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Biological Roots of Psychiatry

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A current joke has it that neurotics build castles in the air, psychotics live in them, and psychiatrists charge both of them rent. In like vein, I suppose I should add, the biologist tries to supply pilings down to earth. This is implied also by the metaphor of my title, for roots notoriously get down to and into the earth. They are less lovely, perhaps even less immediately useful, than the flowers and fruits, but they seem to be a fairly essential condition for the latter. The roots and fruits of psychiatry differ from one another as sharply as do those of plants, and the reasons for this will be worth our brief attention.

The biological roots penetrate from the individual, through the organ, to the cell or even the subcellular level. At such "kitchen" levels of the living, the turnover of substance and energy is the dominating concern, and the primary drives are for an adequate continuing supply of these for the metabolic turnover essential to dynamic, open-ended, equilibrium systems. The fruits, on the contrary, although they also start at the individual, expand to the levels of group and society. Here communication and meaning dominate rather than matter and energy, and the secondary drives become more important—those favoring group existence and involving interpersonal relations.

Interpersonal behavior is but a small sector of the entire range of animate behavior but, like the single octave of visible light in the entire electromagnetic spectrum, it has a unique importance to social man. It therefore deserves the intense scrutiny it is now receiving; it well merits examination under the oil-immersion lens. Biology supplies an arm and fingers, a skeleton and muscles, and a reflex and "voluntary" control of movement; but it cannot yet account for the individual characteristics of each person's handwriting. Biology can pretty well characterize the violin but is only on the edge of understanding why one person plays sweetly and another does not. The biologist is happy to recognize that two men or two violins are more like each other than like anything else in the world; psychiatric practice takes the violins for granted and is concerned with the sour notes that come from certain ones. Biological science seems to deal with the Cheshire cat; mental science, with its smile. But psychiatry, perhaps somewhat in contrast to psychology, is firmly based on its biological and medical origins. In this epoch of rapid transition, psychiatry is indeed unhappily schizophrenic, rooted in biological science and the body, and fruiting in social science and the nuances of human interaction. Like the mother church, in the speaker's eulogy, "There she stands; one foot firmly planted on the ground, the other raised to heaven."

Meaning and information, in turn, imply a knower and a user and, thus, a purpose. It is no accident that teleological explanations come so easily in this area and that nonmaterial causes are so readily accepted. It is simple to grasp the significance of a sterile wife dreaming of babies or of a thirsting desert wanderer hallucinating oases. More, it is possible to see a purpose or function, at least in the second instance; the need of water somehow increases restlessness to seek and focuses attention and perception on the object sought. The trick is in the word *somehow*. To understand the reason for, or object of, an act or experience is not yet to understand it adequately; a mechanism must also be revealed. Only when the action of an increased plasma osmotic pressure on the appropriate specialized neurones in the hypothalamus is laid bare, and dozens of additional mechanisms, does understanding approach the level of mastery and control. "Mechanism adds utility to truth"; we still have to discover the osmoreceptors of hallucinations and the chemoreceptors of dreams!

Incidentally, the problems of stress, in its most general use, and of psychosomatic disturbances and the organ neuroses in particular, bear an inverse relation to mental disease in that they tend to root in the social sphere, with faulty interpersonal relations, and to fruit in the biological sphere, with disturbed body or organ function. It is also worth comment that psychiatry, as compared with neurology, for example, is dynamic and vague, as is perhaps physiology as compared with anatomy. From physiology (*physiologoi,* which included all who sought *knowledge of nature*) were born successively: anatomy, asking "where" and concerned with the spatial relations of living things (the space or centimeter or *c* dimension); biochemistry, asking "what" and concerned with the materials of living things (the matter or gram or *g* dimension); and, in birth, biophysics, asking "when" and concerned perhaps equally specially with change and action (the time or second or *s* dimension). But the relatively amorphous and holistic physiology, asking "why" and "how," remains undiminished; it will yet be fertilized by many seeds from the unknown and give birth to many daughters, as yet unenvisioned. Perhaps psychiatry is cast in a comparable role.

We all agree today that brain and mind are related; that, contrary to Alice's experience in Wonderland, the grin cannot remain after the cat is gone. But the implications of this are often overlooked. A vital force does not move a molecule, and an emotion does not discharge a neurone. When experience leaves an enduring trace, it must be some sort of material imprint; and, so to speak, there can be no twisted thought without a twisted molecule. Perhaps the simplest

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generalization to keep in mind is that all behavior in the external world, as well as all awareness of it, depends explicitly on the discharges of neurones. Certain neurones are fired by a given sensory input, these activate others and still others, and in time certain final neurones activate particular muscles to contract or glands to secrete. Clearly, the properties of the neural units and of their relations are crucial to all normal and disturbed behavior.

Mental Disease

In fact, the simple recognition of a dichotomy between unit and pattern at once sheds considerable light on mental disease, for a disturbance in the unit is likely to be quite a different affair from a disturbance in the pattern. Let me exemplify the point with recent illumination on muscular dystrophy. This disease has been regarded by many as resulting from a deficiency, comparable to the muscle pathology produced by lack of vitamin E, or to some endocrine error, or to some other unfavorable condition in the organism; and the importance of a hereditary factor has also been much debated. It proved not too difficult for workers in my laboratory to prepare tissue cultures of muscle from normal men and from dystrophy patients. Although both kinds of culture were maintained for months, in identical media and with repeated transfers, the dystrophy muscle continued throughout to exhibit characteristic abnormalities in size, striation, nuclear position and division, and so forth. Such findings are direct evidence of a difference in the unit itself, whether or not additional organismic disturbances are involved. Moreover, it makes a hereditary defect highly probable, although it does not entirely exclude the possibility of an irreversible change in the cells, produced, after they were formed, by some abnormal experience.

Another example of close relevance would be a blindness resulting from damage to the visual units, as when the retinal receptors actually degenerate under sufficiently severe and maintained vitamin-A lack, contrasted with damage to the normal connections in the optic system (more accurately their failure to develop), as when chimpanzees raised in total darkness cannot later in life recover usable vision. Again, the degeneration of anterior horn cells in polio patients constitutes a lesion at the unit level, but the comparable muscle weakness or paralysis that appears in cases of periodic family palsy and results from a block of junctional transmission by abnormal potassium content of the blood is equally clearly a disturbance in the connections. It is perhaps worthy of note, also, in the periodic disease that it is a hereditary defect, even though the malfunction of the neuromuscular system is a secondary one and consequent to disturbances elsewhere in the organism.

Such considerations may help point up, if not resolve, the differing claims regarding schizophrenia. If a characteristic abnormality is regularly demonstrable in cells of schizophrenics, as it is for the carbohydrate metabolism of erythrocytes examined *in vitro* (reported last year by Boszormenyi-Nagy and Gerty, from the Illinois Neuropsychiatric Institute), a biochemical or metabolic lesion at the unit or cellular level is practically certain. This again implies strongly a hereditary defect, in this case well supported by the familiar genetic studies on twins and probands, but it by no means excludes additional factors, organismic or environmental, which contribute to the manifest symptoms. It is indeed possible, as has often been suggested, that there is a disturbance between cortical and hypothalamic or other primitive segmental structures; but this cannot be the "full" explanation. I have personally speculated on the possibility of a disbalance between the specific and nonspecific systems from the more ancient nerve groups that act on the cortex. The specific thalamic system is concerned with the content of consciousness, the nonspecific one, with the degree of attention and of affect associated with consciousness. The dissociation of emotion from experience is perhaps the most characteristic sign of schizophrenia; moreover, it is striking that leucotomy also removes emotion from experience—as for example when the suffering associated with pain is eliminated while the direct pain perception is left unaltered.

In general, there is a sort of pyramid from etiology to symptom. Many different etiologies may initiate the same train of pathogenic events; many different pathogenic sequences may produce a single pathology; and many different pathologies may still lead to a single symptom. Thus blindness, as an example, can result from destruction of any portion of the optic system, from retina to cortex; destruction at the chiasm, say, can follow trauma, tumor, infection, and so forth; an infection and abscess, as the pathogenic process, can result from infection by one of many organisms, as a direct etiologic agent, abetted by defective host resistance, and like factors. Can it be doubted that mental disease, also, presents symptoms and even syndromes that may subsume multiple nosologic entities and are almost certainly based on multiple chains of abnormalities? Nonetheless, the present evidence seems to me to speak strongly for heavy weighting of an inherited biochemical aberration as a dominant factor in the causation of schizophrenia. Indeed, it deserves thought that the psychoses — notably schizophrenia and cyclothymia—may be primarily disturbances of the units of the nervous system, biochemical in nature and genetically carried; whereas the neuroses may be primarily disturbances in the patterns of function and interconnections of the neurone units, weighted on the physiological rather than the chemical, and resulting more from unfortunate relations of the individual to his environment than to his ancestors. Whether or not this sharp dichotomy is valid for all neuroses, it seems probable for the stress, anxiety, and psychosomatic disturbances.

Neural Units

It is time now to turn explicitly to modern neurophysiological knowledge, concerning first the units of neural function and then their patterns. The units, the individual neurones, can vary from one to another or from time to time in their thresholds of excitation, the related membrane potential level, the number and timing of their discharges, and the character of their metabolism. These attributes of a given cell are, in turn, normally controlled by impulses arising from other regions, by fields surrounding them — both electric and chemical — which result from changes in the blood supply or composition or directly from altered activity of other cellular units in their immediate neighborhood, and, as fairly basic to the electric and physiological shifts, by their own metabolic activity. Since I have discussed most of these points elsewhere, so far as their necessary relations are concerned, I should like now only to mention a few new observations from my laboratory bearing on the metabolism of neurones. This is the more pertinent in view of the opinion expressed in the preceding section that the psychoses are predominantly associated with disturbances in neurone metabolism. Many of my colleagues have been responsible for these researches; I shall not name most of them, but must mention at least L. Abood, A. Geiger, and E. Sigg (*1*).

It has long been generally accepted that glucose is the unique and even sole substrate for the central nervous system. Although this was early shown not to hold for peripheral nerve, and although various simpler substrates, such as glutamate, were shown to be metabolizable by brain slices or brei, the R.Q. of practically 1.0 and the extreme malfunction with hypoglycemia kept glucose in the fore of our thinking. It has now proved possible, using the perfused cat brain, left in physiological connection with desired parts of the organism but supplied exclusively by known nutrients, to demonstrate the maintenance of essentially normal function for hours in the complete absence of glucose. Since the fluid entering and leaving the brain was analyzed, as well as appropriate samples from the brain itself, it can be stated positively that no carbohydrate is utilized under these conditions. Further, when the cortex is excited by stimulation of the brachial plexus, there is a considerable increase in the nonprotein nitrogen of the effluent and an even larger and fully reversible decrease in the nitrogenous groups of the brain lipoproteins and nucleoproteins. Convulsive brain activity, induced by Metrazol or electric stimulation, is associated with a large increase of oxygen consumption; but, even when adequate glucose is available in the perfusion fluid, the corresponding increase in glucose uptake occurs after the increased oxygen use is past and, moreover, it can be accounted for entirely in terms of lactic acid output. Indeed, it is even possible under appropriate conditions, such as curarization, to obtain perfectly characteristic convulsive discharges from the perfused brain with no increase in oxygen utilization.

Perhaps even more surprising, according to contemporary views, is the finding that activity is associated with a decreased formation of energy-rich phosphates—a decrease that might entirely account for the fall in creatin phosphate and ATP, even if there were no increased breakdown. This decreased formation has been demonstrated with the aid of tracer phosphate — in rat brains convulsed with Metrazol *in vivo,* in frog muscle subject to polarizing or stimulating currents, with or without actual contraction, and in peripheral nerve tetanized in the usual way. Since a decrease in these compounds resulting from slowed production, rather than from hastened destruction, would not be associated with increased energy output, these findings—along with several others already reported — suggest that the energy-rich phosphates may have some other function than as an energy source for action. In muscle, they are clearly related to the magnitude of the membrane potential and this, in turn, to the threshold for excitation; and similar relations almost certainly obtain for nerve fibers and neurones.

The level of ATP and CrP might thus be associated with the irritability of the brain rather than with its actual response; with communication rather than with energy. In accord with such considerations, we have found that the content of energy-rich phosphates in the brain of audiogenic mice is definitely below normal during just that period of the lifespan, approximately 30 days after birth, when the animals are susceptible to sound-induced convulsions. Since the lowered organic phosphates are found in the brains of animals that are sensitive to convulsions—as identified by the purebreeding genetic stock—but have not in fact been convulsed, the low level could not be a consequence of convulsive activity but must be antecedent to it.

Comparable findings have been made on the isolated mitochondria of brain, which also decrease their phosphorylation, while increasing their oxygen consumption, under the influence of exciting electric pulses. These changes, characteristic of normal physiological responses, are in turn related to the presence of sulfhydryl groups and to a shift in potassium ion between the inside of the particulate and the surrounding medium. In fact, the failure of liver or kidney mitochondria to show this metabolic response to excitation may well be associated with the different potassium content or ratio of these organelles. That the particulates in neurones may indeed normally participate in the excitation and recovery processes is further shown by the finding that the microsomes of cortex neurones disappear reversibly when they are stimulated, in the perfused brain given drug convulsions or in tissue culture subjected to electric currents.

With the incompleteness of our knowledge of neurochemistry and of the metabolic concomitants of normal activity, as exemplified by such recent findings, it is not surprising that whatever changes may be present in particular psychoses have not been previously firmly established. It also seems reasonable, with the rapid increases in interest in and knowledge of neurochemistry, to expect that major advances in this direction are imminent.

Neural Patterns

Turning now from the units to the patterns, attention also shifts focus from neurochemistry to electrophysiology. In this domain are the properties of synaptic connections, the structure and reverberating characters of nerve nets and loops, the shape, intensity, and spread of electric and of chemical fields and the associated synchronization of electric rhythms and discharges. Under the influence of the modern theoretical and engineering considerations that have become known under the term *cybernetics,* much attention has been given to the continuous or discontinuous character of the interactions in the nervous system; and perhaps this is as useful way as any to open the discussion of patterns.

The nerve impulse itself is atomic or discontinuous *par excellence.* It behaves in characteristic all-or-none fashion; the impulse, if it occurs at all, is the "all" or maximum of which the nerve fiber is capable at the time. This behavior, in turn, is a necessary consequence of the high factor of safety in the nerve fiber. The eddy current that flows from an active region and constitutes the stimulus for a new region to be activated is normally some 8 times greater than the threshold of the inactive region. If the original stimulus, then, exceeds some critical intensity and fires one part of the nerve, the stimulus generated there is far more than enough to propagate excitation to other regions. Even considerable changes in the size of the action potential or in the threshold of the fiber are thus swamped out by the overpowering drive.

In contrast, most synapses show a low factor of safety—in fact, a factor less than 1. With few exceptions, a single impulse reaching a synapse does not suffice to fire the postsynaptic neurone; only when several impulses have managed to sum their effects, spatially or temporally, does a message carry through and the postsynaptic neurone fire. Synaptic action is thus continuous or analogical rather than discontinuous or digital, as has often been assumed; and graded effects, rather than trigger or threshold ones, operate there. The same is true for electric or chemical fields in the brain; these are by nature continuous and graded and can shift smoothly in intensity or position. In fact, even nerve nets, with multiple neurones and myriad connections, although discontinuous in the impulses shooting about them, are in effect continuous in their operation because of the statistical averaging over large numbers of individual units.

Messages thus enter, leave or rattle around in the nervous system as discrete signals, yet the interactions within the nervous system—which determine the patterns of activity—are mostly continuous, in actuality or in effect. It is no accident that modern information theory, concerned with factual bits of *yes-no* alternatives, and probability theory, concerned with continuities of expectation, both find increasing application in unraveling the tangled patterns of neural interaction; nor is it surprising that the two-valued Aristotelian logic is yielding to its more permissive multivalued modern derivative in rendering assistance. These considerations, moreover, are not remote from the immediate future of psychiatry. I am satisfied that the greatest barrier to rapid advance in psychiatric research today is the continuous and anecdotal character of the descriptive material on which psychiatric insights and generalizations are almost exclusively based. When more useful categories have been recognized and at least ordinal scales established, when it is possible to group the phenomena into classes and categories in a meaningful manner, rapid progress is certain to follow. This is really the familiar problem of nosology in disease or typology in individuals or populations. But this implies just the kind of interplay between continuous and discontinuous that has been under discussion. When the input to our biological calculators has been effectively coded, the rules of operation already built into these nervous systems will suffice to grind out important answers in the mental area, as they have already in the physical and biological ones.

Electric and chemical fields can strongly influence the interaction of neurones. This has been amply expounded in the case of the electric fields. Changes in direct-current potentials have been shown to start, stop, or modify brain rhythms; and changes in the potentials have been seen to accompany changes in activity evoked in other ways, for example the diphasic direct-current shift accompanying cortical depression waves. The influence of potential fields and the resulting local currents in bringing about neurone synchronization are also well known, and I have suggested a hypersynchronization of beating neurones as a neural mechanism underlying causalgia, motion sickness, and neurosis. It will, therefore, be more profitable now to direct attention rather to specific chemical effects and to the influence of one molar brain region upon another, by whatever mechanism. Of special interest in recent years have been the hypothalamic and medullary reticular formation, the interlaminar nuclei in the diencephalon, and other particular structures at the upper end of the old segmental brain stem; and the influence of these upon cerebral activity is obviously of primary concern to psychiatry.

Sympathin and Consciousness

Not only can stimulation of these deeper structures lead to increased or decreased electric and functional activity of the brain and cord; we have recently found a small region, near the mammillary bodies, stimulation of which can double the oxygen consumption of the cerebrum. This increased metabolism, moreover, may outlast the period of stimulation by many minutes—a point to be considered shortly in connection with the action of epinephrine. Indeed, the specific chemical and metabolic properties of these "autonomic" centers almost insure a rather special functional role. Thus, the reticular formation is particularly sensitive to narcotics; mescaline and like agents are reported to cause spiking in the hypothalamus; most autonomic centers are highly resistant to low oxygen and carbohydrate and to high carbon dioxide; these diencephalic structures are rich in sympathins; and, as we have recently found, both bulbocapnine and chlorpromazine inhibit phosphorylations specifically in the basal ganglia-thalamus region of the brain, while affecting that of cortex little or none. Moreover, adrenalectomy in rats leads to an increased ratio of creatine phosphate to inorganic phosphate in these basal structures only, and large epinephrine doses inhibit phosphorylation in this same region.

Many workers are now relating the level of activity of these deep structures—exactly which is far from agreed upon—to the level of normal awareness, from sleep to alertness, and associate their overactivity with disturbed mentation. The psychosomimetic action of mescaline, lysergic diethylamide, amytal, and some adrenalin derivatives has been seen as a paradigm, if not as the actual mechanism, of the pathogenesis in schizophrenia. A faulty epinephrine metabolism has been specifically suggested, and schizophrenic blood has been reported to contain a different adrenalin than normal, perhaps adrenoxime, and to be able to degrade injected epinephrine only abnormally slowly. Whatever the disturbances may be in psychoses, it is of some interest to reexamine the significance for normal behavior of epinephrine action on the central nervous system.

Most behavior is unconscious. Why is consciousness attached to or concomitant with certain acts and experiences? It is certainly true that awareness is most acute in association with disturbing events and is most in abeyance when the surface of existence runs smoothly and placidly. Extensive and splendid mechanisms have evolved to meet, adaptively and automatically, the usual situations encountered in the life of an organism; it is only when such adaptive behavior fails that innovative or creative behavior and the attendant consciousness are called into action. In neurological terms, if the automatic response fails to remove the disturbing stimulus, if the simple negative feedback mechanism fails, then impulses will continue to arrive at particular neurone groups in greater numbers than normal. Some kind of summation is highly probable—the mechanisms for this, at least at synapses, are reasonably well understood—and impulses will now irradiate to additional neurone groups beyond those normally activated. Progressive radiation of activity in the nervous system, under cumulative stimulation, is a well-known and fully documented phenomenon. As judged by the subjective and objective evidence of mounting affect when a disagreeable experience is continued, as well as by the physiological evidence of increased autonomic activity, one important direction of radiation is to the hypothalamus and related structures. From such activation, in turn, result an outflow of impulses up and down the neuraxis and, quite possibly, a direct liberation of sympathins. But the conditions just described are those of emergency or stress, long known to be associated with activity of the adrenals.

The adrenal medullary hormone, epinephrine, but not the closely related norepinephrine, has fairly dramatic actions on the nervous system, and a considerable outpouring of epinephrine does follow hypothalamic stimulations. This substance considerably increases the oxygen consumption of the cerebrum, assumed to be by a direct action on these neurones. In view of the evidence mentioned earlier—of the existence of hypothalamic centers, excitation of which doubles cerebral oxygen consumption, and of the excitant action of the sympathins on such centers—it should be considered whether this effect also is an indirect one from the diencephalon. Epinephrine can, moreover, considerably enhance or, especially with larger doses and deeper anesthesia, depress motor responses obtained from stimulating the motor cortex or those of the knee jerk; and, in the latter case, not all the changes are abolished when diencephalic and medullary influences have been eliminated by spinal section. In general, parasympathetic activity overbalances that of the orthosympathetic system in sleep, and increased orthosympathetic activity leads to arousal; indeed, a moderate epinephrine injection can rouse an animal from moderately deep anesthesia. Perhaps the concentration level of adrenalins, or more generally sympathins, acting on the brain is a significant determinant of the level of consciousness.

We have been able to show, by infusing healthy young adults with epinephrine solutions at only 2 or 3 gamma a minute, that psychological effects are produced in the complete absence of vascular or other peripheral signs. (By contrast, much larger infusions of norepinephrine can produce vigorous cardiovascular changes, even abdominal cramps, with no change in mental state.) Minimal epinephrine does produce a fine tremor, increased unsteadiness, and enhanced word fluency; no other tests revealed differences. More striking than any change revealed by objective tests, was the subjective report of a feeling of anxiety and apprehension. Such feelings have been experienced by all subjects; and some individuals, presumably with a high preexisting level of conflict and apprehension, approached collapse.

It is tempting to think, then, that an unresolved and therefore stressful situation leads to neural activation of primitive brain-stem structures, this to the liberation of sympathin-type agents, and these, by a positive feedback upon the brain, to increased attention, alertness, and anxiety. It is not an unlikely extrapolation that still larger doses or more active derivatives could stimulate still further and produce hallucinations and disorientation and, in general, be psychosomimetic. An oversusceptibility of neurones might be an additional factor in the true psychoses. In fact, such considerations lead us back to a reconsideration of consciousness and memory, this time in terms of circuits and neural nets rather than of electric and chemical fields.

Memory and Circuits

The notion of neurones connected in a network, not merely in linear series, and of nerve impulses passing about the connections in a circular, more or less continuing, fashion, is now widely accepted. Actually, such reverberating circuits have been demonstrated only over gross levels of the nervous system, as between cortex and thalamus (we are finding suggestive evidence of their functioning in the frog's olfactory bulb in normal olfaction), but the sort of dynamic action that is possible in such circuits or assemblies is just what the physiologist ordered to account for the less automatic and immediate aspects of behavior. So, whether or not it is finally correct, it will be useful to explore further some of the behavioral consequences that can flow from reverberating neurone circuits. It was early pointed out that such circuits free behavior from being time-bound to the stimulus. Conduction and synaptic times no longer set the limits between stimulus and response; a neurone chain, once activated by a stimulus, might continue to reverberate indefinitely and so to serve for a maintained new behavior, for behavior appearing intermittently, or even for memory records that could play into consciousness on appropriate triggering. There are, in fact, some highly interesting relations possible between memory traces and nerve impulses running in circuits.

We were able to show that memory does not depend on the continuing operation of active neurone circuits or assemblies, by stopping brain activity with deep cold or by discharging all neurones simultaneously with an electric shock—either of which maneuvers should terminate any active patterns of reverberation. Hamsters, so treated after mastering a maze, showed full retention of their learning. But it was also found, by altering the interval between each learning experience and electric shock, even though a set of runs and a shock were given every 24 hr, that memories required a certain time to become fixed in the nervous system. Thus, when shocks followed trial runs by an interval of 4 hr or longer, the learning curve was as good as when no shocks were delivered; when the interval between experience and shock was reduced to 1 hr, some defects began to show; at 15 min learning was seriously retarded; and at 5 min or less it simply did not occur. Human experience takes meaning in the light of these experiments; after a concussion, memories may be much disturbed and then return in order from earlier toward more recent times, but the events over the few minutes to an hour or so prior to the brain shock are usually lost forever. Presumably, here also the necessary time for fixation, between initial experience and the laying down of a firm mnemonic trace, was lacking.

We have further found that the temperature coefficient of this fixation process is well over 2, perhaps closer to 3, since hamsters kept cool during the interval between experience and electroshock show as great a disruption of learning at an interval of 1 hr as warm ones do at an interval of 15 min. Whether or not this stout temperature coefficient indicates a chemical process in laying down the engram—an issue that is irrelevant to present considerations—it is satisfactory to find such physical regularities in the memory process; especially since the temperature coefficient is comparable to that reported decades ago for the passage of subjective time.

Our immediate concern is the possible relation of these phenomena to reverberating circuits. It may be that the single passage of an impulse over a neurone loop leaves no significant trace but that repeated passages in a limited time sum their reversible effects until some irreversible level is passed. A single water drop can leave a sandhill undisturbed, but a series of drops produces a runoff channel. If messages continue to circulate in a neurone loop, their continuing reappearance at particular junctions over minutes or hours might be required before the critical material change that constitutes a relatively permanent memory record could be produced. In much the same way, tetanization of a presynaptic nerve fiber for a few seconds can lead to marked and enduring enhancement of the number of postsynaptic units that it can excite. The temperature coefficient might thus be determined by the rate of reverberation, the speed of chemical fixation, or one of several other possible variables; but, whatever the details, something of this general character is strongly indicated.

A final point on memory has to do with localization. This again is not part of the main theme, but it is significant that, if memory traces are deposited at multiple loci in an activated neurone assembly, several conflicting phenomena concerning localization seem explicable. Punctuate stimulation of the temporal cortex evokes, at least under some conditions, highly specific recall of past experiences; this indicates a sharply localized engram. Conversely, localized lesions in the brain, even fairly extensive destructions, are unlikely to abolish memories, at least beyond the major modalities encountered in the aphasias. If the neurone assembly involved in a given experience is, as the term *assembly* implies, not a single loop but a multiply linked network of loops, a memory would not be entirely lost unless all parallel paths of the net were destroyed, whereas it might still be elicited quite specifically by stimulating any one appropriate locus. Thus, as is shown in Fig. 1, a memory would be lost only when both *A* and *B* were destroyed; it could be evoked by stimulation of either one alone. Such a picture would, of course, predict that a given memory could be evoked on stimulation of more than one point; but, since the anatomical distribution of such loops is completely unknown and observations on man are difficult, it is not a serious objection that such multiple loci have not been encountered. It is only half a decade since specific memory loci were discovered; half a century elapsed between the discovery of primary motor and sensory areas of the cortex and the discovery of secondary ones.

Consciousness and Circuits

If circuits enduring for minutes or hours may be required to fix experience in memory, perhaps circuits reverberating for seconds or fractions may be necessary even for the initial consciousness of an experience—or of some inner-triggered awareness. Such a hypothesis would deny that any subjective experience accompanies a single activation of any given neurone assembly (whether certain exceptions may exist is not now important) and would require the summative effect of at least a few reverberations before consciousness is aroused. This postulate leads to some interesting consequences. First, it fits the foregoing discussion concerning irradiation in the nervous system with unresolved problem situations. Consciousness and creative behavior are both evoked by the reverberation of circuits, while routine unat-

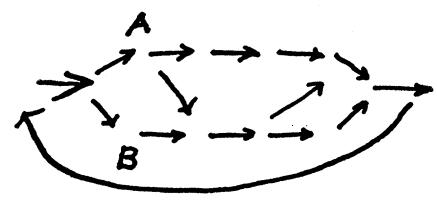

Fig. 1

tended behavior is presumably handled by messages running quickly and with no or minimal repetition through well-grooved "reflex" channels. Along the same lines, dreams might result from unresolved pressures left from the day or generated from the environment and would represent such continuing reverberation and irradiation in brain neurones (2). If dreams represent maintained brain activity—as borborygmi accompany a maintained digestive activity—their presence with unresolved situations is physiologically reasonable. The maintained stimulation might result from lingering concerns of the day, perhaps represented in reverberating loops in the diencephalon-cortex system sensitized or activated by an accumulation of sympathins; or from a maintained barrage of interoceptive messages, such as that produced by a filling urinary bladder; or from a similar insistent input of exteroceptive messages, say a ringing bell—all would favor the existence of dreams.

Much the same considerations would apply to hallucinations, such as those of water that are associated with thirst, to delusions, and the like. When neural activity is maintained, more and more neurone loops will be activated to the level that is associated with conscious awareness and with focusing of attention. Such a neurophysiological picture is obviously congruent with the psychodynamic one of drives or pressures that are unsatisfied, with the accumulation of something—unfortunately called energy—that finally overflows in healthy or unhealthy ways. If such biological considerations serve to account effectively for the existence of consciousness under given conditions, we need not be disappointed if the content of consciousness can be described at all now, and perhaps forever most usefully, only in terms of recent or early experience.

One final instance of a psychodynamic consequence of this postulate regarding consciousness must suffice. It has long bothered me that learned physical prohibitions remain fully conscious while those associated with enculturation are largely unconscious. Thus, a child learns by physical suffering that it must not touch hot objects, avoids touching them, and remains throughout entirely aware

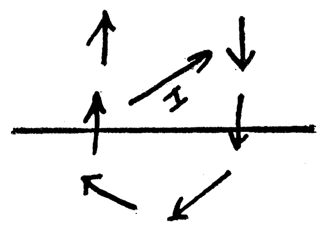

Fig. 2

of the complete relationship; but the same child, punished for hitting someone, gradually develops a superego which not only forbids the act but represses the entire constellation of urge and censoring. Aside from this difference in repression—which may itself have something to do with the repetition of the experience and the gradual accumulation of the inhibition—the following aspect of repression seemed quite inexplicable. Since the superego rules are learned, they are presumably associated with the cortex, and if their censoring action is to be evoked by a drive, this also should somehow involve the cortex. Yet, both the drive and the censoring remain unconscious. This is in conflict with our normal experience and expectation that activation of the appropriate cortical memory elements should be associated with conscious recall or awareness. In simple words, how can the censor censor and be censored without knowing what is happening?

Exactly the same problem arises with the recognition of words exposed tachistoscopically. Neutral four-letter words are perceived and correctly recognized after an exposure of about 0.01 sec; "dirty" four-letter words are not recognized unless exposed for twice as long. Clearly, these words must have been correctly identified in the usual time in order to be rejected from conscious recognition; again, learned patterns in the cortex must have been activated but not sufficiently to arouse conscious awareness. The hypothesis we are considering, that awareness results only with repeated activation of the appropriate assembly, by a brief reverberation, happily accounts for these phenomena if the first activation leads to inhibition. (In Fig. 2, *I* blocks impulses on the way to the cortex; so one passage only occurs.) And the same reverberation requirement for consciousness can simply account for subliminal perception and learning; it may even account for the seeming occurrence of perception in 0.1-sec frames.

Whether the various guesses I have dared to present here should prove, as is highly probable, partly or entirely incorrect is not so important as is the fact that today it is possible for neurophysiologists to make such informed guesses. Not many years ago such viewpoints were not only unavailable but would have been entirely unjustified by the evidence then at hand. I am particularly encouraged by the fact that this postulate concerning consciousness and the consequences that follow with regard to mental activity were triggered by very limited discussion with a psychoanalyst. Such discussion is one of the opportunities presented at the Center for Advanced Study in Behavioral Sciences, where psychiatrists and psychologists, as well as a neurophysiologist, happen to be fellows at the same time. With growing attention to interdisciplinary behavioral science, I am very optimistic regarding the progressive and increasingly valuable application of biological knowledge to mental phenomena in general and to psychiatry in particular.

Notes

1. Our thanks are due to the Office of Naval Research, to the National Institute of Neurology and Blindness and the National Institute of Mental Health of the National Institutes of Health, U.S. Public Health Service, to the Surgeon General's Office of the Army, to the Illinois Department of Public Welfare, to the Muscular Dystrophy Association, and to other agencies whose support has made these studies possible.

2. Incidentally, Freud's asusmption that dreams exist to preserve sleep is not only unnecessary to his important interpretations of latent and manifest dream content and of the nature of dream work; but it also seems unsound physiologically. Physiological evidence is pretty conclusive that there is no dreaming during the deep sleep of most of the night, that dreams do occur in light sleep and during the waking-up process, but that their presence does not prevent the arousal from proceeding to awakeness. Conversely, internal or external stimuli may produce, during complete wakefulness, a wandering of attention and kaleidoscopic conscious content quite similar to that of sleep dreaming, and well called daydreaming. The hypnogogic awareness, associated with actually falling asleep, is also comparable to the dreams during sleep, supposed to prevent wakefulness. This physiological explanation of the existence of dreams in no way detracts from the validity of psychodynamic interpretations of the dream content, latent or manifest, or of the nature of dream work—all of which are now beyond neurophysiology.

The really great school and college teachers are not primarily teachers of biology, English or economics. They are teachers of young men and women. Their success can be measured by the degree to which they correct, humanize and enrich the student's perspective, and give him wider interests, new horizons, enlarged frames of reference, and those sounder habits of working and thinking which make it possible for him to discover the relevant facts in any field, and in his own reach valid conclusions.—CHRISTIAN GAUSS.