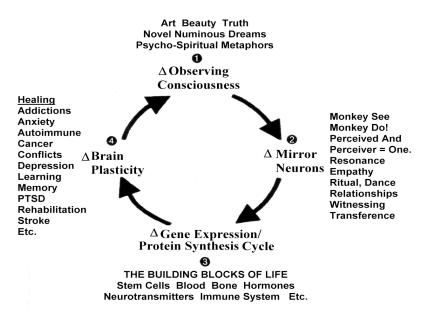
How the Mind and the Brain Co-Create Each Other Daily

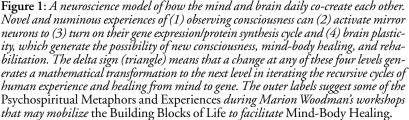
Mind-Brain-Gene Research on the Foundations of Consciousness, Creativity, Imagination, and Psychotherapy

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1. MIRROR NEURONS AND THE MIND-GENE CONNECTION IN PSYCHOTHERAPY

The eternal mystery of how consciousness and nature seemingly reflect each other in the mirror of the human mind was the essence of the Woodman/Rossi dialogues in the Blossoms Bloom in the Fire Conference at Pacifica Graduate Institute in Carpinteria in 2006 (Rossi 2007). We discussed a new neuroscience approach to Carl Jung's (1918/1966) synthetic approach to mind-body healing and psychotherapy. We presumed to boldly go where no one had gone before in outlining the newly emerging field of "the bioinformatics of art, beauty, truth, and creativity in psychotherapy." Figure 1 is a very broadly sketched overview of how the mind updates the brain daily via the mirror neuron system encoding the novel and numinous experiences of consciousness and dreaming (Rossi 2007).





Initial research on the discovery of mirror neurons by Rizzolatti and Arbib (1998) and his research team at the University of Parma in Italy during the early 1990s was described by Miller (2005) as follows:

The finding was exciting, Rizzolatti says, because it fit with ideas that were coming together at the time in philosophy and cognitive science, such as the hypothesis that understanding the behavior of others involves translating actions we observe into the neural language of our own actions. The monkey mirror neurons seemed to do just that, providing a potential neural mechanism to support that proposal. Subsequently, researchers used functional magnetic resonance imaging (fMRI) and other techniques to investigate brain activity as people made—and observed others making—*hand movements and facial expressions*.

These studies identified mirror-like activity in several regions of the human brain, including a region of frontal cortex homologous to F5. This human frontal region, known as *Broca's area, is also involved in speech production—a connection that snared the attention of researchers studying the evolution of language. . . .* Rizzolatti and others have argued that mirror neurons could facilitate the imitation of skilled movements like *the hand and mouth movements used for communication . . .* the mirror system in the frontal cortex is active as novices learn to play chords on a guitar by watching a professional guitarist. Similar learning by imitation is a key feature of language acquisition in infants and is widely considered a prerequisite for language evolution. (946, emphasis added)

In retrospect we can now see that the excitement about the frontal cortex mirror neuron concept was because it was the first to demonstrate convincingly how specialized neurons not only interface with the outer psychosocial environment but how that interface generates mirroring psychophysiological activity within the brain and body of the observer (Fogassi et al. 2005; Gallese et al. 1996; Iacoboni et al. 2005). Figure 1 outlines my theoretical neuroscience model of how novel and numinous experiences of our observing consciousness update and reconstruct the brain at the levels of gene expression and brain plasticity within mirror neurons. This model is speculative and controversial, however, because no one has yet directly demonstrated how activity-dependent gene expression and brain plasticity are actually generated in the F5 region of the human cortex, which is the brain region originally identified as containing mirror neurons defined by Rizzolatti's research team. My theoretical model is, however, entirely consistent with the Nobel Prize-winning research of Eric Kandel (2006), who first described the relationship between activity-dependent gene expression, brain plasticity, and psychotherapy as follows (Kandel 1998):

> Insofar as psychotherapy or counseling is effective and produces long-term changes in behavior, it presumably does so through learning, by producing changes in gene expression that alter the strength of synaptic connections and structural changes that alter the anatomical pattern of interconnections between nerve cells of the brain. As the resolution of brain imaging increases, it should eventually permit quantitative evaluation of the outcome of psychotherapy . . . Stated simply, the regulation of gene ex

pression by social factors makes all bodily functions, including all functions of the brain, susceptible to social influences. These social influences will be biologically incorporated in the altered expressions of specific genes in specific nerve cells of specific regions of the brain. These socially influenced alterations are transmitted culturally. They are not incorporated in the sperm and egg and therefore are not transmitted genetically. (460, emphasis added)

The value of adding Kandel's concept of activity-dependent gene expression and brain plasticity to Rizzolatti's mirror neuron concept is that it avoids the problem of infinite regress implied in the mirror concept of mind and consciousness. Rizzolatti uses the concept of the mirror as a metaphor of how the mind works. *But in reality there are no physical mirrors in the mind or brain!* Many brain neurons, however, do respond to novel, salient, and numinous psychological experiences by turning on activity-dependent gene expression and brain plasticity to construct and reconstruct new neural networks that encode images, memories, words, concepts, etc., which actually are the contents of consciousness that function as metaphorical mirrors or windows to the outside world (Rossi 2007).

A generation before Rizzolatti's research on how consciousness seems to mirror and internalize the outside world, I conceptualized how our dreams function as a "self-reflective apparatus" that mirrors our internal world (Rossi 1972/1985/2000). At that time I described this internal mirror neuron system as a "self-reflective apparatus" that could account for two basic categories of dreams I was learning to distinguish in my college student clients: (1) the more common "experiential dreams" in which the dreamer experienced the dream as a vivid here-and-now drama that was really happening, versus (2) the "observer dreams" wherein the dreamer observed herself in a dream drama. Alan Moffit's research team at the Sleep Laboratory in the Department of Psychology at Carleton University in Canada then developed a nine-point Dream Self-Reflectiveness Scale to quantify my phenomenological observations on experiential and observer dreams (Moffit 1994; Moffit et al. 1988, 1982). This scale was constructed as a developmental tool to study the evolution of consciousness in dreams (see table 1).

TABLE 1: DREAM SELF-REFLECTIVENESS CATEGORIES (ROSSI 1972/1985/2000)

- 1. Dreamer not in dream; objects unfamiliar; no people present.
- 2. Dreamer not in dream; people or familiar objects present.
- 3. Dreamer completely involved in dream drama; no self-perspective.
- 4. Dreamer present predominantly as an observer.
- 5. Dreamer talks over an idea or has communication with someone.
- 6. Dreamer undergoes a transformation of body, role, age, emotion, etc.
- 7. Dreamer has multiple levels of awareness; simultaneously participates in dream drama and observes it. Notices oddities while dreaming; experiences a dream within a dream.
- 8. Dreamer has significant control in, or control over, dream story; can wake up deliberately.
- 9. Dreamer can consciously reflect on the fact that he/she is dreaming; lucid dreaming.

A corresponding *Daytime Self-Reflectiveness Scale* (see table 2) was constructed as well by Moffit's student, Susan Purcell (1987; Purcell et al. 1984, 1985, 1986, 1993).

TABLE 2: DAYTIME SELF-REFLECTIVENESS CATEGORIES (ROSSI 1972/1985/2000)

- 1. While performing the task, attention is focused on a scene with no people in it (e.g., "watching the screen and the bullets wiping out the ships").
- While performing the task, attention is focused primarily on a scene with people and/or things that are familiar but without awareness of self (e.g., "these two people are in love, and they want to be together, but people are interfering in their relationship").
- The person is completely involved with tasks or ambitions that command all attention (e.g., "I was watching the show; I was really involved in it").
- 4. The person is involved in the task and also watches passively (e.g., "I was watching this soap opera, and this girl is in a hospital bed, and her coach and another lady come in to visit her").

- 5. While performing the task, the person thinks over an idea and/or thinks over an interaction that involves someone else, involving words and/or definite communication (e.g., "I was thinking about my sister yelling at me in the morning for borrowing her sweater").
- 6. The person tries to take on the role of another person or undergoes a personal transformation, for example as a different age, a different character(s), as a change of state (from sick to healthy, from human to animal) (e.g., "I thought how pleased I was when I got the score; then I thought I must be nervous because my mouth was dry").
- 7. The person has multiple perspectives on self, participating and watching at the same time. Noticing something unusual, odd, or bizarre, imagining the loss of consciousness or dying while still watching the scene (e.g., "I was sitting here thinking about falling asleep and what a great room this would be to have as a bedroom").
- 8. Something in the experience is not right, so the person tries to change it: deliberately stopping thinking about something; removing oneself from an unpleasant experience; deliberately falling asleep in response to an unpleasant experience (e.g., "I started to think about the time my boyfriend got all dressed up and took me to a really nice restaurant for our first anniversary; it was really romantic and then thoughts of the fight we had yesterday kept coming into my mind, so I decided not to let them stay and moved my thoughts back to the fond memory").
- 9. While involved in the task, the person realizes it is only a dream or an experiment, is transitory, not real in any absolute sense, and may proceed to direct the experience/task (e.g., "I was getting really frustrated with the video game, and suddenly I realized that this was only an experiment and that it doesn't really matter how well I do").

The exciting proposal of this chapter is that these psychological scales of our internal mirror neuron system of self-reflection can now be used by a new generation of students and researchers for assessment of the development of consciousness and creativity in dreams, everyday life, and psychotherapy at the deep psychobiological levels of gene expression and brain plasticity. How to actually do such research into the foundations of mind-gene psychotherapy requires a new vision of how it can be conducted with the million dollar *in silico* databases that are available free on the Internet.

2. A New *In Silico* Model of Research in Consciousness, Creativity, Imagination, Psychotherapy, and Medicine: The New Computer Alchemy Without Chemicals and Test Tubes

In the best of all possible worlds it seems obvious that each of the therapeutic arts and sciences would have an equal share of funding and governmental and academic support. In our real world, however, it is ever more obvious that this is not the case now and probably will never be. Our medical-biological-pharmaceutical industrial complex is able to command billions of dollars annually for new technology and research. Neuroscience, by contrast, manages to get by on hundreds of millions a year. Psychotherapy is scarcely a blip on this radar with only a few million in a good year. In this chapter I propose a new method of *in silico* conceptual research in psychotherapy and medicine that takes an initial step toward equalizing this uneven distribution of research funding and resources by utilizing the million dollar databases of biology that are available free to all on the Internet.

In silico is a popular expression in the biological, computer, and bioinformatic sciences to describe simulations of life processes on all levels, from mind and behavior to genomics. These simulations of complex life processes are performed via information processing models on silicon chips in computers as a more economical approach to experimentation. In silico research is the key to data mining: the exploration, assessment, and integration of the meaning and implications of the research literature in many biological and psychological disciplines that cannot be integrated in any other way. Such interdisciplinary in silico research is possible because our current genomic revolution has made the concept of information the common denominator of all the databases in the life sciences.

The Allen Brain Atlas (ABA) is one such database recently assembled at the cost of \$100 million, which is now being made available free to anyone with access to the Internet via a personal computer. The ABA will make it possible to integrate medicine, neuroscience, and bioinformatics to shed light on how activity-dependent gene expression is associated with brain development, dysfunctions and therapies of mental illness, psychosocial stress, memory, learning, behavior, cognition, and consciousness itself (Rossi 2007).

Let us now explore how the ABA of gene expression can be uti-

lized to facilitate the theory, research, and practice of psychotherapy and medicine in the near future by students and faculty of graduate schools of psychology (such as Pacifica Graduate Institute) who do not yet have multimillion dollar laboratories of molecular-genomics and neuroscience on campus. *In silico research is the great equalizer in all interdisciplinary research exploring mind-gene communication in psychotherapy and complementary medicine*.

The New Allen Brain Atlas of Gene Expression

The ABA (http://www.brain-map.org) is available free as a webbased database showing the location and activity level of approximately 23,000 genes in the mouse brain, which shares about 90% homology (similarity) with the human brain. Plans are now underway for making a complete human brain atlas of gene expression. This anatomical reference for understanding the role of gene expression for approximately 50 million Americans suffering from brain dysfunctions such as Alzheimer's, epilepsy, and Parkinson's as well as addiction, depression, and stress is already being described as the foundation for a new neuroscience of mind and behavior. In the ABA the data of 250,000 microscope slides, a million brain sections, and 85 million anatomical photo files are assembled for viewing gene expression in three-dimensional cross sections of the brain.

An initial surprising finding revealed by the ABA is that approximately 80% of genes are expressed in brain cells. The high-resolution digital microscopy images of the ABA show the exact location of the genes in brain tissues and cells that are expressed (turned on) to produce the proteins for carrying out all biological functions of mind and behavior in health and dysfunction.

At the present time research and publications involving the ABA (http://www.brainatlas.org/aba/) are still dominated by biology and medical applications. Of particular interest for psychotherapy, however, is the ABA potential for exploring genes expressed during brain plasticity (synaptogenesis and neurogenesis) in response to normal memory, learning, and behavior, stress-induced dysfunctions, as well as any form of cognitive-behavioral therapy whose effects can be located in the brain by fMRI (Liu et al. 2007; Wang et al. 2006).

Researchers in psychology have been slow in recognizing the implications of activity-dependent gene expression and brain plasticity for the practical applications of psychotherapy because, until now, there has been no obvious and simple way of assessing these deep biological genomic sources of cognition, emotion, and behavior. Gene expression is usually measured by complex and very expensive laboratory procedures, such as DNA microarrays that involve taking invasive tissue samples from the brain, blood, saliva, and body (Rossi 2004, 2007; Rossi et al. 2006). Such invasive procedures have never appeared to be appropriate for assessing psychotherapy in any form. This stumbling block motivates us to outline how the ABA in association with other currently available technologies can enable us to bypass these invasive biological methods with new *in silico* models of exploring the mind-gene connection in all forms of psychotherapy.

Figure 2 outlines how the bioinformatic technologies of the ABA, functional magnetic resonance imaging (fMRI) (Siegel et al. 2006), and the Connectivity Map (Lamb et al. 2006) can be integrated into a new *in silico* model of the theory, research, and practice of psychotherapy by students, researchers, and psychotherapists with nothing more than a personal computer and an Internet connection. This type of *in silico* data mining of existing scientific literature, which I am now proposing for a new conceptual approach to research in psychotherapy, was originally described in a more limited biological context by Blagosklonny and Pardee (2002) as follows:

Millions of easily retrievable facts are being accumulated in databases, from a variety of sources in seemingly unrelated fields, and from thousands of journals. New knowledge can be generated by "reviewing" these accumulated results in a concept-driven manner, linking them into testable chains and networks . . . Connecting separate facts into new concepts is analogous to combining the 26 letters of the alphabet into languages. One can generate enormous diversity without inventing new letters. These concepts (words), in turn, constitute pieces of more complex concepts (sentences, paragraphs, chapters, books). We call this process "conceptual" research, to distinguish it from automated data-mining and from conventional theoretical biology... Can a review provide new knowledge? A review can constitute a comprehensive summary of the data in the field-this type of writing educates but does not directly generate new knowledge. But a "conceptual" review, on the other hand, can generate knowledge by revealing "cryptic" data and testing hypotheses by published experiments ... Conceptual biology [and psychotherapy] should be recognized and criteria established for its publications - new,

testable conclusions, supported by published data. In *[psycho]*biological systems, everything is interconnected, and ostensibly unrelated fields are related —the separation of biology into different disciplines is artificial. Conceptual research *[in psychotherapy]* can encompass many fields without limitation. *In comparison with labour-based research, conceptual research is more cost-effective; indeed, verification of a hypothesis using existing data does not limit research to scientists in well-resourced fields or countries.* Hypothesis-driven, experimental research will continue to be a cornerstone of biology, but it should strike up a partnership with the essential components of theoretical and conceptual research [in psychotherapy]." (373, emphasis added)

As can be seen in figure 2, *in silico* conceptual research proceeds in four steps when applied to psychotherapy to discover new associations that may never have been considered by the original laboratory researchers, who first published their data in an apparently unrelated field of pure biology, bioinformatics, genomics, neuroscience, etc.

I illustrate an *in silico* approach to explore how scientific data on the molecular-genomics of psychotherapy can proceed with nothing more than a home computer and an Internet connection in figure 2. Figure 2 illustrates the circular biofeedback flow of information between mind and gene, which is the neuroscientific basis of the transformations of consciousness, creativity, imagination, and healing in psychotherapy and medicine. A full appreciation of the implications of this *in silico* approach for current and future development of the theory, research, and practice of mind-gene psychotherapy proceeds from a comparison of figures 1 and 2.

Figure 1 is a *theoretical neuroscience model* of how the novel and numinous experiences of observing consciousness updates and reconstructs the brain on a daily and hourly basis via mirror neurons.

Figure 2 is a practical *in silico model* of how everyone who knows how to access the Internet with an ordinary home computer can actually do mind-gene research in psychotherapy with existing free databases.

Theoretically one could win a Nobel Prize for doing original research with a home computer utilizing the best peer-reviewed mindgene research published in our most highly cited peer-reviewed scientific journals. But can all this really be true? Can we really explore all the pathways between mind and gene for free with existing mil-

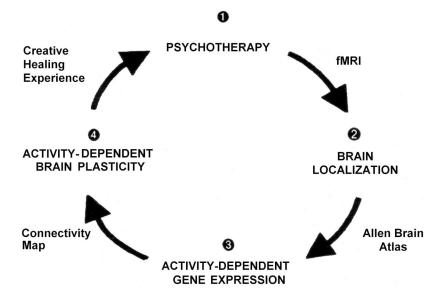


Figure 2: An in silico model for mind-brain-gene psychotherapy. This in silico model traces the circular and recursive path of information transduction between mind, activity-dependent gene expression, and brain plasticity during psychotherapy. (1) The novel, numinous, and salient experiences of consciousness in psychotherapy evokes activity in brain neurons that can be (2) localized in the brain with functional Magnetic Resonance Imaging (fMRI). (3) The Allen Brain Atlas then can be accessed free on the Internet to determine what profiles of activity-dependent gene expression were evoked on these brain locations by psychotherapy. (4) The Connectivity Map is another free database on the Internet that can be accessed to determine what molecular-genomic transformations within brain cells were evoked by the activity-dependent gene expression originally evoked by psychotherapy. (4) Some of these molecular-genomic transformations in brain neurons will lead to the generation of new proteins that will evoke activity-dependent brain plasticity (synaptogenesis and neurogenesis) to create new neural networks, which will stimulate and encode new and numinous transformations of consciousness, which will in turn evoke yet another recursive exponential spiral of continuing cycles of the co-creation of brain and consciousness (Rossi 1972/2000, 2002, 2004, 2007).

lion dollar databases? Well, I've actually been exploring this *in silico* path for the past half a dozen years or so, and it has lead to many publications (Rossi 2002, 2004, 2007; Rossi et al. 2006). But it has been tough going.

The main problem is that all the free databases that make up the *in silico* model in figure 2 were developed by biologists and neuroscientists for their own specialized world of research concerns. These biological researchers are intensely concerned with solving basic problems in medicine—cancer, organic brain diseases, immunological dysfunctions, etc. All certainly praiseworthy preoccupations. These databases are concerned with stress and its associated dysfunctions on the brain and body at the molecular-genomic level, but they are not concerned with psychotherapy. Enter terms like "psychotherapy, cognitive, creative, imaginative, and behavior" in their search boxes and they usually respond with a standard phrase indicating that they do not index these terms in their literature searches and database. In short, most of these million dollar databases of biology and medicine are still blind to psychology, psychotherapy, and the humanities.

What is now desperately needed are new psychological front ends to these *in silico biological databases*. That is, we must add to their capacity to search for the molecular-genomic foundations of our world of psychology and psychotherapy by responding appropriately to search terms such as "addiction, behavior, cognition, creativity, dance, depression, drama, genius, imagination, joy, happiness, meditation, metaphor, mythology, prayer, ritual, storytelling, spiritual, stress," etc. Certainly there is enough fundamental and applied research here for dozens of Ph.D. dissertations for expanding coverage of the biological and medical databases to include all the life sciences and humanities. We would certainly expect that our National Institutes of Health would fund such research by qualified students in the arts as well as in the sciences.

All four technologies tracing the circular, recursive flow of information transduction between mind and gene in figure 2 (i.e., fMRI, the Allen Brain Atlas, Connectivity Map) are well defined in the existing scientific literature except the first: psychotherapy. With over 500 psychotherapies cited in the current literature, it is difficult to specify which psychotherapeutic techniques we should try to localize in the brain with fMRI in figure 2. Since we are specifically looking to document psychotherapy as a flow of information transduction between mind and gene, however, the choice of psychotherapeutic techniques can be narrowed to those originally designed for this purpose. Many brief cognitive-behavioral therapies, such as the novel approaches to activity-dependent creative work, which I outline in chapter 10 of my book The Psychobiology of Gene Expression (Rossi 2002), for example, can be explored easily. These structured, permissive, and easyto-learn psychotherapeutic techniques that now need to be documented scientifically are described as Creative Healing Experiences (CHE) in the next section.

3. THE MIND-BRAIN-GENE DIALOGUES: CREATIVE REPLAY AS THE ESSENCE OF PSYCHOTHERAPY: *THE CREATIVE HEALING EXPERIENCE* (CHE)

In this section I outline a new neuroscience approach to learning and documenting what I call the *Creative Healing Experience (CHE)* (Rossi 2002, 2004a, 2007). It turns out that any novel, salient, or surprising *activity* in our social and cultural milieu impacts us by turning on what biologists call activity-dependent gene expression. Stressful *activities* and relationships, for example, can modulate activity-dependent gene expression in a manner that makes the proteins that can suppress our immune system leading to illness. This, of course, is what psychoneuroimmunology is all about. Likewise, I hypothesize, novel, numinous, positive, salient, and interesting *activities* like art, drama, meditation, music, storytelling, spiritual rituals, and psychotherapy can turn on the genes that generate the proteins that facilitate what biologists call activity-dependent gene expression and brain plasticity—the growth and transformation of the synaptic connections making up the neural networks of our brain, mind, and consciousness.

I propose that this is the psychobiological essence of what is now called Positive Psychology and what we may presume is the scientific basis of healing in Marion Woodman's BodySoul Workshops outlined in figure 1. This means that if you believe that you are initiating novel, and important *activities*, interpretations, and behavioral interventions in your client's life, then *ipso facto* you are facilitating their activity-dependent gene expression and brain plasticity!

As with any truly new theory, however, the role of activity-dependent gene expression and brain plasticity in human experience and social affairs is still controversial. *No one has yet done a single study that clearly documents how psychotherapy modulates activity-dependent gene expression and brain plasticity.* The psychosocial genomic perspectives we apply to psychotherapy here, however, are derived directly from the implications of current research in neuroscience, genomics, and bioinformatics (the sciences of biological information). Of most direct relevance for psychotherapists is the new research on how the mind, brain, and gene are constantly engaged in dialogues on unconscious (implicit) and conscious (explicit) levels (see p. 29 update).

I propose that these dialogues are an emerging model for the deep psychobiological foundation of virtually all schools of psychotherapy (Rossi 2007), which can be explored with the new complementary computer alchemy of tracing the *in silico* flow of information transduction between mind, brain, and gene, as illustrated in figure 2. Interesting and promising hypotheses initially explored and assessed very economically *in silico* can then be validated with the multimillion dollar "wet-ware" biological laboratories of classical molecular medicine.

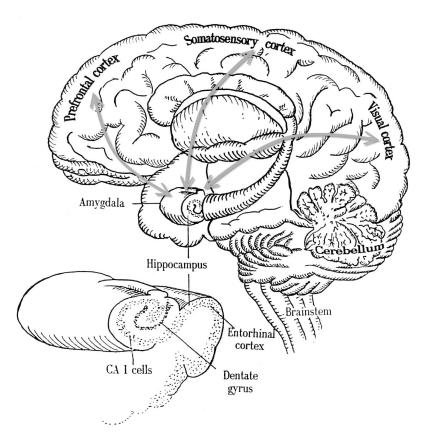


Figure 3: The mind-brain-gene dialogues: Creative replay between the hippocampus and the cortex is the essence of psychotherapy. The enlarged cutout of the hippocampus illustrates the dentate gyrus that is a temporary storage location of new memory, learning, and behavior, which is then transferred to various areas of the cortex during the offline creative dialogues replayed during slow-wave sleep and REM dreaming (Rossi 2002, 2004, 2007). I hypothesize that these natural off-line creative dialogues are facilitated by novel, enriching, and salient dialogues between psychotherapist and client during psychotherapy.

Figure 3 is a profile of the human brain with a cutout of the hippocampus, which is the part of the brain that first records a memory of anything novel, salient, or surprising. The hippocampus only makes a temporary recording of new memory, learning, or behavior, however. Later, during "off-line periods" of sleep, dreaming, and rest when the conscious mind is not actively engaged in dealing with outer realities, the hippocampus and the neocortex engage in a neural dialogue to update, replay, and consolidate the new memory in more permanent storage locations throughout the brain. *These mind-braingene dialogues activate and creatively replay the "local-global computations"* of the cortex (Buzsáki 2007), which are now believed to be the neural correlates of consciousness long sought by the late Francis Crick (Crick and Koch 2003).

Lisman and Morris (2001) describe how this off-line dialogue activates and replays novel and significant life experience between the cortex and hippocampus of the brain as follows:

> ... newly acquired sensory information is funneled through the cortex to the hippocampus. Surprisingly, only the hippocampus actually learns at this time —it is said to be on-line. *Later,* when the hippocampus is off-line (probably during sleep), it replays stored information, transmitting it to the cortex. The cortex is considered to be a slow learner, capable of lasting memory storage only as a result of this repeated replaying of information by the hippocampus. In some views, the hippocampus is only a temporary memory store—once memory traces become stabilized in the cortex, memories can be accessed even if the hippocampus is removed. *There is now direct evidence that some form of hippocampal replay* occurs... These results support the idea that the hippocampus is the fast on-line learner that "teaches" the slower cortex off-line. (247– 248, emphasis added)

I now hypothesize that this entirely natural psychobiological dialogue between our cortex and hippocampus is the essential process that we attempt to facilitate in our emerging mind-brain-gene model of creativity, imagination, and psychotherapy. From this neuroscience perspective, therapeutic suggestions, interpretations, metaphors, cognitive behavioral interventions, art, drama, music, spiritual rituals, etc. can be more aptly described as *implicit processing heuristics* (highly permissive and open-ended suggestions), which facilitate the natural updating dialogues between our hippocampus and the cortex every day. I propose that the conscious, explicit dialogues between therapist and client in psychotherapy are effective to the extent that they facilitate the appropriate, corresponding off-line, unconscious, and implicit dialogues between the cortex and hippocampus that daily update consciousness by turning on activity-dependent gene expression and brain plasticity. Implicit processing heuristics in the therapist/client dialogue are explicit hints and creative cues that we use to facilitate the off-line cortex/hippocampus dialogue that evokes activity-dependent gene expression and brain plasticity for adaptive behavior change.

Until recently the molecular-genomic and anatomical mechanisms of activity-dependent gene expression and brain plasticity during offline psychological states were not understood (Stickgold 2005; Walker 2006). One of the most interesting lines of research, however, has found that when mice experience novelty, environmental enrichment, and physical exercise, the *zif-268 gene* is expressed during their REM sleep (Ribeiro 2004; Ribeiro et al. 1999, 2002, 2004, 2008). *Zif-268* is an *immediate-early gene* and *behavioral-state related gene* that is associated with activity-dependent gene expression that facilitates brain plasticity. Ribeiro et al (2004) have summarized their research as follows:

> The discovery of experience-dependent brain reactivation during both slow-wave (SW) and rapid eye-movement (REM) sleep led to the notion that the consolidation of recently acquired *memory traces requires neural replay during sleep*... Based on our current and previous results, we propose that the two major periods of sleep play distinct and complementary roles in memory consolidation: pretranscriptional recall during SW sleep and transcriptional storage during REM sleep. .. In conclusion, sustained neuronal reverberation during SW sleep, immediately followed by plasticity-related gene expression during REM sleep, may be sufficient to explain the beneficial role of sleep on the consolidation of new memories." (126–135, emphasis added)

Such research documenting how *novelty, enriched environments, and exercise (mental and physical)* can initiate activity-dependent gene expression and brain plasticity is the basis of my hypothesis about *positive, creative, therapeutic replay and reconstruction during off-line periods* as the essence of mind-gene healing on a wide variety of levels, illustrated in the recursive circles of figure 4. I have noted how these three psychosocial experiences that evoke gene expression and brain plasticity are similar to the three qualities of original spiritual experience described by Rudolph Otto (1923/1950) as the *numinosum (fascina-*

tion, mysteriousness, tremendousness). I summarize the similarity of these three psychological and spiritual experiences associated with activitydependent gene expression and brain plasticity as the Novelty-Numinosum-Neurogenesis Effect (NNNE) in creative experiences and the placebo response on all levels from mind to molecule. I propose the NNNE as the creative common denominator between art and science in a new bioinformatic theory of esthetics. Experiences of art, beauty, and truth as well as Einstein's eternal mystery epistemology are the phenomenological correlates of the activation of mirror neurons, the gene expression/protein synthesis cycle, and brain plasticity via the novelty-numinosum-neurogenesis effect (Rossi 2002, 2004a, 2004b, 2007; Rossi et al. 2006, 2008a, 2008b).

From this new neuroscience perspective we can define consciousness itself as a novelty-seeking modality of psychological experience that turns on activity-dependent gene expression and brain plasticity to encode new transformations of consciousness and adaptive behavior. Experiencing the novel, numinous, and salient (the NNNE) turns on activity-dependent gene expression and activity-dependent brain plasticity, leading to an ever-expanding spiral of co-creation between the brain, mind, and consciousness that is the essence of Carl Jung's (1916/1960) ever-shifting creative connection (circumambulatio) between the conscious and the unconscious, which he called the transcendent function. This is the essential connection between the deeply humanistic world of Jungian scholarship, the classical studies of the evolution of consciousness in mythology (Campbell 1959, 1959/1968; Neumann 1962), and our current neuroscience of mind, memory, and learning via activity-dependent gene expression and brain plasticity (Kandel 1998, 2006).

More recently Richard Dawkins (1999) explores the possibility of an exponential evolutionary spiral of co-creation between mind, consciousness, and the brain, whereby "homo sapiens' brain size has approximately doubled every 1.5 million years" (286). He calls this the "self-feeding of co-evolution" (289). Dawkins speculates about the possible mechanisms of this co-evolutionary spiral between the "software" of the mind, language, and consciousness and the "hardware" of the biological neural networks of the brain but comes to no definite conclusion about them. I propose that Dawkins' co-evolutionary mechanism between the mind and the brain is none other than the recursive feedback spiral between the novel and numinous experiences of consciousness that are capable of turning on activity-dependent gene expression and brain *plasticity*, which then evokes another set of the transformations of consciousness and imagination, which in turn evoke yet another round of activity-dependent gene expression and brain plasticity, etc. (illustrated in the varying contexts of figures 1, 2, 3 and 4). To use a rather wild biblical metaphor, these figures all illustrate how "the word is made flesh" and vice versa. In mathematical language we seek to formulate a set of *recurrence equations* that express how transformations of consciousness (C) and adaptive behavior (B) are functions of activity-dependent gene expression (G.E.) and brain plasticity (B.P.) under the impact of the NNNE (http://mathworld.wolfram.com/top-ics/RecurrenceEquations.html).

What motivates our exploration of this co-evolutionary spiral between the software of the mind and consciousness, on the one hand, and the hardware of activity-dependent gene expression and activitydependent brain plasticity, on the other, in psychotherapy? If people have problems it usually means they are stuck somewhere in stage two of the creative process in one area or another of their lives. This is when most people tend to fall into a crisis and come to psychotherapy looking for help. The wise therapist, however, knows that the presenting problem is usually only a ripple on the surface of the deeper waters of self-care and creative life management. Ultimately every creative individual needs to learn how to break out of previously learned limitations on all levels from mind to gene expression and brain plasticity. Facilitating this creative process is called the "breakout heuristic" in my early growth-oriented model of psychotherapy with college students, illustrated in figure 4 of the next section (Rossi 2007).

The Breakout Heuristic: Darwin's Hourly and Daily Natural Selection of Adaptive Behavior

Recent research in evolutionary anthropology is clarifying what may have been the greatest breakout saga in human history. The story begins in Africa when a small group of hunter-gatherers, perhaps just a few hundred, left their homes to migrate over the entire globe between 50,000 to 70,000 years ago. While the anthropology tells the *outer* story of the human breakout of the physical territory of Africa, psychotherapy is focused on the *inner breakout heuristic* as we all experience it on a daily and hourly basis within the living territory of our mind-brain, as the deep psychobiological basis of adaptation and behavior (Rossi 2007). Charles Darwin, in a prescient statement on natural selection in chapter 4 of *The Origin of Species*, commented on the significance of this daily and hourly process of behavioral adaptation:

> It may be said that natural selection is daily and hourly scrutinising, throughout the world, every variation, even the slightest; rejecting that which is bad, preserving and adding up all that is good; silently and insensibly working, whenever and wherever opportunity offers, at the improvement of each organic being in relation to its organic and inorganic conditions of life. We see nothing of these slow changes in progress, until the hand of time has marked the long lapses of ages, and then so imperfect is our view into long past geological ages, that we only see that the forms of life are now different from what they formerly were" (http://www.literature.org/authors/darwin-charles/ the-origin-of-species/chapter-04.html).

We utilize current research on Darwin's natural selection of adaptive behavior to distinguish between the experience of humans and other primates at the levels of brain anatomy, neuronal activity, gene expression, and brain plasticity. This is summarized in figure 4 wherein the large outer circle presents a new context for understanding the creative process in art, science, and psychotherapy. The outer recursive cycle of figure 4 outlines the evolutionary dynamics of waking, sleep, and dreaming in the consolidation of new memory and learning as we break out of old hang-ups, perspectives, and problems (Rossi, Erickson-Klein, and Rossi 2007). The large outer circle illustrates how (1) novel and salient experiences while awake, ranging from trauma and stress to positive, creative breakthroughs, are (2) replayed in a natural dialogue between the neocortex and hippocampus in the slow-wave (SW) stages of sleep, which are followed by (3) rapid eye movement (REM) dream sleep wherein activity-dependent genes such as zif-268 are turned on to generate the proteins for (4) facilitating activity-dependent brain plasticity that transforms and encodes the future orientation of constructive memory, imagination, and behavioral adaptation.

Is it now possible to create a mind-gene biofeedback device?

A direct implication of figures 1, 2, 3, and 4 is that it may be possible to create a mind-gene biofeedback device, which I describe as follows (Rossi 2004a; Rossi et al. 2006):

Will it be possible to develop a mind-gene biofeedback device in

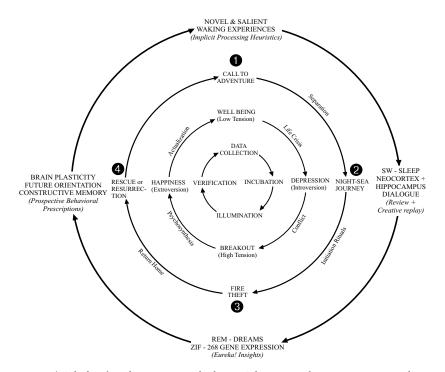


Figure 4: The breakout heuristic in psychotherapy. The outer circle is a neuroscience update of the four-stage creative process (innermost circle), the breakout heuristic during life crisis and psychotherapy (next circle), and the monomyth of the hero (next circle) originally published forty years ago as a metaphor and model of humanistic psychotherapy (Rossi 2007).

the future that would allow us to modulate gene expression and brain plasticity just as we now use inexpensive biofeedback devices to modulate muscle relaxation? This would be the ultimate kind of mind-body biofeedback that theoretically could facilitate to any type of psychophysiological healing at the molecular-genomic level. ... To make a mind-gene biofeedback device we need a *mind-gene transducer*. That is, we need to invent a transducer or "transformer" that converts a subjective psychological experience (thought or neural energy) into some kind of molecular signal that would turn on gene expression and brain plasticity. Recent research in nano-technology suggests how this may be possible (Rossi 2004a, pp. 304–305).

As illustrated in figure 4, we now need to assess whether we can indeed facilitate mind-gene information transduction with the breakout heuristic in psychotherapy with (1) *implicit processing heuristics* that (2) *activate* and facilitate the *natural dialogue between the neocortex and hippocampus* via the *review and creative replay* that typically takes place during sleep, dreaming, and the *novel and salient therapist/patient dialogues*, which (3) tend to *facilitate creative insights (eureka!)* that generate (4) *prospective behavioral prescriptions* that optimize brain plasticity, problem solving, and mind-body healing in psychotherapy. Let us now review the four-stage creative process in psychotherapy in greater detail before we introduce the simple and easy-to-learn approaches to Creative Healing Experiences (CHE) from mind to gene, which we now need to document with further research (Rossi 2002, 2004, 2007).

An Outline of the Four-Stage Creative Process in Psychotherapy

Stage One: Initiation—Symptom Scaling, Accessing Problems and Resources. A natural introduction to activity-dependent psychotherapy begins with the typical history-taking of the initial interview. More than mere words are involved. The typical tears and distress in an initial interview indicate that people are already accessing and replaying the important memories that signals they are embarking on a potentially healing adventure. The therapist's main job here is to recognize that therapy has already begun and simply facilitate it. Basic accessing questions (implicit processing heuristics) can optimize the client's inner work even before the therapist knows all the details about the problem. The therapist may begin by symptom scaling the patient's current emotional state. A 1 to 10 scale (10 being the worst, 5 average, and 0 a satisfactory state) can be used to assess and validate inner work before, during, and after every psychotherapeutic encounter.

Stage Two: Incubation—The Dark Night of the Soul. Review and Creative Replay. This is the valley of shadow and doubt or the storm before the light that is portrayed in the poetry and song of many cultures. When people become stuck in stage two they fall into conflict and become agitated or depressed. This is when they are most likely to seek psychotherapy. The emotional conflicts and symptoms that come up at this time are actually mind-body language about unresolved problems at implicit or unconscious levels that require review, creative replay, and reconstruction. The therapist's main job is to: (1) offer open-ended therapeutic questions (implicit processing heuristics) designed to access the state-dependent memory-encoding symptoms and (2) support the signs of arousal that are typical of creativity and problem solving. Less is often more at this stage of emotional catharsis, offering respectful listening rather than giving advice.

Stage Three: Illumination—the "Aha" Eureka Experience of the Breakout Heuristic. This stage is characteristic of the famous aha or eureka experience celebrated in ancient and modern literature when the creative process is described in the arts and sciences. Some people smile and seem surprised when they receive an unexpected and creative thought. Many patients habitually dismiss their own originality as worthless since it has never been supported in their early life. The therapist's main job at this stage is to help the person recognize and appreciate the value of the new that seems to emerge spontaneously and unheralded. Often the patient will have already thought of the possibilities and options that come up for problem solving at this stage but dismissed them rather than testing them in reality. Stage three is the essence of the creative process wherein I hypothesize that activitydependent gene expression and brain plasticity are becoming manifest as the so-called aha or eureka experience of insight.

Stage Four: Verification—Reality-Testing and Self-Prescribed Behavior Change. What changes does the client want to experience as a result of this therapy? The therapist's job here is to: (1) facilitate a followup discussion to validate the value of the psychotherapeutic process, (2) reframe symptoms into signals and psychological problems into inner resources, and (3) help the client formulate a behavioral prescription for new creative cognitions and behavior. The symptom scaling of the subject's subjective state of being before and after psychotherapy can be a validation of therapeutic progress, problem solving, and healing.

Figure 5 illustrates the *four-stage creative process with hand mirroring* and the types of implicit processing heuristics that therapists can utilize to facilitate the entire process (chapter 9 of Rossi 2002). While this therapeutic process is highly structured as presented here, everyone experiences it differently. An understanding of the psychotherapeutic process and its significance is always co-creative art that engages healing dialogues between the patient and therapist rather than being a standardized procedure. To evaluate the efficacy of their creative experience, clients can be asked to estimate the intensity of how much the problem (or symptom) is experienced before and after this creative process, on a scale of 0% to 100%.

A Creative Activity-Dependent Approach to the Breakout Heuristic in Psychotherapy Illustrating the Four-Stage Creative Process

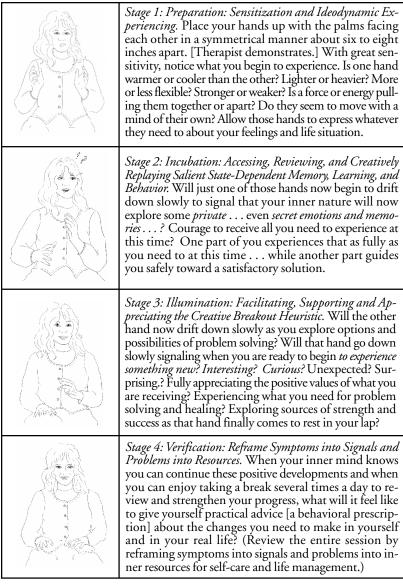


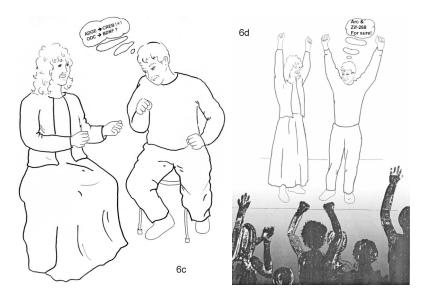
Figure 5: Implicit processing heuristics for facilitating the four-stage creative process with hand mirroring. This illustrates one of ten easy-to-learn novel and alternative approaches to creative psychotherapy (Rossi 2002, chapter 10).



Figure 6: An activity-dependent approach to the breakout heuristic in psychotherapy. This illustrates an emerging model of the mind-gene approach to psychodynamic psychotherapy (Rossi 2002, 2004, 2007).

Figure 6 illustrates a highly permissive, psychodynamic, and unstructured approach to psychotherapy originally derived from Ericksonian therapeutic hypnosis. This approach utilizes the client's own spontaneous ongoing behavior rather than the more highly structured approach illustrated in figure 5 (see Rossi 2002, chapter 10, for more novel, alternative approaches). It requires more extensive professional training to recognize and utilize the client's minimal mind-body language as symbolic cues and calls for the implicit processing heuristics that are now needed to facilitate the mind-brain dialogues of problem solving and healing.

The therapist's mirror neuron system needs to be empathetically alert to facilitate the constantly shifting borderline between the four stages of the creative experience (Rossi 2007). In everyday life people rarely progress through the four stages of the creative process in the idealized order illustrated in figures 4 and 5. Clients typically shift spontaneously between stages two and three with varying degrees of creative uncertainty, confusion, discomfort, and/or excitement. Sometimes psychosomatic symptoms are momentarily experienced more vividly. Such transitional states of the breakout heuristic can even be



experienced as mini-emotional crises. This is well-illustrated in chapters 7 and 8 of *The Psychobiology of Gene Expression* (Rossi 2002), which provides a verbatim transcript and psychodynamic analysis of a onehour videotape from which figure 6 is drawn. "A sensitive fail-safe approach to therapeutic hypnosis" (IC-92-D-V8) is available to students and professionals from the Milton H. Erickson Foundation (Office@erickson-foundation.org; www.erickson-foundation.org.)

Figure 6 is an artistic sketch of how a volunteer client with rheumatoid arthritis experienced the four-stage creative process of psychotherapy in front of a large professional audience of her peers. The thought balloons of the therapist are his conjectures of what the client may be experiencing on all levels, from the molecular-genomic to the cognitive-emotional-behavioral. Research is now required to assess these conjectures with the construction of standardized profiles of the four-stage creative process validated with fMRI, DNA microarrays, the Connectivity Map, etc. (Rossi 1972/2000, 2004a, 2007). Note that we are calling for measurements of the *ongoing creative process of psychotherapy*—not the measurement of *fixed traits* so typical of existing psychological scales and tests.

The Psychosocial and Cultural Genomics of Activity-Dependent Gene Expression and Brain Plasticity

The final image in figure 6 was drawn from a live *action* scene of an enthusiastic response by an audience of thousands of professionals who witnessed this videotaped demonstration at an Ericksonian congress of psychotherapy. Such a positive enthusiastic response requires some comment. Why do we have audiences to witness therapeutic process or, more generally, to participate in significant artistic and dramatic social events ranging from secular business and political meetings to the spiritual rituals of most cultures? It is generally believed that such audiences are there for education, to support a cause, etc. But what could actually be happening at a deep psychobiological level?

I offer figure 7 as a highly speculative interpretation that is consistent with the psychosocial genomic perspective we are presenting. Figure 7 is the result of recent bioinformatic research on fruit flies that illustrates how activity-dependent gene expression and brain plasticity within an individual fruit fly is related to the size of the social group it is participating in. *Nothing, it seems, turns on gene expression and brain plasticity as much as the presence of others of the same species*! Of course, this is documented here for fruit flies only. Genomic researchers consider this an example of *the deeply conserved and constitutive nature of molecular-genomic experience at this psychobiological level.*. This means that it is highly likely that it is a life process that is common to most species—including humans.

This generalization to the human level certainly has many interesting implications for understanding the psychosocial and cultural genomics of human behavior and society, ranging from the dynamics of personal relationships to families, group processes, the madness of crowds, politics, war, and peace. It can also provide us with fascinating insights into the seemingly uncanny efficacy of public demonstrations of brief psychotherapy that were a frequent source of amazement, discussed by the author with teaching therapists of the previous generation as widely diverse as Carl Rogers, Milton H. Erickson, and Fritz Pearls.

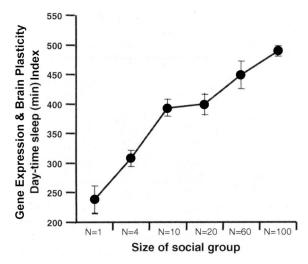


Figure 7: Preliminary evidence of an association between the size of a social group and gene expression and brain plasticity that needs to be confirmed for humans (modified from Ganguly-Fitzgerald et al. 2006).

SUMMARY: AN INVITATION TO OPEN SOURCE INTERNATIONAL RESEARCH

I have outlined a series of images from neuroscience and psychosocial genomics, which I propose as an emerging but still controversial deep psychobiological foundation for all the psychotherapies and medicine in general. Although this creative approach is consistent with a great deal of current research and generations of practical clinical experience, it has not been validated to meet the criteria of evidencebased medicine (EBT) and Cochran meta-analysis at this time. We therefore invite students, researchers, and clinicians to cooperate with us in evaluating these creative approaches in at least five areas that are now ripe for documentation via master's and doctoral dissertations (Rossi et al. 2006):

(1) Advance our understanding of the internal mirror neuron system and the development of consciousness via the Self-Reflectiveness Scales during dreaming and waking (Rossi 1972/1985/2000). From our new perspective, consciousness, creativity, imagination, and selfreflectiveness are the novelty-seeking *software of the mind* that facilitate a continuous, adaptive, positive, biofeedback spiral of co-evolutionary adaptation with the *hardware of the brain* via *activity-depen*- *dent gene expression and brain plasticity.* This is how the mind and the brain co-create each other via the *novel and numinous activities* of art, science, drama, and dreaming in everyday life as well as in psychotherapy.

(2) Construct new psychological processing scales for measuring *the Creative Healing Experiences (CHE)*, as illustrated with their many innovative and novel numinous variations (Rossi 2002, chapter 10). The Creative Healing Experiences are easily learned modules of psychotherapy that enable both client and therapist to continually assess the efficacy of their ongoing co-creative work in facilitating activity-dependent gene expression and brain plasticity for problem solving and healing.

(3) Evaluate the four-stage creative process of mind-body healing with the combined resources of CHE process and the *in silico technologies* of functional Magnetic Resonance Imaging (fMRI), the Allen Brain Atlas (ABA) of Gene Expression, and the Connectivity Map on the Internet. Utilize such research to update our understanding of medicine, psychotherapy, and rehabilitation as co-creative processes of daily adaptation whereby mind, brain, and gene are engaged in positive and constructive dialogues of self-creation at the levels of activitydependent gene expression, brain plasticity, and adaptive behavior.

(4) In language-discrete mathematics we seek to formulate a set of *recurrence equations* indicating how *in silico* data of the transformations of consciousness (C) and adaptive behavior (B) can be expressed as functions of activity-dependent gene expression (G.E.) and brain plasticity (B.P.) under the impact of the Novelty-Numinosum-Neurogenesis Effect (NNNE).

(5) The most profound implication of research on mind-braingene communication, as illustrated in the recursive cycles of figures 1, 2, 3, and 4 of this chapter, is that it may now be possible to create a mind-gene biofeedback device to more precisely facilitate problem solving and mind-body healing in psychotherapy, rehabilitation, and medicine. I hypothesize that not all genes can be accessed and turned on by such a mind-gene biofeedback device but, rather, only those *activity-dependent genes* that nature is already turning on and off during our normal everyday *activities* while awake, asleep, or dreaming. The range and possible clinical applications of a mind-gene biofeedback device are completely unknown at this time. This is a challenge to be explored in experimental and *in silico* research by a new generation of students.

So much to do, so little time to explore these profound avenues of research on how the mind and brain daily and hourly co-create each other. This research is all doable right now, however, as a new neuroscience approach to unfolding the classical mysteries of consciousness, creativity, imagination, individuation, and healing in psychotherapy and medicine in the future.

Psychosocial Genomics 2009 Update

Since the original presentation of this chapter a number of outstanding papers have been published on the psychosocial genomics of dreaming (Ribeiro et al. 2008), meditation (Dusek et al. 2008), and therapeutic hypnosis (Lichtenberg et al. 2000, 2004; Rossi et al. 2008a & b). These papers all document how psychological processes can turn on gene expression and, by implication, brain plasticity (synaptogenesis and neurogenesis).

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