PART FOUR

The Creative Psychosocial Genomics Healing Experience for Creating Consciousness

Chapter Fourteen*

The Creative Psychosocial Genomics of Human Resilience and Resoucefulness:
The Therapeutic Value of Music Appreciation

Ernest Rossi, Jane Blake-Mortimer & Kathryn Rossi

Abstract

This chapter introduces our new creative psychosocial genomics perspective for facilitating human resilience and resourcefulness on all levels from mind to gene. We view human resilience and resourcefulness as a Darwinian evolutionary adaptive response to novel environmental challenges that heighten consciousness and creativity for coping with transformative life situations. When acute trauma (physical accidents, war, etc.) or chronic stress (overwork, illness etc) disrupt communication between mind, body, gene, and environment, however, we fall into physical and emotional crisis (post-traumatic stress disorders). We document how our new *Creative Psychosocial Genomic Healing Experience* reduces (*1) dysfunctional inflammation* (associated with chronic pain and delayed healing) and *(2) oxidative stress* (associated with many chronic medical conditions and the ageing process) as

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well as (3) increasing a *"molecular-genomic signature of stem cells"* (activation of stem cells associated with healing and the rehabilitation and in many tissues of the body) as the deep psychobiological source of human resilience and resourcefulness.

In addition, as an important corollary, we propose that art, beauty, and truth activate experience and qualia-dependent gene expression and brain plasticity in a new theory of aesthetics, dialectics, empathy, meaning, and rehabilitation. We discuss the molecular-genomic dynamics of music appreciation as a clear illustration of the contribution of the arts and humanities to health, recovery and rehabilitation from stress, trauma, and post-traumatic stress disorder. We illustrate how to facilitate qualia-dependent gene expression and brain plasticity to optimize resilience and resourcefulness in the here and now creative moments of our psychosocial genomic approach to creating new consciousness in psychotherapy, the arts, humanities and sciences.

KEY WORDS: Art, beauty, truth, consciousness, psychosocial, PTSD, molecular -genomics, music appreciation, qualia, resilience, resourcefulness

INTRODUCTION

The Creative Psychosocial Genomics of Human Resilience and Resourcefulness

Among the many modern meanings of Plato's foundational philosophical concept of the *eidos* or archetype is "appearance," "pattern," "symmetry" or "ground plan of existence." More generally, the *eidos* could be understood as a general theory of knowledge and in*form*ation (*in-form-ation)* (Spencer-Brown, 1979; Stonier, 1990). Information is implied in theories of the coherence of consciousness and culture (Antonovsky, 1987-1994), and related concepts such as resiliency and resourcefulness in health psychology (Rosenbaum, 1990; Simonton et al., 1992, 2002). While the molecular-genomic revolution initiated by Watson & Crick is the current biological foundation for medicine and health psychology, its impact on our understanding of the human condition remains controversial. We believe the reason for this can be found in the contrast illustrated in figures 1a and 1b. Figure 1a illustrates Watson & Crick's (1953a, 1953b) original linear view of what they called "the basic dogma of molecular biology:" how (1) the linear DNA code of nucleotides that makes up the *sequence* of our genes generates (2) the *structure* of the proteins of our body, which in turn generates (3) all the physiological *functions* of the body.

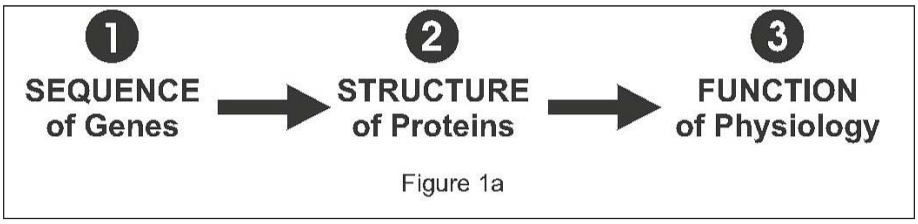

Figure 1a. The Watson and Crick (1953a, b) Original Linear "Dogma of Molecular Biology" with No Explicit Role for the Qualia of Consciousness and Psychological Experience.

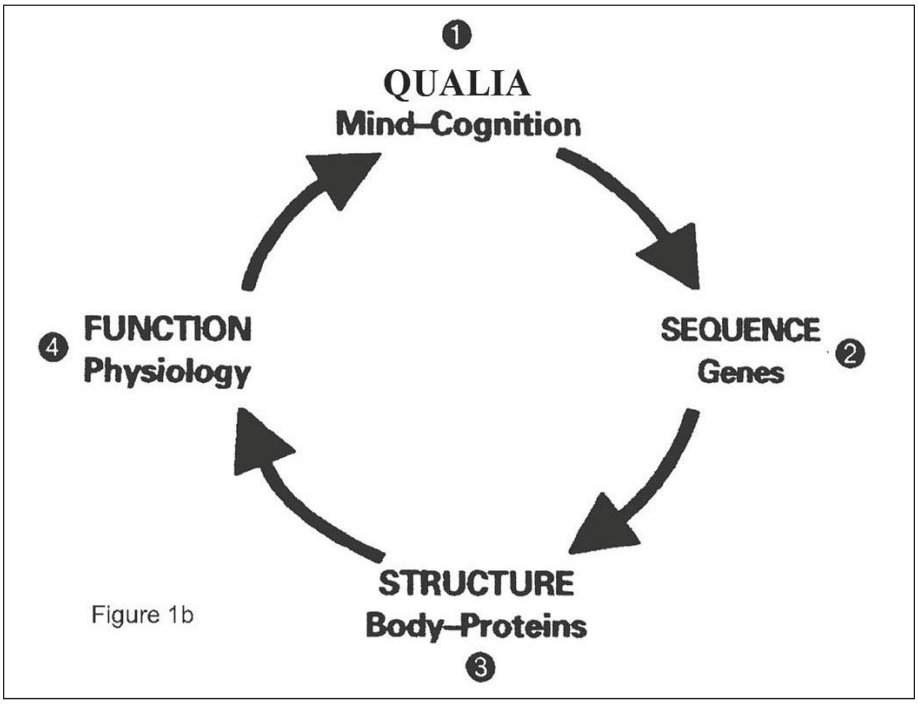

Figure 1b. Adding the Complex Sensory-Perceptual Qualia of Mind and Cognition to the Watson and Crick's Linear "Dogma of Molecular Biology".

Mind, cognition, and the psychological qualia of human experience, however, have no place in Watson & Crick's (1953 a, b) original biological formulation of the basis of life as illustrated in figure 1a. Current neuroscience, however, demonstrates transformative informational links between mind, brain and body in their cyclic reciprocal effects on each other at the molecular-genomic level. This interaction together with processes emerging from the current pioneering research in bioinformatics of memory and learning (Kandel, 2006; Rossi, 2002, 2004a, 2007, 2009), leads us to introduce the

qualia of psychology (mind, cognition, and emotions) into Watson & Crick's *linear outline* to illustrate our *cyclic, multilevel, and transformative process* of mind-body information and communication as illustrated in figure 1b. This cyclic process we call, "psychosocial genomics" that leads to a deep psychobiological perspective of the source of human individuality (Whitney et al., 2003) and the creative process of intuition (Dragoi & Tonegawa, 2011; Moser & Moser, 2011) in the arts and sciences as well as creativity in psychotherapy and health psychology.

Psychosocial Genomics and the Transformative 4-Stage Creative Process

A cartoon of the classical 4-stage creative process is presented in figure 2 illustrating a student attempting to prove a mathematical theorem (Tomlin, 2005). The first two panels represent *Stage One* (preparation) *of the classical 4-stage creative process* when "the wheels start turning" in the mind and the student begins making diagrams and writing equations trying to solve the problem.

Figure 2. Experiencing the Four-Stage Creative Process. *Reproduced with permission, Tomlin, 2005.*

As is typical of many problem solving efforts in the arts and sciences as well as psychotherapy and everyday life, however, the student soon finds himself in difficulty. He feels "stuck" in S*tage Two* (incubation) *of the creative process*, when emotional conflict and despair is evident in the middle panel showing smoke arising from his overheated brain. *Stage Three* (insight) *of the creative process* is illustrated in the next panel as a flash of light surrounds the student's head (Durstewitz et al., 2010). Stage three is the essence of creating new consciousness. Current research documents how the positive expectations and practicing new life scenarios can enhance future success in the real world (Dragoi & Tonegawa, 2011; Moser & Moser, 2011). In the cartoon the student is so surprised by his new insight or intuition that he drops his pencil! *Stage Four* (verification) *of the creative cycle* is evident as the student smiles with happiness about his success and exclaims, "Magic!"

The Creative Cycles of Mind-Gene Communication in Myth and Psychotherapy

Figure 3 illustrates our broad psychosocial genomic perspective of how this creative, so-called "magic," operates on many levels from myth, culture, and psychotherapy to experience-dependent gene expression and brain plasticity. Figure 3 illustrates the 4-stage creative process as the inner-most circle of our psychosocial genomic perspective. The next larger circle illustrates how this 4-stage creative cycle is experienced as "The Breakout Heuristic" in the arts, sciences, psychotherapy, and everyday life (Rossi, 1968, 2007, 2009) The breakout heuristic illustrates how people outgrow and transcend their previous life perspectives to construct an updated and more adaptive worldview or personal myth; this is the essence of what has been called "resilience" and "learned resourcefulness" (Rosenbaum, 1990). The next larger circle is the 4-stage creative cycle conceptualized as the mono-myth of humanity as a paradigm of the evolution of consciousness and culture (Campbell, 1956; Rossi, 1972/1985/2000, 2007). The outer circle summarizes our psychosocial genomics perspective on all levels of human experience from mind and memory to the molecular-genomic level.

The outer circle of figure 3 draws upon Ribeiro's (2004, 2008) evolutionary theory of sleep and dreaming. The basic idea is that dreams often are creative replays of novel past events that try to update the dreamer about new possibilities for our life. Dreams generalize from surprising and unexpected events of the past few days to explore future expectations and possibilities of more adaptive behavior in the future. The evolutionary adaptive function of dreaming is to construct and explore novel behaviors for future survival. Ribeiro et al. (1999, 2002, 2004, 2008) describe the cognitive role of

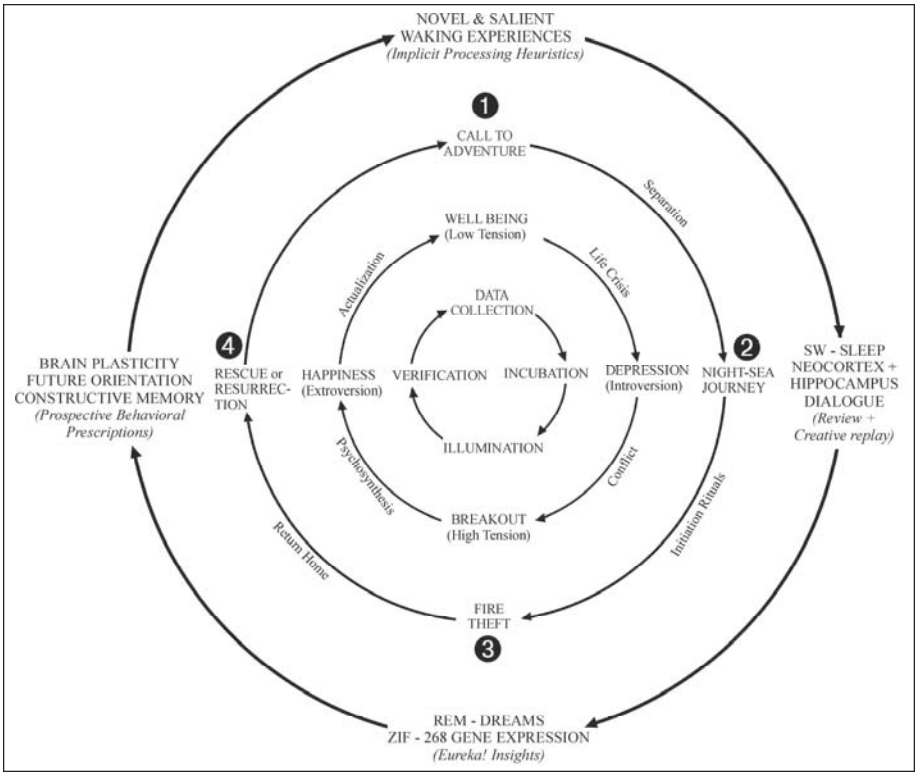

Figure 3. The Psychosocial Genomics of Consciousness and Culture.

experience-dependent gene expression and brain plasticity as a two-step process during the two major phases of sleep, namely rapid eye movement (REM) and slow wave (SW) sleep.

Ribeiro's theory recognizes specific roles for the two major phases of sleep. He proposes that the first phase of slow-wave (SW) sleep evolved from rest in early reptiles as a quiescent, "offline state" suitable for the consolidation of new memory and learning. Consistent with much current neuroscience, researchers believe that this cognitive role takes place through the reverberation of novel daytime waking patterns of neuronal activity during SW -sleep. The second major phase of sleep, characterized by rapid-eye-movements (REM) dreaming and heightened cerebral activity, first evolved in early birds and mammals as a post SW-sleep state that was capable of facilitating memory consolidation. REM dreaming activates experience-dependent gene expression to make the proteins needed for generating synaptic plasticity and new neural networks, which then became the neural correlates of adaptive future behavior. Mammals then evolved extended REM

states of dreaming to prolong neuronal reverberation in novel ways that could promote memory reconstruction for future adaptive behavior rather than a mere rote recording of past events.

In brief, sleep and dreaming became an inner experimental theater for integrating memories of past events with current novel experiences to simulate and creatively replay the past and present as a rehearsal for future adaptive behavior. It is precisely here that we need to understand the most profound fact about the basic mechanism of creative mind-gene communication and the construction of new forms of consciousness. Stage three, the Eureka, Aha! or Illumination experience usually takes place when novel, surprising, and salient events turn on the experience-dependent zif-268 and arc genes, which initiate the process of brain plasticity. If there is no novelty in the previous day's experience – there is no turning on of the zif-268 genes – and no brain plasticity develops! Life becomes dull and the individual is prone to depression, fatigue, and other dysfunctional states and behaviors. The hippocampus actually shrinks in volume just as would an unused muscle. That's why people need exciting life adventures, dreams, art, beauty, and truth, all of which turn on experience-dependent gene expression and adaptive brain growth. This is what we call the "novelty-numinosum-neurogenesis effect (NNNE)" (Rossi, 2002, 2004a & b, 2007). This perspective of mind-gene communication is the basis of our new psychosocial genomic model of psychotherapy as a creative dialogue between the hippocampus and the cortex as illustrated in figure 4.

We propose this new psychosocial genomic approach to psychotherapy that facilitates the novelty-numinosum-neurogenesis effect to optimize adaptive activity and experience-dependent gene expression and brain plasticity for problem solving and healing. The NNNE can be engaged by the novelty of surprising events in the outside world as well as the apparently spontaneous evolution of inner events of our REM dreams and early morning thoughts. Facilitating the NNNE effect is the goal of our new psychotherapeutic protocol, "The Creative Psychosocial Genomic Healing Experience" (Rossi & Rossi, 2011).

A Time Profile of the Psychosocial Genomic 4-Stage Creative Process

Figure 5 is a time profile of the 4-stage creative process on many levels from mind to gene. The upper portion of figure five outlines our psychosocial genomic perspective of how a single psychotherapy session may be conceptualized as the creative utilization of one natural 90–120 minute ultradian rhythm of arousal and relaxation characteristic of Kleitman's Basic Rest-Activity Cycle (BRAC) (Lloyd and Rossi, 1992). We have outlined extensive

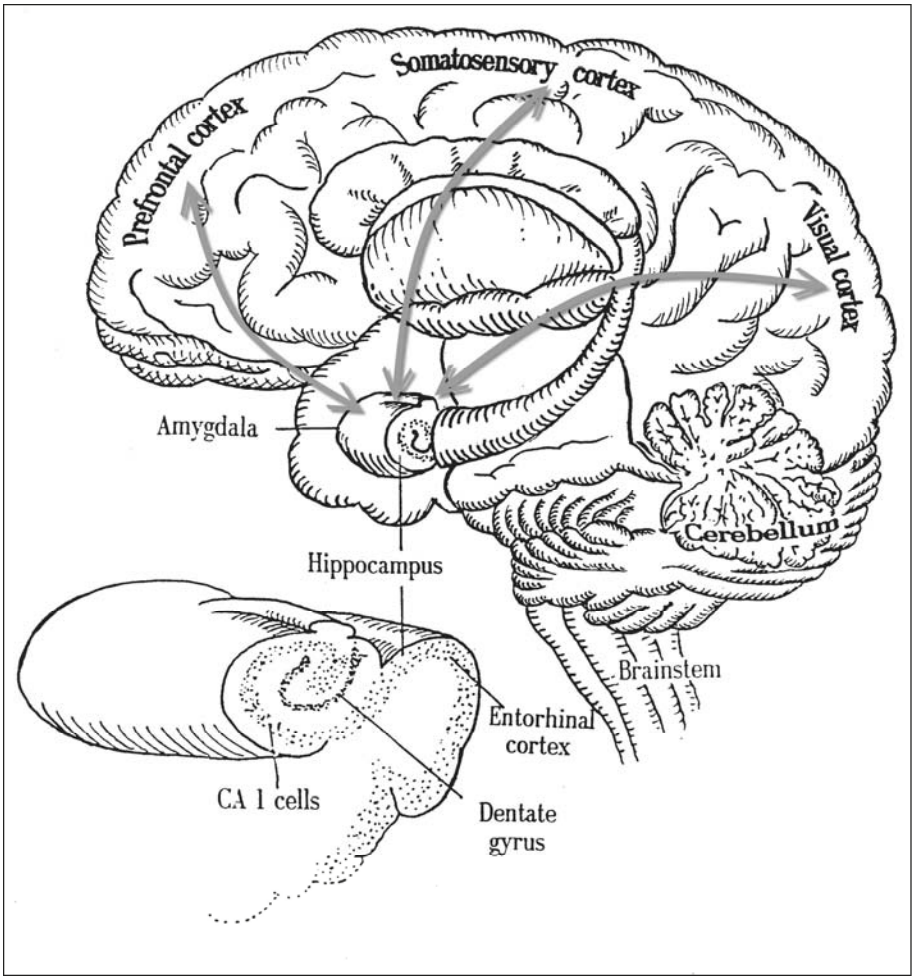

Figure 4. The Psychosocial Genomics of Mind-Gene Communication.

research that documents how the classical four stages of the creative process (data collection, incubation, illumination, and verification) are often experienced as Jung's four basic psychological functions (sensations, feeling, intuition, and thinking) (Rossi, 2002, 2004a, 2007, 2009).

The large upper curves in figure five illustrate how the psychosocial genomic experience of the 4-stage creative process (upper curve) emerges from the proteomics (protein) level (middle curve) depicting the energy landscape for protein folding into the correct structures needed for psychobiological functioning (adapted and redrawn from Cheung et al. 2004). This proteomic level emerges from the genomics level illustrated by the curve below it

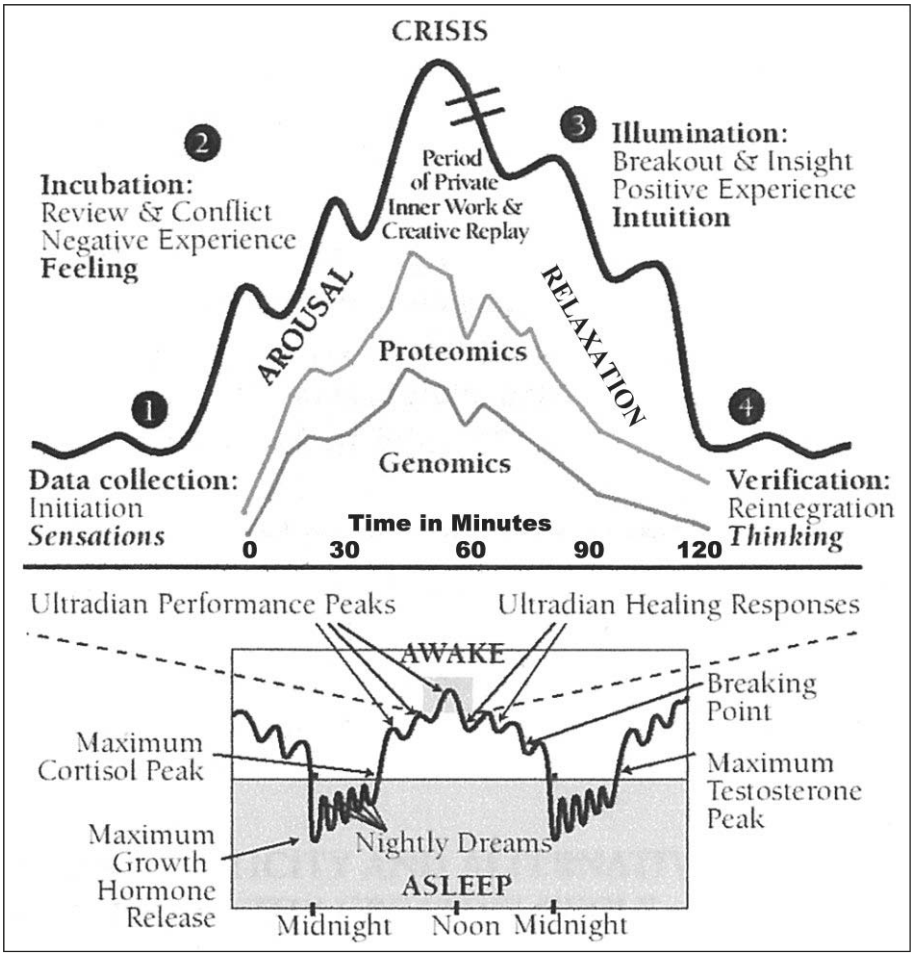

Figure 5. A Time Profile of the Circadian and Ultradian 4-Stage Creative Process.

(adapted from Levsky, et al., 2002). This psychosocial genomics curve represents the actual gene expression profiles of the immediate-early gene *c-fos* and 10 other genes (alleles) over the typical Basic Rest-Activity (BRAC) period of 90-120 minutes. The lower part of figure 5 summarizes the normal circadian (~ 24 hours) and ultradian (less than 24 hours) sleep, dreaming, and wakefulness (Lloyd & Rossi, 1992, 2008; Rossi & Nimmons, 1991). The ascending peaks of rapid eye movement (REM) sleep typically occurring every 90–120 minutes or so are illustrated along with the more variable ultradian rhythms of activity, adaptation, and rest in the daytime. The lower part of figure 5 also illustrates how many hormonal messenger molecules of the en-

docrine system such as *growth hormone*, the activating and stress hormone *cortisol,* and the sexual hormone *testosterone* typically have ultradian peaks at different times of the 24-hour circadian cycle.

The Psychosocial Genomics of Information Transduction in Mind-Body Healing: The Molecular-Genomic Sources of Human Resilience and Resourcefulness

Our psychosocial genomic perspective of the cyclic flow of transformative information from mind to gene is illustrated in figure 6. Gene expression (genomics) and the dynamics of proteins (proteomics) are the ultimate bioinformatic foundation of the classical 4-stage creative process in the dialectical method of philosophy as well as psychotherapy and mind-body medicine. These psychobiological transformations (that is, *information transduction*) at the genomics and proteomics levels are typically experienced as Kleitman's 90-120 minute Basic Rest-Activity Cycle in our normal human psychophysiological rhythms. Our psychosocial genomics hypothesis implies that these psychobiological rhythms can be entrained and utilized to modulate the genomics and proteomics levels for therapeutic purposes by many of the diverse and seemingly unrelated approaches of mind-body medicine.

Current psychosocial genomic research is documenting how many mental processes such as memory and learning (Kandel, 2006), REM dreaming (Ribeiro et al. 2008), meditation (Dusek et al., 2008) and therapeutic hypnosis (Lichtenberg, 2000, 2004; Rossi, 2009; Rossi et al. 2008) can modulate activity and experience-dependent gene expression and brain plasticity in the construction and re-construction of the mind, brain and body illustrated in figure 6. The time parameters of cyclic (1) mind-body information transduction as well as (2) the dynamics of energy production and utilization via the ADP-ATP (Adenosine Di-phosphate and Adenosine Tri-phosphate) cycle are ultimate inner resources of health, resourcefulness and resilience at the molecular-genomic and cellular level in figure 6. The cyclic flow of information transduction between mind and gene in figure 6 now leads to the question of what genes are associated with the complex human phenotypes (characteristics) of resourcefulness and resilience.

The Creative Psychosocial Genomic Healing Experience: A Pilot Study

In a recent pilot study we used DNA microarrays to explore the molecular-genomic basis of human resilience and resourcefulness (Atkinson et al., 2010 in press; Rossi, Iannotti et al., 2008). DNA microarrays are a tool for assessing the expression of the entire human genome (~21,329 gene probes) in a

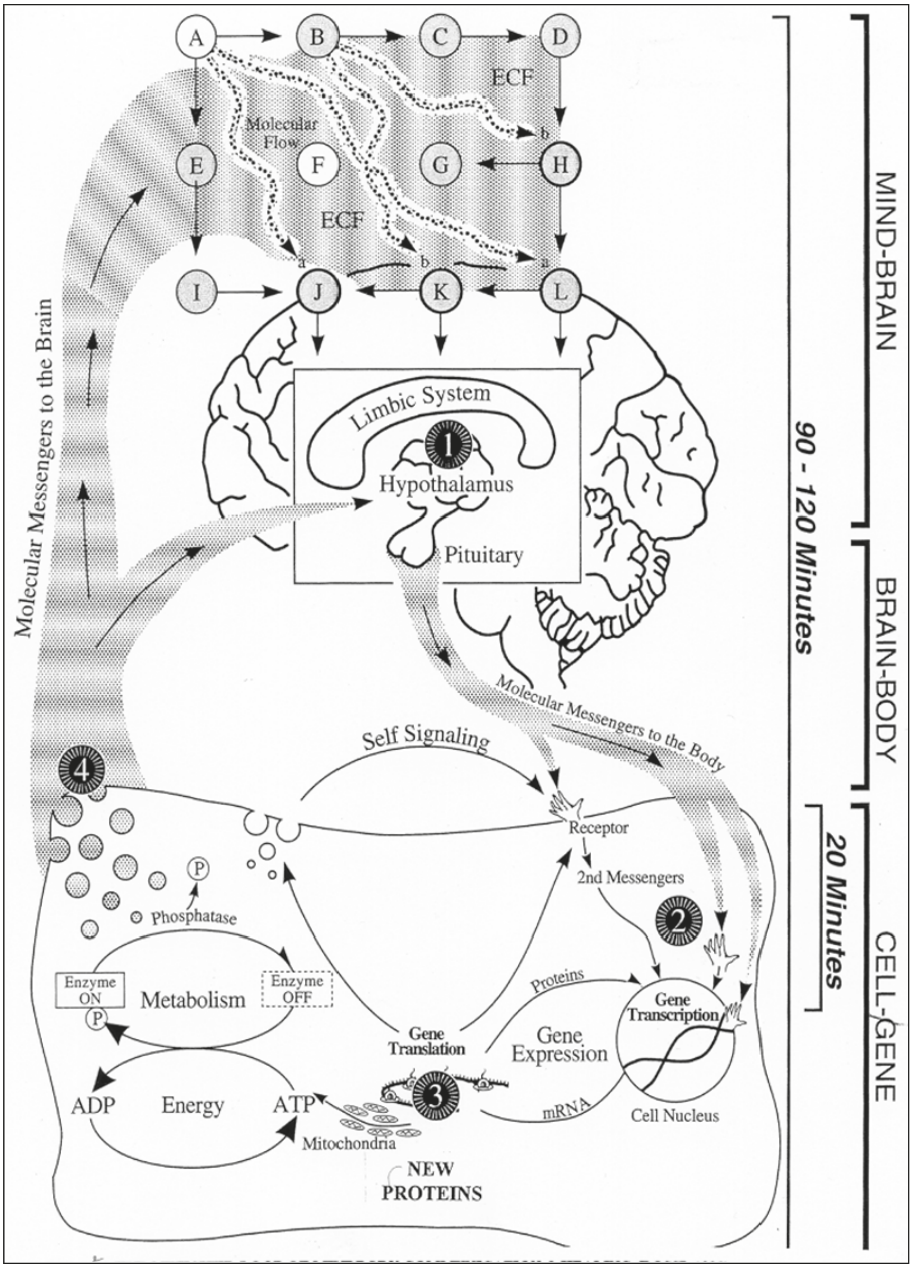

Figure 6. A 4-Stage Profile of the Cyclic Creative Dynamics of Transformative Information Transduction from Mind and Brain to the Molecular-Genomic Level.

single experiment. This pilot study assessed the hypothesis that a top-down creatively oriented positive human experience could modulate experience-dependent gene expression. A DNA microarray analysis of the white blood cells of three human participants (with a total of more than 191,961 data points for statistical analysis) was performed immediately before, one hour after, and 24 hours after the administration of *The Creative Psychosocial Genomic Healing Experience* (Rossi, 2004a), an easy-to-learn approach to therapeutic hypnosis. We documented changes in the expression of 15 early response genes within one hour that initiated a further cascade of 77 genes 24 hours later. This proof-of-principle pilot study now requires cross validation with more participants with a variety of diagnostic classifications to document the validity, reliability, and limitations of using DNA microarrays to assess the value of our new creative psychosocial genomic therapeutic protocol for facilitating human resilience and resourcefulness.

We used Gene Set Enrichment Analysis (GSEA), the free bioinformatics software program from MIT (http://www.broadinstitute.org/gsea/) to assess the meaning and therapeutic implications of our findings. We documented how The Creative Psychosocial Genomic Healing Experience reduces (1) dysfunctional chronic inflammation and (2) oxidative stress (Ning et al., 2004) while (3) increasing the activation of stem cells (Ivanova et al., 2002) to facilitate the deep psychobiological sources of human resilience and resourcefulness. We propose that this is a new psychosocial genomic foundation for facilitating Antonovsky's coherence of consciousness and culture as well as Rosenbaum's learned resilience.

We hypothesize that the healing factors illustrated in figures 7a and 7b, plus others such as microRNAs (Taubes, 2009) associated with human resilience and resourcefulness (Vialou et al., 2010) to be determined by further research, defines what we call, *"The Psychosocial Genomic Healing Response."* Such research could eventually determine if this is the molecular-genomic signature of human resilience and resourcefulness as well as the healing placebo (Benedetti, 2008). Our results are consistent with other research that documents how interventions via therapeutic hypnosis (the Ultradian Healing Response) and meditation (the Relaxation Response) reduces stress and promotes healing on the molecular-genomic level (Dusek et al., 2008; Lichtenberg, 2000, 2004; Rossi, 2002, 2004, 2007; Rossi, Iannotti et al., 2008; Yehuda et al., 2009). Much of this research documents how opportunity as well as stress during important life turning points can modulate activity and experience-dependent gene expression and brain plasticity.

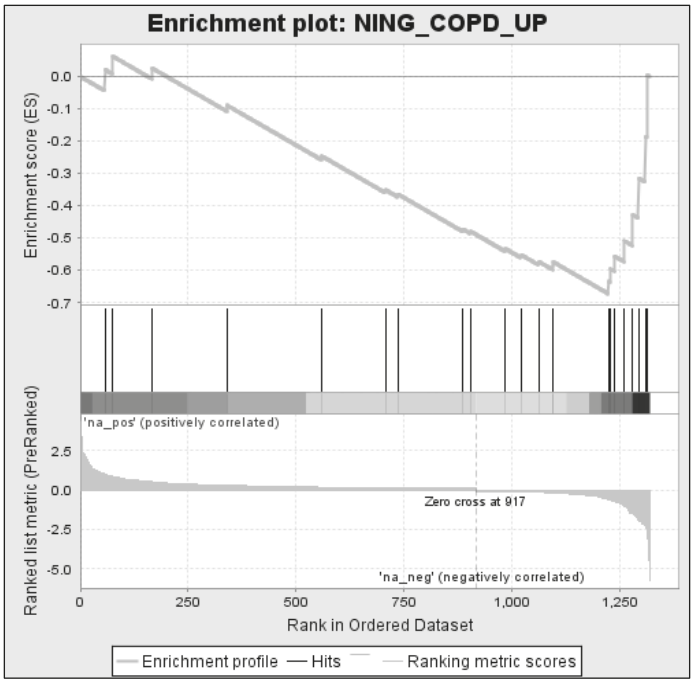

Figure 7a: Within 1 hour of The Creative Psychosocial Genomic Healing Experience, a gene set representing genes associated with heightened states of chronic inflammation and oxidative stress is negatively correlated with treatment. Nominal p-value < 0.0023. False Detection Rate q-value < 0.238.

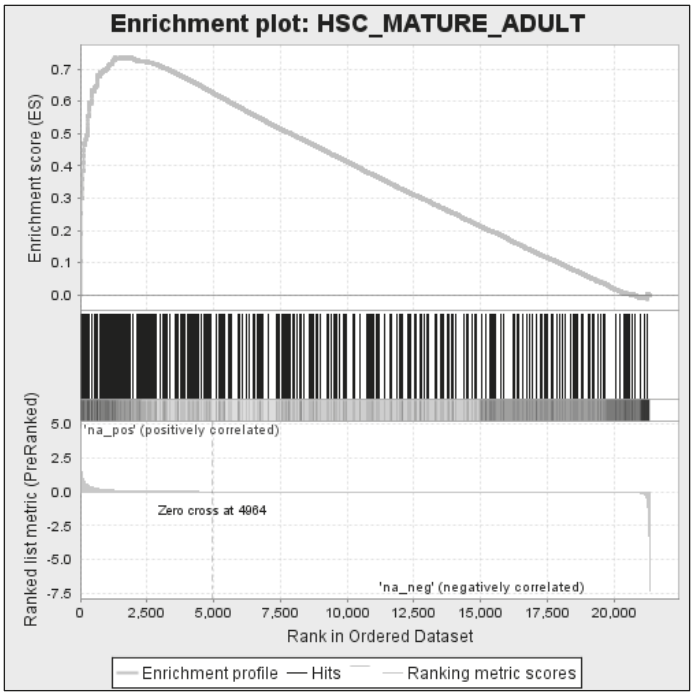

Figure 7b: Within 24 hours of *The Creative Psychosocial Genomic Healing Experience*, a gene set representing "a molecular signature of stem cells" (Ivanova et al., 2002) is positively correlated with treatment. Nominal p-value < 0.000 False Detection Rate q-value < 0.259.

Life Turning Points, Big Dreams, Gene Expression and Brain Plasticity

Figure 8 illustrates how psychosocial genomics portrays life turning points on many levels. Big dreams are typically vivid, dramatic and unusual in their clarity of expression, which mirrors the experience-dependent gene expression and brain plasticity cycle. In brief: (1) Significant Life Turning Points and transitions generate (2) Big Dreams, which are associated with (3) the Gene Expression/Brain Plasticity Cycle that (4) updates and reconstructs memory, learning, behavior, and consciousness in an evolutionarily adaptive manner.

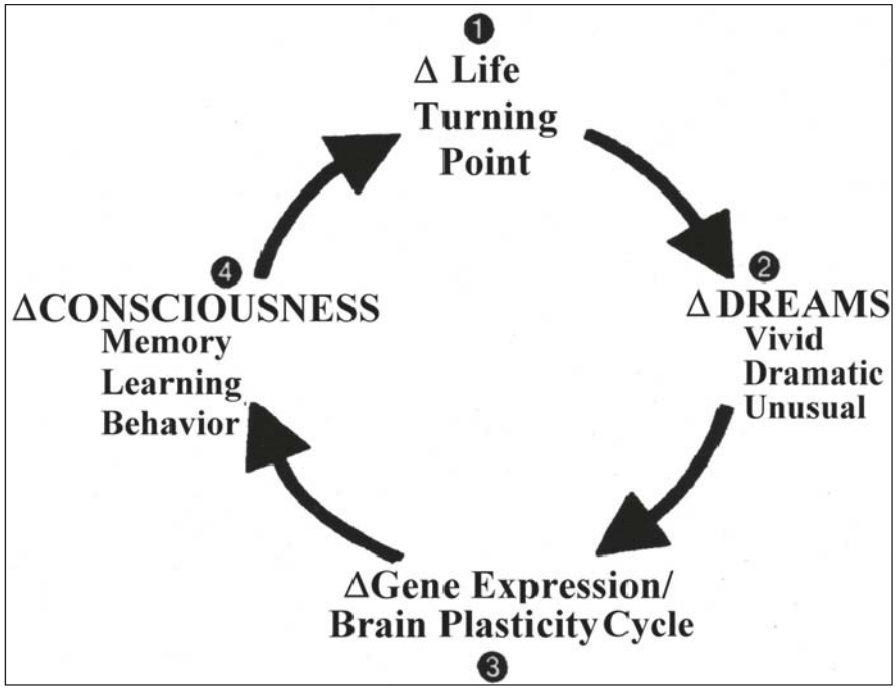

Figure 8. The Psychosocial Genomics of Profound Life Turning Points.

The delta signs (small triangles) in figure 8 indicate that a change at any of these four levels generates mathematical transformations of information, form, and energy to the next level in the perpetual growth of human consciousness and experience over a lifetime well lived with rich experiences of art, beauty and truth. But what does this really mean?

The Neuroscience of Art, Beauty, Truth and Psychotherapy: Lighting the Lamps of Human Consciousness

What do art, beauty and truth really have in common? Figure 9 is our psychosocial genomics perspective of how art, beauty and truth may function as numinous psycho-spiritual metaphors that update and reconstruct the neural networks of the brain, mind and consciousness to resolve psychological problems. We have designated this as the *Novelty-Numinosum-Neurogenesis Effect* (NNNE) Rossi, 2002, 2004a & b, 2007). Art, beauty, and truth are not the simple superficial frills of life! Figure 9 illustrates how novel and numinous experiences of psychotherapy could turn on activity and experience-dependent gene expression and brain plasticity to light and brighten the lamps of human consciousness (Rossi, 2002, 2004a, b, c, 2009; Rossi, Iannotti, et al., 2008).

Novel (Eriksson et al., 1998) and numinous experiences of fascination, mysteriousness, and the tremendous (Otto, 1923/1958) drive the creative

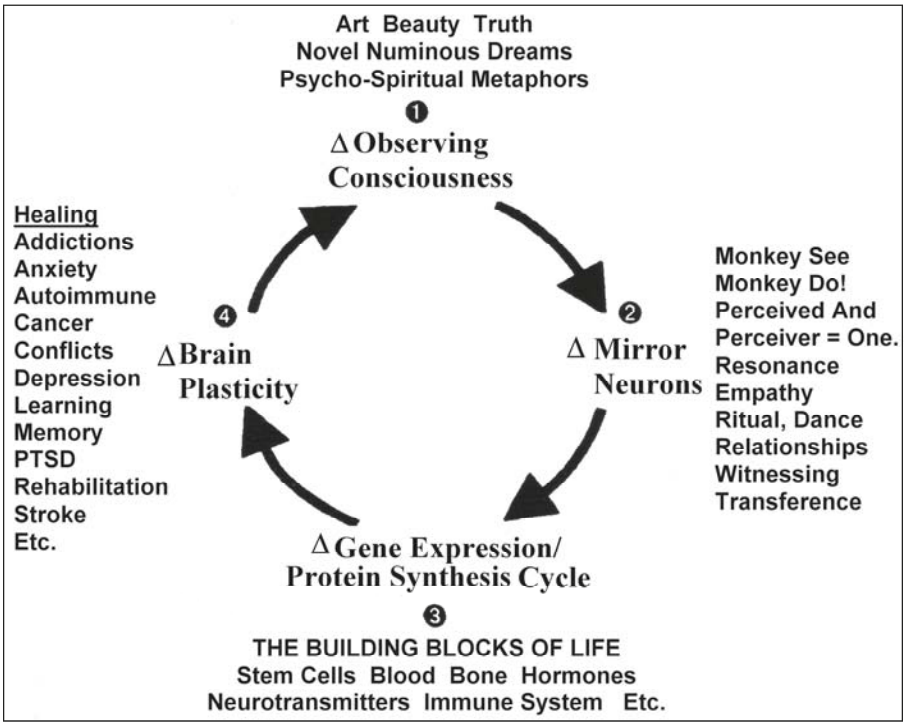

Figure 9. The Creative Psychosocial Genomics Healing Cycle.

psychosocial genomic healing cycle of figure 9. Figure 9 illustrates how (1) Observing Consciousness can (2) activate Mirror Neurons to (3) turn on their Activity and Experience-Dependent Gene Expression/Protein Synthesis Cycle and (4) Brain Plasticity, which generates the possibility of new consciousness and capacities for problem solving, mind-body healing, and rehabilitation. The outer labels in figure 9 suggest how the *Psycho-Spiritual Metaphors* and numinous experiences of psychotherapy, art, truth and beauty that may activate *Mirror Neurons* to mobilize *The Building Blocks of Life* to facilitate *Brain Plasticity and Mind-Body Healing*.

Neuroscience has documented how psychological experiences of novelty (Eriksson et al., 1998), environmental and psychosocial enrichment (Kempermann, et al. 1997; Van Praag et al., 2000), and activity, both *physical* (such as running on a treadmill, and *mental* (such as experiencing and making choices) turn on activity and experience-dependent gene expression and brain plasticity (Van Praag et al., 1999, 2002).

Most recently a very important new functional role for neurogenesis (brain plasticity) in the adult mammalian hippocampus (where new learning is first encoded) has been discovered. Researchers found that newborn neurons are necessary for normal pattern separation in the dentate gyrus of the hippocampus (Clelland et al. 2009). This means that the generation of new neural networks is place where fine sensory-perceptual discrimination takes place. This implies that new patterns of awareness and consciousness become manifest in the 4-stages of our psychosocial genomic healing cycle of figure 9. We propose this creative psychosocial genomic healing cycle is the mind-body mechanism by which the psycho-spiritual metaphors of art, beauty, and truth light and brighten the lamps of human consciousness in psychotherapy as documented in our pilot study reviewed above (Rossi. Iannotti et al, 2008). From a philosophical perspective this is how we can resolve the conundrum of the so-called "Cartesian Gap" between mind and body. This is our answer to the question, "What is the nature of the link from the nonmaterial mind to the material body?" (Langer, 2009).

In the past decade neuroscience has documented the activity of mirror neurons as a mechanism whereby we experience empathy and recognize of intentions of others by observing their behavior and automatically matching their brain activity on an implicit or unconscious level (Iacoboni, 2007, 2008). This neural basis of empathy finds support in research on dysfunctions in the mirror systems of humans with autism and fMRI research on normal participants designed to assess intentionality, emotions, and complex cognition. Such empathy research now appears to be consistent with the historical and research literature on hypnotic induction, rapport, and many of the classical phenomena of suggestion, placebo effects (Benedetti, 2008), and mind-body

healing across many cultures (Greenfield, 2008). A preliminary outline of how mirror neurons may function as a rapport zone mediating between observing consciousness, the experience-dependent gene expression/protein synthesis cycle, and brain plasticity in therapeutic hypnosis and psychosomatic medicine has been documented (Rossi & Rossi, 2006). Experience and qualia-dependent gene expression and brain plasticity is generalized in our theory, research, and practice of utilizing mirror neurons as an explanatory framework in developing and training new skill sets for facilitating "The Creative Psychosocial Genomic Healing Experience" (in volume two of Celinski and Gow, 2010). Current psychosocial genomic research is documenting how music appreciation is example of how the 4-stage creative process of art, beauty, and truth can turn on activity, experience and qualia-dependent gene expression to facilitate therapeutic responses on many levels from mind to gene (Bittman et al., 2005).

The Psychosocial Genomics of Music Appreciation: The Sonata Form of the 4-Stage Creative Process

The psychological experience and meaning of music appreciation has been under intense scrutiny by amateurs and virtuosi and for centuries (Patel, 2008). In this section we review how music can be an expression of the 4-stage creative process that facilitates the transformations of consciousness and behavior in our daily lives. Students of music appreciation will note the similarity between the four stage creative cycle profiled above in figure 5 and the four parts of the classic s*onata form* profiled in figure ten. The term "*sonata form*" refers to the first movement of a symphony. The opening fast movement of a classical symphony (*sonata-allegro*), for example, is usually in sonata form. The sonata form has 3 main sections (the *exposition, development*, and *recapitulation*) that are often followed by a fourth and concluding movement called, "the *coda*." The sonata form illustrates how composers of the classical period (1750-1820) such as Hayden, Mozart, Beethoven and their followers expressed human *conflict, crisis, and their resolution* in music for over 200 years (Kamien, 2006).

In figure 10, the 4-stage outline of the sonata form in classical music illustrates of how the creative arts (dance, drama, literature, music, myth, poetry, song, stories, etc.) may be understood as performance modalities for creating new therapeutic consciousness. Music appreciation can be utilized to facilitate the therapeutic replay, reconstruction, and reframing of negative human experiences into new positive perspectives and expectations that many cultures regard as therapeutic. Numinous experiences of art, beauty, and truth are positive experiences precisely because they generate the activ-

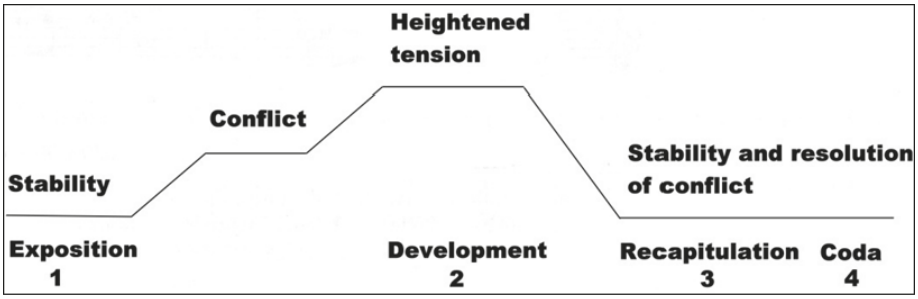

Figure 10. The 4-Stage Outline of the Sonata Form in Classical Music

ity-dependent creative reconstruction of the mind-brain at the molecular-genomic, brain plasticity, and psychological levels. Kamien (2006, p. 163-164) describes the sonata form in the following quotations.

> "The amazing durability and vitality of sonata form result from it capacity for drama. The form moves from a stable situation toward conflict (in the exposition), to heightened tension (in the development), and then back to stability and resolution of the conflict."

This reminds us of the creative process in psychotherapy. We propose that the durability and vitality of the sonata form for over 200 years comes from its integration of creative human experiencing from cognition and emotion to the molecular-genomic.

STAGE ONE: EXPOSITION: INTRODUCTION TO THEMES

> "The exposition sets up a strong conflict between the tonic key and the new key. It begins with the first theme in the tonic, or home, key. There follows a bridge, or transition, leading to the second theme, in a new key." (Kamien, 2006, pp. 163-164)

This first stage of the sonata form corresponds to Stage One of the Creative Process when therapist and patient seek to identify the problem (first theme) and the life changes (second theme) that are at the source of patient's conflicts of Stage Two.

STAGE TWO: DEVELOPMENT: INCUBATION, CONFLICT, AND DRAMA

> "The development is often the most dramatic section of the movement. The listener may be kept off balance as the music moves rest-

> lessly through several different keys. Through these rapid modulations, the harmonic tension is heightened. In this section, themes are developed, or treated in new ways. They are broken into fragments, or motives, which are short musical ideas developed within the composition. A motive may take on different and unexpected emotional meanings." (Kamien, 2006, pp. 163-164)

This second part of the sonata form corresponds to Stage Two, the incubation stage of the Creative Process with its characteristic conflicts, drama, emotions, and symptoms.

STAGE THREE: RECAPITULATION: RESOLUTIONS OF CONFLICTS AND DRAMAS

> "The beginning of the recapitulation brings resolution, as we again hear the first theme in the tonic key. . . .Earlier in the exposition, there was a strong contrast between the first theme in the home key and the second theme and closing section in a new key; that tension is resolved in the recapitulation." (Kamien, 2006, pp. 163-164)

This third section of the sonata form obviously corresponds to Stage Three of the Creative Process when there is an initial resolution of the conflict, problems, and symptoms of Stage Two.

STAGE FOUR: CODA: A SATISFACTORY COMPLETION OF THE 4-STAGE DRAMA

> "An even more powerful feeling is attained by following the recapitulation with yet another section. The coda rounds off a movement by repeating themes or developing them further. It always ends in the tonic [home] key." (Kamien, 2006, pp. 163-164)

This fourth and final part of the sonata form obviously corresponds to Stage Four of the Creative Process in psychotherapy when the patient returns home to reality test the new problem and symptom solutions found in Stage Three. (All quotations from Kamien, 2006, pp. 163-164.)

The integration of the musical and psychological perspectives of the sonata form was described intriguingly by Sullivan (1927) in his brief and prescient book, *Beethoven: His spiritual development*. Sullivan proposes a "revelation" theory of art and "higher consciousness" that Beethoven experienced in composing his last string quartets.

> The four-movement sonata form corresponds to a very fundamental and general psychological process, which is the reason it is found so

> satisfactory and has been so often employed. The general scheme of a first movement, usually representing a conflict of some kind, followed by a meditative or consoling slow movement, and that by a section easing the way to a vigorous final statement, to a conclusion won, is in its main lines, admirably adapted to exhibit an important and recurrent psychological process. The life histories of many major psychological processes can be accommodated within this framework. But in the quartets we are discussing Beethoven's experience could not be presented in this form. The connection between the various movements is altogether more organic than that of the four-movement sonata form. In these quartets the movements radiate, as it were, from a central experience. They do not represent stages in a journey, each stage being independent and existing in its own right. They represent separate experiences, but the meaning they take on in the quartet is derived from their relation to a dominating, experience. This is characteristic of the mystic vision, to which everything in the world appears unified in the light of one fundamental experience. In these quartets Beethoven is not describing to us a spiritual history; he is presenting to us a vision of life. In each quartet many elements are surveyed, but from one central focus. (Pp. 153-154, italics added)

> Therefore a work of art may communicate knowledge. It may indeed be a "revelation." The "higher consciousness" of the great artist is evidenced not only by his capacity for ordering his experience, but also by having his experience. His world may differ from that of the ordinary man as the world of the ordinary man differs from that of a dog in the extent of his contact with reality as well as in his superior organization of it. We may continue to maintain, then, the "revelation" theory of art. Indeed, our business as critics is to make it more explicit. The highest art has a transcendental function, as science has. In saying this, however, we must be careful to distinguish between these functions." (Pp. 15-16)

The four stages of the sonata form as described by many scholars of classical music (Kamien, 2006; Rosen, 1988, 1997; Sullivan, 1927) are a striking examples of how the creative arts may be understood as performance modalities that carry out "psychological work" (Haukappe & Bongartz, 1992; Unterwegner, Lamas & Bongartz, 1992). What is this psychological work? The various forms of artistic expression (cinema, dance, drama, literature, music, myth, poetry, song, stories etc.) are psychological work on the implicit (unconscious) levels of the therapeutic replay, reconstruction, and reframing

of negative (stressful) human experiences into positive "inner resources" that many cultures have called "healing," "therapeutic," "truth" or "wisdom." Numinous experiences of art, beauty, and truth become positive experiences when their initially surprising and unexpected activation of novelty stress generates the activity-dependent creative reconstruction of the mind-brain at the molecular-genomic level (Rossi, 2002, 2004a, 2004b, 2005a).

We now illustrate the therapeutic value of music appreciation with poignant examples from the life of Beethoven and Schubert as recounted by Maynard Solomon who is on the Graduate Faculty at the Juilliard School of Music (Solomon, 2003).

During her sojourn in Vienna in the years 1809 to 1812 Frau Antonie Brentano was often ailing for weeks at a time, suffering to such an extent that she withdrew to her room, where she remained by herself, unfit to see anybody. On such occasions Beethoven was regularly in attendance; he came in, seated himself without further ado at a piano in her antechamber and improvised; when he had "said everything and given solace" to the sufferer in his own language, he left as he had come, without taking notice of anybody else. (p. 229)

In a 1811 letter to her sister-in-law Bettina, Frau Brentano described these Beethoven visits and the healing power she experienced:

Beethoven has become for me one of the dearest *[liebsten]* human beings . . . His whole nature is simple, noble, good-natured, and his tenderheartedness would grace the most delicate woman. It speaks in his favor that few know him, and even fewer understand him. He visits me often, almost daily, and then he plays spontaneously because he has an urgent need to alleviate suffering, and he feels that he is able to do so with his heavenly sounds . . . That there is such power in music I hadn't yet known until Beethoven informed me of it. (Solomon, pp. 229-230)

Other examples of the healing power of music and dreaming are recounted in the senior author's recovery from a stroke experienced at the age of 69 (Rossi, 2004c, 2007). Taken together the theory, research and practice illustrated in the 10 figures of this chapter present a new psychosocial genomic perspective of the creation of consciousness and therapeutic experience. Psychotherapy and the creative arts, in the highest sense, are modalities for the therapeutic replay, reconstruction, and transformation of negative human experiences into positive possibilities. A primary creative function of culture is to initiate therapeutic rituals leading to social integration and wisdom on many levels from mind to gene. The deep psychobiological arousal of stress, struggle, and conflict during stages one and two of the creative process generates the activity, experience and qualia-dependent creative reconstruction of the mind-brain on the molecular-genomic levels that are experienced as joyful, positive life expectancies in stages three and four. Nu-

minous experiences of art, beauty, and truth are positive experiences of stage three and four of the creative process that are experienced after coping successfully with the stress and labor of stages one and two. Art, beauty, and truth are creative experiences that mirror qualia-dependent gene expression and brain plasticity on the DNA and neural levels during REM dreaming as well as inspirational states of consciousness while we are awake.

Conclusion

We document how The Creative Psychosocial Genomic Healing Experience reduces (1) dysfunctional chronic inflammation and (2) oxidative stress while (3) increasing the activation of stem cells to facilitate the deep molecular-genomic sources of human resilience and resourcefulness. This new psychosocial genomic foundation for facilitating Antonovsky's coherence of consciousness and culture, as well as Rosenbaum's learned resilience embraces the eternal verities of art, beauty, intuition, and truth on many levels from mind to gene. We document how the three psychological experiences of novelty, enrichment, and activity (mental and physical) and the three "spiritual" experiences of the numinosum (fascination, mysteriousness, tremendousness) can turn on activity, experience and qualia-dependent gene expression and brain plasticity. We propose that these experiences and their positive cognate states such as awe, bliss, curiosity, ecstasy, expectancy, love, passion, surprise, and wonder can create new consciousness. This implies that our 4-stage creative psychosocial genomics healing cycle bridges the so-called Cartesian gap between the mind and the body. These principles of psychosocial genomics are manifest in the *classical music of the sonata form* as an unusually clear illustration of the 4-stage creative cycle in the humanistic arts and sciences as well as psychotherapy.

- The psychological appreciation, experience and meaning of music are expressions of the four stage creative process on many levels from mind to gene and molecule. This is a new molecular-genomic theory of music appreciation.
- Composers of the classical period (1750-1820) such as Hayden, Mozart and Beethoven expressed human conflict, crisis, and their resolution in the 4-stage creative process of the "sonata form."
- Music that evokes the deep psychobiological arousal of stress, struggle, and conflict during stages one and two of the creative process may facilitate the activity-dependent creative reconstruction of the mind-brain on the molecular-genomic and brain plasticity levels that are experienced as joyful and positive in stages three and four.

Extensive research is now required to identify the experience-dependent profiles of gene expression evoked by psychotherapy as well as the arts, humanities and sciences in creating new consciousness.

Our psychosocial genomic protocol for facilitating creative states of consciousness, art, beauty, truth and healing receives documentation with DNA microarray and RNA technology in our emerging neuroscience of psychotherapy and the creative arts.

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Chapter Fifteen*

A Pilot Study of Positive Expectations and Focused Attention via a New Protocol for Optimizing Therapeutic Hypnosis and Psychotherapy Assessed with DNA Microarrays:

The Creative Psychosocial Genomic Healing Experience

Ernest Rossi, Salvatore Iannotti, Mauro Cozzolino, Stefano Castiglione, Angela Cicatelli & Kathryn Rossi

We extend the use of DNA microarrays to explore a new psychotherapeutic therapeutic protocol, *The Creative Psychosocial Genomic Healing Experience,* an easy-to-learn approach to facilitating therapeutic hypnosis, psychotherapy, rehabilitation, meditation, and pastoral counseling. This pilot study assessed the hypothesis that a top-down creatively oriented positive human experience can modulate gene expression on the molecular level. A DNA microarray data analysis of the white blood cells of three human subjects was performed immediately before, one hour after, and 24 hours after The Creative Psychosocial Genomic Healing Experience. We documented changes in the expression of 15 early response genes within one hour that

* *Sleep and Hypnosis*, 10:2, 2008

apparently initiated a further cascade of 77 genes 24 hours later. This could provide the mind/molecular genomic foundation of new therapeutic models for optimizing human consciousness, health, and well being via therapeutic hypnosis, psychotherapy, pastoral counseling, and psychiatry. This proof-of-principle pilot study now requires cross validation with more subjects with a variety of diagnostic classifications to document the validity and reliability of using DNA microarrays to assess our new creative psychosocial genomic therapeutic protocol in a variety of cultures. (Sleep and Hypnosis 2008;10 (2):39-44)
KEYWORDS: Creative Experience, DNA microarray, gene expression, therapeutic hypnosis.

INTRODUCTION

In the past decade DNA microarray technology has made it possible to measure the expression levels of many thousands of genes simultaneously. This novel experimental approach has revolutionized research in molecular biology and become a new standard in personalized medicine (Eisen et al. 1998). Recent research has documented the use of DNA microarrays for assessing therapeutic responses to psychological relaxation and meditative practices on the molecular-genomic level (Duseket al., 2008; Rossi, 2002, 2004, 2007; Rossi,2005/2006). This has lead to calls for further research on the pathways of psychotherapeutic processes on all levels from mind to gene (Abbott, 2008; Nestler, 2008; Rossi et al., 2006).In this pilot study we use DNA microarrays to assess a new therapeutic protocol, The Creative Psychosocial Genomic Healing Experience, is a relatively brief, easy-to-learn process for facilitating a wide range of therapeutic approaches, such as therapeutic hypnosis, psychotherapy, rehabilitation, meditation, and pastoral counseling (Rossi, 2005/2006; Rossi and Rossi, 2008a and 2008b).

MATERIALS AND METHODS

Three highly susceptible hypnotic subjects, one male and two females, experienced therapeutic hypnosis following the new protocol called, "The Creative Psychosocial Genomic Healing Experience" established by Rossi (2004). Peripheral blood, about 10 ml, was collected immediately before, within one hour of therapeutic treatment (the length of each treatment depended by the subject, but never went more than one hour). A total of 6 blood samples were employed to purify total RNA from leukocytes (the nucleated part of peripheral white blood cells) using the kit LeukoLOCK(TM) Total RNA system following the instruction supplied by the manufacture

(Ambion, USA). The amount of total RNA extracted from each blood sample was quantified using the NanoDrop ND-1000 photometer (Wilmington, DE). The purity of RNA samples was determined based on the ratio of spectrophotometric absorbance of the sample at 260 nm to that of 280 nm (A260/A280). However not all the RNA samples resulted pure enough (A260/A280 ratio of 1.8) to go through the microarray procedure, in fact protein contamination was still present in some of the samples. A further purification stepby means of one phenol chloroform and one chloroform treatment was necessary to eliminate the contaminants.

Total RNA of each purified sample was further quantify using the NanoDrop apparatus and its integrity was ascertained by means of electrophoresis in agarose gels followed by ethidium bromide staining on the ribonucleic acid. Around 2.5 μg of total RNA was delivered to the MicroCRIBI Service (University of Padova, Italy) for microarray analysis. MicroCRIBI Service performed the microarray analysis on 21,329 - 70 meroligonucleotides (Operon version 2.0) designed on Human Unigene clusters.

For each sample, 1.0 μg of total RNA was reverse transcribed and labeled using Amino Allyl cDNA Labeling Kit (Ambion, USA) following the manufacture instruction. Cy3/Cy5 was from Amersham Biosciences (Amersham, United Kingdom). Cy3/Cy5 dye incorporation into aRNA yielded incorporation rates of 30 to 60 dye molecules per 1000 nucleotides by spectrophotometric analysis, as requested by the manufacturer.

The microarrays were scanned with a two-channel confocal microarray scanner (ScanArray# Lite, Perkin Elmer, USA) using its dedicated software (ScanArray Express 3.0.0., Perkin Elmer). The laser power and the photomultiplier tube (PMT) were set between 70% and 80% of maximum. The excitation/emission settings were 543/570 nm for Cy3and 633/670 nm for Cy5. After laser focusing and balancing of the two channels, scans were conducted at a resolution of 5 μm. For any scan, two separate 16-bit TIFF images were produced. Data were normalized by ScanArray Express using the LOWESS (Locally Weighted Regression Scatter Plot Smoothing; Cleveland, 1979) algorithm.

After normalization, data from each slide were split in two, by using Microsoft Excel, since each probe is spotted twice. Thereafter, each spot value was considered to be independent and subjected to SAM (Significance Analysis of Microarrays; Tusher et al., 2001) analyses.

Since each comparison (S1/S1-1h, S2/S2-1h, S3/S3-1h,) was repeated at least twice, there were at least four values for each gene to be used in the SAM analyses.

Lists of genes with significant changes in expression among at least two experimental samples were identified at delta values that gave a false discov-

ery rate (FDR) of 0%.

The possible role played by therapeutic hypnosis via "The Creative Psychosocial Genomic Healing Experience" on three subjects in up-regulating gene expression in leukocytes in the peripheral blood was investigated. To accomplish this, transcriptome changes were first monitored in untreated subject, just after the treatment. The transcriptome variations were analysed by means of the Operon Human Genome Oligo Set Version 2.0 platforms. The effect of positive and creatively oriented therapeutic hypnosis immediately after the session was investigated using a direct comparison experimental design, with four repetitions ofwhich one was a dye swap. As each probe was spotted twice on human array, the following SAM (Significance Analysis of Microarrays, Tusher et al., 2001) analysis was performed on a dataset of eight values for each gene.

Experimental Design

The effect of positively oriented therapeutic hypnosis via the administration of our Creative Psychosocial Genomics Healing Experience on gene transcription was monitored and the subject's measurements before the treatment were the common references. Each comparison (S1/S1-1h,S2/S2-1h; S3/S3-1h) was repeated at least twice, so that at least four values for each gene were used in the subsequent SAM analyses. The dataset was tested with SAM using a 'one class' study design. This analysis was carried out on the following three subgroups of data: S1/S1-1h, S2/S2-1h; S3/S3-1h. Using a delta of 0.2 and a median false discovery rate (FDR) of 0.00%, the analysis yielded 3207 genes as differentially expressed, six groups of genes were selected (the up- and down-regulated for each of the three subgroups of data). By crossing these data, it was possible to show the different up- and down-regulating effects.

Results

DNA microarray results on the three subjects in response to the therapeutic protocol within one hour after the treatment indicated that expression of 15 early response genes were up-regulated between 1.2 and 1.8 folds and no single gene was down-regulated. The list of the up-regulated genes is presented in Table 1.

Table 1. The Gene Bank Accession, Gene Symbol, Gene Description and results in fold changes in response to therapeutic hypnosis.

GB_accession	Gene_Symbol	Description	Fold changes
AK057104		Homo sapiens cDNA FLJ32542 fis, clone SMINT2000537	
		Sodium-coupled neutral amino acid transporter 2	1,777714817
NM_000329	RPE65	Retinal pigment epithelium-specific protein (65kD)	1,664647867
AK055997		Homo sapiens cDNA FLJ31435 fis, clone NT2NE2000612	
		Ring Finger protein 165	1,617968537
AK056729		Homo sapiens cDNA FLJ32167 fis, clone PLACE6000450	
		Serpin B Proteinase Inibitor	1,596523872
NM_001074	UGT2B7	UDP glycosyltransferase 2 family, polypeptide B7	1,578875081
BC018130	F2RL1	Coagulation factor II (thrombin) receptor-like 1	1,506199199
NM_030824	FLJ14356	Hypothetical protein FLJ14356 zinc finger protein 442	1,469687506
NM_021122	FACL2	Fatty-acid-Coenzyme A ligase, long-chain 2	1,380622376
NM_004126	GNG11	Guanine nucleotide binding protein 11	1,372082479
NM_020980	AQP9	Aquaporin 9	1,366899043
NM_001186	BACH1	BTB and CNC homology 1, basic leucine zipper transcription factor 1	1,330834867
NM_002921	RGR	Retinal G protein coupled receptor	1,312291611
NM_024911	FLJ23091	Hypothetical protein FLJ23091	
		G protein-coupled receptor 177 Isoform 1 and Isoform 2	1,274787709
NM_000860	HPGD	Hydroxyprostaglandin dehydrogenase 15-(NAD)	1,224585804
NM_002110	HCK	Hemopoietic cell kinase	1,190732546

DISCUSSION

The major limitation of this pilot studywas the small number of subjects and the lack of appropriate controls. The lack of statistical power in this pilot study, due to the limited number of treated subjects, for example, does not enable us to assess the degree to which our results coincides with previous research supporting the hypothesis that therapeutic hypnosis could modulategene expression (Lichtenberg et al., 2000,2004). Well funded major research studies in psychiatric genetics utilizing DNA microarrays typically include as many as2,000 to 20,000 subjects (Abbott, 2008). Our results, however, suggest that this pilot study provides documentation consistent with the hypothesis that our new therapeutic protocol, The Creative Psychosocial Genomic Healing Experience, may modulate gene expression in human white blood cells.

These preliminary findings suggest that positive expectation via The Creative Psychosocial Genomic Healing Experience, anew protocol for facilitating therapeutic hypnosis, generated the up-regulation of 15early response genes within one hour.

The expression of these early response genes apparently initiated a larger cascade of gene expression 24 hours later. This unexpected finding may have important implications for the role of time and post-hypnotic suggestion in therapeutic hypnosis and many other psychological experiences. We are currently investigating the unexpected finding that a gene associated with bipolar disorder may be over expressed in response to our new protocol of therapeutic hypnosis.

We propose that the genes expressed in response to this new protocol may be related to a variety of functions associated with stress (Dusek et al. 2008), cognition and dreaming (Riberio et al., 2007), and psychiatric conditions (Tsankova et al., 2007). Suggestions for further research in this area have been recommended previously (Kustraet al., 2006; Nestler, 2008; Nuzzo, 2008).

We introduced a new therapeutic protocol, The Creative Psychosocial Genomic Healing Experience, for assessing the contribution of positive expectation, focused attention, therapeutic hypnosis, and psychotherapy to stress reduction and mind-body healing (Rossi, 1986/1993, 2002, 2004, 2007; Rossi and Rossi, 2008b). A salient feature of this new protocol is that it was found to be more acceptable, with high face validity for the subjects who experienced it and the psychiatrist who administered it, as a positive therapeutic process in contrast to the more research oriented classical scales of measuring hypnotic susceptibility, which have been questioned regarding their appropriateness for therapeutic applications (Fromm & Shor,1972 Wester and Sugarman, 2007).

Our new protocol, The Creative Psychosocial Genomic Healing Experience, however, now requires standardization in relation to the classical assessments of therapeutic hypnosis such as the Stanford Hypnotic Susceptibility Scale (Hilgard, 1965)and the Harvard Group Scale of Hypnotic Susceptibility (Shor and Orne, 1978) as well as the more general evaluation of consciousness and focused attention with objective measures such as the Tellegen Absorption Scale (Tellegen, 1981, 1982,1992; Tellegen & Atkinson, 1974).

The successful utilization of this new Creative Psychosocial Genomic Healing Experience protocol for assessing research on humans with DNA microarrays may foreshadow a new psychosocial genomic paradigm to facilitate "top-down" therapeutic approaches from mind to gene (Rossi, 1986/1993, 2007; Rossi and Rossi,2008a & b). This could provide the mind/molecular genomic foundation of new therapeutic models for optimizing human consciousness, health, and well being via therapeutic hypnosis, psychotherapy, pastoral counseling, and psychiatry.

CONCLUSIONS

This pilot study assessed the hypothesis that a creatively oriented positive human experience of therapeutic hypnosis could modulate gene expression on the molecular level. We documented changes in the expression of 15 early response genes within one hour that apparently initiated a further a further cascade of 77 genes 24hours later. This proof-of-principle pilot study now requires cross validation with more subjects to document the validity and reliability of using DNA microarrays to assess our therapeutic protocol,

The Creative Psychosocial Genomic Healing Experience, as a new approach for facilitating therapeutic hypnosis, psychotherapy, rehabilitation, meditation, and pastoral counseling.

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Chapter Sixteen*

A New Bioinformatics Paradigm for the Theory, Research, and Practice of Therapeutic Hypnosis

David Atkinson
University of Pittsburgh School of Medicine, USA
Salvatore Iannotti
La Nuova Scuola Di Neuroscienze Ipnosi Therapeutica, San Lorenzo Maggiore, Italy.
Mauro Cozzolino
University of Salerno, Italy
Stefano Castiglione
University of Salerno, Italy
Angela Cicatelli
University of Naples, Italy.
Bhaskar Vyas
The M.S. University of Baroda, Vadodara, India
Jane Mortimer
University of Adelaide, Australia
Richard Hill
Western Sydney University, Australia
Erika Chovanec
Institut of holistic-motivational Psychotherapy, Vienna, Austria
AlessiaChiamberlando
Scuola Bolognese di Psicoterapia Cognitiva, Italy
Jorge Cuadros
Grupo Hipnológica, Spain
Claude Virot
Emergences, Rennes, France
Michel Kerouac
Institut Milton H. Erickson du Québec, Québec, Canada
Thierry Kallfass
Institute of Human Perspectives, Geneva, Switzerland

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Stanley Krippner
Saybrook University, USA
Claire Frederick
Saybrook University, USA
Bruce Gregory
Ryokan College, Los Angeles, California, USA
Michael Shaffran
MHE Institute of the California Central Coast, Los Osos, USA
Margaret Bullock
MHE Institute of the California Central Coast, Los Osos, USA
Ella Soleimany
MHE Institute of the California Central Coast, Los Osos, USA
April Cybelle Rossi
MHE Institute of the California Central Coast, Los Osos, USA
Kathryn Rossi
MHE Institute of the California Central Coast, Los Osos, USA
Ernest Rossi
MHE Institute of the California Central Coast, Los Osos, USA

ABSTRACT

In a 2008 pilot study we used DNA microarrays to explore the historical ideo-plastic faculty of therapeutic hypnosis. We documented how to measure changes in activity or experience-dependent gene expression over relatively brief time periods (1 hour and 24 hours) following a single intervention of therapeutic hypnosis (about 1 hour). In the present paper we utilize bioinformatic software to explore the possible meaning and significance of this ideoplastic faculty of therapeutic hypnosis. Indications suggest that the ideoplastic process of therapeutic hypnosis may be associated with (1) the heightening of a molecular-genomic signature for the up-regulation (heightened activity) of genes characteristic of stem cell growth, (2) a reduction in cellular oxidative stress, and (3) a reduction in chronic inflammation. We identify these three empirical associations as an initial beta version of the molecular-genomic signature of the ideo-plastic process of therapeutic hypnosis, which can serve as a theoretical and practical guide for clinical excellence by beginners as well as senior professionals. We propose this molecular-genomic level of discourse as a supplement to the traditional cognitive-behavioral description of therapeutic suggestion, hypnosis, and psychotherapy that is consistent with "translational research" currently funded by the National Institute of Mental Health (NIMH).

KEYWORDS: Bioinformatics, DNA microarrays, epigenetics, hypnosis, ideoplastic faculty.

Introduction: Our 2008 Pilot Study of the Epigenetics of Therapeutic Hypnosis

Epigenetics is becoming recognized as a new scientific approach for exploring the interaction of nature and nurture: how genes interact with the environment to modulate behavior and cognition in sickness and health(Hsieh & Eisch, 2010). Recent research has demonstrated that complex 'epigenetic' mechanisms regulate gene activity without altering the DNA code (Tsankova, Renthal, Kumar, & Nestler, 2007). Epigenetics focuses on a special class of genes, often described as activity or experience-dependent genes, which can be turned on (activated) by signals from the physical and psychosocial environment to modulate the complex functions of physiology and psychology (Rossi, 2002, 2004, 2007; Lloyd & Rossi, 1992, 2008). Experience-dependent gene expression is contrasted with constitutive genes, which are inherited by the Mendelian laws of physical inheritance to generate the relatively simple functions of physiology that cannot be modified by the psychosocial signals of culture, learning, and motivation.

In this paper we will first present the basic hypothesis and motivation for our first pilot study utilizing the positive expectations and focused attention of therapeutic hypnosis to modulate activity or experience dependent gene expression (Rossi, Iannotti, Cozzolino, Castiglione, Cicatelli, & Rossi, 2008). We will review the methods, procedures, participants, data analysis, and results of this initial study. We will then discuss the limitations of this pilot study and our current approach for dealing with these limitations by introducing a bioinformatics paradigm into the scientific literature of therapeutic hypnosis. While this new bioinformatics paradigm is new to literature of professional hypnosis, it has recently become a standard operating procedure for the analysis, meaningful organization, and understanding of the epigenetics of experience-dependent gene expression and brain plasticity in the biological and medical sciences (Akil et al., 2010; Insel, 2009, 2010).

Hypothesis and Motivation of Our Original 2008 Pilot Study

Our original 2008 pilot study addressed the hypothesis that a creatively oriented, positive experience of therapeutic hypnosis, which we call, *"The Creative Psychosocial Genomic Healing Experience "(CPGHE),* could modulate the expression of activity or experience-dependent genes as measured by DNA microarrays (Rossi, Iannotti, Cozzolino, Castiglione, Cicatelli, & Rossi, 2008). DNA microarrays are new technology that enables researchers to identify and assess the biological and psychological states and changes in activity or experience-

dependent gene expression in cells and tissues of the brain and body during health and disease with a single experiment (Rossi,2005/2006).While most of this research has been done with animals for biological and medical research, this paper reviews new epigenetic models of how this DNA technology can be applied to a new era of foundational research on the clinical applications of therapeutic hypnosis and psychotherapy (Rossi, 2002, 2004, 2007).

The *CPGHE* is a new, easy to learn, professional protocol for the induction of focused attention, expectancy, and positive motivation that is characteristic of clinical or therapeutic hypnosis. A manual for the administration, rationale, scoring, and research on the *CPGHE,* which we used in our original 2008 pilot study is freely available (http://www.ernestrossi.com/ernestrossi/Neurosciencresearchgroup.html). The original hypothesis of our 2008 pilot study was motivated by recent research, which documents how many activity or experience-dependent genes assessed by DNA microarrays are expressed in the normal processes of learning, memory, and brain plasticity. The psychobiological states of being awake, asleep, and REM dreaming for example, each have their own characteristic pattern of gene expression (Ribeiro et al., 1999, 2002, 2004, 2007, 2008). Many psychiatric conditions such as addictions, depression, obsessive-compulsive disorder, and posttraumatic stress syndrome can now be identified by their characteristic patterns of activity or experience-dependent gene expression (sometimes described as their "molecular-genomic signature") assessed with DNA microarrays (Insel, 2009, 2010). Further, many mind-body approaches to ameliorating psychological and psychiatric dysfunctions via meditation (Dusek et al., 2008), Qigong (Li et al., 2005), and music (Bittman et al., 2005), have used DNA microarrays to assess their characteristic patterns of experience-dependent gene expression. Such research suggests that the focused attention, absorption, and positive expectancy associated with therapeutic hypnosis also could modulate experience-dependent gene expression as measured with DNA microarrays. We propose that the analysis of activity or experience-dependent gene expression to identify the molecular-genomic basis of psychopathology and the therapeutic approaches for resolving such psychopathology may become a new way of assessing evidence based mind-body medicine (Eisen, Spellman, Brown, & Botstein, 1998; Rossi, 2002, 2004a, 2007).

Material, Method, and Participants of Our Original 2008 Pilot Study

We used DNA microarrays to explore the molecular-genomic basis of the historical ideo-plastic faculty of therapeutic hypnosis (Wetterstrand, 1902; Tinterow, 1970). The DNA microarray is a standard tool for assessing the expression of the entire human genome in a single experiment. Our initial cohort of

three highly susceptible hypnotic subjects (two females and one male) all had advanced academic degrees and were recruited from a university environment by the second co-author (Iannotti) on the basis of a General Psychiatric Evaluation, The Minnesota Multiphasic Personality Inventory (MMPI-2), The Tellegen Absorption Scale (highly correlated with Standard Scales of Hypnotic Susceptibility), and the Spiritual Intelligence Self Report Inventory (high scorers on the SISRI-24 acknowledge heightened experiences related to critical existential thinking, personal meaning production, transcendental awareness, and conscious state expansion). These subjects scored within the normal range of personality characteristics with no evident psychopathology on the MMPI-2. They were all volunteers who responded well to the *CPGHE* with a positive sense of focused attention, expectancy, absorption, and therapeutic well being. A full description of the clinical intervention, rationale sample collection, and microarray analysis has been made publically available (Rossi, Iannotti, et al., 2008). For the purpose of this paper, the clinical intervention of our original 2008 pilot paper can be described briefly as an application of the 4-stage creative process to therapeutic hypnosis as follows.

Stage 1: The induction of hypnosis via permissive ideodynamic suggestions.

Stage 2: Deepening hypnosis via incubation and past problem review to activate positive motivation, expectancy, and inner resources.

Stage 3: Supporting the positive aha or eureka experience of insight.

Stage 4: Awakening with post-hypnotic suggestions for re-integration and reality testing.

Briefly, the overall research procedure can be summarized as follows. Peripheral blood was obtained from these three adult subjects immediately prior to, 1 hour after, and 24 hours after a single session of therapeutic hypnosis according to the protocol of the *CPGHE* initially formulated by Rossi (2004a). Total RNA was extracted from leukocytes, quantified, and purified. Approximately2.5 ìg of purified total RNA was delivered to the MicroCRIBI Service (University of Padova, Italy) for microarray analysis. MicroCRIBI Service performed the microarray analysis on 21,329 - 70mer oligonucleotides (Operon version 2.0) designed on Human Unigene clusters. For each sample, 1.0 ìg of total RNA was reverse transcribed and labeled with Cy3 and Cy5 fluorophores for two-channel scanning. Fluorophore labeling of "control" (Immediately before hypnosis) versus "treated" (1 hour or 24 hours after hypnosis) samples was counterbalanced, to control for dye bias. The microarrays were scanned

with a two-channel confocal microarray scanner (ScanArray# Lite, Perkin Elmer, USA) using its dedicated software (ScanArray Express 3.0.0., Perkin Elmer).

Data Analysis, Results, and Limitations of Our Original 2008 Pilot Study

The DNA microarray analysis of the white blood cells of three human participants (with a total of more than 191,961 data points for statistical analysis) was performed immediately before, within one hour after, and 24 hours after being administered the *CPGHE.* DNA microarray results on the three subjects in response in our original 2008 pilot study to the therapeutic protocol within one hour after the treatment indicated that expression of 15 early response genes were up-regulated between 1.2 and 1.8 folds and no gene was down-regulated. The list of the up-regulated genes in our original 2008 pilot study is presented in Table 1.

While Table 1 is a standard listing of the raw data of experience-dependent gene expression assessed via DNA microarrays as typically reported in the biological and medical literature, it would be a daunting challenge to understand its meaning and significance for the practitioner of therapeutic hypnosis. While our uniform cohort of three highly susceptible hypnotic subjects were controlled for time of day (9:15 - 11:30 am), therapist, and hypnotic technique (CPGHE), many other possible sources of genomic variation were a major limitation of this pilot study. A way of coping with some of these limitations is the application of bioinformatic software such as *Gene Set Enrichment Analysis (GSEA),* which presents us with the rational for using it as a computational tool in conceptualizing a new paradigm for the research and clinical practice of therapeutic hypnosis at the molecular-genomic level.

A New Bioinformatic Paradigm of Therapeutic Hypnosis at the Molecular-Genomic Level

In this and the following sections we explore the bioinformatic theory, research, and practice of linking experience-dependent gene expression with the cognitive-behavioral phenotypes (observables), which are traditionally associated with therapeutic hypnosis. To create an appropriate context for understanding the significance of current bioinformatics, we begin with a review of the historical conception of the ideo-plastic faculty in the theory and practice of therapeutic suggestion and hypnosis. We view this ideo-plastic faculty as complementary to the dissociative component of experimental hypnosis measured by the Stanford and Harvard Hypnotic Susceptibility Scales (Hilgard, 1965, 1977; Hilgard & Hilgard, 1975).

Table 1: The Modulation of Gene Expression in Human Leukocytes By a New Protocol for Optimizing Therapeutic Hypnosis and Psychotherapy, "*The Creative Psychosocial Genomic Healing Experience.*" The Gene Bank Accession, Gene Symbol, Gene Description and results in fold changes in up-regulated gene expression within one hour in response to therapeutic hypnosis.

GB Accession	Gene Symbol	Gene Description	Fold Change
AK057104		Homo sapiens cDNA FLJ32542 fis, clone SMINT2000537 Sodium-coupled neutral amino acid transporter 2	1.778
NM_000329	RPE65	Retinal pigment epithelium-specific protein (65kD)	1.665
AK055997		Homo sapiens cDNA FLJ31435 fis, clone NT2NE2000612 Ring Finger protein 165	1.618
AK056729		Homo sapiens cDNA FLJ32167 fis, clone PLACE6000450 Serpin B Proteinase Inibitor	1.597
NM_001074	UGT2B7	UDP glycosyltransferase 2 family, polypeptide B7	1.579
BC018130	F2RL1	Coagulation factor II (thrombin) receptor-like 1	1.506
NM_030824	FLJ14356	Hypothetical protein FLJ14356 zinc finger protein 442	1.470
NM_021122	FACL2	Fatty-acid-Coenzyme A ligase, long-chain 2	1.381
NM_004126	GNG11	Guanine nucleotide binding protein 11	1.372
NM_020980	AQP9	Aquaporin 9	1.367
NM_001186	BACH1	BTB and CNC homology 1, basic leucine zipper transcription factor 1	1.331
NM_002921	RGR	Retinal G protein coupled receptor	1.312
NM_024911	FLJ23091	Hypothetical protein FLJ23091 G protein-coupled receptor 177 Isoform 1 and Isoform 2	1.275
NM_000860	HPGD	Hydroxyprostaglandin dehydrogenase 15-(NAD)	1.225
NM_002110	HCK	Hemopoietic cell kinase	1.191

Theory: The Historical Ideo-Plastic Faculty of Therapeutic Hypnosis

Our proposed bioinformatic paradigm of therapeutic hypnosis finds its historical source in the pioneering works of Bernheim (1886/1957) and others who described the dynamics of therapeutic suggestion and hypnosis as follows.

> The one thing certain is that a *peculiar aptitude for transforming the idea received into an act* exists in hypnotized subjects who are susceptible to suggestion. In the normal condition, every formulated idea is questioned by the mind. . . In the hypnotized subject, on the contrary, the transformation of thought into action, sensation, movement, or vision is so quickly and so actively accomplished, that the intellectual inhibition has no time to act. When the mind interposes, it is already an accomplished fact, which is often registered with surprise, and which is confirmed by the fact that it proves to be real, and no intervention can hamper it further. . .There is, then, *exaltation of the ideo-motor reflex excitability, which effects the unconscious transformation of the thought into movement, unknown to the will* . . .There is also, then, *exaltation of the ideo-sensorial reflex excitability, which effects the unconscious transformation of the thought into sensation, or into a sensory image*. . . The mechanism of suggestion in general, may then be summed up in the following formula: *increase of the reflex ideo-motor, ideo-sensitive, and ideo-sensorial excitability*... In the same way in hypnotism, the ideo-reflex excitability is increased in the brain, so that any idea received is immediately transformed into an act, without the controlling portion of the brain, the higher centers, being able to prevent the transformation. (p. 137-139, italics in the original).

The idea that hypnosis involved activity via an increase in "sensitivity" and "ideo-reflex excitability" was later described as the "ideo-plastic faculty" by Wetterstrand (1902) who presented the dynamics of therapeutic suggestion and hypnosis with these words.

> The *ideo-plastic* idea, the suggestive theory, must be explained and how it is possible to dominate and cure pathological conditions by ideas and volition. They [patients] must be told that no restraint is put upon them, that they are merely shown the way and that their present conditions [pathology] will change, not by any preponderance of another's will. But as the result of a proper effort to aid by us-

ing their own will. They are helped to develop the *ideo-plastic* faculty, whereby is meant the power that ideas possess to influence physical conditions, as, for instance, the production of cholera symptoms by fright, or by bleeding marks on hands and feet from profound and continued contemplation of or meditation upon the "Saviors" wounds. They are guided by word and thought without restraint, authority, and command. . . Suggestion, or, rather suggestibility, is composed of two elements: ability to receive an impulse from without, and the *ideo-plastic* faculty. As these are absolutely independent of each other, we must distinguish between them. There are patients, who are very impressionable, and who accept a suggested idea with absolute confidence; the influence, however, of the idea upon their physiological functions is feeble. They do not realize the suggestions, and their morbid symptoms yield with great difficulty, as their *ideo-plastic* conception is small. Others, on the contrary, accept suggestions slowly; they are incredulous and even resist them. Nevertheless, clinical therapy has repeatedly shown that physiological and pathological processes are often easily modified by the psychic influence, sometimes by autosuggestions. Here, then, the suggestibility is undeveloped and small, being surpassed by the *ideo-plastic faculty*. . .

Above all, the methods in each particular case should be varied with proper guidance and moderation, not because the suggestibility is thereby increased, but because the *ideo-plastic* faculty is thus developed and placed under the influence of a will that knows and directs its tendencies. What we look for is, therefore, a slight receptivity for outside impulses and as great a centralization of psychic functions and the *ideo-plastic* capacity as possible. It is rare to find this combination, but it can be attained by training and education." (Quoted from Tinterow, 1970, pp. 534-537. Italics added here.)

These historical conceptions regarding the "peculiar aptitude for transforming the idea received into an act," "ideo-reflex excitability," and the "ideo-plastic faculty" as the basis of therapeutic suggestion and hypnosis were published approximately a century before our current understanding of "activity or experience-dependent gene expression and brain plasticity" in current neuroscience. From a *neuroscience* perspective "activity or experience-dependent gene expression" is a bridge over the so -called, "Cartesian gap" between body and mind, nature, and nurture. Experience-dependent gene expression and associated brain plasticity is the

putative molecular-genomic mechanism underpinning a neuroscience model of the transformations of consciousness, cognition, and behavior observable in everyday life as well as the arts, sciences, and psychotherapy. Activity or experience-dependent gene expression and brain plasticity mediate psychobiological adaptation and creativity in coping with mind-body issues in health, psychosomatic medicine, and rehabilitation (Rossi, 1986/1993, 2002, 2004a, b, 2007).

Pioneering neuroscience research has documented how psychological experiences of novelty (Eriksson et al., 1998; Ribeiro et al., 2008), enrichment (Kempermann et al., 1997; Pinaud, 2004), and exercise (Gordon, Kollack-Walker, Akil, & Panksepp, 2002), *both mental and physical,* can facilitate immediate early and experience-dependent gene expression and brain plasticity (Guzowski et al., 2001; Van Praag et al., 1999, 2000, 2002). Our activity-dependent protocol for therapeutic suggestion and hypnosis, the *CPGHE,* was constructed to facilitate these psychological experiences of novelty, enrichment, and exercise (mental and physical) to optimize experience-dependent gene expression and brain plasticity generating new neurons. Current neuroscience research documents how these new neurons are not necessary for easy navigational tasks, but they are important for complex tasks that required new memory for finer distinctions in the cognitive-behavioral spatial organization of the environment and consciousness itself (Clelland et al., 2009). Experience-dependent profiles of gene expression associated with higher levels of neuronal activity and brain plasticity with broad implications for understanding the creative transformations of human consciousness, cognitive, and adaptive behavior has been noted by Cáceres et al. (2003).

> Our results indicate that the human brain displays a distinctive pattern of gene expression relative to non-human primates, with higher expression levels for many genes belonging to a wide variety of functional classes. The increased expression of these genes could provide the basis for extensive modifications of cerebral physiology and function in humans and suggests that the human brain is characterized by elevated levels of neuronal activity" (p. 13030). . . Higher levels of neuronal activity are likely to have important consequences in cognitive and behavioral capacities, and of the genes up-regulated in humans (p. 13034).

Likewise Nestler (2008) and Preuss et al. (2004) have discussed the implications of such research on the molecular-genomic level for understanding the evolution of the special qualities of human consciousness as follows:

> Microarray analyses of gene-expression differences in humans and chimpanzees have allowed researchers to begin uncovering some of the changes that characterize human brain evolution at the molecular level, including the up-regulation (heightened activity) of many genes. Connecting these data to the critical phenotypes of interest, such as the emergence of language in humans, theory of mind and our particular susceptibility to certain neurological diseases, will require careful gene-by-gene research into the structural and functional context of the neural systems that underlie our remarkable human qualities (p. 859).

This paper now reviews research with innovative bioinformatic software to assess how therapeutic hypnosis modulated experience-dependent gene expression during our original 2008 DNA microarray pilot study. What is the relevance of such bioinformatic research for the typical professional using psychotherapy and clinical hypnosis today? We propose that bioinformatic research will extend the cognitive-behavioral perspective and efficacy of evidence-based therapeutic hypnosis to include the molecular-genomic level, which is now the standard of clinical excellence recommended by Thomas Insel, the current director of NIMH (Insel, 2009, 2010).

Research: Bioinformatics Software, Gene Set Enrichment Analysis (GSEA)

Researchers at the Broad Institute of MIT have made freely available on the internet a highly innovative bioinformatic tool, *Gene Set Enrichment Analysis (GSEA),* which generates meaningful information from DNA microarray data such as our initial pilot study. In contrast to methods based on single gene analysis (e.g. Lichtenberg et al., 2000, 2004), GSEA software detects changes in sets of genes that have been previously defined based on data from numerous microarray studies across a breadth of topics in biological research, exploring genome-wide gene expression in various functional, developmental, and disease states. GSEA is a computational method that determines whether a set of genes, typically defined by a DNA microarray exploration of a biological or behavioral activity (such as our 2008 pilot study) shows statistically significant associations between two psychobiological states (e.g. phenotypes or observable states). These gene sets are used to track the biological pathways from the molecular-genomic levels to their phenotype levels of observable expression on the cognitive-behavioral level. This paper pioneers a new application of the GSEA bioinformatics software to therapeutic hypnosis. Details of the theory, research, and practice of bioinformatics via GSEA software for molecular biology may be

found on its web site http://www.broadinstitute.org/gsea/ (Bild & Febbo, 2005). We extended the use of DNA microarrays and GSEA to explore the psychobiological underpinning of the ideo-plastic processes of therapeutic suggestion and hypnosis.

Genes rarely, if ever, act alone to generate the complex functions of consciousness, cognition, and behavior that are the outcome of dynamic interactions between genomic and environmental factors in health and dysfunction. Current research, for example, is identifying thousands of relatively small single nucleotide polymorphisms (SNPs) and other variations in the DNA of patients with schizophrenia, that collectively add up to a third of the genetic risk (Sanders, 2009) with important associations to the major histocompatibility complex (MHC) of the immune system (see the special issue of *Nature*, 460 (7256, pp. 744-757). In bioinformatics the coordinated activity of many genes is described as "the functional concordance of co-expressed genes" (Eisen et al., 1998). Figure 1 illustrates GSEA's integration of the two basic operations required to identify the functional concordance of co-expressed genes with an observable cognitive-behavioral state such as therapeutic hypnosis. As portrayed in Figure 1, for example, GSEA identified the best match between (1) the checkered pattern of gene expression we actually found in our 2008 pilot study with (2) several thousand gene sets in the GSEA "Gene Set Database" that are associated with a variety of psychobiological processes. GSEA then automatically generates a diagram profiling an "Enriched Set" of genes. This enriched gene set identifies a complex psychobiological state, such as therapeutic hypnosis, that we can observe on the cognitive-behavioral level (Mootha et al., 2003; Subramanian et al., 2005). These GSEA enriched gene sets have been used to trace the epigenetic pathways between the environment and experience-dependent gene expression found in illness, rehabilitation, and health. Recent research, for example, has used epigenetic associations between hippocampal neurogenesis and neuropsychiatric disorders to unravel the role of the genome to understand the mind (Hsieh & Eisch, 2010, Petronis, 2010).

Table 2 illustrates the significant, positive association we observed between therapeutic hypnosis and the expression of gene sets related to the Zif-268 activity, an immediate-early gene (IEG) that functions as a transcription factor (early growth response; EGR 1,2,3,4), which is associated with adaptive brain plasticity evoked by experiences of novelty, memory, learning, and dreaming, etc. (Baumgartel et al., 2009; Guzowski et al., 2001; Ribeiro et al., 1999, 2002, 2004, 2007, 2008). The up-regulation of this Zif-268 related gene set is significantly associated with therapeutic hypnosis via the *CPGHE* at both 1 hour and 24 hours following the intervention.

Table 3 illustrates genes related to a "molecular-genomic signature" of the

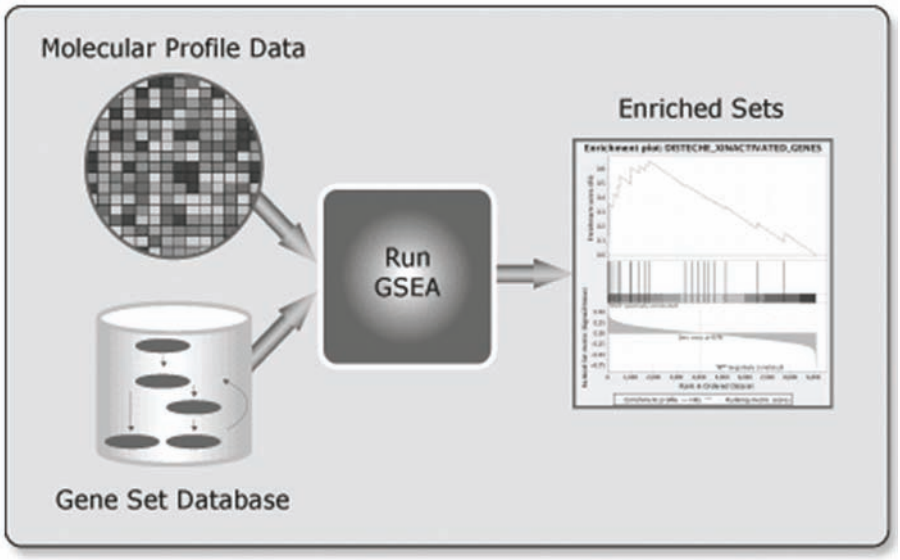

Figure 1: Gene Set Enrichment Analysis (GSEA) is a computational method that can be used to determine whether two sets of genes determined by experiment shows statistically significant differences between two different psychobiological states (e.g. phenotypes such as before and after therapeutic hypnosis in our original 2008 pilot study).

up-regulation of genes characteristic of stem cell growth and proliferation in the GSEA molecular database (HSC_MATURE_ADULT, Ivanova et al., 2002) that is positively associated with therapeutic hypnosis via the *CPGHE* at both 1 and 24 hours. In this study, we have looked at gene expression in white blood cells, rather than specifically stem cells, which live in the bone marrow. We are not observing the activation of stem cells directly, but we are seeing, in white blood cells (descendants of stem cells), the up-regulation of genes that are characteristic of stem cell growth and proliferation. This "molecular-genomic signature" of stem cells is a pro-growth and pro-proliferative expression pattern, characteristic of stem cells and observable in perhaps a variety of stem cell descendants, including peripheral white blood cells.

Table 3 also illustrates genes from the GSEA molecular-genomic database involved in the cellular response to ionizing radiation and oxidative stress (UVC_HIGH_All_DN, Gentile et al., 2003) display a reversed pattern of expression in the context of therapeutic hypnosis at 1 and 24 hours. That is, the pattern of gene expression we observed following therapeutic hypnosis is opposite of that observed in cells subjected to ultraviolet C radiation. Additionally, genes from the GSEA database related to chronic inflammation (NING_COPD_UP, Ning et

			1 HOUR			24 HOURS		
GENE SET	DESCRIPTION: Genes with promoter regions near transcription start sites...	# OF GENES	NES	NOM p-val	FDR q-val	NES	NOM p-val	FDR q-val
V$EGR_Q6	containing a motif matching annotation for EGR1, EGR2, EGR3	215	1.67	0.004	0.017	1.64	0.001	0.039
V$NGFIC_01	containing a motif matching annotation for EGR4: early growth response 4	196	1.55	0.010	0.045	1.54	0.014	0.066
V$EGR1_01	containing a motif matching annotation for EGR1: early growth response 1	203	1.51	0.008	0.063	1.49	0.006	0.095

Table 2: Genes associated with the immediate-early gene Zif-268 (early growth response 1; EGR 1, and related forms (EGR 2, 3, 4) are significantly associated with therapeutic hypnosis.

			1 HOUR			24 HOURS		
GENE SET	DESCRIPTION	# OF GENES	NES	NOM p-val	FDR q-val	NES	NOM p-val	FDR q-val
HSC_MATURE_ ADULT	Up-regulated in mouse mature blood cells from adult bone marrow	290	1.62	0.001	0.151	1.84	0.001	0.001
UVC_HIGH_ ALL_DN	Down-regulated in fibroblasts following high-dose UVC	271	1.60	0.001	0.139	1.44	0.013	0.147
NING_COPD_ UP	Up-regulated in lung tissue of smokers with COPD	139	-1.63	0.013	0.231	-1.25	0.148	0.712

Table 3: Genes characteristic of stem cell growth and proliferation in the GSEA molecular database are up-regulated, that is, positively associated with therapeutic hypnosis within 1 and 24 hours. Genes from the GSEA molecular database related to ultraviolet radiation, oxidative stress, and inflammation are negatively associated with therapeutic hypnosis within 1 hour.

al., 2004) are down-regulated at 1 hour ($p = 0.013$) but not 24 hours ($p=0.148$) after therapeutic hypnosis. These findings have face validity regarding our expectations of the ideo-plastic faculty of therapeutic hypnosis. These results are consistent with the concept that stress reduction and relaxation associated with therapeutic hypnosis reduces excessive activity and oxidative stress on the molecular level as well as some chronic immune system dysfunctions via the molecular mechanisms of psychoneuroimmunology (Ader, 2007).

Figure 2 illustrates the normalized values for changes in the DNA microarray expression of 15,508 genes within 1 hour and 24 hours of therapeutic hypnosis via our ideo-plastic protocol, the *CPGHE*. This correlation within each subject at 1 and 24 hours (Pearson's r coefficient > 0.80, p <0.001) is a validity and reliability check of our DNA microarray data prior to analysis with the

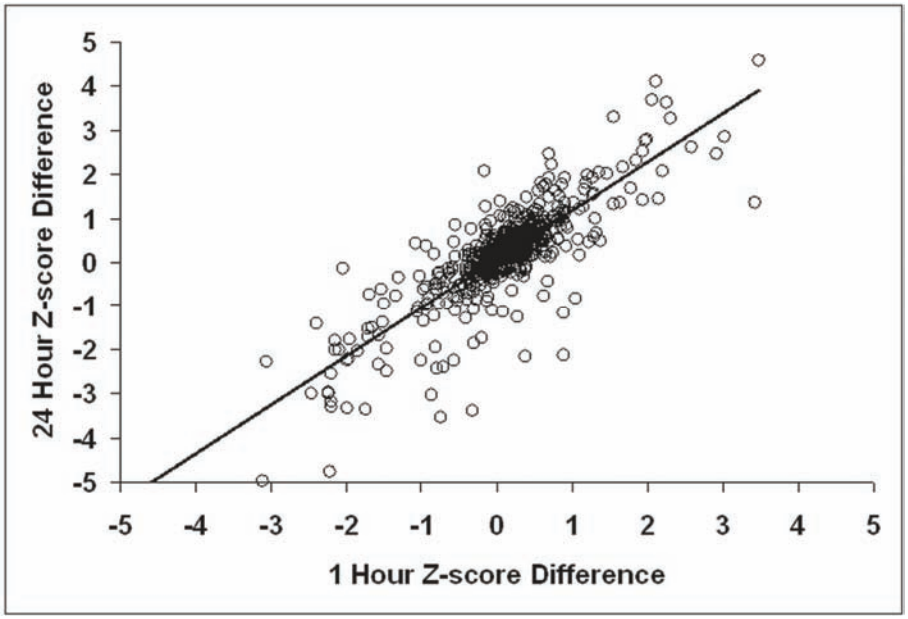

Figure 2: Normalized expression values for the change in the expression of 15,508 genes 1 hour and 24 hours after therapeutic hypnosis via our protocol, The Creative Psychosocial Genomic Healing Experience. Each data point represents the expression of a single gene. Gene expression at 1 hour and 24 hours is strongly correlated (Pearson's r coefficient > 0.80, $p < 0.001$).

GSEA software.

Figure 3 is a new type of scientific diagram characteristic of the GSEA bioinformatic computational software illustrating the intensity and dynamics of gene expression, which is explained in detail at http://www.broadinstitute.org/gsea/. Figure 3 illustrates how within 24 hours of administering the *CPGHE,* a GSEA gene set representing a molecular-genomic signature of the up-regulation of genes characteristic of stem cell growth and proliferation is positively correlated with therapeutic hypnosis. This finding appears to be a desired outcome of the ideo-plastic faculty of therapeutic hypnosis at the molecular-genomic level. This molecular -genomic signature for the up-regulation of genes characteristic of stem cell growth and proliferation, for example, could be associated with the molecular-genomic pathway for facilitating the rehabilitation of strokes and heart attacks (Ohtaki et al., 2008) as well as psychoneuroimmune system dysfunctions (Ader, 2007). The horizontal strip that looks like a financial bar code on the lower part of the Figure 3 actually marks the location of individual genes and their relative degree of expression in our original 2008 pilot study.

Genes on the left side are over-expressed and genes on the right are under expressed. Genes toward the center of this bar code are neither over nor under expressed, implying that they are not modulated by the experimental variable of therapeutic hypnosis.

Figure 4 illustrates how genes associated with *cellular stress and damage by UVC radiation* in the GSEA molecular database are negatively associated with therapeutic hypnosis within 1 hour ($p < 0.001$) and 24 hours ($p < 0.013$) of therapeutic hypnosis with our protocol for the *CPGHE*. This certainly is a desirable outcome of the ideo-plastic processes of therapeutic hypnosis.

Figure 5 illustrates how genes related to *chronic inflammation* in the GSEA molecular database are negatively associated with therapeutic hypnosis via our protocol for the *CPGHE* within 1 hour ($p < 0.013$) but not within 24 hours ($p = 0.148$). The difference between the 1 hour and 24 hour is statistically significant (paired t-test $p < 0.013$). This desirable outcome of reducing chronic inflammation for at least 1 hour via the ideo-plastic faculty of therapeutic hypnosis apparently does not extend for 24 hours. Further research will be needed to replicate the range and limitations of this important finding with various clinical populations.

Figure 6 illustrates Venn diagrams of the logic of the beta version of our proposed molecular-genomic signature of therapeutic hypnosis via our ideo-plastic protocol, the *CPGHE*. Seventy-three experience-dependent genes were identified from GSEA's molecular-genomic database for their relationship to dynamic cellular processes involved in (1) plasticity associated with memory, learning, novelty, dreaming, etc., (2) molecular-genomic signature of the up-regulation of genes characteristic of stem cell growth associated with mind-body healing and rehabilitation, and (3) stress reduction.

DISCUSSION

Bioinformatics of the ideo-plastic faculty of therapeutic suggestion and hypnosis

Since our original 2008 pilot study of the bioinformatics of the ideo-plastic faculty of therapeutic hypnosis had only 3 subjects, cross validation is now required with more subjects with a variety of diagnostic classifications to document the validity, reliability, and limitations of using DNA microarrays and bioinformatics to assess the value of therapeutic suggestion and hypnosis via the *CPGHE*. At this point we prefer to refer to our proposed "molecular-genomic signature of suggestion and therapeutic hypnosis" as a temporary *beta version* until it is replicated by independent research groups. It will require fur-

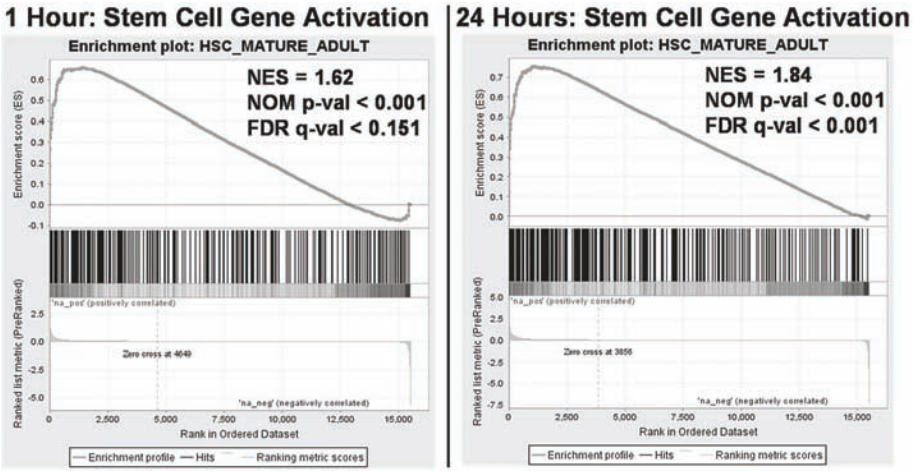

Figure 3: Genes associated with a molecular signature of stem cell activation in the GSEA molecular database are positively associated with therapeutic hypnosis within 1 hour *(p* < 0.001, FDR < 0.151) and 24 hours *(p* < 0.001, FDR < 0.001). False discovery rate (FDR) is a new statistical method characteristic of research at the molecular-genomic level, which is used in multiple hypothesis testing to correct for multiple comparisons. The experience-dependent gene facilitation by therapeutic hypnosis was greater at 24 hours than at 1 hour (paired t-test $p < 0.0007$).

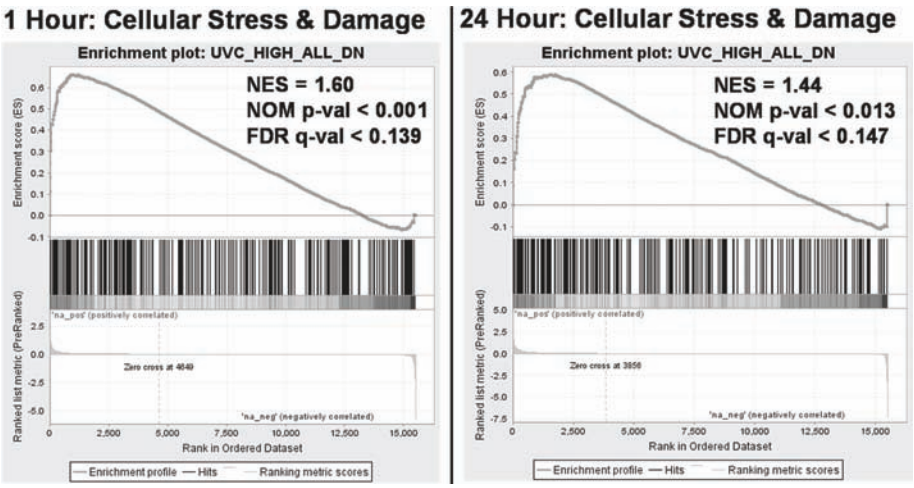

Figure 4: Genes associated with cellular stress and damage by UVC *radiation* in the GSEA molecular database are negatively associated with therapeutic hypnosis within 1 hour *(p* < 0.001, FDR < 0.139) and 24 hours *(p* < 0.013, FDR < 0.147) of treatment.

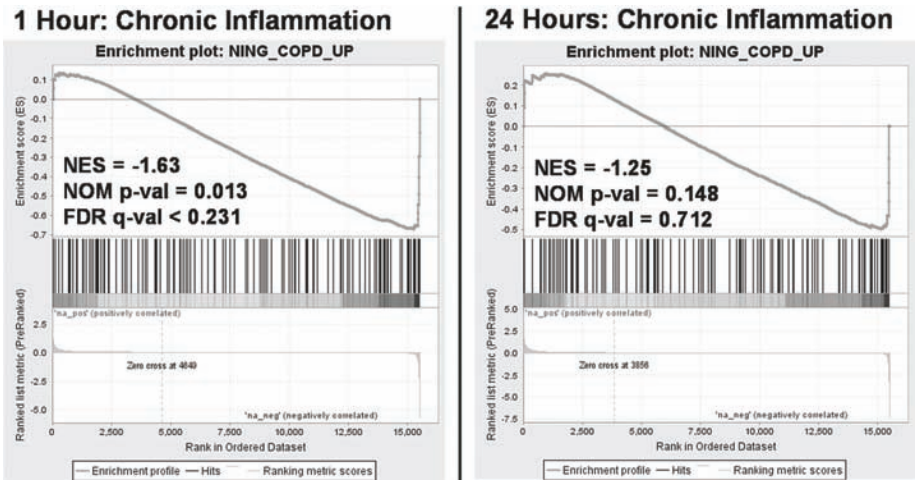

Figure 5: Genes corresponding to chronic inflammation in the GSEA molecular database are negatively associated with therapeutic hypnosis within 1 hour ($p < 0.013$, FDR < 0.231) but not within 24 hours ($p = 0.148$, FDR < 0.712). The difference between the gene set enrichment at 1 hour and 24 hours is statistically significant (paired t-test $p < 0.013$).

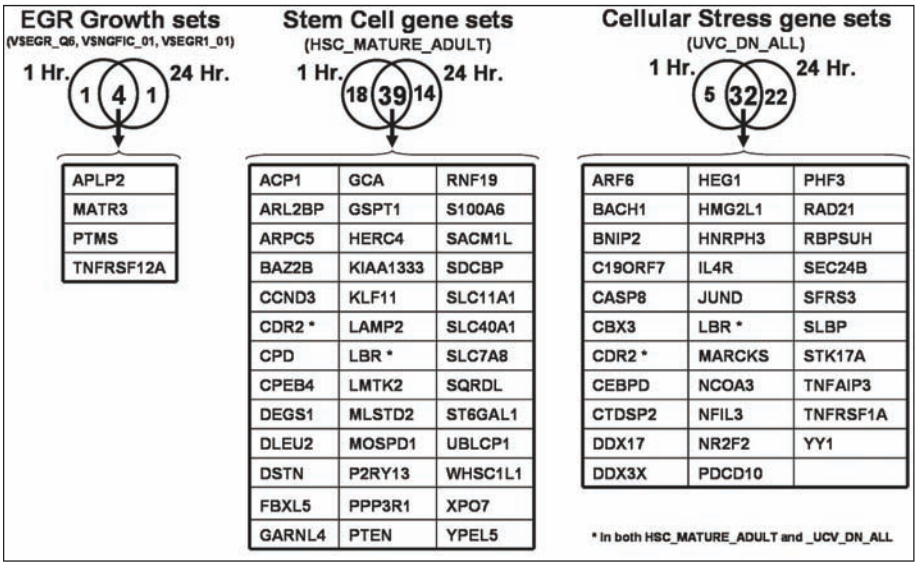

Figure 6: Venn diagrams of a beta version of our proposed molecular-genomic signature of therapeutic hypnosis.

ther assessment by students and researchers who are able to compare our results with a similar DNA microarray and bioinformatic methodology (Figure 1) to update the traditional measures of hypnosis such as the Stanford Scale of Hypnotic Susceptibility (Hilgard, 1965, 1977), The Harvard Group Scale of Hypnotic Susceptibility (Shor & Orne, 1962), and The Hypnotic Induction Profile (Spiegel & Spiegel, 1978). We hypothesize that these well-documented scales, with their stronger emphasis on the *dissociative component* of hypnosis rather than the *ideo-plastic* processes of *The Creative Psychosocial Genomic Healing Experience,* would identify different molecular-genomic signatures.

This bioinformatic process of identifying the molecular-genomic signatures of psychological states of consciousness as well as diagnostic classifications assessed by clinical interview and self-report inventories is more general than the limited scope of this paper's focus on the ideo-plastic process of therapeutic hypnosis. Integrative, translational research now is required to document the efficacy of the molecular-genomic approach (Nestler, 2008) to define and differentiate between the biological underpinnings of stress, trauma, and PTSD (Yehuda et al., 2009) and the ameliorating responses of therapeutic hypnosis in mind-body medicine (Cuadros & Vargas, 2009). We propose that the deep psychobiological correlates of many classical hypnotic phenomena such as *dissociation* (agnosia, amnesia, etc.) and the *ideo-plastic faculty* (ideosensory, ideomotor, ideodynamic, etc.) could be conceptualized and measured more precisely on the molecular-genomic and bioinformatic level of human individuality (Whitney et al., 2003).

There is as yet no comprehensive program of research investigating psychotherapy and therapeutic hypnosis via the methodology of DNA microarrays and bioinformatic analysis illustrated in this paper. This may be part of the reason why the National Institutes of Health (NIH) and the National Institute of Mental Health (NIMH) are limiting funding for psychosocial research on a purely cognitive-behavioral level without regard for the fundamentals of mental illness on molecular-genomic level (Holden, 2004; Kaiser, 2004, 2009).

The lack of a firm molecular-genomic foundation for therapeutic suggestion and hypnosis also could be related to the recent American Medical Association's (AMA) concern about the American Society of Clinical Hypnosis (ASCH) and the Society of Clinical and Experimental Hypnosis (SCEH) making the inaccurate statement that hypnosis is approved by the AMA as a legitimate therapy for medical or psychological purposes.

We therefore proposed the formation of an International Psychosocial and Cultural Bioinformatics Project to coordinate integrative psychobiological insights on the role of activity and experience-dependent gene expression and brain plasticity in facilitating translational research with therapeutic suggestion and hypnosis (Rossi, E., Rossi, K., Yount, Cozzolino & Iannotti, 2006).

The number of activity and experience-dependent genes that are linked to psychosocial activities, mental illness, psychological health, and resilience is unknown at the present time. Extensive exploration of the DNA microarray and bioinformatic model of psychological adaptation, mental illness, and psychotherapy will be required to fully answer the question of whether it can contribute to a new epigenetic and psychosocial genomic paradigm for clinical practice of therapeutic hypnosis.

Summary

This selective review emphasizes that therapeutic hypnosis is an ideoplastic aptitude for transforming an idea into an act in receptive subjects. The idea that therapeutic hypnosis involves an *increase in "sensitivity" and "ideo-reflex excitability"* has been described as its ideodynamic or *"ideoplastic faculty."* We explored an emerging bioinformatic theory, research, and practice of linking epigenetic, experience-dependent gene expression and brain plasticity with the positive experiences we traditionally associate with therapeutic hypnosis. We proposed that such bioinformatic theory and research will extend the cognitive-behavioral perspective and efficacy of evidence-based therapeutic hypnosis to include the molecular-genomic level, which is the current standard of clinical excellence being promoted by the NIMH. We documented how we can measure changes in activity or experience-dependent gene expression (1) over relatively brief time periods (1 hour and 24 hours) following (2) a single experience of therapeutic hypnosis (about 1 hour). This ideo-plastic process of therapeutic hypnosis was associated with (1) the heightening of a molecular-genomic signature for the modulation of experience-dependent gene expression characteristic of stem cell growth, (2) a reduction in cellular oxidative stress, and (3) a reduction in chronic inflammation. We propose these three empirical associations as an initial beta version of the molecular-genomic signature of the ideo-plastic process of therapeutic hypnosis via the *CPGHE,* which can serve as a practical guide for the professional practice of psychotherapy and clinical hypnosis.

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Chapter Seventeen*

The Creative Psychosocial Genomic Healing Experience©: Administration, Rationale & Research

An Open Invitation to Positive Psychotherapy, Clinical & Experimental Research

Ernest Rossi & Kathryn Rossi

Introduction

The Creative Psychosocial Genomic Healing Experience (CPGHE) evolved out of 50 years of exploring the history of creativity, counseling, psychotherapy, and mind-body healing (Rossi, 1967, 1968, 2002, 2007). The CPGHE is a diagnostic and therapeutic protocol for facilitating creative psychological experience and the positive transformations of consciousness by optimizing gene expression and brain plasticity. The CPGHE utilizes the easy-to-learn 4-stage creative process for optimizing private therapeutic inner work without the need for traditional psychodynamic analysis and clinical diagnosis.

Most people are surprised to learn how a sense of wonder, wisdom, truth and beauty can turn on gene expression and brain plasticity during creative experiences. It is profound to realize that our highest and most in-

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spired states of consciousness can facilitate psychological health and well-being, while stress and trauma can distort and suppress it.

Mind-gene communication engages the transformational alchemy of mind, body, and spirit, which generates health and well-being as well as personal illness and the clash of cultures. Theory and research on gene expression and neural circuits is recommended for the future of mental health by noble prize winners in policy forums on the highest national level (Akil et al., 2010). *The Creative Psychosocial Genomic Healing Experience* for creating consciousness via positive qualia-dependent gene expression and brain plasticity is a new tool for facilitating such research by students, counselors, coaches, teachers and therapists of all schools of health, peak performance and well-being.

The Deep Psychobiological Basis of the Creative Psychosocial Genomic Healing Experience (CPGHE)

The Creative Psychosocial Genomic Healing Experience is integrated with current theory and research in epigenetics (Petronis 2010), functional genomics (Geschwind & Konopka, 2009), bioinformatics, neuroscience, and psychosocial genomics (Atkinson et al., 2010; Rossi, 1972/1985/2000, 2002, 2004, 2007; Rossi & Iannotti et al., 2008; Rossi & Rossi, 2010; Rossi, Vyas et al. 2010). The intriguing breakthroughs that are now taking place on the deep biological level in our understanding of mind-gene communication and healing via our new epigenetic psychosocial genomic approach was outlined in an enthusiastic manner in recent issue of *Nature* (Nobrega, 2010).

Gene expression is the cellular process that decodes the genetic information in DNA and converts it into proteins. It is regulated at many levels: when messenger RNA is transcribed from DNA; when mRNA is translated into proteins; and at the epigenetic level, when the structure of chromatin, coils of DNA wound around histone proteins, is altered. Although most discussion of gene expression focuses on the regulation of transcription, the other components of the process are also crucial. Yet little is known about how they are integrated.

Work by Tom Misteli at the National Cancer Institute in Bethesda, Maryland, and his team provides a striking example of the integration of seemingly disparate components in gene-expression regulation (Luco et al., 2010). They describe how patterns of alternative splicing of newly made RNA, a key regulatory mechanism, can themselves be regulated by specific chemical modifications in the chromatin. They also found that a given set of modifications to histones predicts patterns of RNA splicing. The authors conservatively estimate that this mechanism occurs in dozens to hundreds of genes in

the human genome.

This remarkable study makes a connection between a quintessential transcription-regulation mechanism, histone modification, and a post-transcriptional process, alternative splicing. It shows that chromatin can regulate not only how much of a protein, but also which protein, is made in a cell.

We have seen a surge of intriguing studies suggesting that molecules that were thought to regulate transcription also direct epigenetic modifications, modify alternative-splicing patterns and participate in the intracellular transport of RNA. These findings and the work of Misteli and colleagues provide insight into how the components of gene regulation are integrated. (p. 11)

If we believe that counseling, psychotherapy, mind-body healing and therapeutic hypnosis is an *ideo-plastic aptitude for transforming an idea into an act in receptive subjects,* we can say that the history of counseling, psychotherapy and therapeutic hypnosis has anticipated current research in epigenetics and neuroscience on activity or experience-dependent gene expression and brain plasticity by more than a century (Wetterstrand, 1902). We propose that this epigenetic and molecular-genomic level of discourse is a much needed expansion of our traditional cognitive-behavioral conception of therapeutic hypnosis (Luco et al., 2010). Our new ideo-plastic healing scale, *The Creative Psychosocial Genomic Healing Experience* (CPGHE) could become a standardized way of assessing the molecular-genomic impact of many approaches to mind-body healing (meditation, hypnosis, active imagination, music, etc.) that is consistent with the translational research that is now recommended, supported, and funded by the National Institute of Mental Health (Aikl et al. 2010; Insel, 2009, 2010).

The administration of the *Creative Psychosocial Genomic Healing Experience* as presented here requires about 20-30 minutes. A Scoring Form included here is usually filled out by the therapist but may be adapted for group administration. Considerable research is now required to establish the validity and reliability of this initial version of the CPGHE on many levels from the cognitive-behavioral to the molecular-genomic level as outlined in the research section presented below.

This administration protocol and rational for the *Creative Psychosocial Genomic Healing Experience* is a new therapeutic approach for facilitating human resilience and resourcefulness for health, healing, and rehabilitation (Rossi et al., 2011). The Creative Psychosocial Genomic Healing Experience facilitates problem solving and healing by activating experience-dependent gene expression to modulate a variety of epigenetic interactions between mind and body that are the essential mechanisms of psychoneuroimmunology, consciousness, creativity, dreaming, memory, learning, and personality

transitions via brain plasticity (Atkinson et al. 2010; Rossi, Iannotti et al. 2008; Rossi, Vyas et al., 2010).

We propose that scores and response profiles on the CPGHE will be associated with unique profiles of activity and experience-dependent gene expression (measured with DNA microarrays) and brain plasticity (measured with fMRI, etc.) that can make unique contributions to psychological development as well as personalized medicine and rehabilitation. We outline a series of hypotheses and research proposals in this presentation that now require careful scientific assessment to compare and contrast the CPGHE with other standardized mind-body therapeutic protocols in psychology, psychotherapy, and therapeutic hypnosis. We invite academic and research groups engaged in creative approaches to mind-body healing in alternative and complementary medicine to join us in this open research project on our new Ideo-plastic Healing Protocol: *The Creative Psychosocial Genomic Healing Experience* on all levels from the cognitive-behavioral to the molecular-genomic.

We have documented how our ideo-plastic Creative Psychosocial Genomic Healing Experience reduces (1) dysfunctional inflammation (associated with chronic pain and delayed healing) and (2) oxidative stress (associated with many chronic medical conditions and the ageing process) as well as (3) increasing a "molecular-genomic signature of stem cells" (activation of stem cells associated with healing and the rehabilitation and in many tissues of the body) as the deep psychobiological source of human resilience and resourcefulness (Rossi, Iannotti et al. 2008; Atkinson et al., 2010; Rossi et al. 2011).

The Administration and Rationale of the Creative Psychosocial Genomic Healing Experience (CPGHE)

Introduction: Identify the Initial Stress, Symptom, or Problem Initial Time_____ am pm Initial Stress & Symptom: 0%. . .50% . . .100%

We record the *Initial Time* when *the Creative Psychosocial Genomic Healing Experience* takes place for two reasons. (1) Time of day is an important factor determining when activity or experience-dependent genes are expressed in our normal circadian and ultradian rhythms of the Basic Rest-Activity Cycle (Lloyd & Rossi, 1992, 2008). (2) This initial time is needed to measure of the subject's mental engagement and therapeutic response in their scoring profile presented below.

We record the Initial Stress or Symptom to calculate Stress or Symptom Reduction later in item #10. Initial Stress or Symptom is the subject's subjective estimate before they begin *The Creative Psychosocial Genomic Healing Experience.* The therapist initiates the healing experience with these words.

"What level of stress (symptom, problem) are you experiencing right now - where 100% is the worst stress level you have ever experienced, 50% is average, and 0% is no stress?"

Stage 1: The Wonder of Observing Consciousness - Curiosity, Focused Awareness, and Positive Expectancy
1. Warmer – Cooler? Reality % 0%. . . . . 50% 100%

Facilitating the wonder and meta-cognition of the subject's self-observing consciousness of is the hallmark of the Creative Psychosocial Genomic Healing Experience. We want the subject to be fully awake and sensitive to the nuances of self observation, self empowerment and self healing via their own natural patterns of mind-body communication. Supporting the subject's curiosity, focused attention, and positive expectations of a healing journey is the first step in the Four-Stage Creative Process of Psychotherapy that optimizes The Creative Psychosocial Genomic Healing Experience on all levels from mind to gene (Lloyd & Rossi, 1992, 2008; Rossi, 2002, 2004).

The therapist models the activity-dependent mirroring hands protocol with the palms of her/his hands about 6 to 8 inches apart facing each other at chest level as illustrated in figure 1a. The hands in this initial position function as a metaphor for a safe inner space (temnos) or container within which the person can experience a creative dialogue or drama between symptoms, problems, or issues projected into one hand and the "opposite," the unknown solution of the problem in the other hand. The solution is unknown because it has not been created yet on the levels of gene expression and brain growth within the person. That's why the person has a problem.

The therapist, of course, does not know at this point what the answer to the person's problem is either. Together therapist and person now embark on a quest for experiencing the wonder and joy of new consciousness that will express a possible resolution of the person's issues by exploring what Carl Jung (1923, 1963) called "The Problem of the Opposites." Awareness of the conflicting opposites within tends to activate a person's inner resources accumulated from previous life experience that often holds keys for initiating a therapeutic dialogue that may generate new consciousness for a satisfactory resolution of the presenting problem. We have outlined the rational for exploring the "opposites" in the Creative Psychosocial Genomic Healing Experience in the research section below.

Figure 1a illustrates the initial hand position in stage one of our 4-stage creative process via the *Creative Psychosocial Genomic Healing Experience.*

Ask the subject, **"Which hand seems warmer or cooler?"** Subjects may sometimes ask therapists what they mean by this question. The therapist sim-

ply responds with, "**Most people don't realize how their hands and other parts of their body usually feel slightly warmer or cooler when they pay attention to it. This is a good exercise heighten your consciousness and awareness of yourself. It helps activate your focused awareness, creativity, and positive expectation of your natural self healing ability. The simple idea of one hand being warmer or cooler will heighten your actual sensations of warmth and coolness.**"

Figure 1a: The initial mirroring hand position for stage one of the 4-stage creative process facilitated by the Creative Psychosocial Genomic Healing Experience (Rossi, 2002, 2004, 2007).

After two minutes ask the subject "**How real, strong or vivid does the feeling in your hands seem to be on a scale of 100% (completely real) to 0% (not real)?"** (Therapist records whatever "Reality %" the subject reports experiencing.)

Recording this Reality % begins to focus the therapist's own mirror neurons on subjects and provides an immediate impression of the subject's level of focused attention, sense of reality, and positive expectancy of *The Creative Psychosocial Genomic Healing Experience.*

2. Stronger – Weaker? Reality % 0%. . . . . 50% 100%

Ask the subject, "Which hand seems stronger or weaker?" After two minutes ask the subject, "How real, strong or vivid does the feeling in your hands seem to be on a scale of 100% (completely real) to 0% (not real)?" (Therapist records whatever "Reality %" the subject reports experiencing.)

3. Child – Adult? Reality % 0%. . . . . 50% 100%

Ask the subject, "**Now let's turn to a personal memory . . . Which hand seems to be you right now—and which hand seems to feel more like you as a child?**" After two minutes ask the subject, "**How real, strong or vivid does the feeling in your hands seem to be on a scale of 100% (completely real) to 0% (not real)?**" (Therapist records whatever "Reality %" the subject reports experiencing.)

This contrast between the present and the remembered past tends to deepen focused inner attention, curiosity, and expectancy on one's self and prepares for stage two of the creative healing experience that follows.

Stage 2: Incubation, Past Problem Review to Activate Positive Motivation and Inner Resources via the Activity-Dependent Mirroring Hands Protocol

The initial position of the Activity-Dependent Mirroring Hands Protocol of the CPGHE Requesting a subject to lower a hand very slowly as they review the origin and history of their problem is a precise way of focusing their attention and expectancy to access the neural networks of their brain that encode their problem, maladaptive behavior, and consciousness (Rossi, 2002, 2004, 2007). These neural networks encode memories that are to be updated by allowing therapeutic processes of activity and experience-dependent gene expression and brain plasticity to operate in an evolutionary adaptive manner (Rossi, Erickson-Klein & Rossi, 2008).

4. Problem & Opposite Reality % 0%. . . . . 50% 100%

Ask the subject, "Which hand experiences your issue (concern, problem or symptom) and which experiences the opposite of that?"

After two minutes ask the subject, "**How real, strong or vivid does the feeling in your hands seem to be on a scale of 100% (completely real) to 0% (not real)?**" (Therapist records whatever "Reality %" the subject reports experiencing.)

Recording "Reality %" is a way of focusing attention, heightening expectancy, and activating the subject's neural networks that encode the issues, problems, and motivations for seeking a creative healing experience on all levels from mind to behavior and psychophysiology via activity and experience-dependent gene expression and brain plasticity.

5. Negative Past Review Reality % 0%. . . . . 50% 100%

Tell the subject, "**Let the hand that experiences your issue (concern, problem or symptom) now begin to drift down very slowly . . .all by itself. . . as your inner mind privately reviews the history, memories,**

and feelings of your issue (concern, problem or symptom) from the beginning to the present moment."

Therapist's model for the subject by very slowly lowering one hand as illustrated in figure 1b. If the subject begins to show negative cathartic reactions (frowning, weeping, etc.) the therapist can offer emotional support with empathetic *implicit processing heuristics* (positive permissive suggestions, Rossi, 2002, 2004; Rossi & Rossi, 2007) such as these.

Figure 1b: Stage 2 of the four-stage creative process in the activity-dependent mirroring hand process of The Creative Psychosocial Genomic Healing Experience (Rossi, 2002, 2004, 2007).

"That's right! Do you have the courage . . . to allow that hand and arm to drift down a bit. . . with each memory you find yourself reviewing?"

"Allowing your inner mind to feel only as much of that as you need to . . . and then move on to the next memory that comes up more or less by itself."

"That's right . . . let yourself have the courage to continue . . . only as long as you need to . . . to experience everything as fully as you need to . . . privately."

"That's right . . . while another part of you observes wisely . . . as you learn how to take care of yourself . . . and expect the best possible outcome."

This therapeutic review is "fail-safe" in the sense that the only so-called, "failure" is that some people do not understand how to become engaged with their issues in a meaningful way. The easiest way of helping people under-

stand how to have a therapeutic experience is to provide them with opportunities to observe others become optimally engaged in The Creative Psychosocial Genomic Experience. Such observations in group therapy, for example, provide the subject's mirror neurons with appropriate psychosocial experiences, which they learn to use as models for their own therapeutic experiences.

This therapeutic review is "safe" in the sense that persons do not undergo a so-called, "re-traumatization of themselves" in this review of negative past experiences because they are experienced in a safe context (Foa, 2008). The safe context is that the negative memories and emotions are carefully circumscribed and limited when they are externalized by being projected into one hand only. The negative memories are always balanced by experiencing their complementary opposite on the other hand (presumably positive inner resources activated in step #4 above: Experiencing a Problem and its Opposite).

When the problem hand finally touches down in the subject's lap, the therapist asks, **"How real, strong, and vivid do your memories and feelings seem to be on a scale of 100% (completely real) to 0% (not real)?"** (Therapist records whatever "Reality %" the subject reports experiencing.)

The therapist now facilitates the transition to stage three of the creative process with: **"Wonderful . . . appreciating a job well done . . .and now getting ready to move on to the resolution of this issue (concern, problem or symptom).**

Stage 3: Illumination, Facilitating Creative Mind-Gene Replays

This the famous "Aha" or "Eureka" experience of insight celebrated in ancient and modern literature as well as current neuroscience (Ehrenberg, 2010) is illustrated in figure 1c. Creative insight, problem solving & healing often seem to happen spontaneously. Subjects are usually surprised and delighted when they receive a creative thought. Many people automatically dismiss their own originality as worthless since it has never been reinforced in their early life experience. The therapist's main job at this stage is to help the subject recognize and appreciate the value of the "new" and creative that usually emerges spontaneously and unheralded. Often the subject may have already thought of the options that come up for problem solving at this stage but dismissed them since they were never validated. Here we strongly support them!

Figure 1c: Stage 3 of the four-stage creative process in the activity-dependent mirroring hand process of The Creative Psychosocial Genomic Healing Experience (Rossi, 2002, 2004, 2007).

6. Positive Now & Future Reality % 0%. . . . . 50% 100%

The following implicit processing heuristics prompt people experience the Novelty-Numinosum-Neurogenesis Effect: The *novelty* of this *Creative Psychosocial Genomic Healing Experience* tends to turn on the numinosum (a highly motivated state of focused attention, expectancy, wonderment, and fascination), which evokes activity and experience-dependent gene expression and brain plasticity (Atkinson et al., 2010; Rossi, 2002, 2004, 2007; Rossi et al., 2008). The therapist continues to model the subject's behavior by slowly lowering the other hand as illustrated in figure 1c with these words.

"**Now allow your other hand to drift down slowly as you explore new possibilities about how to solve your problem today . . . Will that hand now begin go down slowly as you begin to experience something new? . . . Explore all your hopes . . . the most interesting and wonderful possibilities of healing and well being . . . Speculate about exciting and fascinating turning points in your life . . . Create the best of all possible worlds for yourself . . . Enjoy your best dreams about yourself! "**

This fragile and tenuous transition from the difficulties of the previous stage two reviews of past problems to the new joyous possibilities of stage three that now emerge can often be read in the delicate shifts of the subject's facial expressions. Notice carefully the shifts from negativity, stress, sadness, and conflict (of stage two) to the more searching expressions of expectation in stage three that are often punctuated with a slight smile and even a short laugh. Sometimes subject's will manifest other minimal behavioral cues of

their positive attitude and enjoyment of this third stage of their creative experience by spontaneous head nodding "yes" and shaking, rocking, or caressing themselves comfortably. The therapist now supports these positive shifts with a few warm implicit processing heuristics such as these.

"Something pleasantly surprising you can look forward to? . . . What you really need that is most interesting and important to you?

"Simply receiving and continuing to explore the sources of your strength for dealing successfully with that issue."

"Yes, appreciating the value of that as fully as you need to while taking good care of yourself as that hand finally comes to rest in your lap."

When the hand finally touches down in the subject's lap, the therapist asks, **"How real, strong, and vivid do these new positive possibilities and feelings for changing your life seem to be on a scale of 100% (completely real) to 0% (not real)?"** (Therapist records whatever "Reality %" the subject reports experiencing.)

The therapist now facilitates the transition from stage three of the creative process to stage four with: **"Wonderful . . . really appreciating yourself for a job well done! . . . And now getting ready to move on to the resolution of this issue (concern, problem or symptom)!"**

Stage Four: Integration, Self-Care and Reality Testing:

The therapist optimizes stage four illustrated in figure 1d by (1) facilitating a follow-up discussion to validate the value of the subject's experiences and (2) helping the subject reframe symptoms into signals and psychological problems into inner resources. Here is a four part implicit processing heuristic to mediate these creative transitions (Rossi, 2002, Chapter Nine).

Figure 1d: Stage 4 of the four-stage creative process in the activity-dependent mirroring hand process of The Creative Psychosocial Genomic Healing Experience (Rossi, 2002, 2004, 2007).

"When . . . [pause]

1. A part of you knows it can continue this creative work entirely on its own at appropriate times throughout the day . . . [pause]

2. And when your conscious mind knows it can simply cooperate in helping you recognize when it is the right time to tune in . . . [Pause]

Will that give you a feeling, a signal that it's time for you to stretch, open your eyes and come fully alert so you can discuss how you can use this to help yourself and others in your real everyday life?"

Mentioning "appropriate times throughout the day" and "the right time to tune in" are ultradian cues that help people utilize their entirely natural Basic Rest Activity Cycle that takes place every 90-120 minutes throughout the 24 hour day. Such implicit processing heuristics help people access the state dependent encoding of behavior state related gene expression, brain plasticity, and mind-body healing that can take place most easily at "appropriate times" of their circadian cycle. The therapist can further facilitate with these implicit processing memes that can optimize the evolutionary, adaptive, and constructive aspects of future mind in caring for one's self and others (Rossi, Erickson-Klein, Rossi, 2008).

"Something interesting you would like to share about that?

"What is surprising and unexpected about this that is new to you?

"What is most significant and life changing about this for you?

"How will you remind yourself to do this several times a day?

"What does this lead you to now?

"How will this change your life?

"What will you do in your life that is different now?

The stress and symptom scaling of the subject's state before and after the Creative Psychosocial Genomic Healing Experience is a measure of therapeutic progress, problem solving, and healing that is used to validate the value of the therapeutic process

Repeats If Necessary: If stress and symptom reduction of less than 50% is reported, facilitate further therapeutic progress with, **"If your inner nature knows it can do another unit of creative work right now so you can reach a more satisfactory state, will those eyes close for a few moments so you can fully receive everything you need at this time?"**

If stress and symptom reduction of less than 50% continues after two or three repeats reassure the subject, **"You know that your mind and body go through a natural cycle of ultradian healing and problem solving every couple of hours throughout the day and at night even when you are asleep & dreaming. Notice how your progress will continue all by itself and how you can improve your self-care every day."**

Final Stress & Symptom (0% is Best)_____.
Confidence (100% is Best) _____.

7. Positive Self-Change 0%. . 100%
8. Positive Self-Prescription 0%..100%

This corresponds to stage four of the creative experience wherein the subject has an opportunity to assess the value of the insights gained in their stage three "Aha" and plan how they will reality test them now and in the future. Self Change 0%. . . .100% is the degree that the subject recognizes and accepts how they will change their own thinking emotions, and behavior.

Self-Prescription 0%. . . .100% is the "reality %" which each subject believes they can give themselves positive and satisfactory Self-Prescriptions for changing themselves.

Subjective Time Est. Min: 0-5 6-10 11-20 21-30 31-40 41-50 51- 60+
Immediately after the experience (following stage four when the subject usually opens their eyes, although they are usually not asked to close them in the first place), the subject is asked (without looking at their watch) to estimate how much time passed since the beginning of their experience. This is their Subjective Time Estimate in Minutes.

Real Time (Min.): 0-5 6-10 11-15 16-20 21-25 26-30 31-40 41-50 51-60+
This is the real time of the subject was involved in the creative experience that the therapist records here,

9. Mental Absorption: (Real Time / Est. Time) X 100 = _____ %

Now the therapist can calculate the subject's degree of mental absorption or engagement via so-called "time distortion," which research has recently noted as being a reliable indicator of positive engagement and expectancy, which are characteristic of creative and therapeutic states of mind (Naish, 2007).

For example, a person might be engaged in The Creative Psychosocial Genomic Healing Experience for 20 minutes in "real time" as measured by the therapist's stop-watch. When asked by the therapist immediately after this experience (typically when the person opens their eyes, stretches, adjusts themselves, etc.), "How long would you estimate you were you doing that inner work (trance, hypnosis, meditation, etc.)?" however, the person might guess, "about 5 minutes." Doing the calculation: 20 minutes/ 5 minutes X 100 = 400% mental absorption or engagement. "400% mental absorption" may sound a bit peculiar initially but it is an indication that people are more focused and active mentally during this ideo-plastic protocol for their The

Creative Psychosocial Genomic Healing Experience. We interpret this to mean that people can become so deeply engaged (absorbed) in their inner work that they "forget time" and underestimated how long they were creatively engaged. This is very typical of people when they are engaged in creative, important, and highly motivating activities, which we propose, actually turns on "activity-dependent gene expression and brain plasticity" for healing and problem solving at the molecular-genomic and neural level.

11. % Stress Reduction: Initial Stress / Final Stress X 100 = _____%

The therapist now asks the subject how much stress (or symptoms) the subject is now experiencing in comparison with the subject's initial stress score recorded in the beginning before *The Creative Psychosocial Genomic Healing Experience* began. The therapist now calculates the % Stress Reduction as indicated.

For example, a person might estimate that their initial stress level is at the 90% level. At the end of *The Creative Psychosocial Genomic Healing Experience* he/she might estimate stress has been reduced to the 10% level. Doing the math: 90% / 10% = 0.90 / 0.10 = 9 X 100 = 90% stress reduction.

11. Surprise: 0%. . . .100%

The therapist asks the subject to estimate on a scale of 0% to 100% how surprised they were by any aspect of their therapeutic experience. Neuroscience has established how experiences of surprise, novelty, and creative experience turn on Activity and Experience-Dependent Gene Expression and Brain Plasticity, which is the molecular-genomic basis of The Creative Psychosocial Genomic Healing Experience, psychotherapy, and rehabilitation that we seek to assess and facilitate with this scale.

12. Confidence: 0 %. . . .100%

The therapist asks the subject to estimate on a scale of 0% to 100% how confident they are of the value of their therapeutic experience in resolving the problems, symptoms, or issues of self-care they worked with.

Education: Elementary High School College Masters Doctorate
Age: 0 – 9 10 – 19 21 – 29 30 – 39 40 – 49 50 – 59 60 – 69 70 – 79 +
Sex: M F
Night Sleep Length: 1h 2h 3h 4h 5h 6h 7h 8h 9h 10h 11h 12h +
Dreams: 1 2 3 4 5 6 7 **Days/Week. Est. Dreams Per Night**_____
Comments:

Comments by the subject indicating any happy, surprising or unexpected, positive aspects of the experience are recorded by the therapist.

Th[illegible]spontaneous manifestations of the creative healing experienced, particularly during stage three and four, are worthy of further reinforcing by remarks by the therapist.

An Open Invitation to Research: The Creative Psychosocial Genomic Healing Experience

Facilitating Creative Consciousness: The Rational for Exploring the "Opposites" in the Creative Psychosocial Genomic Healing Experience

Experiencing the opposites for the creation of new consciousness, identity, healing, and conflict resolution via the Creative Psychosocial Genomic Healing Experience has a profound but little known history ranging from the ancient origins of eastern and western philosophy to modern neuroscience and computer technology. Here we briefly review a few highlights for understanding this deep rational for our *Creative Psychosocial Genomic Healing Experience*.

The earliest record of the role of the opposites in the creation of new consciousness goes back to the Chinese philosopher, Lao Tzu (Zi), the author of the *Tao Te Ching* in the 7th century BC (Wilhelm, 1990).

> Occasionally Lao Zi puts forward a curious deduction of his own from the Book of Changes, as when he says that the One creates the Two, the Two creates the Three and the Three creates all things. In this way he sets forth and develops the complementarity of opposites. . .Similar ideas can even be found in more recent philosophy: Hegel's dialectic, with its thesis, antithesis and synthesis, where synthesis then becomes the thesis for the next series, the departure point for all that follows – is based on an approach very much like Lao Zi's. The two primal powers from which the visible world as the Third is born, are Heaven and Earth, yang (the light power) and yin (the dark power), the positive and negative line, the temporal and the spatial – in other words the opposites from which the phenomenal world proceeds. (pp. 73-74)

Examples of the most recent evolution of the central role of the opposites are illustrated by Melanie Mitchell (2009) in her recent book on Complexity, wherein she describes how she wrote a computer program to model the function of the opposites in the emergence of new analogies, metaphors, consciousness and meaning.

> The cognitive scientist Douglas Hofstadter, in his book *Gödel, Escher, Bach,* makes an extended analogy between ant colonies and brains, both being complex systems in which relatively simple components with only limited communication among themselves collectively give rise to complicated and system-wide ("global") behavior. In the brain, the simple components are called neurons. The brain is made up of many different types of cells in addition to neurons, but most brain scientists believe that the actions of neurons and the patterns of connections among groups of neurons are what cause perception, thought, feelings, consciousness, and the other important large-scale brain activities. . . No one knows exactly how any community of social organisms – ants, termites, humans – come together to collectively build the elaborate structures that increase the survival probability of the community as a whole. Similarly mysterious is how the intricate machinery of the immune system fights disease: how a group of cells organizes itself to be an eye or a brain: how independent members of an economy, each working chiefly for its own gain, produce complex but structured global markets; or, most mysteriously, how the phenomena we call "intelligence" and "consciousness" emerge from non-intelligent, non-conscious material substrates. (pp. 4-6)

Mitchell goes on to describe how previous generations of biologists assumed that during natural evolution our genes were accidently slapped together in a kind of "molecular Rube Goldberg machine." She presents "a countering thesis: most of the beautiful order seen in ontogeny is a spontaneous, natural expression of the stunning self-organization that abounds in very complex regulatory networks. . . Order, vast and generative, arises naturally." Stuart Kauffman (1993) has proposed how such complex *gene regulatory networks* have an innate tendency to become more complex ultimately giving rise to the cognitive-behavioral levels of human experience that we describe as art, beauty, and truth. The link between these gene regulatory networks and cognitive-behavioral levels of consciousness is now thought to be mediated by the ribonucleic world of microRNA's. Current epigenetic research, for example, documents how FOXP2, a gene implicated in human speech, also plays a significant role in bird-song learning (Balter, 2010). Clayton, one of the scientists involved in this research, believes "this is the first time a microRNA has been shown to respond to a particular thought process" (Saey, 2010; Kim et al.,2010; Warren, Clayton, et al., 2010). This leads us to propose how future research on the *Creative Psychosocial Genomic Healing Experience* may document how the 4-stage creative process could access and facilitate

the microRNA gene regulatory network underpinning stress, health, and well -being (Atkinson et al., 2020; Rossi, 2002, 2004, 2007; Rossi, Vyas et al., 2010).

Since our initial pilot study (Atkinson et al., 2010; Rossi, Iannotti et al. 2008; Rossi, Vyas et al., 2010) had only three subjects it is important to replicate it with larger populations (~ 30 subjects) and many diagnostic categories. Our initial cohort of three highly susceptible hypnotic subjects all had advanced academic degrees and were recruited from a university environment by the second co-author (Iannotti) on the basis of a General Psychiatric Evaluation, The Minnesota Multiphasic Personality Inventory (MMPI-2), The Tellegen Absorption Scale (highly correlated with Standard Scales of Hypnotic Susceptibility), and the Spiritual Intelligence Self Report Inventory (high scorers on the SISRI-24 acknowledge heightened experiences related to Critical Existential Thinking, Personal Meaning Production, Transcendental Awareness, and Conscious State Expansion). These subjects scored within the normal range of personality characteristics with no evident psychopathology on the MMPI-2. They were all enthusiastic volunteers who responded well to the "Creative Psychosocial Genomic Healing Experience" with a positive sense of focused attention, expectancy, appreciation, wonder, and therapeutic well being.

A full description of the clinical intervention, sample collection, and microarray analysis can be found in Rossi, Iannotti et al. 2008. Briefly, peripheral blood was obtained from three adult subjects immediately prior to, 1 hour after, and 24 hours after a single session of therapeutic hypnosis according to the protocol "Creative Psychosocial Genomic Healing Experience" established by Rossi (2004). Total RNA was extracted from leukocytes, quantified, and purified. Approximately 2.5 µg of purified total RNA was delivered to the MicroCRIBI Service (University of Padova, Italy) for microarray analysis. MicroCRIBI Service performed the microarray analysis on 21,329 - 70mer oligonucleotides (Operon version 2.0) designed on Human Unigene clusters. For each sample, 1.0 µg of total RNA was reverse transcribed and labeled with Cy3 and Cy5 fluorophores for two-channel scanning. Fluorophore labeling of "control" (Immediately before hypnosis) versus "treated" (1 hour or 24 hours after hypnosis) samples was counterbalanced, to control for dye bias. The microarrays were scanned with a two channel confocal microarray scanner (ScanArray# Lite, Perkin Elmer,USA) using its dedicated software (ScanArray Express 3.0.0.,Perkin Elmer).

Table one notes some similarities and differences in the Stanford Hypnotic Susceptibility Scales (SHSS) (Hilgard, 1965, Table 96, p. 402), which emphasize pathological dissociation, and this initial beta version of the Creative Psychosocial Genomic Healing Experience (CPGHE), which focuses on the ideo-plastic processes of activity-dependent gene expression and brain plasticity.

CLASSIC HYPNOSIS (SSHS) VS PSYCHOSOCIAL GENOMICS

CLASSICAL HYPNOSIS	PSYCHOSOCIAL GENOMICS
Agnosia (not knowing)	4-Stage Creativity
Amnesia	Enhanced Memory
Time Distortion	Time Condensation
(+) Hallucinations	Ideo-Sensory Signaling
(-) Hallucinations	Ideo-Motor Signaling
Dreams & Regression	Dream & Consciousness
Loss of Self Control	Self-Empowerment
Posthypnotic compulsion	Self-Prescriptions

Table One: A comparison of the Classical Stanford Scale of Hypnotic Susceptibility (SSHS) with the ideo-plastic Creative Psychosocial Genomic Healing Experience (CPGHE).

Table one highlights the differences between the SSHS and the CPGHE to draw attention to a series of hypotheses that motivate the type of epigenetic creative psychosocial genomic research that is now required. The classical measures of hypnosis like the Stanford Scale of Hypnotic Susceptibility (SSHS) and related scales were based on the classical population genetics of Fischer, Haldane, and Wright, which provided a mathematical description of the dynamics of Mendelian inheritance and natural selection over the generations (Mitchell, 2009). This is in sharp contrast with the dynamics of epigenetics, functional genomics, and modern complexity theory (Mitchell, 2009), which provides the research base for understanding how mind-body therapy is possible within an individual in real time here and now via the ideo-plastic dynamics of gene expression assessed by the Creative Psychosocial Genomic Healing Experience (CPGHE). The theory and applications of the SSHS and the CPGHE each have a appropriate function in psychotherapeutic practice but they are different as highlighted here.

- The classical hypnosis scales (SHSS) were constructed so that only 5-7% of the general population is scored as "highly susceptible." This implies that only 5-7% of the general population would be suitable for therapeutic hypnosis. We hypothesize, however, that with appropriate psychosocial experience and training everyone will be able to score highly on the CPGHE. Therefore it will be well suited for facilitating translational research and the clinical practice of therapeutic hypnosis, psychotherapy, meditation, and counseling with everyone.

- Research on the effects of training people to optimize their score on the classical scales of hypnotic susceptibility has been discouraging. Since people are not able to improve their classical hypnotic susceptibility, SHSS scores are conceptualized as a "fixed trait" that is investigated with the paradigms of classical population genetics (e.g. Lichtenberg et al., 2002, 2004; Szekely et al., 2010). This would imply that most subjects cannot improve their self-care and psychotherapeutic skills as measured by the SHSS.

- This is the opposite of what neuroscience and psychological research demonstrates about humans – we are very responsive to psychosocial learning opportunities for improving our psychotherapeutic skills and well being! Crowds and social activity actually turns on experience-dependent gene expression (Ganguly-Fitzgerald et al. 2006). This means that the CPGHE is a measure of epigenetics (Atkinson et al., 2010) assessing the natural moment-to-moment effects of evocative, on -going cognitive-behavioral and psychosocial experiences on activity or experience-dependent gene expression is in sharp contrast with the SHSS, which assesses hypnosis as "fixed trait" of classical population genetics. Experience with the CPGHE suggests that most people can improve their performance when (a) they are given appropriate, positive instruction and illustrations about how the 4-stage creative process is typically experienced; (b) they are given optimal opportunities to actually experience the CPGHE and openly share their experiences in supportive groups; (c) when their privacy is respected during self-motivated sharing of their positive creative experience. We hypothesize that creative therapeutic achievement on the CPGHE is enhanced by psychosocial learning in positive, constructive, and non-competitive groups.

- We hypothesize that the CPGHE is a means by which people can empower themselves by learning how to experience the 4-stage creative process in everyday life as well as in academic, artistic, scientific, and therapeutic situations on all levels from mind to gene.

- We hypothesize that scores and response profiles on the CPGHE will be associated with unique profiles of activity and experience-dependent gene expression (measured with DNA and Micro RNAs microarrays) and brain plasticity (measured with fMRI). The Gene Set Enrichment Analysis (GSEA) computer program available free on the

internet from MIT can be used to assess the meaning of DNA microarray findings for practical therapeutic purposes.

- The characteristics of classical hypnosis as measured by the SHSS in table one are associated with undesirable states of extreme dissociation such as agnosia (not knowing), and pathology (amnesia, hallucinations, regression, loss of self control), which are typical of psychological dysfunctions. We hypothesize that the characteristics of the CPGHE, by contrast, are associated with the positive, creative ideo-plastic processes of psychological resilience, resourcefulness, self-empowerment and mind-body healing (Atkinson et al., 2010; Rossi, Vyas, et al. 2010; Rossi et al., 2011, in press; Wetterstrand, 1902). This may be the reason why research and professional commentators over the past two generations have cast doubt on the value and validity of "hypnotherapy" practiced as a method of putting people into a "sleep-like trance" and programming them with post-hypnotic suggestions and commands while they are misperceived to be vulnerable and robot-like in their behavior.

- The historical misconceptions of classical hypnosis as a negative and possibly harmful process of "power, programming, manipulation, and control of human cognition and behavior" has led to the unfortunate reality that today classical hypnotic scales (SHSS) are no longer easily available, perhaps because of fears of liability with their misuse. We hypothesize that the positive and creative activity-dependent ideoplastic" experiences facilitated by the CPGHE are consistent with what neuroscientists call "activity-dependent gene expression and brain plasticity." We propose that this creative ideo-plastic faculty will have greater face validity as a definition of modern mind-body healing, rehabilitation, and therapeutic hypnosis that will be welcomed by the general public.

Considerable research will be required to assess the validity and reliability the administration of the *CPGHE* with the typical statistical methods of standardizing any psychological scale with item analysis, factor analysis, etc. We need to explore, for example, the art of questioning subjects about their experience in a manner that will not distract them from the creative flow of their inner processing. Variations in the language of the *CPGHE* for individual and group administration need to be assessed. Details about optimizing this creative approach to facilitating activity and experience-dependent gene expression and brain plasticity are presented in chapter nine of *A Discourse with Our Genes: The Psychosocial and Cultural Genomics of Therapeutic Hyp-*

nosis and Psychotherapy (Chapter nine, Rossi, 2004). More extended theoretical and practical presentations of our new psychosocial genomic concept of psychotherapy from mind to gene may be found in Rossi (2002, 2004, 2007; Rossi, Vyas, et al., 2010).

SELF-ORGANIZING MIND-GENE MAPS OF *THE CREATIVE PSYCHOSOCIAL GENOMIC HEALING EXPERIENCE*

We expect that the subjective experiences that are assessed by *The Creative Psychosocial Genomic Healing Experience* will contribute valuable insights when they are entered into the subject's experience-dependent gene expression matrix (the data from the DNA microarray gene chips) for the construction of Heat Maps and Self-Organizing Mind-Gene Maps, which will provide a picture of mind-body relationships via the epigenetics of genomic regulatory networks (Geschwind & Konopka, 2009; Petronis, 2010; Mitchell, 2009)

Note that the 12 points scored on this scale together with the subjects scores on the *Tellegen Absorption Scale, The Stanford and Harvard Group Scale of Hypnotic Susceptibility, The Minnesota Multiphasic Personality Inventory 2 (MMPI 2), The Spiritual Intelligence Self Report Inventory (SISRI)* http://www.dbking.net/spiritualintelligence/sisri.htm - and any other variables researchers would like to study – can be transformed into standard scores and entered into the same data matrix with the subject's gene expression data. The matrix of gene expression scores and psychological scores could be used to make Heat Maps and Self-Organizing Genomic/Psychological Maps. Visualized Mind-Gene Maps could give us more understanding of the evolving theory, research, and practice of psychosocial genomics (Dusek et al. 2008; Eisen et al., 1998; Jiang, et al. 2004; Kim, 2008; Kustra et al., 2006; Mahony, et al., 2004; Rossi et al. 2008).

The Use of DNA Microarrays (Rossi, 2005/2006) and bioinformatics software programs such as GSEA (http://www.broadinstitute.org/gsea/) and DAVID (http://david.abcc.ncifcrf.gov/) for the annotation, meaning, and therapeutic implications of *The Creative Psychosocial Genomic Healing Experience* are now being investigated. Such research already suggests that it reduces (1) chronic dysfunctional inflammation (associated with chronic pain and delayed healing); (2) oxidative stress (associated with many chronic medical and psychological conditions as well as the ageing process); (3) increases a "molecular signature of stem cells" (possibly associated with activating stem cells throughout the body). We hypothesize that these three deep molecular-genomic processes, plus others to be determined by further research, could eventually define what we call, "The Creative Psychosocial Ge-

nomic Healing Response."

Such research could determine if this is also the molecular-genomic signature of the healing placebo (Benedetti, 2008). This is consistent with research that documents how interventions via therapeutic hypnosis (the Ultradian Healing Response) and meditation (the Relaxation Response) reduces stress and promotes healing on the molecular-genomic level (Dusek et al., 2008; Rossi, 2002, 2004, 2007; Rossi, Iannotti et al., 2008; Yehuda et al., 2009). Future research could examine these therapeutic effects directly using novel markers of inflammation and oxidative stress such as 5'-ectonucleotidase (NT) in humans as described by Blake-Mortimer et al (1996, 1998, 2000). We invite other research groups to coordinate with us in the standardization and further documentation of the therapeutic value of *The Creative Psychosocial Genomic Healing Experience* on all levels from the cognitive-behavioral to the molecular-genomic. http://www.ernestrossi.com/ernestrossi/Neuroscienceresearchgroup.html.

THE CREATIVE PSYCHOSOC  GENOMIC HEALING EXPERIENCE
(Scoring & Assessment Form)

Initial Time_____ am pm Initial Stress: 0%. . . .100%

Accessing Resources:

1. Warmer – Cooler 0% . . . .100% 2. Stronger – Weaker 0%. . . .100%

Engaging Issues:

3. Child – Adult 0%. . . .100% 4. Problem – Opposite 0%. . . .100%

Creative Replays:

5. Negative Past Review 0% . . .100 6. Positive Now & Future 0%. . . .100%

Integration:

7. Positive Self Change 0%. . .100% 8. Positive Self-Prescription 0%. . .100%

Real Time (Min.: 0-5 6-10 11-15 16-20 21-25 26-30 31-40 41-50 51-60 61+
Est. Time (Min.): 0-5 6-10 11-15 16-20 21-25 26-30 31-40 41-50 51-60 61+
9. Mental Engagement: Real Time / Est. Time X 100 = _____ %
10. Stress Reduction: Initial Stress / Final Stress X 100 = _____%
11. Surprise: 0%. . . .100% 12. Confidence: 0%. . . . 100%
Education: Elementary High School College Masters Doctorate
Age: 0 – 9 10 – 19 21 – 29 30 – 39 40 – 49 50 – 59 60 – 69 70 – 79 +
Sex: M F
Night Sleep Length: 1h 2h 3h 4h 5h 6h 7h 8h 9h 10h 11h 12h +
Dreams: 1 2 3 4 5 6 7 **Days/Week.**
Est. Dreams per Night_____

Comments

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Chapter Eighteen*

A Brief Protocol for the Creative Psychosocial Genomic Healing Experience:
The 4-Stage Creative Process in Therapeutic Hypnosis and Brief Psychotherapy

Ernest Lawrence Rossi
Milton H. Erickson Institute, California Central Coast, Los Osos, CA, USA
The Mind-Body Institute of San Lorenzo Maggiore, Benevento, Italy

Mauro Cozzolino
University of Salerno, Italy

Jane Mortimer
University of Adelaide, Australia

David Atkinson
University of Pittsburgh School of Medicine, USA

Salvatore Iannotti
Neuroscience School of Therapeutic Hypnosis Psychotherapy & Rehabilitation, Solopaca (BN), Italy

Kathryn Lane Rossi
Milton H. Erickson Institute, California Central Coast, Los Osos, CA, USA
The Mind-Body Institute of San Lorenzo Maggiore, Benevento, Italy

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ABSTRACT

We present empirical data on therapeutic hypnosis and brief psychotherapy as a 4-stage creative process of focused attention and positive expectancy in professional training workshops of the American Society of Clinical Hypnosis, the National Institute for the Clinical Applications of Behavioral Medicine, and the Milton H. Erickson Foundation. We developed a brief protocol for assessing the 4-stage creative process, which is the core dynamic of the Creative Psychosocial Genomic Healing Experience. We report that the 4-stage creative process for resolving many psychological problems and symptomatic behavior in a satisfactory manner can be learned within three trials during two day professional workshops. The theory, research and practice of private problem solving, stress reduction, and mind-body symptom resolution in professional and public settings is discussed.
KEYWORDS: Brain plasticity, 4-stage creative process, ideo-plastic, psychosocial learning, psychosocial epigenetics, professional training workshops.

INTRODUCTION

The theory, research and practice of utilizing the 4-stage creative process as a protocol for facilitating personal problem solving and symptom resolution in psychotherapy began with two seminal papers in the *Journal of Humanistic Psychology* by the senior author (Rossi, 1967, 1968). Since that time the 4-stage creative process has been used to train two generations of students and clinicians in professional training workshops of the American Society of Clinical Hypnosis, the National Institute for the Clinical Applications of Behavioral Medicine, and the Milton H. Erickson Foundation. The 4-stage creative process is the core dynamic of the Creative Psychosocial Genomic Healing Experience, which recently is associated with molecular-genomic signatures consistent with the (1) up-regulation of stem cell activity and (2) the down-regulation of chronic inflammation and (3) cellular oxidation (Rossi et al., 2008, Atkinson et al, 2010).

It has been hypothesized that this association between the 4-stage creative process of psychology and the molecular-genomic signatures of biology may be a fundamental mechanism of therapeutic hypnosis and the placebo response as well as healing aspects of meditation, holistic medicine and psychosocial epigenetics (Rossi, 2007,. 2011b). We propose that psychosocial epigenetics is an emerging science of interactions between social and psychological levels of experience and qualia-dependent activation of gene expression and brain plasticity (Rossi & Rossi, 2011). The complex psychosocial epi-

genetics between behavior, gene expression, chronic inflammation, and the environment have been reviewed recently in *Nature* for its far reaching implications even in cancer prevention by Brower (2011) as follows.

> Researchers are finding that epigenetic changes frequently precede and can induce genetic mutations that cause cancer. If these early epigenetic alterations can be detected and reversed, it might be possible to prevent certain cancers. . . *If the genetic code is the hardware for life, the epigenetic code is software that determines how the hardware behaves — and as such it can be rewritten.* . . The move from a purely genetic to an epigenetic model is crucial for prevention strategies. . . Epigenetics has also provided clues that link environmental factors with cancerous genetic changes. . . *A prime candidate at the interface of environment and genetics is chronic inflammation, which is known to precede the development of numerous types of precancerous lesions* — and indeed certain cancers themselves, including esophageal, liver and colon cancers. Inflammation has been linked with increased DNA methylation in otherwise healthy looking tissue. . . . *chronic inflammation "a truly epigenetic phenomenon".* . . Slowly the importance of the epigenome in cancer development is being appreciated. "Geneticists are hugely more aware of the importance of epigenetics in the development of cancer," . . . When it comes to cancer prevention, the future could lie in arresting the reversible epigenetic changes before irreversible mutations take hold. (pp. s12-s13, italics added here).

We propose that this recent acknowledgement of the role of epigenetic interactions between behavior and gene expression in mind-body health and dysfunctions as intractable as cancer has profound implications for developing a new neuroscience mind-body paradigm of brief psychotherapy and therapeutic hypnosis (Rossi, 2002, 2007, 2011). The Creative Psychosocial Genomic Healing Experience, with its core 4-stage creative protocol, is explicitly designed for optimizing the ideo-plastic epigenetic modulation of acute and chronic stress reduction via experience-dependent gene expression, brain-plasticity, and mind-body healing, which is appropriate for 100% of the general population seeking positive psychological transformations (Rossi, 2011). This is in sharp contrast to the classical dissociative model of hypnosis measured by the Stanford (Hilgard, 1965) and Spiegel and Spiegel (1978) Scales of Hypnotic Susceptibility, which are most appropriate for identifying the 5% to 7 % of the clinical population who are prone to pathological dissociation that can be corrected by authoritative, direct suggestion. With

this distinction between the *pathological dissociative* versus the *creative ideoplastic* models of therapeutic hypnosis clearly in mind, we now outline the methodology and results of presenting the 4-Stage Creative Process and the Creative Psychosocial Genomic Healing Experience as a teaching protocol in professional training workshops of the American Society of Clinical Hypnosis, the National Institute for the Clinical Applications of Behavioral Medicine, and International Institutes of Milton H. Erickson Foundation.

METHOD

Our teaching plan for each professional training workshop proceeds in four steps.

1. A 20 minute PowerPoint presentation of six slides illustrating of the nature of the 4-stage creative process as experienced in everyday life, therapeutic hypnosis and brief psychotherapy. These slides and their scientific rational in six languages are available at http://www.ernestrossi.com/ebook/index.html.
2. A 20 minute experience of the 4-stage creative process via the Brief Protocol for the Creative Psychosocial Genomic Healing Experience that is presented as supplementary material at the end of this paper.
3. A 15 minute group voluntary sharing of interesting and surprising aspects of problem solving with the 4-stage creative process in the Brief Protocol for the Creative Psychosocial Genomic Healing Experience.
4. Five minutes to fill out the 4-stage Creative Process Scoring and Assessment Form presented as supplementary material at the end of this paper.

HYPOTHESES AND RESULTS

The four hypotheses that motivated this study and analysis of the data collected are as follows.

HYPOTHESIS ONE: THE 4-STAGE CREATIVE PROCESS CAN BE LEARNED IN PROFESSIONAL TRAINING WORKSHOPS.

Figure 1 illustrates how three trials during a professional training workshop the National Institute for the Clinical Applications of Behavioral Medicine at Hilton Head in 2010 over two days were sufficient to learn the 4-stage creative process in a group presentation. The two way analysis of variance was significant at the P value of 0.0128 for trials variable and very significant at the P value of 0.0018 for the 4-stage creative process variable. Figure 2 illustrates the same data with a focus on the 4-stage creative process on the horizontal axis. Table one presents the two way analysis of variation for figures one and two.

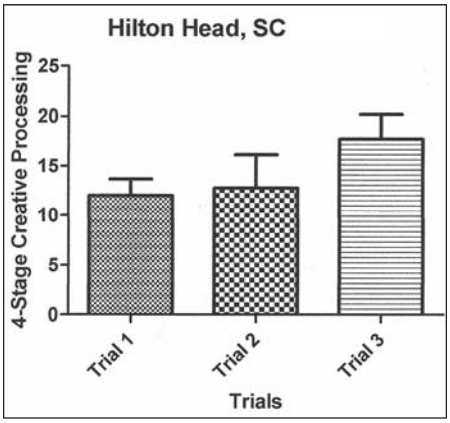

Figure 1

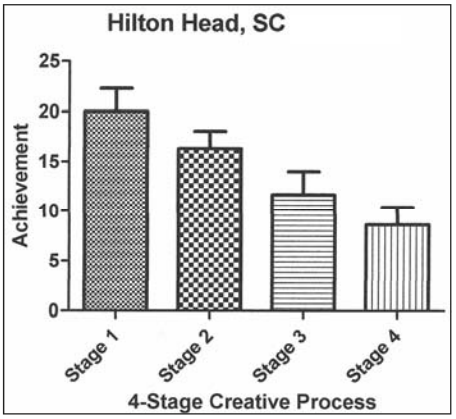

Figure 2

	2way ANOVA Tabular results				
1	Table Analyzed	Data 1			
2					
3	Two-way ANOVA				
4					
5	Source of Variation	% of total variation	P value		
6	Trials	23.86	0.0128		
7	Stage of Creative Process	68.87	0.0018		
8					
9	Source of Variation	P value summary	Significant?		
10	Trials	*	Yes		
11	Stage of Creative Process	**	Yes		
12					
13	Source of Variation	Df	Sum-of-squares	Mean square	F
14	Trials	2	78.17	39.08	9.839
15	Stage of Creative Process	3	225.7	75.22	18.94
16	Residual	6	23.83	3.972	
17					
18	Number of missing values	0			

Table 1

HYPOTHESIS TWO: THERE IS A SIGNIFICANT GAP IN LEARNING TO BRIDGE STAGE 2 AND 3 OF THE FOUR-STAGE CREATIVE PROCESS IN PROFESSIONAL TRAINING WORKSHOPS.

Figure 3 illustrates how combining the data of successful achievement on stages 1 & 2 and contrasting it with the combined data on the successful experience of stages 3 & 4 narrowly missed significance at the P values of

0.0544 for the stages variable and a P value of 0.5888 on the trials variable presented in table two.

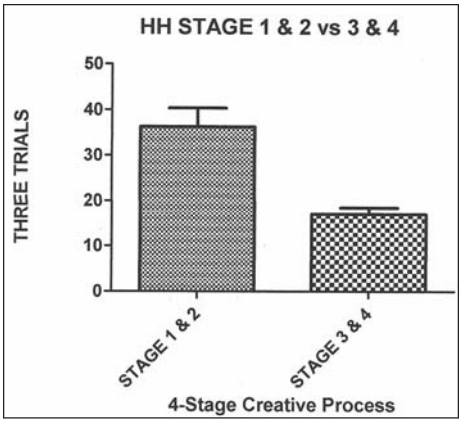

Figure 3

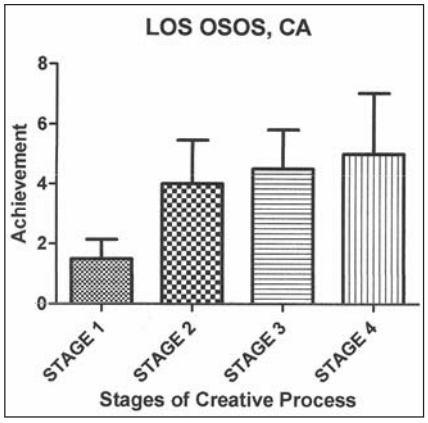

Figure 4

	2wayANOVA Tabular results				
1	Stages 1 & 2 vs 3 & 4	Figure 3 Data			
2					
3	Two-way ANOVA				
4					
5	Source of Variation	% of total variation	P value		
6	4-Stage Creative Process	83.27	0.0544		
7	Trials	6.88	0.5888		
8					
9	Source of Variation	P value summary	Significant?		
10	4-Stage Creative Process	ns	No		
11	Trials	ns	No		
12					
13	Source of Variation	Of	Sum-of-squares	Mean square	F
14	4-Stage Creative Process	1	560.7	560.7	16.90
15	Trials	2	46.33	23.17	0.6985
16	Residual	2	66.33	33.17	
17					
18	Number of missing values	0			

Table 2

HYPOTHESIS THREE: MORE EXPERIENCED SUBJECTS WILL ACHIEVE HIGHER SUCCESS AT STAGES 3 AND 4 OF THE FOUR-STAGE CREATIVE PROCESS IN PROFESSIONAL TRAINING WORKSHOPS.

While a visual comparison of figure two (initially inexperienced subjects) and figure 4 (highly experienced subjects with more than 3 trials) suggests that this hypothesis is true, it actually fails to achieve statistical significance.

A careful inspection, however, reveals that there is a wider range of variation in the achievement of stages 2, 3 & 4 in the more experienced group. These highly experienced subjects appeared to spend less time in stage one (selecting a problem) and immediately jumped to stages 2, 3, & 4 with gusto. They appeared to be less methodical and orderly in progressing from one stage to the next. They often shifted rapidly back and forth between stages 2, 3 & 4 *while working on several related problems and their implications at the same time!* The subjective reports of these more experienced subjects suggested that their growing expertise led them to take many intuitive, non-rational short cuts leading to more efficient multiple and simultaneous problem solving which, however, was unexpected and difficult to quantify at this early stage of research on the 4-stage creative process. This means that further research with a larger number of subjects and a more detailed analysis of the subject's performance strategies could clarify what contributes to advanced achievement on the 4-stage creative process for therapeutic purposes These unexpected findings suggests that future research may employ Bayesian inference, which combines experience of the *prior probability* of a hypothesis with new observed evidence (Bolstad, 2010).

HYPOTHESIS FOUR: TEACHING THE 4-STAGE CREATIVE PROCESS CAN BE EFFECTIVE THROUGHOUT THE TYPICAL CIRCADIAN DAY (MORNING AND AFTERNOON) OF PROFESSIONAL TRAINING WORKSHOPS IN THERAPEUTIC HYPNOSIS AND PSYCHOTHERAPY.

Aldrich and Bernstein (1987) reported that hypnotic susceptibility is bimodal with peaks occurring in the morning (11 am - noon) and afternoon (4 - 6 pm). This circadian factor was closely approximated in figure 5, which illustrates how the trials and 4-stages variables were both very highly significant (P = 0.0001) as presented in table three.

These very highly significant P-values were due, in part, to figure 5 representing the combined data of all the subjects participating at two major national 2010 workshops offering training in therapeutic hypnosis and psychotherapy (the National Institute for the Clinical Applications of Behavioral Medicine at Hilton Head, South Carolina, and the Milton H. Erickson Foundation in Orlando, Florida). The three columns on the left side of figure 5 represent data for the combined groups in the morning (between 9 am and

noon), which were almost identical with the data of the combined groups in the afternoon (between 3 pm and 6 pm). This means that teaching and learning the 4-stage creative process can be equally effective throughout the typical circadian day of professional workshops sponsored by two very different national organizations offering beginner and advanced training in therapeutic hypnosis and psychotherapy. This implies that our model of training professionals in learning to experience the 4-stage creative process is very robust and worthy of scientific replication with other populations representing the various interests of the general public, different age and educational levels, and the many clinical dysfunctions that may be treated more economically in group settings.

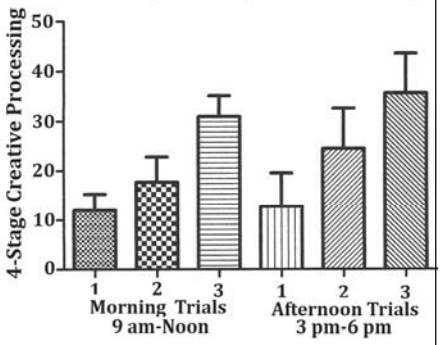

Figure 5

	2wayANOVA Tabular results				
1	Circadian Factor	Figure 5 Data			
2					
3	Two-way ANOVA				
4					
5	Source of Variation	% of total variation	P value		
6	Trials	73.56	< 0.0001		
7	4-Stage Creative Process	21.49	< 0.0001		
8					
9	Source of Variation	P value summary.	Significant?		
10	Trials	****	Yes		
11	4-Stage Creative Process	****	Yes		
12					
13	Source of Variation	Of	Sum-ot-squares	Mean square	F
14	Trials	5	1918	383.5	44.55
15	4-Stage Creative Process	3	560.1	186.7	21.69
16	Residual	15	129.1	8.608	
17					
18	Number of missing values	0			

Table 3

DISCUSSION

Data Limitations of Our Clinical-Research Workshop Model.

The data collected in the clinical-research workshop model of this study contained uncontrolled and unreliable situational factors typical of such professional training workshops. The number of subjects participating was sometimes uncertain, for example, because subjects occasionally walked in and out of the workshops. Most groups, however, contained about 30 subjects (plus or minus ~5) in a wide age range between the twenties to the sixties with about 70% females and 30% males in each group.

Not everyone present in the workshops participated; about 10% of the subjects apparently preferred to simply observe rather than actively engage in the 4-stage creative process exercise. We found that to secure optimal participation in this clinical-research teaching workshop, it is important for potential participants be advised ahead of time (in the workshop brochure) that they agree to participate as research subjects in a novel approach to learning how to experience the 4-stage creative process in therapeutic hypnosis and psychotherapy.

Psychobiological Dynamics from Mind to the Molecular-Genomic.

Why do subjects need more practice time to bridge the gap between state 2 and stage 3? We hypothesize that in any truly creative process more time is needed for experience-dependent gene expression and brain plasticity to bridge the performance gap between stages 2 & 3. This hypothesis achieved some experimental support with murine (mice) subjects that require about four weeks for brain stem cell to develop into young neurons and four months to reach their mature size and functions (Rossi, 2002, 2007).

Enhancing Psychosocial Skills via Positive Transformations of the 4-Stage Creative Process in Professional Training Workshops.

A noteworthy feature of empirical data of this study is how quickly psychotherapists are able to learn how to enhance their personal experiences of the 4-stage creative process privately in a public setting. A remarkable aspect of the 4-stage creative process is its inherent bias toward facilitating positive psychosocial transformations. The concept of "clinical or therapeutic hypnosis as well as "brief psychotherapy" in the medical model, which implies that people are "sick" and need "therapy" to get well. Our more benign creative psychological genomic healing experience model of the 4-stage creative process implies, instead, that people are temporally "stuck" in stage two of a creative process that simply requires a little more time, focused concentration

and conscious self-care for a satisfactory resolution. This radical perspective shift could account for the positive attitudes and rapid transformations many of our subjects experienced.

It has long been assumed that psychotherapy is a very private affair with many secrets that must be hidden from public scrutiny. We have demonstrated, however, that our professional training workshops can be robust psychosocial venues for doing private inner work rapidly in public. The instructions given throughout our approach to the 4-stage creative process is that "it is private but appropriate aspects of the experience can be shared publically" to help others in the workshop. This appropriate psychosocial sharing could account for the richness, rapidity and satisfaction of learning in professional training workshops. Future research will be required to evaluate the extent to which such private psychosocial genomic creative work in public settings can be extended to other groups.

SUMMARY

We formulated a brief protocol for the Creative Psychosocial Genomic Healing Experience and the 4-Stage Creative Process in therapeutic hypnosis and brief psychotherapy suitable for administration to groups as well as individuals. This robust protocol of the 4-stage creative process for resolving psychological problems and symptomatic behavior in a satisfactory manner can be learned within three trials during two day professional workshops. The theory, research and practice of private problem solving, stress reduction, and mind-body symptom resolution on all levels from mind to gene in professional workshops is discussed. Immediate knowledge of results, positive peer support, and the development of new psychosocial skills in learning how to appropriately communicate live here-and-now novel and therapeutic experiences is an exhilarating exercise in creating new consciousness that facilitates the confidence and maturation of psychotherapists.

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Supplemental Material

THE CREATIVE PSYCHOSOCIAL GENOMIC HEALING EXPERIENCE: A BRIEF PROTOCOL FOR THE 4-STAGE CREATIVE PROCESS

Introduction

The therapist begins with: ***It is wonderful to know how our best thoughts and positive feelings can improve health and well-being. Here are a few exercises that will inspire you explore some interesting questions that can help you solve your own creative problems in your own way.***

[Optional facilitation of stage one: If needed, the therapist may add a few empathetic statements to individualize this Brief Protocol to clarify whatever concerns and questions some people and groups may have.]

[Introduce the 4-Stage Creative Process Scoring & Assessment Form here.]

Therapist begins with: ***"An important aspect of creative problem solving is to realize how you can explore new life possibilities by looking at things from many points of view at the same time. These creativity exercises will ask you to carefully observe yourself and carefully remember what you are experiencing. Later you will be asked to remember your experiences so you can fill out the 4-Stage Creative Process Scoring & Assessment Form. You can begin by filling out the first line of this form right now. [Pause for a moment] Notice the last item on the first line asks you to record what level you are experiencing right now on a scale of 0% to 100%. Where 0% is no stress or discomfort and 100% would be the worst stress or discomfort your have ever experienced in your whole life. 50% would be your average level of stress in everyday life. Go ahead circle or write in your initial stress level right now on the dotted line." [Pause for a moment]***

[**Optional Research:** A protocol for research on the molecular-genomics of **The 4-Stage Creative Process** and **The Creative Psychosocial Genomic** Healing Experience has been presented (Atkinson et al., 2010; Rossi et al., 2008). The first step in collecting samples for DNA microarray and bioinformatic analysis of the molecular-genomic analysis of each stage of the 4-stage creative process is conducted at this time.]

STAGE 1 ONE: FOCUSING CONSCIOUSNESS

The therapist models the first stage of the creative process with the palms of the hands about 6 to 8 inches apart facing each other at about chest

level. [Presenting Figure 1 illustrating this initial hand position in stage one of the 4-stage creative process is optional.]

"You can begin by looking at your hands like this. . ."

1. Warmer or cooler? The therapist asks ***"Which hand feels a bit warmer or cooler?"*** Subjects may sometimes seem puzzled about what this question means. The therapist simply responds with, ***"Most people don't realize how their hands or other parts of their body usually feel slightly warmer or cooler when they really pay attention to it. This is a good exercise help you become more aware of yourself. It helps to focus your attention and positive feeling about your natural abilities. The simple idea of one hand being warmer or cooler could heighten your real feeling of warmth and coolness."***

Figure 6: The initial hand mirroring position for stage one of the 4-stage creative process (presenting an image of Figure 6 is optional).

After a minute the therapist adds support and states emphatically, ***"Notice and remember how warm or cool your hands seem to be".*** [Allow another minute for the subject's inner focus.]

2. Stronger – Weaker?

The therapist now asks, ***"Now notice which hand feels stronger or weaker?"*** After one minute the therapist adds support by stating emphatically, ***"Notice and remember how strong or weaker your hands seems to be!"*** [Allow another minute for the subject's inner focus.]

3. Lighter – Heavier?

The therapist asks, ***"Now notice which hand feels lighter or heavier?"*** After one minute the therapist adds support by stating emphatically, ***"Notice and remember how light or heavy your hands seems to be!"*** [Allow another minute for the subject's inner focus.]

[Facilitating stage one for the uniqueness of groups and individuals: If

needed the therapist may add a few empathetic statements to individualize this Brief Protocol to clarify whatever concerns and questions that some subjects and special groups may have.]

STAGE 2: INCUBATION, PROBLEM REVIEW

4. Child – Adult?

The therapist asks, *"Now let's explore your imagination . . . Which hand seems to be you today - and which hand feels more like you as a child?"* After one minute the therapist adds support by stating emphatically, ***"Notice and remember which hand seems to be you at*** *your present age and which hand seems to be more like you as a child*!" [Allow another minute for the subject's inner focus.]

5. Problem – Opposite

The therapist now asks, ***"Which hand represents some problem you would like to solve right now - today in this exercise? . . .*** [Therapist pauses for one minute.] ***And which hand seems to be the opposite . . . perhaps holds an answer to your problem?"*** After one minute the therapist adds support by stating emphatically, ***"Remember which hand represents your problem and which hand seems to hold the opposite – perhaps an answer even if you do not know what it is yet!"*** [Allow another minute for the subject's inner focus.]

6. Problem History

The therapist states emphatically, ***"Now let the hand that represents your problem begin to drift down very slowly . . . as you privately review the history, memories, and feelings of your problem from the beginning to the present moment."***

The therapist's models by very slowly lowering one hand as illustrated in figure 7.

Figure 7: Stage 2 of the four-stage creative process in the hand mirroring protocol (presenting an image of Figure 7 is optional).

The therapist states offers motivational support with these remarks administered one minute apart.

"That's right! Do you have the courage . . . to allow that hand and arm to drift down a bit. . . with each memory you find yourself reviewing?"

"Allowing yourself feel only as much of that as you need to . . . and then move on to the next memory that comes up more or less by itself."

"That's right . . . let yourself have the courage to continue . . . only as long as you need to . . . to feel everything as fully as you need to . . . privately."

"That's right . . . while another part of you observes wisely . . . you learn how to take care of yourself . . . to imagine and create the best possible outcome for yourself."

This therapeutic review is "safe" because people are **not** encouraged to fully recall any difficult situations or traumatic memories of the past. In this safe context *memories and emotions are carefully circumscribed and limited because they are externalized by being projected into one hand only.* In this brief protocol negative memories are always *balanced by encouraging people to simultaneously experience the opposite or solution in their other hand* that holds solutions to problems even if they remain unknown at this point.

When the problem hand finally touches down in the person's lap, the therapist adds support and offers empathetically, ***"That's Right! Allowing your problem hand drift down to your lap and come to a comfortable rest . . . Wonderful . . . appreciating your job well done! . .***

Remember as much of this Stage 2 of your creative process as you need to build a better future! . . . and now getting ready to move on to the solution of your problem with your other hand. Let your other hand holding the solutions to your problem remain up for a moment so you can now turn your full attention to it!

STAGE 3: AHA! PROBLEM SOLVING

The therapist now facilitates problem solving via the famous "Aha" or "Eureka" experience of insight celebrated in ancient and modern literature as illustrated in figure 8. Creative insight, problem solving & healing often seem to happen spontaneously. Subjects are usually surprised and delighted when they receive a creative thought. Many people automatically dismiss their own originality as worthless since it has never been reinforced in their early life experience. *The therapist's main job at this third stage of the creative process is to help people recognize and appreciate the value of the "new" and creative that usually emerges spontaneously and unheralded.* Often people may have already thought of the options that come up for problem solving at this stage but dismissed them since they were never validated. Here the therapist strongly supports exploring them for their real life possibilities!

Figure 8: Stage 3 of the 4-stage creative process in the in the hand mirroring protocol (presenting an image of Figure 8 is optional).

7. Problem Solving

The therapist continues to model by slowly lowering the other hand as illustrated in figure 8 with these words.

"Now allow your other hand to drift down slowly as you explore new possibilities about how to solve your problem today . . . Allow that hand to begin drifting down slowly as you begin to explore something new . . . Explore your best hopes and imagination for today and the future . . . what could be some interesting and wonderful possibilities of problem solving, healing and well being . . . Speculate about exciting and fascinating turning points in your life . . . Create the best of all possible worlds for yourself . . . Enjoy your best dreams about yourself!"

This fragile and tenuous transition from the difficulties of the previous stage two reviews of past problems to the new joyous possibilities of stage three that now emerge often can be seen in the delicate shifts of people's facial expressions. Notice the shifts from negativity, stress, sadness, and conflict (of stage two) to the more searching expressions of positive expectation in stage three of the creative process that are often punctuated with a slight smile and even a short laugh. The therapist supports these positive shifts with a few warm implicit processing heuristics such as these administered at one minute intervals.

"Something pleasantly surprising you can look forward to? . . . What you really need that is most interesting and important to you?

"Simply receiving and continuing to explore the sources of your strength for

dealing successfully with that issue."

"Yes, appreciating the value of that as fully as you need to while taking good care of yourself as that hand finally comes to rest in your lap."

When the hand finally touches down in the subject's lap, the therapist states in supportive manner, ***"Remember this Stage 3 of your creative process! Remember how real and strong these new positive possibilities and feelings for changing your life for the better are!***

The therapist now facilitates the transition from stage three of the creative process to stage four with: ***"Wonderful . . . really appreciating yourself for a job well done! . . . And now get ready to move on to the resolution of this issue (concern, problem or symptom)!"***

STAGE FOUR: REALITY TESTING AND SELF-CARE

The therapist optimizes stage four by (1) facilitating group sharing and positive discussion to validate the value of their experiences, (2) helping them reframe symptoms into signals and psychological problems into inner resources, (3) reality testing, and (4) self prescriptions for self care. Here is a four part implicit processing heuristic to mediate these creative transitions.

Figure 9: Stage 4 of the four-stage creative process in the activity-dependent hand mirroring protocol (presenting an image of Figure 9 is optional).

8. Reality Testing & Self Prescription for Self Care

The therapist brings this brief protocol to its creative conclusion with this four part implicit processing heuristic, each part administered at 30 second intervals:

"When . . . [brief pause for emphasis] **A part of you knows it can continue this creative work entirely on your own at appropriate times throughout the day . . .** [30 second pause]

And when . . . [brief pause for emphasis] **your conscious mind knows it can simply cooperate in helping you recognize when is the right time to tune in and continue this creative work privately on your own . . .** [30 second pause]

Learning how you can explore and practice your new ideas in the real world and give yourself positive prescriptions for taking good care of yourself . . . [30 second pause]

You will bring this creative exercise to an end for now so you can stretch and come fully alert. Some of you may wish to share how you can help yourself in your real everyday life."

While the group is evidently completing their inner work the therapist can support with:

All this creative work can remain private within you . . . although some of you may wish to share a few of your insights with the group . . . some appropriate ideas that may help others learn how to continue this creative work.

9. Reinforcing the Psychosocial Learning of the 4-Stage Creative Process via Group Sharing of Appropriate, Interesting and Surprising Aspects of this Creative Exercise.

The therapist now encourages group sharing with supportive remarks such as these:

"Something interesting some of you would like to share about your creative inner work?

"What is surprising and unexpected about this that is new to you?

"What is most significant and life changing about this for you?

"How will you remind yourself to do this several times a day?

"What interesting possibilities are opening up for you to now?

"How will this experience contribute to a positive change your life?

"What new attitudes and ideas will you now explore in your life?

The therapist carefully monitors a positive sharing of experiences. People are encouraged to "learn how to appropriately share a few their private experiences that support psychosocial learning." People are discouraged from negative evaluation of these share experiences! Compassionate, empathetic, and supportive listening to each other is the most important creative psychosocial process to be learned.

[Optional facilitation of stage four: If needed the therapist may add a few empathetic statements to individualize this Brief Protocol to clarify whatever concerns and questions some people and groups may have.]

10. Finish the 4-Stage Creative Process Form.

The therapist completes the protocol: **"Please complete the 4-stage creative processing form by filling in what your stress level is now at the end of your creative exercise:**

[**Optional Research:** Research on the molecular-genomics of this **4-Stage Creative Process** is the same as the pilot studies of **The Creative Psychosocial Genomic Healing Experience** (Atkinson et al., 2010; Rossi et al., 2008). The second step in collecting samples for DNA microarray and bioinformatic analysis of the molecular-genomic analysis of each stage of the 4-stage creative process is conducted at this time. Further follow up collections of samples for DNA microarray and bioinformatic analysis of the molecular-genomic analysis then may be carried out to determine how long the psychosocial genomic changes last.]

The 4-Stage Creative Process Scoring & Assessment Form

Initial Time_____ am pm Age____ Sex: M F
Initial Stress: 0% . . . . 50% 100%

Stage One: Focusing Consciousness (Circle your response: Yes or No)

1. Warmer – Cooler? Yes No. 2. Stronger – Weaker ? Yes No.
3. Lighter – Heavier? Yes No.

Stage Two: Incubation, Problem Review
4. Child – Adult? **Yes No.** 5. Problem – Opposite? **Yes No.**
6. Problem History? **Yes No.**

Stage Three: Aha! Problem Solving
7. Problem Solving? Yes No.

Stage Four: Reality Testing and Self-Care
8. Reality Testing? Yes No. 9. Self Care? Yes No.
10. End Stress: 0% . . . . . 50% 100%

11. Confidence: 0% . . . . . 50% 100%

12. Time Estimate: _____ minutes.

Education: High School College Master Doctorate

COMMENTS: _____

_____

_____

_____

Do not fill in this box: Staff Only.

Real Time (Min.: 0-5 6-10 11-15 16-20 21-25 26-30 31-40 41-50 51-60 61+

Est. Time (Min.): 0-5 6-10 11-15 16-20 21-25 26-30 31-40 41-50 51-60 61+

Mental Engagement: Real Time / Est. Time X 100 = _____%

Stress Reduction: Initial Stress / Final Stress X 100 = _____%