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From the Physiological Laboratory, University of Cambridge, England

# The Control of the nervous System by the Sense Organs*

By

E. D. ADRIAN

With 3 Figures in the Text

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A lecture on the sense organs cannot begin without an apology for neglecting what will soon become the most important line of research into their action. This, however, must be left to the biophysicist and the biochemist who can speak of molecular transformations, protein structure and enzyme chemistry. The physiology of the sense organs is rapidly coming down to a molecular level where I cannot pretend to follow it.

This kind of advance is in fact transforming almost every branch of physiology. In the sense organs the essential elements are the receptor cells which respond to physical and chemical disturbance and transmit information about it to the central nervous system. And so like nerve and muscle they have now become fascinating material for the cell biologist. We have the electron microscope to give all kinds of new data about their structure and there are all the new biophysical and biochemical techniques for investigating the changes which take place in them when they are stimulated. If all goes well, our understanding of the physical and chemical events which take place at the receptor level will soon become part of a general picture of cell organisation in terms of molecules and intermolecular forces.

It is true, of course, that the sense organs still provide problems and material for the electro-physiologist who studies them as part of the nervous system. The technique of recording nervous activity inside as well as outside the central nervous system has reached much greater precision and in the animal kingdom there is still a great range of receptor apparatus not yet investigated—even in the vertebrate this field is far from exhausted, particularly that part of it which concerns the receptors which signal the internal rather than the external environment.

But the physiology of the sense organs implies the study of their function as well as of the properties which make them react to stimuli and their function is to control the nervous system so that the behaviour of the organism suits its environment. The control must be on a long

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term as well as on a short term basis. In the human organism behaviour must be planned in relation to past and future events but the plan must be adapted to conform with the immediate state of the environment. Our behaviour may need to be temporarily suspended by the appearance of a friend or an enemy, by a warning sound or an unpleasant smell, for the environment is constantly changing and the organism must do whatever is necessary to adjust itself to the immediate changes without letting the adjustments interfere too much with its general policy.

It is necessary, therefore, to consider the sense organs not only as the groups of receptors which are excited by particular physical or chemical events. We must think of them as the organs which have to determine the general direction of activity in the central nervous system from moment to moment. Their collective report must give prominence to the events which call for an immediate response, but it must be comprehensive and must be detailed enough to enable the events to be compared with others of the same class which have occurred before. The sound we hear must be recognisable as the voice of a particular person, and what we see must be recognisable not only as a human figure but as someone we have often seen and can label with a name.

There are two main problems therefore which confront us. One is the old problem of sensory discrimination. How do our sense organs enable us to recognise so many different events? Each will have it own methods of analysing the events which affect it but the nervous signals are all of the same pattern and there should be some general principles which show how they can convey so much information.

The other problem is that of their access to the controlling regions of the brain. How does it come about that a particular element of the visual field 'catches our eye' and that our behaviour is then given a new direction, almost without relation to all the other reports which are arriving simultaneously from other sense organs?

This problem of sensory attention must be dealt with first and it can be approached by referring to a recent paper by Dr. HERNANDEZ-PEON and his colleagues (1957). They made records from the visual cortex of a cat, with no anaesthetic but with electrodes permanently fixed in the skull. When the cat was relaxed and exposed to a brief flash of light this would produce a train of electric waves in the visual area of the cortex, but when the cat was roused by an olfactory or an auditory stimulus all but the first wave of the visual response was suppressed. They found that the suppression occurred at the subcortical level as well as at the cortical, in the optic tract and in the reticular formation. One must suppose, therefore, that when the attention is aroused by a non-visual stimulus some change occurs in the pathway from the eye to the cortex so that the flash of light is unable to produce its full effect.

In the human brain the most striking effect of a change of attention is on the $\alpha$ rhythm of the electroencephalogram, the effect discovered by Berger nearly 30 years ago. Records from the human brain are scarcely comparable with those from the cat, for vision plays a far more important part in human than in feline behaviour. What is found is that the $\alpha$ rhythm is suppressed when the attention is on the visual field and it can be made to reappear by diverting the attention to a sound. As BERGER pointed out, the $\alpha$ rhythm is blocked by any stimulus which claims the whole of our attention and it is usually absent when the eyes are open, but if the visual field is made uniform and featureless, attention to a sound will restore the rhythm, provided that the shift of attention does not involve a concentrated effort (ADRIAN 1944).

In the human brain the sensory stimuli other than visual which will block the $\alpha$ rhythm are those that are unexpected, a sudden loud sound for instance; a series of sounds may keep it blocked if they are very loud, but if they are not the rhythm soon returns. Again an unexpected touch on the hand of the subject will give a temporary blocking, but a series of touches will soon fail. And the same is true of the animal brain. There have been many studies recently with electrodes permanently implanted in the brains of cats and monkeys and it is the regular finding that in the normal unanaesthetised animal a stimulus which will arouse attention and will produce the characteristic record of the alert brain will soon lose its effect when it is repeated many times. It will soon fail to change the pattern of the electroencephalogram from large slow waves to small rapid oscillations and it may also fail to produce its own localised response in the receiving area (SHARPLESS and JASPER 1956).

It is not necessary, however to make records from the brain to show that repeated sensory stimuli soon become ineffective. We have only to listen to a clock ticking to realise how soon we cease to hear it. Perhaps for the same reason in the formation of a conditioned reflex the conditioning stimulus must not be repeated too often without being followed by the unconditioned stimulus which emphasises its importance.

Evidently therefore if signals from the sense organs are to influence the course of behaviour, to lead to some new pattern of activity and in man to reach consciousness, they must be intense in themselves, or unexpected, or associated with some previous experience which gives them a particular significance. If they have these qualities they will produce considerable changes in the activity of the cerebral cortex, but if not they may never reach it and will soon fail to do so if they are repeated at short intervals.

At what level in the pathway from sense organ to cortex does the failure occur? When we cease to be aware of the clock ticking is there any difference in the intensity of the signals from the cochlea or are they as strong as before at the periphery but unable to pass some barrier in the auditory pathway? Why are sounds with particular associations able to reach the highest levels when a meaningless noise will only do so when our attention is not held in some other direction?

The first point where the block might occur is in the sense organ itself, owing to some kind of inhibition imposed by the central nervous system.

It is clear, I think, that the barrier, wherever it may be, is imposed by the central nervous system and that it may involve a positive inhibitory effect at some level below the cortex. Some of you may recall cases of hysterical deafness during the war of 1914—18 when the patient would show no startle reaction to the loudest sounds, but could be made to hear normally again by the simple form of psychotherapy which we used in those days. And there were some interesting records of the electroencephalogram made by TITECA (1938) on a case of hysterical hemianaesthesia. When his eyes were closed the patient had a well developed $\alpha$ rhythm: this could be abolished by a touch or a pin prick on the normal side of the body but was quite unaffected by one on the anaesthetised side.

The barrier imposed by the central nervous system might well be at the receptor level, for the sense organs are under central control. If we are to use these to the best advantage, there must be a constant adjustment by efferent signals from the central nervous system to keep them focussed on the stimulus and working with the right degree of sensitivity. We must turn our head to hear a faint sound and we must sniff to detect a smell: if all the movements of the oculomotor muscles were suppressed we should see very little and if our fingers were paralysed we should get far less information from their tactile receptors. Recently too we have become more aware of the existence of efferent nerve fibres to the receptors, distributed not to the accessory muscles of the sense organs but apparently to the receptors themselves. There may well be some direct control of their sensitivity by this route.

Though I do not suggest that this is the only or the most important factor in deciding whether we react to a sensory stimulus or not, it is worth remarking that almost all the investigation of the sense organs has been carried out by methods which are bound to prevent us from recognising any such central control.

The classical method of investigating the human sense organs is to relate the stimulus to the resulting sensation, to compare wave length with colour, chemistry with smell, etc. The classical investigations of VON KRIES and SKRAMLIK at Freiburg bear witness to the great value of the method. But in all such experiments it is a necessary condition that our attention should be concentrate on the test stimulus. Again, in the newer method of investigating sense organs by recording the nervous discharges from them any kind of efferent control from the central nervous system is usually impossible because the organ is isolated by nerve section.

It might seem possible, however, to measure the response of receptors with all their central connections intact by recording the potential change which develops at the receptor level. The potential between the cornea and the back of the eye is influenced by the activity of the rods and cones and the initial potential change to a flash of light seems to be an adequate measure of the retinal response. It is not difficult to record the potential change at the exposed part of the human eyeball when it is exposed to a very feeble flash of light, but unfortunately it is extremely difficult to be sure that attention has ever been much diverted from the test stimuli. In the few experiments I have made on myself I found no clear evidence of any change in the receptor response when my attention was intentionally concentrated on the visual field or diverted from it, but nothing short of a very large change would have been at all convincing in an experiment where so many factors had to be left uncontrolled.

The same sort of difficulty arises with the olfactory organ. OTTOSON (1956) has recently shown that the receptors of the organ develop a surface negativity when they are stimulated by smell. This has not yet been recorded in man, but it can be recorded in intact animals with implanted electrodes. The difficulty in this case is that attention to smell changes the rate of breathing. The nose is the sense organ which depends more than any other on the active movements which are needed to bring the stimulus to the receptors, for they are excited by the molecules brought to them by the current of air which passes through the nose at each inspiration, and the intensity of stimulation varies both with the concentration of the molecules in the inspired air and with the rate at which they are brought to the organ by the air current. If the concentration is small a rapid inspiration will bring more molecules up to the organ in a given time and so when a rabbit is interested in a smell it begins to sniff rapidly. The stimulus to the organ will be increased and the electric response will be larger. When the rabbit ceases to attend the breathing will become slower and the response of the organ will be smaller. Since we cannot prevent such changes in the rate of respiration and therefore in the stimulus it is scarcely possible to decide whether there is any change in the sensitivity of the organ when the direction of attention is changed.

But I have mentioned the olfactory organ because in man, at all events, it gives the best example of repeated sensory stimulation ceasing very soon to affect the higher levels of the central nervous system. When we listen to a clock ticking we may soon cease to notice it, but we can hear it again by listening, by making the effort of turning our attention to it. When we are exposed to a smell we soon become unaware of it and no amount of attention will restore the sensation. Either the organ ceases to signal the smell or else the signals are blocked at some point in the olfactory pathway.

It might be thought that the failure of the sensation is due to stimulation fatigue in the olfactory organ. Certainly continuous stimulation, by drawing a steady current of air through the nose, will soon lead to

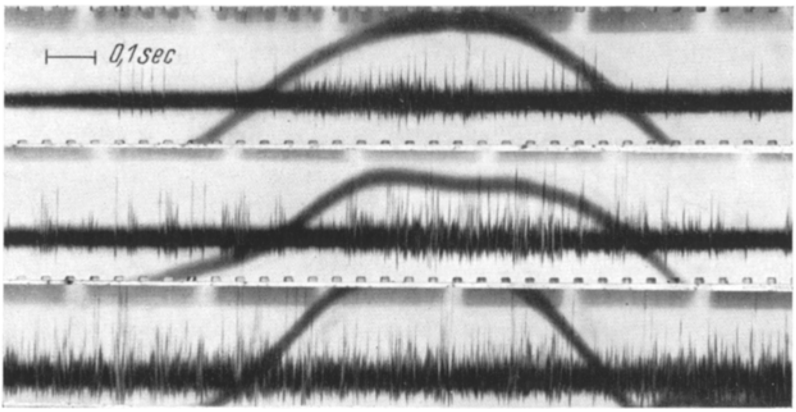


Fig. 1. *Masking of olfactory signals by spontaneous activity developed in the olfactory bulb.* Record (from a rabbit under Urethane) with an electrode in the olfactory bulb showing the effect of breathing air with amyl acetate vapour. Movement of inspiration shown by signal line. A Deep Anaesthesia. The olfactory discharge is seen clearly. B Lighter Anaesthesia. Discharge partly obscured by irregular activity. C Still lighter Anaesthesia. Discharge completely obscured

receptor fatigue and decline in the response, but in the normal working of the organ the stimulation is always intermittent and there is always an interval for recovery between one inspiration and the next. In the rabbit there is a gradual failure with certain smells, most of them vapours which might be expected to injure the receptors, ether or xylol for instance, but with many others the olfactory potentials or the nervous discharges from the organ occur at each inspiration with no signs of failure whatever the length of time the animal has been exposed to the stimulus. One ought not to put too much emphasis on such evidence, for our knowledge of olfactory adaptation is derived from man and not from the rabbit, but in the rabbit it appears that the olfactory organ is capable of signalling the same smell for an hour or more with no sign of fatigue.

There is, however, some evidence to suggest that the failure may occur not in the olfactory organ but in the olfactory bulb where the signals are passed on from the primary neurones to the mitral cells and the olfactory tract. In deep anaesthesia the mitral cell discharge gives a faithful reflection of each stimulation of the olfactory organ, but as the anaesthesia becomes lighter there is increasing activity in many of the nerve cells in the bulb and the mitral cell discharge becomes irregular and continuous. In very light anaesthesia a smell will usually suppress the irregular activity and give a succession of impulses at each inspiration, but after a variable time groups of impulses appear again at irregular intervals and the effect of the repeated olfactory stimulation is far less obvious (ADRIAN 1950).

In records with so much general activity it is difficult to pick out the response of the individual mitral cells, yet the impression they give is that afferent signals may be blocked or may become unrecognisable at an early stage in their passage into the brain because the pathway is not kept clear of other traffic. If this is so, the failure would be an example of what FORBES has described as the ,line-busy' effect. In the olfactory bulb the line may be kept busy by discharges which are too irregular to convey the information, and evidently the same kind of interference might occur at each synaptic gap in the pathway to the cerebral cortex. In fact to work effectively the signalling system must not transmit too much meaningless noise as well as or instead of the messages which convey specific information from the receptors, and there will be an opportunity for noise to confuse the transmission wherever the neurones are likely to be affected by the general level of activity in the synaptic areas.

Although this may be one or indeed the main factor in the failure of olfactory signals, it is clearly only a small part of the whole story. It does not explain why the signals succeed at first in quieting the noise and are afterwards swamped by it, or why signals with associations which make them important to behaviour can reach the higher levels unimpaired, when less important signals make no impression on them.

I shall not suggest reasons, for they can only be speculative, and it is time to deal with the other problem mentioned at the beginning, that of the way in which the sense organs can transmit information which may be important. The olfactory organ would be of little use to an animal if it could only signal the occurrence of a smell without also giving some indication of its nature, and in fact even the human olfactory organ, though much smaller than that of most mammals, will allow us to distinguish a vast number of different smells.

By making records of the olfactory discharge when it reaches the mitral cells of the bulb we can record from the individual units. This allows us to see what kind of information is provided and the important point is that it seems to depend not on any one aspect of the discharge but on a variety of features, all of which may differ to some extent according to the particular smell which is used to stimulate.

There are first the differences in the sensitivity of particular receptors to different smells: one of the mitral cells may give a discharge at each inspiration when the air contains a low concentration of one smell, but will need a high concentration of another to stimulate it. A different mitral cell will respond with a lower concentration of the second smell but will need a higher concentration of the first. Thus in a record where the impulses from several mitral cells can be recorded together as spikes of different size, one smell at low concentration can be made to give a discharge of one series of spikes and another will give spikes of smaller or larger size.

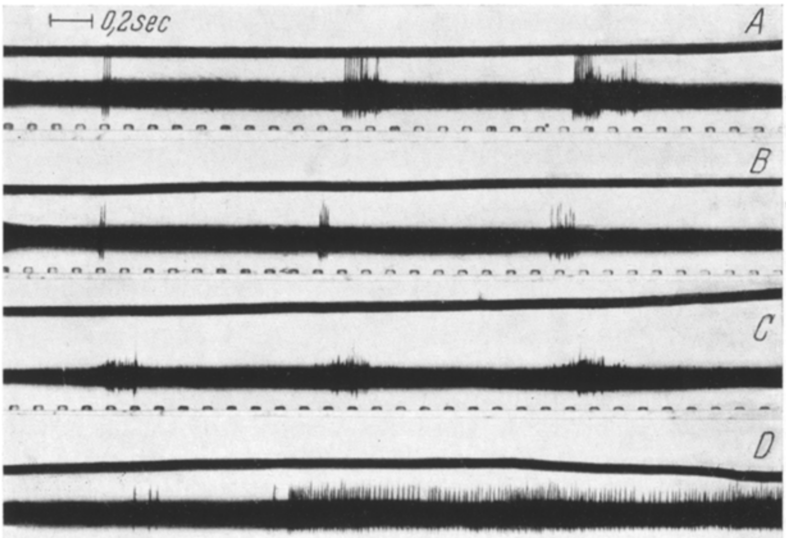


Fig. 2. *Olfactory discharges from different mitral cells, showing specific sensitivity of different receptors.* Records (rabbit under urethane) with an electrode leading from the mitral cell layer. All records made with same electrode position but various smells. Increasing concentration of smell shown by rising signal line. Discharges occur at each inspiration. A Response to Amyl Acetate. B Response to Dipentene. C Response to Cedar Wood Oil. D Response to Acetone. The potential spikes are of different size and therefore of different origin with each smell

Tested in this way the receptors in the rabbit's nose show differential sensitivity to a good many different smells. They can be ranged roughly in four or five groups, sensitive to esters, aromatic substances, terpenes, oils and so on, but the sensitivity is not sharply restricted and I think it would be extremely difficult to fit every compound into one of a restricted number of compartments. Clearly this differential sensitivity of the receptors will give some of the information on which the reaction of the central nervous system may be based (Fig. 2).

But the olfactory discharge has other features related to the character of the stimulus, features which modify the general pattern of excitation over the olfactory membrane. The organ has a large surface and the areas excited by different smells may differ in extent or position. There are certain substances, associated with oils, coal gas, kerosine, etc., which excite the aboral part of the organ much more readily than the oral, and certain substances, more soluble in water, which excite the oral part more readily or give a uniform excitation in both regions. And there may well be parts of the organ which are less accessible and are only reached by certain smells. I have not tried simultaneous recording from more than two, or occasionally three, places in the bulb, but it is possible that multiple records would show a patchy distribution of excitation like that of a chromatogram. At all events it would be surprising if the concentration of stimulating substances at different regions showed no variation with the physical and chemical properties of the molecules; the variations may

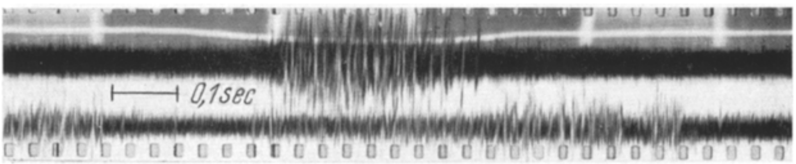


Fig. 3. *Simultaneous records from two points in the olfactory bulb, showing differences in the evolution of the discharge.* Rabbit under urethane. Signal shows suction of air with Amyl Acetate through the nose. The upper oscillograph tracing is from the aboral region of the bulb, the lower tracing from the lateral

well depend on differences in the receptor surface, rate of air movement in different regions, etc. There are also differences in the temporal pattern of excitation according to the smell. Substances partly soluble in water usually give an abrupt discharge with a short latency, whereas substances soluble only in lipoids give a discharge which rises more slowly after a longer latency and continues for a time after the air movement has ceased. Thus the time relation of the discharge to paraffin oil (kerosine) makes it easily distinguishable from the discharge to amyl acetate, etc.

The electro-physiologist with all these records before him would be able to say which of the substances under examination had been used to stimulate and if he can do as much in the way of discrimination it is likely that the brain which receives the pattern can do still more. I should add that some of the elements in the pattern may become less sharply defined after the first few breaths as the smell becomes more evenly distributed. This loss of definition may well be another factor in olfactory adaptation—in the progressive loss of a distinct olfactory sensation.

But we must not regard the pattern of the olfactory discharge as the only source of our information about the smell. The ends of the $V^{th}$ nerve in the nose may add something to it, and the relation of the afferent signals to the inspiratory movements which are needed to produce them will give information about the intensity and time course of the excitation. Many different sorts of receptor may be involved besides those of the olfactory organ itself and with all of them the pathways must be kept clear of noise injected at the synaptic regions.

I am suggesting that many afferent signals may fail to reach the cerebral cortex because the pathway is not fully insulated from activity taking place in the neurones which surround it and this may obscure the signal by filling the pathway with continous and meaningless disturbance. So much continuous activity can be found throughout the controlling parts of the central nervous system that only very well insulated pathways would escape its effects. But the noise can be suppressed for a time. In the olfactory pathway a strong smell will succeed in controlling the spontaneous activity when it is first presented and no doubt the level of activity can also be controlled from above. Unexpected and intense stimuli must be able to clear the whole pathway to the cortex.

When the spontaneous discharge or the 'noise' returns, as it does when the stimuli is repeated many times, the signals will lose their clear outlines and will cease to transmit information about the smell. But all that can be said is that the noise does return; why it should do so remains uncertain and until this has been explained an essential part of the scheme is missing. There are possible explanations related to the factors which control spontaneous activity in groups of cells, but for the present the hypothesis which I have given is no more than a preliminary survey. Its only value is to indicate possible lines of attack on the general problem of attention and adaptation.

My apology for such an unfinished story is that it will serve to indicate the great prospects which there are now for solving some of the major problems of the central nervous system. The new development is that it has already become an established technique to make records from single nerve cells and to make them from cells and pathways in the normal unanaesthetised brain. Studies on the human brain have been made in many neurological centres. JASPER and his colleagues havemade records with micro-electrodes in the cortex of monkeys during the performance of conditioned reflexes and in states of rest or attention and there are similar researches on different animals going on in laboratories in all parts of the world. I need not draw your attention to the work of my friend Professor JUNG and of his colleagues. It is enough to say that it has put Freiburg in the front rank as a centre for research on the brain.

Most of our present theories will no doubt be broken down by the new evidence which will soon be available to us, for it can show what is actually happening in the different cell units of the brain under normal conditions of cerebral activity. It is from records of this kind that we can expect to understand why the behaviour of the organism is dominated first by one sensory field and then by another. And the problem of attention is only one of many which will soon be far nearer solution.

I will end, then, by reminding you of the great advances in our knowledge of the brain which came of Hans Berger's work 30 years ago. That was the beginning of the direct recording of normal cerebral activity and it gave us new and quite unexpected facts to digest. We are now entering the second stage where we shall have records from units as well as from large cell masses and from deep in the brain as well as from its surface. I have little doubt that the results will be as unexpected and as illuminating as Berger's were, and I think our younger neurophysiologists are very much to be envied. It will fall to them to disprove our theories and I hope we shall be grateful.

I began by saying that the investigation of the receptor side of the sense organs now demands a knowledge of the latest results and methods of cytology, biophysics and biochemistry. Those who are more concerned with the function of the sense organs may still be able to dispense with a knowledge of molecular physics, but they will need to fortify their physiology with the latest techniques of psychology and the study of animal behaviour. They will have much to discover and difficult experiments to carry out: but I am sure we can congratulate them on being so close to some of the ultimate problems both of the central nervous system and of the mind.

**Zusammenfassung**

Allgemeine Fragen der peripheren und zentralen Sinnesphysiologie werden besprochen und an speziellen Beispielen des Geruchssinnes mit Registrierung vom Bulbus olfactorius erläutert.

Funktion der Sinnesorgane ist die Signalisierung von Vorgängen der Außenwelt an das Zentralnervensystem, um adäquate Handlungen zu ermöglichen. Die Aufmerksamkeit muß sich jeweils neu auf die wechselnden äußeren Ereignisse richten, damit das Verhalten darauf eingestellt werden kann. Bedeutsame Sinnesmeldungen, die diese Ereignisse beschreiben, müssen Zugang zu den Kontrollregionen des Gehirns finden, damit andere einlaufende Signale vernachlässigt werden können.

Elektrophysiologische Untersuchungen haben gezeigt, daß Sinnesmeldungen nur dann das Gehirn erreichen und das Verhalten beeinflussen können, wenn sie entweder intensiv oder unerwartet oder mit vorangehender Erfahrung assoziiert sind und dadurch einen besonderen Bedeutungscharakter erhalten.

Warum bleiben andere Signale unwirksam, wenn eine Sinnesbahn die Aufmerksamkeit bestimmt und kontrolliert? Diese Frage kann durch neuere elektrophysiologische Befunde am Geruchssinn wenigstens zum Teil beantwortet werden. Offenbar entstehen auf verschiedenen Ebenen des Nervensystems oder sogar im Sinnesorgan selbst Hemmungsvorgänge, die eine Fortleitung der Sinnessignale verhindern. Doch scheint im olfactorischen System die Passage eher durch eine dauernde unregelmäßige Hintergrundsaktivität gestört zu werden, welche die Synapsen

der olfactorischen Nervenzellen beinflußt. Dieses ,,Grundgeräusch" verhindert eine klare Übertragung der Sinnesmeldungen.

Wahrscheinlich sind auch nicht-olfactorische Sinnesbahnen dort, wo sie anderen Einflüssen zugänglich sind, einer solchen Störung durch das ,,Grundgeräusch" ausgesetzt. Ungestörte Übertragung ohne ein solches Grundgeräusch ist notwendig, wenn die Signalmuster spezielle Informationen bringen sollen. Intensive Reize können das Grundgeräusch unterdrücken und die Bahn vorübergehend freimachen.

Im Riechorgan können die Signale verschiedener Gerüche nach ihrem Zeitverlauf, ihrer räumlichen Verteilung und der spezifischen Empfindlichkeit einzelner Receptoren unterschieden werden. Wahrscheinlich ist die Erkennung eines Geruches von dem komplexen Effekt aller dieser olfactorischen Informationsquellen abhängig, wie auch von Receptormeldungen außerhalb des Geruchsorgans.

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Lord Adrian, The Masters Lodge, Trinity College, Cambridge (England)