A Biophysical Approach to Altered Consciousness

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Ordinary chemical and biological thinking tends to emphasize special functions at the expense of general and organismic processes. I want to suggest some of the ways in which "physical state" ideas can bring generality to the complex biochemistry of consciousness and behavior.

I use the phrase "physical state" to suggest that life, and its pathological and evolutionary modifications, can profitably be considered as a special "state of matter." The liquid crystalline state, with its various degrees of order, is a good example of another special state of matter. Living material is peculiar in being able to use external energy to increase its order without having to reduce its temperature; nerves and muscles, for example, consume ATP and CrP when they "fire," and they are able to return to their resting, sensitive state as long as energy is available. These active and resting states differ in various ways, such as preference for sodium or potassium ions, volume (Morocz-Juhasz and Orkenyi, 1966), and even in the freedom and average alignment of their water molecules (Damadian, 1971; Fritz and Swift, 1967).

These two states, active and resting, can also be characterized, respectively, as hydrophilic and hydrophobic (Tasaki and Hallett, 1973; Ungaret al., 1959); as sodium-loving, and potassium-loving; as inefficient and efficient (Peat and Soder-wall, 1973).

The all-or-nothing impulse of a neuron is not the only known or plausible (Ressler, 1972; Cope, 1971) mechanism of nervous communication. Nevertheless, all forms of cell conductivity are subject to modification by any process which shifts the equilibrium in either direction from the normal resting state— toward excessive "readiness," or toward incomplete restoration of the resting sensitive state. Russian biologists are most active in studying the changes that occur in tissue exhaustion (Nasonov and Aleksandrov, 1940) —e.g., increased dye uptake, decreased electrical conductivity—but Crile (1936) and others several decades ago discovered some of the basic electrical properties of tissue related to consciousness.

If such tissue conductivity is a gross aspect of the kind of conduction which maintains our perceptual model of the world, we would expect a disturbed "state equilibrium," through its effect on conductivity, to alter our perceptions in general ways, such as spatial expansion

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or foreshortening (Newbold, 1972a; Leonov and Lebedev, 1971). Since such perceptual changes are common in depression, mania, "schizophrenia," paranoia, delirium, etc., this "physical state" theory would predict that ionic and metabolic intervention would be possible to relieve those conditions. There is a long history of "resonance" models of consciousness, and some of them are highly relevant to this holistic and physical approach (Pribram and Baron, 1973; Barrett, 1969).

There are many examples of gel hysteresis, in which a transition in one direction is easier than a return to its previous state. This seems to be what happens in the cornea after a prolonged riboflavin deficiency: even very high doses of riboflavin fail to restore its concentration in the cornea to a normal level, as if its solubility in the corneal gel had been reduced.

The monovalent alkali metal ions "bind" to themselves more water molecules as their radius becomes smaller, i.e., in the series rubidium, potassium, sodium, lithium. In this sense, lithium can be considered to be "super-sodium," and rubidium would be "super-potassium." Their affinities for cell proteins are apparently determined by their own radius and by the charge concentration of sites on the proteins (Ling, 1962; Ling, 1969). The presence of these ions in turn stabilizes the conformation of the protein-water system in such a way that the charge concentration of the protein sites continues to favor those ions, barring the intervention of a stronger influence. These stronger influences may include powerfully adsorbed polyions such as ATP (Ling, 1969), or certain changes in amino acids, or disturbed electronic conditions (Szent-Gyorgyi, 1968). Glutamic acid increases the cell's ability to take up other amino acids, while glycine acts in the opposite direction (Troshin, 1966); glutamic acid also acts as a "cofactor" with ATP, probably sterically, in enabling the cell to take up potassium (Ling, 1972). This steric function could account for the interference of synthetic (i.e., a mixture of levo and dextro forms) monosodium glutamate with brain development in rodents, and sometimes with nerve function in humans. Natural glutamic acid would be predicted by this theory to facilitate recovery of sensitivity in a depressed brain.

Lithium and rubidium have opposite influences on neuroexcitability, as predicted by this physical theory of the living state. Damadian (1972) emphasizes the importance of this point, because "if one tries to explain these data in terms of conventional membrane pumps, one is at a complete loss to explain why lithium quiets the neuro-excitable state and rubidium enhances excitability."

The usual definition of a cell's "energy charge" is given in terms of ATP, ADP, and AMP (Atkinson, 1968), with a high energy charge —an abundance of ATP— corresponding to what I am calling the resting state of "readiness." According to Szent-Gyorgyi (1972) there is probably another sense in which cell proteins can be charged, namely, by addition to their "electron pool," which is a capacity of washed proteins to reduce large amounts of glutathione (discovered in 1925 by Hopkins; this capacity is what Racker has referred to in his cute phrase "nothing dehydrogenase"). Szent-Gyorgyi feels that this electron pool may provide the energy used to drive cell division. This energy seems to be derived mainly from glycolysis, which operates in the liquid phase of the cytoplasm. A related observation is that agents —e.g., estrogen —that promote mitosis also cause a proportionate increase in oxygen consumption and reducing capacity of whole tissue (Peat, 1972), but that this capacity is lost if the cells are disrupted. This would suggest that the Hopkins electron pool is only a remnant of a larger and more delicately balanced pool, which can be kept in balance by draining electrons into oxygen as long as that is available; some pigments might serve as substitutes for oxygen in an emergency. Peroxidase and age pigment

could catalyze this “draining” process (Peat, 1972).

If such an electron pool is an integral part of the protein structure of the cell (Szent-Gyorgyi, 1972, has suggested the protein nitrogens as a likely site), then Szent-Gyorgyi's approach becomes a perfect complement to Ling's (1969), since the charge concentrations on the ion-binding sites of proteins are crucial factors in cell regulation in Ling's theory. It is well known that electron releasing or attracting groups have inductive effects through adjoining atoms, and Ling's view is that the strong ("cardinal") adsorbents can act through such inductive effects on adjoining charge concentrations. Szent-Gyorgyi also believes that these electrons could regulate the degree of protein hydration (1972).

The source of these electrons is likely to be NADH and/or NADPH, which are produced abundantly in the cytoplasm and which contain high-energy electrons (NADPH provides the energy for many biosynthetic reactions). For example, NADH and NADPH are the source of electrons for reducing glutathione, which in turn is in equilibrium with the SH groups of proteins (Peat, 1972). Niacin is a component of these molecules that are so important in energy delivery. In a niacin-deficient animal, estrogen has no effect, so if estrogen is acting through its influence on the electron pool, NADH and NADPH seem to be necessary for energizing that pool. Of course the biosynthetic function would also be damaged in a niacin deficiency.

The fact that large doses of niacin can often cure schizophrenia (Hoffer, 1966; Cott, ASA Publication) suggests that in this disease the energy charge of neurons may be low. This would affect the ability of cells to retain certain ions and the known mineral changes that occur in schizophrenia (Newbold, 1972b) may be similar to those that appear in general stress reactions, though possibly with the brain being most affected. A low electron pool in schizophrenia might account for the claim that schizophrenics seldom develop cancer, since the cancer state, like other mitosis-favoring -states, presumably requires a very large or excessive electron pool. (The resistance of schizophrenics to virus infections, allergies, and histamine, Carter and Watts, 1971, would suggest lower susceptibility to cancerization by viruses or irritation.) In the normal states, proteins would be "charged" only enough to function, bind water, etc., and then energy production would be limited. In a sense, the schizophrenic would be "too weak" even to produce cancer.

Szent-Gyorgyi (1951) has shown that a given process can have opposite effects in different tissues, depending on whether that tissue is already above or below its maximum capacity to produce the particular effect. Recognizing that cells can have different degrees of structure according to their normal function and position in the developmental gradient, we should look for concepts that can combine generality with recognition of individuality, rather than grasping for undergeneralized answers such as "special receptor" theories.

Many people have suggested that pigments such as melanin may be able to function as electron acceptors, as an alternative to oxygen —no one has yet thought of a better explanation for the occurrence of pigments in the nervous system (e.g., the substantia nigra**),** in association with rapid mitosis (Florey, 1966), e.g., melanoma and skin irritation, or in hormone imbalance or vitamin deficiency (Davis, 1965), e.g., pellagra, Addison's disease, "melasma of pregnancy." We could imagine the pigment receiving electrons that "overflowed" from the electron pool, in case of a control error, or that leaked out of the pool, in case of structurally defective protein-gel systems. A phase shift of the cytoplasm toward "melting" would be the common event. Discontinuity of the proteins probably causes the low conductivity.

The fact that abnormal pigmentation occurs in a niacin deficiency and in

association with psychosis (Creinor, 1970; Proctor, 1972) suggests that a metabolic or structural energy problem may be the key to both conditions. The observation that ascorbic acid with its high electron energy can be helpful in psychosis (Cott, ASA Publication) as well as in B-vitamin deficiencies has the same implication — ascorbic acid has both structural (Davis, 1965) and energetic effects. The electron donor potential of a substance has been successfully used to predict its effect as a hallucinogen (Kang and Green, 1970), and combinations of donor and acceptor substances induce muscle contraction (Kaminer, 1962) and may be involved in dyskinesias (Proctor, 1972).

Usually we think of both "error" and correction as being on the molecular level. However, control processes are likely to be of a physical nature first, followed by a chemical adaptive response. For example, if oxygen is physically restricted, the resulting lactic acid tends to restore the oxygen supply by causing vasodilation. Transmitter granules in nerve endings likewise are believed to be ruptured by physical changes in the cytoplasm, leading to the release of transmitter substances. Thus, we might look first for unusual functional states, such as stressed consumption of oxygen or glucose, or a nutritional block to such consumption, as provoking the release or synthesis of unusually high or low amounts of regulatory substances. Even vasodilators or vasoconstrjctors are ultimately regulators of the cytoplasmic "phase"; some hormones may do this more subtly, though. In this connection, it is interesting that a vasoconstrictor action has finally been demonstrated for LSD. The action of niacin as a vasodilator may be significant in its ability to block intoxication by hallucinogens (personal observation), as well as to block the symptoms of schizophrenia.

Schizophrenics typically have an abnormal serotonin concentration in their pineal gland. The pineal is rich in both serotonin and its N-acetylated, O-methy-lated derivative, melatonin, which has the function of concentrating melanin, making it seemingly disappear by withdrawing it from the extremities of the melanocytes. An interesting complexity is that the hormone is chemically closely related to the pigment that it regulates. The enzyme peroxidase, which is almost universally induced by irritation or stress, is involved in the synthesis of melanin (Proctor, 1972). The same enzyme can efficiently dispose of both electrons and oxygen (Peat, 1972).

The pineal is closely associated with the optic thalamus and the reticular system, and is functionally involved in response to light, and is antagonistic to the gonads' production of sex hormones (Kinson and Peat, 1971). Its involvement in the visual system suggests it would be important in perception and dreaming, and related to agents that either stimulate or suppress the dream-consciousness, such as LSD or alcohol.

A common item of folklore is that alcoholics are likely to be lightly pigmented people; sexual problems are often suggested, but usually are treated as an effect rather than a cause of alcoholism. Sensitivity and imaginativeness are frequently attributed to alcoholics. **(Newsweek,** July 2, 1973, reported successful use of lithium salts to treat alcoholism; this could be interpreted as acting to depress the "dream process," lowering excitability.)

Rat experiments (Celle, 1971; **Science News,** 1973) have shown that the pineal gland is involved in preference for ethanol: injected melatonin makes them prefer alcohol, as does keeping them in the dark. Removal of the pineal prevents this response to the dark.

It is well known that alcohol suppresses dreaming, usually for several days following intoxication, while the alcohol remains in the body. The body's "need to dream" is temporarily suppressed, but catches up later with a night or two of unusually intense dreaming. Continuous intoxication presumably builds up an increasing "dream pressure" that can eventually break through as waking dreams, or "delirium tremens."

LSD works the other way, stimulating intense dreams even when awake, but causing a few dreamless nights when its direct effect wears off. (Para-chloro-phenylalanine, which blocks serotonin synthesis, not only interferes with sleep — especially R.E.M. sleep —but it causes rats to reject alcohol, and to become hypersexual, Campbell, 1970). The dream process involves greater conductivity through the head, whether it happens during sleep or when awake (my unpublished observations). This suggests that it corresponds to a high efficiency "resting" state.

It seems likely that human alcoholics, like the alcoholic rats, have excessive melatonin. This would account for the idea about their light pigmentation and possibly for an associated sex problem, since melatonin also suppresses the sex hormones (Kinson and Peat, 1971). Serotonin and reticular formation implants also have this suppressive action; male and female hormones may respond differently to serotonin and melatonin (Kinson and Peat, 1971).

Drinking would tend not only to suppress the dream consciousness (imagination may be a source of frustration), but may also antagonize the antigonadal action of the overactive pineal, though I don't know of any study that would indicate this —alcohol's occasional ability to increase sex hormone action is generally attributed to liver damage.

To the extent that psychosis is associated with excessive pigmentation, we might guess that it corresponds to a deficiency of melatonin; abnormal levels of serotonin (precursor of melatonin) in the pineals of schizophrenics could be interpreted in this way.

Stress, among its many effects, causes an increased synthesis of uric acid (Davis, 1965), possibly as a useful adaptation, since uric acid levels correlate positively with mental activity and efficiency. However, uric acid can catalyze the oxidation of epinephrine (Proctor, 1972), and if this leads to elevated adrenochrome levels, it might interfere with cytoplasmic gel structure by acting on glutathione (Mattock and Heacock, 1965).

Migrainoids typically have unusually vivid visual imagery and high electrical activity of the brain stem; a sudden drop in serotonin level is considered to be responsible for the swelling blood vessels that cause the pain, scotoma, etc. The travelling symptoms described by Reich and others may indicate that a certain mass of vessels exceeds the organism's vasoconstriction capacity; the demonstration that autonomic training can stop a migraine (by raising the temperature of the hands), the fact that sleep or orgasms can often end the symptoms, or that rectal stuffing can induce a headache, would be consistent with this idea. The "substitution" of bronchitis or piles (both involving vasodilation) for migraine would probably be conditioned by factors such as diet, activity, posture, etc. A high metabolic rate of any tissue will tend to cause reflexive vasodilation to maintain adequate blood circulation, as will relative starvation of the tissue, as in a riboflavin deficiency. In the migrainoid person, high brain activity, low blood sugar, and disturbed intestinal absorption may be interacting factors. Chernigovskii (1967) has discussed some of the ways in which brain, blood sugar, and the intestine can interact.

The pituitary hormone, MSH (melano-phore-stimulating hormone), which causes darkening by dispersion of melanin, seems to act by way of interfering with glycolysis (Turner, 1966, Wright, 1955). High pH and hypo-osmolarity (Turner, 1966) can also cause dispersion, which suggests that a phase transition (gel to sol) is involved. Kinosita (1953) has reported exactly this gel-sol transition and has also demonstrated that the pigments seem to follow electrical gradients within the cell.

The idea of an altered state of the protein-water system makes it easier to see the darkening event, pigment dispersion, as a single process: deficient melatonin, excess MSH, deficient niacin, or irritation, would all promote the low

conductivity, low efficiency, anti-dreaming state.

During exhausting fevers and after drinking too much, I have experienced a defective kind of dream, a kind of analytical, verbal delirium, in which one word only leads to another word. In place of fluid and integrated imagery, there was just a kind of fizzly yellow, or swarming orange, activity. Mental satisfaction becomes impossible in that state. (Green and blue usually seem to be suppressed in that kind of state.)

Since I believe mental imagery is the real, working structure of language, I think a related kind of damage to the dream system, or dream metabolism, would account for the peculiar nature of "schizophrenic" verbalization.

The damage would be both energetic and structural and would act by an effect on tissue conductivity. (An important difference between the cancer state, Peat and Soderwall, 1973, and schizophrenia, on the cell level, would be that cancer depends on glycolysis, while glycolysis is specifically depressed in schizophrenia, according to this view.)

This theory, unlike others used as a basis for Orthomolecular psychiatry, offers a great range of substances that may be used simultaneously and possibly provides a better and more general basis for understanding synergisms (such as Ling's ATP-glutamate-potassium interaction). It specifically opposes the premature assumption that any particular metabolic error is genetic and proposes instead the investigation of environmental factors (including the uterine environment) that could alter the physical state of the cytoplasm. The observations of poor muscle tone in very young infants who later become schizophrenic has been used to argue for a purely genetic origin, but it could as well reflect a bad uterine environment, such as could be caused by an inadequate placenta.

IMPLIED THERAPEUTIC APPROACHES

This biophysical theory argues that altered consciousness (and the behavior it produces) is a question of both bioenergetics and "bio-microstructure," and implies that a therapy should attempt to create the desirable state of structure and energy by intervention at crucial —and possibly numerous-points.

If it is possible to introduce ATP directly, its use would be suggested by the theory, since it is one of the central points in both energy metabolism and structure. Creatine phosphate, which is in equilibrium with ATP, might be an alternative way of raising ATP concentration since it is at a higher energy level and would not introduce additional adenosine, thus allowing a higher ratio of ATP to AMP, if not an absolutely higher concentration of ATP. ATP has been found to improve the functional state of the brain (vestibular analyser) when used with Pyridoxine, increasing its stability and shortening postrotatory nystagmus (Lapayev et al., 1971). Also, ATP promotes healing of corneal wounds at high altitudes, when applied locally with 4-methyluracil (Vovsi, 1972). Since ATP hydrolyzes rapidly in blood, it might achieve these effects partly through vasodilation. Recent in vitro studies show that ATP prevents leaking of enzymes and other proteins from cells **(Science News,** 1974).

Other "orthomolecules" besides niacin would, according to this view, include potassium, magnesium, vitamin E (improving oxygen supply, facilitating cell retention of proteins, and even, according to Matusis, 1971, increasing ATP content), L-glutamic acid, inositol (stabilizer of cells and proteins against denaturing or "dehydrating" influences, Webb, 1965), the other B vitamins, vitamin C, and anabolic steroids (e.g., testosterone, progesterone, ginseng, el-eutherococcus) to promote protein synthesis and retention of potassium and creatine and ATP. Progesterone may be particularly important in female schizophrenics, since it commonly seems to promote emotional stability and even has an anesthetic function in large doses (Selye, 1967). Vitamins A, E, C, and B-|2

either mimic or potentiate testosterone to some degree (Sharaf and Comaa, 1970). I am currently investigating the function of folic acid in allergic, immune, and perceptual processes.

The electronic aspect of the cell's energy charge suggests that cysteine or reduced glutathione might be desirable, especially if there is evidence that glutathione is being destroyed by something like adrenochrome. (Sulphydryl blocking can impair glycolysis, as can a niacin deficiency.) The theory of donor-acceptor interaction might eventually lead to a specific understanding of the "electronic leak" and how best to intervene, though it might not be such a discrete problem as some theorists have hoped.

The glutathione peroxidase which is released when mitochondria swell (Green and O'Brien, 1970) might be involved in the "electron leak," and so things which cause uncoupling of oxidative phosphorylation and mitochondrial swelling, such as unsaturated fatty acids (Racker, 1965) should probably be controlled in the diet.

Since the normal person has sharp diurnal cycles of brain activity (reflecting a proper concentration of the "brain" amines) and many psychotics have flattened cycles, involving disturbed sleep as well as disturbed waking consciousness, cyclic light stimulation of skin and head might be desirable to support regular cyclic activity of the pineal gland and brain. This would also tend to increase sex hormone production by the gonads (Kinson and Peat, 1971). The brain's "background activity" might have what in the heart is called the "staircase" effect, in which structural readiness seems to leak away if the tissue doesn't become active often enough-"function builds structure, and structure produces function" (Szent-Gyorgyi,1972).

"Rhythmotherapy," the imposition of normal rhythms, is being done with the apparatus called "LIDA," which produces pulsed light, sound, and UHF currents, and a breeze on the face (Belenkiy, 1973).

Hyperbaric oxygen therapy has been used in relieving psychotic symptoms (Kondrashchenko et al., 1971), but this doesn't seem appropriate for creating lasting improvement. The opposite condition, i.e., high elevation, has caused lasting improvement in psychosis (Mir-rakhimov, 1972) and many somatic and psychosomatic conditions, and the mechanism (according to the animal studies of F. Meyersonet al., 1972) is the adaptively increased number and efficiency of mitochondria in the brain, resulting in improved learning ability. Also, MAO activity decreases at high elevation while respiratory effectiveness increases (Khvatova et al., 1973).

In a pharmacological approach, reduced expenditure of glycogen, ATP, and creatine phosphate (Dardymov, 1971), combined with increased protein synthesis (Rozin, 1971) and increased resistance of cells and organisms to stress, can be achieved with ginseng, eleutherococcus, and 2-benzyl-benzimidazole (Rusin, 1971), used singly or in combination. Piracetam, an analog of GABA, improves learning, increases resistance to toxins or oxygen deprivation, and increases bilateral symmetry of function in the cerebral hemispheres (Giurgea, 1973).

The importance of improving protein synthesis is implied by the observation that serum from schizophrenics inhibits protein synthesis in rat cerebral hemispheres, hypothalamus, and cerebellum (Us and Bozhko, 1971).

Several people (e.g., Manukhin and Turnayev, 1971) have suggested an identity of acetylcholine, epinephrine, and serotonin "receptors," and this structural-energetic theory similarly would suggest that "specific receptor" psychopharmaceutical approaches lack a proper physiological basis. But studies of psychoactive agents can contribute to a general understanding of cell and brain function and can possibly support an Orthomolecular approach. For example, when excessive cholinergic activity is involved in nervous dysfunction (and excessive acetylcholine can block cholinergic synapses, ll'yuchenov, 1971),

cholinolytic cell stabilizers (e.g., acetylcholine or tetramethylammonium with the adamantyl radical substituted for the N-methyl group, Kharkevich, 1971), might be used to stabilize nerve function while actual repair processes occur under Orthomolecular therapy. The adamantyl radical is also useful in treatment of Parkinsonism and viral infections (ll'icheva, 1973) again suggesting a general biophysical structuring effect, as in cholinolytic processes. The "Pavlovian dose" of caffeine which produces sedation is very small and probably acts by increasing the degree of structuring of cells; larger doses, which would promote an "adrenergic" state, might intensify the symptoms of schizophrenia or alcoholism. The cholinergic and muscarinic drugs (e.g., prostigmine) might shift the nervous balance in the right direction if the cholinergic synapses aren't blocked by excess acetylcholine.

The Russians have two electronic techniques that may serve as alternatives to ECT and which may in fact give some insight into the effects of ECT on the brain. Electrosleep (produced by 5-100 Hz. pulses, with peak current of 5-8 m.a. applied to the eyes— negative pole— and mastoid process —positive pole) has been used in treating "functional disorders of the CNS," autonomic and endocrine functional disorders, etc. (Studnitsyna, 1972). High frequency (5000-6000 Hz.) currents have been found to stimulate the brain (Rubakov, 1973).

In embryonic muscle cells, when the "depolarizing fast acetylcholine receptors" are blocked by snake venom, then the cell's "slow polarizing acetylcholine receptors" are revealed (Patrick et al., 1972). This type of receptor may be responsible for the "trophic" influences which maintain high polarization and which seem to be involved in such things as the "Bowditch staircase." Electrical stimulation may act on similar "receptors" in neurons.

Vitamin B6 is a coenzyme in carboxyl-ation reactions and as such is involved in the synthesis of serotonin from 5-hy-droxy-tryptophan, and also in the formation of GABA (gamma-aminobutyric acid) from glutamic acid. In the "resting" state, cell water seems to be more orderly, as if it had a lower "structural temperature." Some enzymes are inactivated by cold and presumably would be inactive in the resting state. GAD (glutamic acid decarboxylase) has been found to be among these peculiar enzymes, and this is the enzyme which decarboxylates glutamic acid, producing GABA. GABA has been shown to be a mediator of nervous inhibition on the basis of several criteria, including heightened GABA liberation in sleep and near-sleep (Sytinskiy, 1973).

This would seem appropriate if the physical state of cell water is participating in brain regulation. During brain "activation" or exhaustion, this enzyme should become more active, producing more GABA and presumably thereby promoting rest and restoration. Since hydroxylamine is an inhibitor of GABA degradation, it would be interesting to see what effect it has on psychoses, though it may be too toxic to be practical; the same might apply to hydrazine, which is used with considerable success in inoperable cancer and often induces sleep as well as preventing cachexia. It raises the level of ATP systemic ally. Injected GABA is usually considered to enter only the fetal or infant brain, because of the "blood brain barrier" of the more mature organism. However, Nasonov and his students have shown that many kinds of stress will eliminate the barrier and that it can be interpreted as a physical state of the neuron, governing solubility. This suggests that GABA itself may be able to enter the brain and exert a beneficial inhibitory action if the brain is in a state of exhaustion from stress.

Another enzyme that should be investigated from this point of view is NADase, since it too shows what may be a sensitivity to structure: in cell homoge-nates, it is sufficiently active to destroy NAD and thus stop glycolysis at the triose phosphate stage (Florey, 1966); it is inhibited by nicotinamide, but is also

relatively inactive in the intact brain, at least in the intact non-schizophrenic brain.

Magnetic fields presumably act biologically by acting on the structure of water, and Kholodov has established that a continuous sinusoidal magnetic field has a sedative and inhibiting effect, modifying the EEC and raising the level of GABA in the brain (Speranskiy, 1973). The activity of oxygen increases in magnetically treated water (Speranskiy, 1973), so there might be a direct effect on energy production.

Since DMSO has been used successfully for treating mental retardation, with removal of cataracts as a side effect, its effect of "structuring" water, or lowering its "activity" according to a Soviet study, and of promoting oxidation of glucose by quinone (my unpublished observation) suggests that it might improve the function of nerves and other cells by promoting the desired high energy state.

During an epileptic seizure, a localized vascular "blanching" has been observed in the exposed brain. Since vasoconstriction occurs in the brain when the concentration of carbon dioxide is low, such a spasm might occur when metabolic inefficiency interferes with the production of carbon dioxide. Thus epilepsy and schizophrenia might benefit from similar treatments. This theory suggests that we should look for more general mechanisms in known therapies: for example, the ability of Dilantin to lower insulin levels could improve the supply of glucose to the brain.

One of the older therapeutic uses of niacin is in the treatment of "trench mouth," which is a reaction to stress (Cohen, 1973), though a protein deficiency is also probably involved. Since the gums are responsive to many agents (including Dilantin and cigarette smoking) and are easy to inspect, they may provide an additional means for following the course of recovery when schizophrenia is being treated with niacin.

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