

12

Psychoneuroimmunology- The Bridge Between Science and Spirit

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A new field of science and medicine, psychoneuroimmunology (PNI), has evolved out of the interaction of psychology, neurobiology, immunology, theology, yoga, shamanism, and the space program. The union has not been an easy one, nor is it condoned by all its peers - yet. PNI started off on the shaky ground of psychosomatic medicine, which claimed that emotions and stress influence illnesses such as asthma, allergies, and rheumatoid arthritis. That the psyche could influence the soma was not a popular idea in academic medicine forty years ago. Now, some "accidents" of science, corroborated by the unprejudiced observations of astute investigators add impetus to PNI's theories of mind-body connectivity.

ANATOMICAL CONNECTIONS

Underlying the beginnings of this infant discipline was the quest to identify biological links between the nervous system and the immune system¹⁻³ It must be kept in mind that until recently, it was believed that the immune system operated independently of any other system in the body. Because immune cells could function normally in the test tube, it was assumed that they were outside regulation by any internal or external factors.

Initial studies showed that there were nerves connected to the thymus, the primary organ of the immune system. Damage to the brain, specifically the hypothalamus and left cerebral hemisphere, was shown to damage the immune system.⁴ Similarly, vaccination, which stimulates an immune response was seen to accelerate the electrical firing of specific (noradrenergic) neurons in the hypothalamus.⁵ In other words, there was now anatomical evidence that the nervous and immune systems can communicate with each other. Further evidence came when it was demonstrated that cells of the immune system, the lymphocytes, have receptors for many of the chemicals synthesized in the nervous system, such as growth hormone, adrenalin and noradrenalin, prolactin, acetylcholine, substance P, endorphins, and enkephalins.⁶⁻⁹ Lymphocytes also can synthesize some of the same substances made by the nervous system, such as cortico-tropin and endorphins.¹⁰ Conversely, astrocytes, cells in the brain, can produce interleukin-1, an effector of immune reactivity once thought to be made only by the immune cells.¹¹ Not only are there anatomical links between these two systems of the body, but they also share many of the same biochemical functions.

CONDITIONING THE IMMUNE SYSTEM

The coup de grace that launched PNI into legitimate interdisciplinary dimensions was the controversial discovery by Robert Ader, a psychologist, and Nicholas Cohen, an immunologist, that the immune system could be trained just like a reflex. In other words, it could be conditioned to do new things.¹² A new assumption came to modern science: If the immune system could learn behaviorally, then it must be part of or at least influenced by the mind. Conditioning, one form of learning, often occurs without conscious perception of the process.

Pavlov's classical conditioning of the dog with a dinner bell set the stage for a scientific protocol to study learning and the immune system.¹³ Ader set out to discover how animals are conditioned to adverse stimuli. In his experiment, he fed rats saccharin-sweetened water paired with a one-time injection of a drug that would cause gastrointestinal upset. The association of the ill feeling with the sweet taste resulted in subsequent aversion to the saccharin-sweetened water. When thirst overpowered the aversion, the rats were obliged to drink the saccharin water. Unexpectedly, some of the animals died of infections during the extinction trials, and the mortality rate tended to vary directly with the amount of saccharin originally consumed. What was happening? Ader, in discussing the pharmacology of the drug he used, cyclophosphamide (Cytoxan), with immunologist Cohen, learned that this chemotherapeutic agent used in cancer treatment also suppresses the immune system. Even when the rats were no longer exposed to Cytoxan, they continued to suppress their immune system in response to the sweetened water alone. Together, Ader and Cohen went on to confirm that the immune system can be suppressed through a classical conditioning paradigm. Subsequently many investigators have substantiated and expanded their work.

Other findings have shown that the senses are powerful triggers for conditioning the immune system. In the 1920s and 1930s, Metal'nikov at the Pasteur Institute, injected bacteria into animals while simultaneously scratching their skin. Later, scratching alone evoked a large increase in white blood cell count and antibodies to the bacteria previously injected.¹⁴ Besides taste and touch, the smell of camphor as well as visual cues have been used in association with agents that suppress or enhance immune capabilities.^{13,15} In a series of experiments, Spector and associates conditioned interferon and natural killer cell activity by using a synthetic immunostimulant, Poly I:C, paired with the odor of camphor. Conditioning occurred after nine sessions. Poly I:C mimics the action of a virus, which acutely raises levels of interferon and natural killer cell activity. The odor of camphor alone, before conditioning, had no effect on immune functions.¹⁵ In human studies, conditioning stimuli have been the odor of incense, rhythmic drum patterns, and unusual patterns of stroking the skin..

Jeanne Achterberg, author of *Imagery and Healing*¹⁶ and *Bridges of the Bodymind*,¹⁷ once suggested that perhaps someday people with cancer could take a mint paired with an antitumor drug. Eventually they could stop taking the drug and get the same beneficial effects with the mint, eliminating toxic side effects such as vomiting and hair loss.

PLACEBO EFFECT

Any effect produced in the absence of an identifiable causal agent raises the question of whether a placebo (from the Latin for "I shall please") response is being triggered. The placebo effect has long been a nuisance to drug companies doing placebo-controlled studies to test new pharmaceutical agents. After all, how can a new sleeping pill be proved effective and commercially viable if experimental subjects who are strong placebo-responders sleep even better with an inert pill?

Although the mechanisms of the placebo response are not well understood, factors that influence placebo effects include the physician-patient relationship, the person's belief system, and environmental and cultural components. The existence of the placebo response implies that beliefs about one's own curative abilities can stimulate the necessary physiological systems that mediate healing. The psychological factors most commonly implicated are suggestion, expectation, anxiety reduction, and the hope and will to live. It has been suggested by Ader, Wickramaskera, and others that conditioning also may account for the placebo effect.^{18,19} Wickramaskera says: "All effective interventions have the potential for Pavlovian conditioning and triggering a placebo response. The response to any active ingredient includes two components: a placebo and an active component."

Virtually every physiological response in the body, including blood flow, pain control, and cancer cytotoxicity has been subject to a placebo effect, and in most studies the placebo accounts for at least 30% of all observed effects.²⁰ Its changes can be positive or negative, producing the same effect as the active drug and the same unpleasant side effects.

In the one area of placebo studies, the biological mechanism is understood. Jon Levine and his colleagues at University of California San Francisco' reported that placebos appear to modulate pain relief through release of endorphins, the brain's opiate-like pain-killing substances.²¹

ATTITUDES AND SURVIVAL

The existence of the placebo effect opened the door for seeking to understand if and how belief, attitude, and states of mind affect the physical body. Much of the initial work in this area looked epidemiologically at the psychological differences between those people who stayed well and those who get sick. An excellent overview of the historical work is found in Blair Justice's book, *Who Gets Sick*.²² Suzanne Kobasa, a pioneer in attitudes and health, studied executives from the Illinois Bell Telephone Company during the stressful time of federal deregulation and showed that certain mind states contributed to health and hardiness.²³ In Kobasa's subjects, the factors most predictive of healthy coping were the three Cs: *challenge* - the perception of a threat or change as a challenge, a problem looking for a solution; *control* - the ability to do something about the situation versus a feeling of victimization, and *commitment* - the sense of purpose in life, that there is something important to accomplish. The three Cs, which Kobasa deems the *hardiness factor*, have been shown to be the basis for resilience and survival in brutal circumstances, such as during the Holocaust and in prisoner-of-war camps.

Many attitudes, such as trust and nurturing, that contribute to health and well-being are formed, for the most part, during childhood. It is widely known that loving touch is essential in human infant survival and growth. One study found that if baby rats were gently handled every day from birth to weaning (22 days), they showed much smaller stress hormone responses than unhandled rats, an effect that lasted until "old age"-24 months.²⁴

The importance of childhood upbringing is implicated in the relation between learned hostility and coronary heart disease. Cultural differences in children shed some light on how attitudes learned as children influence later health and behavior. For example, a central feature of the typical Japanese personality is *amae*, the expectation of being treated well and with kindness by others. Child-rearing practices in Japan include close physical contact, little separation from the mother, and preference for maternal-child closeness over strict discipline. The child abuse common in the United States is virtually nonexistent in Japan.²⁵ Traditional Japanese mothers avoid expressing negative emotions toward or about the child and take care to spare the child embarrassment. The parental attitude toward the child is that he or she is good, wonderful, and clever. This early benevolent environment coupled with preliminary research findings of lower hostility scores among urban Japanese men led Williams and co-workers to postulate that the attitude of the Japanese toward their children is a contributing factor to lower rates of coronary heart disease in Japan compared with these in the United States, where child-rearing is very different. As discussed below, hostility has been identified as a key psychological factor in coronary artery disease.

The challenge for researchers and practitioners of PNI is to find ways to teach healthful attitudes to those who haven't learned them as children. A specific goal is to help people shift from a helpless mode to one in which they experience control and mastery. Subjected to uncontrollable stress from which they could not escape, animals were more likely to experience infections, increased tumor growth, and other experimentally induced diseases.^{27, 28} This led to the understanding that in people, too, helplessness and lack of control have long-range effects on mental and physical health. Furthermore, helplessness and optimism can be learned. As suggested by Martin Seligman, helplessness in one stressful situation often is carried over to others.²⁹

The importance of a sense of control to overall health increases as we age. Research in the area of aging and autonomy has suggested that the ability to choose one's environmental surroundings is important in healthy aging. Adverse effects on health after admission to a nursing home were in part a function of the amount of individual control over the move. Prospective residents given a choice about when and where they moved as well as about some specifics of the living arrangements showed little decline in level of health and psychological well-being. Lack of control has adverse effects on emotional states, performance, and subjective well-being.³¹ As we age, the locus of control often changes from internal, or directed from within, to external, or imposed from without.

PNI provides a scientific structure for understanding the biology and psychology of how attitudes or emotional states, like optimism, or internal locus of control impact the immune system, the quality of life, and longevity.³² PNI research also provides us with the rational incentives to search for empirical ways to alter consciousness to improve health. Negative emotional states, such as depression,³³ loneliness,³⁴ hopelessness,³⁵ and bereavement³⁶ suppress immune function, making a person more prone to illness. Anger, another so-called negative emotion,

appears to have its first effects on the cardiovascular system rather than the immune system. In the 1950s, Meyer Friedman and Ray Rosenman introduced the concept of coronary-prone or Type A behavior - the fast-paced, impatient "hyper" person - to help explain the increased incidence of coronary artery disease in twentieth-century Western societies.³⁷ More recently, Redford Williams and others showed that not all Type A behaviors were life-threatening.^{38,39} Hostility, lack of trust, and cynicism seem to be the damaging components of Type A behavior.⁴⁰

Are there ways a person can counterbalance or change self-defeating attitudes and emotions and continue in a state of health despite great upheavals? It is the mandate of PNI to search for and develop these behaviors. With the benefit of Soviet science, we find clues to altering emotional behavior and physical responses -the mind-body dialogue.

THE SPACE PROGRAM, ATHLETICS, AND YOGA

Pioneering work on stress by Nobel laureate Hans Selye established that our emotions and mental states dramatically influence activities of the autonomic nervous system, such as hormonal activity and blood flow.^{41,42} Excitement or anxiety can increase blood pressure and heart rate and cause blood vessel constriction, producing cold hands and feet. Worry, depression, or performance anxiety can slow other body and brain functions.

During our day-to-day existence, we all experience emotional ups and downs, but there was one arena in which emotional instability was unacceptable -the Soviet and American space programs. In the early 1950s, initial efforts of the Soviet space program were aimed at exploring the possibility of using the techniques of yoga to teach cosmonauts to control psychological and physiological processes while in space. Yoga is an ancient Eastern mental and spiritual system in which the practitioner can learn to regulate functions such as temperature, heart rate, and mental concentration. Using the traditional teachings, the Soviets developed methods of control that depend on feedback signals between the body and the mind. The training emphasized voluntary control of heart rate and muscle tension as well as of emotional reactions to stressful situations like zero gravity. Before this work, most scientists, unfamiliar with or skeptical of yoga, believed that these autonomic, automatic functions were outside conscious control.

Similarly, in the early phases of the American space program, National Aeronautics and Space Administration (NASA) scientists predicted that during prolonged lunar spaceflights, astronauts would experience irregular blood pressure and heart rate along with emotional lability. To combat these effects, rather than risk drugs that had never been tested at zero gravity, NASA began to explore self-regulation through meditation and biofeedback. In a spaceflight simulator, the astronauts were taught how to preprogram their minds and bodies for optimal space performance. Yet even with their self-regulation abilities perfected, when the astronauts returned from orbit, they showed some damage to immune function and decreased bone density. The latter was in part attributed to hypersecretion of adrenal stress hormones, the corticosteroids.⁴³

What was learned in space projects like Apollo -the disciplined use of imagination, the importance of mental rehearsal, and biofeedback - contributed to PNI's investigations into which specific self-regulatory methods are most effective in reversing the negative effects of stress, emotions, and thoughts.

From their success with controlling automatic responses in the cosmonauts, Soviet scientists set out to discover how emotional reactions, detrimental to peak athletic performance, could be regulated consciously before competition. They discovered that certain mental training techniques helped to combat stress and heighten physical abilities. The power of visualization and imagery to alter physical performance was first evident in recent times in weight lifting, golf, skiing, and tennis. Many *Inner Games* of - books were written in the 1970s, using imagery, mental rehearsal, and relaxation to improve performance in these sports.

Superior athletic performance brought to public awareness the effects of stress, attitude, and mental training on physical training and prowess. In his book *Peak Performance*, Charles Garfield describes how athletes identify the signs of stress and negative emotions as shortness of breath, lost coordination, cramped muscles, and the inability to perform optimally.⁴⁴ In other words, when an athlete is worried about his or her performance, the body responds in ways that makes performance less successful.

The body-mind methods that have been perfected for optimal performance in astronauts and athletes are finally entering the health arena. From the traditions of yoga, a new body-mind technology is achieving scientific respectability and proving to be useful "medicine" in many health-promoting settings.

RELAXATION RESPONSE, MEDITATION, AND PRAYER

Harvard physician Herbert Benson studied yogis and other people engaged in meditation practices for biological clues to possible health benefits. His work has contributed substantially to integrating yoga with a modern understanding of stress. Central to Benson's definition of the relaxation response is his idea that the body operates in a yin-yang, on-off manner. For every *on* reaction, or stress response, he believes that there must be a corresponding *off* response.^{45, 46}

Benson showed that the relaxation response, exemplified in transcendental meditation, improves hypertension and irregular heart rhythms. Since his initial studies, it has been learned that meditation is effective in alleviating presurgery anxiety and the adverse effects of cancer chemotherapy and can decrease a diabetic's need for insulin. By putting the body in a state of altered consciousness and lowered biochemical arousal, a more balanced homeostasis is achieved.

Benson expanded his study of the biological effects of meditation to discover its heart- and consciousness-opening abilities;. He began to see a relation between meditation and prayer. The study of prayer seems to have no place in science, yet a much-quoted study done by cardiologist Randy Byrd at San Francisco General Hospital looked at the effect of prayer in 343 patients who had suffered a myocardial infarction (heart attack).⁴⁷ Compared with a control group of 201 patients, the 192 patients named in prayer had fewer complications while in the cardiac care unit. The prayed-for group had between five and seven Protestants, Catholics, and Jews across the United States praying for them each day. Those praying were given the patient's name, diagnosis, and condition and were asked to pray for the beneficial healing and quick recovery for each person. In this experiment, the patients were not told or the prayers, nor did the people praying personally know those whom they were praying for. Although such a unique study is highly suggestive, it is difficult to design and execute studies in the accepted methodologies of science to test these subtleties.

SOCIAL TIES THAT BIND

Similarly, characterization of the potential of personal relationships to benefit health and longevity has seemed implausible 'as a biological experiment. Work by dedicated investigators, however, is beginning to show what we intuitively might expect: that the kinds of relationships we have affect our risk of disease. The residents of Roseto, Pennsylvania, have most of the risk factors for heart disease - a high-fat diet, obesity, smoking -yet they have significantly lower rates of heart disease than the rest of the United States.⁴⁸ Why? The conclusion was that this is a close-knit community in which the social ties are strong.

Other ground-breaking work on the importance of the quality of relationships, intimacy, and health came first from epidemiological studies and then from research by James Pennebaker and his associates. Prospective epidemiological studies showed greater morbidity and mortality in people with fewer close relationships.⁴⁹ Both the quality of relationships and their disruption influence immune function. Furthermore, Pennebaker, Janice Kiecolt-Glaser, and Richard Glaser showed that being able to express emotions from past traumatic events improves not only immune function in the test tube, but also health.⁵¹ In Pennebaker's original experiments, college students who had been sexually or physically abused as children spent fifteen minutes a day writing about their early traumas.⁵² In their journals, they emphasized their feelings -rather than the narrative of the events. After a trial of only four consecutive days of writing, long-range effects were apparent. The students had stronger lymphocyte reactivity, used the student health service significantly less frequently for illness, and had less subjective distress than a control group of students who wrote about random, nonemotional things. Failure to confront a buried trauma forces the person to live with it in an unresolved manner; actively confronting it allows for understanding and assimilation.

The salutary effects of intimate relationships and the ability to disclose emotional traumas were further demonstrated in support groups for breast cancer patients in research by Stanford psychiatrist David Spiegel.⁵³ After one year, patients reported only subjective changes such as mood improvement and pain reduction. Then, unexpectedly, in a ten-year follow-up, a difference in survival time was discovered in those patients who had been in the support group. Such compelling evidence of prolonged survival resulting from group psychotherapy suggests

that one major change in the practice of medicine should be the inclusion of psychosocial support as an integral part of any cancer therapy program.

FUTURE HEALTH AND MEDICINE

PNI is in a position to create a solid theoretical framework for preventive medicine. By continuing to provide experimental data, as much as possible, on the mind-body connection, PNI will clarify how mental states confer susceptibility to and protection from illness. Concomitantly, PNI clinicians will define practical means of strengthening the internal environment.

The clinical applications of this information may be of profound value for people with AIDS (acquired immune deficiency syndrome), cancer, and autoimmune diseases such as rheumatoid arthritis. Even in the absence of unequivocal laboratory data on the beneficial effects of imagery and relaxation on immune function and longevity, these modalities are being effectively used for improving the subjective quality of life in people with illness or stress.

This chapter has focused on the objective aspects of PNI. It provides the reader with a context in which to interpret future work on the effects of consciousness~altering modalities on health. Medical science tends to emphasize quantitative, reproducible outcomes from quantifiable, reproducible interventions. In our efforts to seek out the hard facts, we also must acknowledge the role of spirit in healing. The effects of subtle energies may be more elusive, less universal than those of, say, penicillin. But the results for the individual are no less dramatic.

Medically, PNI will offer insight into how, beyond the chemical changes, consciousness affects the body. Philosophically, PNI promises to leap from its formal proofs to an elucidation of the spiritual component of healing and the quest for purpose essential to health and quality of life.

NOTES

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Rest of notes omitted.