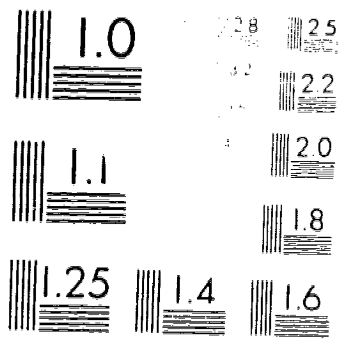
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ABSTRACT

Described is research using computer techniques to study the brain's perceptual systems in both normal and pathological groups, including hyperactive children (6-12 years old). Reviewed are the early studies of A. Petrie, M. Buchsbaum, and J. Silverman using the electroencephalograph to obtain AER (average evoked response) records of schizophrenics. The use of the AER to investigate how the brain reacts to changes in stimulus intensity is explained. Summarized are major findings concerning AER abnormalities in schizophrenics, manic-depressives, pure depressives, hyperactive children, and in normal behavior. It is proposed that stimulus intensity control serves as an adaptive protective role in the face of potentially excessive stimulation; that schizophrenics might be representing this adaptive tendency to an exaggerated degree; and that hyperactive children who improve with drug therapy are those who, prior to treatment, have the most abnormal AER patterns. (SBH)

National Institute of Mental Health

The Roots of Individuality

Brain Waves and Perception

an nimh program report

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service • Alcohol, Drug Abuse, and Mental Health Administration

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FOREWORD

The brain has been an enigma—at times inscrutable, at times divulging minute bits of information that act as "teasers," encouraging scientists to pursue elusive answers and experimental investigations. Now technological advances have enabled researchers to unearth information about the brain that heretofore was impossible.

This monograph describes a research program, being conducted in the National Institute of Mental Health's intramural research laboratories, that utilizes computer techniques to extract responses of the brain's perceptual systems from surface electroencephalographic recordings. By presenting short bursts of light and noise ranging in intensity from weak to strong and by studying the brain's activity, the investigator has found marked differences between people's responses—between men and women, hyperactive and normal children, pain-tolerant and pain-intolerant persons, and between various groups of psychiatric patients.

The research has also identified abnormalities of perception and attention, suggested that treatment effectiveness for some mental illnesses can be predicted at a pretherapy stage, and confirmed signs of clinical improvement in patients undergoing therapeutic intervention.

This report exemplifies still another NIMH research endeavor to sharpen our knowledge of the dynamics of human behavior—how our environment can affect each of us—and is important because it provides insight into some reasons for our actions.

Bertram S. Brown, M.D.
Director
National Institute of Mental Health

The Roots of Individuality: Brain Waves and Perception

At the core of medicine is an elaborate typology of human differences that forms the basis for diagnosis and therapy. As biomedical research progresses, these distinctions are refined, with increasing emphasis on particular characteristics and functions underlying clinical differences among patients.

A physician-researcher at the National Institute of Mental Health, Dr. Monte Buchsbaum, has for many years been fascinated by the differences in the ways people react to sensory stimulation. As he put it:

> Clinical practice in an emergency room quickly dramatizes individual differences in pain tolerance. I remember a Swedish carpenter who, declining analgesia, stoically allowed me to dig out a splinter from under his fingernail with a scapel as he gaily discussed baseball. Holy men rest on their beds of nails; Lesch-Nyhan patients mutilate themselves; rock groups blast listeners with sounds above normal auditory pain threshold—all of which raises the question: How do combinations of experiential and neurophysiological mechanisms work together to produce these variations in tolerance of extreme intensities of sensory input?

During the past decade or so, Dr. Buchsbaum and many coworkers joining him in his unprepossessing but well-equipped laboratory in Bethesda, Maryland have attempted to probe the brain's response to sensory input. Out of their research has come a better understanding of the differences between many groups of individuals: schizophrenics and normals, manic-depressives and pure depressives, men and women, children and adults, pain-intolerant and stoic individuals, both normal and pathological. These studies have also suggested new diagnostic tools for several types of mental illness and have given some clues to the aberrant brain mechanisms accompanying these conditions.

Measuring the Brain's Responses: Background

This research has focused on comparing differences in people's reactions to the same stimuli and attempting to account for them.

The approach combines techniques of several disciplines. Like an experimental psychologist, Dr. Buchsbaum studies how people react to controlled little fragments of sensory stimulation, such as short bursts of light or sound. But instead of scrutinizing people's observable behavioral responses (although he will sometimes do that, too), with his colleagues, both humans and computers, he pores over brain responses recorded by the electroencephalogram—or EEG. Were it not for relatively recent advances in computer technology, these studies would be impossible because the tiny electrical messages the brain emits in response to sensory stimulation ("evoked responses" or "evoked potentials") could not be detected amid the roar of the rest of the brain's ongoing activity.

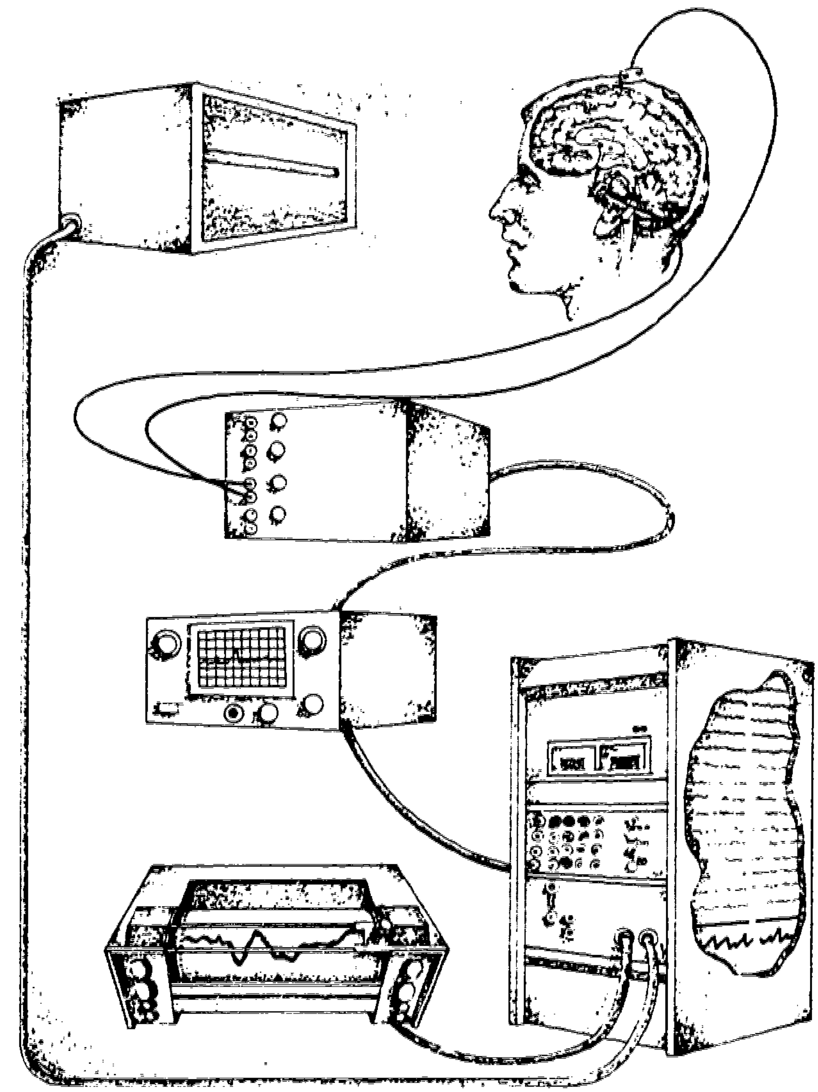
Ever since 1924, when the German psychiatrist Hans Berger first put electrodes on the human scalp and tried to read the brain's electrical messages in the almost illegible scrawl of the EEG, scientists had been simultaneously challenged and frustrated by this tantalizing clue to the human brain's responses to the outside world. Clearly, the brain's electrical activity, as reflected in the EEG, must be affected by events in the external environment. Even Berger knew that loud noises would change ongoing electrical activity. But the changes he saw were slow and inconsistent shifts of EEG rhythm, and not the clean, repeatable response patterns scientists love to work with. The EEG gradually became an invaluable diagnostic tool for clinical neurologists, providing consistent and identifiable patterns associated with epilepsy, brain masses, and other neurological disorders. But scientists trying to identify evoked responses in the EEG were stymied; finding evoked responses was like picking out the ripples stirred by a pebble thrown into an angry tossing sea.

Researchers interested in the basic question of how the brain responds when the senses are stimulated could not get a satisfactory answer using the EEG technique until, in the early 1960's, rapid progress in computer technology provided a simple way to detect evoked potentials: "signal averaging." By aggregating or averaging many EEG records of an individual's evoked responses to a given sensory stimulus, it was possible to make the relatively small ripples of evoked responses stand out against the sea of background activity—now mathematically calmed by the averaging process. The evoked response, now an "average evoked response"—or AER as it is commonly called—was finally visible and available for study.

In the 1960's, as relatively inexpensive special-purpose computers became more or less commonplace in neurophysiological and psychological laboratories (only to be replaced by even more useful, economical, and programable general-purpose computers), many scientists became intrigued with the AER, testing out and describing people's brain responses to all kinds of stimuli. Dr. Monte Buchsbaum was one of these. After hearing of some provocative behavioral findings by Dr. Asenath Petrie, an English psychologist, Dr. Buchsbaum turned to an exploration of brain activity evoked by changes in just one dimension of sensory stimuli—their intensity.

Dr. Petrie had found consistent differences in the way certain people performed on a standard perceptual task (Kinesthetic Figural Aftereffect, or KFA). Asked to judge the size of a standard bar after feeling other bars of different diameters, some normal subjects repeatedly overestimated: others repeatedly underestimated. Dr. Petrie called the overestimators "augmenters"; their opposites were dubbed "reducers." What made Dr. Petrie's experiments particularly interesting was her finding that these perceptual tendencies carried over to another, somewhat unexpected, sensory dimension. Dr. Petrie found that on a pain-tolerance test, those who had been "reducers" on the KFA test tended also to minimize pain stimulation: they were "pain-tolerant." By contrast, the KFA augmenters were prone to exaggerate pain stimuli and were considered "pain-intolerant." That is, a shock to the arm that a reducer might stoically rate as "mildly unpleasant" might be rated as "painful" by an augmenter. Dr. Petrie and others believed at the time that reducers' pain tolerance reflected an overall tendency to diminish the intensity of all incoming stimulation, regardless of the senses involved; some central nervous system mechanisms seemed to be regulating the level of sensory input.

About the same time that Dr. Petrie was exploring the sensory reactions of normal subjects, Dr. Julian Silverman, another psychologist, was using the KFA perceptual test with



schizophrenics, trying to understand how distortions of sensory perception in schizophrenia might affect and reflect schizophrenics' grossly altered views of reality. He and others had found that most schizophrenics were extreme reducers on the KFA task. On the basis of this and other evidence, he suggested that stimulus reduction by schizophrenics reflects "stimulus intensity control"—the action by some internal neurophysiological mechanism to regulate the degree of sensory stimulation.

A collaborative effort by Drs. Buchsbaum and Silverman provided the opportunity to explore stimulus intensity control in schizophrenics—behaviorally, using the KFA test, and electrophysiologically, using the AER combined with other tests of perception. One major finding by these investigators was that schizophrenics, who are generally extreme reducers on the KFA test, are also "reducers" neurophysiologically; that is, their brain responses (as measured by the AER) decreased somewhat in size (amplitude) as stimuli became more intense. This AER pattern differs from that seen in normal subjects, who generally tend to show increased AERs (greater amplitude) when stimulus intensity increases.

On the basis of this and other findings, these two investigators proposed what has been referred to as the "Buchsbaum-Silverman hypothesis": Stimulus reduction among schizophrenics probably reflects a self-protective mechanism to prevent excessive sensory stimulation. Schizophrenics may protect themselves from high-intensity stimulation because they are already loaded (or perhaps overloaded) with low-level stimulation, to which they are particularly sensitive.

The Buchsbaum-Silverman hypothesis represented a departure from Dr. Petrie's earlier speculation. She thought that stimulus reducers minimized stimuli at all levels of intensity; the Buchsbaum-Silverman hypothesis suggested that reducers only minimize relatively high-level stimuli. This issue was examined experimentally through another study. If the Buchsbaum-Silverman hypothesis was right, schizophrenics should be extremely sensitive to low-intensity stimulation; in fact, they should be able to perceive sensory stimuli others might miss (subthreshold stimuli). The prediction was confirmed experimentally, but other studies have presented a mixed picture of this sensory sensitivity. Supportive evidence, however, arose from a somewhat tangential direction. Studies of people exposed to environments with minimal sensory stimulation (which can cause discomfort and hallucinations) had shown that those who were pain-tolerant were better able to endure sensory deprivation than those who were pain-intolerant. Since pain-tolerant individuals tend to be reducers and reducers tend to be sensitive to low-level stimulation, these people seemed to be able to "feed" their nervous systems at least some paltry stimulation from subtle little environmental cues; the pain-intolerant augmenters, on the other hand, unable to perceive these tiny scraps of stimulation, essentially suffered "sensory starvation" in the same impoverished environment.

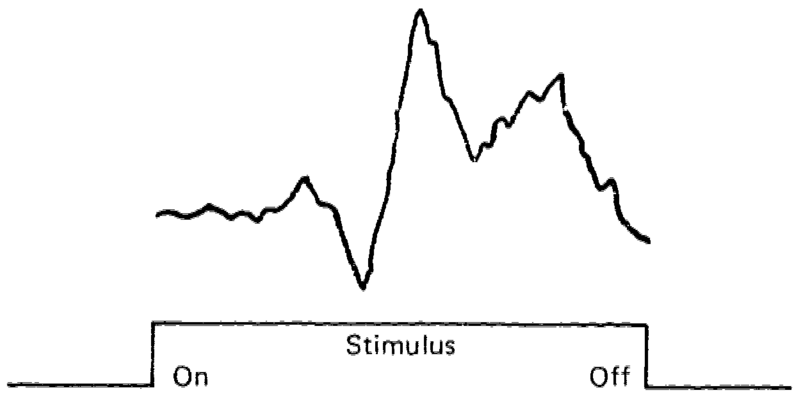
The early collaborative studies of Drs. Buchsbaum and Silverman convinced Dr. Buchsbaum that the AER was a useful approach to studying brain events evoked by sensory stimulation. For almost 10 years he has studied stimulus intensity control in normal and abnormal subjects, using their AER records as evidence of underlying characteristics and consistent perceputal styles. In some ways Dr. Buchsbaum is like a naturalist, hunting down and netting AERs as lepidopterists lunge after rare butterflies, pinning them down, and describing their special identifying characteristics when compared with either run-of-the-mill butterflies or with certain exotic types that closely resemble them. But Dr. Buchsbaum's pursuit is more abstract. He is studying the shape of an abstraction (average) of an abstraction (EEG) of unknown events that occur in the brain—usually when people are exposed to different sights and sounds.

Before launching into a description of Dr. Buchsbaum's work, let us pause for a moment to describe how scientists catch and label AER "specimens."

Netting and Naming AERs: The Wavecatcher's Craft

The AER record is the basic raw material for Dr. Buchsbaum's studies. One can stretch it, or squeeze it, run it through a computer grinder or a gauntlet of critical researchers. But whatever one makes of it, all the information is secreted in the record itself and the events that seem to elicit it. The record itself is deceptively simple. By the time the computer has finished its initial averaging handiwork, the almost undecipherable scribble of the EEG record has been translated into a relatively clear monogram: a voltage wave, with a few crests and troughs, and scattered Hokusai-like wavelets riding on top.

By itself, the wave has only limited meaning: one person's averaged brain responses when a stimulus of a given intensity (say a quick, medium-bright light flash) is presented repeatedly. But when this record is compared with a person's average evoked responses to other light flashes of different intensities, and when the response patterns of many different individuals are compared, important differences begin to emerge. In

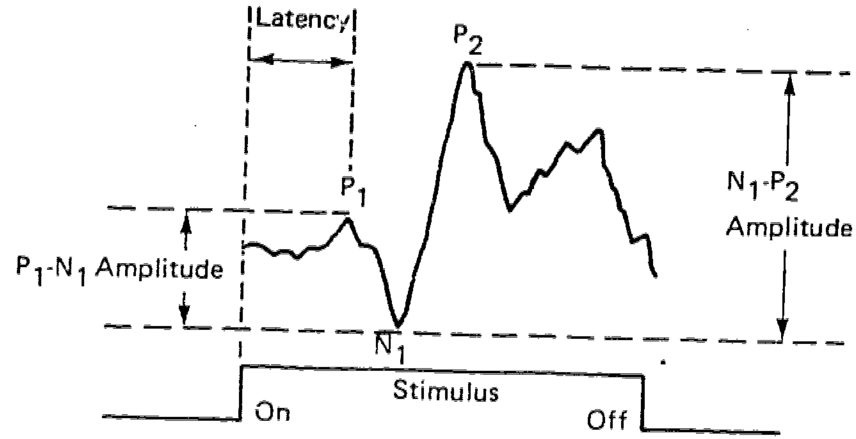


A TYPICAL AVERAGE EVOKED RESPONSE to a stimulus (for example, a light flash). This picture of an AER is "snapped" after the ongoing brain activity is averaged out.

a typical AER the first dip is followed by a rapid rise to a higher peak, followed by another dip and peak before the record levels off. "Crests," "troughs," and "dips" are descriptions too vague for the scientist; more precise labels are needed, preferably ones that permit exact measurements, such as latency and amplitude of the AER. Although a scientist can measure other features of the wave, Dr. Buchsbaum's experience and that of others have suggested that these features carry important aspects of the brain's message when we perceive, for example, a light flash. The ambiguity of even these few features, coupled with inherent variability in human AERs, presents more than enough challenges to a scientist's interpretive powers. Whatever untold riches are locked in other unmeasured aspects of the wave will have to await the attention of future research.

The $P_1 - N_1$ amplitude has some interesting properties. For any person, when the stimulus intensity changes (in this case, the light), the $P_1 - N_1$ amplitude changes. Thus, for the scientist interested in how the brain reacts to changes in stimulus intensity, there is an objective way to measure these changes: One can compare the heights of $P_1 - N_1$ under different conditions of known stimulus intensity.

The neurophysiological origin of this $P_1 - N_1$ peak is only partially understood, but it reflects the collective action of probably millions of neurons in the brain somehow induced to fire (or not fire) by messages coming in from light receptors in the eyes that say effectively, "Wow, something exciting just happened." In many ways Dr. Buchsbaum, reading



FEATURES OF THE AER. P_1 is the first reliable peak and is often used to measure how long it takes the nervous system to respond to the stimulus—a time called the "latency." The amplitude, P_1–N_1, is the voltage difference (in microvolts) between the crest at P_1 and the trough at N_1. The amplitude, N_1–P_2, is the following trough to crest.

AERs averaged from EEGs picked up from the brain by electrodes on the skull, is like the football fan described by Robert Benchley in "How to Watch Football":

> As almost everyone is late in arriving at a football game, there is a period of perhaps twenty-five minutes after the kick-off when you are milling around outside the gate in the crowd, looking for your proper entrance. This is perhaps the most trying period for the spectator. He hears occasional barkings from the quarterback, followed by terrible silence, and then a roar from one side or the other, he can't tell which. Almost anything may have happened. The visiting half-back may be racing down the field for a touchdown, or good old Grimsey of the home-team may have caught a forward pass on the enemy's three-yard line. Alternate waves of apprehension and elation sweep up and down the fur-clad back of the tardy partisan. What to do? What to do?

In Dr. Buchsbaum's case, it might be more accurate to say he is trying to hear the reactions of one part of the crowd to one or several footballs hurled into the stadium while the game is going on. At any rate, it is clear that he is not sitting in a $50 seat on the 50-yard line. (Other researchers are investigating what is going on inside the brain, but they are watching quite different teams. Electrodes can be placed in the brain, but usually box seats for brain activity are only permitted in animal research. In humans, scientists usually have to be satisfied with a shadow of th phenomenon, a kind of Platonic peek inside the brain.)

Dr. Buchsbaum has relied on the changes in the latency and amplitude as they respond to different stimulus intensities.

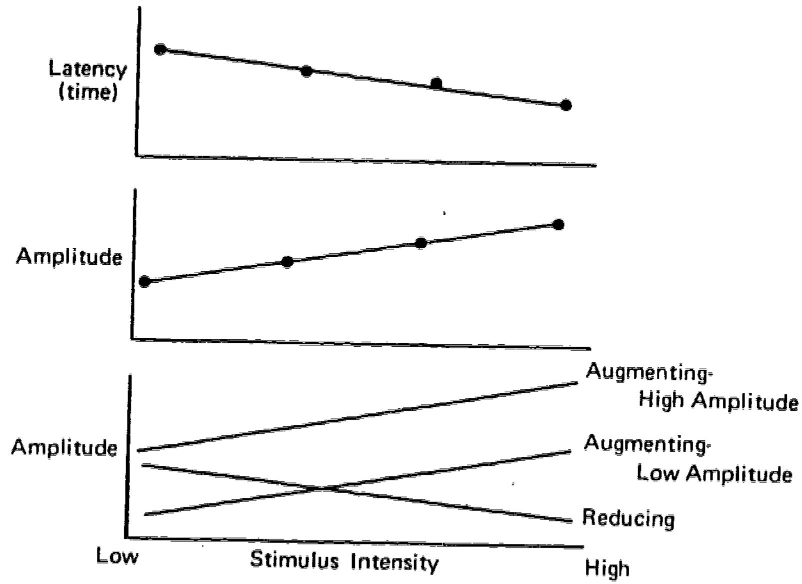
All the helter-skelter $P_1 - N_1$'s can be represented by just two properties—the average amplitude of $P_1 - N_1$ and the slope of the $P_1 - N_1$ responses when plotted against stimuli of increasing intensity. Surprisingly enough, the slope—a simple straight line at various angles for different people—can provide clues to their personalities, their emotional stability, and even to their thoughts. At the heart of Dr. Buchsbaum's research might be found the maxim: "Different slopes for different folks."

For Dr. Buchsbaum, the $P_1 - N_1$ (and sometimes $N_1 - P_2$) is a wedge to divide and compare people—man or woman, insomniac or not, schizophrenic or normal—all on the basis of the relative steepness of a line that is an idealization of an individual's evoked responses to four stimuli of different intensities, such as light flashes. (Actually, each of the four points that determine the line is the result of averaging 64 or more of an individual's responses to repeated presentations of each of the four stimulus intensities.)

Although there is wide variation in the response slopes of different people as they respond to stimuli of increasing intensity, a given individual will tend to show the same general slope whenever he or she is tested. Furthermore, people with the same type of slope often share other enduring characteristics in common—both behavioral, and, sometimes, in other aspects of their AERs.

Following the terminology of Dr. Petrie, Dr. Buchsbaum called the steeper lines (reflecting a rise in AER amplitude to increasing stimulus intensity) "augmenting" slopes, and the shallower lines (reflecting, in some instances, an actual diminution of AER amplitude to increasing stimulus intensity) "reducing" slopes. So, for any sample of the population, whether randomly chosen as "normals" or deliberately chosen to reflect some behavioral or genetic characteristic, the differences among individuals can be characterized as those with relatively steep AER amplitude slopes ("augmenters") and those with relatively shallow slopes ("reducers"). Not only can the slopes of different individuals be compared within groups, they can also be compared across different groups. For example, if the AER amplitude slopes of several women are compared, there is quite a bit of variation; but on the average, when women are compared to men, women tend to have more augmenting slopes (a finding which, as we shall see later, Dr. Buchsbaum has studied in considerable detail).

One exciting result of this research has been the demonstration that groups of people with certain forms of mental illness (such as schizophrenics, manic-depressives, pure depressives, and hyperactive children) have, on the average, AER slopes



IDEALIZATION OF AER LATENCIES AND SLOPES. The latency (top) typically decreases as the stimulus intensity increases, whereas the amplitude (middle) typically increases with greater stimulus intensity. The line connecting the four idealized P_1–N_1 responses can, depending on the individual and the conditions, appear dramatically different from the one shown. For example, those shown in bottom diagram show other possible P_1–N_1 responses to the same stimuli.

that differ from one another and from groups of normal individuals. In addition, the AER amplitude slopes of individuals with the same illness can be used with some success to predict who will and will not respond to treatment. It is too soon to know whether the AER technique can ever be developed to the point that it can be used for diagnosis and treatment-outcome prediction, but at least the promise is there. The problem, of course, is that use of the technique requires that patients show a distinctive AER pattern that will practically shout out: "I am a schizophrenic" or "I am a manic-depressive patient who is likely to respond to lithium treatment." Currently, while there are typical differences in AER slopes (and other AER characteristics) when groups of mental patients are compared with one another or with normal subjects, these differences are not always sufficiently consistent or large enough to permit accurate diagnosis.

For example, as mentioned earlier, Drs. Buchsbaum and Silverman found that schizophrenics, in addition to being reducers on the KFA test, are AER reducers as well. That is, their AER amplitudes generally slope downward as the stimulus intensity increases. However, not all groups of schizophrenics will show the same slope. In fact, in some of Dr. Buchsbaum's latest studies, using somewhat different visual stimuli, other groups of schizophrenics barely have a reducing slope; rather, they show more of a level straight line. Still, groups of schizophrenics never seem to show a strongly augmenting slope (although, of course, individual schizophrenics might). Since normal subjects tend to have augmenting slopes (though not very dramatically), schizophrenics, as a group, can be distinguished from normal subjects.

Among the sources of problems in trying to find stable correlations between various AER slopes and various forms of mental illness are, of course, the patients themselves, whose behavior, even on a simple perceptual test, can be quite varied, and whose thought processes (which can affect the AER) are even more skittish. (What might schizophrenics think of sitting in a room, with eletcrodes attached to their scalps, while lights continually flash at various intensities?) In addition, there is the problem of psychiatric labels. Psychiatric diagnosis is still in a crude state of development. A given patient may receive somewhat different labels from different psychiatrists, with the result that groups of patients diagnosed as schizophrenics may differ widely in their behavior—and even in their neurophysiological functions.

AERs and Psychopathology

Dr. Buchsbaum and his fellow researchers have been more interested in studying human perceptual styles—both normal and abnormal (as indicated by the AER)—than in investigating the causes of mental illness per se. Nonetheless, their research has yielded some potentially significant approaches to more accurate diagnosis and treatment of several types of psychopathology. Their findings have also suggested that, as many scientists have shown behaviorally, abnormalities of perception and attention often accompany many forms of mental illness. By showing that perceptual abnormalities occur at the level of brain function (whatever the AER represents, it is surely brain activity), these studies lend support to the view that abnormal neurological processing of sensory information may have a significant role in mental illness. Whether such abnormalities are root causes in and of themselves or a reflection of yet other biological problems and tendencies remains to be seen. And of course, the existence of AER abnormalities in mental illness does not suggest which specific anatomical and neurophysiological aspects of the nervous system are implicated.

We will now summarize some of the major findings of Dr. Buchsbaum and his colleagues concerning AER abnormalities in schizophrenia, manic-depression, and depression, concluding with a related study of hyperactivity in children. These studies have been addressed to several major questions:

How do the AERs of groups of individuals with these types of mental illness differ from the AERs of groups of normals?

Between patient groups that present similar clinical pictures (e.g., manic-depressives in the manic phase vs. pure depressives) are the AERs different?

What happens to the AER before, during, and after treatment in patients given various disease-specific treatments?

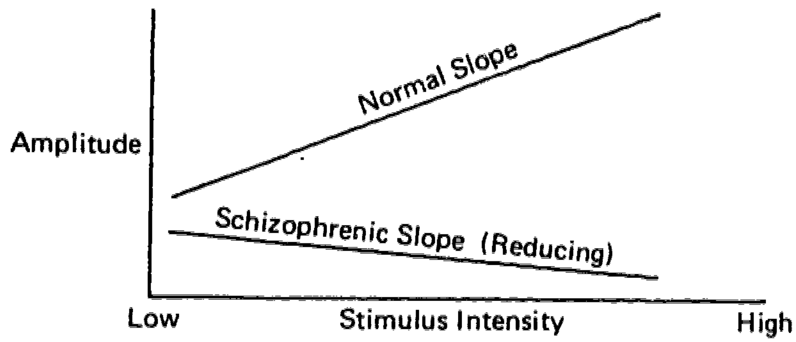
To what extent can the AER predict treatment response?

What might AER characteristics seen in various patient groups suggest about their neurophysiological functions?

Dr. Buchsbaum and his associates have found a number of provocative, though preliminary, answers to these questions. First, before treatment there are relatively distinctive AER patterns for each type of illness that permit one to distinguish patients from normals. Second, in some cases relatively clear distinctions can be made among patient groups with different diseases, based upon AER patterns. Third, pretreatment AERs can often indicate who will and will not respond to treatment. Fourth, during effective treatment, AERs can confirm signs of clinical improvement, as AERs return to more normal patterns.

Schizophrenia

Compared to normals, whose slopes usually rise, schizophrenics have reducing slopes. Although the result was not striking, Dr. Buchsbaum found that those schizophrenics who had been the most extreme reducers at the beginning of hospitalization showed a slight tendency to respond more favorably to treatment later in their hospital stay. This pattern of better treatment response among those initially most abnormal has been found in subsequent studies—often more obviously than in the case of schizophrenics. At present there is no explanation of this finding (one might expect those mildly abnormal to return more readily to normal). It should be borne in mind, however, that if the Buchsbaum-Silverman hypothesis is right, and stimulus intensity control enables schizophrenics to protect themselves by reducing their response t‹ high-intensity stimuli, then extreme reducers are better protected. In that sense, although their extreme reduction is abnormal, it may be adaptive; and from the point of view of self-protection, these schizophrenics may be "healthier" than those with more normal AERs. Obviously, there is



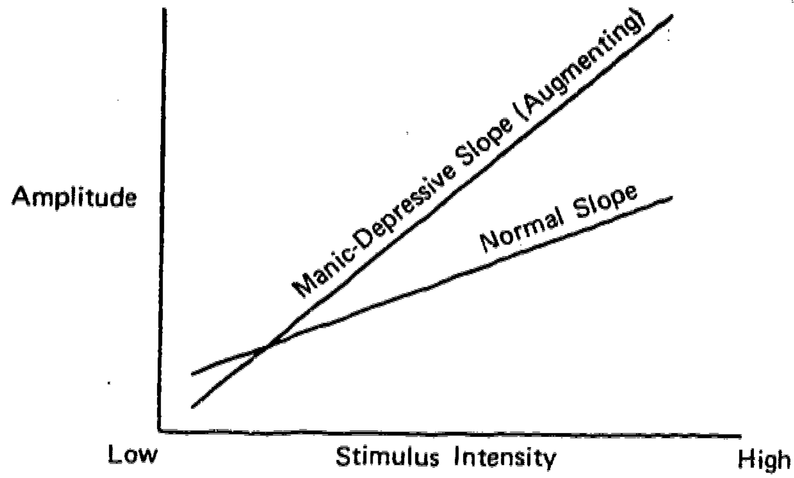
SCHIZOPHRENIC AND NORMAL AER AMPLITUDE SLOPES

much room for speculation, but for the moment the mystery remains.

Manic-Depression

Continuing their studies of mental patients, Dr. Buchsbaum and other colleagues turned to manic-depressives. Several studies by these investigators revealed that such patients, many of whom seesaw between euphoria and melancholy (although some seem to stay more often in one phase), generally show augmented AER slopes steeper than those of normals. These rather augmented AER slopes are seen regardless of the manic or depressive phase in which the patient is tested.

For some time, lithium carbonate has been used to treat manic-depressives. As often happens with medication, patients with the same disease labels respond differently; some get better, some are unchanged, and a few may even get worse. And, as also happens, lithium treatment has some undesirable side effects; physicians would like to assure that those who must undergo the risk of side effects are likely to benefit from the medication. Some of Dr. Buchsbaum's findings suggest that in the future it may be possible to use the AER to predict a patient's response. In studying manic-depressive patients before, during, and after lithium therapy, Dr. Buchsbaum and his colleagues have found that those patients with rather extreme AER augmenting slopes prior to lithium therapy are more likely to improve than those with more "normal" slopes. Again, the principle of the most abnormal being the most improved seems to follow here. In addition, in patients responsive to lithium treatment, changes in AER amplitude slope are correlated with clinical improvement; as patients return



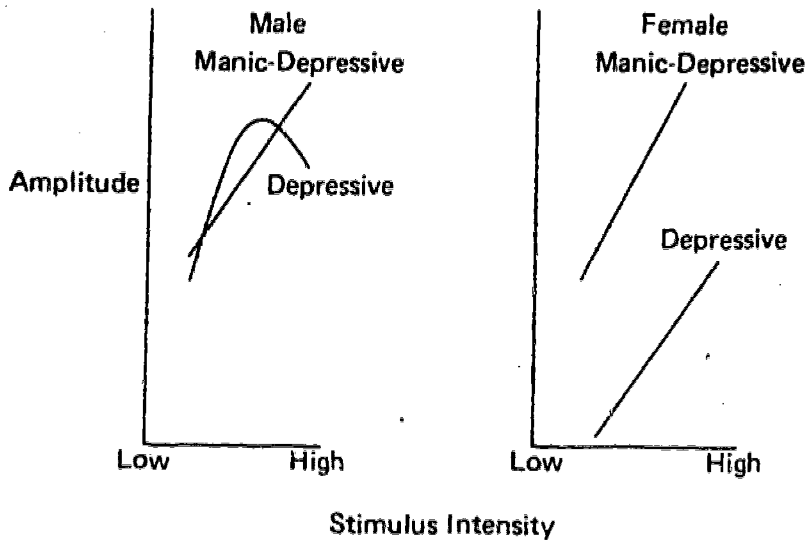
MANIC-DEPRESSIVE AND NORMAL AER AMPLITUDE SLOPES

to more normal behavior, their AERs also become more normal.

Depression

Another group of mental hospital patients has also captured Dr. Buchsbaum's research attention: pure depressives. These people, who sometimes clinically resemble manic-depressive patients during their depressive phase, are not simply manic-depressives minus the mania. Recent biological evidence points to the fact that different biochemical factors underlie the two illnesses. And clinical experience has shown that they respond to different medications. Because of the clinical similarities between the two diseases, it would be helpful to have as many objective ways as possible to distinguish between them. Again, the AER technique shows promise, although results are only preliminary. Distinguishing manic-depressive from pure depressive patients is easier with men than with women.

Manic-depressives—whether male or female—tend to have augmenting slopes. Male manic-depressives are thus easily differentiated from male depressives because the former have augmenting slopes while the latter have reducing slopes. Female manic-depressives present more of a problem, since they, like female depressives, have augmenting slopes; however, their high-amplitude AERs are usually a diagnostic giveaway. Thus, the AERs of the depressives are different from manic-depressives, and AERs might offer the clinician yet another way of distinguishing among the faces of gloom.



MALE AND FEMALE RESPONSES BY DEPRESSIVES AND MANIC-DEPRESSIVES. Note the male depressive response pattern, which does not seem to be a linear slope. More patients will need to be tested to determine whether this inverted "U" is indeed characteristic of all depressives. Male depressives appear to be distinguishable from manic-depressives by their pattern of response while females are distinguished by the difference in magnitude.

"Hyperactive" Children

Among the most challenging children for parents, teachers, and researchers alike are those restless "hyperactive" youngsters medically diagnosed as having "minimal brain dysfunction" or MBD. As Dr. Buchsbaum has observed: "Minimal brain dysfunction (MBD) is apparently the single most common cause of behavioral and educational problems in childhood." As yet there is no cure for hyperactivity, but many such children, seemingly boundless in energy and typically flitting from task to task (or trouble to trouble) like nervous hummingbirds, can be brought calmly to earth through carefully regulated doses of amphetamine. (Paradoxically, while amphetamine acts as a stimulant in most adults, it has a calming effect in children—at least in hyperactive ones.)

Comparing the AERs of hyperactive and normal children of the same ages (6–12 years), Dr. Buchsbaum found that the hyperactive children tend to have AERs characteristic of younger normal children. Hyperactive children also have considerably more variability in their AERs than normal children, with latencies and amplitudes that change from stimulus to stimulus more than they do in normal children. In addition, compared to normal children, hyperactive children tend to show shorter latencies; that is, their AER response-times tend to be faster.

Since hyperactivity may be, as some have supposed, a disorder of attention, and differences in attention have been shown to affect the later parts of the AER record (that is, the $N_1 - P_2$ peak), Dr. Buchsbaum speculated that the later portions of the AER record would show distinct differences between hyperactive and normal children. Indeed they did. He found that the amplitude of a later AER peak was higher in hyperactive children than in normal children.

By studying the AERs of hyperactive children before, during, and after treatment with amphetamine, Dr. Buchsbaum has been able to identify some response patterns that seem to correlate with therapeutic success. Treatment-responsive hyperactive children are those who, before treatment, have the most abnormal—that is, immature—AER latency patterns; conversely, those whose AERs seem relatively mature before treatment are unlikely to respond. According to Dr. Buchsbaum, 64 percent of hyperactive children who will respond to amphetamine treatment can be identified by their AER latency patterns before treatment. Once treatment has started, potential treatment-responders can be distinguished from nonresponders by changes in their AER amplitudes: Compared to their pretreatment AERs, those who will benefit from amphetamine show a more reduced AER amplitude slope, while in those who will not benefit, the slope augments somewhat. (Clinical improvement is also related to significantly reduced AER variability during successful treatment.) As in the findings above, hyperactive children who improve with amphetamine are those who, prior to treatment, are most unlike normals.

AERs and Normal Behavior

Dr. Buchsbaum has explored AERs in a variety of humans, some of whom are ostensibly "normal," and others who, for a variety of reasons (often largely behavioral), are labeled as "abnormal." His AER studies have revealed a rather wide spectrum of brain responses when these different individuals view the same stimuli, such as four lights of four different intensities. For the most part, as we have seen, groups of behaviorally abnormal people show a band of AER patterns that cluster differently from normal people—usually tending toward the extremes of normal response tendencies (for example, appreciably steeper slopes of augmentation or reduction, or shorter response latencies, or greater than normal average amplitudes). In some instances, normal AER characteristics for one sex or the other are changed (as in the case of manic-depressive women). Clearly, the concept of abnormality would be meaningless without some notion of what is normal. But as Dr. Buchsbaum has discovered, there is considerable variation in AER patterns even among people who have served as his "normal" subjects. (It is even possible to find, scattered among these subjects, individuals whose AERs might suggest to a careless observer that they should immediately volunteer to enter a mental hospital rather than an experimental laboratory—but as far as anyone knows, they, too, are "normal.") One continuing focus of Dr. Buchsbaum's work has been to identify the relatively stable differences in AERs among groups of normal individuals, and try to understand why they exist. In normal individuals, their response differences may reflect inbuilt and enduring differences in the ways humans process sensory information. If normal human differences can be understood, they may provide some clues to understanding the exaggerated responses we see in mental illnesses.

As we have seen, the AER amplitudes of normal persons may have augmenting or reducing slopes (although usually these patterns can be distinguished from the steeper augmenting and reducing slopes characteristic, say, of a hyperactive child or a schizophrenic). What is the biological basis for such AER differences among normal individuals? To what extent are they genetically determined, and to what extent does prior experience play a part in these relatively stable characteristics of individuals? To answer questions such as these, scientists often turn to twins, comparing the degree of similarity between pairs of identical twins (who, coming from the same fertilized egg, share an identical genetic makeup) and the degree of similarity between fraternal twins (who come from two different fertilized eggs and are no more alike genetically than any two siblings). If genetic factors are at play in the AER, then the AER patterns of identical-twin pairs should be more alike than those of fraternal-twin pairs. (Ideally, the search for pure genetic effects should be conducted with identical twins who have been raised apart, to offset the effects of their common upbringing; however, such subjects are a rarity.)

In a study of 60 twin pairs—30 identical and 30 fraternal—Dr. Buchsbaum found support for the thesis that AER patterns reflect genetic endowment: The AERs of pairs of identical twins were far more alike than those of pairs of fraternal twins. Both identical twins of a pair tended either to have augmenting or reducing slopes, while fraternal-twin pairs sometimes showed conflicting AER patterns. Such findings must be qualified by the recognition that, since identical twins frequently are raised more uniformly than fraternal twins, their prior experiences, rather than their greater genetic similarity, may account for these results. Nonetheless, it seems unlikely that such differences in upbringing would affect AERs significantly. One may reasonably assume that stable AER patterns may reflect, at least in part, one's genetic makeup.

Many lines of biological and psychological research, including Dr. Buchsbaum's, suggest that the minds of women are physically and functionally different from those of men. Whether the differences are the result of genetic factors and/or cultural conditioning is not yet known. The preceding twin study, like many conducted by Dr. Buchsbaum and others, revealed that normal women tend to show a greater degree of AER augmentation than do men. Also, on the critical $P_1 - N_1$ first AER peak, women's responses are about 25 percent greater than those of men.

However, emotional states can modify—and even reverse—these sex-typical response patterns. For example, anxious and neurotic men tend to have augmenting slopes while equally distressed women tend to have reducing slopes. In short, maladjusted individuals tend to respond like normals of the opposite sex.

Why do men and women have different AER patterns? The answer has been elusive and still is only fragmentary. Sex-linked hormones seem an unlikely cause, since, as we have seen, sex-linked response patterns can be reversed by anxiety and neurosis (unless we assume these emotional problems reflect or affect the level of sex hormone present). Furthermore, AER differences between boys and girls can be demonstrated as young as 6 years of age—long before the gonadal hormones appear. In addition, sex-linked AER differences exist in the 40-to-60-year-old group when women's estrogen levels are diminished.

Could the cause be differences in brain weight or in skull size? Women do have slightly lighter brains than men, suggesting that for purely physical reasons we would find differences in AERs between men and women. However, other studies have shown no relationship between brain weight or size and the AER. In summary, the answer does not seem to lie in the anatomy or physiology of the sexes, but rather in some underlying neural style.

Pursuing one more biological possibility—the genetic chromosomal differences between men and women—Dr. Buchsbaum and his coworkers found some encouraging clues. They examined the AERs of patients with abnormal sex chromosomes. This study suggested that there is some relationship between sex chromosomes and AERs. Normally, males have one X and one Y chromosome (XY), while females have two X chromosomes (XX). Looking at patients with XO chromosome patterns, where the sex-determining chromosome is absent, these researchers found the AERs of XO males to be very much like those of women. One possible hypothesis is that the Y chromosome exerts some genetic effect that attenuates AER amplitude.

Dr. Buchsbaum's interest in individual differences, fueled by Dr. Petrie's earlier discovery that variations in individuals' pain tolerance were correlated with other perceptual tendencies, has led him to see how AER patterns are related to pain and noise tolerance. In one study, subjects were given relatively mild electrical shocks of various intensities on the forearm, and asked to rate each shock as "just noticeable," "distinct," "unpleasant," or "painful." AER reducers were more pain tolerant than augmenters, making little of stimuli that augmenters found painful.

Exploring another dimension of pain tolerance, Dr. Buchsbaum looked at the effect of suggestion on pain. The AERs of three groups of subjects were compared. One group simply experienced shocks of various intensities; a second group heard music during the shock-test period; a third group, told in advance that music would reduce pain, also heard music during the test period. Subjects in the third group, who had received a form of suggestion, tended more toward a reducing slope—and to be more pain tolerant—than those in the other groups. This appears to be what Dr. Buchsbaum calls a "neural placebo reaction"; that is, suggestion actually seemed to fool the nervous system into "believing" that the painful stimulus was less intense than it was. A belief in the analgesic powers of Beethoven may not enable you to sleep on a bed of nails, but it may help on the next trip to the dentist—if he, before drilling, turns on the stereo and says, "You won't feel a thing."

The AER is a particularly useful research tool in part because AER patterns are relatively stable for different individuals over time. Response patterns of individuals may vary slightly from trial to trial with the same stimulus, but these variations are relatively small compared to AER differences between and among subjects. Generally, a person with a reducing or augmenting slope will show the same pattern rather consistently (unless, as we have seen, abnormal subjects are given medications that change their AER patterns). Indeed, Dr. Buchsbaum's twin study suggests that the tendency to respond with an augmenting or reducing slope in adulthood may be genetically predetermined. However—and there are always "howevers"—many short-term situational factors can modify a person's evoked-response patterns. As the experiment with shock and music has shown, expectations can color one's response patterns. Several studies have demonstrated that the AER is closely related to a person's short-term psychological state; in fact, what he or she thinks, feels, or expects may determine the shape and size of the AER more than the actual intensity of the stimulus. Dr. Buchsbaum, like many scientists, has found that, by understanding the conditions that make AERs unstable, he can learn to control them better in subsequent experiments. Thus, while basically interested in relatively stable AER patterns, he has explored how subjects' expectations can change their AERs over very short time periods.

Let us imagine, for a moment, that you are the subject in an experiment, which is a carefully contrived variation of the standard light-flash study. After EEG electrodes are attached to your scalp, you are invited merely to watch the coming light show. You see a long, uninterrupted series of brief light flashes of various intensities that seem to fall into some pattern. Perhaps you will note that they seem to run in sequences of four, in ascending order of intensity; at other times the pattern may be less apparent. In fact what you are seeing is a complex series of light flashes made up of two subpatterns which alternate irregularly. In light pattern A, four light flashes are presented in order of increasing intensity, let us say 1, 2, 3, 4, from weakest to brightest. In light pattern B, the order is changed to 1, 3, 2, 4. The weakest light is still first and the brightest is last, but the middle intensities are switched. You, the subject, actually are presented with a string of flashes in the sequence AAABAB, so that the regular, ascending light pattern appears three times, followed by alternations of the irregular and regular light patterns.

If you are like most of Dr. Buchsbaum's subjects, your AER will show an interesting expectation effect, even if you were not consciously trying to figure out the sequence. For the regular, ascending A pattern, your AERs will reflect the actual intensities of the stimuli. But for the B pattern, your AER will be somewhat strange; you will give an excessive response to stimulus intensity 2, responding as if it were the more intense stimulus 3. In Dr. Buchsbaum's view, this inconsistent response reflects the incorrect expectation that pattern B will be exactly like pattern A; in essence, your AER response reflects what you think should be there, and not the actual stimulus. (Believing is seeing!)

If you enjoy being an imaginary subject, there is another experiment in which to participate. In this study, which uses the same light sequence (AAABAB), you will be taught the total sequence in advance, so you know exactly what to expect. You will know, therefore, that the second stimulus in each group of four indicates whether it is a regular, ascending sequence (the A pattern) or an irregular sequence (the B pattern). This time, your AERs probably will be even more peculiar than in the preceding experiment, reflecting more about your internal state and less about the actual intensities of the light flashes. For both the A and B patterns, your AERs probably will be elevated (that is, will have greater amplitude) for the second stimulus in each group of four. To Dr. Buchsbaum, this elevated AER reflects the significance of this stimulus to the viewer. Seen another way, each time the second stimulus appears, it confirms what you were led to expect; your elevated AER is like a confirmatory "uh-huh." The important point, for Dr. Buchsbaum, is to recognize that, although people appear to have relatively stable AER tendencies, a person's AER at a given instant may reflect what matters most to him at that moment, rather than his overall AER pattern or the particular stimulus characteristics. In short, even in the humdrum task of perceiving light flashes, we do not simply process perceptual information mechanically and "objectively"; the very act of perception is infused with our own subjective meaning.

Beyond the implications of such findings for those who seek to find some "objective" reality, there are some practical caveats for scientists engaged in AER research. Identifying stable AER patterns for individuals and groups requires great care in the design, conduct, and analysis of studies, lest a moment's meaning be mistaken for an enduring mind-set.

Toward a Theory of Sensory Overload

From birth to death, biological organisms continually struggle to maintain their identity, equilibrium, and integrity in the face of environmental flux. At every level of biological existence—from individual cells to the total organism—there seems to be a defined band of environmental conditions for optimal performance; too much or too little of even a good thing can be lethal. Living organisms are in a constant tizzy, trying to maintain stability despite the vagaries of the environment. In his book *The Wisdom of the Body*, the eminent early 20th-century American physiologist Walter Cannon called this process "homeostasis." He and others have identified innumerable mechanisms by which the body keeps itself in dynamic equilibrium. To take one example, all animals must keep their body temperature within relatively narrow limits to survive. Warm-blooded animals such as mammals have the equivalent of a thermostat (the hypothalamus) at the base of the brain that senses and controls body temperature—turning on flushing and sweating when hot and turning on shivering when cold. Some scientists believe that the ancient capacity for homeostatic regulation of body temperature once gave mammals an adaptive edge over the gigantic cold-blooded reptiles; when the great Ice Age came, we mammals shivered our way to survival, while dinosaurs froze to death and extinction.

Does our homeostatic equipment include some general mechanism that attempts to maintain a continuous optimal state of overall nervous system activation? This view is attractive but as yet not well supported. However, the research is suggestive. For example, studies have shown that temporary or permanent mental impairments can arise from either sensory overload or underload, and, since the 19th century, it has been repeatedly demonstrated that humans do not respond behaviorally in direct linear proportion to increasing intensities of sensory stimulation. At the AER level, at very high levels of stimulation (extremely loud noises or brilliant lights) our brain responses normally level off or reduce, as if something says, "That's more than I can take." For those with reducing slopes, this point seems to come at fairly low stimulus intensities; for those with augmenting slopes, at much higher intensities.

As yet, there is no way to demonstrate conclusively that the nervous system is designed to maintain some optimal level of activation, nor does anyone know exactly how such a process might occur anatomically and neurophysiologically. The central nervous system has been shown to exert some control over the peripheral sensory receptors, but how this happens is unknown. There appears to be some control across the different sensory modalities, so that, for example, we do not usually give equal attention simultaneously to information from all the senses; when we are attending visually, our receptivity to sounds diminishes, and vice versa. The whole field of attention and its neurophysiological basis is fascinating, but fraught with contradiction and controversy. The search to understand stimulus intensity control may well be bound up with investigations of attention and expectancy. (It should be remembered that both schizophrenia and hyperactivity have been characterized by some scientists as disorders of attention.)

Drs. Buchsbaum and Silverman have not gone so far as to suggest a homeostatic model to explain augmentation and reduction. But they have proposed that stimulus intensity control serves an adaptive, protective role in the face of potentially excessive stimulation. Those with strong reducing slopes, hypersensitive to low-level stimulation, seem to close out the world's clangs, pains, and glare in a bid for neurophysiological survival. Schizophrenics might be seen as representing this adaptive tendency to an exaggerated degree. Those with strong augmenting slopes on the other hand, prone to be understimulated because of their insensitivity to low-level stimuli, seem to turn up the amplification of the world, allowing themselves to be flooded with sensations at higher levels. In some ways, hyperactive children may represent exaggerated versions of this potentially adaptive response.

At present, the studies of Dr. Buchsbaum and his coworkers present us with many unresolved chicken-and-egg problems. Do schizophrenics respond to high levels of stimulation because they are hypersensitive to low-level stimulation? Do they have reducing slopes because they are schizophrenic? Does schizophrenia represent a failure of protective stimulation-reduction mechanisms? Do schizophrenics suffer from sensory deprivation effects caused by closing out high-intensity stimulation? Do all of these effects reflect yet another mechanism at work —for example, a shift of responsiveness from perception of the outside world to internal perception? Might the brain's "background noise," deliberately excluded by the AER technique, encompass other essential components of the total dynamic equation? As yet we have no way to know. We have barely found a way to document electrophysiological responses to external stimulation; a new frontier awaits us concerning internal stimulation, perhaps requiring, as did AER research, another technological breakthrough.

Supplementary Readings

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