Recent research has led to the evolution of an important clinical relationship among psychology, neurobiochemistry, and nutrition. The result has been the development of the multidisciplinary field of psychoneuro-nutritional medicine. The successful application of this medical model to mental health problems ranging from behavior disorders in children to cognitive/emotional disorders in adults has opened the door to new lower-technology, cost-effective approaches to improving functional neurobiochemistry. This review describes the psychoneuro-nutritional medicine model and its application to a variety of biobehaviorally related health problems. (Alternative Therapies in Health and Medicine. 1995;1(2):22-27)

The nature-nurture debate continues: are our attitudes, beliefs, and behaviors established as a consequence of our genetic nature, or are they grounded in the environment in which we were nurtured? Although this discussion holds relevance for scholars, it may be of minimal importance in the clinical management of psychological problems. During the past decade it has become apparent that these two aspects of personality development are really one and the same, and both are part of a holographic description of behavior. We now recognize that the phenomena that bathe our nervous system daily with experience serve as energy field inducers to translate the potential that lies resident within our genetic structure into the agents of action that ultimately produce muscle contraction, nerve excitation, hormone secretion, gastric activity, cell reparation, and changes in immune system activity. An example of this phenomenon is the unexpected pregnancy of a woman who, until she went on a long vacation with her husband, had for years been unable to conceive a child. Or consider the man whose “heart disease” symptoms vanish as soon as he is honest about the problems he faces in his life. These hypothetical examples represent the powerful physiologic connection our perceptions and attitudes have to our neurochemistry and its effects upon our physiologic status.

We now recognize that the central nervous system is both an energy producer and an energy transmitter that communicates with the rest of the body through electrical and chemical signals that have been compared with quantum mechanical events and chemical communications through the secretion of neurotransmitters and neuromodulators. We know that phenomenologic messages originating from sight, sound, taste, touch, and energy fields are transduced by specific structures within our nervous system that give rise to physiologic responses. The translation of observation into response is in part governed by messages encoded within our unique genetic inheritance factors. The translation of this genotype into the phenotype of function in any individual is dependent not only upon the intensity, duration, and frequency of the stimulating factor(s), but also upon the presence or absence of specific effectors that help translate the genetic message into physiologic activity. Many of these effectors are agents derived from our diet, a fact that ties the functional status of our nervous system to our nutritional status. Richard Wurtman, PhD, was one of the first brain chemistry investigators to report the role of nutrition in the regulation of neurotransmitters.

The relationship between our behavior and our environment is complex, but it is clear that genetic inheritance factors, environmental stimuli, and nutritional factors work together in a well-controlled system to regulate neuronal function, which to a great extent determines cognition and behavior. Significant questions have been raised concerning this mechanistic view of behavior. Does it mean, for example, that a person with antisocial or criminal behavior is a product of such determinants as bad diet or faulty genes? It is premature to jump to the conclusion that behavior is governed by a single determinant, but evidence suggests that the genes we carry through life have been modified in their expression by the intensity and pattern of exposure of the nervous system to experiences and environmental.
factors, including nutrition. The flexibility, complexity, regulatory activity, filtering, organizational structure, and mind-body interactions of the nervous system are related in part to the nutritional status of the person, from conception through old age, which is a major factor contributing to the regulation of brain chemistry. Experts in the field including Sidney Cohen, MD, have gone so far as to suggest that there is "no crooked thought without a crooked molecule in the brain."

**NEURONAL FUNCTION AND ITS RELATIONSHIP TO NUTRITION**

Nutritional status influences all phases of the nervous system, including activities at the axons and synapses. The brain is fueled principally by glucose, which is metabolized in the mitochondria in the axon, in the presence of vitamins and minerals, into energy intermediates such as adenosine triphosphate (ATP), which are required for the synthesis and secretion of neurotransmitters. The neurotransmitters regulate the physiologic processes associated with such diverse activities as perspiring when we are nervous, a racing heartbeat when we are frightened, increased appetite before a meal, and thirst when our bodies require fluids. Even dream states and the way our brains process information are related to the nutritional status of our nervous system. Numerous studies published during the past 2 decades, including those of Ruth Harrell, PhD, indicate that poor nutritional status is associated with reduced performance on tests of cognitive function and alterations in neuropsychologic performance, irrespective of the age of the individual. Investigators at the US Department of Agriculture Research Service (Grand Forks, ND), for example, found that performance on cognitive tasks in individuals 65 years or older was tied closely to nutritional status. A person who is deprived of the B vitamins is less able to cope with mentally demanding tasks, and test results show alterations in psychologic and neurophysiologic performance.

Similarly, studies have shown that children with higher intake of B vitamins and other brain-active micronutrients performed better in school than did those with lower intake of these nutrients. Also, children who are exposed to low levels of the neurotoxicant lead through their food, water, and air have impaired learning and memory and a reduced intelligence quotient. Lead is known to prevent proper central nervous system metabolic activity. Cadmium and mercury in the diet and environment have also been identified as potential behavioral teratogens, adversely affecting the functioning of the central nervous system.

**NUTRITIONAL RELATIONSHIPS TO NEUROTRANSMITTERS**

Research in neurophysiology has increased rapidly in recent years, and new neurotransmitters have been identified. Among this increasing family of neuroactive substances, the neurotransmitters acetylcholine, serotonin, and the dopamine family have been the most studied in relation to the control of brain activity. Whereas acetylcholine is related to the availability and metabolism of the B-complex nutrient choline, serotonin, a mood-normalizing neurotransmitter, is derived from the essential amino acid tryptophan, which is found in dietary protein. Lack of availability of tryptophan in the diet, or an imbalance of tryptophan in relationship to other amino acids found in dietary protein, can result in the depression of the serotonin level. Studies have indicated that the pain threshold, which is partly controlled by serotonin, falls as dietary tryptophan levels decrease in animal diets, and that mood indication scores are related to the availability of tryptophan.

**FIGURE 1 Influence of nutrients on the synapse**

Nutritional status may also play a role in controlling synaptic function. Nervous system messages that must pass across the synaptic cleft require the release of acetylcholine, as shown in Figure 1. Acetylcholine is derived from the B-complex nutrient choline, which is derived from the diet. Insufficiencies of choline and other members of the B-complex vitamin family can have an adverse effect upon the synthesis, release, and metabolism of acetylcholine, thus altering neuronal function.
The dopamine (catecholamine) family of neurotransmitters, which is involved with arousal, includes adrenaline and noradrenaline. This family of neurotransmitters is created from another protein-derived essential amino acid, phenylalanine, and its companion amino acid, tyrosine. Considerable evidence indicates that imbalances of phenylalanine and tyrosine relative to tryptophan as well as insufficient vitamin B₆ levels can alter the balance between mood arousal and mood inhibition, resulting in changes in sleep patterns, affective states, response to stimuli, and arousal.²⁰

The fact that acetylcholine, serotonin and its metabolites, and dopamine and its metabolites are all derived from essential nutrients indicates that the nutritional status of the individual, based on unique genetic needs, may play a significant role in determining that person’s functional neurobiochemistry, cognition, and behavior.

In a sense, what we have learned during the past decade is that the activity and function of the nervous system are related to the availability and metabolic activity of various nutrient-derived substances, including amino acids, vitamins, minerals, essential fatty acids, and such other “conditionally essential” nutrients as taurine, carnitine, glutamate, and tetrahydrobiopterin.²¹

**‘CONDITIONALLY ESSENTIAL’ BRAIN-ACTIVE NUTRITIONALS**

Extensive research indicates that the conversion of phenylalanine and tryptophan into their respective neurotransmitters is in part regulated through the nutrition-related substance tetrahydrobiopterin. This substance, which is closely related to the B-complex nutrient folic acid, is actively involved in the stimulation of various metabolic activities in the brain that help control the conversion of phenylalanine to the dopamine family of neurotransmitters, and of tryptophan into its neurotransmitter metabolites.²¹ Interestingly, tetrahydrobiopterin also has an impact on the activity of the immune system. We now recognize a close relationship between the activity and function of the nervous system and that of the immune system. Some anatomists, in fact, have advocated rewriting textbooks that treat the nervous and immune systems separately, to describe neuroimmunology as a single interacting system. Candace Pert, PhD,²³ has identified neurotransmitter-binding sites on the surface of white blood cells, which, according to Pert, indicates that the nervous system can “communicate” directly with the immune system. Since that discovery, it has become more obvious that the nervous and immune systems interrelate in a number of ways. What is new information is the recognition that both nervous and immune system functions are dependent on specific nutrient factors they share for modulation of their activity.²¹

These nutrients are listed in the Table.

Research in psychobiology and neurology has revealed the amino acid relationship of a number of neurotransmitter systems that regulate neuronal activity. Three major systems that have been identified include the NMDA (N-methyl-d-aspartate), kainate and AMPA (alpha-amino-3-hydroxy-5-methyl isoxazole-4-propionic acid) systems.²⁶ The most thoroughly studied of these is the NMDA pathway, discovered by neuropharmacologist John Olney, PhD, who explained that the NMDA pathway is an excitatory pathway for neuronal activity; when it is overstimulated, the result can be “neuronal burnout.”²⁶ Substances such as monosodium glutamate are implicated as potential excitatory substances that, in sensitive individuals, may overstimulate the NMDA pathway, resulting in aberrant brain biochemical activity. The nutrients magnesium and zinc help normalize the NMDA pathway and retard the hyperexcitability that can occur from exposure to excess glutamate. Glutamate is produced in the nervous system through a variety of metabolic processes, many of which have nothing directly to do with monosodium glutamate. This research does indicate, however, that substances in a person’s diet or environment could contribute to hyperexcitability of the nervous system.

Another indication of neurotoxic substances in our environment is that certain cases of Parkinson’s disease in younger patients may be traced to exposure to a neuroexcitatory substance that is a byproduct of an extensively used street drug.²⁷ The recognition that certain young men developed a Parkinson’s-like disorder after consuming this neurotoxin has given rise to an environmental toxin theory of Parkinson’s disease. This extreme
example of how an environmental substance can alter the brain’s biochemical function and produce neurologic disorders suggests that many subtle factors in our environment and diet could cause alteration of the biochemical function of the brain and subsequent behavioral, perceptual, or cognitive changes.29

NUTRITIONAL TOXINS, HALLUCINOGENS, AND PERCEPTIONAL CHANGES

Certain edible plants have been known for centuries to have “magical,” or hallucinogenic, properties. The first Western report of a hallucinogen was recorded by Francisco Hernandez, personal physician to Philip II of Spain. Between 1570 and 1575 Hernandez reported on the hallucinogenic effects of the Aztec preparation ololiuqui: “When the priests wanted to commune with their gods and receive a message from them...they ate this plant; and a thousand visions and satanic hallucinations appeared to them.”29 Today we regularly employ a number of socially accepted mood-altering substances derived from plants. The most common of these are caffeine, theophylline, and theobromine, derived from coffee, tea, cola, and cocoa. Evidence now exists in the medical literature that excess consumption of these substances can result in significant alteration of both the central and peripheral nervous systems, creating changes in sleep patterns, cognitive function, and peripheral nervous system activity, as well as elevating blood pressure.30

A number of alkaloids found in various food products, particularly derived from mold that infects grain, can also alter brain chemistry. The suggestion has been made that the Salem witch trials occurred after a particularly mild winter and a rainy spring and summer, during which time grains became moldy, causing flour products to be contaminated with ergot alkaloids. Exposure to even small concentrations of these hallucinogenic alkaloids can dramatically alter perception and behavior; therefore, many of the altered states of behavior in Salem during that time could be traced to grain contamination.29 Today we recognize a number of mold metabolites such as aflatoxin, a powerful liver toxin, and other hallucinogenic alkaloids found in our food supply. People’s systems respond in different ways to exposure to these toxins. People with compromised detoxification systems may have a high level of sensitivity to these substances and therefore may display altered behavior from consumption of these toxins well before other people do. These people may be analogous to the caged canaries that were carried into coal mines to alert miners to the presence of toxic gases. If a canary was overcome by fumes and fell unconscious to the bottom of its cage, the miners knew to evacuate the mine shaft. Similarly, the response of our societal “canaries” to a toxic substance may be the first warning sign that the toxin could have an impact on physiologic functioning in the population at large.

Excess alcohol consumption also can have a significant impact on the function of the central and peripheral nervous systems. Based on genetic variations in the body’s ability to metabolize alcohol, some people have a higher sensitivity to alcohol than others.22 The liver of an Oriental person, for example, has a lower level of activity of alcohol dehydrogenase, one of the principal enzymes responsible for metabolizing alcohol. Therefore, that person may become inebriated quickly and develop flushing and other adverse reactions at a low level of alcohol consumption. Drinking alcohol may therefore be an unpleasant experience and people may avoid it as a consequence of their unique metabolism. A person who is able to consume more alcohol without adverse reactions, on the other hand, may suffer from the more direct nervous system effects of the higher level of alcohol. Excess alcohol consumption also results in the loss of magnesium, vitamin B12, and zinc, further complicating the control of brain chemistry and perhaps causing such conditions as Wernicke’s syndrome.31

THE IMPACT OF THE NUTRITIONAL ENVIRONMENT ON THE ANATOMY AND PHYSIOLOGY OF THE BRAIN

Both nutritional status and agents such as toxicants that influence brain biochemistry can affect perception, cognitive function, and behavior. These effects strongly suggest that the environment has a profound influence on brain anatomy and physiology. In 1874 Charles Darwin noted that the brains of domestic rabbits were considerably smaller than those of wild rabbits. He suggested that the small brain size might have resulted from generations of close confinement of domestic rabbits, which restricted the exercise of their intellect, instincts, sense, and voluntary movements. This argument seems to belie the genetic paradigm of our day.

However, after nearly 30 years of research, Marian Cleeves Diamond, PhD, at the University of California at Berkeley, has written that brain anatomy and function are significantly altered by environmental experience.30 Diamond’s work with animals has conclusively demonstrated that environmental enrichment through sensory and nutritional stimulation results in an increased number and size of synapses, cortical thickening of the brain, and increased potential to secrete the neurotransmitters that regulate neuronal function.32 Animals placed in an impoverished environment have fewer and smaller synapses and thinner cortices of the brain, and they are much less successful in learning and problem solving than are animals raised in an enriched environment. Diamond’s observations may have profound implications for the emergence of an integrated form of medicine, because they suggest that brain function, from infancy through old age, may benefit from sensory and nutritional stimulation.

In a study of elderly nursing home residents, those who appeared to be suffering from depression and dementia demonstrated significant improvements in intelligence quotient and mood when they were read to daily and supported in playing board games.33

Medical researchers have reported that cases of presumed senile dementia may result from vitamin B12 insufficiency.35 This condition is not uncommon in older individuals whose digestive problems cause them to consume suboptimal diets.
and inadequately absorb vitamin B₁₂. Correction of this problem often requires therapeutic administration of vitamin B₁₂ by intramuscular injection.

Infants who have suffered brain trauma also have been found to respond dramatically to a sensory and nutritionally enriched environment in a program called the Doman-Delica method. Thousands of parents around the world have been taught to employ this method, developed and refined throughout the past 40 years at the Institutes for the Achievement of Human Potential. Results of these studies are remarkable. They indicate that as a child’s neurologic and physiologic functioning improves through the training provided by this program, the brain metabolites tend to normalize.

INTERFACE OF PSYCHOLOGY, NEUROBIOLOGY, AND NUTRITION

No single factor appears to be paramount in improving brain biochemical, cognitive, or emotional function. Instead, what emerges is a pattern of multiple factors related to an enriched environment that includes improved nutrition. This more comprehensive view of the nature-nurture debate concerning behavior results from the recognition that a converging interface exists among psychology, neurobiology, learning theory, and nutrition. We now recognize that our sensory organs, working in conjunction with our central and peripheral nervous systems, help translate messages from the outside world into functional changes in our physiology.

The map upon which these relationships are drawn is each person’s unique genetic blueprint. In part, the translation of these messages from observed phenomena into physiologic functioning helps one discriminate “friendly” from “hostile” exposures. When confronted with a life-threatening situation, for example, the nervous system arouses response so one can either avoid danger by fleeing or prepare to face the threat head-on. Similarly, in the safe environment of the family, the nervous system facilitates communication, bonding, and closeness. If the nervous system loses the ability to discriminate friendly from hostile stimuli, everyday encounters might result in unusual responses.

In the physiologic equivalent of this relationship, 70% of the immune system is clustered about the digestive system. The purpose of this positioning is to help the digestive system recognize nutritional “friends” from hostile substances that appear in the diet as toxins. Because the immune system is constantly communicating with the nervous system through neurotransmitter receptor sites on the surface of immune-active cells, cross-talk takes place between the brain (which controls behavior) and toxic agents in the diet. This fact should not come as a great surprise. It is well known in hospital-based medicine that older patients who consume a high-protein diet frequently develop psychosis and hallucinations associated with hepatic encephalopathy. This condition is a consequence of the conversion of dietary protein by bacteria in the gut into toxic molecules that are absorbed into the bloodstream. Because the liver detoxification functions of older individuals are impaired, these toxic molecules pass on to the brain, where they can alter nervous system function.

Many people suddenly feel sleepy, tired, or aggravated, or develop a headache after they consume certain foods. We now know that such foods as red wine, cheese, chocolate, and bananas contain tyramine, which causes “toxic” side effects when ingested by an individual in whose liver the activity of the enzyme monoamine oxidase is genetically reduced. Similarly, some people are sensitive to sulfites in their foods. Because they have genetically impaired activity of the enzyme sulfite oxidase, these people experience adverse nervous system effects after ingesting foods containing sulfites. Other people are sensitive to proteins in dairy products or wheat and may experience alterations in brain biochemical functions when they ingest these proteins. These reactions are not true food allergies but what clinical immunologist JO Hunter, MD, refers to as enterometabolic disorders. Hunter originated this term to describe reactions to substances consumed in the diet and metabolized in the intestinal tract that produce metabolic effects on the nervous and other physiologic systems.

As Figure 2 illustrates, all the new insights into behavior, physiologic function, and nutrition can be combined into a comprehensive new paradigm called psychoneuro-nutritional medicine. This new concept allows clinical psychologists, psychotherapists, psychiatrists, and primary care physicians to develop integrated insight into the assessment and evaluation of patients with complex biobehavioral symptoms. The medical paradigm that emerges is more integrated and holographic (eg, networked in time/space) than the traditional differential diagnosis and treatment model. The new model deals with the functional aspects of the nervous system in connection with the environment and diet. Using this model, one evaluates the algorithm that is developed from the interaction of a person’s genetic potential and environmental factors that modify the expression of this genetic structure into function. From a nutritional perspective, this model is valuable as both an assessment and treatment tool, because it examines the interrelationship of the patient’s diet, lifestyle, environment, and genetic family history with the presenting symptoms. This method of patient evaluation, called patient-centered assessment, leads to a more complete understanding of the interrelationship of these factors in determining the severity, duration, and frequency of the patient’s problems and how those problems relate to modifiable factors such as diet and environment. Nutritional intervention derived from this model is directed at reducing one’s exposure to substances that cause a neurotoxic response and enhancing
Psychoneuro-nutritional medicine model

Patient presenting with cognitive-emotional-physical problems

Evaluation of degree of impairment: severity, frequency, duration

Physical examination: personal and family history

Psychological evaluation

Physiological and nutritional evaluation

Integrated treatment program

Diet prescription
Nutritional pharmacology
Psychotherapy and counseling
Exercise prescription
Environmental counseling

one's intake of nutrients and nutritional substances that help normalize neurochemical activity. Specific nutritional intervention, therefore, can improve cognitive and emotional function. This model can benefit people of all ages—from infants suffering brain injury to the elderly exhibiting the first signs of senile dementia—as well as those with affective personality disorders. In the future the psychoneuro-nutritional medicine model may play a major role in alleviating problems that are presently controlled through chemical incarceration with mood-altering medications.

References