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PRIVATE EVENTS FOR BEHAVIOR ANALYSTS: A Review of *An Introduction To Neuroendocrinology* by Richard E. Brown (Cambridge University Press: New York, 1994, 360pp. $79.95, $34.95 paper)

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The title of the book, *An Introduction to Neuroendocrinology*, may raise questions among behavior analysts concerning the value of such a book to behavior analysts. The history of behavior analysis with its emphasis on environmental variables suggests that a book of this nature has little value for a behavior analyst. I believe this position, though never tenable, is certainly untenable today as behavior analysts are becoming increasingly aware of the importance of internal variables and their relationship to behavior. Consequently, I can envisage a growing interest among behavior analysts in books and journal articles that are concerned with internal variables. The importance of information about neural and endocrinological constructs to behavior analysts will certainly increase as there is greater interest in the development of an effective behavior theory. Although one book will not an expert make, I believe that it behooves behavior analysts to acquire the vocabulary of those scientists who are working on internal variables and constructs.

The author indicated that the book was designed to deal with the interactions of brain and hormones (the primary products of the endocrine system) and behavior. The book, therefore, is addressed to a rather broad and diverse audience, including students of biology, neurosciences, psychology, physiology, and behavior analysis as well as students of related disciplines. The first 13 chapters are concerned primarily with a description of the endocrine system, the hormones produced by the endocrine system, the neuropeptides, and other features of the structures and functions of the neuroendocrine system. Though the information contained in these chapters is very important to understanding the complexity of the relationships between the neural, endocrine, and immune systems, the major thrust of this review will be on the relationships between neuroendocrine functioning and behavior. There are occasional descriptions of relationships between neuroendocrine functioning and behavior in many of these chapters, most of this description is in Chapter 12 relating neuropeptides to behavior, Chapter 14 dealing with methods for studying behavioral neuroendocrinology, and Chapter 15 which is concerned with an overview of the past, present, and future of behavioral neuroendocrinology. More detailed information about these chapters will be presented later in this review. The reason for emphasizing the relationships between neuroendocrinology and behavior is because the review is being written primarily for behavior analysts. The emphasis on

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neuroendocrine-behavior relationships should not be construed as deemphasizing the importance of the material in those chapters dealing with neural-endocrine relationships.

The author has systematically and carefully described, sometimes in considerable detail, the structure and function of the neuroendocrine system. He has made very effective usage of table, charts, and figures to assist the reader, especially the reader with little or no knowledge of the neuroendocrine system, through the complex of relationships among neural and endocrine structures. Despite the author's efforts the material is not easy reading for the individual with a limited or no history with respect to the vocabulary of neurology, neurophysiology, and endocrinology. There is a whole new language that may have to be acquired. There is an extensive usage of abbreviations that are commonly used in describing the material. The author has provided a list of abbreviations at the beginning of the book. The reader will probably find this list to be very helpful and may have to refer to it many times in the course of reading the book.

Brown has taken great pains to describe the relationships as clearly and simply as possible. However, the relationships are frequently so complex that the reader may occasionally be very confused. It may be necessary for some readers to re-read sections several times before comprehending the described relationships. Some of the relationships that have been described in elementary or introductory textbooks in some of the behavioral sciences are not as simple as they been described. Many introductory textbooks in the behavioral sciences describe the pituitary gland as just an endocrine gland when it is both an endocrine gland and a part of it is neural tissue. Much of discussion of the initial chapters addresses some of the difficulties and problems of determining what is a hormone and the dual or more functions of the neuroendocrine system.

The chapter dealing with the hypothalamus may be of special interest to behavior analysts. The hypothalamus is an extremely important neuroendocrine structure that has numerous functions that ultimately may be related to the behavior of the organism. The hypothalamus has been subjected to an enormous amount of research by a variety of investigators from several different disciplines. As a result of this extensive and intensive investigation the regulatory functions of the various nuclei of the hypothalamus are well known. The neurosecretory cells of the hypothalamus have been the subject of increased research since these cells are stimulated by various neurotransmitters to release their hormones. This relationship among the neurosecretory cells, the neurotransmitters, and the nervous system provides the means whereby external stimuli may be developed as a source of control over hypothalamic functioning. Since the various nuclei regulate many functions, including the autonomic nervous system, the development of external stimuli as a source of control over hypothalamic functioning may be of special interest to behavior analysts. Emotional responding for many behavior analysts involves the reactions of various organs regulated by the autonomic nervous system.

The relationship between the neurosecretory cells of the hypothalamus and the limbic system may also have special interest for behavior analysts since the limbic system has been considered by some to be involved in motivation and emotion. The hypothalamus has also been considered by some to be part of the limbic system.

Whether it is or isn't considered to be a part of the limbic system the hypothalamus does have a neurohormonal relationship with the limbic system. One way or the other, the hypothalamus is intimately involved in the activity of the limbic system and may have important consequences for behavior.

The author points out that the autonomic nervous (ANS) can stimulate what he calls the "true" endocrine glands. Since the ANS activity is controlled or regulated to a large extent by the hypothalamus, it means that the endocrine activity can be conditioned to external stimuli through the hypothalamus' regulation of the ANS. There is an abundance of evidence in the literature that supports the conditioning of ANS activity both through operant and classical conditioning procedures. Through this chain of activities, it is possible for environmental factors to have a significant effect on hormonal output from the endocrine glands. The complex interactions of neural activity and hormonal activity suggest a very complex chain of internal events that may have some behavioral reaction that may be of great interest to the behavior analyst. A change in environmental events can in turn affect hormonal activity through the hypothalamus and ANS which may be associated with a change in behavior. All of this suggests that various internal responses, particularly responses involving the hypothalamus, the ANS, and the endocrine glands may develop either as discriminative stimuli (S^Ds) or establishing operations (EOs). These relationships are complicated by the fact that a lot of the evidence involving the relationship between the release of hypothalamic and pituitary hormones is contradictory and many of these relationships are still unknown.

The author has a short section on the effects of psychotropic drugs on hormone release which should interest behavior analysts, particularly applied behavior analysts who may be working with clients who are taking such drugs. Some of the antidepressant and antipsychotic drugs alter the levels of dopamine and noradrenaline in the central nervous system (CNS) which, in turn, can have a disruptive effect on the endocrine system. Consequently behaviors that have various endocrine outputs as important links in the chain or functioning as EOs may be markedly affected.

In another short section on the relationship of neuroendocrine correlates of psychiatric disorders the author sounds somewhat reductionistic. On p. 107 he says, "The disorders of neurotransmitter systems which underlie psychiatric disorders may cause neuroendocrine disorders since certain psychiatric disorders are associated with abnormal neuroendocrine responses." The question of what produces the disorders of the neurotransmitter systems is left unanswered, although the author has from time to time indicated that environmental events may come into play and exercise some control over the neurotransmitter systems. The brevity of this section does not include any suggestions about what produces the disorders of the neurotransmitter systems.

Hormones are classified as steroid or non-steroid. Many of the non-steroid hormones are synthesized from one or more amino acids and the steroid hormones are synthesized from cholesterol. The author discusses the synthesis of the steroid and non-steroid hormones. The two types of hormones also differ in the way they are stored.

Hormone release occurs when the endocrine cell is stimulated in some way. Events occurring in the environment can affect the release of the hormones through

interaction of the environment and the electrical and chemical activities that stimulate hormonal release. This situation illustrates another area of potential interest to behavior analyst. Since environmental events can eventuate in the release of hormones, research in the kinds of environmental events that will effect the hormonal release may be important to an understanding of the variables and conditions that affect behavior.

The author points out in a very convenient table the research methodologies used to identify cellular sites of hormone synthesis, storage, and secretion. The level of a hormone in the blood stream may be measured either directly or estimated through saliva, urine, or feces, urinary metabolites or bioassays. None of these methods lends itself to continuous monitoring, a situation that behavior analysts tend to prefer. In spite of this shortcoming in the measurement of hormonal level, it certainly does not preclude doing behavior analytic type research.

The regulation of the amount of hormones in the blood may be carried out through several different mechanisms. These mechanisms include the ANS, non-hormone chemicals in the blood or GI tract, hormonal feedback, and neurotransmitters and neuropeptides in the brain. The nervous system responds more rapidly than the endocrine or vascular system and the nervous, especially the ANS, has been demonstrated to be amenable to environmental manipulations. Therefore, it may be possible to manipulate the amount of hormones in the blood through the manipulation of environmental variables that are known to affect the ANS and hormonal level. The increase in epinephrine through increased activity of the sympathetic nervous system component of the ANS and the conditionability of this entire sequence have been demonstrated many times. This may be an example of when the hormone regulatory system fails. There is a balance between secretion of a hormone and the subsequent reduction in the amount of the hormone in the blood system. The regulatory system may fail temporarily as in the above described situation or it may fail on a more permanent basis. When the regulatory system fails there may be an elevation or reduction of the hormone in the blood system. This situation may result in a number of physical and behavioral changes. One example is Cushing's Syndrome which results from an excess secretion of corticosterone. This elevation of corticosterone may be a function of hypersecretion of ACTH as well as corticosteroid tumors of the adrenal glands. The behavioral consequences of Cushing's Syndrome may include depression, disturbances of perceptual and cognitive functions (thinking), paranoia, hallucinations, and confusion.

Though much of the research described in this book has been conducted on lower order mammals, it is sometimes difficult to determine if the author is referring to conditions in the lower organisms or if these conditions also occur in the human. There are some major and significant differences in the endocrine system of the lower order mammals and the human. An experimental result obtained from lower mammalian organisms may or may not be applicable to the human. Since many of the conditions can occur in both the lower organisms and the human, it would be beneficial to the reader to have it clearly stated that the condition occurs in the lower organisms and may or may not occur in the human. In discussing steroid and thyroid receptors the author notes that both Type I and Type II receptors are down-regulated in chronic stress as well as diabetes mellitus, diabetes insipidus, and aging. Does this

situation occur in the human as well as the rat or mouse? Probably.

The author raises the possibility that the second messenger system may be involved in the prolongation of events such as long term memory. The second messenger system involves hormones and other biochemical agents that can affect the effectiveness of the first messenger system, the neurotransmitter system. Receptor disorders which may involve the second messenger system may include a variety of behavior disorders such as schizophrenia and depression. One hypothesis asserts that glucocorticoid disruption of serotonin receptors' mediated second messenger system may be the basis of depression. There also appears to be a relationship between concentration of neuropeptides in brain areas and the regulation of sexual, agonistic, and feeding behavior.

Beta endorphins bind to receptors that are most heavily concentrated in neural structures that are associated with pain regulation. The receptors to which enkephalins, dynorphins, and neoendorphins tend to bind are most heavily concentrated in neural structures that may be involved in the regulation of olfaction, motor integration, and cognitive functioning. Since pain and avoidance or termination of pain may play important functions in the acquisition and maintenance of a lot of behavior, it may behoove behavior analysts to be familiar with some of the private events that may be involved.

The exact number of neuropeptides is not known at this time and it seems that additional neuropeptides are discovered every year even though their functions may not be identified until much later. The neuropeptides have a profound effect on the functioning of the neuroendocrine system and the central and autonomic nervous systems. These effects, in turn, may affect a wide range of behaviors, especially behaviors that may relate to many different functions such as pain reactions that may be involved in avoidance responses. The influence of the neuropeptides on the limbic and hippocampal systems may, in turn, affect behaviors associated with food and water consumption, sexual arousal, emotional, and motivational conditions.

The opioid peptides may also have an indirect effect on behavior as a function of their blockage of the paleospinothalamic pathway. The paleospinothalamic pathway has been associated with dull chronic pain. Acupuncture, for example, is believed to stimulate beta endorphins which inhibit the pain signals. Running and other forms of exercise stimulate the release of beta endorphins which may account for the euphoria frequently reported by people who engage in exercise. The opioid peptides affect the autonomic nervous system, especially the gastrointestinal and cardiovascular systems that are regulated to a large extent by the autonomic nervous system. These peptides tend to suppress the release of hormones and peptides that tend to stimulate the sympathetic component of the ANS. Opiate agonists, at least in small doses, tend to increase eating and drinking behavior and opiate antagonists tend to reduce both behaviors. Opiate agonists are associated with a reduction in sexual behavior. Some researchers contend that an imbalance in endogenous opiates, particularly beta endorphin, may be a factor in the asocial behavior of autistic children.

Cholecystokinin (CCK), a gastrointestinal peptide, has received considerable attention from researchers. CCK-8, the eight amino acid cholecystokinin, is widely distributed throughout the brain. CCK-8 is a very powerful analgesic, facilitates sleep, and reduces food intake in humans. It has been hypothesized that

schizophrenics have an overactive CCK system, but this hypothesis has not been strongly supported by the data.

Angiotensin II raises blood pressure and some anti-hypertensive medicine blocks the conversion of angiotensin I to angiotensin II as the method of controlling blood pressure. Bradykinin, another neuropeptide, is considered one of the most potent pain transmitting substances.

Behavior analysts who are interested in aging may find that an understanding of the thymus gland and its functions in the immune system are important in the aging process. The thymus gland is located in the chest above the heart. It is involved in the maturation of T-cells and the development of cell-mediated immune responses. The thymus gland declines in size and function with aging, thereby reducing the effectiveness of the immune system in combating disease. Consequently, the aged are more susceptible to the development of cancers and infectious diseases. This situation profoundly affects the reactions of the elderly to a wide range of environmental events.

The author discusses methods for the study of behavioral endocrinology. The methodology of behavior analysis is very appropriate for behavioral neuroendocrinological research since behavior analytic methodology stresses the observation and recording of behavior in quantitative terms.

One method of investigation is correlational. That is, the emphasis is on the correlation between hormonal and behavioral changes. As in correlational studies in general, the behavioral variables and hormonal levels are measured simultaneously to determine if there is any relationship between the two measures. For example, it may be possible to determine the relationship between hormone levels and behaviors during the period immediately preceding the menstrual period. These hormonal changes are considered to be naturally fluctuating. It would be necessary to have a measure of the relationship between hormonal level and behaviors at other times of the month.

One problem with the correlational studies is that the hormonal level should be ascertained at the time the behavior is occurring. If an invasive technique is used, it could have an effect on the hormonal level. This difficulty may be circumvented by implanting a chronic cannula. Though this procedure may be satisfactory with animals, it may present difficulties with humans. An effective noninvasive method for ascertaining hormone levels that is especially useful with children and other humans is through urine analysis. Steroid hormone levels can be analyzed from the saliva through the use of cotton swabs or chewing gum.

One of the more widely used experimental methods is the hormone removal and replacement experiment. There are several techniques that can be used for hormone removal. A behavioral baseline should be obtained before the hormone removal procedure is implemented. One procedure for hormone removal is surgical removal. This procedure is designed primarily for infrahumans. However, there are situations in which hormone removal is surgically removed from humans as a function of some disease, e.g., cancer of the thyroid. If behavioral measures can be taken before the surgery, then it may be possible to determine the effect of hormone replacement on the behavior. Other techniques of hormone removal include pharmacological and immunological methods. The pharmacological method involves the use of drugs to

prevent hormone synthesis and release from endocrine glands or act as hormone antagonists at a receptor site. The immunological method involves antibodies for hormones that deactivate the hormone and prevent it from activating a receptor.

The author discusses methods of hormone replacement that include gland replacement, e.g., liver or kidney transplant, injection of purified hormones, and injection of synthetic hormones. He describes a number of factors to be considered before giving hormone replacement therapy. These factors include chemical preparation of hormone, dose to be used, vehicle in which hormone is given, route of administration, and timing of injection. He describes some considerations in each of these factors, especially the timing of hormonal replacement and behavioral testing.

A second type of experimental study involves endocrine responses to environmental stimuli. The neuroendocrine response is measured as a function of some environmental change such as noise or temperature. Other environmental changes can involve social interactions and their effect on endocrine levels. Both of these kinds of studies are designed to determine the effect of environmental changes on endocrine responses.

Environmental events may control a hormonal change which, in turn, may be a source of control of a behavior which controls another or different hormonal change. This form of environment-hormonal change-behavior change-hormonal change may be of special interest to behavior analysts, especially behavior analysts who are interested private events. The hormonal events or changes may not be readily amenable to verbal description by the individual and can be assessed only by blood or urine analysis.

Though the author tends to discuss various environmental events in cognitive terms, it is relatively simple for the behavior analyst to substitute appropriate behavioral language or eliminate the cognitive language altogether. For example, the author says that "cognitive factors in the emotional response to an external stimulus may determine the pattern of neuroendocrine responses to that stimulus. Emotional arousal involves a physiological response to a stimulus and *the cognitive appraisal* of that stimulus" (p. 365 italics added). The behavior analyst may be comfortable without the cognitive appraisal as a necessary part of the emotional response. The physiological responses may set into motion a chain of neuroendocrine responses that may have a particular verbal response as the terminal link in the chain. In this way an individual may have acquired a particular verbal response such as "I am angry" or "I am happy" as the terminal link in a chain that may include an extensive chain of physiological and neuroendocrine responses.

Evidence from animal studies indicates that both neuroendocrine and immune responses can be acquired or conditioned. Consequently this means that these responses can become discriminative stimuli in a chain with some behavior, verbal or nonverbal, as the terminal link. Since the neuroimmune responses can be conditioned, behavior analysts may find this entire area to be an area of research interest to them, especially since this kind of research may have a reasonable chance of gaining financial support. It may be possible for certain environmental events that apparently attack the immune system (e.g., eating carcinogenic foods or cigarette smoking) to be conditioned to facilitate the neuroimmune system rather than attacking

it. In a similar vein, it may be possible to modify the neuroendocrine or neuroimmune system functioning to affect serious behavior problems such as schizophrenia, depression, and anxiety attacks. The medication that is currently the preferred method of treatment affects the neuroendocrine system, thereby modulating some of the discriminative stimuli in the chain. Unfortunately, all too often when the medication is halted, the associated behavior returns.

Differentiating short-term and long-term neuroendocrine changes may be very significant to behavior analysts who are working with moderate to severe behavior problems. The moderate to severe behavior problem may have had a long-term change in the baseline of various neuroendocrine responses. An individual may enter an environmental situation neuroendocrinally predisposed to respond behaviorally in a way that has led him/her to be called a moderate or severe behavior problem. That kind of problem may be markedly different from the individual who responds to the situation with an increase or decrease in some neuroendocrine response that in turn may be related to physiological changes, such as changes in the cardiovascular system with an attendant increase in blood pressure. When the environmental situation passes, the neuroendocrine response returns to a previous baseline and so does the blood pressure.

The author discusses how hormones, neuropeptides, and cytokines affect behavior indirectly through their influence on sensory receptors and input to the brain, the motor pathways that control behavior, and central integrative functions. The last function is discussed solely within the context of animal behavior. The discussion of genomic mediating mechanisms is especially pertinent in light of the developments in genetic and molecular biology. As there are more and more attempts to develop a genetic basis of behavior, it behooves behavior analysts to be aware of the relationships between genetic and molecular biological factors and the neuroendocrine and neuroimmune systems. The behavior analyst is in the best position to remind these researchers of the importance of environmental variables and their potential influence on neuroendocrine and neuroimmune response systems. It is relatively easy to slip into some biological reductionistic system to account for human behavior and the behavior analyst has to be aware of this possibility. But if the behavior analyst isn't aware of some of these relationships, he/she then may have difficulty developing cogent arguments against a reductionistic approach.

The author makes it very clear that conducting behavioral neuroendocrinological research is fraught with difficulties and numerous confounding variables. Some of these confounding variables occur in other areas of behavior analytic research but some of them are unique to research in behavior-hormone interactions. One special problem for behavior analytic researchers is getting continuous measures of some of the hormones. Technological advances are making possible more and more of these continuous measurements, but there are others that are not so amenable to continuous observation and measurement. The author discusses in some detail each of these confounding variables, but does not present possible ways to avoid or minimize the confounding. The discussion may provide some clues to potential ways of controlling these confounding variables.

The discussion of confounding variables includes a separate section on humans hormone-behavior research. The author notes that all of the confounding variables

of animal research apply to humans plus some additional confounding variables. Some experimental methodologies may not be feasible in light of legislative and judicial actions. Consequently, less rigorous research methods are frequently used with humans. Often it is necessary to use as subjects patients who have a condition that involves the hormone of interest. Very often questionnaires or interviews of such patients may be used, a much less rigorous research methodology. There is no doubt that the safeguards of human subjects and to a lesser extent many animals have and will continue to have an impact on the kind of environment-hormone-behavior research that may be conducted.

As I have said before, the book is not easy to read unless one has a history that includes the languages of neurophysiology, biochemistry, and neurochemistry. The author has made extensive use of tables and charts that are very helpful to the reader. It would have been helpful to many readers if the author had included a glossary of terms.

Since the environment can affect the functioning of the neuroendocrine system and the neuroendocrine system, in turn, can affect behavior, I believe the book can be helpful to many behavior analysts who have an interest in these kinds of private events.