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# The Bioinformatics of Psychosocial Genomics in Alternative and Complementary Medicine

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**Key Words**

Bioinformatics · Gene expression · Healing · Novelty · Numinosum · Neurogenesis · Psychosocial genomics · Rehabilitation · Replay · Stress

**Summary**

The bioinformatics of alternative and complementary medicine is outlined in 3 hypotheses that extend the molecular-genomic revolution initiated by Watson and Crick 50 years ago to include psychology in the new discipline of psychosocial and cultural genomics. Stress-induced changes in the alternative splicing of genes demonstrate how psychosomatic stress in humans modulates activity-dependent gene expression, protein formation, physiological function, and psychological experience. The molecular messengers generated by stress, injury, and disease can activate immediate early genes within stem cells so that they then signal the target genes required to synthesize the proteins that will transform (differentiate) stem cells into mature well-functioning tissues. Such activity-dependent gene expression and its consequent activity-dependent neurogenesis and stem cell healing is proposed as the molecular-genomic-cellular basis of rehabilitative medicine, physical, and occupational therapy as well as the many alternative and complementary approaches to mind-body healing. The therapeutic replaying of enriching life experiences that evoke the novelty-numinosum-neurogenesis effect during creative moments of art, music, dance, drama, humor, literature, poetry, and spirituality, as well as cultural rituals of life transitions (birth, puberty, marriage, illness, healing, and death) can optimize consciousness, personal relationships, and healing in a manner that has much in common with the psychogenomic foundations of naturalistic and complementary medicine. The entire history of alternative and complementary approaches to healing is consistent with this new neuroscience world view about the role of psychological arousal and fascination in modulating gene expression, neurogenesis, and healing via the psychosocial and cultural rites of human societies.

**Schlüsselwörter**

**Zusammenfassung**



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## Introduction

Although it is believed that the molecular-genomic revolution initiated by Watson and Crick [1, 2] and others fifty years ago could serve as a common scientific foundation for the medicine and psychology [3, 4], it has had relatively little impact on the field of alternative and complementary medicine. This conceptual review introduces a new bioinformatic foundation for alternative and complementary medicine that is called 'psychosocial genomics.' Psychosocial genomics complements traditional Mendelian behavioral genetics by exploring how psychological experiences can modulate gene expression in health, optimal performance, stress, disease, and rehabilitation [5].

Classical Mendelian genetics and its modern application to behavioral genetics documents how genes modulate behavior, psychological traits, and psychological experience. *The new question explored by psychosocial genomics is the opposite: How does psychological experience modulate gene expression?* This most surprising question that emerges from the human genome project is well expressed by Stahl [6].

But can behavior modify genes? Learning as well as experiences from the environment can give rise to changes in neural connections. In this way, human experiences, education, and even psychotherapy may change the expression of genes that alter the distribution and strength of specific synaptic connections. Thus genes modify behavior and behavior modifies genes. Psychotherapy may even induce neurotropic factors to preserve critical cells and innervate new therapeutic targets to alter emotions and behaviors [6, p 37].

Because there are as yet no systematic experimental programs of research investigating how psychotherapy, alternative and complementary medicine modulate gene expression, I will outline a bioinformatic approach with 3 hypotheses to guide future research and practice.

## Bioinformatics and Psychosocial Genomics in Stress and Healing

*Hypothesis 1: A bioinformatics approach to alternative and complementary medicine is the essential foundation for understanding the dynamics of stress, mind-body communication, and healing via psychosocial and cultural genomics.*

The concept of biological stress was originally developed by Selye [7] to describe the deleterious effects of toxic, traumatic, excessive, and chronic demands on the organism's physiological level of functioning as manifest on 3 organ and tissue systems.

…a stereotyped syndrome (a set of simultaneously occurring organ changes), characterized by (1) enlargement and hyperactivity of the adrenal cortex, (2) shrinkage (or atrophy) of the thymus gland and lymph nodes, and (3) the appearance of gastrointestinal ulcers…

… It soon became evident from animal experiments that the same set of organ changes caused by the glandular extracts were also produced by cold, heat, infection, trauma, hemorrhage, nervous irritation, and many other stimuli… This reaction was first described, in 1936, as a 'syndrome produced by various nocuous agents' and subsequently became known as the General Adaptation Syndrome (GAS), or the biological stress syndrome. Its three stages are: (1) 'the alarm reaction; (2) the stage of resistance; and (3) the stage of exhaustion' [7, p 24–27].

Current research is extending Selye's biological concept of stress and the GAS to the molecular-genomic level [5]. Kaufer et al. [8], for example, document how 'acute stress facilitates long-lasting changes in cholinergic gene expression' by forced swimming in rats. Meshorer et al. [9] describe a number of molecular mechanisms whereby stress could modulate gene expression in humans experiencing posttraumatic stress disorder (PTSD). What they call 'stimulus-induced changes in alternative splicing [of genes]' will be discussed here because it clearly demonstrates how psychosomatic stress in humans modulates gene expression. This is an example of psychosocial genomics: how 'mental experiences' could modulate the molecular-genomic core of 'body physiology' in alternative and complementary medicine as well as the many cognitive-behavioral psychotherapies [5, 10].

Traumatic stress is often followed by long-term pathological changes. In humans, extreme cases of such changes are clinically recognized as PTSD. Although the immediate response to acute stressful insults has been extensively studied, the molecular mechanisms leading to the long-term neuronal hypersensitivity that is characteristic of PTSD are yet unknown. 'Stimulus-induced changes in alternative splicing [of genes] have recently emerged as a major mechanism of neuronal adaptation to stress, contributing to the versatility and complexity of the expression patterns of the human genome' [5, p 508].

To understand the meaning and implications of the alternative splicing of genes we need to understand a few basic concepts of bioinformatics. It is important to realize that genes exist within long strands of DNA which are made up of several billion base pairs (in humans) of the 4 nucleotides that make up the molecular code of life (bases: adenine, cytosine, guanine, and thymine). The (1) sequence of these nucleotides that make up DNA is a code that determines the order in which amino acids will be strung together to build the (2) structure of proteins, which in turn determine the (3) physiological functions of the organism. When the splicing of genes is changed by stress it means that the (1) sequence of nucleotides is changed so that (2) the structure of proteins is changed in a manner that leads to (3) corresponding changes in physiological functions of the organism for good (a little stress can facilitate healing) or for ill (too much chronic stress results in dysfunction).

This relationship between sequence, structure, and function is a basic concept of molecular biology that is now called 'bioin-

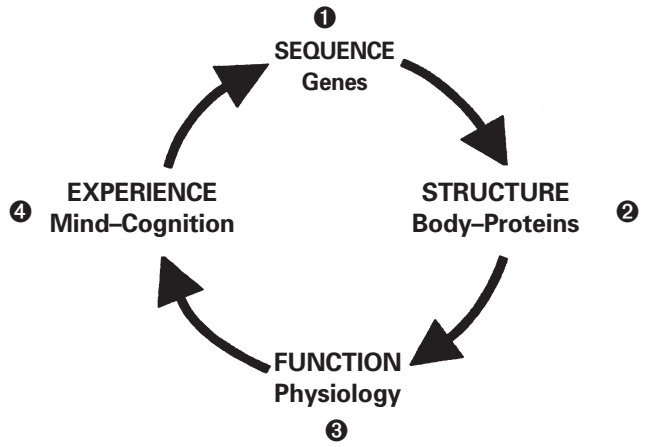


**Fig. 1.** The adaptive bioinformatic cycle of sequence, structure, function, and experience that integrates mind-body communication and healing in the alternative and complementary approaches to medicine. This could more properly be called a 'psycho-bioinformatic cycle of psychosocial genomics' since I added the level of experience to the current standard textbook bioinformatic progression of sequence, structure, and function.

formatics' [11]. To this standard textbook concept of bioinformatics I now add a 4th link so that human experience on the cognitive-emotional-behavioral level completes the bioinformatic cycle of information transduction between mind and matter as illustrated in figure 1. It is of essence for alternative and complementary medicine to realize that the bioinformatic levels of sequence, structure, function, and experience are all related in figure one. This means that if you enter the cycle at any level with any of the various approaches to alternative and complementary medicine, it is possible to modulate and possibly heal dysfunctions on any other level.

The second fundamental concept of bioinformatics is to understand a few surprising facts about genes and how they are expressed (that is, turned on and off). The essential regions of genes are sequences of nucleotides called 'exons' that code for the structure of proteins. These exons, however, are frequently interrupted by non-coding regions of 'junk DNA' (that is, nucleotide sequences with no generally agreed upon function at this time) that are called 'introns'. Before genes can be expressed (transcribed) these non-coding introns must be cut out and eliminated so that the coding exons can be spliced together to make up a useful piece of messenger ribonucleic acid (mRNA). When the exons are spliced together they are shipped out the cell nucleus to ribosomes (the protein factories of the cell) where the sequence of nucleotides in the mRNA is translated into a string of amino acids that fold into the structure of proteins that determines their physiological function.

The research of Meshorer et al. [9] now tells us how this splicing of exons is modulated, at least in part, by the molecular messengers of trauma and stress (the hypothalamic-pituitary-adrenal hormones of Selye) that humans experience as PTSD. This is just one example of a psychosocial genomic mechanism that completes the cycle of information transduction between the sequence and structure of matter with the physiological function of the body and the experiences of the mind [5]. As noted above, healing can be initiated by entering the bioinformatic cycle of figure 1 at any of the four levels of sequence, structure, function, or experience. Modern molecular medicine usually chooses entry at the purely physical and molecular-biological levels of sequence, structure, and physiological functions. The alternative and complementary approaches (including the cognitive-behavioral approaches, meditation, therapeutic hypnosis etc.), by contrast, tend to focus on the psychobiological levels of function, especially psychological experience, in facilitating the bioinformatic cycle of mind-body communication and healing in figure 1.

## Brain Growth, Healing, and Rehabilitation via Activity-Dependent Gene Expression in Stem Cells

*Hypothesis 2: Alternative and complementary medicine facilitates gene expression, neurogenesis, and healing via the growth, differentiation, and maturation of stem cells throughout the life cycle.*

A new view of how stem cells, stress, gene expression, and healing are interrelated is currently emerging in the health sciences [5]. Stress on all levels from the social and psychological to the physical and traumatic leads to injury and aging of the individual cells that make up the tissues and organs of the body. What is the most general mechanism of recovery from such stress, trauma and injury? New answer: stem cells! Adult stem cells are self-replicating, multi-potent cells that continue to exist in adult tissues and may be used as a source of 'spare parts' which can replace injured cells and tissues [12]. Stem cells have been described as 'mother nature's menders' when they function as reserves of the brain and body [5]. Stem cells are embryonic in the sense that they retain the ability to express whatever genes are needed to replace the damaged cells that are no longer fully functional [13, 41]. Stress, trauma, injury, and diseases of many types leave a trail of molecular signals that activate the bioinformatic gene expression-protein synthesis cycle in stem cells that are still residing in malfunctioning tissues throughout the brain and body. The molecular messengers generated by stress, injury, and disease can activate immediate early genes within stem cells so that they then signal the target genes required to synthesize the proteins that will transform (differentiate) the stem cells into mature well-functioning tissues. These new tissue cells can then replace injured, aging, and dysfunctional cells that die by a process of apoptosis (so-called 'cell suicide' that takes place due to stress, injury, genetic mutations, senescence, etc.).

The emerging evidence of stem cells as a general source of healing in stress-related physical and psychological medicine is implied in the existing scientific literature even though many

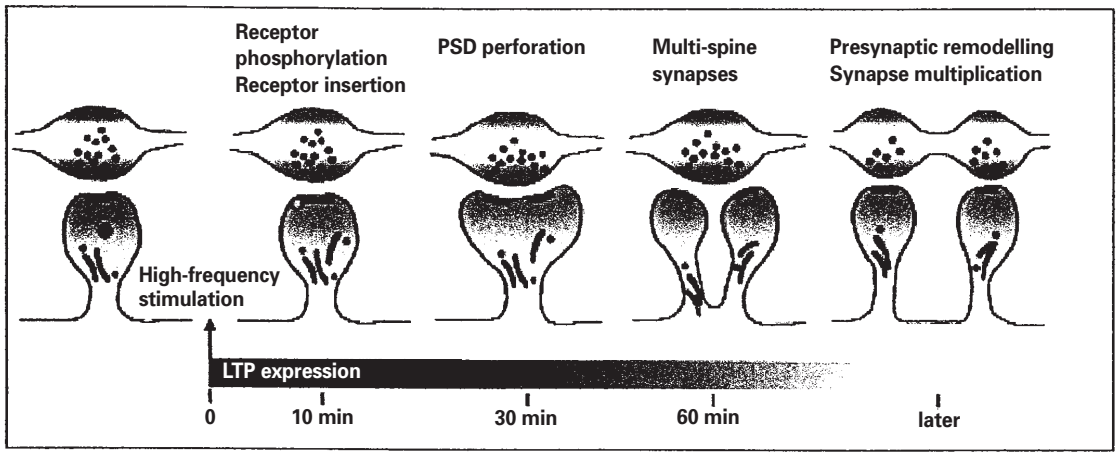


**Fig. 2.** Proposed stages in the genesis of new synapses with long-term potentiation (LTP). Within 10 min of appropriate stimulation there is series of molecular signals that activate AMPA receptors and an increase in their single-channel conductance. Within 30 min the size of the post-synaptic density increases and divides in the receiving neuron. Within 60 min some synapses divide to generate multi-spine synapses where 2 or more post-synaptic spines connect with the same pre-synaptic bouton. Concomitant retrograde communication from the post- to the pre-synaptic bouton increases, so that the total numbers of functioning synapses proliferate over time (90–120 min to hours) [with permission from 18]. AMPA = …..; PSD = …….

of the exact molecular mechanisms are not yet well known. Scores of growth factors that can activate the gene expression and the protein synthesis cycle in stem cells have been isolated to date. Stimulation by varying combinations of these growth factors and other signals from the environment leads to varying patterns of gene expression that generate the proteins that lead stem cells to differentiate into healthy, mature, functioning tissues. Healing via this pattern of gene expression has been well documented in self-renewing stem cells in the brain (including the cerebral cortex, hippocampus, and hypothalamus), muscle, skin, intestinal epithelium, bone marrow, liver, heart and many other tissues [14].

Some of the most well-documented evidence of a relationship between psychosocial stress and a healing response via stem cells comes from the area of neurogenesis and brain growth [15]. Kandel [16], a Nobel laureate in medicine in 2000, discussed this issue after a lifetime of research on activity-dependent gene expression in the molecular-genomics of memory, learning, and behavior.

Insofar as psychotherapy or counseling is effective and produces long-term changes in behavior, it presumably does so through learning, by producing changes in gene expression that alters the strength of synaptic connections and structural changes that alter the anatomical pattern of interconnections between nerve cells of the brain. As the resolution of brain imaging increases, it should eventually permit quantitative evaluation of the outcome of psychotherapy…….Stated simply, the regulation of gene expression by social factors makes all bodily functions, including all functions of the brain, susceptible to social influences. These social influences will be biologically incorporated in the altered expressions of specific genes in specific nerve cells of specific regions of the brain. 'These socially influenced alterations are transmitted culturally. They are not incorporated in the sperm and egg and therefore are not transmitted genetically' [16, p 140].

Kandel's last 2 sentences emphasize once again that we are not dealing with classical Mendelian genetics with it laws regarding the distribution of traits from one generation to the next. We are dealing with the new field of psychosocial genomics, which investigates the molecular biology of the entire genome of an organism as it adapts creatively to the challenges and stresses of its environment in daily life.

The organism responds to any challenge with activity – fight, flight or whatever on a molecular-cognitive-emotional level as well as a physical level. Sensory and behavioral activity on any level stimulates neurons and neurotransmitters, which generates activity-dependent gene expression [17]. Activity-dependent gene expression generates the proteins, which in turn make up the enzymes of metabolism and energy dynamics as well as the hormones, neurotransmitters, growth factors, and immune system factors etc. that carry out the daily housekeeping and defense of the organism. The most profound outcome of the neuroscience research of Kandel and others [18–20] is that activity-dependent gene expression leads to the formation of new synapses and neurons (neurogenesis or brain growth), as illustrated in figure 2. There are 3 well replicated psychosocial genomic factors that generate activity-dependent gene expression, neurogenesis, and stem cell healing: novelty, enrichment, and exercise.

1) novelty [15, 21, 22],
2) environmental enrichment [19, 23],
3) exercise [20, 24].

While the details are still controversial [25], it is generally agreed that such recent research documents how activity-dependent gene expression facilitates the generation of functional neurons in the hippocampus of the brain, which encodes new memory, learning, and behavior [26, 27]. Most significantly for alternative and complementary medicine is how neurogenesis takes place in three neocortical association areas (prefrontal, inferior temporal, and posterior parietal cortex) that

are involved in behavioral plasticity (that is, behavioral change) and associated transformations of psychological experience [26, 27]. Gould et al. [26] conclude: 'These new neurons, which are continually added in adulthood, may play a role in the functions of association neocortex' (p 548).

I now propose that this process of activity-dependent gene expression and its consequent activity-dependent neurogenesis and stem cell healing is the molecular-genomic-cellular basis of current approaches to rehabilitative medicine, physical, and occupational therapy as well as the many alternative and complementary approaches to mind-body healing. Physical activity and exercise initiates the molecular-genomic basis of rehabilitation in cardio-vascular accidents such as stroke, heart attacks etc. [5, 28]. Hood [29], for example, has documented activity-dependent gene expression in mitochondrial (the energy factories of the cell) biogenesis in skeletal, cardiac and smooth muscle in response to physical exercise that is consistent with this proposal. Consistent with Selye's original conception of stress, it is now well documented that the stress hormones such as the glucocorticoids inhibit neurogenesis [30]. We now need a systematic research program to investigate the degree to which the many different approaches of alternative and complementary medicine can actually generate the novelty, environmental enrichment, and exercise, which are required to evoke activity-dependent gene expression in stem cells of the body to initiate the bioinformatic cycle of healing as well as stem cells of the brain to facilitate neurogenesis.

Figure 2 is a schematic illustration of how activity-dependent gene expression initiates the formation of new synapses to facilitate the development and growth of the brain throughout the entire life span. What is of greatest interest for the practical applications of alternative and complementary medicine is the 1.5 to 2 hour time frame within which new synapses can be developed in the brain. This relatively brief time frame means that therapists can expect that actual brain growth could take place at the synaptic level within a single therapeutic session. Once initiated, synaptogenesis and neurogenesis in the brain and, presumably, stem cell healing in the body could, in the ideal case, continue for days, weeks, and months when the patient has been given an adequate way of facilitating his own healing [5, 28].

## Creative Replay and Healing in the Arts, Humanities, and Cultural Rituals

*Hypothesis 3: Alternative and complementary medicine facilitates the psychosocial genomics of encoding new experience, memory, learning, and behavior in the molecular dynamics of healing and physical rehabilitation by engaging creative replays of the novelty-numinosum-neurogenesis effect.*

The therapeutic replaying of enriching life experiences that evoke the novelty-numinosum-neurogenesis effect during creative moments of art, music, dance, drama, humor, literature, poetry, spirituality, as well as cultural rituals of celebration and life transitions (birth, puberty, marriage, illness, healing, and death) can optimize consciousness, personal relationships, and healing in a manner that has much in common with the psychogenomic foundations of alternative and complementary medicine [5]. The entire history of alternative and complementary approaches to healing including ancient and modern spiritual rituals of exorcism, shamanism, fire walking and the still 'mysterious methods' of acupuncture, body work, therapeutic touch, and biofeedback that evoke a positive experience of wonder and expectation are the experiential data base for this hypothesis about the role of psychological arousal and fascination in the humanities and cultural rites of human societies [31–33]. We speculate that psychobiological healing during ecstatic religious experiences of the 'numinosum', consisting of a combined sense of fascination, the mysterious, and the tremendous [34], has much in common with traditional and modern rituals of healing associated with the self-help groups, twelve-step programs and the so-called 'miracle cures' in clinical demonstrations of hypnosis [5].

All such holistic and spiritual approaches to healing involve the repetition and replay of numinous experiences developed over the history of a culture. The value of repetition, replay, and reconstruction is recognized also in the popular psychotherapeutic concept, 'Every replay is a reframe' [5], which has found experimental support by Shimizu et al. [35], who demonstrate how the processes of repetition, recall, replay, and reconstruction are manifest in the transformations of consciousness, memory, and behavior on the neurobiological level. They found that the NMDA (N-methyl-D-asparate) receptor in the CA1 region of the hippocampus serves as a 'gating switch' in the construction and reconstruction of memory.

Our results indicate that memory consolidation may require multiple rounds of site-specific synaptic modifications, possibly to reinforce plastic changes initiated during learning, thereby making memory traces stronger and more stable. Recent studies report that the learning-induced correlation states among CA1 neurons are reactivated spontaneously in a post-learning period. Such a co-activation of these neurons might suggest the existence of the natural condition within the hippocampus by which recurrent synaptic strengthening can occur during memory consolidation. We hypothesize that such a synaptic re-entry reinforcement (SRR) process can also be applied to explain how the hippocampus transfers newly created memories to the cortex for permanent storage. As the hippocampus undergoes reactivation during consolidation, it may also act as a coincidence regenerator for activating neurons in the cortical area such as the association cortex. This would allow cortical neurons previously corresponding to the different sensory modalities to be reactivated together, leading to the strengthening of the connections between them through SRR. Indeed, such a coordinated reactivation of hippocampal-cortical neurons after learning has been observed recently……..Once these cortical connections are fully consol-

idated and stabilized, the hippocampus itself becomes dispensable for the retrieval of the 'old memory' . . .Therefore, we postulate that the hippocampus, by serving as a coincidence regenerator, may induce the reinforcement of synaptic connection within the cortex during memory consolidation as the cellular means to convert short-term memories into long-term memories' [35, pp 1172–1173].

A recent review of these psychobiological dynamics of the 'multiple rounds of site-specific synaptic modifications, possibly to reinforce plastic changes initiated during learning' [35, p 1172] by Cohen-Cory [36] provides more detail about the actual time parameters of activity-dependent synaptogenesis that are illustrated in the four stages in figure 1.

During development, more synapses are established than ultimately will be retained. Therefore, the elimination of excess synaptic inputs is a critical step in synaptic circuit maturation. Synapse elimination is a competitive process that involves interactions between pre- and postsynaptic partners. The dynamics of synapse formation and of synapse elimination may be much more rapid in the CNS than at the neuromuscular junction (NMJ), where synapse elimination has been well characterized. At the vertebrate NMJ, a single muscle cell is initially innervated by multiple motor axons. The transition from multiple innervations to innervation by a single motor axon occurs gradually as some terminal branches retract from each muscle fiber before others, a process requiring about 24 hours for withdrawal of the presynaptic terminal…..In the CNS, as with the NMJ, a developmental, activity-dependent remodeling of synaptic circuits takes place by a process that may involve the selective stabilization of coactive inputs and the elimination of inputs with uncorrelated activity. The anatomical refinement of synaptic circuits occurs at the level of individual axons and dendrites by a dynamic process that involves rapid elimination of synapses. As axons branch and remodel, synapses form and dismantle with synapse elimination occurring rapidly, in less than two hours. . . hippocampal neurons in which glutamate receptor function was altered demonstrated that synapse disassembly in the CNS occurs rapidly, within 1.5 hours after synapses are no longer functional [36, p 771] . . . Studies investigating the effects of long-term synaptic plasticity have generally used experimental paradigms in which repetitive, high-frequency stimulation gives rise to synaptic potentiation (called long-term potentiation, LTP) that is accompanied by structural and molecular changes at the level of single synapses…..Recent imaging experiments reveal that both NMDA and AMPA receptor activation are indeed involved in synapse formation and maturation [36, p 773].

I hypothesize that just as negative states of emotional arousal can evoke the psychosocial genomic network to initiate gene expression cascades leading to the synthesis of stress proteins and illness, so can the replay of positive psychological experiences initiate cascades of healing at the gene-protein level [5]. This implies that the experience of positive fascination, novelty, numinosum, mystery, surprise and insight experienced in the dramatic cultural rites of many cultures could access and facilitate gene expression cascades leading to the synthesis of healing proteins. This concept of positive therapeutic replay as the essence of psychogenomic healing on the level of brain neuroanatomy is suggested by the research of Lisman and Morris [42] as follows: '. . . newly acquired sensory information is funneled through the cortex to the hippocampus. Surprisingly, only the hippocampus actually learns at this time – it is said to be online. Later, when the hippocampus is offline (probably during sleep), it replays stored information, transmitting it to the cortex. The cortex is considered to be a slow learner, capable of lasting memory storage only as a result of this repeated replaying of information by the hippocampus. In some views, the hippocampus is only a temporary memory store – once memory traces become stabilized in the cortex, memories can be accessed even if the hippocampus is removed. There is now direct evidence that some form of hippocampal replay occurs . . . These results support the idea that the hippocampus is the fast online learner that 'teaches' the slower cortex offline' [42, pp 248–249].

The neuroscience research reviewed above describing how novelty and enriched environments can initiate gene expression leading to the formation of new proteins and neurogenesis is the basis of this hypothesis. When combined with voluntary exercise such as running researchers found that the number of cells generated in the hippocampus of the brain is doubled [21, 24, 26, 27]. It is tempting to make a speculative leap between these highly arousing activities that facilitate neurogenesis in current neuroscience research in the laboratory and the high level of sensory stimulation and movement found in many colorful cultural rituals of passage [33]. Most of these anthropological reports note that after the period of high sensory stimulation and emotional arousal there is a compensatory period of rest, relaxation, and sleep during which healing is experienced. This reminds us of the mathematical models of therapeutic hypnosis and the holistic healing arts presented previously wherein there is a high phase of ultradian arousal followed by a low phase of ultradian arousal characteristic of Kleitman's 'basic rest-activity cycle' [5]. This suggests that both high and low states of psychosocial genomic arousal utilized in alternative and complementary medicine make important contributions to what we could call a 'continuum of healing associated with behavior state-related gene expression'.

This concept of a continuum of healing ranging from high to low states of psychobiological arousal is confirmed by many studies that suggest that different belief systems about alternative and complementary medicine as well as spiritual healing may be emphasizing different parts of the same continuum. Glik [37], for example, compared the belief system and spiritual healing rituals of 93 members of charismatic Christian healing groups whose healing rituals emphasized hyperarousal with 83 members of New Age healing groups whose meditative approach to healing emphasized hypoarousal. The

two groups were apparently emphasizing and facilitating opposite psychobiological states. Glik found, however, that people in both groups reported more healing experiences than people who did not frame their health problems from a spiritual perspective. The positive expectancy associated with their spiritual perspective could utilize both the high and low psychobiological states for healing.

This is consistent with classical studies that classify meditative states into two major categories: Via Positiva or active meditation versus Via Negativa or passive meditation. The Via Positiva is an active approach wherein there is a focusing of attention on an external or internal object, concept or image such as a religious figure with numinous overtones that generates high psychobiological arousal. The Via Negativa is passive in the sense that they attempt to clear the mind by eliminating sensory input and activities such as thinking, emotions so that a low state of psychobiological arousal is experienced. Current research in neurotheology utilizing brain imaging of practitioners on either the active or passive path, however, indicate that they both can achieve the desired 'absolute unitary being' (AUB) state [38]. The significance of such studies is that they may be developing a universal psychobiological paradigm that could investigate the therapeutic values of all cultural and spiritual practices in an objective manner. They also imply a more general hypothesis about the role of psychosocial genomics in the positive expectations and experiences of the placebo response [5].

The science writer Ridley [39] provides a deep albeit speculative perspective on the implications of current research on psychosocial genomics.

It is time to put the organism back together again. It is time to visit a much more social gene, a gene whose whole function is to integrate some of the many different functions of the body, and a gene whose existence gives lie to the mind-body dualism that plagues our mental image of the human person. The brain, the body and the genome are locked, all three, in a dance. The genome is as much under the control of the other two as they are controlled by it. That is partly why genetic determinism is a myth. The switching on and off of human genes can be influenced by conscious or unconscious external action [39, p 148] ... genes need to be switched on, and external events – or free-willed behavior – can switch on genes [39, p 153]…Social influences upon behavior work through the switching on and off of genes [39, p 172]…The psychological precedes the physical. The mind drives the body, which drives the genome [39, p 157].

Ridley's final sentence is somewhat startling and controversial. In the creative bioinformatic cycle of sequence, structure, function, and experience of figure 1, it is actually impossible to answer which comes first in the 'chicken or egg' question of mind or body. Mind and body always involves the circular, non-linear, and chaotic dynamics that make a linear cause and effect answer impossible to prove; mutual relationship is the essence of their structure and function [40]. Figure 1 does illustrate, however, how the alternative and complementary approaches to holistic medicine and rehabilitation that enter and engage the bioinformatic cycle of mind-body healing on any level can facilitate healing on all other levels; it gives modern meaning and reification to the ancient mystical utterance 'All is One'.

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