AUTONOMIC IMBALANCE *and the Hypothalamus*

IMPLICATIONS FOR PHYSIOLOGY, MEDICINE PSYCHOLOGY, AND NEUROPSYCHIATRY

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. . . human truths, however valuable they may seem, are always open to challenge, to revision, to refinement, to refutation, to repeal. Only the quest is eternal.

A. Guérard, *Bottle in the Sea* (1954)

Happiness consists in devotion to a dream or to a duty.

E. Renan, *Recollections of My Youth*

To

Mr. A. A. Heckman, Executive Director,
and to the Board of Directors, of the
Louis W. and Maud Hill Family Foundation

PREFACE

Only lunatics can be completely original.
Will Durant, *The Age of Faith* (1950)

THE experiments described in this monograph had their origin in the clinical observation of Funkenstein, Greenblatt, and Solomon that the intensity of the hypotensive action of mecholyl showed greater variations in neuropsychiatric patients than in controls, and particularly in the fact that this effect of the drug changed with the change in the mental condition of the patient. This finding was illustrated in a number of publications, but not evaluated in its theoretical significance.

In view of my earlier studies on the relation between the diencephalon and psychic disorders (86, 87, 90, 94), the original observation of Funkenstein *et al.* suggested to me the possibility of measuring the excitability of the hypothalamus in the intact organism through autonomic tests. Since this idea would have far-reaching consequences for clinical medicine and neuropsychiatry, the problem was attacked on a broad basis. The experiments proving the validity of the idea, the application of the underlying principle to the parasympathetic system, and the results obtained with these tests in normal persons and psychiatric patients, are reported in this monograph. In addition, it became necessary to subject the closely related problem of autonomic imbalance and its ramifications (including hypothalamic-cortical relations, somato-autonomic integration, and homeostasis) to an experimental analysis.

If it is correct that a disturbance of functions is the first observable sign of the disease process long before an anatomical lesion appears, the physician must be interested in the physiological analysis of functional changes and abnormal reactions of the autonomic nervous system which seem to throw some light on numerous clinical problems. In view of the central role which the hypothalamus plays in the physiology of the emotions and behavior, psychologists and neuropsychiatrists, it is hoped, will find the studies reported in this book of value in solving their problems.

Readers who are not well acquainted with neurophysiological research or cannot spare the time to read the detailed report of the

physiological experiments and their evaluation are advised to substitute pp. 217–221, 225–228, and 239–242 for Chapters 1, 2, and 7. An attempt has been made to correlate the experimental findings with medical, psychiatric, and psychological problems, in the hope of stimulating further research.

Although the major part of the experimental work reported in this book has been performed during the last few years, its roots go back to my student days when, under the influence of my teachers in the medical sciences and the humanities, my interest in the nervous system was aroused and the ideals took shape which have guided me through the vicissitudes of academic life and through personal tragedy. Neurophysiology, when seen in its larger aspects, is charged with the task of explaining the mind, and yet it is deeply rooted in the natural and biological sciences. Its area lies at the crossroads between the sciences and the humanities, separated at the present time by an ever widening gulf. In these circumstances it is perhaps not superfluous for a teacher, at the end of his career, to make a profession for the sake of the younger generation: first, to acknowledge his indebtedness not only to the teachers of physiology who influenced his scientific goals but also to the representatives of the humanities who helped him to develop his personality; secondly, to express his desire that these sources of information and moral strength should be utilized to a greater extent than today in the education of scientists. "The very summit of man's achievement," said Goethe, "is the capacity to marvel." "Wonder," writes J. Pieper, in quoting these words, "is the *principium*, the lasting source, the *fons et origo*, the immanent origin of philosophy." Of experimental science the same could be said. Indeed one might even say that the fundamental, perhaps the physiological, basis of the creative act is the same, whether in philosophy, the arts, or the sciences. What Pieper writes about philosophy, that "the joy that accompanies wonder is the joy of the mind and spirit that is always open to what is fresh, new, and as yet unknown," is just as applicable to science. In the sciences as well as in the humanities, should not the teacher by his enthusiasm, checked of course by rigorous criticism but undaunted by failure, attempt to transmit this joy and this wonder to the younger generation? If he could do so, then a generation of humanistic scientists might develop who would not recognize a schism between scientific and humanistic endeavors. On the contrary, they would attempt, in their life and work, to reconcile these main foundations of the creative life. Such scientific humanists would agree with Goethe, "Das Leben ist keine Lust, das Leben ist

aber auch keine Last; das Leben ist eine Aufgabe," * and act according to the precepts of Euripides:

> When you are about to take some action by yourself, call then on the powers above.
> For divinity also takes a hand to help him who tries to help himself.

My thanks are due to the Hill Family Foundation and its executive director, Mr. A. A. Heckman, who made the present work possible; to the President and Regents of the University of Minnesota for a short leave and a sabbatical leave used to write the monograph; to my collaborators H. M. Ballin, W. P. Koella, H. Nakao, R. Nelson, E. S. Redgate, and T. Tokizane for their devotion to the work.

I am deeply grateful to my friends for reading the manuscript, and particularly to Dr. G. N. Loofbourrow for his keen criticism; to Mrs. Vera Clausen of the Biomedical Library of the University of Minnesota for her continued cooperation; to the staff of the University of Minnesota Press, and especially to my friend Dr. Doris Franklin, for unfailing help.

A large part of the experimental and clinical material in this book is presented here for the first time. Of its 101 illustrations, 70 are from unpublished investigations. The author wishes to express his grateful appreciation to the editors and publishers of the *Journal of Neurophysiology*, *EEG*, *Clin. Neurophysiol.*, *Journal of Physiology*, and *Arch. Internat. Pharmacodyn.* for permission to reprint illustrations from these journals.

E. Gellhorn

2 Fellowship Circle
Santa Barbara, California
December 1956

* "Life is no pleasure, but neither is it a burden; life is a task."—The quotations from Pieper are from his book *Leisure, the Basis of Culture* (1952). According to information kindly supplied by Professor W. Jaeger of Harvard, the lines from Euripides are from the lost version of the *Hippolytus*.

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INTRODUCTION

IT IS a long-established fact based on experiments on various nerve-muscle preparations that a given stimulus acting on an autonomically innervated organ produces diametrically opposed effects on this organ in different physiological states. Thus, stimulation of the hypogastric nerve elicits a relaxation of the virginal uterus but a contraction of the pregnant uterus of the cat (49), and the smooth muscles of the gastrointestinal tract react to various stimuli differently in different states of tone.

Without adding further examples, it may be said that fundamental alterations and even a reversal in the responsiveness of autonomically innervated structures have frequently been observed in physiological experiments, pharmacological tests, and under clinical conditions; but the site of action where such changes are bound to occur most frequently, the central structures of the autonomic nervous system, has not yet been subjected to a systematic experimental analysis.

It seemed desirable, therefore, to study autonomic reactions in conditions of centrally induced autonomic imbalances. These investigations form the core of this book. From the physiological point of view they appear to be rewarding, since they throw light on the nature and the limits of some of the laws governing the activity of the autonomically innervated organs of the body. To some extent also, the study explains the mechanism underlying the alteration and reversal of autonomic reactions seen in certain clinical conditions.

The procedure, in principle, was this: to alter the reactivity of the autonomic system through a stimulus and to determine this alteration ("tuning") by a test stimulus. In order to analyze such a case, the laws governing summation within the sympathetic and parasympathetic nervous system must be understood. Therefore these laws are discussed first; later they are applied in conditions in which the autonomic centers had been altered ("tuned") reflexly either toward a greater sympathetic or parasympathetic responsiveness (Chapter 1).

This problem was investigated further at the hypothalamic level (Chapter 2). The hypothalamus was selected because of its great significance for the physiology and pathology of the emotions and the

adequate separability of parasympathetic and sympathetic functions.* Moreover, the experiments gave an opportunity to investigate the relation between the hypothalamus and the medulla oblongata, and to show that the threshold of important vascular and respiratory reflexes that were thought to act primarily on the medulla is determined by the excitability of the hypothalamus.

States of autonomic imbalance were produced by directly altering the excitability of either the anterior or posterior division of the hypothalamus through physiological or pharmacological means. The responsiveness of the autonomic system to various stimuli was greatly altered, and the laws operating in reflex tuning were found to be valid in states of hypothalamic imbalance. In addition, the investigations led to a result of considerable importance for medicine and neuropsychiatry by showing that certain simple autonomic tests measure semiquantitatively the excitability of the parasympathetic and sympathetic divisions of the hypothalamus in the intact mammalian organism: the effect of mecholyl and other hypotensive drugs on the blood pressure is determined by the excitability of the posterior hypothalamus, whereas the pulse slowing resulting from a given rise of the blood pressure (induced by noradrenaline, for instance) depends on the excitability of the anterior hypothalamus.

The study of sympathetic discharges over a wide range of intensities made it necessary to clarify the relation of the neurogenic to the adrenomedullary discharges (Chapter 3). The experiments showed that the adrenomedullary discharges do not reinforce the sympathetic discharges, as Cannon believed, but inhibit them, and thereby fulfill an important role in homeostasis. Moreover, the ratio of neurogenic to adrenomedullary discharges depends on the excitability of the central nervous system in general, and on that of the hypothalamus in particular. Among the physiological factors which greatly influence hypothalamic excitability and this ratio are the proprioceptive impulses (Chapter 4). This work has important implications for the

* In recent years the important discoveries of Magoun and his school (73, 75, 213, 214, 221–223, 241, 289, 290) have shifted the interest from the hypothalamus to the reticular formation. Both structures have certain functions in common, and the excitability of the posterior hypothalamus seems to depend on the reticular formation (251). Nevertheless, it should not be forgotten that the hypothalamus controls highly integrated actions (151, 153) and is intimately related to the emotions and the endocrine system (94, 141). However, the anatomical and functional connections between the hypothalamus and the reticular formation and the fact that both structures send diffuse impulses to the cortex and receive impulses from the cortex and cerebellum (327) make it very probable that the posterior hypothalamus and the reticular formation undergo similar changes in a variety of conditions.