SOME SUGGESTIONS FOR THE NEURAL BASIS OF THE ANAESTHETIC STATE*

BY
D. A. BUXTON HOPKIN†
Charing Cross Hospital, London, England

The purpose of this paper is to put forward some ideas about the neural basis of the anaesthetic state and to see what support, if any, can be adduced for these by a survey of present knowledge of the neural mechanisms of consciousness and how these can be altered by psychotropic drugs.

THE NATURE OF CONSCIOUSNESS

Consciousness still defies precise definition although knowledge of some of the neural processes involved has widened considerably in recent years.

It is known, for example, that the watchful, alert, or attentive state is dependent on the ability of the ascending reticular system to induce electroencephalographic and behavioural arousal in the cerebral cortex. Without this "arousal reaction" messages arriving at the sensory receiving areas of the cortex cannot undergo the complex integrative processes necessary for their elaboration into consciousness (Magoun, 1958a).

These integrative processes appear to be of at least two distinct kinds. The first concerns perception—that is to say recognition of the identity of an incoming signal. The second and more complex is the endowment of this perception with conceptual value (Herrick, 1949; Herrick, 1956), which involves memory, association, emotion, and learning.

It can be argued that ability to perceive is itself an adequate definition of consciousness. To a certain extent this is true, for otherwise a newborn babe could not be said to be conscious, since it has not had time to develop conceptual values. To do this requires experience and memory. It may be that this is why it is not thought necessary to anaesthetize an infant for the operation of circumcision whilst laparotomies can be performed at this age under d-tubocurarine and oxygen.

Only as growth proceeds does the power of endowing perceptions with conceptual values develop. These find expression in behavioural and emotional responses which it is the task of the anaesthetist to overcome or modify. Consequently it is of interest to see how far it is possible to define the neuronal processes involved and the extent to which they are susceptible to different classes of sedative drugs.

THE NEURONAL MECHANISMS OF CONSCIOUSNESS

It seems probable that perception is the consequence of the interaction of neuronal processes which a peripheral stimulus sets up in the ascending reticular activating system and at the sensory cortex. This manifests itself by alertness, the focusing of attention and desynchronization of electroencephalographic rhythms (Lindsley, 1957).

However, in order for the perception to acquire conceptual value the participation of the temporal lobe and the rhinencephalon appears necessary. Wilder Penfield (Penfield, 1958) has drawn attention to the importance of the temporal lobe in the exercise of the function of memory. He has suggested that it should be distinguished from the sensory and motor cortex by receiving the name of "interpretive" cortex. The temporal lobe is necessary for the recall of past experience and through the medium of this structure signals arriving at the sensory cortex are able to reactivate old patterns of neural activity set up by similar signals in the past. Clearly this supplies the basis for creation of conceptual value. The underlying rhinencephalon (the old brain or the visceral brain) has also received increasing attention in recent years for the part it could play in determin-
ing behavioural responses which are also closely related to the conceptual component of consciousness.

The rhinencephalon is intimately connected with, and under the influence of, the ascending reticular activating system. Connections have been traced from the intralaminar nuclei of the thalamus through the septum and dorsal fornix to the hippocampus, whilst a return pathway has been described which leads back to the midbrain reticular system by way of the external capsule, anterior commissure and the stria medullaris (Adey, 1955; Adey, Merrillees and Sunderland, 1956). This re-entrant circuit furnishes a pathway for the initiation of the autonomic and endocrine disturbances which accompany conditions of predicament and emotional stress. The hippocampus receives fibres from all the surrounding parts of the brain—visual, auditory, olfactory, visceral, parietal and temporal (Papez, 1957). It thus provides a common field for a variety of reactions expressing emotional moods as well as a place for the integration of cortical processes from several different sources into the conceptual component of consciousness.

Animal experimentation also supports the view that this part of the brain is responsible for behavioural response to environmental situations (Green, 1957). Everything points to the limbic system as a key structure in the formation of the conceptual processes of consciousness which arise through the interaction of the ascending reticular activating system, the neocortex, the temporal lobe and limbic system. The site of the final integrative processes is not known but Penfield's suggestion is that they occur in a subcortical "centrencephalic" system which he defines as "coordinating and organizing fibre and cell connections in the higher brain stem" (Penfield, 1957).

Expressed in a simplified form consciousness may be said to depend on:

(a) The integrity of a nonspecific subcortical system known as the ascending reticular activating system. This extra-lemniscal sensory pathway seems to be kept in activity by afferent stimuli from all modalities of sensation much of which reaches it by means of collaterals from the lemniscal pathways. These stimuli give rise to diffuse neuronal activity which results in alertness and wakefulness and puts the cerebral cortex in a position to integrate the specific sensory messages, which continue to pass direct to the cortex.

(b) Two cortical integrative mechanisms subserving perception and conception both of which must converge in a central subcortical "centrencephalic" system before consciousness can be said to exist.

**SOME PHARMACOLOGICAL CONSIDERATIONS**

The susceptibility of these neural processes to certain types of drugs makes it possible to modify or abolish consciousness without simultaneous suppression of activity in the remainder of the central nervous system. For example, there have been several convincing demonstrations that small amounts of anaesthetic agents bring neuronal activity in the ascending reticular activating system to a standstill and render it impervious to afferent stimuli. The arousal reaction (behavioural or electroencephalic) no longer can be produced, although other parts of the brain remain active since it has been shown that signals continue to be transmitted up the lemniscal pathways to the sensory cortex, where the responses they evoke often show increased amplitude (Magoun, 1958b).

However, loss of consciousness can also result from depression of the mechanisms which it has been suggested are responsible for the perceptive and conceptual components of consciousness, by centrally acting drugs, which so far as is known, do not have any direct depressant action on the neurones which comprise the ascending reticular system.

Thus, it is possible to induce a light plane of anaesthesia by the simultaneous intravenous injection of a powerful tranquilizing drug (chlorpromazine) and an opiate (morphine or pethidine) although neither of these given separately and in similar dosage exhibits this property.

It is widely agreed that opiates reduce sensation of pain; that is to say, they reduce intensity of perceptive processes. Their lack of effectiveness in the presence of pain complicated by exaggerated conceptual processes and behavioural responses is well known, for example in the distressed primagravida in active labour. Whilst precise knowledge about the exact place and manner of the action of opiates is lacking, there is very suggestive evidence of an action in the region of the corona radiata (Wikler, 1950; Seevers, 1954). A depression at this site could inter-
rupt integrative neuronal activity between the cortex and the subcortical systems which appear to be concerned in subserving the perceptive component of consciousness.

The tranquilizing drugs as typified by chlorpromazine have no apparent depressant action on perceptive processes but have a remarkable ability to depress mechanisms responsible for formation of conceptual processes. This type of sedation has been variously described as "ataraxia", "antiphobia" and "tranquilization" but on analysis this turns out to be a loss or modification of the behavioural response to different environmental situations, especially those that are "stressful" (using that term in its widest sense). There is no interference with perception but the emotions which perception arouses are reduced or absent; or, put in another way, there is interference with the elaboration of conceptual processes. Studies of the central actions of these drugs appear to lend support to this hypothesis.

In spite of many claims that the more powerful tranquilizers abolish the "arousal reaction" by a direct repression of the ascending reticular activating system these effects have not been confirmed. Bradley has shown that chlorpromazine (and other tranquilizers of similar potency) reduce neuronal activity in the ascending reticular system by means of a depressant action on afferent input at the point where collaterals from the lemniscal pathways enter the reticular system (Bradley, 1958-59; Bradley and Key, 1959). The neocortical arousal response is little altered but there seems to be a definite depression of the hippocampal arousal reaction (Vogt, 1958). This differs from the neocortical arousal in that the characteristic alterations of rhythm which accompany the change from the inattentive sleepy state to one of wakefulness and alertness are the opposite of those which take place in the neocortex (Magoun, 1958c; Adey, 1955).

The opiates and the tranquilizers can therefore be said to have a selective depressant action on two of the neuronal processes necessary for full consciousness; one responsible for pain perception and the other for the accompanying conceptual processes. Their combined action is sufficient to abolish consciousness without any simultaneous direct action on the ascending reticular activating system.

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**HBERNATION AND ATARALGESIA**

This furnishes us with a method of inducing anaesthesia at a small cost in terms of depression of cellular activity elsewhere in the body, such as must occur to some extent when more powerful general protoplasmic poisons are used for this purpose.

The state of "hibernation" is nothing more than anaesthesia of a light plane produced by intravenous injection of opiates and tranquilizers. Once induced it is possible to allow surgery to begin, sometimes without further medication, or supplemented by a small dose of thiopentone, or nitrous oxide given with a high percentage of oxygen.

The interesting condition known as "ataralgesia" can be explained in terms of the actions of the drugs used on perception and conception. To induce this state large doses of opiates (much larger than those used in hibernation) are combined with one of the less potent tranquilizing agents. The effect of this combination is to induce a state where consciousness is still retained but pain sensation abolished to the extent that in many instances operations can be performed without additional anaesthetic agents. Perception is effectively dulled by the rather large doses of pethidine used (200–300 mg) but conceptual mechanisms are not depressed to the point where consciousness is lost. If an attempt were made to carry out this method using a powerful agent like chlorpromazine together with these large amounts of opiates a deep state of anaesthesia would ensue sufficient for surgery but recovery would be very prolonged. This is, in effect, what happened when chlorpromazine was first introduced into anaesthesia; the heavy opiate premedication (papaveretum and hyoscine) which preceded injection of the "cocktail" produced deep unconsciousness ("anaesthesia without anaesthetics!") and a much delayed recovery. This gave the method a bad name amongst those surgeons who like a rapid postoperative recovery. However, by keeping down the amount of opiates (never in excess of 100 mg pethidine) a state of unconsciousness or light anaesthesia can be obtained which only needs the addition of minimal quantities of stronger agents. After operation the return of consciousness is rapid and side effects are minimal.
LIGHT ANAESTHESIA AND MOTOR RESPONSES

"Hibernation" then is nothing more than a very light plane of anaesthesia produced by abolishing perceptive and conceptual processes. There are, however, several other ways of inducing a light plane of anaesthesia. Whatever method is chosen, it must be appreciated that this does not guarantee that the patient will not respond by limb movements to surgical stimulation. This response does not necessarily indicate a return of consciousness. Adrian and Moruzzi (1939) showed some years ago that these movements occurred in animals anaesthetized by various agents and that they depended on the rate of neuronal discharge evoked in the pyramidal tracts by the arrival of signals at the sensory cortex. This discharge was continuous in all but the deepest planes but when it reached a certain intensity it gave rise to movements of the limbs.

This motor response which is involuntary can, in clinical practice, be prevented by increase of the overall anaesthetic concentration (undesirable except in short procedures), by intravenous injection of opiates, or by paralyzing the patient with a muscle relaxant which ensures an unresponsive patient, albeit lightly anaesthetized.

This last practice is not without its drawbacks. From time to time there are reports of patients becoming conscious during anaesthesia and finding themselves immobilized or paralyzed, a situation which is unpleasant to contemplate. However, it is doubtful whether consciousness is complete in its fullest sense. Powers of perception may well be present but the effect of the drugs (usually nitrous oxide and a barbiturate) seems sufficient to prevent the elaboration of conceptual values for these circumstances, so that the full emotional response which such an experience would induce in a person not under the influence of any sedatives does not occur. It is a constant impression that these patients do not express keen resentment or horror and that their recollections appear detached and free from rancour.

SUMMARY

Consciousness could be the consequence of the interaction of two different neural mechanisms, one responsible for perception and the other for conception. This hypothesis is discussed in the light of recent neurophysiological research into the neural basis of consciousness.

Certain drugs used for sedation and in anaesthesia appear to have a selective action on the neural mechanisms underlying perception and conception whilst their combined actions abolish consciousness and produce a light plane of anaesthesia. Effective anaesthesia does not demand overall depression of central nervous activity. The specific sensory and motor mechanisms are little affected in the lighter planes of anaesthesia.

These considerations offer an explanation for the states known as artificial hibernation, ataralgesia and for the popularity of anaesthetic techniques which depend on the maintenance of a light plane of anaesthesia whilst ensuring immobility of the patient by means of muscle relaxants or small intravenous doses of analgesics.

Further thought about the neuronal mechanisms of consciousness and the action of psychotropic drugs may help to remove some of the empiricism in which our specialty has been shrouded ever since the day when Oliver Wendell Holmes coined the word "anaesthesia".

REFERENCES

BOOK REVIEW


This is a book of absorbing interest and represents the collected work of the author together with a critical assessment of the work of others and it has resulted from many years of study and thought on this subject. Professor Beecher's specific interest in the subject of pain appears to date from his war experience and thus extends back over nearly twenty years. During this time he has formulated principles based on a vast amount of careful and meticulously controlled observation particularly directed towards the investigation of the subjective aspect of pain. This is exemplified by his studies of "placebo reactors" of the "psychic" component of the pain experience and its relation to the significance of the pain to the individual. The book, however, collects together not only these studies but also a great deal of information concerning the techniques which may be used for their objective study and their evaluation.

The first part of the book is concerned with these preliminary principles and includes sections on statistical planning, the reaction factor of the pain response and on pain thresholds. To be facetious for a moment, it is surprising to find in this section "Constancy" and "Purity" as main headings. Part two deals with studies in which these techniques have been applied and compares analgesia with sedation. There is a consideration of the euphoric and dysphoric components of drug activity and experiments are described which, interestingly enough, attempt to "quantify" the action of drugs on anxiety and hunger. There is even an examination of the drugs which have been claimed to be useful to control postoperative nausea and vomiting and pruritus, and a very original chapter on "experimental and pathological cough in man", in which are examined various antitussive agents and their value assessed.

Anaesthetists who received their training before the war will recall their gratitude to Professor Beecher for his classical collection of data published as The Physiology of Anaesthesia, and it seems that in this book he has produced a volume likely to be a work of reference and study for a long time to come. Its scope is demonstrated by a bibliography containing 1,063 references. Its value too arises from the fact that it is a study concerning man—animal work is not his interest. It is therefore an example of the valuable contribution that can be made to pharmacology by those who have the opportunity to study the effects of the basic principles of their science applied to homo sapiens and it is an encouragement to the applied pharmacologist not to lower the objective and scientific standards which he would apply to work on animals.

Despite a certain repetitiveness which will be found irksome to some, the book is readable and very pleasantly produced. Cecil Gray