RECEPTORS AND SENSORY PERCEPTION

A Discussion of Aims, Means, and Results of Electrophysiological Research into the Process of Reception

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MEMORIAL LECTURES

Preface

THE title and with it the theme of these lectures was suggested by my friend and colleague John Fulton and tempted me immediately because I thought it might be of interest at this particular moment to comment on the achievements of a quarter century of work by electronic methods on the special senses. It was clear that there was no need for an annual-review type of book, or for one expanded to deal with the results textbook fashion. Again, a complete general physiology of the special senses, apart from the danger of being too pretentious for the present age, might easily turn out to be too general for the specialist, yet too special for the general scientific reader.

Thus I felt I had good excuse for following my natural inclination to go into detail only in the fields where I felt I had mastered the details, to extract general principles from them, and to look for applications in adjacent fields. It seemed to me also that what we as experimenters individually pay a price for is laboratory experience and that therefore my innumerable omissions might be more generously forgiven if, as a counterpoise, I inserted chapters based on first-hand knowledge acquired by experimentation. The sections on the eye, on the muscle receptors with their reflexes, and on centrifugal control of sense organs serve this purpose.

My major omissions concern audition, which as a subject of electrophysiological research has been so beautifully developed by several workers in the United States. I try to follow the work on the ear but am not expert enough in the field to include a separate chapter on it.

Now, why is this an appropriate moment for commenting on the aims, means, and results of research by electrical methods on various aspects of perception? Clearly, the main reason is that we have actually arrived at principles which ought to be formulated and held to a mirror in order to prevent them from becoming immersed in the steady stream of annual contributions from many different points of view. Such principles concern, among others, "receptive fields," "generator potentials," "centrifugal control," "specific and unspecific afferents," and "organization of the frequency code." These and many others will be dealt with below.

Much as I speak about results obtained by electrical methods, my secret plea between the lines—I emphasize it now—is really for this kind of work *combined* with adequate stimulation of sense organs. I see no other way to a real understanding of the principles of organization of the central nervous system. This, in a different way, was emphasized very long ago by John Locke (see below, introductory quotation). The brain, after all, is the great interpreter of the senses.

While preparing these lectures I occasionally felt some apprehension that the time required was being spent less profitably than for laboratory work. I then derived some solace from the thought that the generation of postgraduate students about to enter this field may find the book useful as an introduction to the principles involved. At other times, in other moods, I have greatly enjoyed both the excuse for writing and the writing itself, feeling stimulated by the hope of, perhaps, gathering something of what, with Walter B. Cannon, one might refer to as the "durable results of the perishable years."

In the preparation of the manuscript my secretary, Gunvor Larsson, has given freely of her spare hours in order to make it possible to finish the book in time for the lectures. Evi Reigo and Anne-Marie Bengtson took charge of the illustrations and legends. At Yale John F. Fulton and Mary P. Wheeler devoted a great deal of unselfish care and labor to the perusal of the manuscript, suggesting improvements and corrections. The book and its author owe a great deal to these collaborators.

Several members of the staff of the Nobel Institute for Neurophysiology, as well as guest workers, have read parts of the manuscript and made valuable suggestions. Friends in Stockholm, London, and Cambridge have read sections of the book and given me the benefit of their criticism. Many more in different parts of the world have liberally lent me originals of illustrations from their papers and given me access to data in the course of publication. Though no one is specifically mentioned, none is forgotten, and I thank them all.

It is seldom that one has an opportunity of expressing one's gratitude to the foundations which have supported the Nobel Institute and made its work possible. This seems such an occasion, and I therefore wish to put on record my great indebtedness to the Knut och Alice Wallenbergs Stiftelse, the Royal Caroline Institute, the Nobel Foundation, the Rockefeller Foundation, and the Swedish Medical Research Council. Originally my Institute was set up in 1940 by a generous combined gift from the Wallenberg and the Rockefeller Foundations.

Finally, to the officers of Yale University and the members of the

Silliman Committee I wish to convey my sincere thanks for the invitation to deliver the Silliman Lectures. The great care taken by the Yale University Press in publishing this book is gratefully acknowledged.

If it shall be demanded, then, when a man begins to have any ideas? I think, the true answer is, When he first has any sensation. For since there appear not to be any ideas in the mind before the senses have conveyed any in, I conceive that ideas in the understanding are coeval with sensation; which is such an impression or motion made in some part of the body as produces some perception in the understanding. It is about these impressions made on our senses by outward objects, that the mind seems first to employ itself in such operations as we call "perception, remembering, consideration, reasoning," &c.

John Locke, *An Essay concerning Human Understanding*

Contents

Chapter 1

Historical Background. The Electrophysiological Approach to Primary Processes

1. Introduction

AT the time when the psychophysical era of sensory research was beginning to feel the impact of electrophysiological analysis J. von Kries in his Allgemeine Sinnesphysiologie (1923) gave a masterly presentation of the main principles discovered in the last epoch of research, as well as the psychological and epistemological background. To show how ripe the time was for Adrian's discovery of the frequency variation in single sensory afferents, I offer this translated quotation from Von Kries' book (pp. 51–2):

> For skeletal muscle we now regard the rhythmic nature of the motor innervation as certain. We see in this one of its most important distinctive features, and the frequency of this rhythm has been the subject of much research. It is a question of fundamental importance whether in a similar way the activity in the sensory nerves is rhythmical, but on this question it is not yet possible to pass definite judgement. Fröhlich has observed action potentials of very regular rhythms in certain sensory nerves of cephalopods. In afferent nerves of higher animals corresponding phenomena have not yet been established. Nevertheless, Fröhlich is inclined to accept the rhythmical nature of activity for all sensory nerves, and he assumes that it has escaped notice in higher animals because the frequency is relatively high, so that the string galvanometer fails to record it.

Von Kries goes on to discuss the all-or-none law of the nerve impulse and concludes, "If we transfer these notions—which, at least for motor nerves, seem probable—to sensory nerves, we have to assume that stronger stimuli give a more frequent, weaker stimuli a rarer, reiteration of the same process" [viz. the action current].

Having made the distinction—somewhat artificial, like all such distinctions—between the mainly psychophysical epoch of sensory research and the present era dominated by electrophysiology, I feel obliged to consider briefly the background of the latter in order to indicate its legitimate claim to a title of its own. In a recent lecture Adrian (1953) captured something of the atmosphere of the early twenties when he said:

> No one in those days who was interested in electrophysiology could have failed to realise what it might mean to his own work when the initial difficulties were overcome, and then came the papers of ALEXANDER FORBES and of GASSER & NEWCOMER * to show that the difficulties were already yielding. The technique they were using was clearly not to be undertaken lightly; it involved all sorts of unfamiliar components, high tension batteries, condensers and resistances—electrical gear which now overflows our store cupboards but then had all to be made by hand in the laboratory. But the technique could be used for physiological purposes. It was a practical method for magnifying the very small electrical changes which had been beyond the reach of our recording instruments. It promised direct information about events which formerly we had only been able to study by inference.
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> Reading some of the early papers of that time one cannot help remembering what a pleasure it was to find that most of the inferences had been correct. Impulses arising in sense organs or nerve cells were accompanied by action potentials like those in a nerve trunk stimulated electrically. They followed the all-or-nothing rule inferred from KEITH LUCAS's † work on the frog's dorso-cutaneous muscle. They appeared where and when we had reason to expect them, in sensory and in motor nerves. In fact there was no need to revise the accepted theories of the nature of nervous communication. It was carried out by impulses of the familiar type.

Having myself from the beginning been interested in the special senses and consequently in psychophysics, I can well remember how deeply stirred I was when Adrian's first contributions began to appear (1926, 1926–27; see also his summaries of 1928 and 1932b). It suddenly became clear that both sense organs and neurones (cf. Denny-Brown, 1929) delivered a message of repeated brief, electrical im-

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* The papers intended I take to be Forbes and Thacher (1920) and Gasser and Newcomer (1921). For these and all other references see pp. 303 ff.

† See Lucas (1917) in References.

pulses, so-called spikes, all of which were of the same size but increased in frequency when the stimulus was made more intense. Such spikes are shown in Fig. 1 in response to touch (*A*) and a painful stimulus (*B*). The message in the individual nerve fibers thus had the character of a simple frequency code! And it was all made more exciting by the fact that one could listen through the loudspeaker (Adrian and Bronk, 1928) to the code of the nervous message in the act of being delivered. An immense field was opened up for research. The code itself had to be studied in various sense organs. The retina and the organ of Corti seemed particularly fascinating. For these organs there was available an enormous body of psychophysical information to direct further research by the new method. Adrian immediately showed that impulse frequency diminished during continuous stimulation and so put sensory adaptation to the stimulus on a firm basis. It was obvious, too, that with such a definite measure available as spike frequency many new sense organs would be discovered. This expectation has been fulfilled. So far the only serious disappointment of this technique has been with the very thin nerves from some insect sense organs, which even expert technicians have attacked in vain (Hartline, Waterman, in personal communications).

Fig. 1. Discharges in dorsal cutaneous nerves of frog. *A* shows large rapid impulses due to touching skin; *B*, slow impulses produced by 2% acetic acid on skin. (Adrian, The mechanism of nervous action, Oxford University Press, London, 1932b.)

Another source of inspiration around the same period was Erlanger and Gasser's work (see e.g. their summary, 1937). This provided a clear picture of the properties of the nerve impulse in terms of fiber size and conduction rate and thus laid the basis for the precise analysis of electrical events which plays such a great role in contemporary work. In the physiology of the special senses its general significance has been obvious in the study of primary mechanisms, impulse generation, and sensory discrimination.

Forbes and his collaborators (1937) introduced the microelectrode technique for the study of neurone responses.* This method (cf. Buchthal, 1934) became an important supplement to nerve dissection (see Adrian, 1928) which technically had culminated in Hartline's (1938a) work on single fibers in the frog retina. First the retina (for a summary see Granit, 1947, 1950b) and then the organ of Corti (Galambos and Davis, 1943, 1944, 1948) were studied with the aid of microelectrode records, and a vast amount of new information was obtained. Perhaps the main advantage of the technique at this stage was that it made the mammalian eye and ear, as well as several nervous centers, available for analysis. Most of our detailed information about the elementary properties of sensory end organs and neurones has come from later improvements of the microelectrode technique, about which a great deal more will be said below.

The discovery by Wever and Bray (1930) of what is nowadays called the cochlear microphonic potential, even though first not understood, should rightly be mentioned in this place because it created very great interest at the time and served as a starting point for much important work.

Berger's rediscovery of the electrical potentials of the brain, popularly called "brain waves," his early fundamental results, subsequent scepticism as to the value of such mass analysis, and the final justification of this mode of approach, also had repercussions in the sensory field (1929; for a good historical review in English see Gibbs and Gibbs, 1948). These will be dealt with below when sensory projections and specific and unspecific relays are discussed. Adrian in England, Bremer in Belgium, and Bard and Fulton in the United States took up the study of sensory and motor projections and thus pioneered the large amount of important work that is being carried out today. It is well known that modern psychosurgery, which began as frontal lobotomy, owes its origin to experimental work carried out at Yale Uni-

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* A number of reports of the new method were published, but the most complete description of it was given by Renshaw, Forbes, and Morison (1940). In this paper will be found a full account of the physical principles involved in recording with microelectrodes from a volume conductor. As early as 1934 Buchthal had used microelectrodes for electrophysiological work on single muscle fibers.

versity by Jacobsen and Fulton (for a review see Fulton, 1949a,b; 1951).

I recall these events in passing as memoirs of a sense-organ man, because it may be of some historical interest to put such impressions on record. In retrospect they seem to me formative influences. At that time the electrophysiology of the sense organs did not as a field enjoy the popularity that has fallen to its lot today. One of the reasons for the revival of interest seems to be the appeal of the microelectrode technique, with its emphasis upon general principles of cellular behavior. This puts a premium on easily accessible reactive structures wherever such structures may be found. It is particularly convenient to use sense organs because they are accessible to both adequate and electrical stimulation.

May I also venture to suggest that the general importance of receptors has been emphasized by such discoveries as that by Heymans and Heymans (1927) of chemoreceptive regulation of respiration from glomus caroticum; by Verney (1947) of osmosensitive structures in the brain stem; by Ranson (see e.g. 1940) of heat-sensitive structures in the hypothalamus; followed more recently by C. von Euler's and Söderberg's (1952a,b) demonstration that the region in the medulla which is sensitive to carbon dioxide has in every respect properties of receptors such as those to be described below. It has been realized for a century to be sure, that the body contains a considerable number of internal measuring instruments—Sherrington (1906) used to speak of interoceptors as opposed to exteroceptors—but electrical methods have invited close analysis of their effects and made it imperative for both general physiologists and neurophysiologists to cross the boundaries of their own limited territories and invade each other's domains of research. For instance, the heart specialist must know something about receptors because study of cardiac afferent impulses, important for reflex self-regulation within the vascular system, has again attracted a large body of workers. (See e.g. Amann and Schaefer, 1943; Jarisch and Zotterman, 1948; Whitteridge, 1948; Dickinson, 1950; Schaefer, 1950; Paintal, 1953b.) The recent pioneer work in this field was begun by Jarisch (1940, 1941), who took up the well-known problem of the Bezold reflex.

2. *Scope of the study*

The sense organs are our "private" measuring instruments and, like other instruments, they have properties such as sensitivity, range, speed, and power of resolution. The study of these is common to both psychophysics and electrophysiology. A great deal of experimental work has gone into determining the limitations of the senses as interpreters of the external world in terms of perception. The analysis by electrical methods of primary processes in sense organs is part of this study but at the same time is also part of general neurophysiology.

At this point it is appropriate to remember that in the course of evolution the sense organs have developed by being in intimate contact with movement to or from external objects. This principle of organization is preserved in the reflex arcs of man and all animals. Indeed, highly important receptors, e.g. the vestibular ones, adjust balance by reflex postural contractions—according to most authors—without ever entering the world of perception. Many sense organs have pathways which do and others which do not evoke that particular conscious state which is called perception or sensation. We are not aware of our pupillomotor reflexes; yet their afferent path is that of light. All this is significant because the electronic era of work on sense organs has made some of its greatest contributions to the understanding of first principles by analyzing receptors lacking psychological equivalents in perception. It is not untrue perhaps to state that by comparison the previous era was one of great psychophysical discoveries.

In vision I can think of only one major psychophysical discovery from the same period, the "directional effect" (Stiles and Crawford, 1933; Stiles, 1939), which implies that the effect of light falling on the cones depends upon its angle of incidence. Of course there has been brilliant work done in sensory physiology with methods involving little or no electronics. I should like to mention the discovery of the "supersonic radar" of bats in flight (Griffin and Galambos, 1941; Galambos and Griffin, 1942; Galambos, 1942) suggested by Hartridge's early experiments (1920); Von Frisch's (1946, 1949, 1950) beautiful results on the orientation of bees; Waterman's (1950) precise analysis of the polarizing properties of the eye of *Limulus;* and Dethier's (1953) study of taste receptors on the legs of flies. Several others will be mentioned below when the subjects are discussed.

In many instances it is exceedingly difficult to translate electrophysiological results into sensory equivalents at the psychological level. I shall return to this point in Chapter 8 and when discussing microdissection and microelectrode techniques, which set problems that cannot be translated into perceptual terms. I do not mean problems which by definition are purely physicochemical propositions, e.g. ion transfer in impulse generation, but problems concerning the organiza-