International Foundation for
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The Neurobiology Basis of Mind Body Medicine

Convergent Traditional and Scientific Approaches to Health, Disease, and Healing

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Concepts of **HEALING**

For many centuries and in virtually every society, long before the appearance of evidence-based medicine, people with medical problems have turned to healers. It is striking to realize that only a handful of the drugs that were prescribed at the turn of the last century by Western physicians are still in clinical use (opiates, digitalis, aspirin, and quinine). Presumably, most of the rest of what physicians were doing at that time, and what they did for millennia before that, relied upon the healing effects of internal (endogenous) physiological systems activated by state of mind.

The universal concepts of traditional healing practices, ranging from the prehistoric shamans to the practitioners of Western Hippocratic, Traditional Chinese, Aryuvedic (a tradition in India), and Native American Medicine include the following beliefs:

- The belief in a universal life force (pneuma, chi, prana, animal magnetism, vis medicatrix naturae, bioenergy)
- The belief in the unity between mind, body, and universe
- The conceptualization of health as a state of harmony between mind and body, and between the organism and nature
- The conceptualization of disease as a loss of such harmony

The role of the healer was seen as a catalyst who uses subtle interventions to stimulate the body's own healing abilities, with the goal to re-establish harmony and the undisturbed flow of the universal life force. Even though the placebo effect is considered Western Medicine's eternal and most formidable competitor, it is agreed by all that placebo is effective at relieving pain and suffering. In fact, some of our best and most established therapies fall far short of the 30–60% placebo response rates seen in controlled clinical trials in many chronic disorders.

In the context of Mind-Brain-Body Medicine, the placebo response (even though poorly understood) is the manifestation of the remarkable self-healing abilities of the organism against a wide spectrum of diseases, ranging from coronary heart disease and cancer to rheumatoid arthritis and chronic pain. If we are honest with ourselves, treatment practices do not necessarily have to be better than placebo to find a useful place in medical practice, and honest practitioners have used this approach to the benefit of their patients for many years. Conversely, practitioners who eschew the healing arts in favor of only offering their patients scientific evidence-based therapies may be justifiably accused of doing their patients a serious disservice.

In the last century, in the movement to compare treatment to placebo, and to relinquish practices that were not superior to placebo, we have moved medical technology forward by enormous strides. At the same time, many patients and some physicians have come to expect that treatments, which meet this standard, should be available for all conditions and that evidence-based medicine should be able to provide cures, or at least effective treatment, for all ills. Alas, this has not proved to be the case. As a result, many patients in disillusionment have sought care from *alternative* healers and treatments, and many have received benefits that they value. The range of alternative

treatments[1] is enormous, from such generally accepted modalities as acupuncture and relaxation therapies, to herbal treatments and homeopathy, to meditation and spiritual practices such as prayer.

The current wave of interest in holistic (i.e., mind-brain-body) medicine practices has been generated by an unlikely alliance of forces, including breakthrough in neuroscience, economic considerations of managed care organizations, a popular demand for more natural healing approaches, and a general political concept of self-reliance (self-efficacy) applied to health and disease.

There is a tendency for many physicians to look down upon these therapies as "unscientific" or at best "unproven," and therefore not acceptable for patient management. Other physicians have recognized that patients often respond to kindness, human contact with perceived healers, and the attractiveness of a *holistic* view of health and disease as providing benefits, despite the absence of an effective evidence-based therapy. Interestingly, most of the popular alternative healing practices (e.g., homeopathy, acupuncture, bodywork, hypnosis, and Native American healing) share holistic views. These views are reminiscent of the historic concepts of health as a state of internal and external harmony, self-healing abilities of the body, and the health promoting effects of re-establishing the flow of "energy" or "life-force" within the body-mind continuum.

The disparity between patients' preferences or demands and traditional belief systems of health care providers has produced a national debate on the validity of alternative medicine. It has induced a major investment by the U.S. National Institutes of Health (NIH) in finding which parts of it may include therapies that can pass the test as evidence-based, meaning superior to placebo. Not only has the NIH recently established a National Center for Complementary and Alternative Medicine (NCCAM), but also a major resources have been made available to establish national NIH-sponsored Mind Body Research Centers. The current wave of interest in holistic (i.e., mind-brain-body) medicine practices has been generated by an unlikely alliance of forces, including breakthroughs in neuroscience, economic considerations of managed care organizations, a popular demand for more natural healing approaches, and a general political concept of self reliance (self-efficacy) applied to health and disease.

[1] In the context of this publication, *alternative treatment* means practices not generally taught in U.S. medical schools or available in U.S. hospitals.

The Sedona **MEETING**

In the spring of 1998, Emeran Mayer from the University of California, Los Angeles, and Clifford Saper, from Harvard Medical School—with the help of an organizing committee made up of Nancy Norton from the International Foundation for Functional Gastrointestinal Disorders (IFFGD), Bruce Naliboff, Margaret Kemeny, and Lobsang Rapgay—invited 48 individuals to Sedona, Arizona to discuss for 3 days the emerging convergence of science and ancient and modern comprehensive approaches to health and disease. Invited guests also included representatives from the Noetic Sciences Foundation and the Fetzer Institute. The multidisciplinary symposium, *The Science and Practice of Mind Body Interactions*, was in many ways a unique and first of its kind undertaking. The fact that the meeting was supported by the consumer products giant Proctor & Gamble, and the interest of Elsevier Science to publish the proceedings in their prestigious neuroscience book series, *Progress in Brain Research*, are by themselves testimony to a paradigm shift in society towards a more holistic view of health and disease.

The magic of Sedona, a mystical place amidst the red rocks of the Arizona desert a few miles from the Grand Canyon, facilitated communication between the participants resulting in marathon sessions which often started with Yoga and Mediation sessions in the early morning and ended with spirited scientific and philosophical discussions well into the night. The active participants were comprised of outstanding and internationally recognized scientific leaders in neurophysiology[2] and anatomy, and a group of prominent and unique practitioners of *mind-body medicine*. The interactions between these two disparate groups of individuals, who under other circumstances would not be likely to meet—let alone spend several days listening to one another's view points—was remarkable.

How do the mind and body interact with each other and with the environment... and in this process actively maintain health and prevent disease.

[2] *Neurophysiology* is the study of the functions of the nervous system—particularly how, why, and when nerve cells fire.

Mind Body Interactions in Health and Disease: **FROM ANCIENT HEALING TRADITIONS TO MODERN NEUROSCIENCE**

The meeting started out with some fascinating presentations by Lati Rinpoche, a Tibetan dignitary from Shartse Monastery, Mundgod, South India and Ursula Noki Wilson, a Native American Healer from the Navaho (Dine) tribe. Lati Rinpoche reviewed some key aspects of the Tibetan view of the mind, and discussed a series of meditative practices aimed at strengthening the abilities of the mind. The Tibetan Buddhist view of mind, its divisions, and the elaborate practices to achieve ideal states is a complex presentation of psychological, behavioral, and spiritual concepts. It is intriguing to consider some of the parallels of these *empirically* derived concepts, with the evolving scientific concepts of *cognitive neuroscience* related to mind-brain-body interactions.[3]

Ursula Noki Wilson gave a vivid presentation of the Dine way of looking at health, disease, and healing. By showing a series of sandpaintings, she demonstrated the sophisticated spiritual system, which views the individual as firmly integrated into a web of interactions with Nature, the Universe, and with other members of the tribe. The disturbance of the harmony in these interactions is viewed as the cause of disease, and reestablishment of the original harmony by elaborate rituals is essential for effective treatment.

> Even though (specific systems within the brain) are a major determinant of health of mind and body, we are only beginning to acknowledge these factors in Western clinical medicine.

As outlined by Emeran Mayer from UCLA, these concepts of harmony (at the level of the body, the mind, and in relationship of the individual to Family, Nature, the Environment, and the Universe) are at the core of healing traditions throughout the history of mankind, including the Chinese and Aryuvedic traditions, Shamanistic thought, and pre-scientific Western Medicine. The concept of disruption of harmony as cause of disease, and the role of the healer as a catalyst facilitating the reestablishment of lost harmony, or the uninterrupted flow of energy, was shared by many of these traditions. The healing process was not viewed as an heroic battle between the healer and the disease, but as a process in which the healer facilitates the body's own capacity for healing.

Up to the 17th century, Western medical thought (best summarized in Hippocratic writings) was based on the ancient holistic view of mind, body, and the Universe. It has only been with the advent of western science that a different, reductionist view replaced the ancient teachings. In this view, mind was separate from body and disease was viewed as a mechanical malfunctioning of parts of the body machine, which had to be fixed or replaced.

Following this overview of the traditional view of mind body interactions, Brent Vogt from the Bowman Gray School of Medicine, North Carolina attempted to address the mind from a very different, and typically Western perspective: Where in the brain is the mind located? Following a review of theoretical considerations, reports about patients with brain lesions and recent evidence from brain imaging studies, Vogt proposed that the fundamental components of mind are located in distinct brain regions (the cingulofrontal and parietotemporal confluence regions), that the mind is divided into functionally specialized regions (lateralized), and that the distributed mental activity is associated with a unified mind through various "binding" mechanisms, which link the involved brain regions into a unified functional circuit. The fact that a neuroscientist can discuss topics such as the spatial localization of the mind and of consciousness[4] within the brain clearly demonstrates the end of the Cartesian paradigm that relegated the Mind to the Church and as a topic non-suitable to scientific investigation.[5]

[3] *Empirically* derived concepts are formulated based on repeated experience and observation. *Neuroscience* is the study of the nervous system. *Cognitive neuroscience* looks at how the brain gives rise to processes by which we gain knowledge, become aware, and apply what has been learned.

[4] *Consciousness* may seem understandable and self-evident. But how can it be explained in scientific terms? The focus of neuroscience is physical neuro processes. How physical processes give rise to subjective experiences—to awareness, thoughts, and feelings—is a question only recently addressed by neuroscientists.

[5] We can distinguish the brain anatomically and study its function. But what and where is the mind? The *Cartesian paradigm* equated mind with consciousness, and consciousness with the soul. Inquiry into its nature, therefore, was assigned to the realm of theology, not of science.

The Neurobiological Mechanisms Underlying the
CENTRAL STRESS RESPONSE [6]

Several parallel pathways are activated by the organism in order to maintain a relatively constant internal stability (*homeostasis*) when faced with an actual or a perceived threat. These pathways, which have also been referred to as the emotional motor system[7], include several systems. One is the involuntary *autonomic nervous system*, which controls smooth muscle of the internal organs (viscera) including the gut, the glands, and the cardiovascular system. It is divided into the *sympathetic system*, which among many other functions, stimulates increased responses of the cardiovascular system and the *parasympathetic system*, which stimulates increased responses of the gastrointestinal system, in an effort to restore homeostasis. The *hypothalamic-pituitary-adrenal axis*, or HPA is a system that responds to stress by stimulating or inhibiting the release of various hormones, in particular cortisol, into the blood which then stimulate systems essential to self-preservation. Finally, the body has its own pain modulation systems. Examples include endogenous production of chemical neurotransmitters (endorphins) that are able to suppress and lower pain, and neural pathways that can inhibit as well as facilitate pain perception.

The concept of the organism's ability to maintain a state of balance within itself and with the environment through activation of central stress circuits is remarkably similar to the traditional concepts of harmony as a basis of health. However, it is important to realize that while the body's response systems normally have a protective (or adaptive) effect on the health and survival of the individual, their impact on various functions of body and mind can also become inappropriate or harmful (maladaptive). This may occur when a system's output is altered by genetic factors, early life events, or certain types of abnormal or repetitive (pathological) stressors—such as life threatening experiences, abuse, or chronic stress.

Bruce McEwen from the Rockefeller University, New York, discussed how the attempt of the organism to adapt to chronic stress can result in a maladaptive response with harmful effects on health, resulting in such common disorders as hypertension, coronary heart disease, obesity, and immune related disorders. McEwen calls this accommodation to chronic stress *allostatic load*, referring to the wear and tear that results from chronic overactivity or underactivity of systems that try to achieve stability through change.[8]

Esther Sternberg from the National Institutes of Health discussed the effects of over and under activity of the neural and hormonal (neuroendocrine) arm of the stress response, the HPA axis, on the immune system. Hyporesponsiveness (under activity) of the HPA axis—as seen in patients with rheumatoid arthritis, and a variety of so-called functional disorders such as fibromyalgia, chronic fatigue, and possibly irritable bowel syndrome (IBS)—appears to predispose to increased activity of the immune system. On the other hand, hyper-responsiveness (overactivity) of the HPA axis predisposes to enhanced susceptibility to certain infectious diseases.

> Alterations in the responsiveness of this system, on a genetic basis or due to environmental influences, are important factors in the pathophysiology of a wide range of chronic diseases ranging from coronary artery (ischemic) heart disease to irritable bowel syndrome (IBS).

Charles Nemeroff from Emory University in Atlanta discussed the evidence and the underlying mechanisms that link affective disorders (related to mood or emotional states), in particular major depression, with the development of atherosclerotic heart disease (a type of arteriosclerosis), and with the increased frequency of cardiac disease (morbidity) and mortality after an index myocardial infarction (heart attack). He identified chronic activation or hyperactivity of the HPA axis, increased sympathoadrenal responses (rapid sympathetic nervous system stimulation of the adrenal medulla and the "fight or

[6] Stressors are internal or external factors or stimuli that produce stress. They can be physical, biological, environmental, or situational. Each can activate central stress circuits in an individual. *Stress* is the neurophysiological and subjective response to the stimuli.

[7] The *emotional motor system* regulates different activities crucial to our survival. It controls systems such as heart rate, blood pressure, digestion, and respiration.

[8] Allostasis is the ability to achieve stability through adaptation or change. This process, which is critical to our survival, involves the autonomic nervous system, the HPA axis, and the cardiovascular, metabolic, and immune systems which act to protect the body by responding to internal and external stimuli. Paradoxically, these same systems, when activated by stress, can protect and restore as well as damage the body. *Allostatic load* refers to the damage that can result from chronic overactivity or underactivity of these systems.

flight" response), and diminished heart rate variability (corresponding to decreased *cardiovagal tone, or control of the heart rate)*) as major components in providing the link between an alteration of the mind (depression) and cardiovascular disease. These insights have already resulted in large-scale clinical trials aimed at evaluating the impact of antidepressant therapy on cardiovascular morbidity and mortality after a myocardial infarction.

Paul Sawchenko from the Salk Institute in La Jolla, California addressed the issue of how the central stress response is not only activated by outside stimuli, or psychological stressors (such as pain, major life events, trauma) but can also be activated by internal events, such as inflammation, blood loss, hypothermia, or possibly even food intake. In particular he addressed the question of how these different types of stressors result in specific hypothalamic responses to stress, even though both types of stressors result in activation of the HPA axis and sympathoadrenal systems. The effects of interoceptive stressors (stimuli that originate within the body, such as various cytokines that act as messengers between cells) on hypothalamic effector (responsive) neurons may be conceived as simple reflex responses. On the other hand, exteroceptive (outside) stressor effects mediate adaptive visceromotor responses[9] which require involvement of forebrain activation, including medial prefrontal and anterior cingulate cortices—areas of the brain involved in problem solving or planning, memory or imagination, and integrating emotional information in cognitive responses.

In summary, the outputs of the central stress response play an important role in the modulation of many chronic illnesses. Alterations in the responsiveness of this system, on a genetic basis or due to environmental influences, are important factors in the pathophysiology of a wide range of chronic diseases ranging from coronary artery (ischemic) heart disease to irritable bowel syndrome.

The Effect of Early Life Events on the **CENTRAL STRESS RESPONSE**

A series of speakers addressed the question of how environmental factors occurring early in life of an organism are able to permanently alter the neurocircuitry of the developing central nervous system, in particular the different components of the central stress response discussed in the previous section. Together with genetic factors, such permanent biasing (predisposition) of the mind-body relationship and the way an organism responds to environmental stressors occurring later in life is likely to have important consequences for the mental and physical health of the affected adult throughout life. Two such situations in which early traumatic life events become major risk factors for chronic disease later in life, were addressed by Ghislain Devroede from Centre Universitaire de Santédel L'Estrie, Sherbrooke, Québec and Sunny Anand from Arkansas Children's Hospital, Little Rock. Devroede discussed the relationship between physical and sexual abuse, and organic and functional gastrointestinal disorders.[10] Anand discussed the ill effects that stress and pain in newborn infants can have on later development of the individual.

Paul Plotsky from Emory University, Georgia presented an animal model of stress occurring around the time of birth (perinatal) in the form of short-term maternal separation, which in many ways mimics many of the physiological abnormalities seen in humans with early life trauma and abuse. The changes in neurocircuitry resulting from this type of perinatal stressor are associated with the expression of enhanced anxiety-like behavior, anhedonia (inability to experience pleasure or enjoy life), alcohol preference, and HPA axis hyper-responsiveness to psychological stressors which persist throughout the lifetime of the adult animal. Preliminary results also suggest that the adult animals that had experienced perinatal stress also develop features analogous to irritable bowel syndrome. For example, in response to psychological stress, rats with a history of perinatal stress show greater colonic motility responses, and develop increased sensitivity of the colon to mechanical stimuli. Both features (altered colonic motility and colonic hypersensitivity) are currently believed to underlie symptom generation in IBS patients.

> The human mind has developed powerful ways of modulating the output properties of stress systems… (that)… include the role of belief systems in mediating effects on health and disease.

[9] Stimulation of the visceral motor region of the brain can cause gastric contractions or changes in blood pressure. It is part of a region in the brain (cingulate cortex) associated with emotional reactions to external stimuli.

[10] Although abuse has not been shown to cause gastrointestinal disorders, it may influence the perception of symptoms in individuals who have the disorders. In other words, it may make symptoms feel worse.

Ned Kalin from the University of Wisconsin, Madison presented evidence from studies in non-human primates related to the development and neural structures (substrates) of defensive behaviors, on an organism's behavioral response to fear. He presented a hypothesis that conceptualizes pathological anxiety in humans, such as anxiety disorders, as the inappropriate expression of fear-related behaviors, related to specific substrates within the central nervous system. Such inappropriate expressions can be assessed as alterations in the various outputs of the central stress response as addressed in an earlier paragraph. In addition, he discussed the evidence for lateralization of brain responses in individuals with inappropriate defensive behaviors, such as preferential activation of the right hemisphere associated with pathological anxiety, behavioral inhibition, and enhanced cortisol (an adrenal stress hormone) responses. It is of interest that recent studies using functional brain imaging (PET scanning) showed a right hemispheric lateralization in IBS patients.

In summary, rapid progress is being made in identifying specific substrates, pathways, and transmitter systems within the brain that are altered in response to early adversive environmental influences, permanently biasing the individual's brain/mind to respond to the influences later in life. Even though these systems are a major determinant of health of mind and body, we are only beginning to acknowledge these factors in Western clinical medicine.

Our Internal Interface with the World: INTERACTIONS OF THE DIGESTIVE AND NERVOUS SYSTEMS

When we think about influences of the environment, most people generally think about events in the world around us, interfacing with our special senses, and our external surface. However, several pieces of evidence suggest that our interactions with the world are much more extensive and intimate when we include in this interaction our *internal surface*—the lining of the digestive system. Simply comparing the surface areas of external and internal interfaces, we have over a 2,600-fold difference between the approximate 2 square yards of our external body surface and the 5,250 square yards of our internal surface (the size of a football field). In addition, while our external surface under normal circumstances is fairly "tight", our internal surface is notoriously leaky and open to fluxes of fluids and nutrients. Furthermore, the "leakiness" of our internal surface is under control by the autonomic nervous system, and is enhanced in situations of stress. In addition, our internal surface is in very close contact with billions of microorganisms (our bacterial flora) which interact with the digestive system in unknown ways. And finally, food intake—the incorporation within a short period of time of chunks of our external environment—represents a major stressor to our internal stability (homeostasis), activating some of the same circuits of our central response that stressors in our external environment can activate.

Due to its large and leaky surface, the gut is protected against external influences by distinct subsystems of the immune, the nervous, and the endocrine systems. John Furness from Melbourne University, Australia discussed the unique role of these subsystems, and of the gastrointestinal tract and its sensory innervation as an interface with our internal environment. A significant amount of preprocessing of this sensory information is achieved at the level of the gut within "sensors" on immune cells and specialized endocrine cells (hormones that regulate cellular activity), and of the enteric nervous system,[11] (the "little brain") before it reaches the central nervous system (the "big brain"). Despite this complex innervation pattern, the great majority of events that occur within our digestive tract are not consciously perceived, but presumably play crucial roles in maintaining homeostasis.

Tim Maher from the University of Massachusetts in Worcester reviewed the evidence that dietary components, primarily in the form of precursors (substances from which another is formed) of different amino acids can cross the blood brain barrier.[12] They then can have distinct effects on a variety of behavioral and affective (mood related) responses. For example the amino acid composition of food can influence mood and pain sensitivity. This lends indirect support to the claims of ancient traditions, such as the Indian Aryuvedic system, about very specific influences of diet on health, disease, and mental function.

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[11] The *autonomic nervous system* is essential to maintaining homeostasis. It conveys messages away from the central nervous system (the brain and spinal cord) to the motor system that help regulate the visceral organs (like the intestines), the glands, and the cardiovascular system. The *enteric nervous system* is the part of the autonomic nervous system that controls function of the gastrointestinal tract. The enteric nervous system can function autonomously and is relatively independent of the central nervous system. It contains roughly as many neurons as are found in the spinal cord.

[12] The *blood brain barrier* is a protective system of cells and capillaries that keep certain substances in the blood from penetrating cerebral neural tissue.

> Autonomic pathways that… play important roles in stress-mediated modulation of the immune system, the heart, and a wide range of other organ systems… can be activated in the form of simple reflexes, but also in response to complex mental activity.

Emeran Mayer from UCLA, Los Angeles discussed evolving concepts about the role of visceral afferent information (neural messages from the body's internal organs to the brain or central nervous system) in modulating mental functions, including both emotional (affective) and reasoned or intellectual (cognitive) aspects. Starting with the lay concept of "gut feelings" he discussed recent results from functional brain imaging studies identifying distinct brain regions which are activated in association with perception of and autonomic responses to visceral stimuli.

In summary, our interactions with the world through our internal interface is in many ways more intimate but less glamorous than our interactions with the world via our special senses (sight, hearing, smell, touch, taste). Even though special dietary manipulations play a central role in traditional concepts of healing, we are only beginning to understand how molecules that are either part of our diet, or secretary products of our intestinal flora, interact with sensory mechanisms (involving sensory neurons, immune cells, and endocrine cells) influence not only our digestive system, but have important influences on our feelings, cognitive processes, and other organ systems. According to this concept, our digestive system is not only an organ system concerned with assuring our nutritional needs, but a fundamental modulator of some of our most important mental and physical functions.

How the Brain PERCEIVES AND RESPONDS TO PAIN

Several speakers dealt with the issue of sensory feedback[13] from the body to the brain and the ways by which the brain is able to modulate the subjective experience of pain. Robert Foreman from the University of Oklahoma, Oklahoma City discussed the integrative role of the upper cervical spinal cord in processing sensory information from visceral organs separated by function and distance. This provides not only a way for intraspinal communication between different viscera but also for the convergence of somatic bodily input and visceral organ input. Furthermore, it appears that change in function of one visceral organ can alter responses in another organ. This line of research is not only important for the understanding of clinical aspects of visceral pain and headaches, but may have profound implications as a possible neurological correlate for such esoteric concepts of Chinese Medicine as the meridians, and the connection and energy flow between different organs.

Brent Vogt discussed the role of the medial pain system as a mental process that is primarily aimed at predicting, rather than localizing the outcome of life-threatening events. Drawing on extensive evidence from studies in animals and functional brain imaging studies in humans he described the role of subregions within the brain (the anterior cingulate cortex), and projections to other cortical and subcortical regions in the experience of, response to, and prediction of painful (nociceptive) events.

Howard Fields from the University of California in San Francisco reviewed the role of endogenous (internal) pain modulation systems in altering the experience of pain. Inhibitory and facilitatory systems act on the subjective experience of pain, which is produced by a specific spatiotemporal[14] pattern of neural activity called "representations." These pain modulation systems are able to internally produce analgesia (opioid peptides called endorphins that can reduce pain sensation) under conditions of threat, and "virtual" pain under situations of suggestions and expectations. In other words, the mind is able to manipulate our subjective experience of pain via well-defined pathways reaching the spinal cord. The balance between simultaneously activated pain inhibitory and pain facilitatory pathways determines our "net" sensitivity to sensory information reaching the spinal cord.[15]

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[13] *Feedback* refers to a bi-directional or loop-like pattern of information flow. For example, the body senses pain, or a variable level of stimuli. This information is relayed to the brain where it triggers a regulatory response. The regulatory response modulates the pain, which in turn affects the level of stimuli.

[14] The *spatiotemporal* pattern refers to awareness of pain based on perception of the location, size, nature, duration, and changes in magnitude of the stimulus. Pain is subjective. It involves a complex perception that takes place in the central nervous system. It is influenced by emotional states and environmental circumstances, is dependent on experience, and varies from person to person.

[15] This balance between simultaneously activated pain inhibitory and pain facilitatory pathways is related to the *pain*

Donald Price from the University of Florida, Gainesville reviewed the different mechanisms of analgesia produced by hypnosis and placebo suggestions. In the case of hypnotic analgesia, these mechanisms include inhibition of pain sensation traveling from the periphery to the brain (afferent nociceptive signals) originating at the level of the spinal cord via descending pain inhibitory pathways, as well as cerebral mechanisms selective for modulation of pain affect within the anterior cingulate cortex. In the case of pain relief from placebo (analgesia), these mechanisms include a change in emotional (affective) state, cognitive response bias, and activation of descending spinal control systems that can inhibit pain. Price suggested that these differences could be useful in the design of specific therapeutic approaches to chronic pain.

Several clinical studies have demonstrated the effectiveness of hypnotherapy on symptoms in IBS patients. Wilfrid Jänig from the University of Kiel, Germany discussed the role of a set of specialized sensory nerves (vagal afferents) originating in the gut in the modulation of pain originating from another body region, the joints. He showed that subdiaphragmatic vagal visceral afferents can modulate pain resulting from movement of an arthritic joint. Jänig provided evidence that this gut triggered analgesia system involves an as yet unknown endocrine signal, which is released via sympathetic nerves from the adrenal medulla. These results show how the brain is able to regulate sensitivity of pain receptors (nociceptors) in the periphery by this hormonal signal, and how the sensitivity of nociceptors can be influenced by changes in body parts that are remote from the location of the sensitized nociceptor. Again, similar to the presentation by Robert Foreman, these concepts derived by strict Western scientific methods are reminiscent of the ancient, empirically derived concepts of Chinese Medicine. In particular, the notion that activity in one part of the body can influence the function of a distant, seemingly unrelated organ was a recurrent theme in this conference.

In summary, it is becoming clear that the experience of pain is not a simple chain of events starting in an injured body part and ending in some pain center in the brain. Rather, it results from a bi-directional interplay between affected body regions, the digestive system, and the mind/brain. The nervous system can either directly influence events in an injured body region, or it can manipulate the representation of the injury in "virtual space." These mechanisms form the basis for a variety of alternative therapies used in the treatment of pain, such as guided imagery and hypnosis.

> The mind is able to manipulate our subjective experience of pain via well-defined pathways reaching the spinal cord.

How the Mind/Brain **TALKS TO THE BODY**

While the circuits of the central stress response determine the basic response patterns of an organism to real, expected, or imagined changes in its internal or external environment, the human mind has developed powerful ways of modulating the output properties of the stress system. These powers of the human mind include the role of belief systems in mediating effects on health and disease. They also include the role of brain regions and networks in temporal organization of action, in unconscious emotional processing, in different emotional coping styles, and in function-specific autonomic regulation including autonomic regulation of the heart and of the immune system.

Margaret Kemeny from the University of California, Los Angeles discussed the evidence supporting the links between the mind and the immune system, focusing on newer evidence that cognitive and emotional states have immunological correlates. Specific cognitive factors (such as negative expectancies, self-blame, psychological inhibition) may be related to immunological processes relevant to health. These concepts form the basis of the field of *psychoneuroimmunology*.

Richard Bandler from the University of Melbourne, Australia reviewed functional neuroanatomical evidence supporting the concept that different sub regions of a specific brain area, the periaqueductal gray (PAG), coordinate opposite modes of emotional coping in the form of engagement or disengagement with the external environment. For example, while stimulation of one subregion of the PAG results in a parasympathetic behavioral response of withdrawal, activation of another region results in the typical fight or flight sympathetic response. The PAG thus represents a brain correlate of

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gate theory. Not only does the brain sense pain, but it also can block pain by "closing" the gate. Different techniques by which individuals may attempt to influence pain modulation include relaxation, imagery, hypnosis, and cognitive-behavioral therapy.

fundamental different coping styles in an individual confronted with stressful situations. Bandler also presented evidence for function-specific networks involved in different patterns of emotional coping, made up of projections between discrete subregions of prefrontal cortex, PAG, amygdala, and hypothalamus—areas in the brain associated with autonomic responses.

Wilfrid Jänig from the University of Kiel, Germany reviewed the neurophysiological evidence that demonstrate the function-specific organization of sympathetic (autonomic) outflow from the central neuroaxis to the body. This organization is the basis for precise neural regulations of all homeostatic body functions activated to maintain equilibrium, and is in sharp contrast to the traditional concept of the functioning of the sympathetic nervous system as an all or none system, stereotypically activated in the context of stress.

Richard Verrier from the Beth Israel Hospital, Harvard discussed distinct physiological processes that play a role in the mediation of potentially life-threatening effects of stressors and emotions in patients with coronary artery (ischemic) heart disease. These effects are mediated by output patterns of the autonomic nervous system characterized by high sympathetic and low vagal tone. Low vagal tone is associated with increased and less effective work of the heart, and predisposes the patient to development of fatal arrhythmias. Low vagal tone has been found in many patients suffering from depression, and is one of the factors that underlies the greatly enhanced risk of depressed patients to die from an arrhythmia after a myocardial infarction.

David Felten from Loma Linda University in California discussed aspects of neural-immune signaling, in particular the role of the hormone norepinephrine in modulation of immune function. Distinct branches of the sympathetic nervous system innervating lymphoid tissue in the spleen and gastrointestinal tract play a prominent immunoregulatory function. Based on studies evaluating the effect of naturalistic and experimental stressors on immune function, increased stress-induced activation of the sympathetic system is associated with an immunosuppressive effect. A well-known example illustrating these scientific findings is the increased susceptibility to viral infections during times of stress.

In summary, specific roles of different branches of the autonomic nervous system are being identified, which play important roles in stress-mediated modulation of the immune system, the heart, and a wide range of other organ systems. Activation of these autonomic influences is highly target specific and is organized in distinct patterns within the brain. Autonomic pathways can be activated in the form of simple stereotypic reflexes, but distinct patterns can also be activated in response to complex mental activity. They are one of the major mechanisms by which feelings, thoughts, and coping styles are directly translated into changes in organ function and into behavior.

The Practice of **MIND BODY MEDICINE**

There is good evidence that simple, safe, and relatively inexpensive behavioral medicine interventions can dramatically improve health outcomes and reduce the need for more expensive treatments of both chronic organic disease and of so-called functional disorders. Cost effective mind-body interventions, particularly when offered to groups of patients, are likely to become important strategies for health care delivery systems to deal with escalating costs, rising public expectations, limited access, and an aging population with multiple chronic illnesses. Several speakers dealt with comprehensive disease models (biopsychosocial models) and with practical implications of comprehensive approaches to chronic disease, in particular the *functional* disorders.[16]

Bruce Naliboff from the University of California, Los Angeles focused on a common functional disorder, irritable bowel syndrome (IBS), to present a biobehavioral model that integrates neurophysiological, perceptual, and behavioral processes. This model may be generalizable to other common functional syndromes—such as fibromyalgia, dyspepsia, and chronic pelvic pain—and forms a rationale basis for effective behavioral treatment strategies. Treatment that utilizes a combination of strategies may be most effective. The use of fiber, visceral analgesics, and antispasmodics can modify the interaction between enhanced contractility (alterations in bowel motility) and enhanced sensitivity of the digestive tract to

[16] A *functional* disorder refers to a disorder or disease where the primary abnormality is an altered physiological function, rather than an identifiable structural or biochemical cause. It characterizes a disorder that generally can not be diagnosed in a traditional way; that is, as an inflammatory, infectious, or structural abnormality that can be seen by commonly used examination, x-ray, or laboratory test.

stimuli. If emotional or autonomic hyperactivity is present, a treatment strategy may also include ways to decrease the hyperactivity through relaxation techniques, including hypnosis. Finally, cognitive behavioral techniques can be used to help the individual control symptoms.

Nicholas Read from Northern General Hospital, Sheffield, UK presented an alternative model of functional disease, which is based on a psychoanalytical understanding of how disease may result from the impact of psychosocial stresses on a fragile and vulnerable personality structure. Even though the psychoanalytical model and the preceding biobehavioral model arise from fundamentally different traditions of psychology, in the end, they both converge with neurobiological concepts presented in this publication.

David Eisenberg from Beth Israel Hospital at Harvard addressed the issue of complementary and alternative medicine (CAM). He gave a brief overview of the different approaches that are usually referred to as "alternative," which he defined as medical interventions neither taught widely in U.S. medical schools nor generally available in U.S. hospitals. Examples include chiropractic, homeopathy, herbal medicine, and massage. He presented information about the wide spread utilization of such treatment options by the U.S. population.[17]

David Mayer from the Medical College of Virginia, Richmond focused on one of the most established alternative treatment strategies, acupuncture, and discussed possible neurobiological mechanisms, in particular the role of endogenous opoids (endorphins) underlying the effectiveness of such treatments.

Don Johnson from the California Institute of Integral Studies, San Francisco discussed the concepts and general therapeutic strategies shared by different schools of Western Integrative Bodyworks (various methods of touch and massage). He suggests that this "intricate tactile sensitivity," which includes the therapist's sensitivity for certain patterns of the patient's body, and a unique contact between therapist and patient may become amenable for scientific evaluation.

Finally, Rolf Sovik from the Himalayan Institute in Buffalo, New York reviewed the central role of breathing in the practice of yogic techniques. Breathing is the only body function that in the normal state is fully under automatic control by circuits in the central nervous system, but which instantly can be switched to conscious control. This unique property is probably responsible for the fact that for thousands of years, breathing techniques have been essential components of meditation techniques and healing practices.

Scientific mechanisms are being unraveled which form the basis to understand the mechanism(s) of action of (mind-body or complimentary interventions.

Switching between different breathing patterns—such as from shallow and rapid breathing into the chest to deep diaphragmatic—has profound effects on a variety of body functions such as pain sensitivity, acid reflux from the stomach into the esophagus, and function of various pelvic floor structures. Within yogic traditions, voluntary control of breathing is used to foster self-awareness and to reduce unnecessary, autonomic arousal, thereby exerting important effects on physiologic and psychologic functioning.

In summary, the presentations in this section made it clear that many aspects of mind body medicine or complementary medicine clearly have come of age. Acupuncture, bodywork, breathing, and relaxation techniques are widely accepted and valued by the lay public. Scientific mechanisms are being unraveled which form the basis to understand the mechanism(s) of action of these interventions. At the same time, controlled studies have demonstrated the cost-effectiveness of behavioral medicine approaches that target cognitive constructs in patients with chronic disease to help them control symptoms and thereby improve health and quality of life. And finally, the seriousness of many of these approaches, only recently ridiculed by the medical establishment, is being validated by the involvement of the U.S. National Institutes of Health (NIH) in funding studies into the effectiveness of non-traditional treatments and the underlying mechanisms.

For most participants at the conference there was a growing awareness of the evolving convergence of many ancient concepts of health and disease with cutting edge concepts proposed by science. What initially was feared by some of the participants to turn into two parallel meetings without a common language, became a "watershed" experience by many, with profound influences on thoughts and feelings about Mind Body Medicine.

[17] Approximately 40% of adult Americans visited alternative therapy practitioners in 1997 according to an article in the *Journal of the American Medical Association*, November 11, 1998.

The **PUBLICATION**

The proceedings of the Sedona conference have been published in January of this year as volume 122 of the prestigious book series *Progress in Brain Research* by Elsevier Science, entitled *The Biological Basis of Mind Body Interactions*. In this volume, the authors address key issues relevant to the ongoing debate over the validity of traditional, holistic, and alternative or complementary approaches to health, disease, and healing.

In the book, the authors are asking the question of how the mind and body interact with each other and with the environment, from the first days of life to adulthood, and in this process actively maintain health and prevent disease. They are examining mechanisms by which early disruptions of the mind/body/environment homeostasis can predispose the individual to chronic disease. Finally, they are asking the question of how a few selected "alternative" practices, either aimed at the body or at the mind are able to re-establish balance and thereby a state of health.

The book is divided into two parts. The first part examines the physiological basis for the bi-directional interactions between mind/brain and the body. The second component involves the work of various practitioners of *mind body medicine* which give a sample of approaches considered alternative to Western Medicine, ranging from Yogic Breathing techniques, Tibetan meditation, Bodywork, and Acupuncture.

The different programmatic sections of the book address different aspects of the mind/brain/body interactions in health and disease. After establishing the relationship between mind, brain, and emotions, sections III and IV deal with neurobiological mechanisms underlying the organism's response to stress and how this response is altered by events occurring early in life. The next two sections (V and VI) address different aspects of how the body (from its internal and external interfaces with the environment) communicates to the brain, and section VII reviews different mechanisms by which the mind/brain communicates back to the body. Finally, in section VIII, authors from widely differing disciplines address aspects of the practical application of mind/body approaches to health and disease.

If you are interested in more information about the Sedona Conference, the participants, or the publication, *The Biological Basis of Mind Body Interactions*, contact the UCLA Mind Body Clinical Research Center at our web site at www.med.ucla.edu/ndp/.

The Biological Basis of Mind Body Interactions may be ordered online from the publisher by going to www.elsevier.nl/ and entering the title in the Publication Search field. The hardbound edition is available at a cost of $223.50 U.S. dollars.