Chapter 4
How Can We Reconstruct the Health Anticipation?

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Our thoughts are changing day by day, but belief systems are not so flexible and usually resist even positive changes. Various belief systems interact with each other and construct our webs of belief and, consequently, our forms of life. Our beliefs are vastly heterogeneous, from the delusional to the experimental, and the amazing fact is that an irrational or bizarre belief may overcome plenty of concordant rational beliefs even from our responses in a maladaptive manner. Various health beliefs such as "depression is a disease", "my illness is due to evil eye", "my spouse's behavior is the cause of my anxiety", "smoking is an unhealthy behavior", "energy enhancement of kidney meridian cooks ameliorate glomerohephritis", and "I can control my pain" could be categorized in sociocultural, individual, and healing belief systems. The examples mentioned demonstrate some of the different beliefs which are aroused from various healing systems (biomedicine, acupuncture), subcultures (transitional, modern) and personal belief systems. Each of these beliefs, separately and/or in interaction with other beliefs, can determine our locus of control, self-efficacy, coping strategies and expectations, ultimately changing our illness behavior and psychoneuroimmonologic responses.

Quine and Ullian (1978), in their influential book *Web of Beliefs*, defined believing as "a disposition to respond in certain ways when the appropriate issue arises" (p. 4). To believe in something this way means the tendency to interpret the relevant stimuli and the effect of the relevant objects in a particular manner. Thus, a belief is a symbolic sign in itself, which can conduct a special flow of psychophysical signs to/in/from our body. Let us draw on one of previously mentioned examples: When

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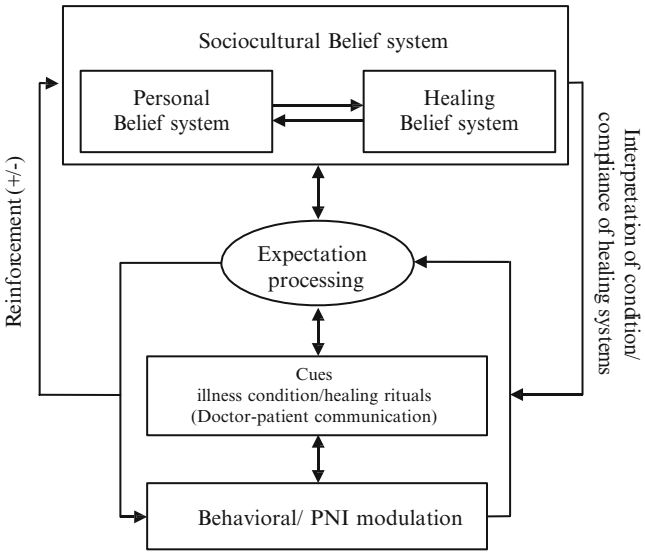

Fig. 4.1 Through the webs of belief

I believe in my pain control ability (sign), it can change my expectations and consequently, my somatic (neuroimmune modulation), psychological (calmness/anxiety, hopelessness/hopefulness), and social (seeking behavior/aggression) responses (interpretant). The flow of signs through intra/intercorporeal fields is determined via biopsychosocial interpretations in the cultural, social (healing systems), psychological and physical contexts. Cultural beliefs such as "pain is a divine examination" can change the patient's attitude towards an assertive and generative manner. Not only can this interpretation make a hopeful and positive meaning but it can also moderate our illness behavior, relationships, and even the interpretation of our T cells.

In Fig. 4.1, we have summarized the hypothesis of this chapter, and displayed the relationships between personal and healing belief systems in the frame of sociocultural beliefs and the role of expectations in healing response. Each person, due to his/her schemas, attachment, history and narrations, constructs a belief network which addresses causes, consequences, control, and anticipations around his/her life, and, finally, health and illness.

Healing systems have their own worldviews and interpretations of health and illness conditions. You can imagine that a psychoanalyst, a neurologist, an acupuncturist, and a physical therapist each have their specific narration of a particular health condition. They then induce their indirect suggestions to the client. The interaction between the personal and healing belief systems are configured in a sociocultural belief system, which can facilitate or disturb compliance and meaning responses of clients. These interactions shape expectations and are embodied in the

form of clinical rituals and tasks. The expectation-ritual interactions mediate the belief network as well as psychoneuroimunologic and behavioral responses.

The implicated and manifest meanings of procedures and remedies are formed in the personal and social context and actualized through performing clinical rituals. These psychosomatic dynamisms can be activated even when we intend to perform a particular prescription. It is not uncommon to hear reports such as: "Just when I decided to go to the doctor, I felt better" or "I got better right after I had visited the physician."

Through the expectation-rituals interactions, biosemiotic procedures not only can anticipate illness behavior, but also modulate vital systems. In this chapter we will develop this model and present documents which can explain how meaning formation in the context of belief network leads social and physiological behavior to a special way of healing.

4.1 Belief System and Expectation

Believing, whether defined as disposition of action in a certain manner, judgment of reality (Freud 1895, p. 333), or cognitive-emotional acceptance of an idea as being a truth (See Thagard 2007), could be considered as a pattern of bioenergy distribution and bodily attunement which is configured to a linguistic pattern. This pattern systemically forms certain sign processes and determines our cognitive, emotional, and behavioral responses. Belief is closer than knowledge, and have darer but more stable relation with action in comparison with emotion (See Frijda et al. 2000, p. 46). Therefore, dysfunctional beliefs can evidently distort our lifeworld and bring about complexities and facilitate health. The renunciation of belief is then an educational task and a psychological struggle, both liable to encounter great resistance. The idea has been proposed that many faith-based beliefs are actually delusional beliefs (Dawkins 2001; Harris 2004). Myths and irrational beliefs are also responsible for behaviors which could be harmful to one's health. Albert Ellis (2004), in his rational emotive behavior therapy theory (REBT), showed the role of irrational beliefs in illnesses, their formation, and aggravation.

Belief system is an organized way of trying to explain the world around us. It is something that distinguishes human beings and becomes an integral part of our culture. As belief systems grow in complexity beyond simple common-sense generalizations, these systems attempt to also explain and understand. There are two forms of belief systems: evidence-based and faith-based (Siegel 2004). Science is used to build an evidence-based belief system under the premise that the world is ultimately understandable through observation, experiment, and prediction. The key element of science is the recognition that human beings possess individual beliefs, and are consequently capable of introducing biases into their interpretation of the world. As a result, science attempts to militate against such biases by requiring strict definitions of terms and conditions, as well as demanding that any evidence be capable of independent verification by others. This ensures that accepted

results have been subjected to trials. These may not be free from bias, but by strict adherence to procedure, such biases will cancel each other out and produce conclusions that are largely objective.

Faith-based belief systems are mental constructs, which are not necessarily based on evidence. This is not meant to disparage them or to diminish their value, but rather to define an important difference. In short, a faith-based belief system does not have a foundation based on evidence. It is usually defined by the properties such as archetypal and subconscious conceptions, and/or evidence, which may be impossible to collect (ibid.).

Based on these descriptions, it would be easy to consider faith-based beliefs as somehow lesser in value, but this would be incorrect. We tend to draw these conclusions because we are all convinced that our particular beliefs are correct, regardless of what we individually believe. It is this fascination with being "correct" that leads to such discrepancies. Thus, we tend to defend our particular belief systems vigorously as being the only means by which one can experience "truth" or "reality". However, it is important to note that not all beliefs are subject to verification, and that this is precisely where these two forms of belief may often collide.

Therefore, beliefs coming from either evidence or faith can introduce our personal sense (or narration) of "reality" (Johari-Fard 2012). Both interpersonal and scientific beliefs were often seen as the outcomes of emotional responses to issues or persons (Frijda et al. 2000). As human beings, we tend to use all of these belief systems to varying degrees in order to cope with events in our lives. One of these events is to patent. When we get sick, our belief system about disease, doctors, healing, etc. can affect our behaviors and what we then plan to do. But there is a mediating variable between belief systems and behavior called "expectation" (Stewart-Williams and Podd 2004).

An expectation is a belief about the probabilities associated with a future state of affairs (Olson et al. 1996). The expectancy approach holds that the placebo effect is driven by anticipation that a treatment will result in a particular outcome (Bootzin 1985; Kirsch 1999; Stewart-Williams and Podd 2004). Expectation is what is considered to be the most likely outcome. An expectation, which is a belief that is centered on the future, may or may not be realistic.

Thus, simply put, expecting the suggested reaction is said to lead to the generation of that reaction. The expectancy framework that has received the most attention in the placebo literature is that of response expectancy theory (Kirsch 1997, 1999). According to this framework, response expectancy is one's anticipated automatic reaction to situational and behavioral cues. Response expectancies are believed to be directly self-confirming (Kirsch 1997). Figure 4.2 displays the circular relationships between the belief system, expectation, and experience.

Glover (2011) suggested that beliefs have to be considered holistically and that no belief exists in isolation in the mind of the believer. They always implicate and relate to other beliefs. Glover provided the example of a patient with an illness who returned to the doctor and the doctor said that the prescribed medicine was not working. At that point, the patient had a great deal of flexibility in choosing what

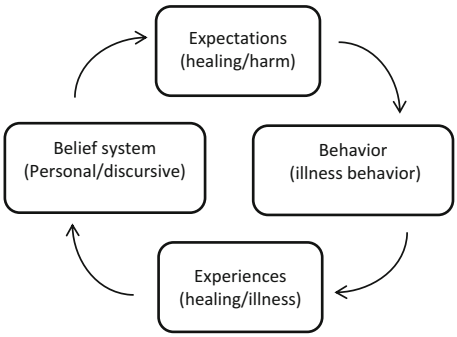

Fig. 4.2 Cycle of belief, expectation, behavior, and experience (adapted from Kirsch 1997)

beliefs to keep or reject – the patient could believe that the doctor is incompetent, that the doctor's assistants made a mistake, that the patient's own body is unique in some unexpected way, that western medicine is ineffective, or even that western science is entirely unable to discover truths about ailments.

Thus, the associative network around a simple fact-based belief (the treatment does not work) can switch the patient's mind to the other fact or faith-based beliefs which determine his/her illness experience and behavior. These biopsychosocial responses are formed in a complex network of webs of beliefs on the personal, healing system, and sociocultural levels. The role of the webs of belief in the sign processing of symptom formation, and especially healing response, is being discussed in this chapter.

4.2 Personal Belief System

A personal belief system is built upon our life experiences. Every word that has been spoken to us, every personal success or failure, our family, education, friends, work, dating experiences and even physical trauma and illness will lead us to build our personal belief system, for good or bad. These are the things that make up who we are, and how we feel and act. In this part, we discuss more about the interactions of these factors in personal belief system formation.

John Bowlby (1969), an English psychiatrist who pioneered attachment theory, argued that the primary motivation of the infant was to attach itself to a stable caretaker. From the perspective of developmental neuropsychology, the goal of attachment is to promote maturation of the brain regions responsible for configuring a progressive hierarchy of behavioral organization (Main 1995). This is achieved by progressively bringing lower levels of primitive reactivity, such as the spinal reflexes, under the influence of higher cortical brain areas via top-down regulation (Toates 1998). This organization of the early self is integrally linked to and motivated by the brain's affect centers. Psychologists' term of developmental stages are,

in reality, new categories of dynamic skills that emerge with the progressive maturation of the nervous system.

There is general agreement that secure attachment protects against psychopathology (Fonagy 2001). In fact, as Michael Ainsworth, an expert on attachment noted, secure attachment may be "the primary defense against trauma-induced psychopathology" (Kumin 1996). As previously noted, secure attachment develops through reciprocal mutually attuned preverbal interactions between mother and infant. When separated from the mother, the child engages in exploratory behavior and eventually shows signs of missing her, subsequently returns to reestablish physical contact with her. Under good enough circumstances, the child develops the ability to self-soothe and a cohesive sense of self (Kradin 2011). From the developmental neuropsychological standpoints, the function of attachment is the progressive organization of brain and behavior. In other words, the pattern of attachment coordinates cortical and subcortical activities such as neuroimmune responses (See Toates 1998; Main 1995). On the other hand, a secure attachment facilitates optimal doctor- patient communication (Balint 1972) and, subsequently, response to treatment (Siegel 2003).

Beliefs refer to assumptions about reality that form how one interprets events, and can thus be considered as determinants of appraisal. For example, pain beliefs develop during the lifetime as a result of an individual's learning history and cover all aspects of the pain experience (e.g., the causes of pain, its prognosis and suitable treatments). Appraisal and beliefs about pain can have a strong impact on an individual's affective and behavioral response to pain. If a pain signal is interpreted as harmful (threat appraisal) and is believed to be associated with actual or potential tissue damage, it may be perceived more intensely and may evoke more escape or avoidance behavior. For instance, pain associated with cancer is rated as more unpleasant than labor pain, even though the intensity is rated equally (Price et al. 1987). Similarly, Smith et al. (1998) demonstrated that cancer patients, who attributed pain sensation after physiotherapy directly to cancer, reported more intense pain than patients who attributed this pain to other causes. Perception of danger of an experimental pain stimulus (cold-presser test) may also lead to avoidance of this stimulus (Cipher and Fernandez 1997). Arntz and Claassen (2004) experimentally manipulated the appraisal of a mildly painful stimulus (a very cold metal bar against the neck), by suggesting that it was either very hot or very cold. It was assumed that it would be stronger with tissue damage (hot) than cold. As expected, participants rated the stimulus as more painful in the condition where they were informed that it was hot. In addition, the effect appeared to be mediated by the belief that the stimulus would be harmful. These studies demonstrated the important role of people's interpretations regarding the meaning of pain.

Pain appraisal and pain beliefs are also prominent determinants of adjustment to chronic pain (Jensen et al. 1999; Turner et al. 2000; Turner and Aaron 2001). The following pain beliefs have been identified as particularly maladaptive in dealing with pain: pain is a signal of damage, activity should be avoided when one has pain, pain leads to disability, pain is uncontrollable, and pain is a permanent condition (Jensen et al. 1995; Turner et al. 2000). The belief that pain is a signal of damage

and the belief that activity should be avoided in order to recover fro m pain appear to be widespread (Balderson et al. 2004; Ihlebaek et al. 2003). Two months after seeking treatment, a large majority of back pain patients believed that a single wrong movement could have serious negative consequences. Moreover, this belief was associated with reduced activity levels and increased disability (Balderson et al. 2004; Thorn et al. 1999).

Health-related self-efficacy, as a cognitive factor, may be one of the mechanisms of the placebo effect. Perceived self- efficacy refers to a psychological construct concerning the belief that one's abilities organize and execute behaviors with experimental manipulation of self-efficacy impacting stress, autonomic nervous system activation and neuroendocrine changes (Bandura 1997; Buckalew and Ross 1981).

Treatment regimens that actively engage the patient to have some sense of control over their disease process may produce better outcomes than those that are less actively engaging to the patient. Studies with adequate control groups that can clearly differentiate positive expectancy from self-management are, however, lacking (Crow et al. 1999). High-success biofeedback that improves one's sense of control may improve clinical outcomes, independent of the accuracy of the biofeedback (Holroyd et al. 1984). Adherence to a drug regimen may relate to an expectancy of the drug working in this sense of control. Subjects more adherent to a placebo intervention do better than those less adherent to the placebo regimen even with gross major medical outcomes (Hoewitz et al. 1990; Simpson et al. 2006).

However, other than expectancy, subjects more adherent to a prescribed medical regimen may have different characteristics, such as personality or mood (Osterberg and Blaschke 2005; Flegal et al. 2007), which may correlate with compliance and other aspects of medical intervention or health-promoting behavior. A systematic review found that positive expectations towards the outcome were associated with indeed better results (Mondloch et al. 2001).

Personality traits have a tendency to influence selection and reinforcement in beliefs. Plenty of studies have investigated the correlation between personality and placebo response. Currently, the most popular such model emphasizes that the search for a placebo personality factor must be combined with the measurement of situational expectancy. Expectancy is widely considered the central mechanism of placebo phenomena (Price et al. 2008; Tracey 2010), with variability in expectations influencing the variability of the response (Vase et al. 2005; Flatten et al. 2006). The most promising personality traits interacting with the mechanism of expectancy are optimism or pessimism, defined as a generalized and relatively stable expectancy for positive or negative future outcomes (Solbergnes and Segerstorm 2006). A considerable amount of research indicated that optimism is related to the flexible use of adaptive mental and behavioral coping strategies when faced with stressful life situations (Solbergnes and Segerstorm 2006). More importantly, optimists tend to exhibit attentional bias for positive information (Isaacowitz 2005; Geers et al. 2003). Therefore, optimism (and even pessimism) might serve as a moderator of placebo that responds by influencing the strength and/or the direction of the relation between expectancy and specific placebo effects.

Another example of the situation-personality interaction has been demonstrated by the traits of extroversion, as well as agreeableness to a lesser extent (Kelley et al. 2009). Extroversion is closely aligned with the temperament of positive emotionality/affect, referring to people who are described as sociable, talkative, energetic and assertive. With agreeableness, this manifests itself in individual characteristics perceived as kind, sympathetic and cooperative (John and Srivastava 1999). Kelley et al. (2009) examined the relationships between personalities of patients with irritable bowel syndrome and response to placebo acupuncture in different therapeutic settings, such as warm emphatic interaction, neutral interaction or waitlist control. Several personality dimensions were significantly associated with a placebo response, but extroversion was the only independent predictor, holding true for the warm emphatic therapeutic setting. The authors suggested that extroverted and agreeable patients responded in a better way to the efforts of emphatic clinicians; thus, facilitating the warm therapeutic relationship further. At the psychological level, this caring interaction could have reduced anxiety and increased positive expectancies. Conversely, when placebo effects are a consequence of medication with a minimal or neutral patient-clinician interaction, these personality traits will not have such a relevant moderating role.

There have been inconsistent results from studies evaluating whether certain personality traits predispose some to experience improvements from placebo administration more than others. While some studies have been negative (Fercund et al. 1972; Buckalew et al. 1981), other studies suggest there may be contributions to the placebo response from factors such as social acquiescence (McNair and Barrett 1979), suggestibility, or hypnotizability and absorption– which is the degree to which one can focus on a single theme (Evans 1985; Challis and Stam 1999; Raz 2007). This lack of consensus on individual differences to placebo administration may be related to an interaction between personality factors and the specific experimental condition.

The individual response to placebos also differed based on optimism–pessimism scale in the 100 % deceptive, but not in the 50–50 % conditional expectancy of receiving an active drug (Geers et al. 2005). The effect of personality traits such as optimism on placebo response may be dependent on the specific treatment and context (Geers et al. 2007; Hyland et al. 2007). Uncertainty in diagnosis and prognosis produces expectancy effects on health outcomes (Thomas 1987), possibly through some mechanism related to stress or anxiety.

High levels of neuroticism, along with depression and anxiety, helped to predict analgesic responses in patients with discogenic back pain (Wasan et al. 2006). Individual differences may contribute to variations in placebo effects in other ways. The individual experience of actual pain contributes significantly to neurotransmitter activity during placebo analgesia (Zubieta et al. 2006). Personality may relate to placebo responses either through the neurotransmitter systems, which were thought to be related to these traits, or to interactions with these traits. The mechanisms of expectance nausea and vomiting associated with chemotherapy overlap with the placebo effect. Higher anticipatory nausea and vomiting were not related to measures of absorption and autonomic perception (Challis and Stam 1999).

4.3 Healing Belief System

Each healing culture has its belief system, jargon, metaphors, and rituals. Healers and those being healed of each system are living in common cultures all over the world. For example, homeopaths and their clients in Germany, China and Iran all implicitly or explicitly, more or less, believe in a monistic worldview; a bioenergetic explanation of health and illness, the effective role of vibrational medicines in moderation of energetic balance and of course, the law of "like cures like". Many medical-anthropologic studies show the cultural diversity of healing systems and how this symbolic aspect of medical practice can induce physiological, psychological and social effects (Kirmayer 2004; Kleinman 1978). Even in the biomedicine's "culture of no culture", behind its positivistic claims are many recognizable mythical, metaphorical and rituals elements (Lock and Nguyen 2010; Taylor 2003; Coulehan 2003).

At the moment, the majority of people, especially because of worldwide media, live in a cultural marginality, and the nationality borders cannot determine cultural identities (See, e.g., Horback and Rothery- Jackson 2007). We are virtual nomads who travel through the cultures and, in addition to that, live simultaneously in several cultures. Thus, healing systems are a set of global belief systems, which could be more or less compatible with the various personal and cultural belief systems.

A study for the Institute of Noetic Sciences by Paul Ray (1996) had similar findings regarding different health beliefs and behaviors among different subcultures of a society. Ray identified three subsets of American culture that are influencing the demand for health services:

1. Heartlanders preserve traditional or rural values, tend to resist change, are somewhat isolationist, and are most often among middle to lower-income populations.
2. Cultural moderns are found in the mainstream in all income categories.
3. Cultural creatives are most often found in upper income levels, and tend to be leaders of cultural change and see a desirable future.

Cultural creatives have nontraditional values that require a different paradigm of health; they are willing to try a variety of approaches to health care. These consumers believe in holistic health through a unified approach to the body, mind, and spirit. Although this group tends to be fairly healthy, some members have also been described as the worried. They are more prevention–oriented than the two other groups that make up the U.S. population.

Thus, even in a certain society, health care systems should distinguish different subcultures, their belief systems, and their preferences. To minimize the chaotic response to the therapeutic programs and optimize placebo responses, we should mention the compatibility of the healing belief system with the personal and sociocultural systems. The next chapter is focused on the healing belief systems and their biopsychosocial effects. Afterwards, we will discuss further the healing power of the forms of clinical settings, and healing rituals.

4.4 Sociocultural Context

A cultural system is the interaction of different elements of culture. Cultural system is quite different from social system, however, sometimes both are referred to as the socio-cultural system. We live our lives in both the social systems of relationships and institutions, and also in the cultural systems of beliefs and discourses. Wilber (2000) illustrates the human's nest in a window by four fields –I (intentional), IT (behavioral), WE (cultural), and ITS (social) (Fig. 4.3).

He explains how our lifeworlds are formed through these symbolic-intentional and physical-behavioral worlds. Therefore, the sociocultural context indicates a matrix of material, energic, symbolic, and intentional elements of the collective aspect of our life. Healing occurs in such a complex network.

Healing involves a basic logic of transformation from sickness to wellness that is enacted through cultural salient metaphorical actions. Kirmayer (2004) applied the notion of a hierarchy of metaphoric spaces, through which multiple levels of meaning are generated to the range of symbolic healing practices. Figure 4.4 depicts some of the many processes involved in symbolic healing. In the central column of the figure, these are arranged as a hierarchy of organizational levels: first within the central nervous system (CNS), then on to family and to the larger levels of community, the physical and social environment, and the spiritual world. Each of these levels has its own metaphorical logic and dynamics corresponding to specific neuropsychological, interpersonal, social, political, or ecological processes.

Gottman et al. (2002) emphasized that beyond the processes associated with levels of information processing within the CNS, it is useful to distinguish at least two further levels in biological organization: the social groupings of family and community. Families and other groups of people living together develop implicit rules of interaction that may give rise to problems that are not reducible to psychological

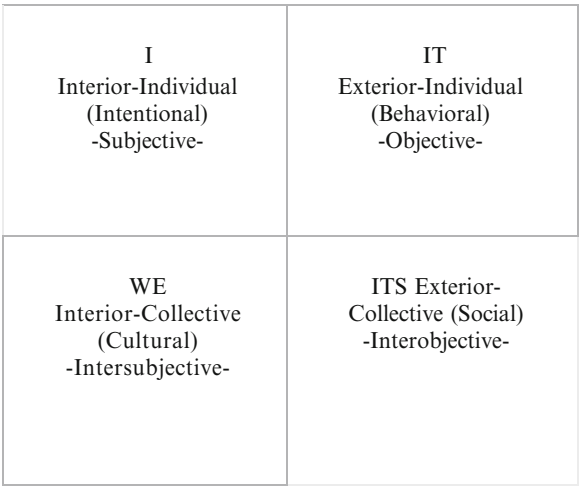

Fig. 4.3 Four quadrants (adapted from Ken Wilber 2000)

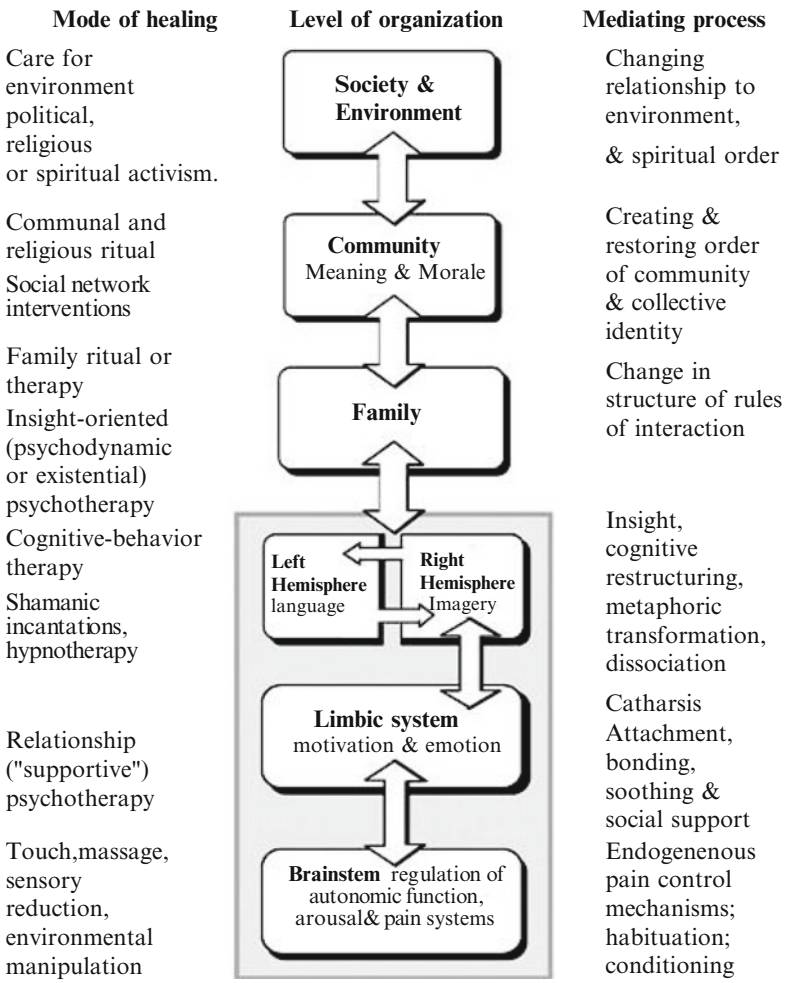

Fig. 4.4 A hierarchy of healing mechanisms (reprinted from Kirmayer 2004, by permission of Oxford University Press)

conflicts within one individual. Consequently, the unraveling of such interpersonal conflicts demands a change in family structure or the rules of interaction. Family rules are rarely articulated as such. Instead, family members conceive their group in terms of family myths and metaphors. Therefore, a change in metaphor prescribed by a therapist and subscribed to even one family member can change the pattern of interaction in widespread ways. The family unit is embedded in a community or larger social grouping with a collective history and way of life. At this sociocultural level of organization, people participate in the construction of institutions and shared symbolic meanings that confer an order, beauty and diversity that surpass individual experiences. Psychological healing at this level employs the extended

metaphors of secular and religious rituals to create and restore the order of the community and the relationship to the environment, the larger cosmos and with it, the sufferer's experience of meaning and morale (Turner 1974).

For example, cultural aspects common to Native Americans usually include being oriented in the present and valuing cooperation. Native Americans also place great value on family and spiritual beliefs. They believe that a state of health exists when a person lives in total harmony with nature. Illness is viewed not as an alteration in a person's physiological state, but as an imbalance between the ill person and natural or supernatural forces (McLaughlin and Braun 1998).

As mentioned before, all cultures have their especial health belief systems, which explain the causes of illness, the consequences, the meaning and how to control them. The consistency of a healing model or even technique in a sociocultural context has a crucial role in compliance and psychoneuroimmunologic response (See McLaughlin and Braun 1998; Roth 2003).

We should know the meaning of therapeutic concepts, tools, and procedures in the various cultural frameworks, otherwise, we cannot recognize their expectations and interpretations of their health and illness, therewith rapport, compliance, illness behavior, and even physiological responses will be affected.

Some cross-cultural studies unfold the psychocultural aspects of physiology. For example, Klein (2003) showed that in Germany 60 % of stomach ulcers were healed by placebos but practically none in Brazil. But it was nearly impossible to treat German hypertension by placebo, whereas Brazilians reacted quite well. It seems that the symbolic meaning of illness and treatment in each sociocultural context can change the pharmacokinetic responses.

4.5 Changing Expectation and Placebo Effect

A ritual is a set of actions performed mainly for their symbolic value. It may be prescribed by the traditions of a community, including a religious community. The term usually refers to actions which are stylized, excluding actions which are arbitrarily chosen by the performers. In psychology, the term ritual is sometimes used in a technical sense for a repetitive behavior systematically used by a person to neutralize or prevent anxiety; it is a symptom of obsessive– compulsive disorder. Among anthropologists, and other ethnographers, who have contributed to ritual theory are Victor Turner, Ronald Grimes, Mary Douglas and the biogenetic structuralists. Anthropologists from Émile Durkheim through Turner and contemporary theorists like Michael Silverstein treat rituals as social actions aimed at particular transformations, often conceived in cosmic terms. Although the transformations can also be thought of as personal (e.g. the fertility and healing rituals Turner describes), they become a sort of cosmic event– one stretching into "eternity" (McNeill 1995).

To reiterate, the term placebo effect will be used to refer to a physiological state anticipating and contributing to the occurrence of some future health-related outcome through learning, conditioning, or other related processes. Other terms used to

describe these effects include expectancy effects (Crow et al. 1999), context effects (Di Blasii et al. 2001) and meaning response (Brody and Brody 2000; Moerman 2002). Expectancy is what people predict will happen, rather than what they desire. Expectancies are primarily based upon social norms and specific characteristics of the communicators. Some placebo researchers have used the term expectancy narrowly to mean placebo effects due to anticipation that has been verbally or consciously mediated. Also, as mentioned in Chap. 1, meaning response evidently includes expectancy effects that impact health aside from the placebo effects such as cultural effects (Moerman 2002), uncertainty in diagnosis and prognosis (Thomas 1987), the impact of pessimism and hopelessness on disease and function (Anda et al. 1993; Maruta et al. 2002), and the nocebo or negative placebo effect (Hahn 1997; Barsky et al. 2002). Placebo effects also encompass neural systems not only simply related to anticipation or expectancy, but also to the desire to achieve a particular goal (Price et al. 2008).

A placebo can be in the form of any clinical intervention including words, gestures, pills, devices and surgery (see Chap. 1). The term "sham" or "trick" is sometimes used to describe a placebo intervention, such as in the context of surgery. Placebo effects do not include methodological factors resulting in improvement that are unrelated and active alterations of outcome measures, for example, natural history, regression to the mean (McDonald and Mazzuca 1983), the Hawthorne effect (Bouchet et al. 1996), or poor experimental designs such as subject biases (Clayden et al. 1974) or the purported inert control condition not being inert (Kienle and Kiene 1997; Ader 2000; Miller et al. 2004).

The natural history is particularly problematic, because it is impossible to infer anything about the frequency or size of placebo effects without a control for the placebo condition. Unfortunately, it is rare in modern clinical trials to have untreated control groups. A recent systematic review of placebo effects found only 114 clinical trials out of all clinical trials spanning several decades that had both a placebo treatment arm as well as a non-treatment arm in a clinical trial (Horbjartsson and Gotzsche 2001). Subject biases resulting from non-blinding, especially in a crossover design, may confound placebo research (Ader 2000).

Meaning effects presumably have different mediators depending on the specific learned association and affiliation to acquisitions or contexts of practice. The CNS is the primary location and mediator of the physiological basis of the placebo effects through its role in learning and memory, and its outputs on sensory, motor and autonomic pathways, as well as the immune and endocrine system. People have individual traits that predispose them to be more or less responsive to certain stimuli; the interaction between the learned associations of the clinical situation and the person's particular biology produces a response. The response could be a basic physiological process, such as modulation of sensory processing, release of neurotransmitters, alterations in the Hypothalamic-Pituitary-Adrenal (HPA) axis, or immune system activity. The placebo response could also be a more complex physiological process including change in mood, change in motivation/effort, or cognitive set-shifting.

Learned associations producing placebo effects can be acquired through conditioning (Vodouris et al. 1989; Price et al. 1999; Wickramasekera 2000; Siegel 2002).

The conditioned pharmacotherapeutic effects have been characterized in animal models (Ader and Cohen 1982; Jones et al. 2008). While the relative contribution of conditioning to placebo effects remains uncertain (Montgomery and Kirsch 1997; Benedetti 2003; Kirsch 2004; Stewart-Williams and Podd 2004), non-conscious mechanisms such as conditioning may be particularly important for immune or endocrine placebo effects (Kirsch 2004). Animal models are useful models of some components of placebo effects but are intrinsically limited placebo effect models because there are no verbally mediated expectancy changes.

Conditioning in placebo research studies has consisted of exposure(s) prior to administration of placebo of either the active drug itself (Laska and Sunshine 1973; Amanzio and Benedetti, 1999), or of an apparent effect of a placebo, for example, due to surreptitiously turning down the pain intensity at the same time as the placebo is administered (Vodouris et al. 1989). Since most adults have had previous exposures to clinical experiences such as taking oral analgesics, clear separation of conditioning from other aspects of the placebo response in human experiments is difficult.

Conditioning is only one aspect of the placebo effect which can form in sociocultural context. Many aspects of placebo effects, including verbal communication, encompass more top-down and cortically mediated change in behavior than the term conditioning usually implies. Some learned anticipations acquired over longer periods of time than are usually studied in the conditioning experiments may be related to: interaction between person and health care provider (Brody and Brody 2000), health care setting and practitioner characteristics (Di Blasii et al. 2001), physical characteristics of a pill (Buckalew and Coffield 1982), type of treatment (e.g., pill versus injection versus surgical) (Kaptchuck et al. 2000), and pill administration frequency (de Craen et al. 1999). Additionally, anticipation or expectancy can refer to a response expectancy or self-efficacy expectancy, which is one's sense of being able to achieve an outcome (Caspi and Bootzin 2002). Desire or motivation for improvement is another aspect of the placebo effect (Hyland et al. 2007; Price et al. 2008). All of these variables can form in the sociocultural context.

There is some data to suggest that placebo effects are greater for psychological and self-rated measures than other objective measures of disease activity (Horbjartsson and Gotzsche 2001). A study that evaluated patients in placebo arms of rheumatoid arthritis drug trials found essentially no change over 6 months on the erythrocyte sedimentation rate, but there was a significant improvement in articular index and morning stiffness (Porter and Capell 1993).

While placebo responses may be generally greater for self-ratings, there are many studies that demonstrate the changes in more objective outcome measures including C-reactive protein (Hashis et al. 1988), elevation of liver enzymes (Merz et al. 1997), changes in pulmonary function (Luparello et al. 1970; Butler and Steptoe 1986; Kemeny et al. 2007), postprandial glucose (Sievenpiper et al. 2007) and the neurobiology studies.

Even though there is no control over the placebo condition, the balanced placebo has shed light on expectancy effects. For example, in a balanced placebo design among cocaine abusers, administration of methylphenidate when the client expects

to receive methylphenidate produces significantly increased brain glucose metabolism compared to the administration of methylphenidate with the expectation of simply receiving placebo (Volkow et al. 2003). Expectation of receiving caffeine produced dopamine release in the thalamus, measured by raclopride positron emission tomography (PET) following administration of placebo (Kaasinen et al. 2004). Therefore, as we displayed in Fig. 4.1, expectation has an effect on the illness condition and healing rituals, and these expectations/rituals change the placebo effect.

4.6 Behavioral-PNI Modulation

The two-way communication between the brain and the immune system (Ader et al. 2001) contributes to aspects of the placebo response, both in its potential relationship to conditioning and in relationships mediated by stress and HPA axis activity (Ader 2000). A beneficial immunosuppressive effect was obtained with placebo through conditioning of administration of cyclophosphamide with saccharine in a murine systemic erythematous model (Ader and Cohen 1982). Even a commonly-used clinical immune marker, the tuberculin reaction, can be significantly diminished through conditioning (Smith and McDaniel 1983).

There are factors related to a clinical interaction that may produce improvement in patient outcomes without directly affecting the underlying pathophysiology of a disease. Methodological artifacts have contributed to confusion about these factors. However, there are clearly effects on outcomes that are dependent on patient expectations, whether these expectations are related to patients, culture, previous interactions with the clinical setting, verbal communication, conditioning, or some combination of factors. Figure 4.5 shows these behavioral-PNI modulation pathways.

In accordance with this model, these meaning effects are mediated through change in neocortical and subcortical systems. It is likely that some therapies and therapists have been successful in improving people's health because of their utilization of these beneficial effects and affective coordination of the healing narration within the psychosocial context. Sustaining these effects is important, and many current placebo effect studies actually serve to extinguish the beneficial placebo response through lack of reinforcement of the response (Oken 2008).

In conclusion, a certain therapy or clinical experience, as a set of signs, is interpreted by different sets of cognitive, emotional and behavioral responses through the various sociocultural contexts. On the other hand, each sociocultural context has its own especial normative attitudes, belief systems, and healing rituals. Health professionals have to be familiar with both the clients' reaction to the scientific management and their own ethnic healing methods. They should also have a non-judgmental attitude, systemic approach, and deep attention to the verbal bodily messages. Reframing, adjustment and reinforcement of both professional and traditional health beliefs should be based on our knowledge and awareness of the cultural belief system.

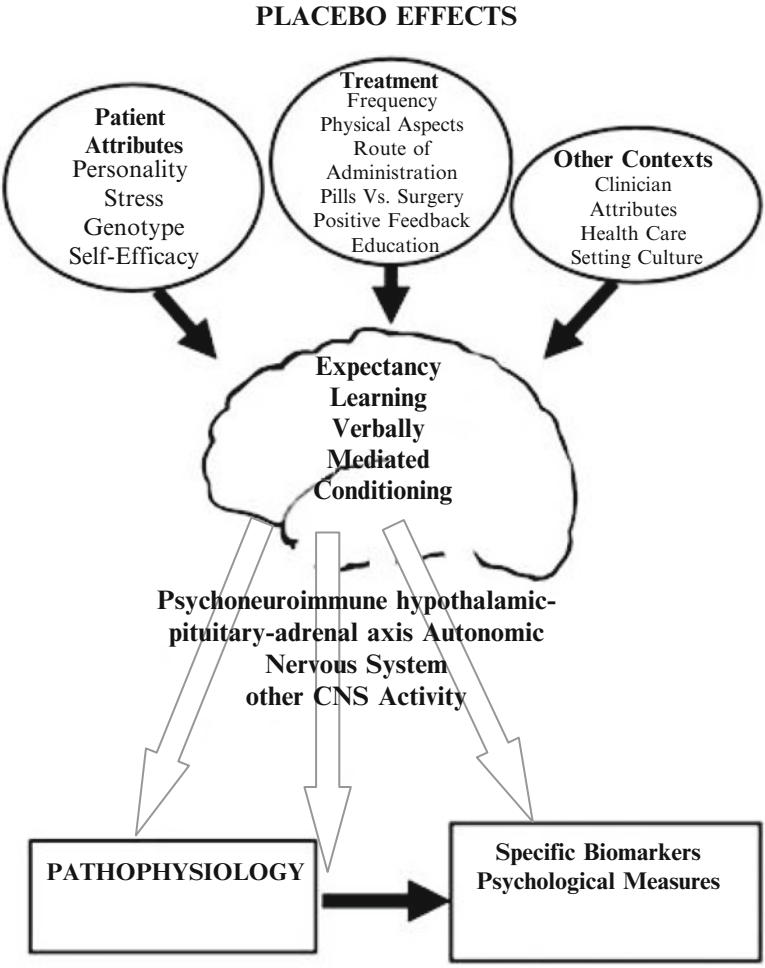

Fig. 4.5 Theoretical model of issues impacting development of expectancy and how brain outputs may produce a placebo effect (reprinted from Oken 2008, by permission of Oxford University Press)

References

Ader, R. (2000). The placebo effect: If it's all in your head, dose that mean you only think you feel better? *Advances In Mind-Body Medicine, 16*(1), 7–11.

Ader, R., & Cohen, N. (1982). Behaviorally conditioned immunosuppression and murine systemic lupus erythematosus. *Science, 512*, 1534–1536.

Ader, R., Felten, D. L., & Cohen, N. (Eds.). (2001). *Psychoneuroimmunology*. San Diego: Academic Press.

Amanzio, M., & Benedetti, F. (1999). Neuropharmacological dissection of placebo analgesia: Expectation-activated opioid systems versus conditioning–activated specific subsystems. *The Journal of Neuroscience, 19*(1), 484–494.

Anda, R., Williamson, D., Jones, D., Moacera, C., Eaker, E., & Glassman, A. (1993). Depressed affect, hopelessness, and the risk of ischemic heart disease in a cohort of U.S. adults. *Epidemiology, 4*(4), 258–294.

Arntz, A., & Claassens, L. (2004). The meaning of pain influences its experienced intensity. *Pain, 109*(1–2), 20–25.

Balderson, B. H. K., Lin, E. H. B., & von Korff, M. (2004). The management of pain-related fear in primary care. In G. J. Asmundson, J. W. S. Vlaeyen, & G. Crobez (Eds.), *Understanding and treating fear of pain* (pp. 267–292). England: Oxford University Press.

Balint, M. (1972). *The doctor, his patient and the illness*. New York: International University Press.

Bandura, A. (1997). *Self-efficacy; the exercise of control*. New York: W. H. Freeman and Company.

Barsky, A. J., Saintfort, R., Rogers, M. P., & Borus, J. F. (2002). Nonspecific medication side effects and the nocebo phenomenon. *JAMA, 287*(5), 622–627.

BenedettI, F., Pollo, A., Lopiano, L., Lanotte, M., Vighetti, S., & Rainero, I. (2003). Conscious expectation and unconscious conditioning in analgesic, motor, and hormonal placebo/nocebo responses. *Journal of Neuroscience, 23*, 4315–4323.

Bootzin, R. R. (1985). The role of expectancy in behavior change. In L. White, B. Tursky, & G. E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 196–210). New York: Guilford Press.

Bouchet, C., Guillemin, F., & Briancon, S. (1996). Nonspecific effects in longitudinal studies: Impact on quality of life measures. *Journal of Clinical Epidemiology, 49*, 15–20.

Bowlby, J. (1969). *Attachment and loss* (Vol. 1), Attachment. New York: Basic Books.

Brody, H., & Brody, D. (2000). Their perspectives on the placebo response: Expectancy, conditioning, and meaning. *Advances in Mind-Body Medicine, 16*, 216–232.

Buckalew, L., & Coffield, K. H. (1982). An investigation of drug expectancy as a function of capsule color and size and preparation from. *Journal of Clinical Psychopharmacology, 2*, 245–248.

Buckalew, L., & Ross, S. (1981). Relationship of perceptual characteristics to efficacy of placebo. *Psychological Reports, 49*, 955–961.

Buckalew, L., Ross, S., & Starr, J. B. (1981). Nonspecific factors in drug effects: Placebo personality. *Psychological Reports, 48*, 3–8.

Butler, C., & Steptoe, A. (1986). Placebo responses: An experimental study of psychophysiological processes in asthmatic volunteers. *British Journal of Clinical Psychology, 25*, 173–183.

Caspi, O., & Bootzin, R. R. (2002). Evaluating how placebo produce change: Logical and causal traps understanding cognitive explanatory mechanisms. *Evaluation & the Health Professions, 25*, 436–464.

Challis, G. B., & Stam, H. J. (1999). A longitudinal study of the development of anticipatory nausea and vomiting in cancer chemotherapy patients: The role of absorption and autonomic perception. *Health Psychology, 11*, 181–189.

Cipher, D. J., & Fernandez, E. (1997). Expectancy variables predicting the tolerance and avoidance of pain in chronic pain patients. *Behaviour Research and Therapy, 35*, 437–444.

Clayden, J. R., Bell, J. W., & Pollard, P. (1974). Menopausal flushing: Double-blind trial of a non-hormonal. *British Medical Journal, 1*, 409–412.

Coulehan, J. (2003). Metaphor and medicine: Narrative in clinical practice. *Yale Journal of Biology and Medicine, 76*, 87–95.

Crow, R., Gega, H., Hampson, S., Hart, J., Kimber, A., & Thomas, H. (1999). The role of expectancies in the placebo effect and their use in the delivery of health care: A systematic review. *Health Technology Assessment, 3*, 1–48.

Dawkins, R. (2001). Has the world changed? *The Guardian*,10–11.

de Craen, A. J., Moerman, D. E., Heisterkamp, S. H., Tytgat, G. N., Tijssen, J. G., & Kleijnen, J. (1999). Placebo effect in the treatment of duodenal ulcer. *Journal of Clinical Pharmacology, 48*, 853–860.

Di Blasii, Z., Harlness, E., Erns, E., Georgiou, A., & Kleijnen, J. (2001). Influence of context effects on health outcomes: A systematic review. *Lancet, 357*, 757–762.

Ellis, A. (2004). *Rational emotive behavior therapy: It works for Me: It can work for you by*. Amherst/New York: Prometheus Books.

Evans, F. J. (1985). Expectancy, therapeutic instructions, and the placebo response. In L. White, B. Tursky, & G. E. Schwartz (Eds.), *Placebo: Theory, research, and meachnisms* (pp. 215–228). New York: The Guilford press.

Fercund, J., Krupp, G. g., Goodenough, D., & Preston, L. W. (1972). The doctor-patient relationship and drug effect. *Clinical Pharmacology and Therapeutics, 13*, 172–180.

Flatten, M. A., Aslaksen, P. M., Finset, A., Simonsen, T., & Johansen, O. (2006). Cognitive and emotional factors in placebo analgesia. *Journal of Psychosomatic Research, 61*, 81–89.

Flegal, K. E., Kishiyama, S., Zajdel, D., Hass, M., & Oken, B. S. (2007). Adherence to yoga and exercise interventions in a 6-month clinical trial. *BMC Complementary and Alternative Medicine, 7*, 37.

Freud, S. (1895). Project for a scientific psychology (1950) [1895]. In J. Strachey (Ed.), *The standard edition of the complete psychological works of Sigmund Freud* (Vol. 1, pp. 283–398). London: Hogarth Press (Originally written 1895).

Frijda, N. H., Manstead, A. S. R., & Bem, S. (2000) *Emotions and beliefs: How feelings influence thoughts*. Cambridge: Cambridge University Press.

Geers, A. L., Handley, I. M., & McLarney, A. R. (2003). Discerning the role of optimism in persuasion: The valence- enhancement hypothesis. *Journal of Personality and Social Psychology, 85*, 544–565.

Geers, A. L., Helfer, S. G., Kosbab, K., Weiland, P. E., & Landry, S. J. (2005). Reconsidering the role of personality in placebo effects: Dispositional optimism, situational expectations, and the placebo response. *Journal of Psychosomatic Research, 58*, 121–127.

Geers, A. L., Kosbab, K., Helfer, S. G., Weiland, P. E., & Wellman, J. A. (2007). Further evidence for individual differences in placebo responding: An interactionist perspective. *Journal of Psychosomatic Research, 62*, 563–570.

Glover, J. (2011). Systems of belief. *Philosophy Bites Podcast*, October 9, 2011. [Online] Available from: http://philosophybites.com/2011/10/jonathan-glover-on-systems-of-belief.html. 12 Nov 2012.

Gottman, J. M., Murrary, J. D., Swanson, C. C., Tyson, R., & Swanson, K. R. (2002). *The mathematics of marriage: Dynamic nonlinear models*. Cambridge: MIT Press.

Hahn, R. A. (1997). The nocebo phenomenon: Concept, evidence, and implications for public health. *Preventive Medicine, 26*, 607–611.

Harris, S. (2004). *The end of faith: Religion, terror, and the future of reason*. New York: W.W. Norton and Company.

Hashis, I., Hai, H. K., Harvey, W., Feinmann, C., & Harris, M. (1988). Reduction of postoperative pain and swelling by ultrasound treatment: A placebo effect. *Pain, 33*, 303–311.

Hoewitz, R. I., Viscoli, C. M., Berkman, L., Donaldson, R. M., Horwitz, S. M., & Murray, C. J. (1990). Treatment adherence and risk of death after a myocardial infarction. *Lancet, 336*, 542–545.

Holroyd, K. A., Penzien, D. B., Hursey, K. G., Yobin, D. L., Rogers, L., & Holm, J. E. (1984). Change mechanisms in EMG biofeedback training: Cognitive change underlying improvements in tension headache. *Journal of Consulting and Clinical Psychology, 52*, 1039–1053.

Horback, S., & Rothery- Jackson, C. (2007). Cultural marginality: Exploration of self- esteem and cross cultural adaption of the marginalized individual: An investigation of the second generation Hare Krishnas. *Journal of Intercultural Communication, 14*. Retrieved from:http://immi.se/intercultural/nr14/horback.htm

Horbjartsson, A., & Gotzsche, P. C. (2001). Is the placebo poweress? An analysis of clinical trials comparing placebo with no treatment. *New England Journal of Medicine, 344*, 1594–1620.

Hyland, M. E., Whalley, B., & Geraghty, A. W. A. (2007). Dispositional predictor of placebo responding: A motivational interpretation of flower essence and gratitude therapy. *Psychosom Res, 62*, 331–340.

Ihlebaek, C., Love, T., Eilertsen, D. E., & Magnussen, S. (2003). Memory for a staged criminal event witnessed live and on video. *Memory, 11*, 319.

Isaacowitz, D. M. (2005). The gaze of the optimist. *Personality and Social Psychology Bulletin, 31*, 407–415.

Jensen, M. P., Turner, J. A., Romano, J. M., & Strom, S. E. (1995). The chronic pain coping inventory: Development and preliminary validation. *Pain, 60*, 203–216.

Jensen, M. P., Romano, J. M., Turner, J. A., Good, A. B., & Wald, L. H. (1999). Patient beliefs predict patient functioning: Further support for a cognitive-behavioral model of chronic pain. *Pain, 81*, 95–104.

Johari-Fard, R. (2012). *Introduction to psychosomatic medicine*. Aahvaz: IAU publication.

John, O. P., & Srivastava, S. (1999). The big five trait taxonomy: History, measurement, and theoretical perspectives. In L. A. Pervin & O. P. John (Eds.), *Handbook of personality: Theory and research* (2nd ed., pp. 102–138). Guilford.

Jones, R. E., Moes, N., Zwickey, H., Cunningham, C. L., Gregory, W. L., & Oken, B. (2008). Treatment of experimental encephalomyelitis with alpha lipoic acid and associative conditioning. *Behavior and Immunity, 22*, 538–543.

Kaasinen, V., Aalto, S., Nagren, K., & Rinne, J. O. (2004). Expectation of caffeine induces dopaminergic responses in humans. *European Journal of Neuroscience, 19*, 2352–2356.

Kaptchuck, T. J., Goldman, P., Stone, D. A., & Stason, W. B. (2000). Do medical devices have enhanced placebo effects? *Journal of Clinical Epidemiology, 53*, 786–792.

Kelley, J. M., Lembo, A. J., Ablon, J. S., Villanueva, J. J., Conboy, L. A., & Levy, R. (2009). Patient and practitioner influences on the placebo effect in irritable bowel syndrome. *Psychosomatic Medicine, 71*, 789–797.

Kemeny, M. E., Rosenwassre, L. J., Panettieri, R. A., Rose, R. M., Berg-smith, S. M., & Kline, J. N. (2007). Placebo in asthma: A robust and objective phenomenon. *Journal of Allergy and Clinical Immunology, 119*, 1375–1381.

Kienle, G. S., & Kiene, H. (1997). The powerful placebo effect: Fact or fiction? *Journal of Clinical Epidemiology, 50*, 1311–1318.

Kirmayer, L. J. (2004). The cultural diversity of healing: Meaning, metaphor and mechanism. *British Medical Bulletin, 69*(1), 33–48.

Kirsch, I. (1997). Specifying nonspecifics: Psychological mechanisms of placebo effects. In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 166–186). Cambridge, MA: Harvard University Press.

Kirsch, I. (1999). *How expectancies shape experience*. Washington, DC: American Psychological Association.

Kirsch, I. (2004). Conditioning, expectancy, and the placebo effect: Comment on Stewart-Williams and Podd. *Psychological Bulletin, 130*, 341–343.

Klein, S. (2003). Ohne rislken und nebenwirkugrn. *GEO, 10*, 48–64.

Kleinman, A. (1978). Concepts and a model for the comparison of medical systems as cultural systems. *Social science & medical anthropology, 12*, 85–93.

Kradin, R. (2011). The placebo response: An attachment strategy that counteracts the effects of stressrelated dysfunction. *Perspectives in Biology and Medicine, 54*(4), 438–454.

Kumin, I. (1996). *Preobject relatedness*. New York: Guilford Press.

Laska, E., & Sunshine, A. (1973). Anticipation of analgesia: A placebo effect. *Headache, 1*, 1–11.

Lock, M., & Nguyen, V. K. (2010). *An anthropology of biomedicine*. New York: Wiley- Blackwell.

Luparello, T. J., Leist, N., Lourie, C. H., & Sweet, P. (1970). The interaction of psychologic stimuli and pharmacologic agents on airway reactivity in asthmatic subjects. *Psychosomatic Medicine, 32*, 509–513.

Main, M. (1995). Attachment: Overview with implications for clinical work. In S. C. Goldberg, R. Muir, & J. Kerr (Eds.), *Attachment theory: Social, developmental and clinical perspectives*. Hillsdale: Analytic press.

Maruta, T., Colligan, R. C., & Malinchoc, M. (2002). Optimism-pessimism assessed in the 1960s and self-reported health status 30 years later. *Mayo Clinic Proceedings, 77*, 748–753.

McNair, D. M., & Barrett, J. E. (1979). Two bass scale factors and response to placebo and anxiolytic drugs. *Psychopharmacology, 65*, 163–170.

McDonald, C. J., & Mazzuca, S. A. (1983). How much of the placebo effect is really statistical regression? *Statistics in Medicine, 2*, 417–427.

McLaughlin, A. L., & Braun, K. (1998). Asian and Pacific Islander values: Consideration for health care decision-making. *Health and Social Work, 23*(2), 116–126.

McNeill, W. H. (1995). *Keeping together in time: Dance and drill in human history*. Cambridge, MA: Harvard University Press.

Merz, M., Seiberling, M., Hoxter, G., Holting, M., & Worthan, H. (1997). Elevation of liver enzymes in multiple dose trials during placebo treatment: Are they predictable? *Journal of Clinical Pharmacology, 37*, 791–978.

Miller, F. G., Emanuel, E. J., Rosenstein, D. L., & Straus, S. E. (2004). Ethical issues concerning research in complementary and alternative medicine. *JAMA, 291*, 599–604.

Moerman, D. E. (2002). Explanatory mechanisms for placebo effects: Cultural influences and the meaning response. In H. A. Guess, A. Kleinamn, J. W. kusek, & L. W. Engle (Eds.), *The science of the placebo*. London: BMJ Books.

Mondloch, M. V., Cole, D. C., & Frank, J. W. (2001). Does how you do depend on how you think you'll do? A systematic review of the evidence of a relation between patient's recovery expectations and health outcomes. *Canadian Medical Association Journal, 165*, 174–179.

Oken, B. S. (2008). Placebo effects: Clinical aspects and neurobiology. *Brain, 131*, 2812–2823.

Olson, J. M., Roese, N. J., & Zanna, M. P. (1996). Expectancies. In E. T. Higgins & A. W. Kruglanski (Eds.), *Social psychology: Handbook of basic principles* (pp. 211–238). New York: Guilford Press.

Osterberg, I., & Blaschke, T. (2005). Adherence to medication. *New England Journal of Medicine, 353*, 487–497.

Porter, D. R., & Capell, H. A. (1993). The natural history of active rheumatoid arthritis over 3-6 Months – an analysis of patients enrolled into trials of potential disease-modifying antirheumatic drugs, and treated with placebo. *British Journal of Rheumatology, 32*, 463–466.

Price, D. D., Harkins, S. W., & Barker, C. (1987). Sensory-affective relationships among different types of clinical and experimental pain. *Pain, 28*, 297–307.

Price, D. D., Milling, L. S., Kirsch, I., Duff, A., Montgomery, G. H., & Nicholls, S. S. (1999). An analysis of factors that contribute to the magnitude of placebo analgesia in an experimental paradigm. *Pain, 83*, 147–156.

Price, D. D., Finniss, D. G., & Benedetti, F. (2008). A comprehensive review of the placebo effect: Recent advances and current thought. *Annual Review of Psychology , 592*, 1–226.

Quine, W. V., & Ullian, J. S. (1978). *The web of belief* (2nd ed., p. 10). New York: McGraw-Hill.

Ray, P. (1996). *The integral culture survey: A study of the emergence of transformational values in America*. Sausalito: Institute of Noetic Sciences.

Raz, A. (2007). Hypnobo: Perspectives on hypnosis and placebo. *American Journal of Clinical Hypnosis, 50*, 29–36.

Roth, R. S. (2003). A biopsychosocial perspective on the placebo effects: Comment on Benedetti et al. (2003). *Prevention and Treatment, 6*(1), 8–17.

Siegel, S. (2002). Explanatory mechanisms for placebo effects: Pavlovian conditioning. In H. A. Guess, A. Kleinman, J. W. Kusek, & L. W. Engle (Eds.), *The science of the placebo*. London: BMJ Books.

Siegel, D. J. (2003). An interpersonal neurobiology of psychotherapy: The developing mind and the resolution of trauma. In M. Solomon & D. J. Siegel (Eds.), *Healing trauma: Attachment, mind, body, and brain* (pp. 1–56). New York: Norton.

Siegel, H. (2004). Faith, knowledge and introduction: A friendly response to hand. *Theory and Research in Education, 2*, 343–353.

Sievenpiper, J. L., Eztagha, A., Dascalu, A., & Vuksan, V. (2007). When a placebo is not a 'placebo': A placebo effect on postprandial glycaemia. *British Journal of Clinical Pharmacology, 64*, 546–549.

Simpson, S. H., Eurich, D. T., Majumder, S. R., Padwal, R. S., Tsuyuki, R. T., & Varney, J. (2006). A meta-analysis of the association between adherence to drug therapy and mortality. *British Medical Journal, 333*, 15–20.

Smith, G. R., & McDaniel, S. M. (1983). Psychologically mediated effect on the delayed hypersensitivity reaction to tuberculin in humans. *Psychosomatic Medicine, 45*, 65–70.

Smith, W. B., Gracely, R. H., & Safer, M. A. (1998). The meaning of pain: Cancer patient's rating and recall of pain intensity and affect. *Pain, 78*, 123–129.

Solbergnes, L., & Segerstorm, S. C. (2006). Dispositianal optimism and coping: A meta-analytic review. *Personality and Social Psychology Review, 10*, 235–251.

Stewart-Williams, S., & Podd, J. (2004). The placebo effect: Dissolving the expectancy versus conditioning debate. *Psychological Bulletin, 130*, 324–340.

Taylor, J. S. (2003). Confrounting "culture" in medicine's "culture of no culture". *Academic Medicine, 78*(6), 555–559.

Thagard, P. (2007). How cognition meets emotion: Beliefs, desires, and feeling as neural activity. In G. Braun, V. Doguoglu, & D. Kuenzle (Eds.), *Epistemology and emotions*. Aldershot: Ashgate.

Thomas, K. B. (1987). General practice consultations: Is there any point in being positive? *British Medical Journal, 294*, 1200–1202.

Thorn, B. E., Rich, M. A., & Boody, J. L. (1999). Pain beliefs and coping attempts. *Pain Forum, 8*, 169–171.

Toates, F. (1998). The interaction of cognitive and stimulus response processes in the control of behavior. *Neuroscience and behavioral Reviews, 22*, 59–83.

Tracey, I. (2010). Getting the pain you expect: Mechanisms of placebo, nocebo and reappraisal effects in humans. *Nature Medicine, 16*, 1277–1283.

Turner, V. (1974). *Dramas, fields, and metaphors: Symbolic action in human society*. Ithaca: Cornell University Press.

Turner, J. A., & Aaron, L. A. (2001). Pain-related catastrophizing: What is it? *Clinical Journal of Pain, 17*, 65–71.

Turner, J. A., Jensen, M. P., & Romano, J. M. (2000). Do beliefs, coping, and catastrophizing independently predict functioning in patients with chronic pain? *Pain, 85*, 115–125.

Vase, L., Robinson, M. E., Verne, G. N., & Price, D. D. (2005). Increased placebo analgesia over time in irritable bowel syndrome (IBS) patients is associated with desire and expectation but not endogenous opioid mechanisms. *Pain, 115*, 335–347.

Vodouris, N. J., Peck, C. L., & Coleman, G. (1989). Conditioned response models of placebo phenomena: Further support. *Pain, 38*, 109–116.

Volkow, N. D., Wang, G. J., Ma, Y., Fowler, J. S., Zhu, W., & Maynard, L. (2003). Expectation enhances the regional brain metabolic and the reinforcing effects of stimulants in cocaine abusers. *Journal of Neuroscience, 23*, 11461–11468.

Wasan, A. D., Kaptchuk, T. J., Daver, G., & Jamison, R. N. (2006). The association between psychopathology and placebo analgesia in patients with discogenic back pain. *Pain Medicine, 7*, 217–228.

Wickramasekera, I. (2000). How to produce not only powerful but, more importantly, reliable placebo healing and analgesia. *Advances in Mind-Body Medicine, 16*, 211–216.

Wilber, K. (2000). *Integral psychology: Consciousness, spirit, psychology, therapy*. Boston: Shambhala.

Zubieta, J. K., Yau, W. Y., Scott, D. J., & Stoher, C. S. (2006). Belief or nedd? Accounting for individual variations in the neurochemistry of the placebo effect. *Brain Behave Immun, 20*(1), 15–26.