PROBLEMS RAISED BY ANAESTHESIA FOR THALAMIC AND CORTICAL EXPLORATION IN NEUROSURGERY

BY

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SUMMARY

Surgical treatment of Parkinson's disease involves the destruction (by diathermy) of localized areas of the thalamus. The accurate location of those areas is made possible by stereotactic approach; but this does not allow for anatomical variations. Electrical stimulation by unipolar electrodes to produce motor responses is equally inaccurate, due to the diffusion of the current. Our team has tried to apply to man techniques used in the laboratory on the cat. A high degree of accuracy has been achieved in locating the various cerebral structures, and even thalamic nuclei, using bipolar electrodes, recording the activity (spontaneous or evoked potentials) of different groups of cells.

However, a major difficulty was to find a suitable anaesthetic, which would induce light anaesthesia, while preserving those activities. It has been found that chloralose and hydroxydione (Viadril) work in a similar way; the former has been used extensively for animal experimentation, since it preserves synaptic responses; the latter has been used on man with satisfactory results, which are presented.

During the past few years, the neurosurgical treatment of Parkinson's disease has been undertaken by various workers. The aim is the destruction of localized and limited areas of the thalamus. We shall not discuss the topography of those areas, upon which there is not yet complete agreement; this is a neurophysiological problem and we shall leave it to the specialists (Albe-Fessard, 1961a, b). In addition to thalamic structures, we have tried to explore cortical activity in sensory areas.

The accurate localization of the area to be destroyed by electrocoagulation has been the subject of many studies. Stereotactic explorations (Talairach et al., 1957) have made possible an approximate localization of those areas, by various landmarks (foramen of Monro; anterior and posterior commissures; premamillary notch), but as Guiot et al. (1958) have shown, with Brierley and Beck (1959), those landmarks are rather inaccurate, and cannot account for individual variations. Their are statistical means, and each patient can vary from the average anatomical picture. However, any mistake (and it is a matter of millimetres) may result in failure or even severe disorders.

Stimulation with unipolar electrodes has made possible, to a point, the localization of some structures; it induces motor responses, more or less localized. Unfortunately, the diffusion is such that a really accurate localization is impossible. Standard techniques of e.e.g. recording have not been successful in locating the position of the electrode; they cannot even identify grey or white matter (Ribstein, 1960; Chatrian et al. 1960; Bickford, 1961).

The neurophysiologists, however, have solved this problem in the animal. Exploration of deep structures with bipolar electrodes can determine the boundaries of the thalamus and even recognize the various thalamic nuclei by their responses. This has already been tested in man by various workers (Ervin and Mark, 1960; Jouvet, 1961) using techniques different from ours.

Ascending Connections to Somatic Thalamic Relays.

The thalamus is an important sensory relay between peripheral receptors and cortical centres. Sensory fibres, coming from a limb, for example relay in the medulla, in the dorsal column nuclei of Goll and Burdach, and reach the thalamus on the opposite side (lemniscal pathway). Stimulation of the receptors will induce a response (evoked potential) in the posterolateral ventra...
nucleus (PLV); a section of the dorsal columns abolishes the response nearly completely. The spatial representation of the various parts of the body, in the posterolateral ventral nucleus, is somatotopic and specific; some cells corresponding to a very localized area will only respond to the stimulation of a given receptor (light touch to the skin, flexion or extension of a joint). Information so recorded is transmitted to the sensory cortex, where it induces recordable potentials.

However, it has been found that all sensory impulses do not follow this pathway. There is another, extralemniscal, pathway, supplying non-specific nuclei, among them the centrum medianum. For instance, if section of the dorsal columns of the cord abolishes the activity of the posterolateral ventral nucleus, that of the centrum medianum is hardly affected (neither is that of the red nucleus, nor the non-specific cortex). The reticular formation of the mesencephalon may receive a lemniscal component but the extralemniscal one is markedly predominant. The centrum medianum is mostly fed with impulses travelling along the interolateral columns of the cord (spinothalamic pathway).

While the posterolateral ventral nucleus has a marked somatotopic disposition (each region of the opposite side of the body having its representation in a definite region of the nucleus), non-specific nuclei (such as the centrum medianum) respond to widespread stimulation, hom- or contralateral, somatic, visual, auditory, coming from everywhere, without any accurate localization. That system has accordingly been called associative or converging.

This distinction between the two systems is probably too sharp. It is known that an interrelation between the two systems exists. A neospinothalamic system, small in the cat, but more important in primates, has been described, including a small component of fibres from the anterolateral columns to the lemniscal system; and a paleothalamic system, directly feeding the associative, converging, nuclei of the thalamus, found in all vertebrates, and corresponding to a more primitive form of somatic sensitivity; it is associated with spinobulbar-thalamic fibres. This classification recalls Head’s views of epicritic (dorsal columns and neospinothalamic system), and protopathic sensation (paleothalamic system).

For the sake of simplicity, however, the distinction between the two systems, primary dorsal columns and associative anterolateral, will be maintained.

The two systems differ in some points:

Recuperation phase.

When a subject is submitted to repeated electrical stimulation the responses of the centrum medianum soon decrease and disappear, while those of the primary relays are not modified.

The activities of the associative nuclei are characterized by their long latency period, their bilateral nature and their long duration.

Action of anaesthetic drugs.

The difference between the two groups can be emphasized in a remarkable manner by various anaesthetic drugs. Some, like chloralose and hydroxydione, do not alter the responses of either, and can even increase them. Others diminish or abolish the responses of both (nitrous oxide). Others abolish the activity of centrum medianum, but increase that of the posterolateral ventral nucleus (halothane).

It can therefore be concluded that chloralose and hydroxydione facilitate the associative responses, while other agents so far assessed depress them but leave intact the primary responses and sometimes even increase them.

Interrelations between the thalamic centres and the cortex.

The primary thalamic centres have their projection on the cortex; their stimulation induces cortical potentials in the corresponding primary areas.

However, the destruction (through surgery or drugs) of those cortical areas has very different actions on the thalamic nuclei. Excision of the cerebral cortex, or anaesthesia with chloralose or hydroxydione, increases the responses of the centrum medianum, for instance, but does not affect the primary responses of the posterolateral ventral nucleus.

It may therefore be concluded that, if the thalamic nuclei have their projections on the cortex, the cortex, in turn, exerts an inhibitory action on the associative thalamic nuclei (centrum medianum), but affects the primary areas (posterolateral ventral nucleus) in a different way. The degree of attention of the conscious subject may
also interfere with them; sleep and inattention increase the associative responses; concentration and vigilance decrease them, without altering the primary thalamic response.

As for the thalamic associative nuclei, there are no such well-defined direct connections; it can only be said that there are cortical areas recording associative activities (fed through the extra-lemniscal pathway).

**Principles of our Method of Anaesthesia.**

The localization of these nuclei has been determined with extreme precision in the cat. The cats are first anaesthetized with ether, tracheotomized, curarized with large doses of gallamine (200 to 400 mg), and ventilation is controlled mechanically. Anaesthesia is maintained with chloralose, which depresses spontaneous cortical activity, while preserving the evoked cortical and thalamic activity. After craniotomy, electrodes are inserted in the thalamus; precision is such that localization of various nuclei is made possible, among them, the centrum medianum and posterolateral ventral, used most commonly to assess the actions of drugs.

Various factors can undoubtedly interfere with and alter the responses recorded, apart from anaesthesia: ventilation, circulation, muscle relaxants, or carbon dioxide retention, affect notably the cellular activities (Davis et al., 1957, 1958). Body temperature must be kept within normal limits (34° to 37°C). Below 32° C, the evoked potentials are depressed, even earlier for the associative responses. Multisynaptic pathways seem to be more sensitive to oxygen lack.

The problems in man, however, are entirely different. In this particular case (surgical treatment of Parkinson's disease), it is necessary to:

1. Sedate the patient with agents acting like chloralose, that is agents which depress the cortical spontaneous activity and induce a state of inattention, but leave the thalamic activity normal, and even increase the associative one. Animal experimentation has shown that most anaesthetic agents depress cellular activity, at various levels, in the cortex and thalamus. A drug was required, therefore, that would work in man like chloralose in the cat; and to

2. Preserve the motor activity so that tremor can be maintained or induced at will, in order that the surgeon can control the result of the destruction made. It is well known that any anaesthesia (and even sleep) stops the tremor.

Those requirements contradicted each other, and the answer was not easy. It was impossible to use in man, the neurophysiologist's technique. Chloralose is too toxic, induces uncontrollable motor activity, and reflex over-activity, incompatible with operating conditions. Curarization could have been used; neurophysiologists use gallamine which is devoid of central effects, but gallamine abolishes the motor component of Parkinson's disease (tremor, rigidity). As for anaesthetic drugs most depress cerebral electrical activity, and evoked potentials, both cortical and thalamic. Therefore we were in some difficulty when asked to find an agent capable of fulfilling these various requirements. Some drugs had already been tested (Davis et al., 1957, 1958, 1961). It was known that barbiturates, nitrous oxide, halothane cyclopropane, ether, di-vinyl ether, chloroform trichloroethylene, and volatile agents in general stop synaptic transmission and cellular activity sometimes for a long time. The same is true of morphine and morphine-like drugs, and of tribromethanol. Our own studies have endorsed some of these observations in the cat; even small doses of nitrous oxide depress thalamic and cortical activities and make all recording impossible; halothane depresses cortical activity and the centrum medianum but increases the posteroverentral lateral nucleus responses.

However, these studies have had a practical implication. Neurophysiologists used to anaesthetize their animals by throwing swabs soaked with ether into the cage, after which they performed tracheostomy and venesection, and injected chloralose. The elimination of ether, however, is a slow process, and they had to wait for some hours until the cat's brain could be used for recording. We thought that this technique could be improved. Zauder and Orkin (1959) have described a cage for the anaesthetizing of small animals. We did not try to match such a luxury of equipment, but used a cage into which was injected a mixture of oxygen and halothane, at a known percentage, through a Fluotec vaporizer. The cat falls asleep in a few minutes; anaesthesia is carried out with halothane (with a mask) while tracheostomy is done,
nd then followed with the chosen agent and allamine. The rapid wash out of halothane saves an appreciable period of time. Half an hour later, the cat can be used for experimentation. Halothane used by Davies et al., 1961) has the advantage over cyclopropane of being non-explosive.

Since most common anaesthetic drugs were ruled out, it was necessary to investigate the possibilities of new drugs, or even old ones, not yet fully assessed. We are still in nearly complete ignorance about the mode of action of anaesthetic drugs. Their actions on the various organic functions are well known, without being fully understood. Pharmacological research provides many drugs, but cannot determine, with certainty, from a given formula, whether a substance will be useful or not.

A large number of drugs, as different as possible, and not yet investigated, were tested in order to find out which could eventually be shown to work like chloralose.

We were lucky, in that one of the first drugs we tried, hydroxydione (Viadril) provided us first on the cat and then in man, with satisfactory conditions. Others (such as Ro.4.0403, chlorprothixene, Taractan), have variable actions, and more are still being investigated. Hydroxydione has already been used for thalamic and cortical investigations, in patients operated on for Parkinson's disease, or for the surgical treatment of intractable pain by topectomy. It seems to work, more or less, like chloralose. Tracings, both cortical and thalamic, are quite comparable with those recorded in the laboratory on the chloralosed cat, and the neurophysiologists have always been able to read them, and lead us to localize the area we were seeking.

One point must be emphasized which we have not yet seen described: some patients (often, but not always, with Parkinson's disease) have shown, after rapid injection of average doses (1 g to 1.5 g of hydroxydione, excluding any other drug), curious bouts of motor activity, with spasmodic, regular contractions of muscles of the limbs and face, short, unco-ordinated spasms, with flexion, extension, adduction, mumbling, and hypertony. The condition is quite different from that of Parkinson's disease and different also from that induced by chloralose, but more like it. We have no explanation to account for this state; it

![Fig. 1A](https://academic.oup.com/bja/article-abstract/35/4/208/255310/fig1a)

**FIG. 1A**
- **H**: Recording of four spontaneous activities in man, during retrothalamic exploration.
- **g1**: Recording in a cortical area (13 mm below brain surface).
- **b1**: In white matter, just below g1.
- **g2**: Grey matter, 29 mm below brain surface.
- **b2**: White matter, some millimetres further.

![Fig. 1B](https://academic.oup.com/bja/article-abstract/35/4/208/255310/fig1b)

**FIG. 1B**
- **C**: Recording of spontaneous activities in cat; same electrode as in man.
- **g**: In grey matter.
- **b**: In white matter; position of electrodes histologically controlled.
may be a manifestation of cortical liberation. One may wonder to what extent results achieved in the cat can be applied to man. However, it seems that tracings recorded in both are quite comparable, and sometimes cannot even be distinguished (fig. 1A and B).

TECHNIQUE
Two types of electrodes have been used. One has a central core of steel, and records mostly the cellular impulses (spikes). The other has a copper core, and records mostly slower rhythms, emerging through the background of spikes. Both have a tip diameter of less than 50μ. The bigger cellular bodies vary between 70 and 120μ, in the area to be explored.

Recording is made on an oscilloscope. A loudspeaker is branched in parallel, through which the rhythmic impulses can be heard. This makes possible the detection of cellular nuclei and the localization, with reasonable accuracy, of the various structures met: grey, white matter; ventricle; thalamus and its various nuclei; internal capsule. Neurophysiologists can even identify, by their type of response to peripheral stimulus, the various thalamic nuclei, and can detect the cellular activities induced by sensory stimulations (evoked potentials).

Pre-operative recording under hydroxydione. Three upper tracings: bipolar occipital leads Bd and Bg: forearm myogram (Bg=affected side).
Sixth tracing: e.c.g.
St=light signal.
R=patient's response.
I=hydroxydione 1.85 mg/kg. No action on alpha rhythm. Myogram of affected limb still obvious. Reaction time normal (St—R).
II=hydroxydione 5.5 mg/kg. Slight action on tracing; left arm myogram markedly depressed. Patient obeys order but response is incoherent.
Patients are submitted, before the operation, to a preliminary exploration under e.e.g. control, in order to assess the individual reaction to hydroxydione. We have noted that this varies considerably, the dose used ranging from 3 to 8 mg/kg. We try to find out the dose which, in a given period of time, brings the subject into a state of indifference and lack of attention. Tremor (recorded on a mecanogram, or by electromyography), decreases, then disappears, but it can be induced again by stimulating the patient (doing additions, asking questions). With larger doses, the patient becomes unconscious; tremor cannot be induced, and occasionally the muscular phenomena already mentioned may occur (fig. 2).

Hirsch and colleagues (1961) have described the e.e.g. under deep anaesthesia with hydroxydione as showing intermittent bursts of rhythmic activities. We maintained a lighter plane of anaesthesia, so that the alpha rhythm retains its spatial localization, and its frequency; but it is still present when the patient has his eyes open (showing lack of attention), and disappears only if he is asked to concentrate.

The operation itself involves the introduction of an electrode through the occipital region, following a parasaggital route, 16 mm from the medial plane (mean, this being determined by the size of the third ventricle as previously assessed by encephalography).

The electrode meets successively: cortex; white matter; sometimes loops of cerebral cortex buried within the brain; splenium of corpus callosum; ventricle; thalamus. Within the thalamus, the electrode meets various nuclei: the pulvinar, or the posterolateral nucleus; then the ventroposterior. As it emerges, it meets the internal capsule and then the globus pallidus. Figure 3 shows this on sagittal (A) and horizontal sections (B).

The electrode is inserted when the patient is already under hydroxydione infusion, the dosage being adjusted according to the results of the pre-operative e.e.g. and the patient's behaviour. Simultaneous e.e.g. and e.e.g. recordings, provide information about the level of anaesthesia, and may help in the interpretation of the thalamic tracing by showing the artefacts produced by the pulse.

**RESULTS**

**Application to Surgical Treatment of Parkinson Disease.**

**Retrothalamic exploration.**

The electrode meets, as already stated, three types of structure: grey and white matter, and ventricle. They are easily identified on the oscilloscope and loudspeaker. Figure 4 shows the comparison between the activities recorded on the surface of the brain and within the cortex by the electrode.

**Thalamic exploration.**

The electrode marks the limits, with adequate accuracy, of the posterior and anterior boundaries of the commissure.
FIG. 4
Comparison between activities recorded on surface of the brain (upper tracing), and at deep electrode (3 mm below). The two tracings are not synchronous but have been recorded at the same time, the time bases being equalized.

FIG. 5
Man, hydroxydione. Recording following a laterosagittal plane. This figure shows the variation in spontaneous activity, as the electrode goes through white matter (34); ventricle (33); thalamus (28); posterolateral nucleus (24 to 22); then posteroverentral nucleus, upper part (17).

FIG. 6
Man, hydroxydione. Shows differences between tracing recorded in posteroverentral nucleus (18,17), and internal capsule (8). 15 represents ventrolateral nucleus; 12, reticularis thalami.
In 5, activity corresponds to globus pallidus.
(A) Recording of evoked potentials in the posterolateral ventral nucleus, on patient under light hydroxydione anaesthesia.
A and B: Bouts of tremor spontaneously stopped. The electrode was in the area corresponding to the forefinger, as shown by two potentials (C1 and C2) evoked by tactile stimulation of tip of the finger.

(B) Recording of evoked potentials in the same area in another patient, induced by electrical stimulation (A1, A2, B1), and tactile stimulation (B2); note the secondary slow wave in B2.

Fig. 7
marked by a progressive decrease in the cellular activity as the electrode leaves the thalamus and goes into the nucleus reticularis (or zona incerta), where cells are scanty. This is shown in figures 5 and 6.

Identification of intrathalamic structures. The identification of the thalamic nuclei is made possible by oscilloscope recording and the loudspeaker.

The posteroventral nucleus is the secondary synapse of somaesthesia. It can be identified by inducing evoked potentials, by stimulating cutaneous receptors on the opposite side of the body. This can be determined with extreme precision (for example for only the pulp of the index finger). In that area we have recorded rhythmic activities synchronous with tremor and possibly due to evoked potentials induced by it (figs. 7 and 8).

The ventrolateral nucleus can be identified by a decrease of the basic activity, with bursts of 25 cycles per second; evoked potentials disappear. The tracing is the same, whether the patient has received hydroxydione or not (fig. 9).

FIG. 8
Four different examples of cellular units, bursting rhythmically in the thalamus. In each tracing the upper recording is thalamic and the lower one is the limb myogram.

A: Pulvinar; the three slow waves are artefacts, due to e.c.g.
B and C: Recording in the neighbourhood of posteroventral nucleus.
D: Electrode in posteroventral nucleus corresponding to wrist.
Recording starting at ventricle (30) to globus pallidus (8). The electrode only touched the edge of the posterovenal nucleus (20). S is the occipital e.e.g., with the same time scale. In 28 and 25 (electrode in posterolateral nucleus), rhythmic activities are noted which correspond to cortical tracing and which disappear later.

Cortical Exploration.
Apart from thalamic explorations, we have applied the same technique to the localization of cortical areas to be destroyed by topectomy, for the cure of intractable pain due to cancer of the cervix.

The anaesthetic technique consisted of premedication with atropine, induction with halothane, nitrous oxide and oxygen, intubation after injection of suxamethonium and topical spray with amethocaine. Previous e.e.g. recording had been carried out under hydroxydione anaesthesia to which the patient showed a marked resistance. The patient had previously received large doses of various analgesic drugs. During the first part of the operation (opening of the scalp, and trephining), anaesthesia was maintained with the same drugs. As the dura was opened, the endotracheal tube was disconnected and the patient left to breathe atmospheric air while she was given hydroxydione (total dose 4 g). Cutaneous stimulations were induced by electric shocks. The result has been satisfactory. The localization of the sensory area to be destroyed and to be identified by evoked potentials was easily made. The patient was relieved and suffered no motor or intellectual impairment.

A similar approach has already been made to this problem by Pertuiset and associates (1959), under local analgesia.

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REFERENCES


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**SUMMARY**

Le traitement chirurgical de la maladie de Parkinson implique la destruction (par coagulation) de régions précises du thalamus. La localisation de ces régions est rendue possible par le repérage stéréotaxique; mais les variations individuelles sont grandes. La stimulation électrique, à l'aide d'électrodes unipolaires, est également imprecise, à cause de la diffusion du courant. Nous avons cherché à appliquer à l'homme les techniques utilisées au laboratoire, sur le chat. Une extrême précision a été obtenue, dans la localisation des structures cérébrales, et des noyaux thalamiques, grâce à des électrodes bipolaires, qui recueillent les potentiels, spontanés ou évoqués, des cellules. Les principales difficultés résident dans le choix d'un anesthésique, qui puisse provoquer une anesthésie légère, tout en conservant ces activités. Nous avons constaté que la chloralose, et l'hydroxydione (Viadril) ont le même mode d'action; le premier a été utilisé de façon courante dans l'expérimentation animale; le second chez l'homme, avec des résultats satisfaisants, que nous présentons.

**ZUSAMMENFASSUNG**


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**THE IX ARGENTINE CONGRESS OF ANAESTHESIOLOGY**

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The Secretary-General is Dr. Fausto J. Molina, Guemes 4070, Buenos Aires, Argentina.