

PSYCHONEURO-IMMUNOLOGY: The Bridge Between Science and Spirit

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A field of science and medicine, psychoneuro-immunology (PNI), has evolved out of the interaction of psychology, neuro-biology, immunology, theology, yoga, shamanism, and the space program. The union has not been an easy one, nor is it totally embraced by mainstream medicine. Yet, PNI started off on the shaky ground of psycho-somatic 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 once infant discipline was the quest to identify biological links between the nervous system and the immune system. (1-3) It must be kept in mind, that it was once 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 of 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 or changes to the brain, specifically the hypothalamus and left cerebral hemisphere, was shown to damage or alter immune functions. (4) Similarly, vaccination, which stimulates an immune response, accelerated electrical firing of noradrenergic neurons in the hypothalamus. (5) In other words, growing anatomical evidence confirmed that the nervous and immune systems could communicate with each other. Further evidence came when it was demonstrated that lymphocytes, the cells of the immune system, 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) In addition, lymphocytes also can synthesize some of the same substances made by the nervous system, such as corticotropin and endorphins. (10) An effector of immune reactivity, interleukin-1, once thought to be made only by immune cells can be produced by brain cells. (11) Not only are there anatomical connections between nervous and immune systems, they also share many same biochemical properties.

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, immune cells could be conditioned to do new things with sensory input. (12) A new assumption and branch of medicine – PNI - came to modern science: If the immune system could learn behaviorally, then it must be part of, or at least influenced by the mind. (13, 14) Conditioning often occurs without conscious perception of the process. Sensory conditioning can trigger an automatic, unconscious physiologic response.

Pavlov's classical conditioning of salivation in a dog with the sound of a dinner bell set the stage for the scientific protocol to study learning and the immune system. (15) To discover how animals are conditioned to adverse stimuli, Ader fed rats saccharin-sweetened water paired simultaneously with a one-time injection of a drug that would cause gastrointestinal upset – the adverse response. The association of the ill feeling with the unusual taste resulted in subsequent aversion to the saccharin-sweetened water. However, when thirst overpowered the aversion, the rats were obliged to drink the saccharin water. Unexpectedly, after about thirty days some animals began dying of infections; those that died had consumed the most saccharin-sweetened water. What was happening? Ader, in discussing the experiment with immunologist Nick Cohen, learned that the drug he used to cause GI upset (cyclophosphamide - Cytoxan), a cancer chemotherapeutic agent known to cause nausea, also

suppresses the immune system. In this experiment, the rats were exposed to Cytoxan once and even though the rats were no longer exposed to immunosuppressive Cytoxan, they continued to suppress their immune systems by drinking the saccharin-sweetened water. Ader and Cohen went on to confirm the unexpected, that the immune system could be suppressed through a classical conditioning paradigm. Subsequently many investigators have substantiated and expanded their work.

Other studies have shown that all the physical senses are powerful triggers for conditioning the immune system as well as other autonomic behaviors. In the 1920s and 1930s, Metal'nikov, at the Pasteur Institute, injected bacteria into animals while simultaneously massaging their skin. Later, that touch alone evoked an immune response showing a large increase in white blood cell count and antibodies to the bacteria previously injected. (16) Besides taste and touch, smell (of camphor) and visual cues have been used in association with agents to suppress or enhance immune capabilities. (15, 17) In a series of experiments, Spector and associates conditioned the production of interferon and natural killer cell activity by pairing a synthetic immuno-stimulant, Poly I:C, with the smell of camphor. Conditioning occurred after nine sessions. Poly I:C mimics the action of a virus, which rapidly raises levels of interferon and natural killer cell activity. The odor of camphor alone, before conditioning, had no effect on immune functions. (17)

Jeanne Achterberg, author of *Imagery and Healing* (18) and *Bridges of the Bodymind*, (19) once suggested that perhaps someday people with cancer could take a mint paired with an anti-tumor drug. Eventually they could stop taking the drug and get the same beneficial anti-tumor effects with the mint alone, eliminating any toxic side effects of the drug.

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 proven 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 yet well understood, factors that influence the effects include 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. Ader, Wickramasckera, and others suggested that conditioning also might account for the placebo effect. (20, 21) Wickramasckera 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 many studies, the placebo accounts for at least 30% of all observed effects. (22) Changes can be positive or negative, producing the same expected effect as the active drug and the same unpleasant side effects. In one area of placebo studies – pain control – a biological mechanism is understood. Jon Levine and his colleagues at University of California San Francisco reported that placebos appear to modulate pain relief by releasing endorphins, the brain's opiate-like pain-killing substances. (23)

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 got sick. An excellent overview of the historical work is found in Blair Justice's book, *Who Gets Sick*. (24) Suzanne Kobasa, a pioneer in attitudes and health, studied executives from Illinois Bell Telephone Company during the stressful job-changing time of federal deregulation. She showed that certain mental states contributed to health and hardiness. (25) In these executives, 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 or helplessness; and Commitment-the sense of purpose in life or to family, that there is something important to accomplish. Those executives who faced the crisis at work with the three Cs stayed healthy. Kobasa calls the three Cs, the hardiness factor; these same factors 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. The hardiness factor also plays a role in survival from HIV and AIDS. (26) One biochemical explanation for this effect on health – when people feel challenged rather than threatened, they produce far less immune-suppressing cortisol. In addition, an attitude of hardiness means being able to take action; mental states influence behaviors.

Many attitudes, such as trust and feeling nurtured, that contribute to health and well-being are formed, for the most part, during childhood. It is widely known that loving touch is essential for survival and growth of babies, both human and other animals. In addition, touch in newborns alters the stress response. One study showed when baby rats were gently handled every day from birth to weaning twenty-two days later, they had lower stress hormone released than rats not touched, an effect that lasted until "old age" of twenty-four months. (27) Baby rats licked by their moms thrived long after the grooming practice was over. New epigenetic studies indicate that future offspring of the nurtured rats also thrive. (28)

Childhood upbringing is implicated in how attitudes and emotions affect later health particularly in the relationship between hostility and heart disease. Cultural differences between American and Japanese children shed some light on how attitudes learned as children influence later adult health and behavior. Child-rearing practices in Japan include close physical contact, little separation from the mother, and preference for maternal--child closeness over strict discipline. A feature of the "typical" Japanese personality is *amae*; the expectation of being treated well with kindness. Child abuse, unfortunately so common in the United States, is virtually nonexistent in Japan. (29) Traditional Japanese mothers avoid expressing negative emotions toward 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. (30) The early nurturing environment coupled with preliminary research findings of lower hostility scores among urban Japanese men led Redford Williams and coworkers to postulate that the attitude the Japanese have toward their children is a contributing factor to lower rates of coronary heart disease in Japan compared with the United States. (29) As discussed below, hostility has been identified as a key psychological factor in coronary artery disease.

A challenge for our society and practitioners of PNI is to find ways to learn and teach healthful attitudes to those who haven't learned them as children. One specific goal is to help people shift from a helpless mode to one in which they experience control and mastery. We learned that animals subjected to uncontrollable stress from which they could not escape, were more likely to experience infections, increased tumor growth, and other experimentally induced diseases. (31, 32) This led to the understanding that in people, helplessness and lack of control have long-range negative effects on mental and physical health. As suggested by Martin Seligman, helplessness in one stressful situation often is carried over to others. (33) Furthermore, helplessness and optimism can be learned. (34)

The importance of having a sense of control rather than helplessness to overall health increases as we age. (35) Research in the area of aging, attitudes 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 specifics of the living arrangements showed little decline in level of health and psychological well-being. (35) Conversely, lack of control has adverse effects on emotional states, subjective well-being, and longevity. (36) 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 framework for understanding how attitudes like optimism, emotional states, or a sense of control impact the immune system, quality of life, and longevity. (37, 38) It also provides us with the rational incentives to search for empirical ways to alter consciousness to improve health and quality of life. Emotional states, such as depression, (39) loneliness, (40) hopelessness, (41) suppress immune function, making a person more prone to illness. Depression and stress also put

people more at risk for coronary artery disease. (42) Inappropriate anger, another so-called negative emotion, appears to have its first effects on the cardiovascular system rather than immune functions. In the 1950s, Meyer Friedman and Ray Rosenman introduced the concept of coronary-prone or Type A behavior- the fast-paced, impatient, competitive "hyper" person- to help explain the increased incidence in coronary artery disease (CAD) in twentieth-century Western societies. (43) Redford Williams and others showed that not all Type A behaviors were negative or life-threatening. (44, 45) Hostility, lack of trust, and cynicism seem to be the damaging components of Type A behavior. Yet our culture still holds to Type As having more heart disease; the data don't support that. Now it's about Type H, the hostile, cynical character.

Dr. Dean Ornish added another piece to the mind-body puzzle of heart disease by initiating for people at risk for CAD, a lifestyle program of meditation, yoga, support group, and vegetarian diet with only 10% calories from fat. By engaging in a year-long program, many people reversed their cardiac blockages by simple lifestyle strategies. (47, 48) On long-term follow up, stress reduction and group support appeared to be the most important features. (49)

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 early Soviet science, we find clues to altering emotional behavior and physical responses via an effective 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 the autonomic nervous system, such as hormonal activity and blood flow. (50-52) Excitement and anxiety can increase blood pressure, heart rate and blood vessel constriction, resulting in tell-tale stress signs of cold hands and feet. Worry, depression, or performance anxiety can slow body and brain functions.

We all experience emotional ups and downs, yet this kind of emotional instability was totally unacceptable in 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 yoga techniques 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 these traditional teachings, the Russians developed methods of control that depended on feedback signals between the body and the mind. The successful training emphasized intentional control of heart rate, muscle tension, and emotional reactions to stressful situations like zero gravity. Before this work, most scientists, unfamiliar with or skeptical of yoga, believed that these autonomic, automatic processes were outside conscious control. (53)

Similarly, in the early phases of the American space program, National Aeronautics and Space Administration (NASA) scientists predicted that astronauts during prolonged lunar spaceflights would experience irregular blood pressure and heart rate along with emotional instability. To combat these effects, rather than risk drugs that had never been tested at zero gravity, NASA explored 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. (53)

Space projects, like Apollo, taught us that the disciplined use of self-regulatory methods such as imagination, mental rehearsal, and biofeedback, could be effective in reversing the negative effects of stress, emotions, and thoughts.

From their success in the cosmonauts with controlling automatic responses, like heart rate, Soviet scientists set out to discover whether emotional reactions, detrimental to peak athletic performance, could be consciously controlled before competition. In fact, they were able to translate mental training techniques for the cosmonauts, to help combat stress and enhance physical abilities in their athletes. The power of visualization and imagery to alter physical performance was successful for weight lifting, golf, skiing, running, and tennis. The result, in the 1970s, many books -"Inner Games

of" - were written using imagery, mental rehearsal, and relaxation of the astro-cosmonauts to improve athletic performance.

Outstanding athletic performance brought to the public, awareness that stress, attitude, and mental training effect physical training and competence. In his book *Peak Performance*, Dr. Charles Garfield describes how athletes can identify signs of stress and negative emotions as shortness of breath, lost coordination, cramped muscles, and the inability to perform optimally. (53) When an athlete is worried about performance, and doesn't deal with the worry, the body responds in ways that makes performance less successful.

The body-mind methods perfected for optimal performance in astronauts and athletes began to enter the health arena. From visualization by cancer patients to the practice of yoga and meditation for chronic pain, health consumers and medical research are finding that many of the "old ways" work. New body-mind technologies are 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 contributed substantially to integrating meditation with a modern understanding of stress. Central to Benson's definition of the "relaxation response" was his idea that the body operates in a yin-yang, off-on manner. For every on reaction, or stress response, he believes that there had to be a corresponding "off" response. (54, 55)

Benson showed that the relaxation response, exemplified by the practice of transcendental meditation, improves hypertension and irregular heart rhythms. Since his initial studies, it has been learned that meditation is effective in alleviating pre-surgery anxiety, adverse effects of cancer chemotherapy, and decrease a diabetic's need for insulin. By putting the body in a state of altered consciousness and lowered biochemical arousal, a more balanced metabolic state is achieved. Jon Kabot-Zinn and colleagues went on to achieve groundbreaking results teaching yoga and mindfulness meditation to people with unresponsive pain. People who committed to the 8-week program showed decreased pain even two to five years later if they continued practicing meditation. (56, 57) Now these practices are being taught in hospitals and health care settings throughout the United States; many are even covered by insurance.

It turns out that meditation does more than alter physiology, it influences relationships and spirituality. After years of study, Benson saw a relationship between meditation and prayer. Though the study of prayer seems to have no place in science, its tangible results are growing. A seminal study by cardiologist Randy Byrd at San Francisco General Hospital looked at the effect of prayer on 393 persons who had suffered a myocardial infarction (heart attack). About half of the patients were prayed for, the others weren't. The prayed-for group had five to seven people of different religions (Protestants, Catholics, and Jews across the United States) praying for them each day. Those praying were given the patient's name, diagnosis, and condition, prayed for the beneficial healing and quick recovery. (58) The prayed for patients had fewer complications while in the cardiac care unit compared with the control group. The patients were not told of the prayers, nor did the people praying personally know those whom they were praying for. Byrd's unusual results launched many prayer studies since including those of Dr. Larry Dossey and the late Dr. Elizabeth Targ.

SOCIAL TIES THAT BIND - People and our Health

Like prayer, the potential for personal relationships to benefit physical health and longevity seemed implausible as a scientific experiment. However, work by dedicated investigators is showing what we intuitively might expect: that the kinds and number of relationships we have affect our risk of disease. One of the initial studies was an epidemiological look at the residents of Roseto, Pennsylvania, who had the lowest incidence of heart disease in the United States. Yet it turned out they had most of the accepted risk factors for heart disease. They ate high-fat diets, smoked, didn't exercise, and many were obese. So why didn't they have heart disease?

(59) The researchers concluded that the advantageous factor was personal relationship. Roseto was a close-knit Italian-American community in which social ties were very strong. When the next generation started moving away and adopted better health behaviors – they stopped smoking, changed their diets, and began exercising – their health declined; the incidence of heart disease increased dramatically. The breakdown in close social ties was said to contribute to their increased heart disease

Groundbreaking work on the importance of the quality of relationships, intimacy, and health came from both epidemiological studies and research by Seymour Cohen and others. Prospective epidemiological studies showed greater morbidity and mortality in people with fewer close relationships. (60) In controlled human experiments, people exposed to rhinoviruses showed cold symptoms if they had fewer than six social contacts a week. Here the number of relationships influenced health. Cohen et al didn't even account for quality or intimacy. (61) Divorce, how spouses fought, and the quality of relationships affected immune functions more in women than men. (62) Furthermore, James Pennebaker, Janice Kiecolt-Glaser, and Richard Glaser showed that being able to express emotions from past traumatic events improves immune function in the test tube as well as physical health. (62) 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. (63) 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 only wrote about random, non-emotional events. The researchers' explanation for these interesting results - failure to confront a buried trauma forces the person to live with it in an unresolved manner exacerbating the stress response; actively confronting it, through writing, allows for understanding, assimilation, and release of the held-in stress. Pennebaker and colleagues went on to use this strategy with people with asthma or rheumatoid arthritis (RA) showing it to improve lung function in those with asthma and decrease pain in the people with RA. What's amazing about this – they wrote thoughts and emotions about an emotional trauma four days for only fifteen minutes. They enjoyed the benefits for more than six months. (64)

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. (65) After one year in the group, patients reported mood improvement and pain--reduction. Unexpectedly, in a ten-year follow-up, a difference in survival time was discovered in patients who had been in the support group. Such compelling evidence of prolonged survival from participating in a support group 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 or health-enhancing program.

Looking at this material fifteen years later, the history still speaks for itself with substantial evidence supporting how the mind, attitudes and stress influence risk factors and healing from disease. The one area I think relevant for our troubling times is the importance of supportive relationships to our well-being. Human contact and support is essential for any kind of health-changing program, be it for losing weight or changing the course of an illness. (66)

Kiecolt-Glaser showed that caregivers of parents with Alzheimer's Disease suffered considerable unrelenting stress; their health suffered as well. However if they had supportive relationships, their well-being and health improved considerably. (67, 68)

FUTURE HEALTH AND MEDICINE

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

environment. Many successful strategies have been put into play in health-care settings throughout the world. (69)

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, meditation, yoga and relaxation, these modalities are effectively being used for improving the subjective quality of life in people with illness or stress. (70) Fortunately, the relatively new National Center for Complementary and Alternative Medicine (NCCAM) now provides funding for such studies. They may even show how to improve quality of life and longevity. (71)

This chapter has focused on the objective aspects of PNI. It provides a context in which to interpret future work on the effects on health of consciousness-altering modalities. Medical science tends to emphasize quantitative, reproducible outcomes by exercising concrete, measurable interventions. Yet many of the interventions used for reducing stress and anxiety cannot be tested by the conventional placebo-controlled double blind study. We must develop new models for research. In our efforts to seek out the hard facts, we also must acknowledge the role of the individual and spirit in healing. The effects of immeasurable energies may be more elusive, less concrete than that of penicillin. Yet the results for the individual are no less dramatic. There is no 'one size fits all' for healing or diminishing risk factors.

Medically, PNI offers insight into how, beyond the chemical changes, mental, emotional, and spiritual states of consciousness affect the body. Philosophically, PNI promises to leap from formal proofs to an elucidation of the human and spiritual component of healing; an individual's quest for purpose is essential for health and quality of life. Personally, PNI offers the individual options and choices that began in ancient times with the underpinnings of modern science. Each person must be their own testing ground for choosing, exploring and discovering what works best for their well-being, whether they are challenged by an illness or life. It is only when we each make choices to change that we may discover what works for us.

To learn more, see this web site: www.SondraBarrett.com

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