Biochemistry and Behavior

BIOCHEMISTRY and BEHAVIOR

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FOREWORD

THIS LUCID AND COMPREHENSIVE VOLUME ON *BIOCHEMISTRY AND BEHAVIOR* will be a welcome addition to the library of every behavioral scientist, from those interested in metabolic functions to those groping for the new information on DNA and RNA as clues to the complexities of genetics. The book is not easy reading for those whose chemistry is deficient—and this friend and admirer, who is writing the introduction is deficient. Attention is held, and data made clear, in slowly ascending levels of complexity, without the authors' falling into assumptions and speculations, and without ever "taking the word for the deed" where research is concerned.

Almost every aspect of behavior is considered in the light of the findings of biochemistry. At times, the behavioral scientist will want to define his own data more sharply when he sees them as expressions of chemical realities; at times, he will want to ask what the return effect of behavioral changes upon biochemical realities may be; at times, he will ask whether there is truth and reality in "general systems theory" and its assertion that the same basic principles apply at different levels. Sometimes he will just want to sit with the individual findings from limited experiments and slowly absorb their implications; at other times he will want to reach for the stars of biochemistry of the future.

It should be clear that the book is not an attempt at a biochemistry *of behavior*. Note the very last sentence of the book, in which the biochemistry of behavior is conceived to be a problem of tomorrow. The task today is to mobilize today's chemical knowledge, so that the genetic, physiological, behavioral problems of today will be better understood, and those of tomorrow more clearly glimpsed through today's confusion. Though the authors make clear that the "inter-level bridges" required to pass from one scientific level to another have not been constructed, they do nevertheless offer exciting glimpses of the way in which bridges are being constructed: *"Just as anoxia appears to influence emotions, so emotions appear to in-*

fluence the internal oxygen supply of at least certain tissues" (page 52). A more subtle example of the problem of levels appears (page 414) where the relation of the social environment to the inner determiners of heredity is considered: *"The genic composition of an individual may be best understood as that which determines the limits beyond which the organism cannot range. But the exact point within these limits where we may find an individual is determined by a variety of influences, some of which are known, many of which, most certainly, are not."* One has then the attempt of biochemistry not only to throw light on the phenomena of behavior, but to move out into those intricacies, those scientific challenges in which data from chemistry, biology, psychology, sociology interpenetrate one another. The concepts belong to science, not just to a particular science.

"Chemistry is the central science." I thought again of this phrase, so well used by Sherman in his *CHEMISTRY OF FOOD AND NUTRITION*, when I was attempting to fathom the problem of the manner in which hydrogen ion concentration is related to human value systems. The flow is, for the most part, from chemistry on up to the other levels because it is the chemist who is preparing the feast for our delight. When, ultimately, the data of science have reached their own mature integration, it may be that the chemist may be allowed to enjoy a meal prepared by the behavioral sciences. It will, however, be some time from now. In the meantime, let us thank the chemist both for the rich information given and for the broadening of our vision.

GARDNER MURPHY

PREFACE

ONE OF THE GREAT SCIENTIFIC PROBLEMS facing biologists today is the manner in which knowledge of one level of abstraction and generalization can be translated into terms equally suitable and understandable for another level of generalization and abstraction. The consideration of "behavior," both animal and human, involves data from the ion, molecular, cellular, organ, animal, and even the societal strata. Although data are accumulating in all such areas of exploration, there are yet no models (let alone answers) that can furnish the interlevel bridges needed between them. However, attempts can and are being made to ascertain the correspondences, or at least the correlations, that may exist between the data from these different fields of investigation. In terms of the disciplines currently in vogue, there are, among others, attempts to relate biochemical data to physiological data to behavioral data. In view of the nonexistence of bridging models, it seemed of importance to us, because of our bias and training, to look at those correspondences that have been postulated in the literature to exist between biochemistry and behavior. The chapters that follow, therefore, are an attempt to bring together within the framework of biochemistry those kinds of correspondences that may exist or have been implied by the literature in these two related disciplines. Admittedly, it is an incomplete attempt. To some extent, the selection and grouping of the data are determined by the interests and biases of the authors. We would like to apologize therefore for the inevitable omission of some important papers wherever these omissions may have occurred.

The impetus for this work was generated by some casual conversations we had with Professor Horace W. Magoun whose interest in, and excitement about, interdisciplinary relationships were transmitted to us. Insofar as this book is in some measure a successful attempt, we would like to express our thanks to Dr. Magoun; and insofar as it fails in its aims, we hasten to say that we, not he, must be held accountable.

Certainly, a deep sense of gratitude must go to Lila Geller and Alice Yuwiler who, with their children, had to share their husbands

and fathers on countless evenings and weekends with the Eidusons, the library, and the manuscript of this book. It was, we know, not always easy or comfortable to do this.

We wish gratefully to acknowledge the secretarial assistance of Mrs. Lucille Keller who, as we wrote and rewrote, typed and retyped, to what for her must have seemed *ad infinitum*. There are still others we thank who in countless ways contributed in some measure to the task of getting this manuscript to its present form.

In particular we are indebted to our colleagues at the University of California at Los Angeles, the Veterans Administration, Los Angeles, Reiss-Davis Clinic for Child Guidance, and the University of Michigan, who provoked many stimulating ideas. Dr. R. W. Gerard was extremely helpful in reading portions of the manuscript and offering his insightful suggestions.

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E.G.
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TABLE OF CONTENTS

CHAPTER 1

INTRODUCTION

During the last few years, we have had the pleasure and privilege of working with individuals from different scientific disciplines on a variety of collaborative research projects. These multidisciplinary projects were undertaken with the firm belief that looking at a particular problem from many different frames of reference might enhance the kind and the number of questions being asked about the problem, the direct investigational techniques, as well as the ultimate understanding of the phenomena. We held discussions with psychiatrists and psychologists, with anatomists and neurophysiologists, which were admittedly stimulating and rewarding, but which also necessitated an inordinate expenditure of time in simply teaching one another some of the basic approaches, concepts, and myths of our respective disciplines.

Our interest in the "imprinting mechanism," for example, led us to certain aspects of brain biochemistry, to study imprinting from a behavioral point of view, to consider its electrophysiological concomitants, to attempt to determine its genetic components, and to try to understand the way the development of the central nervous system relates to each of these.

Because we who are biochemists were interested in the biochemistry of the brain associated with or concomitant with certain behavioral patterns, it was necessary for us to know something about behavior—especially those aspects or pegs upon which we were going to hang our data. Conversely, the other investigators would then be concerned about the nature, structure, and action of particular chemical substances affecting the behavior they were observing and studying. Many, many questions were asked. Can this or that behavioral segment be quantified? Can the behavior be categorized into specific units of description? Can its magnitude, intensity, and direction be delineated? How could we relate a unit like micrograms per gram of brain tissue to a category like "behavior"? What is a

chemical inhibitor, an antimetabolite? What is the possible relationship of a temporally segmented enzyme system to the sequential activity in behavior? What does a neurohumoral transmitter have to do with the transmission of information to the regulatory mechanisms of the brain? How does the developmental anatomy and the neurophysiology of the brain relate to the developing biochemistry in the embryonic or neonatal brain?

When we looked into the literature to become familiar with these and other vexing questions, we found ourselves trying to become conversant with an enormous spectrum of pertinent data ranging not only from alpha globulin to zeta potential, but also from avoidance behavior in cats to wakefulness in man.

It was at this point that the idea was generated for a book that would be of help to investigators from various disciplines who were interested in the experimental work being done to establish a relationship between biochemistry and behavior, and to relate the thinking that has grown out of this work. In this book our primary aim has been to describe the principal biochemical systems and processes that seem pertinent to behavioral function, and to discuss the basic biochemical concepts that underlie our knowledge of these systems. To a large extent the development of current understanding in the field of biochemistry and behavior will be evident. We hope thus to show the trends in the area of biochemistry and behavior and the questions with which biochemists are now increasingly concerned.

Because we have singled out those aspects of biochemistry that have some relationship to behavior—albeit often a nebulous one—we make no pretense at offering an exhaustive treatment of biochemistry, or even of those areas in which we are interested. This is neither a textbook in general biochemistry nor in neurobiochemistry. At most, this book discusses some of the basic biochemistry that facilitates an examination of the general topic under investigation. Interested readers will find a number of textbooks suitable for more detailed analyses of each area and topic, and a list of those books we think particularly valuable for certain topics is given in Appendix A.

Our intention has been to look at the hundreds of studies that have been primarily biochemical but have cited some behavioral findings. Conversely, we have been interested in the hundreds of studies in the behavioral sciences, particularly psychology, that have

directly or indirectly implicated some biochemical parameter. Our aim is to systematize these studies in a meaningful way. To date, they have lain largely in a state of unrelatedness, making it most difficult for the biochemist and the nonbiochemist interested in the problems of biochemistry and behavior to establish any synthesis from the rapidly accumulating data. We have taken those behavioral studies covering some aspects of biochemical knowledge and tried to relate the particular biochemistry involved to larger or more general sequences and principles. We have checked to see if other studies of the same behavior have implicated the same biochemical parameter. Similarly, we have tried to place the behavioral parameters of the biochemical studies into the more general categories of behavior.

It will be apparent to all, as it was to us, that the experimental work has proceeded largely on a hit-or-miss basis, with far too many misses for the amount of thinking, work, and effort that have been expended. Nevertheless, we have tried to evaluate the studies, see their implications in terms of present knowledge, and determine the avenues they suggest as the most promising for the future. We have looked particularly for the most potentially fruitful cross-avenues, and these and some general relationships of the two disciplines are presented in the final chapter.

The approach we have taken should be evident from the chapter headings—indeed, our treatment of some of the topics shows our intent. We have tried, for example, to treat collectively certain well-known biochemical-behavioral disorders like phenylketonuria, galactosemia, porphyria, and so on. However, we have not done this exclusively. Although these disorders are quite well understood in that a biochemical lesion is known, and they are more or less directly correlated to certain mental defects, we believe that the difference between pertinent aspects of these disorders and many of the more vague and ill-defined mental aberrations, to be mentioned later, is more apparent than real. For example, although the phenylpyruvic oligophrenics (phenylketonurics) are almost invariably mentally retarded and the biochemical lesion known, we do not know which aspect of this lesion is specifically pertinent to the mental retardation or whether the relationship is secondary or even more remote to the biochemical lesion. We have therefore felt it appropriate to

bring in some of these disorders in other aspects of the biochemical orientation.

As to the behavioral side of the picture, we have limited the definition of behavior to normal and abnormal phenomena that are open to direct experimental manipulation or observation, or to clinical data. Both human and animal studies have been included, and, although these have represented a number of theoretical approaches in psychology, we have chosen to consider only the empirical behavioral data. We did not find it pertinent or desirable to get embroiled in those problems of conceptualization or theoretical rationale unique to either discipline. When, however, both the biochemical and behavioral data together merit a theoretical plunge, we are happy to take it.

Although some of the psychological data are presented as parameters which are relatively easily understood by biochemists and other nonpsychologists, and perhaps are already familiar to them, a number of others which are idiosyncratic to the field appear in the literature. Rather than trying to explain these in the scope of the text, we have again taken recourse to an appendix. Thus, in Appendix B, we have discussed the psychological tests generally used, the kinds of measurements and evaluations customarily made by psychologists, and have listed references that give details of some of the basic experimental and clinical procedures. Although we have, by and large, put a biochemical microscope on a behavioral agar plate, in each chapter the psychologist has a chance to reverse subject and object. In this way, we hope to take advantage of behavior as a co-frame of reference.

Furthermore, we have chosen to omit behavioral phenomena which, most appropriately, relate more to physiology or neurophysiology, and with this, almost all of the electroencephalographic data. These data are, of course, very exciting and hold great promise for defining brain mechanisms, but our inability to review the wealth of material currently appearing in the literature and our very limited competency in this area precluded further coverage.

The approach we have taken in trying to understand the problem of biochemistry and behavior has certain general underlying assumptions that should be stated. Whatever behavioral process takes place, whether feeling or overt action, it is our belief that there necessarily must be concomitant or correlative biochemical reactions. Just as

digestion involves biochemistry in making the food we eat available to the metabolism of the body, and as motion involves the conversion of biochemical energy to work, and just as vision and olfaction have an intimate relation to the biochemistry of their receptor cells, so too must behavior be mirrored in the myriad of biochemical reactions. We cannot conceive of even a thought occurring without its counterpart of biochemical and physiological events. If the mind resides in the brain, as we believe, then it follows that thought and consequent behavior are expressions of brain function. But brain function, in turn, can be derived only from the function of its component units. Those units, being living cells, are continually involved in biochemical activity, and alterations in their function must involve alterations in their biochemical activity whether this activity is as subtle as an ion shift or as "gross" as the elaboration of a neurohumor. Different organs of the body subserve different functions, and it is reasonable to expect, therefore, that each organ will carry out specific and unique biochemical processes. The thyroid, for example, is the only organ in the body that produces thyroxin and has the unique property of possessing the necessary biochemical system for the trapping and incorporation of inorganic iodine into the thyroid hormone. The pituitary secretes its tropic hormones and the pancreas elaborates its secretion of insulin, to mention only a few. Thus, it can be anticipated that the brain also will have its own particular biochemical systems so as to fulfill its unique functions and will differ, in part, from functionally different organs like lung and liver, pancreas and pituitary. Underlying these individual peculiarities, however, may be found general metabolic pathways common to all systems, regardless of their specific function. Thus, for example, the myriad of biochemical reactions required to utilize carbohydrate as a fuel and convert it to needed stored chemical energy is essentially common to all metabolizing cells and organs whether they are found in plants, bacteria, or any other living organism. It should, therefore, be clear that general biochemical principles which are applicable to the liver and lungs are found equally applicable to the brain.

We wish to point out that we have not mentioned the biochemistry *of* behavior but have spoken of biochemistry *and* behavior. We have purposefully done so in order to avoid in part the implied causal relationships in the phrase, "biochemistry *of* behavior." We

often speculated, of course, about causal sequences between biochemistry and behavior. As might be expected, among ourselves we held different views. One of us believed that a direct sequential causal relationship existed and that any behavioral process must be preceded by biochemical reactions. Another felt that biochemistry, neurophysiology, etc., simply represented different levels of abstractions of temporally simultaneous phenomena and that causal relationships between them were purely arbitrary. And yet, virtually all felt that the brain (or almost any organ for that matter) was such a complex mechanism that it was indeed difficult even to consider causal relationships. It appeared to us that in a direct causal relationship, biochemistry could cause behavior which then could effect biochemistry to elicit new behavior, and so on and so on until it would be virtually impossible to segregate individual events, even though each may be causally related. With the neurobiochemical, neuroanatomical, and neurophysiological data indicating the possibility of such mechanisms as "feedback systems," "reverberatory circuits," and "inhibitory and stimulatory networks," it was felt that it would not be meaningful to speak of simple causal relationships of these interactional and transactional processes. Despite, or perhaps because of, these disparate views, agreement was obtained in that all believed that the question of causality here cannot be measured and so must be held in abeyance.

These notions only increased our belief that interdisciplinary[1] thinking and approaches to problems involving biochemistry and behavior could indeed be fruitful. In the last chapter we suggest that not only may biochemistry provide some of the bases for behavior and thus greater understanding and explanation of phenomena on a psychological level, but conversely perhaps, behavioral data, once meaningfully schematized, may provide clues and ideas for biochemical research.

Our interest in attempting convergence and correlation between the phenomena of behavior and biochemistry not only reflects our enthusiasm for the work in these sciences, but also has been stimulated by the historical growth of biochemistry.

[1] Here we do not mean a "team approach," which connotes the submission of each of the members for the practical whole, but rather truly interdisciplinary in that each member of a discipline, independently, brings to bear his thinking, his techniques, his biases and orientations on the same or similar problems.

History shows, as Jacques Barzun has stated, ". . . in a civilization like ours, built on records and on continuity, we are willy-nilly the past embodied. Since this is so, no one can understand himself or the institutions at his disposal without historical information" (1).[2] We learn from the history of biochemistry that, first, it in itself is an interdisciplinary product; and secondly, when it engages in an interdisciplinary relationship, biochemistry seems to be in a unique position.

We must remember that biochemistry is a young, almost contemporary science, being, figuratively, a late chapter in the history of scientific chemistry. However, it is not the subject matter that is new. Rather, it embodies and extends the representations and syntheses of advances made in the fields of medicine, physiology, and organic and physical chemistry. Biochemistry as an entity has had to wait for its development until the ideas and notions which have become its generalizations were first generated elsewhere. However, once within the systematic framework that we know today, these generalizations have acquired new application and new meaning. The history of biochemistry is then in essence a history of bridging the gulf between apparently dissimilar phenomena. First establishing a relationship between living and nonliving matter, biochemistry has proceeded to establish relationships between chemistry and physiology, embryology, pathology, genetics, botany, etc.

The whole notion that natural law was applicable to living and nonliving systems developed out of eighteenth century chemistry. Until that time vitalistic theory held sway and life processes were thought dependent on special forces, derived from life itself, that gave organic compounds distinct properties. Enzymic reactions, then attributable to strange "ferments," came under scrutiny via the fermentation of sugar to produce alcohol, and such "ferments" were thought by Liebig and others to be only incidentally related to life and therefore still subject to ordinary physical chemical laws. The vitalist position began to break down with the work of Pasteur, which pointed to the role of the living yeast cell in fermentation. Later, at the end of the nineteenth century, the work of Buchner resulted in the suggestion of the "unorganized" ferments acting within the cell—especially those involved in alcohol production.

[2] Numerals in parentheses refer to references at the end of the chapter.