PRESIDENT'S ADDRESS SOCIETY FOR NEUROSCIENCE WASHINGTON 10/28/71

by
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Ladies and Gentlemen; my colleagues in Neuroscience.

We are gathered here on a happy occasion, in the first plenary session of our Society. The good will which pervades it, - - the obvious joy you have shown at being together - - promises success for our enterprise. It confirms beyond expectation that this was a natural and good idea, now come to its formal beginning.

We are an association of scientists from many disciplines, joined by common aims: to advance understanding of nervous systems by research, to promote education in the Neurosciences, to inform the general public on current knowledge of the brain, and its relevance for the human condition. These are noble aspirations. Together they compose the modern expression of the continuing desire of man to understand the nature of his own life. What makes man human is his brain; what better thing for the life of an investigator than to seek to understand the organ of man's humanity.

The aims of our Society commit us to responsible leadership over a broad spectrum of this most human of human affairs.

II. To advance knowledge of nervous systems by research.

That beautiful phrase strikes a responsive chord in the heart and mind of each of us. This is our business; that is what we know how to do with a finite probability of success, as witness our program of this week. I believe that the last quarter century has seen a series of important advances, built successively one on another, and that we have now reached that plateau of knowledge, still primitive in some aspects, from which truly spectacular discoveries will be made during the decades of the seventies and eighties.

1. <u>The processes of excitation and conduction.</u>

An advance of profoundly heuristic value for Neuroscience was the elucidation of the processes of excitation and conduction in axons, discoveries which at once simplified and established a quantitative basis for understanding the changes in membrane conductance and the resulting ionic fluxes which are an important basis of life itself. Consider how important for the life of a nervous system is that ever so slight staggering in time of the changes in sodium and potassium permeability which allow for impulse conduction! Certainly this, and the explosion of discovery it has engendered, is a major achievement in biological science; one which will soon culminate in descriptions of the molecular alterations in membranes which allow for the changes described.

2. <u>The general biology of neurons, including synaptic transmission.</u>

Nowhere in the field of Neuroscience has there been more successful union of several disciplines than in the general biology of neurons. The mutual, positively reinforcing, methods of electron microscopy, biochemistry, and electrophysiology have yielded already a general understanding of the special metabolic and synthetic processes in neurons; of the axonal and transsynaptic transport of even large molecules, which portends discovery of the mechanism of the trophic influences of a neuron upon the cells it innervates; of the function of glial cells; of the processes of growth and differentiation of neurons and how connectivity develops, of the critical periods in brain development; of the genetic control of neuronal wiring diagrams, surely an information transmission of immense proportions. Most successful of all, the clarification of the various natures of synaptic transmission; both chemical and electrical, the latter prevalent in simpler forms, the former in more complex brains. And for the latter, the identification of transmitter agents and the biochemical and spatial pathways for their synthesis, variety of transsynaptic actions, and destruction. These are major advances in Neuroscience, which will provide a solid base for Experimental and Biological Psychiatry, and Neuropharmacology. No development of our era promises more for the general welfare. Interdisciplinary research at its best, you say? Much more, for here disciplinary lines are wholly blurred, and frequently all are united in one individual, a union marking the healthy development of the science of cellular Neurobiology.

3. The study of small brains.

The history of science suggests that significant advances commonly depend upon an imaginative simplification of naturally complex situations.

A development of this sort of the last decade has been the realization that small brains or ganglia - - frequently containing only a few hundred or a few thousand neurons - - may control a variety of interesting behaviors in some ways analogous to those of animals with complex brains. The successful application of microphysiological and microchemical methods to their study - - combined with measurements of behavior - - has led to significant discoveries concerning how such small brains program and control efferent action. This provides an avenue of attack from the viewpoint of comparative biology, upon what I consider presently to be the central problem of CNS Physiology: that is, to discover the nature and the laws which govern the emergent properties of the action of large populations of neurons. The phrase may evoke visions of vitalism; nothing could be further from my thought. What I mean is the way a population of central neurons operates upon its input to produce its output, an output which may vary widely depending upon an equally wide range of conditions; an operation not wholly explicable by what is known of the integrative properties of single neurons. There is an important something more, something which encompasses and transcends the individual cellular integrations. This problem Sherrington identified but did not solve,. nor any since him. We can measure its result, but know nothing of its nature or general laws. It is the hope of a considerable number of you that the study of small brains will lead the way to what would be a discovery of transcendent importance.

4. Afferent avenues and central processing: Sensation and Perception

A brain is an apparatus which collects information about its environment and by coding, relay, and processing guides efferent actions which maintain within broad limits homeostasis of the organism. Stored and recalled, this information provides the ground for execution of propositions internally generated.

The last decades have marked a change in the conceptual approach of investigators to the study of the central nervous mechanisms in sensation. There are no longer ghosts in our models of what brain operation may be like; no little men within the head. The working hypothesis of many is subsumed by the concept of psychoneural identity. That is, that the neural activity set in motion by sensory stimuli, successively transformed through successively interconnected populations of neurons, complexed against stored information, contributing to and conditioned by those neural locales and activities concerned with set or affect - that these neural activities do themselves lead to and are in fact the very essence of the private event of perception, and at choice its public description. Both private and public happenings result from the same chain of neural events. Thus on this view the processes of sensation and perception merge representing not different entities but the behavioral concomitants of different stages of central processing.

Discovery has ranged from identification of neural codes to elucidation of the processing mechanisms of sensory cortices. I shall not detail them; they compose several of our programs this week. Progress has been possible by a combination of several things: the use of natural stimulation, of the method of single unit analysis to reconstruct *ad seriatim* the events in neuronal populations, and a close correlation with the sensory capacity of the particular nervous system under study. This approach culminated in the last year in a simultaneous application of all these methods in waking, behaving animals, in a number of laboratories, surely an expression of the multi-disciplinary approach which we deem important.

In the field of sensory neurophysiology, I believe that the seventies will be the decade of the association cortices; for here, with the methods available and with some knowledge of events in primary cortices in hand, we can observe directly those interactions between sensory inflows which must be the neural substrates of the complex sensory experiences of everyday life.

5. The control of efferent action.

The externally observable actions of nervous systems are generated only by muscle contraction or gland secretion, the latter of interest in vegetative regulation. Thus the neural mechanism controlling posture and movement, and of such complex movements as those producing speech, continue now as they have for a century to attract the interest of a large number of Neuroscientists. What can we say about the central control of movement which Sherrington would regard as startlingly new?

Not very much.

Nevertheless, considerable progress has been made in preparing the ground. The intricate wiring diagrams at segmental, brain stem and cerebellar levels, and the details of their microphysiology, have been elucidated with remarkable clarity. And a great deal has been learned about the feed-forward and re-entrant systems of the forebrain which project from and play back upon the executant pathways to efferent action. Observation of the activity of neurons in those pathways during specified movements of waking animals promises an understanding of, for example, the function of the cells of origin of pyramidal track comparable with that of the motoneurons upon which they impinge.

What is needed is a new set of theoretical constructs. This is a fresh phenomenon, for most commonly in Neuroscience our theories far outreach the factual data to support them. But in the field of the central control of movement investigators now generate an increasing flood of new facts about one or another part of this complex system of systems. New theoretical ideas are needed, particularly about the initiation of movement, to bring together into a coherent whole the facts already available, and to guide future experiment.

6. Intrinsic and Extrinsic Regulating Systems.

Between major sensory and motor systems there exists the great mass of the central nervous system. Its explosive development has been accompanied by - indeed seems to have required - a parallel development of what I shall term the intrinsic regulating system of the brain. Central to this problem is that of the levels of neural excitability; or, speaking behaviorally, levels of awareness, varying from coma through stages of sleep to wakeful and attentive conscious. The problem of consciousness: That is a dominant theme for Neuroscience, one difficult to approach experimentally. Perhaps it is useful to regard consciousness as the behavior expression of a mechanism which may be the only possible means of achieving appropriate regulation of large brains, and may represent only the most elaborate example of a general biological mechanism for the control and regulation of action.

Studies of these intrinsic regulatory systems have produced monumental contributions to understanding during these last decades. The discovery of the role of the reticular system, and elucidation of the function of the generalized thalamocortical systems upon which projects must be regarded as major advances, and provide a framework for understanding the oscillating states of awareness we call the sleep-wakefulness cycle, and how it is that a brain regulates its own internal excitability. And just recently there comes the discovery that there is a system of neurons within the brain stem which connects by virtue of its adrenergically operated C-fibers with virtually all other regions of the nervous system: a reticulated brain within a brain, a regulator or governor, now revealed largely by the application of new anatomical techniques.

The free and independent life of animals - - that glorious Bernardian phrase -- depends upon the constancy of their internal environments.

And in that homeostasis the nervous system plays a vital role: not only because it regulates the regulators, but because it is at the neural link in these control loops that both slow and rapid adaptations to behavioral and environmental demands are made. In all this vast and rapidly advancing field surely no discovery of these decades has been of greater importance than that of the neurohumoral regulating function of the hypothalamus, the crossroads where humoral and neural factors are titrated for neuro-endocrine regulation, and certainly no other development in the Neuro-sciences promises more for clinical medicine that this flowering of the field of Neuroendocrinology.

7. Behavioral Science

I shall say little about the Behavioral Sciences, nor of what our Russian colleagues call the higher nervous function. To spotlight any one development would neglect a hundred of equal importance. I shall make two points. First, that there is a continuing trend of behavioral scientists to seek explanation of what they measure in terms of brain function, and that aspect of the latter relevant to the former can often now be observed directly and simultaneously. Such a trend gives promise for a future Neuropsychology in which the union will be complete.

My second point is that the study of the higher nervous function leads directly to that of man himself, and to those experiments of nature which disease or injury of the nervous system lay before us. On this score, I believe we have not taken advantage of the opportunities open. What we need is an ever closer blend of concept and technique and effort between our clinical colleagues in the Neurological disciplines and those of us who do not deal with human beings. And we can hope that the time will come when we can discard those divisive descriptors: clinical and basic. Perhaps the several current experiments in which the Neurological Sciences in a University are organized vertically will show us the way to the most productive studies of the human brain, in human beings.

III. To promote education in the Neurosciences.

Now I turn to a difficult problem, education in the Neurosciences. Here we face a dilemma which somehow we must resolve. How can we combine, in the education of young investigators, two superb ideas which are, to a certain degree at least, mutually exclusive? The very raison d'etre of this Society is that the dissolution of disciplinary lines will, and indeed has already, led to rapid advances in knowledge of the functions of brains. We hold that function must be understood in terms of anatomy, physiology, and biochemistry simultaneously considered, together with the behavior engendered. Now, most of us were trained in one or another of the relevant basic sciences; many of you have later added a deep conceptual understanding and technical proficiency in one or perhaps two adjacent fields. The result: some of the remarkable research achievements I have tried to outline earlier. Put bluntly, the problem is this: if a man is trained broadly across all the relevant fields of Neuroscience, can he at the same time achieve the theoretical penetration, scholarly understanding, and technical skill in one of them required of the man who will make fundamental discoveries?

No one has a certain answer to this problem. That is why your program committee has scheduled a special session on it this week. But we are in a fortunate position, for there exist in the universities of the country a wide variety of training opportunities, which vary from one extreme through several intermediate grades to the other. What is needed is an objective study of the success or failure of these many efforts. This is why I have recommended to your council that it establish a group to study these programs marking their success or failure. Such a group must, of course, first discover how to do so. Perhaps within a decade, we may then learn how to retain what is successful from programs of the various types. I myself believe that such an assessment will be difficult; for the success of teacher and taught depends, at least in my own experience, far more on personal attributes and particularly personal motivation than upon programmatic outlines.

IV. To inform the general public on the state and implications of current knowledge of the brain, and its relevance for the human condition.

It is this role, defined as the third objective of our Society, which is most foreign to us. Yet it is one, I believe, that the majority of you agree we should assume, for it provides us with the opportunity for service on a broad scale, and to influence for good the future course of our national life. There are at least three different aspects:

1. Firstly, to provide a consultative resource for those in public life charged with decision-making. This, of course, we share with other learned groups with longer histories and deeper experience. But our nascent state, unburdened by tradition, allows us to approach this role in new and what I hope will be more useful ways than common hitherto. This is why I have hesitated to lead our Society pell-mell into the arena of public and social affairs during our first formative months, desiring first to build our own house. We should discover how to bring to bear on these problems, in an effective way, the collective wisdom and originality and sense of public service so obviously a characteristic of our distinguished membership. I do not yet know that way, but I am convinced that it is not by the usual pyramiding of committees. We must bring to bear on this important function the scholarly process you each use in your daily laboratory research.

2. Secondly, We must inform the general public, not only to guide them in public decision-making, but that they understand what it is for which we ask such large-scale public support. In this regard I believe that our case for a high priority for public support is so strong that we need not, indeed we should not, take the position of special pleaders. I have no doubt that the majority of responsible public officials and

private citizens can be brought to understand the importance of the study of brain function without resort to flamboyant and extravagant promises. Indeed I believe that, if made, such promisory notes will eventually be presented for redemption; default will certainly evoke a negative feedback. And who knows better than we do that we are not likely very soon to solve such problems as the prevention of mental retardation, the genesis and prevention of mental illness, the biological basis of memory and thus a brain-oriented educational system, etc. Let our results over-run our promises; support will follow.

I know that each of you will agree with me we should be grateful for the magnificent support we have been given during the exponentially expansive decade of the sixties. Never before in the history of any country has science, and particularly our own, been given the lavish and continuing support we have enjoyed. Whether we used it well remains for history to decide, but with it we have built the broad and strong Neuroscientific apparat we now possess.

That such support would eventually slow its rate of growth was inevitable; no organism or organization can long sustain a 15%/year growth rate. We should understand, as I believe Dr. MacNichol will document tomorrow, that the public support of Neuroscience continues to grow, and continues on a magnificent scale. The 15% increment years are not likely ever to return. We should put our own houses in order, and use the very large support we have with the greatest skill possible. Support will always follow discovery: it is our business to discover, not lobby. We should voluntarily proclaim what will otherwise most certainly be forced upon us: that we are responsible for the support we receive, and accountable to the public for its judicious use. To think otherwise places us in the position of medieval ecclesiastics, facing an inevitable and perhaps destructive reformation!

The social resposibility of the Neuroscientist

Last, I address some brief remarks to a problem which burdens the Neuroscientist perhaps more than it does any of his scientific colleagues. What is the social responsibility of the Neuroscientist for the effect on human society of the discoveries which come from his work, and particularly for eventual abuses of his discoveries? I know you will agree that a descriptive study of the laws of nature has no moral or ethical quality; no property of good or evil pertains to study of an action potential, of the growth of a neuron, of the identification of a transmitter, or the measurement of behavior. The moral and ethical issues, questions of right or wrong, arise only when scientific research concerns itself with influencing nature; and for us this means influencing behavior. The frightening spectre raised by that thought, the real and present dangers to individual freedom which it poses, are not pipe dreams. They are problems in the real world with which we must deal, and in responsible ways. And on them we should take no positions of superior wisdom by virtue of extensive knowledge, for it is not my experience that scientists are better qualified than other responsible individuals to give advice on social and political questions. Nor do I believe that we are more objective, dispassionate, impartial or tolerant than any other group of people. What We do possess is the detailed knowledge upon which the wisest, most tolerant, and socially just decisions possible can be based.

I do not know how to resolve the host of difficult questions subsumed under the phrase: the social responsibility of the Neuroscientist. I do know that the large majority of you indicate that you desire our Society to be concerned in a responsible way with it, and with this I agree. It is for this reason that I have asked your council to explore the most efficient way to begin study of the problem.