

Article

## Mind-Body Practices in Integrative Medicine

Harald Walach <sup>1,2</sup>, Marie-Louise Gander Ferrari <sup>3</sup>, Sebastian Sauer <sup>4</sup> and Niko Kohls <sup>2,4,\*</sup>

<sup>1</sup> Institute of Transcultural Health Studies, European University Viadrina, Postfach 1786, D-15207 Frankfurt (Oder), Germany; E-Mail: walach@europa-uni.de

<sup>2</sup> Brain, Mind and Healing Program, Samuelli Institute, 1737 King Street, Suite 600, Alexandria, VA 22314, USA

<sup>3</sup> Department of General Internal Medicine, Division of Psychosomatic Medicine, Inselspital, Bern University Hospital, CH-3010 Bern, Switzerland; E-Mail: ganderml@googlemail.com

<sup>4</sup> Generation Research Program, Human Science Center, Ludwig-Maximilians-Universität, Prof.-Max-Lange-Platz 11, 83646 Bad Tölz, Germany

\* Author to whom correspondence should be addressed; E-Mail: kohls@grp.hwz.uni-muenchen.de.

Received: 3 February 2012; in revised form: 11 February 2012 / Accepted: 21 February 2012 /

Published: 23 February 2012

---

**Abstract:** Mind-Body practices have become increasingly popular as components of psychotherapeutic and behavior medicine interventions. They comprise an array of different methods and techniques that use some sort of mental-behavioral training and involve the modulation of states of consciousness in order to influence bodily processes towards greater health, well-being and better functioning. Mind-body practices may thus be interpreted as the salutogenetic mirror image of psychosomatic medicine, where psychophysiological and health consequences of specific psychological states are studied, such as stress arousal, psychological trauma or depression. This contribution examines the empirical evidence of the most common mind-body techniques with regard to their salutogenetic potential. We concisely discuss some aspects of the mind-body problem, before we consider some historical aspects and achievements of psychosomatic medicine. We then turn to some prominent mind-body practices and their application, as well as the empirical database for them.

**Keywords:** integrative medicine; behavioral medicine; psychosomatics; mind-body problem; mind-body techniques; consciousness

---

## Abbreviations

ALS: Amyotrophic lateral sclerosis; IL 1: interleukin 1, IM: Integrative Medicine, ACTH: adrenocorticotrophic hormone, HPA: hypothalamic–pituitary–adrenal axis, CNS: Central Nervous System, NO: nitric oxide, RR: relaxation response, MBSR: mindfulness based stress reduction, TM: Transcendental Meditation, AT: Alexander Technique, OCD: obsessive-compulsive disorder, EEG: Electroencephalography. MBCT: Mindfulness Based Cognitive Therapy.

## 1. Introduction

Mind-Body practices, such as Yoga or mindfulness training, have become increasingly popular among the public and researchers. They are a hallmark of Integrative Medicine (IM), since here the integration of psychological and medical, mental and physical approaches is most clearly visible. Mind-Body-Practices are also frequently utilized as components of psychotherapeutic and behavior medicine interventions [1–3]. Mind-body practices comprise an array of different methods that have one thing in common: they all use some sort of mental-behavioral training and involve modulating states of consciousness in order to influence bodily processes towards greater health and well-being and better functioning. In a sense, mind-body practices are thereby the salutogenetic mirror image of psychosomatic medicine, where psychophysiological and health consequences of specific psychological states, such as stress arousal, psychological trauma or depression, are studied. In this article, we aim to describe, elaborate and evaluate the philosophical background, rationale and value of Mind-Body-interventions. To place mind-body practices philosophically, it seems mandatory to us to discuss some issues around the mind-body problem. Some basic philosophical stances held by researchers and practitioners regarding this question might have a direct practical impact determining which mind-body practices are deemed useful and how they are being employed. Let us therefore start with a brief treatment of the mind-body problem before we consider some of the history and achievements of psychosomatic medicine. We then turn to some mind-body practices and their application, as well as the empirical database for them.

## 2. The Mind Body Problem

The mind-body problem raises the questions of whether mental events and our corresponding first person experience of consciousness are derived from, or secondary to, our physical make-up, our biology, and whether they are produced by the brain and its concomitant neurological processes, or is there such a thing as a soul- or spirit-like entity that is different from material events in the body. One can actually distinguish two levels of the problem [4]. The first concerns the question of how consciousness and brain events are related. Is consciousness a consequence and therefore causally dependent on the brain and its functioning? Alternatively, can a case be made that consciousness and material brain processes are different in kind, as was believed by the founding father of experimental psychology, Wilhelm Wundt (1832–1920)? In other words, is there a satisfying physical explanation for human consciousness? This is the classical mind-body problem. The second level we would like to term the ‘spiritual part’ of the mind-body problem. This deals with questions such as: is there some immaterial or even transcendental essence to human consciousness that could potentially even survive

personal death? How can we understand certain spiritual experiences such as enlightenment experiences within the framework of a physicalist program? Our opinion is that it is useful to distinguish between these two levels of the problem, because frequently some personal spiritual or religious motives lie hidden behind seemingly simple philosophical questions [5].

Since the beginning of the modern scientific era in the 18<sup>th</sup> century the questions of whether there is such a thing as a spirit-like soul, and if so, whether it is amenable to scientific scrutiny. These were central questions of modern physiology and psychology [5,6]. It was a hallmark of the surge of the scientific enterprise that physiologists replaced philosophers in tackling the question of how mental events come about by adopting a reductionist program, which was mainly inspired by Newtonian physics and mechanics, thereby reducing mental events to physical events in the brain. One historically important document is a famous letter written by Emil du Bois-Reymond (1818–1896), destined to become one of the most famous and influential physiologists of his time. This letter that he wrote at the age of 26 to some friends notes a meeting in 1848 of some young researchers, who would all become highly influential thinkers. Among them was du Bois-Reymond and Ernst Brücke (1819-1892), the physiologist who later became the teacher and mentor of Sigmund Freud (1856–1939) in Vienna. *“Brücke and myself,”* the letter notes, *“have conspired to bring forth the truth that there are no other forces active in the human organism than the common chemical-physical ones. And where this is not sufficient as an explanation as yet, the mathematical method of physics needs to be applied in order to search for the way they are active in a concrete case, or else new forces have to be assumed which, however, have to be of the same dignity than the physical-chemical ones, also inherent in matter, and always to be reduced to attractive and repulsive forces.”*<sup>1</sup> [7] This text delineates the program of physicalism: all explanations of mental events are to be reductions of physical laws, and hence mental events will eventually be explained by reference to physical events; much as physics was able to explain seemingly different events, such as lightning and magnetism as instances of electromagnetism. Briefly, the brain was conceived as a complex but rather clockwork-like neuronal machine for producing thoughts and mental sensations. The eighteenth-century French physician Pierre Jean Georges Cabanis (1757–1808) expressed in a famous phrase “the brain secretes thought as the liver secretes bile”. Mind then, in such a view, is simply a consequence of the complex neural assembly that forms our brain. Just how far such a physicalist program will be able to progress is still a matter of heavy debate. Some have said, and still keep saying, that we will not need a mentalist-psychological language any longer, as we will explain everything in terms of neuroscience [8]. Similar to our saying “a bolt of lightning has struck” instead of using the more precise terminology “a strong current of electricity has balanced the large potential difference between clouds and the earth” we will still be talking about “pain”, but will then have a precise definition and description of what it is to have pain in neuroscientific terms. There is a plethora of philosophical positions that differ in just how much of

---

<sup>1</sup> Translation ours. Original: "Brücke und ich, wir haben uns verschworen, die Wahrheit geltend zu machen, dass im Organismus keine anderen Kräfte wirksam sind, als die gemeinen physikalisch-chemischen; dass, wo diese bislang nicht zur Erklärung ausreichen, mittels der physikalisch-mathematischen Methode entweder nach ihrer Art und Weise der Wirksamkeit im konkreten Falle gesucht werden muss, oder dass neue Kräfte angenommen werden müssen, welche, von gleicher Dignität mit den physikalisch-chemischen, der Materie inhärent, stets auf nur abstossende oder anziehende Komponenten zurückzuführen sind" S. 108.

causal efficacy they attribute to our mental events [9]. Some appear to be saying that our subjective impression of agency and will is just an illusion and that there is no such thing as real causal agency driving our mental life [10]. Others would say that, although those mental events of will and causal activity are caused by our material substrate, *i.e.*, the brain, these mental events, once produced, may have some causal repercussions on the physical system [11].

On the whole, physicalist approaches agree on the basic stipulation that mental events are consequences of our brain architecture and are caused by it. When the brain and its sustaining organism cease to live, our individual consciousness will also collapse.

Clearly, this physicalist view has much to recommend itself as a parsimonious and yet adequate theory for explaining consciousness. A host of neuropsychological studies have shown how the brain sustains mental functions [12], and that, where certain brain functions have been damaged, very particular and specific mental functions have also been compromised. The study of coma and anesthesia, for instance, has shown which brain structures are necessary to sustain conscious awareness, and we know pretty well that if such essential structures as the brainstem are severely damaged then consciousness cannot be maintained or regained [13]. We also know that long projection fibers ranging from the brain stem via the thalamus to the cortex seem to form circular structures that are necessary for the sustenance of conscious experience [14]. If these thalamo-cortical loops are deranged, severe chronic pathologies, such as pain syndromes, may result [15]. These pain syndromes can sometimes be influenced by diligent microsurgery in some areas of the thalamus [16]. These and similar experiences have shown without any reasonable doubt that the brain certainly is *necessary* for consciousness to arise.

However, can a rational conclusion be drawn that the brain is also *sufficient* for consciousness? At issue is the philosophical problem of sufficient and necessary cause. A functioning engine, for instance, is a necessary condition for a car to drive. Nevertheless it is not sufficient. Gasoline, oil and a battery are also necessary to start the engine. Moreover, in order to get the car in motion, tires, a gearbox and a clutch are also essential. At another level, a driver is also needed to operate the car. Taken together, these components establish necessary *and* sufficient boundary conditions that allow the car to be driven. In the same sense, it does not seem to make sense to doubt that the brain is a necessary condition for consciousness. However, is it sufficient?

What about, for instance, the gut? Amyotrophic lateral sclerosis (ALS) is a disease that destroys the muscular endplates of motor neurons, leading to complete paralysis. Because this condition also brings about a more-or-less complete destruction of visceral feedback to the brain, patients with this disease can experience a state of consciousness that can sometimes be quite serene [17,18].

This seems to be due to the fact that some feedback from the gut and from other parts of the periphery is missing. The gut has its own system of innervation, for instance, with many millions of neurons and some orders of magnitude more of synaptic connections. These use serotonin as its major transmitter, and in addition acetylcholine [19]. To date, not all of its function is clearly understood. Most has to do with the registering of nutrients and antigens in the bowel, being taken up by the blood, and with the regulation of peristaltic movement. It may well be the case that this complex neuronal system of gut regulation contributes to the tone and color to our consciousness, without us ever knowing [20].

The neuronal system regulating the gut is part of a larger neuronal system, the autonomic nervous system. It has long been thought to be completely separate from the central nervous system, operating autonomously, hence its name. However, we know nowadays that there are multiple ways how the two systems interact and that IM interventions may change their reciprocal action [21]. Imbalances of the autonomic nervous system can severely affect our conscious experience [22]. Chronic pain syndromes such as fibromyalgia and chronic fatigue syndromes are two examples of how an imbalance in autonomic regulation, *i.e.*, in a part of the nervous system that is largely outside the brain and does not contribute to consciousness as such, have a clear and perceptible impact on the sufferers' conscious experience [23,24].

Another system, seemingly autonomous but with a multitude of interactions both with the autonomic and the central nervous system is the immune system. We now know that nearly every molecule used by the central nervous system as a messenger or transmitter molecule can have immunological functions as well. Most molecules used by the immune system for communication between components of itself may also have some function within the central nervous system, or at least will have some receptors in certain brain areas such as the hypothalamus, where the brain seems to scan the immunological situation of the body [25].

Thus, the status of another, highly interlinked and complex system that operates mainly as a system of cells distally linked through very specific messenger molecules, also potentially contributes to the state of our consciousness. To give an example: Whenever we suffer from an infection, the level of the messenger molecule interleukin 1 (IL 1), a protein used by the immune system to activate lymphocytes and commandeer them to a place of infection and stimulate the growth and division of B-lymphocytes, will rise. IL 1 is also now known to exert very specific effects in the brain. It produces a feeling of tiredness, a behavioral withdrawal syndrome with a lack of motivation, a profound sense of fatigue and the feeling of not being able to cope with the world. Under normal circumstances, this is a signal for the organism to withdraw and save energy in order to fight the infection. It appears that in some forms of depression, IL1 also seems to play a role by producing a facsimile of clinical depression. This raises intriguing questions about how our immunological situation plays a role in the way our consciousness is toned [26–29].

These two examples show that defining the brain as a necessary condition for consciousness is by no means equivalent to explaining consciousness sufficiently. They also illustrate that opponents of a physicalist solution of the mind-body problem may have a point which is difficult to counter: saying that something is necessary for consciousness—the brain—is not identical to having a sufficient explanation.

A series of arguments can and have been leveled against a physicalist view. Some of them are of a principal philosophical nature. Some use phenomenological and empirical facts. Several philosophical arguments use the principal difference of our first-person subjective experience and brain events [30,31]. While brain events are always similar—neuron discharges and patterned firing of neurons, as well as chemical transmission of molecules, personal subjective experience is quite varied. One might want to use the differences in transmitter molecules to explain the differences in subjective phenomenology. However it may be argued that there are probably many more subjective feelings and tastes than can be accounted for by types of molecules or any mixture thereof. It is very difficult to jump from the hardwiring of neurochemistry and neurophysiology to the subjective feel of what it is like to be myself,

or yourself, in any particular situation. Although we all know what pain is, it is quite something to think about pain, remember it, even empathize with someone who experiences pain, and having pain oneself. Moreover, pain defies the Cartesian taxonomy, as this phenomenon is actually something in between objective and subjective categories [32,33]. As a matter of fact, no knowledge about our pain-brain circuitry is able to help us understand what someone who suffers from severe chronic pain of a phantom limb actually feels. Although we may be able to describe this in a somewhat objectified manner, for example as abnormally strong patterns of theta-activity reverberations between some thalamo-cortical loops, and also see the result of a therapeutic intervention in the normalization of these patterns, these patterns themselves do not carry any of the subjective flavor of being in pain [16,34,35]. It could also have been the correlate of a strong emotional reaction to one's grandmother. It only happened to be the correlate of strong pain, and nothing in itself tells us so, except the context of the research, and the private experience of the person who suffered from the pain in the first place.

Such arguments have been leveled to bring home the point that an objective, physical description, even an explanation of a subjective content of mind, such as a feeling, an emotion or a particular subjective phenomenological experience, is not identical to that experience itself. As Thomas Nagel has pointed out, such an explanation, no matter how complete, will, in principle, never be able to give us the feeling of “what it is like to be in this state” [36]. This first-person singular, or subjective, view is categorically different from the third person view of scientific description and explanation. In the philosophical literature such phenomenological states have been termed “qualia”, from the Latin “how it is”, and it has been argued that as yet no way leads from a closed external description of the functioning of our brain to the subjective experience itself [37,38].

Some have gone as far as to say that because of this categorical difference between mental and physical events, subjective experience and objective description, the mind must be altogether a different entity [4,39,40]. Such a dualist position was of course first voiced by René Descartes (1596–1650), although Descartes was of course much more sophisticated than to merely postulate two substances. He was aware of the problem: If two completely different substances are unified within the human person, then they need a place of interaction [41]. Descartes saw the pineal gland as this organ of interaction, whereas Wundt, relying on Gottfried Wilhelm Leibniz' (1646–1716) metaphysical ideas of a pre-established harmony, developed the idea of psychophysical parallelism assuming that brain and mind states are two independent yet synchronized layers of description that are both necessary in order to understand and describe consciousness [5,6]. Modern proponents of dualist ontologies or solutions of the mind-body question also face the same problem [4–6]. They have to say how such an interaction can happen in the first place. Some have made the point that the physiology of our brain, more precisely the synaptic vesicles, are of a size that might sustain quantum fluctuations such that our consciousness could actually use these physical events for the purpose of steering the physical make-up of our brain [42,43]. Others have pointed out that the micro-skeleton of the neurons, the so-called neurotubules, are of a size and geometry such as to sustain long-range coherence of electromagnetic vibrations—similar to a laser—which then collapse into a definite state in the act of consciousness [44,45].

Such models derived from quantum theory are implicitly dualistic because the application of quantum theory itself presupposes the fact of a conscious observer in the first place. This is a precondition of quantum mechanics, and hence of all physicalist approaches. Still, this fact is rarely appreciated by proponents of monist-materialist physicalist solutions of the mind-body problem.

Moreover, it is precisely through the thorough analysis of the preconditions of a physicalist position that quantum mechanical models bring up the problem of consciousness as a second entity, different from the physical-material make-up of the world [30,46].

Some empirical arguments stem from the systematic study of near-death experiences [47,48]. Some documented experiences have apparently been reported by persons who have been clinically dead for more than 30 minutes [49]. This is a period which would not allow the heart to keep the brain sufficiently provided with blood, oxygen and nutrients, and which would hence have resulted in a physiologically dead brain that, in theory, should not have been capable of consciousness. Hence, conscious experience of a person with such a physiologically dead brain would be a weighty counter-argument against a physicalist theory of consciousness.

Some have used the formal structure of quantum mechanics, which presupposes a conscious observer to work formally, to make consciousness primary altogether [43,45,50–54]. On this basis, they reinforce what, in the history of philosophy, has been termed idealism. This is the position that ultimately, mind or consciousness is the only “real” thing in the world, and matter is a consequence of, or derived from, consciousness. The German idealists Fichte, Schelling and Hegel were the last influential philosophers to hold such a view. In modern days some mathematicians and physicists sympathized with this view, and some esoteric and transpersonal ontologies that are influenced by Eastern philosophies adopt such an idealist mind-over-matter stance. In fact, most of Yoga or Hindu psychology can be seen as an attempt to work out such a world view. Needless to say, our modern scientific-physicalist program is not easily reconcilable with such an idealist position. On the contrary, it arose despite heavy philosophical criticism from idealist quarters.

A pragmatic solution to the conundrum might be provided by a complementarist solution, a particular form of dual aspect theory [38,55]. Dual aspect theories have a long tradition, going back at least to Spinoza in the 17<sup>th</sup> century. They suggest that mind and matter are just two expressions of the same basic stuff in the universe that happens to have a physical side and a mental side. Some, such as Plotinos in the 2<sup>nd</sup> century AD, have suggested a transcendental origin for this basic stuff. Others, such as the modern philosopher Feigl, have chosen not to address this question [56,57]. The Swiss psychiatrist Carl Gustav Jung (1875–1961) held a similar position by saying that mental and physical events are unified by a common source he termed “*unus mundus*”, using a notion from medieval alchemy [58]. One potential model is to refer back to the basic structure of quantum mechanics, which uncovered complementarity as a basic structuring principle of the quantum realm. Nils Bohr, one of the fathers of quantum mechanics, pointed out that in order to describe matter properly we need to adopt notions that are at the same time maximally incompatible with each other, yet have to be applied to the same thing [59]. This structure he called complementarity, borrowing a term from the psychology of his days [60]. Bohr speculated that this structuring principle may be more general than just applicable to the description of processes in the quantum realm. Following Bohr, one could apply this notion to the relationship of mind and matter [61], and, it should also be noted, also within consciousness itself, as one finds both emotional and cognitive aspects therein that are both necessary in order to explain the human condition. That is, that two maximally incompatible concepts that nevertheless have to be applied at the same time to describe one and the same thing: a conscious human being (or another animal, for that matter). Similarly to quantum mechanics, we do not have another way at talking about the underlying nature of the world than by using such complementary

concepts as a heuristic template in order to grasp the complexity of the phenomenon in question. Neither would it make sense to forfeit one of the sides. There may still be an underlying unifying nature on an ontological level, but we ordinarily do not have epistemological access to it. Hence the world appears to us in these dual aspects of material and mental events which, however, are intimately related with each other. Various ways have been pointed out how this could be conceptualized properly, one being the assumption that mind and matter represent a breaking of an underlying symmetry [62], another one being the idea that the basic structure of quantum mechanics might be applicable to other systems, as well [30,31]. Hence complementarity between mental and physical events could be orchestrated by non-local correlations, similar to quantum correlations proper.

We think that no matter which one of these views will emerge as being “true”, it is important to reflect on the preconditions, consequences and the scope of these philosophical options. For, if one holds on to a narrow materialist-physicalist solution of the mind-body problem, then some forms of mind-body medicine or psychosomatic practices might not sound very reasonable. For instance, in order to sustain a certain type of, say, refinement of altered states of consciousness and spirituality [63–65], it is actually implicitly understood that a materialist ontology would not be compatible. Interestingly, by acknowledging the complementarist functions of cognitions and emotions, the principle of complementarity has been successfully employed to extend the scope of the traditional cognitive theories of mind and it has been suggested as a “generative principle” for explaining visual perception [66]. Thus, it appears to us that a complementarist notion is a promising minimal meeting ground. It ascertains the reality and causal efficacy of mental events, yet does not buy into a dualist or idealist ontology and guarantees the unity of the human person at the same time, thus being true to the thrust of the scientific enterprise of finding unitary explanations and causes. Hence, for pragmatic reasons, we will adopt such a position for the remainder of this chapter.

### **3. Psychosomatic Medicine, Psycho-Neuro-Endocrinology and Psycho-Neuro-Immunology**

Psychosomatic approaches were at the cradle of modern medicine and psychology. By rejecting the old spiritist possession ‘animal magnetism’ model created by Franz Anton Mesmer (1734–1815). He thought that some sort of energy flows through the body that produces health and disease, physical as well as mental [67–69]. Hence, balancing this animal magnetism through his magnetic strokes would create or at least restore health. It later emerged, when his followers and other neurologists took these discoveries further—Charcot, Bernheim and Janet—that despite all their conceptual differences what Mesmer had probably done was use psychological methods, such as suggestion and hypnosis, to affect the physiology of the body [6,70–72].

Treating hysterical women with hypnosis was also the starting point for the young Freud. He not only studied physiology with Ernst Brücke in Vienna, from where he got his physiological ideas, but he also visited Jean-Martin Charcot (1825–1893) at the Salpêtrière in Paris and Hippolyte Bernheim (1840–1919) in Nancy where he became accustomed to the two important French schools of hypnotism [71,72]. Moreover, he translated the most important book of Bernheim into German and not only named his oldest son Jean-Martin, but also wrote a favorable obituary of Charcot, although he was not very favorable towards another French psychologist, Pierre Janet (1859–1947). However, on closer scrutiny it turns out that a substantial amount of Freud’s seemingly original ideas are actually

unaccredited developments of discoveries of these French giants [6,73]. Thus it is not a big surprise to find Freud theorizing and speculating about the possibility that mental problems and psychological trauma could express themselves in the body, or even use a secret code to express psychological problems physically. Although Freud developed only a rough outline, psychosomatic ideas are genuinely at the base of the psychoanalytic enterprise. If the psyche and the subconscious are to have any power at all, this power cannot stop where psychological phenomenology stops. It must reach into the realm of the body. This idea was developed further by Freud's followers and also those who effectively became psychoanalytical renegades. Alfred Adler (1870–1937), who initially considered himself a student and follower of Freud but then broke away, developed the concept of organ inferiority [70]. This is the idea that the inferiority complex, which in Adler's view is one of the driving forces of positive striving as well as of neurosis, manifests also physically [74]. From there it is only a small step to what Freud himself called "organ language", together with early psychoanalytically-inspired psychosomatic theorists, such as Sandor Ferenczi (1873–1933), Wilhelm Reich (1897–1957) and Georg Groddeck (1866–1934) [75]. In the same way that neurosis uses symbols in dreams and thereby develops a certain language to manifest conscious experience, it may also use body function to express itself. Thus, anger that is "swallowed" may express itself as stomach ulcers, or implicit wishes to avoid sexual intercourse may express themselves as skin disease that discourages physical contact, and so on.

Modern empirical psychosomatic research has largely disproved the crude psychosomatic equations fashionable with the early analysts [70]. However, it has also uncovered multiple links between the psyche and the body and thereby potentially expanded the scope of a psychosomatic view. If anything, the psychosomatic view has been solidified and grown in importance by liaising with another important movement: systems theory. Systems theory is a theoretical movement that originated in Austria and Hungary around the 1930s. It was driven mainly by biologists, such as Albert Szent-György (1893–1986) and Ludwig von Bertalanffy (1901–1972), who were dissatisfied with the reductionist view in biology [76–78]. They argued that a living system is different from and more than just its constituent parts. From there it was only a small step to argue that such an abstract systemic view can be applied to a variety of systems. Thus, not only cells, plants and animals can be considered such systems, but also human beings. They not only comprise a physical system, but are also embedded in a social context that creates the meaning that is transported in their psychological world, both of which are intimately related to humans. Hence, systemically, there is not only an intimate connection between the mental and the physical, but also between those two dimensions and the social aspect. Thus a bio-psycho-social view was increasingly applied to medical problems [79,80]. Such a view postulated that one had to consider not only the physical plane but also how this reflected the psychological situation and the social plane as well as their complex interdependencies. Such a systemic view was akin to what German psychosomatic medicine had been teaching since the early 20<sup>th</sup> century, developed out of the Heidelberg school, centering on Victor von Weizsäcker (1886–1957) [81].

Modern psychosomatic research became less dogmatic and more and increasingly pragmatic, trying to uncover the concrete links between the psychological plane and the physical reality of the body [75]. While the crude links of early psychosomatic approaches turned out to be barren, the generic idea seemed to be fruitful and is still inspiring new research programs. Two important developments were instrumental. They are known as psycho-neuro-immunology and psycho-neuro-endocrinology. These

terms denote the programs that try to uncover the links between the psychological system, the brain and the endocrine or the immunological systems respectively. Often, they are now considered one program, and it is mainly for disciplinary reasons that they are distinguished.

The immunological system was long considered fairly self-contained and self-sufficient, operating independently from the central or autonomic nervous system. While some earlier ideas were already around, the idea of a psycho-neuro-immunological connection was boosted by Robert Ader's work *i.e.*, the central nervous system interacting with the immune system, and the immune system with the central nervous system [82–84]. This showed that a supposedly independent immunological reaction, the immunosuppression produced by a pharmacological stimulus, could be classically conditioned. This meant that an immunologically irrelevant but psychologically relevant stimulus could be imbued with immunological meaning. If that was principally possible, then it was conceivable that a host of immunologically mediated responses, and hence diseases also, might be susceptible to conditioning. If rats could be conditioned to show an immunosuppressive reaction in a taste-aversion paradigm, then it was also conceivable that humans could show enhanced or suppressed immune reactions to aversive psychological stimuli [85]. This opened, at least in principal, a route to understanding psychological concomitants of immunologically mediated diseases, such as asthma, atopic dermatitis, colitis or Crohn's disease, to name but a few of the more important diseases.

At the same time, immunologists and endocrinologists discovered that the distinction between hormones, cytokines and transmitters was fairly artificial. Ever more receptors for ever more molecules were discovered on immunocompetent immune cells. Cells, such as lymphocytes or macrophages, not only respond to cytokines proper, *i.e.*, to signaling molecules used by the immune system to communicate and regulate the immune response, but also express receptors for most of the transmitter molecules used by the central or autonomic nervous system, as well as to some hormones. Cortisol, for instance, a hormone that is introduced into the blood stream by the adrenal cortex in response to a perceived stress, not only has a host of reactions in the periphery, such as an increased metabolism, but also via further sympathetic activation leads to a quicker heart rate and a change in temperature, as well as a redirection of blood distribution from the intestines to the periphery. Cortisol receptors are also expressed by some immune cells which then decrease activity. Cortisol receptors have also been discovered in the cortex, for instance in hippocampal areas, amygdala and in the hypothalamus [86]. Hence, what classically used to be seen as a hormone, is now considered to have multiple actions: , as a hormone, as an immunologically active molecule and as a molecule with central nervous system activity. In the same vein, it has been discovered that most of the distinctions previously considered instrumental are rather artificial, due to our ignorance or our failing theoretical models. While we have neither the competence nor the space to give a complete overview, it is sufficient for our purposes to simply note this thrilling fact that research has uncovered a multitude of links between the immune system, the brain and the endocrine system in both directions. This allows for an understanding, at least in principle, of the fact that the brain, and thereby the mental system, can have a direct influence on the body [87,88].

Take stress as an example. The stress response can be distinguished into two phases. The immediate stress response is via autonomic innervation of the adrenal medulla and autonomic reactions [89]. On a threat stimulus, the threat is perceived through sensory input, which then via parts of the thalamus activates the locus coeruleus in the brain stem to stimulate the sympathetic adrenal medullary (SAM)

axis [90]. Adrenalin is injected into the blood stream within several hundreds of milliseconds by the adrenal gland [91].

At the same time, direct connections from perceptual centers in the lower brain areas activate neurons in the amygdala where the emotional valence of stimulus is analyzed even before clear conscious perception is formed by higher centers [92,93]. If a threat stimulus is detected, direct innervations of hypothalamic centers by amygdala neurons activate corticotropin-releasing hormone (CRH). This in turn stimulates the emission of adrenocorticotrophic hormone (ACTH) from the pituitary [94]. This then travels via the bloodstream to the adrenal gland, where, in the cortex of the adrenal, cortisol is released, starting the second phase of the stress response as briefly outlined above. Blood cortisol peak is reached roughly within 10–15 minutes after the perceived stress [95].

The sympathetic system will have reacted to the perception of the fear stimulus within a matter of several hundred milliseconds. It will have not only triggered the release of adrenalin and nor-adrenalin, also known as epinephrine, and norepinephrine from the medulla of the adrenal gland, several minutes before the hormonal regulation of the excretion of cortisol will have started. It will also have increased the heart rate almost instantaneously and rushed the emission of glucose from depots in the liver into the bloodstream to make immediate muscular action possible. If the perceived threat that has triggered this autonomic reaction is shortly afterwards discovered to be a false alarm by more intricate analysis—a stick of wood, say, instead of a dreaded snake—the second phase will be halted immediately and we calm down again. This will be the case at least under normal circumstances. Negative feedback loops will stop the arousal. This is because epinephrine is not only a hormone, but also a neuro-transmitter. The epinephrine level in the bloodstream is monitored by receptors in the hypothalamus and possibly elsewhere in the brain. It will block the respective centers responsible for activating the sympathetic arm of the autonomic nervous system. The cortisol system which starts out a little more slowly will take over the necessary regulation activities if the threat or the challenge persists [96].

Stress response normally subsides once the organism has successfully dealt with it. Then a down-regulation of the system takes place and a rebalancing can be effected. The ability of the body to increase or decrease vital functions to a new steady state on challenge during stress is called allostasis. However, there are four types of reactions describing how a system can mal-adapt to a stressor, which in the long term can increase the probability of disease [97]. The four maladaptive responses to a stressor are: (1) frequent exposure to stress, (2) inability to habituate to repeated challenges, (3) inability to terminate a stress response, (4) an inadequate response. In these four reaction types to challenge, the system accumulates high allostatic load as the cost of chronic exposure to elevated or fluctuating endocrine and neural responses. A high allostatic load is predictive of mortality and morbidity [89,98].

If, however, for some reason, the stress persists and the organism is not effective in coping, the negative feedback winding-down processes will not work. Alternatively, if the stress response is activated too frequently or in too short a period of time, the pituitary-adrenocortical axis will be taxed and worn out. Challenges may not be met with the right level of reaction, exposing the organism to inefficient capabilities to cope with the situation, prolonging the stress situation and hence the potential threat.

Both chronically elevated levels of cortisol and a lack of reaction to cortisol emission are problematic [99]. Chronically elevated cortisol levels may have a host of immunological reactions.

Cortisol in the short term stimulates the immune activity of some cells, but over a longer period has suppressive effects. Elevated stress levels might actually make the organism prone to either infections or deregulated immune responses and auto-immunological reactions, such as elevated inflammatory response. It is a well-known clinical fact that immunologically-mediated diseases such as atopic dermatitis, asthma, rheumatoid arthritis or multiple sclerosis can be triggered or aggravated by stress or emotional upheavals [100,101]. Chronic immune suppression brought about by elevated cortisol levels might also contribute to some forms of cancer, where the immune system fails to attack some cells that have not destroyed themselves as they should have [102,103].

It may even be possible that chronically elevated cortisol levels may inhibit the formation of synaptic diversity in the hippocampus, an area of the brain necessary for the transition of content from short term to long-term memory, and an important comparator of perceived information with expected information [104]. The hippocampus also plays important roles in emotional regulation, and thus elevated cortisol levels may have powerful repercussions in affective tone. For instance, some forms of depression have been associated with chronically elevated cortisol levels [99]. If cortisol levels are chronically elevated, or traumatic challenges of the stress-response system have been experienced in childhood, the responsivity of the hypothalamic–pituitary–adrenal axis (HPA-axis) can be down-regulated and hypocortisolism results [105]. This is an inability of the system to respond adequately to stressors, either because of a fatiguing of the system or because of a protective mechanism against flooding with cortisol. Hypocortisolism is associated with chronic disease, such as atypical depression, fibromyalgia, chronic fatigue syndrome or post traumatic stress disorder [106,107].

Thus, in principle and probably depending on individual vulnerabilities and learning histories, some quite non-specific and ubiquitous stress reactions could be responsible for a wide range of dysregulations and potentially even for chronic disease. This is possible, because immunological reactions, hormone reactions, autonomic nervous system effects and central nervous activity are all intimately linked and all communicate with each other.

In conclusion: While the old psychosomatic theories were certainly much too crude, the general intuition was correct. Psychological content, experiences and traumata, such as anxiety, fear, grief, depression and hopelessness may have profound reactions on the body. What we have discovered through exploring immunological and endocrinological connections within the brain and thus within the sphere of psychological experience is a highly intricate and complicated network of potentially mutual influence. We have also seen that simple equations such as anger leading to stomach ulcers, anxiety to asthma, repressed hostility to myocardial infarction, are nearly always wrong in their linear simplicity. However, the generic possibilities of such connections have been unraveled, based on the discovery that the whole body and not only the Central-Nervous-System (CNS) is a complex network communication system and continues to be researched [108]. It can be expected that in the near future, this research program will generate a more specific and detailed understanding of how some somatic diseases are linked to psychological states. In the next section, we consider the aspiration and the rationale of such interventions.

#### 4. The Hope of Mind-Body Interventions

By now it should be clear that if mental states and psychological experiences can influence the body towards disease, the same connections should also be pathways for therapeutic interventions. If chronic stress, to name but one condition, can produce a host of negative consequences or exacerbate many diseases, then a chronically relaxed state, or the capacity to counteract stress and relax quickly and effectively, could potentially exhibit beneficial health effects. If negative affect and depression can produce profound dysfunctional immunological changes, then the induction of positive and serene affects should be protective, if not therapeutic. This is the basic assumption of Mind-Body Interventions.

One of the first systematic explorations and exploitations of that idea was Benson's Relaxation Response [109,110]. Following this line of reasoning, Benson suggested that similar to the universal stress response that allows the organism to combat a wide variety of challenges and cope with all sorts of difficult situations through a circumscribed set of physiological reactions, there should also be an innate relaxation response that does the opposite: leading the organism back into a state of regeneration. Associated with the parasympathetic arm of the autonomic nervous system, Benson and his associates studied a variety of techniques, mainly derived from meditation techniques, that would trigger such a relaxation reaction. The hallmark of this reaction is an activation of the parasympathetic arm of the autonomic nervous system, which is antagonistic to the sympathetic arm mediating the stress response [111]. The main pathway to accessing and stimulating this is through the regulation of breathing. By regulating one's breathing the sympathetic activation can be modified and eventually countered [112]. A slowing down in breathing slows down the heart rate. It also effects a dilation of blood vessels, mainly in the periphery, but also in the bowels. Glucose is moved back into depots, cortisol emission is down-regulated, endorphins are released, and as a consequence constitutive nitric oxide synthase is stimulated and nitric oxide (NO) is produced. NO is an immune, vascular and neural signaling molecule, and is itself bactericidal and antiviral. It scavenges free radicals and down-regulates endothelial and immunocyte activation and adherence, thus performing vital physiological activities, including vasodilation [113]. Thus, a comprehensive state of regeneration is triggered by this relaxation response [114]. Most, if not all, beneficial effects of mind-body techniques are supposed to work through this generic mechanism of the relaxation response, according to this claim. They all influence breathing and heart rate, and thus exert a stimulating influence on the parasympathetic system.

The question whether the relaxation response is sufficient as an explanation of beneficial effects of mind-body techniques is certainly open at this time, although there is some evidence that it cannot be seen as the sole pathway driving the health connection [21,115,116]. While it is a reasonable assumption that some form of relaxation is germane to most, if not all, mind-body techniques, it might well be the case that more subtle changes that are difficult to measure or are exerted only centrally in the brain with very poor proxy measures in the periphery have so far evaded researchers. Pain often being a subjective phenomenon of immediate experiential directness might nevertheless be highly elusive locally, if the pain is not one secondary to a local inflammatory process but one that has generalized and is now due to a centrally mediated dysregulation of pain perception [117,118]. Effects of mind-body techniques on the experience of pain, for instance, will require more elaborate models of explanation than just the generic activity of the relaxation response.

But it is precisely the fact that some chronic diseases are complex functional diseases with only few local and peripheral abnormalities, where mainly central regulation either of pain perception, or of the immune network or of endocrine-immune-functions are deranged, that attracts people to mind-body techniques. After all, nearly all diseases that are medically difficult to treat or are only treated symptomatically, seem to have a strong component of central functional dysregulation. This is true for all chronic pain syndromes which are not due to injuries or mechanical disruptions, such as for fibromyalgia, chronic idiopathic pain, or some neuropathic syndromes such as sciatica [119,120]. This is also true for chronic fatigue syndrome, for all chronic diseases with an involvement of dysfunctional immune-regulation, such as atopic diseases, and perhaps even for coronary heart disease and atherosclerotic diseases [121–123]. It is certainly also valid for psychological disorders, such as anxiety and depressive disorders, and perhaps even for some compulsive disorders and potentially also for substance abuse disorders [88,124–126].

That is not to say that mind-body techniques are effective in all these cases. Nevertheless, it means that it makes sense to study mind-body techniques in connection with diseases where a component of central regulation: pain, psychological experience or endocrine and immune regulation is involved. In addition, this is true nowadays for nearly all relevant chronic diseases that pose a challenge.

## 5. A Typology of Mind-Body Techniques, Brief Descriptions and a Summary of the Evidence Base

Mind-Body techniques can be ordered according to several components:

1. Self-directed *vs.* other-directed
2. Narrow *vs.* wide focus of attention
3. Direct *vs.* indirect action and intervention
4. Body oriented *vs.* mind-oriented
5. Amount of practice (high *vs.* low)

First, a technique can be more or less completely dependent on the instructions of a trained therapist. This is the case with classical or modern hypnotherapeutic approaches, where the mental states of a patient are modified and modulated by a therapist in order to influence some bodily function. On the other hand, it can be comparatively self-contained after an initial training period. This is the case for most therapeutic meditation programs that are instructed by a teacher such as the relaxation response (RR) program, the Mindfulness Based Stress Reduction (MBSR) program, Qi Gong, Tai Chi, or the Transcendental Meditation (TM) program. Some of the more complex Yoga, Qi Gong or Tai Chi techniques are in-between as they often presuppose the presence of a skilled teacher and a long training period for correct postures and movements. At the extreme end of the self-directed techniques range are simple relaxation programs that are conveyed by self-help books and accompanying tapes and discs and self-hypnosis programs.

Second, most techniques explicitly direct attention towards a clear focus, at least initially. This is certainly true for all meditation techniques that either use the focus of breathing on the body and its function, or on mantras and phrases as a vehicle to redirect attention. After that initial focusing some techniques are quicker than others in broadening out the focus towards observing all mental activities and content, such as mindfulness based techniques, while others encourage practitioners more strongly

to keep this focus and intensify it, such as techniques derived from Yoga traditions, such as TM or Yoga itself, Qi Gong or Tai Chi. However, it should be said here that this distinction seems rather technical and artificial to us. Every technique that targets the capacity to redirect and focus attention will eventually increase mindfulness also outside the context of meditation. Moreover, every technique that intends to increase mindfulness and thus initially favor an open focus has to teach people how to shift and direct their attention in the first place and is achieves this by focusing on breathing. Nonetheless, seemingly orthogonal constructs, mindfulness and focused attention seem to be complementary in the sense that they are both necessary and fostered by mind-body techniques.

Third, some techniques are quite direct in regulating bodily function and prescribe patterns of breathing and moving, such as Tai Chi, Qi Gong or Yoga meditations. Others, such as mindfulness techniques and even TM are more indirect in just having people observe the breath or bodily functions and thus use the simple fact that observation itself changes the function.

Fourth, some techniques use the body directly and influence bodily states through movement, posture or bodily manipulation with the expectation that either psychological or bodily changes will ensue. This is true for techniques such as Tai Chi, Qi Gong, Yoga or the Alexander Technique. Other techniques are in an intermediate position in that they use some body awareness but only in a supportive fashion. That would be true for most meditation techniques that recommend a certain posture, such as upright sitting position, or a certain type of slow movement. Examples for mind-body techniques with little direct emphasis on the body would be hypnosis or self-hypnosis. Table 1 presents a summary classification for some of the more widely known Mind-Body Interventions.

**Table 1.** Summary Classification of Some Better Known Mind-Body Interventions.

	<b>Direction</b>	<b>Focus</b>	<b>Action</b>	<b>Body</b>	<b>Practice</b>
Transcendental Meditation	Self-directed with some emphasis on teacher	Focused	Indirect	Little emphasis	Daily 1 to 2 times 20–30 minutes
Relaxation Response	Self-directed	Focused	Indirect	Little emphasis	Daily, 2 times 15/20min,
Progressive Muscle Relaxation	Self-directed	Focused	Direct	Emphasis	Daily or as needed; no fixed duration
Biofeedback	Self-directed with initial expert component	Focused	Direct	Emphasis	Supervised sessions until resolved or as needed
Alexander Technique	Externally directed	Focused	Direct	Emphasis	Taught lessons until resolved or as needed
Qi Gong/Tai Chi	Externally directed, later self directed	Focused	Direct	Emphasis	Taught lesson with daily practice
Life-style modification	Externally directed, later self directed	Mixed	Indirect	Mixed	Defined programs
Kundalini Yoga, Hata Yoga	Externally directed, later self directed	Focused	Direct	Emphasis	Supervised sessions with daily practice
Mindfulness Meditation	Externally directed, later self directed	Initially focused, later wide focus	Indirect	Little emphasis	Supervised programs with daily practice

Fifth, the degree of practice that is estimated as necessary varies considerably between different Mind-Body-interventions. For example, some mindfulness trainings expect their students to practice for approximately one hour daily, whereas the Alexander Techniques is organized around one or more classes each week.

In the following paragraphs we present brief descriptions of the techniques. The order does not imply any inherent quality rating or judgment of usefulness.

### *5.1. Alexander Technique*

This is a method originally developed by the actor Frederick Matthias Alexander (1869–1955) as a self-help treatment for his failures of voice on stage [127]. This technique places a lot of emphasis on correct anatomical posture, mainly of the spine, but also for movements. It uses mental directives or self-suggestions (“my neck is wide and free”) on top of teacher-directed movements to foster awareness of unfavorable movement and posture habits and eventually change them. It is suggested to be a helpful technique for all anatomy related pain problems, such as for chronic back pain, neck and shoulder pain or speech disorders. The Alexander Technique (AT) normally necessitates a series of single sessions until old movement patterns and postures have been unlearned and new movements incorporated. Later booster sessions are supposed to be beneficial. It is normally not possible to practice AT alone, except the self-hypnotic directives that are supposed to be integrated into daily movements.

The technique has been researched comparatively little. A recent systematic review uncovered four trials, two of which have some relevance and report promising results in back pain patients and Parkinson patients [128]. Another review found no studies allowing conclusions on the efficacy of Alexander Technique in asthma [129]. Our own randomized single-case study showed good effects in two patients with refractory stuttering [130]. A recent Randomized Controlled Trial study with 597 patients suffering from persistent back pain provided an economic evaluation of therapeutic massage, exercise and lessons in the Alexander technique [131,132]. A combination of six lessons in the Alexander technique followed by exercise turned out to be the most effective and cost-effective option.

### *5.2. Qi Gong/Tai Chi*

These Chinese movement meditations are thought to be derived from ancient martial arts training, although most forms have been compiled comparatively recently. They rest on assumptions that Chi, considered to be the universal life energy or force, is continuously used and regenerated by the body and has to be balanced between two opposite polar sides. Chi can be regenerated through breathing and moving. Hence certain prescribed sets of motions are used to regenerate Chi and to balance it within the body. Qi Gong uses slow repetitive patterns of movements with a tight coordination of breathing and moving that can be quite taxing on the muscular system, and different types of exercises are adapted for different sets of tasks. Tai Chi uses a certain series of movement figures that continuously follow each other. Depending on school and type, these movements can differ slightly and are conducted at various levels of speed. Qi Gong exercises can be used singly and incorporated into a daily program of only a few minutes. Tai Chi programs are normally longer and would take roughly 15 to 30 minutes at least. Due to their intricate patterns and their dependence on correct movements, both

techniques need experienced and qualified teachers initially, with tight supervision of correct movements, until students reach some proficiency and can benefit from their own training. Both are supposed to be practiced daily for at least 15 minutes, although Qi Gong can be also practiced for a shorter period when integrated in one's own private program.

Although old by any modern standard and well accepted as general health promoting, relaxing and integrating exercises, Tai Chi and Qi Gong have not been researched to any notable extent. One systematic review of Tai Chi in patients with rheumatoid arthritis concluded that there was very weak evidence for the effectiveness of Tai Chi. In fact only four trials were included in this review, and only one showed a clear benefit [133].

Another review summarizes Tai Chi used in six bone mineral density studies, but the conclusion is limited by the quantity and quality of these studies [134]. [135] showed that community-based Tai Chi interventions could reduce the fear of older people falling in community-accommodation.

Tai Chi as a complement to existing exercise intervention can be useful in low and intermediate risk patients in cardiac rehabilitation [136] and cancer patients [137]. It appears to have beneficial health effects, but due to the small number of studies and the lack of a theoretical foundation, it is difficult to draw firm conclusions [138]. A recent review analyzing 40 studies where Tai Chi was utilized as a clinical intervention suggested improvements in psychological well-being including reduced stress, anxiety, depression and mood disturbance as well as increased self-esteem [139]. It is also noteworthy that another review based on 13 randomized controlled trials recommended Tai Chi as an alternative treatment in older adults for improving balance and reducing falls, although it was not found to be superior to other interventions [140]. A recent trial proved it effective for fibromyalgia [141].

### 5.3. Yoga Interventions

There are large numbers of different programs that are summarized under the heading of Yoga. Yoga literally means union. Some of the yoga programs are more akin to TM or mindfulness meditation programs, as they mainly train attention and awareness whereas other Yoga forms focus more on physical training. In a way, the TM program can be viewed as a derivative and adaptation of an ancient Vedic Yogic meditation technique to modern day requirements. Kundalini Yoga, for example, is a specific type of Yoga practice which emphasizes the awakening/rise of the Kundalini force which is symbolically located as an enrolled serpent at the lower end of the spine. However, in the West, yoga is mostly associated with Hatha Yoga, which emphasizes the overcoming of the physical body limitations as a mirror to the internal mind. Through regular practice of asanas (body positions of stretching and holding) as well as breathing techniques, focusing one's attention and meditation, the union of body and mind is to be achieved. The idea being that this union will have healing and preventive effects, as well as a calming effect on the mind.

Many individual studies exist, some of them promising [142,143] but not followed up, and a bibliography details the earlier research [144]. Two recent reviews conclude that there is too little research for definitive conclusions, but that first results are encouraging [145,146]. Kundalini-Yoga has also shown effects in the treatment of obsessive-compulsive disorder (OCD) [147].

A series of studies document that Yogic meditation has clearly definable effects on the brain as shown in the EEG: mainly the power of lower frequencies (alpha, delta and theta) is enhanced, as is the coherence of the resonators across the brain [148–152].

A systematic review suggests that yoga may reduce insulin-resistant syndrome risk factors for cardiovascular disease, but most of the studies have methodological limitations [153]. There is evidence that meditation techniques (Meditation, Meditative Prayer, Yoga, Relaxation Response) might have health benefits, but that sound methodological studies are missing [154]. However, a recent review that included more than 80 studies found that yoga interventions seemed to be equal or superior to exercise in most outcome parameters measured, except those involving physical fitness [155]. Two recent trials proved Yoga efficient for the treatment of low back pain [156–158].

#### 5.4. *Transcendental Meditation*

Arguably, the best-researched mind-body intervention is Transcendental Meditation. This is a Yogic-Vedic meditation technique introduced in the West by the late Maharishi Mahesh Yogi (1918-2008). Although, strictly speaking, not necessarily dependent on this person, a large community and organization has evolved around this guru and his technique that also drove the research activities. The core of the TM program is a mantra, given out only during personally supervised sessions and supposedly individually chosen. This mantra, consisting of some Sanskrit words, is used to focus attention during the meditation process. The hypothesis is this mantra conveys some subtle spiritual benefit on the meditator, apart from acting as an aid to focus. After some training, which is supposed to consist of two sessions of 20 minutes daily training over a period of 10–16 weeks, the meditator is able to reach a state of transcendence of normal consciousness into a blissful state of pure consciousness, thought to be not only psychologically desirable, but also physically healthy [159–161].

A large number of studies have been conducted, but overviews and reviews are still not clear about the benefit of the program [145,162]. Earlier meta-analyses and reviews comparing randomized studies conducted to date have been largely supportive [163], with moderate to sizeable effect sizes between Cohen's  $d = 0.33$  to  $d = 1.5$  [159]. Skeptics sometimes criticize the non-randomized nature of some of the evidence, for instance for less health care use [164–166] or crime prevention [165,166]. However, the over-rigid adherence to allegedly omnivalent quality standards derived from pharmacological trials may sometimes produce false negative conclusions [162] due to the exclusion of studies that are deemed less valid or due to the insufficient expertise of reviewers in the content area itself [167]. Overall, TM seems to be useful in stress reduction and secondarily in the lowering of blood pressure [168] (although this has been doubted [162]), and in the prevention of coronary artery disease [169]. A series of promising single studies has shown the effects of TM on blood pressure and cardiovascular risk factors [170–175]. Some reviews support this [176–178], and a recent review suggested that TM may have the potential to reduce systolic and diastolic blood pressure in a clinically meaningful way [179].

#### 5.5. *The Relaxation Response*

The development and study of the relaxation response seems to be modeled along the lines of spiritual meditation programs, leading to a completely secularized counterpart. The introduction and

teaching time was radically shortened. The meditation also focuses on a mantra- like syllable, which, however, is meaningless [180]. Posture is less important and a specific content-less state of mind is not the target of the technique, but simply relaxation. Some of the research shows that even this comparatively reduced program seems to have some effects [181–186]. A recent meta analysis embracing 27 studies found that relaxation training showed a medium-large effect size in the treatment of anxiety [187].

### 5.6. Mindfulness Meditation

Mindfulness Meditation is probably one of the oldest meditation techniques, tracing its inauguration to the historical Buddha himself. It consists in mindfully observing the breath and all mental content, both during the exercise and outside it. Ideally, it should lead to a mindful awareness of one's mental activity and in the long term also to a non-judgmental attitude towards one's own mind and other people's actions [188,189]. Mindfulness is both active (actively observing) and passive (not reacting towards what is observed) and in this and other aspects it is dialectical [188]. While the original practice clearly is religious in intent in that it was supposed to be a means to free oneself from suffering through enlightenment, the modern adoptions often use just the technique without the religious and philosophical background. One of the most popular adoptions is Mindfulness Based Stress Reduction (MBSR)[2] and two further developments, Mindfulness Based Cognitive Therapy (MBCT) [190], which is a program for depression relapse therapy, and Dialectical Behavior Therapy [191], in which the principles of mindfulness have been included into a specialized program of therapy for borderline patients. A common feature of these programs is that they use principles of mindfulness and teach formal mindfulness meditation to patients, urging them to daily practice at least within the eight-week programs. In a meta-analysis published in 2003 of studies on MBSR, Baer *et al.* found an effect size of  $d = 0.70$  for anxiety and  $d = 0.84$  for depression [192]. We found in a meta analysis published in 2004 that MBSR was effective in improving psychological and physical health outcomes across various diseases with an effect size of  $d = 0.53$ , which can be considered a medium effect that is worthwhile, considering the chronicity of the diseases studied [193]. However, a more recent meta-analysis published by Bohlmeijer *et al.*, based on 8 studies of moderate to good quality investigating the effect of MBSR on mental health of adults with a chronic medical disease, found only smaller effect sizes ranging from  $d = 0.47$  for anxiety and  $d = 0.26$  for depression [194]. In a similar way, MBCT proved effective in preventing relapse in patients with recurrent depression in controlled studies [195–197] but is at present not seen as a completely reliable intervention by others, as the results of studies are equivocal [198].

Pain patients seem particularly able to profit from mindfulness, although not from pain alleviation as such. Nevertheless, mindfulness seems to install a cognitive distance between the experience of pain and the cognitive reaction towards it. In our study on MBSR in fibromyalgia patients building on an effective pilot study [199,200], one of our patients said: "I have been bossed around by my pain all my life. Now I just don't bother any longer and go on holidays." It was the first time this lady had taken some time out for more than 20 years. She did not go without pain, but with more freedom.

## 6. Final Remarks and Conclusions

Mind-body techniques have a clear place in integrative medical care. They are, together with placebo research, the systematic place where it becomes clear that mental activity, techniques and practices have a clearly recognizable and direct influence on the body [201]. Most mind-body techniques seem to be effective, although conclusive statements cannot be made as yet. They are popular, because patients intuitively want this holistic approach. They seem to understand sometimes more clearly than their physicians that part of their physical problem may be due to some emotional-mental ailment and that treating this mental realm might also be beneficial for their bodies. Although we are only slowly beginning to understand how the interconnections between the psyche and the body operate, due to our greater knowledge of the immunological and endocrinological connections between the brain and the periphery, in principle, we have enough knowledge to understand how stressful and soothing, noci-ceptive and healing reactions and influences can travel either way. Hence, it seems natural also to employ these mind-body techniques as therapeutic options. It is clearly more difficult to study those techniques as they are always complex interventions, operating with an array of potential specific and non-specific effects. Such complex interventions cannot be studied by simple research designs modeled along the lines of pharmaceutical interventions [202,203]. Rather, they need a diligent, stepwise approach in which general effectiveness is established first, before dismantling trials might be able to tackle the question about which component might be important and which component could be dispensed with. A lot of time, money and effort have to be put into research programs like that, and considering the limited amount of funding available it will take a score of years until we have the desired, firm knowledge base. Until then, we will have to rely on proxy-studies and proof of principle evidence. This we have. We have enough knowledge in general to be confident that some of the techniques—meditation and mindfulness relaxation, and body work—can be beneficially employed. Here as elsewhere, these techniques will only be beneficial if patients themselves see a point in involving their mental and psychological lives in their healing process. If they do, a mind-body technique might be the first step towards more wholeness and healing, as patients understand that it does not make sense to cure the body without tackling their psychological wounds and *vice-versa*. We are therefore of the opinion that mind-body techniques constitute a superior approach to attaining holistic health.

## Acknowledgments

Harald Walach and Niko Kohls are grateful for the long standing support of the Samueli Institute, USA. Marie-Louise Gander was supported by the Swiss National Fund at the time this work was conducted.

## References and Notes

1. Latorre, M.A. A holistic view of psychotherapy: Connecting mind, body, and spirit. *Perspect. Psychiatr. C.* **2000**, *36*, 67–68.
2. Kabat-Zinn, J. *Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness*; Delacorte: New York, NY, USA, 1991.

3. Kabat-Zinn, J. *Wherever You Go, There You Are*; Hyperion Books: New York, NY, USA, 1994.
4. Walach, H. Mind - body - spirit. *Mind Matter* **2007**, *5*, 215–239.
5. Kohls, N.; Benedikter, R. The origins of the modern concept of ‘‘neuroscience’’ - wilhelm wundt between empiricism and idealism: Implications for contemporary neuroethics. In *Scientific and Philosophical Perspectives in Neuroethics*; Giordano, J., Gordijn, B., Eds.; Cambridge University Press: Cambridge, UK, 2010; pp. 37–65.
6. Kohls, N. *Aussergewöhnliche erfahrungen - blinder fleck der psychologie? Eine auseinandersetzung mit aussergewöhnlichen erfahrungen und ihrem zusammenhang mit geistiger gesundheit*; Lit-Verlag: Münster, Germany, 2004.
7. Du Bois-Reymond, E. *Jugendbriefe von emile dubois-reymond an eduard hallmann*; Dietrich Reiner: Berlin, Germany, 1918.
8. Churchland, P.S. *Neurophilosophy. Toward a Unified Science of the Mind-Brain*; MIT Press: Cambridge, MA, USA, 1986.
9. Metzinger, T. *Neural Correlates of Consciousness: Empirical and Conceptual Questions*; MIT Press: Cambridge, MA, USA, 2000.
10. Wegner, D.M.; Wheatley, T. Apparent mental causation. Sources of the experience of will. *Am. Psychol.* **1999**, *54*, 480–492.
11. Libet, B. Do we have free will? *J. Conscious. Stud.* **1999**, *6*, 47–57.
12. Damasio, A. *The Feeling of What Happens. Body, Emotion, and the Making of Consciousness*; Vintage: London, UK, 2000.
13. Laureys, S.; Owen, A.M.; Schiff, N.D. Brain function in coma, vegetative state, and related disorders. *Lancet Neurol.* **2004**, *3*, 537–546.
14. Tononi, G. An information integration theory of consciousness. *BMC Neurosci.* **2004**, *5*, 42.
15. Can, R. Are thalamocortical rhythms the rosetta stone of a subset of neurological disorders? *Nat. Med.* **1999**, *5*, 1349.
16. Jeanmonod, D.; Schulman, J.; Ramirez, R.; Cancro, R.; Lanz, M.; Morel, A.; Magnin, M.; Siegemund, M.; Kronberg, E.; Ribary, U.; *et al.* Neuropsychiatric thalamocortical dysrhythmia: Surgical implications. *Thalamus Relat. Syst.* **2003**, *2*, 103–113.
17. Kübler, A.; Neumann, N.; Kaiser, J.; Kotchoubey, B.; Hinterberger, T.; Birbaumer, N. Brain-computer communication: Self-regulation of slow cortical potentials for verbal communication. *Arch. Phys. Med. Rehab.* **2001**, *82*, 1533–1539.
18. Kübler, A.; Kotchoubey, B.; Hinterberger, T.; Ghanayim, N.; Perelmouter, J.; Schauer, M.; Fritsch, C.; Taub, E.; Birbaumer, N. The thought translation device: A neurophysiological approach to communication in total motor paralysis. *Exp. Brain Res.* **1999**, *124*, 223–232.
19. Kim, D.Y.; Camilleri, M. Serotonin: A mediator of the brain-gut connection. *Am. J. Gastroenterol.* **2000**, *95*, 2698–2709.
20. Damasio, A. *The Feeling of What Happens: Body and Emotion in the Making of Consciousness*; Harcourt: New York, NY, USA, 1999.
21. Tang, Y.; Ma, Y.; Fan, Y.; Feng, H.; Wang, J.; Feng, S.; Lu, Q.; Hu, B.; Lin, Y.; Li, J. Central and autonomic nervous system interaction is altered by short-term meditation. *P. Natl. Acad. Sci.* **2009**, *106*, 8865–8870.

22. Heitkemper, M.; Burr, R.L.; Jarrett, M.; Hertig, V.; Lustyk, M.K.; Bond, E.F. Evidence for autonomic nervous system imbalance in women with irritable bowel syndrome. *Digest. Dis. Sci.* **1998**, *43*, 2093–2098.
23. Petzke, F.; Clauw, D.J. Sympathetic nervous system function in fibromyalgia. *Curr. Rheumatol. Rep.* **2000**, *2*, 116–123.
24. Martinez-Lavin, M. The autonomic nervous system and fibromyalgia. *J. Musculoskel. Pain* **2002**, *10*, 221–228.
25. Hiramoto, R.N.; Rogers, C.F.; Demissie, S.; Hsueh, C.-M.; Hiramoto, N.S.; Lorden, J.F.; Ghanta, V.K. Psychoneuroendocrine immunology: Site of recognition, learning and memory in the immune system and the brain. *Int. J. Neurosci.* **1997**, *92*, 259–286.
26. Kiecolt-Glaser, J.K.; McGuire, L.; Robles, T.F.; Glaser, R. Emotions, morbidity, and mortality: New perspectives fro psychoneuroimmunology. *Ann. Rev. Psychol.* **2002**, *53*, 83–107.
27. Ray, O. How the mind hurts and heals the body. *Am. Psychol.* **2004**, *59*, 29–40.
28. Mössner, R.; Mikova, O.; Koutsilieri, E.; Saoud, M.; Ehliis, A.C.; MÃ¼ller, N.; Fallgatter, A.J.; Riederer, P. Consensus paper of the wfsbp task force on biological markers: Biological markers in depression. *World J. Biol. Psychiatry* **2007**, *8*, 141–174.
29. Schins, A.; Dorien, T.; Richel, L.; Gunter, K.; Delanghe, J.; Crijns, H.; Grauls, G.; Stassen, F.; Maes, M.; Honig, A. Inflammatory markers in depressed post-myocardial infarction patients. *J. Psychiatr. Res.* **2005**, *39*, 137–144.
30. Römer, H.; Walach, H. Complementarity of phenomenal and physiological observables: A primer on generalized quantum theory and its scope for neuroscience and consciousness studies. In *Neuroscience, Consciousness and Spirituality*; Walach, H., Schmidt, S., Jonas, W., Eds.; Springer: Dordrecht, The Netherlands, 2011; pp 97–107.
31. Walach, H.; Römer, H. Generalized entanglement—A nonreductive option for a phenomenologically dualist and ontologically monist view of consciousness. In *Neuroscience, Consciousness and Spirituality*; Walach, H., Schmidt, S., Jonas, W., Eds.; Springer: Dordrecht, The Netherlands, 2011; pp. 81–95.
32. Giordano, J.; Kohls, N. Spirituality, suffering, and the self. *Mind Matter* **2008**, *6*, 179–191.
33. Bendelow, G.; Williams, S. Pain and the mind-body dualism: A sociological approach. *Body Soc.* **1995**, *1*, 83–103.
34. Llin ás, R.; Ribary, U.; Jeanmonod, D.; Cancro, R.; Kronberg, E.; Schulman, J.; Zonenshayn, M.; Magnin, M.; Morel, A.; Siegmund, M. Thalamocortical dysrhythmia i. Functional and imaging aspects. *Thalamus Relat. Syst.* **2001**, *1*, 237–244.
35. Llin ás, R.; Ribary, U.; Jeanmonod, D.; Kronberg, E.; Mitra, P.P. Thalamocortical dysrhythmia: A neurological and neuropsychiatric syndrome characgterized by magnetoencephalography. *Proc. Natl. Acad. Sci. USA* **1999**, *96*, 15222–15227.
36. Nagel, T. What is it like to be a bat? *Philos. Rev.* **1974**, *83*, 435–450.
37. Chalmers, D.J. *The Conscious Mind. In Search of a Fundamental Theory*; Oxford University Press: New York, NY, USA, 1996.
38. Hoche, H. *Anthropological Complementarism: Linguistic, Logical, and Phenomenological Studies in Support of a Third Way beyond Dualism and Monism*; Mentis: Paderborn, Germany, 2008.

39. Fahrenberg, J.; Cheetham, M. The mind-body problem as seen by students of different disciplines. *J. Conscious. Stud.* **2000**, *7*, 47–59.
40. McGinn, C. Can we solve the mind-body problem? *Mind* **1989**, *98*, 349–366.
41. Richardson, R.C. The "Scandal" Of cartesian interactionism. *Mind* **1982**, *91*, 20–37.
42. Beck, F.; Eccles, J.C. Quantum aspects of brain activity and the role of consciousness. *Proc. Natl. Acad. Sci. USA* **1992**, *89*, 111357–111361.
43. Pereira, A. The quantum mind/classical brain problem. *NeuroQuantology* **2003**, *1*, 94–118.
44. Hameroff, S.; Penrose, R. Conscious events as orchestrated space-time selections. *NeuroQuantology* **2003**, *1*, 10–35.
45. Hameroff, S.; Penrose, R. Conscious events as orchestrated space-time selections. *J. Conscious. Stud.* **1996**, *2*, 36–53.
46. Schwartz, J.; Stapp, H.; Beauregard, M. Quantum physics in neuroscience and psychology: A neurophysical model of mind–brain interaction. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **2005**, *360*, 1309–1327.
47. Greyson, B. Dissociation in people who have near-death experiences: Out of their bodies or out of their minds? *Lancet* **2000**, *355*, 460–463.
48. Greyson, B. Incidence and correlates of near-death experiences in a cardiac care unit. *Gen. Hosp. Psychiatry* **2003**, *25*, 269–276.
49. van Lommel, P. About the continuity of consciousness. *Adv. Exp. Med. Biol.* **2004**, *550*, 115–132.
50. Atmanspacher, H.; Filk, T.; Römer, H. Quantum zeno features of bistable perception. *Biol. Cybern.* **2004**, *90*, 33–40.
51. Atmanspacher, H.; Primas, H. Epistemic and ontic quantum realities. In *Time, Quantum, and Information*; Castell, L., Ischebeck, O., Eds.; Springer: Berlin, Germany, 2003; pp. 301–321.
52. Hagan, S.; Hameroff, S.R.; Tuszynski, J.A. Quantum computation in brain microtubules: Decoherence and biological feasibility. *Phys. Rev. E* **2002**, *65*, 61901–61911.
53. Penrose, R. Mechanism, microtubules and the mind. *J. Conscious. Stud.* **1994**, *1*, 241–249.
54. Beck, F. Quantum mechanics and consciousness. *J. Conscious. Stud.* **1994**, *1*, 253–255.
55. Grossberg, S. The complementary brain: Unifying brain dynamics and modularity. *Trends Cognit. Sci.* **2000**, *4*, 233–245.
56. Feigl, H. Some crucial issues of mind-body monism. *Synthese* **1971**, *22*, 295–312.
57. Feigl, H. The "Mental" And the "Physical". In *Minnesota Studies in the Philosophy of Science*; Feigl, H., Scriven, M., Maxwell, G., Eds.; Minnesota University Press: Minneapolis, MN, USA, 1958; Volume 2, pp. 370–497.
58. Shamdasani, S. *Jung and the Making of Modern Psychology: The Dream of a Science*; Cambridge University Press: Cambridge, UK, 2003.
59. Bohr, N. *Causality and Complementarity: Essays 1958–1962 on Atomic Physics and Human Knowledge*; Vintage: New York, NY, USA, 1966.
60. Fahrenberg, J. Komplementarität in der psychophysiologischen forschung. Grundsätze und forschungspraxis. In *Widersprüchliche wirklichkeit. Neues denken in wissenschaft und alltag: Komplementarität und dialogic*; Fischer, E.P., Herzka, H.S., Reich, K.H., Eds.; Piper: München, Germany, 1992; pp. 43–77.

61. Walach, H.; Römer, H. Complementarity is a useful concept for consciousness studies. A reminder. *Neuro Endocrinol. Lett.* **2000**, *21*, 221–232.
62. Atmanspacher, H. Mind and matter as asymptotically disjoint, inequivalent representations with broken time-reversal symmetry. *Biosystems* **2003**, *68*, 19–30.
63. Kohls, N.; Hack, A.; Walach, H. Measuring the unmeasurable by ticking boxes and actually opening pandoras box? Mixed methods research as a useful tool for thinking out of the box while investigating exceptional human experiences *Arch. Psych. Relig.* **2008**, *30*, 155–187.
64. Kohls, N.; Walach, H. Exceptional experiences and spiritual practice—A new measurement approach. *Spirit Health Int.* **2006**, *7*, 125–150.
65. Kohls, N.; Walach, H.; Lewith, G. The impact of positive and negative spiritual experiences on distress and the moderating role of mindfulness. *Arch. Psych. Relig.* **2009**, *31*, 1–18.
66. Pöppel, E. Complementarity as a generative principle in visual perception. *Vis. Cogn.* **2005**, *12*, 665–670.
67. Crabtree, A. *Animal Magnetism, Early Hypnotism, and Psychical Research 1766–1925. An Annotated Biography*; Kraus International Publishers: White Plains, NY, USA, 1988.
68. Crabtree, A. *From Mesmer to Freud: Magnetic Sleep and the Roots of Psychological Healing*; Yale University Press: New Haven, CT, USA, 1993.
69. Florey, E. *Ars magnetica. Franz anton mesmer 1734–1815: Magier vom Bodensee*; Universit äsverlag Konstanz: Konstanz, Germany, 1995.
70. Ellenberger, H.F. *The Discovery of the Unconscious. The History and Evolution of Dynamic Psychiatry*; Basic Books: New York, NY, USA, 1970.
71. Makari, G. *Revolution in Mind: The Creation of Psycho-Analysis*; Harper Perennial: New York, NY, USA, 2009.
72. Tinterow, M. *Foundations of Hypnosis: From Mesmer to Freud*; Charles C. Thomas: Springfield, IL, USA, 1970.
73. Kohls, N.; Sommer, A. Die akademische psychologie am scheideweg: Positivistische experimentalpsychologie und die nemesis der transzendenz. In *Spiritualität, krankheit und heilung—bedeutung und ausdrucksformen der spiritualität in der medizin - perspektiven, schriften zur pluralität in der medizin und komplementärmedizin*; Büssing, A., Ostermann, T., Glöckler, M., Matthiessen, P., Eds.; Verlag für akademische Schriften: Frankfurt, Germany, 2006.
74. Carlson, J.; Maniaci, M. *Alfred adler revisited*; Routledge: London, UK, 2011.
75. Danzer, G. Body, mind, and psychosomatic medicine. In *Embodiment in Cognition and Culture (Advances in Consciousness Research)*; Krois, M., Rosengren, M., Steidele, A., Westerkamp, D., Eds.; John Benjamins Publishing Co: Amsterdam, The Netherlands, 2007; Volume 71, pp. 185–194.
76. Drack, M.; Wolkenhauer, O. System approaches of weiss and bertalanffy and their relevance for systems biology today. *Semin. Cancer Biol.* **2011**, *21*, 150–155.
77. Davidson, M. *Uncommon Sense: The Life and Thought of Ludwig von Bertalanffy (1901–1972), Father of General Systems Theory*; Tarcher: Los Angeles, CA, 1983.
78. Szent-Györgyi, A. Drive in living matter to perfect itself. *Synthesis* **1974**, 12–24.

79. Engel, G.L. The need for a new medical model: A challenge for biomedicine. *Science* **1977**, *196*, 129.
80. Engel, G.L. The biopsychosocial model and medical education. *N. Engl. J. Med.* **1982**, *306/13*, 802–805.
81. Meyer-Abich, K.M. Wie ganzheitlich ist die gesundheit? Von hippokrates und platon bis zu einer kuenftigen sozio-psykosomatischen situationstherapie. *Forsch Komplementarmed Klass Naturheilkd* **2003**, *10*, 35–39.
82. Ader, R.; Cohen, N. Behaviorally conditioned immunosuppression. *Psychosom. Med.* **1975**, *37*, 333–340.
83. Ader, R. Behavioral conditioning and immunity. In *Immunoregulation*; Fabris, N., Garaci, E., Hadden, J., Mitchison, N.A., Eds.; Plenum Press: New York, NY, USA, 1983; pp. 283–313.
84. Ader, R.; Cohen, N. The influence of conditioning on immune responses. In *Psychoneuroimmunology*, 2nd ed.; Ader, R., Felten, D.L., Cohen, N., Eds.; Academic Press: San Diego, CA, USA, 1991; pp. 611–646.
85. Ader, R. Conditioned immunomodulation: Research needs and directions. *Brain Behav. Immun.* **2003**, *17*, 51–57.
86. van Stegeren, A.; Wolf, O.; Everaerd, W.; Scheltens, P.; Barkhof, F.; Rombouts, S. Endogenous cortisol level interacts with noradrenergic activation in the human amygdala. *Neurobiol. Learn. Mem.* **2007**, *87*, 57–66.
87. Blalock, J.E. The syntax of immune-neuroendocrine communication. *Immunol. Today* **1994**, *15*, 504–511.
88. Van Praag, H.M.; De Kloet, R.; Van Os, J. *Stress, the Brain and Depression*; Cambridge University Press: Cambridge, UK, 2004.
89. Hellhammer, D.; Hellhammer, J. *Stress: The Brain-Body Connection*; Karger: Basel, Switzerland, 2008; Volume 174, 1–108.
90. Padgett, D.; Glaser, R. How stress influences the immune response. *Trends Immunol.* **2003**, *24*, 444–448.
91. Pollard, T.M. Adrenaline. In *Encyclopedia of Stress*; Fink, G., Ed.; Academic Press: San Diego, CA, USA, 2000; Volume 1, pp. 52–58.
92. LaBar, K.; Gatenby, J.; Gore, J.; LeDoux, P.; Phelps, E. Human amygdala activation during conditioned fear acquisition and extinction: A mixed-trial fmri study. *Neuron* **1998**, *20*, 937–945.
93. Breiter, H.; Etcoff, N.; Whalen, P.; Kennedy, W.; Rauch, S.; Buckner, R.; Strauss, M.; Hyman, S.; Rosen, B. Response and habituation of the human amygdala during visual processing of facial expression. *Neuron* **1996**, *17*, 875–887.
94. Heinrichs, S.C.; Koob, G.F. Corticotropin-releasing factor in brain: A role in activation, arousal, and affect regulation. *J. Pharmacol. Exp. Ther.* **2004**, *311*, 427–440
95. Eriksen, H.R.; Olf, M.; Murison, R.; Ursin, H. The time dimension in stress responses: Relevance for survival and health. *Psychiatry Res.* **1999**, *85*, 39–50.
96. Esch, T.; Stefano, G. The neurobiology of stress management. *Neuro Endocrinol. Lett.* **2010**, *31*, 19–39.
97. McEwen, B.S. Protective and damaging effects of stress mediators. *N. Engl. J. Med.* **1998**, *338*, 171–179.

98. Lazarus, R.S.; Folkman, S. *Stress, Appraisal, and Coping*; Springer: New York, NY, USA, 1984.
99. Melamed, S.; Ugarten, U.; Shirom, A.; Kahana, L.; Lerman, Y.; Froom, P. Chronic burnout, somatic arousal and elevated salivary cortisol levels. *J. Psychosom. Res.* **1999**, *46*, 591–598.
100. Glaser, R.; Rice, J.; Sheridan, J.; Fertel, R.; Stout, J.; Speicher, C.; Pinsky, D.; Kotur, M.; Post, A.; Beck, M.; *et al.* Stress-related immune suppression: Health implications. *Brain Behav. Immun.* **1987**, *1*, 7–20.
101. Glaser, R.; Rabin, B.; Chesney, M.; Cohen, S.; Natelson, B. Stress-induced immunomodulation. *JAMA* **1999**, *281*, 2268–2270.
102. Irie, M.; Miyata, M.; Kasai, H. Depression and possible cancer risk due to oxidative DNA damage. *J. Psychiatr. Res.* **2005**, *39*, 553–560.
103. O'Leary, A.; Brown, S.; Suarez-Al-Adam, M. Stress and immune function. In *Clinical Disorders and Stressful Life*; Miller, T.W., Ed.; International Universities Press: Madison, CT, USA, 1997; pp. 181–215.
104. McEwen, B.S. Stress and hippocampal plasticity. *Annu. Rev. Neurosci.* **1999**, *22*, 105–122.
105. Heim, C.; Ehler, U.; Hellhammer, D. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. *Psychoneuroendocrinology* **2000**, *25*, 1–35.
106. Raison, C.L.; Miller, A.H. When not enough is too much: The role of insufficient glucocorticoid signaling in the pathophysiology of stress-related disorders. *Am. J. Psychiatry* **2003**, *160*, 1554–1565.
107. Fries, E.; Hesse, J.; Hellhammer, J.; Hellhammer, D.H. A new view on hypocortisolism. *Psychoneuroendocrinology* **2005**, *30*, 1010–1016.
108. Meissner, K.; Kohls, N.; Colloca, L. Introduction to placebo effects in medicine: Mechanisms and clinical implications. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **2011**, *366*, 1783–1789.
109. Benson, H. The relaxation response: Its subjective and objective historical precedents and physiology. *Trends Neurosci.* **1983**, *6*, 281–284.
110. Benson, H.; Greenwood, M.M.; Klemchuk, H. The relaxation response: Psychophysiological aspects and clinical applications. *Int. J. Psychiatry Med.* **1975**, *6*, 87–98.
111. Aldwin, C.M. *Stress, Coping, and Development: An Integrative Perspective*; The Guilford Press: New York, NY, USA, 2007.
112. Grossman, P.; Taylor, E. Toward understanding respiratory sinus arrhythmia: Relations to cardiac vagal tone, evolution and biobehavioral functions. *Biol. Psychol.* **2007**, *74*, 263–285.
113. Stefano, G.B.; Fricchione, G.L.; Esch, T. Relaxation: Molecular and physiological significance. *Med. Sci. Monit.* **2006**, *12*, HY21–HY31.
114. Esch, T. Stress, anpassung und selbstorganisation: Gleichgewichtsprozesse sichern gesundheit und überleben. *Forsch Komplementarmed Klass Naturheilkd* **2003**, *10*, 330–341.
115. Tang, Y.; Ma, Y.; Wang, J.; Fan, Y.; Feng, S.; Lu, Q.; Yu, Q.; Sui, D.; Rothbart, M.; Fan, M. Short-term meditation training improves attention and self-regulation. *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 17152–17156.
116. Tang, Y.; Posner, M. Attention training and attention state training. *Trends Cogn. Sci.* **2009**, *13*, 222–227.
117. Giordano, J. Chronic pain and spirituality. *Prac. Pain Manage.* **2007**, *7*, 64–68.
118. Giordano, J. Complementarity, brain/mind, and pain. *Forsch Komplementmed* **2008**, *15*, 2–6.

119. Demitrack, M.; Crofford, L. Evidence for and pathophysiologic implications of hypothalamic-pituitary-adrenal axis dysregulation in fibromyalgia and chronic fatigue syndrome. *Ann. N. Y. Acad. Sci.* **1998**, *840*, 684–697.
120. Kumar, M. Epidemiology, pathophysiology and symptomatic treatment of sciatica: A review. *nt. J. Pharm. Bio. Arch.* **2011**, *2*.
121. Chambers, D.; Bagnall, A.; Hempel, S.; Forbes, C. Interventions for the treatment, management and rehabilitation of patients with chronic fatigue syndrome/myalgic encephalomyelitis: An updated systematic review. *JRSM* **2006**, *99*, 506–520.
122. Fries, E.; Hesse, J.; Hellhammer, J.; Hellhammer, D. A new view on hypocortisolism. *Psychoneuroendocrinology* **2005**, *30*, 1010–1016.
123. von Känel, R.; Mills, P.; Fainman, C.; Dimsdale, J. Effects of psychological stress and psychiatric disorders on blood coagulation and fibrinolysis: A biobehavioral pathway to coronary artery disease? *Psychosom. Med.* **2001**, *63*, 531–544.
124. Schwartz, J. A role for volition and attention in the generation of new brain circuitry. Toward a neurobiology of mental force. *J. Conscious. Stud.* **1999**, *6*, 115–142.
125. Le Moal, M.; Koob, G. Drug addiction: Pathways to the disease and pathophysiological perspectives. *Eur. Neuropsychopharmacol.* **2007**, *17*, 377–393.
126. Li, C.R.; Sinha, R. Inhibitory control and emotional stress regulation: Neuroimaging evidence for frontal-limbic dysfunction in psycho-stimulant addiction. *Neurosci. Biobehav. Rev.* **2008**, *32*, 581–597.
127. Alexander, F.M. *The Use of the Self*; Methuen & Co. Ltd.: London, UK, 1932.
128. Ernst, E.; Canter, P.H. The alexander technique: A systematic review of controlled trials. *Forsch Komplementarmed Klass Naturheilkd* **2003**, *10*, 325–329.
129. Dennis, J. Alexander technique for chronic asthma. *Cochrane Database Syst. Rev.* **2000**, CD000995.
130. Schulte, D.; Walach, H. F.M. Alexander technique in the treatment of stuttering—A randomized single-case intervention study with ambulatory monitoring. *Psychother. Psychosom.* **2006**, *75*, 190–191.
131. Hollinghurst, S.; Sharp, D.; Ballard, K.; Barnett, J.; Beattie, A.; Evans, M.; Lewith, G.; Middleton, K.; Oxford, F.; Webley, F. Randomised controlled trial of alexander technique lessons, exercise, and massage (ateam) for chronic and recurrent back pain: Economic evaluation. *Br. Med. J.* **2008**, *337*.
132. Little, P.; Lewith, G.; Webley, F.; Evans, M.; Beattie, A.; Middleton; Barnett, J.; Ballard, K.; Oxford, F.; Smith, P., *et al.* Randomised controlled trial of alexander technique lessons, exercise, and massage (ateam) for chronic and recurrent back pain. *Br. J. Sports Med.* **2008**, *42*, 965–968.
133. Han, A.; Judd, M.G.; Robinson, V.A.; Taixiang, W.; Tugwell, P.; Wells, G. Tai chi for treating rheumatoid arthritis. *Cochrane Database Syst. Rev.* **2004**, *Issue 3*, Art. No. CD004849.
134. Wayne, P.M.; Kiel, D.P.; Krebs, D.E.; Davis, R.B.; J., S.-G.; Connelly, M.; Buring, J.E. The effects of tai chi on bone mineral density in postmenopausal women: A systematic review. *Arch. Phys. Med. Rehabil.* **2007**, *88*, 673–680.

135. Zijlstra, G.A.; van Haastregt, J.C.; van Rossum, E.; van Eijk, J.T.; Yardley, L.; Kempen, G.I. Interventions to reduce fear of falling in community-living older people: A systematic review. *J. Am. Soc. Geriatr.* **2007**, *55*, 603–615.
136. Arthur, H.M.; Patterson, C.; Stone, J.A. The role of complementary and alternative therapies in cardiac rehabilitation: A systematic evaluation. *Eur. J. Cardiovasc. Prev. Rehabil.* **2006**, *13*, 3–9.
137. Mansky, P.; Sannes, T.; Wallerstedt, D.; Ge, A.; Ryan, M.; Johnson, L.L.; Chesney, M.; Gerber, L. Tai chi chuan: Mind-body practice or exercise intervention? Studying the benefit for cancer survivors. *Integr. Cancer Ther.* **2006**, *5*, 192–201.
138. Wang, C.; Collet, J.P.; Lau, J. The effect of tai chi on health outcomes in patients with chronic conditions: A systematic review. *Arch. Intern. Med.* **2004**, *164*, 493.
139. Wang, C.; Bannuru, R.; Ramel, J.; Kupelnick, B.; Scott, T.; Schmid, C. Tai chi on psychological well-being: Systematic review and meta-analysis. *BMC Complement Altern. Med.* **2010**, *10*, 23.
140. Leung, D.; Chan, C.; Tsang, H.; Tsang, W.; Jones, A. Tai chi as an intervention to improve balance and reduce falls in older adults: A systematic and meta-analytical review. *Altern. Ther. Health Med.* **2011**, *17*, 40.
141. Wang, C.; Schmid, C.; Rones, R.; Kalish, R.; Yinh, J.; Goldenberg, D.; Lee, Y.; McAlindon, T. A randomized trial of tai chi for fibromyalgia. *N. Engl. J. Med.* **2010**, *363*, 743–754.
142. Haslock, I.; Monro, R.; Nagarathna, R.; Nagendra, H.R.; Raghuram, N. Measuring the effects of yoga in rheumatoid arthritis. *Br. J. Rheumatol.* **1994**, *33*, 787–788.
143. Harinath, K.; Malhotra, Pal, K.; Prasad, R.; Kumar, R.; Kain, T.C.; Rai, L.; Sawhney, R.C. Effects of hatha yoga and omkar meditation on cardiorespiratory performance, psychologic profile, and melatonin secretion. *JACM* **2004**, *10*, 261–268.
144. Monro, R.E.; Ghosh, A.K.; Kalish, D. *Yoga Research Bibliography*; Yoga Ciomedical Trust: Cambridge, UK, 1989.
145. Krisanaprakornkit, T.; Krisanaprakornkit, W.; Piyavhatkul, N.; Laobaiboon, M. Meditation therapy for anxiety disorders. *Cochrane Database Syst. Rev.* **2006**, CD004998.
146. Ramaratnam, S.; Sridharan, K. Yoga for epilepsy. *Cochrane Database Syst. Rev.* **2002**, CD001524.
147. Shannahoff-Khalsa, D.S. Kundalini yoga meditation techniques for the treatment of obsessive compulsive and oc spectrum disorders. *Brief Treat. Crisis Interv.* **2003**, *3*, 369–382.
148. Aftanas, L.I.; Golocheikine, S.A. Human anterior and frontal midline theta and lower alpha reflect emotionally positive state and internalized attention: High-resolution eeg investigation of meditation. *Neurosci. Lett.* **2001**, *310*, 57–60.
149. Aftanas, L.I.; Golocheikine, S.A. Non-linear dynamic complexity of the human eeg during meditation. *Neurosci. Lett.* **2002**, *330*, 143–146.
150. Aftanas, L.I.; Golosheykin, S. Impact of regular meditation practice on eeg activity at rest and during evoked negative emotions. *Int. J. Neurosci.* **2005**, *115*, 433–443.
151. Lehmann, D.; Faber, P.L.; Achermann, P.; Jeanmonod, D.; Gianotti, L.R.R.; Pizzagalli, D. Brain sources of eeg gamma frequency during volitionally meditation-induced, altered states of consciousness, and experience of the self. *Psychiatry Res.* **2001**, *108*, 111–121.

152. Lehmann, D.; Faber, P.L.; Gianotti, L.R.R.; Kochi, K.; Pascual-Marqui, R.D. Coherence and phase locking in the scalp eeg and between loreta model sources, and microstrates as putative mechanisms of brain temporo-spatial functional organization. *J. Physiol. Paris* **2006**, *99*, 29–36.
153. Innes, K.E.; Bourguignon, C.; Taylor, A.G. Risk indices associated with the insulin resistance syndrome, cardiovascular disease, and possible protection with yoga: A systematic review. *J. Am. Board Fam. Med.* **2005**, *18*, 491–519.
154. Arias, A.J.; Steinberg, K.; Banga, A.; Trestman, R.L. Systematic review of the efficacy of meditation techniques as treatments for medical illness. *JACM* **2006**, *12*, 817–832.
155. Ross, A.; Thomas, S. The health benefits of yoga and exercise: A review of comparison studies. *JACM* **2010**, *16*, 3–12.
156. Sherman, K.; Cherkin, D.; Erro, J.; Miglioretti, D.; Deyo, R. Comparing yoga, exercise, and a self-care book for chronic low back pain. *Ann. Intern. Med.* **2005**, *143*, 849–856.
157. Sherman, K.; Cherkin, D.; Wellman, R.; Cook, A.; Hawkes, R.; Delaney, K.; Deyo, R.A. A randomized trial comparing yoga, stretching, and a self-care book for chronic low back pain. *Arch. Intern. Med.* **2011**, *171*, 2019–2026.
158. Tilbrook, H.; Cox, H.; Hewitt, C.; Kang'ombe, A.; Chuang, L.; Jayakody, S.; Aplin, J.; Semlyen, A.; Trehwela, A.; Watt, I. Yoga for chronic low back pain. *Ann. Intern. Med.* **2011**, *155*, 569–578.
159. Alexander, C.N.; Rainforth, M.V.; Gelderloos, P. Transcendental meditation, self-actualization, and psychological health: A conceptual overview and statistical meta-analysis. *J. Soc. Behav. Pers.* **1991**, *6*, 189–247.
160. Yunesian, M.; Aslani, A.; Vash, J.; Yazdi, A. Effects of transcendental meditation on mental health: A before-after study. *Clin. Pract. Epidemiol. Ment. Health* **2008**, *4*, 25.
161. MacLean, C.; Walton, K.; Wenneberg, S.; Levitsky, D.; Mandarino, J.; Waziri, R.; Hillis, S.L.; Schneider, R. Effects of the transcendental meditation program on adaptive mechanisms: Changes in hormone levels and responses to stress after 4 months of practice. *Psychoneuroendocrinology* **1997**, *22*, 277–295.
162. Canter, P.H.; Ernst, E. Insufficient evidence to conclude whether or not transcendental meditation decreases blood pressure: Results of a systematic review of randomized clinical trials. *J. Hypertens.* **2004**, *22*, 2049–2054.
163. Alexander, C.N.; Robinson, P.; Orme-Johnson, D.; Schneider, R.H.; Walton, K.G. The effects of transcendental meditation compared to other methods of relaxation and meditation in reducing risk factors, morbidity, and mortality. *Homeostasis* **1994**, *35*, 243–263.
164. Orme-Johnson, D.W. Medical care utilization and the transcendental meditation program. *Psychosom. Med.* **1987**, *49*, 493–507.
165. Alexander, C.N.; Walton, K.G.; Orme-Johnson, D.; Goodman, R.S.; Pallone, N.J., *Transcendental Meditation in Criminal Rehabilitation and Crime Prevention*; Haworth Press: New York, NY, USA, 2003.
166. Dillbeck, M.C.; Banus, C.B.; Polanzi, C.; Landrith, G.S. Test of a field model of consciousness and social change: The transcendental meditation and tm-sidhi program and decreased urban crime. *J. Mind Behav.* **1988**, *9*, 457–486.

167. Orme-Johnson, D.W.; Barnes, V.A.; Hankey, A.M.; Chalmers, R.A. Reply to critics of research on transcendental meditation in the prevention and control of hypertension. *J. Hypertens.* **2005**, *23*, 1107–1110.
168. Schneider, R.H.; Alexander, D.N.; Wallace, R.K. In search of an optimal behavioral treatment for hypertension: A review and focus on transcendental meditation. In *Personality, elevated blood pressure, and essential hypertension*, Johnson, E.H.; Gentry, W.D.; Julius, S., Eds.; Hemisphere: Washington, DC, USA, 1992; pp. 291–312.
169. Calderon, R., Jr.; Schneider, R.H.; Alexander, C.N.; Myers, H.F.; Nidich, S.I.; Haney, C. Stress, stress reduction and hypercholesterolemia in african americans: A review. *Ethn. Dis.* **1999**, *9*, 451–462.
170. Alexander, C.N.; Schneider, R.H.; Staggers, F.; Sheppard, W.; Clayborne, B.M.; Rainforth, M.; Salerno, J.; Kondwani, K.; Smith, S.; Walton, K.G.; *et al.* Trial of stress reduction for hypertension in older african americans. Ii. Sex and risk subgroup analysis. *Hypertension* **1996**, *28*, 228–237.
171. Alexander, C.N.; Langer, E.J.; Newman, R.I.; Chandler, H.M.; Davies, J.L. Transcendental meditation, mindfulness, and longevity: An experimental study with the elderly. *J. Pers. Soc. Psychol.* **1989**, *57*, 950–964.
172. Barnes, V.A.; Johnson, M.H.; Treiber, F.A. Impact of stress reduction on ambulatory blood pressure in african-american adolescents. *Ethn. Dis.* **2003**, *13*, S2–S173.
173. Barnes, V.A.; Treiber, F.A.; Davis, H. Impact of transcendental meditation on cardiovascular function at rest and during acute stress in adolescents with high normal blood pressure. *J. Psychosom. Res.* **2001**, *51*, 597–605.
174. Castillo-Richmond, A.; Schneider, R.H.; Alexander, C.N.; Cook, R.; Myers, H.; Nidich, S.; Haney, C.; Rainforth, M.; Salerno, J. Effects of stress reduction on carotid atherosclerosis in hypertensive african americans. *Stroke* **2000**, *31*, 568–573.
175. Schneider, R.H.; Alexander, C.N.; Staggers, F.; Orme-Johnson, D.W.; Rainforth, M.; Salerno, J.W.; Sheppard, W.; Castillo-Richmond, A.; Barnes, V.A.; Nidich, S.I. A randomized controlled trial of stress reduction in african americans treated for hypertension for over one year. *Am. J. Hypertens.* **2005**, *18*, 88–98.
176. Walton, K.G.; Schneider, R.H.; Nidich, S. Review of controlled research on the transcendental meditation program and cardiovascular disease. Risk factors, morbidity, and mortality. *Cardiol. Rev.* **2004**, *12*, 262–266.
177. Walton, K.G.; Schneider, R.H.; Nidich, S.I.; Salerno, J.W.; Nordstrom, C.K.; Bairey Merz, C.N. Psychosocial stress and cardiovascular disease part 2: Effectiveness of the transcendental meditation program in treatment and prevention. *Behav. Med.* **2002**, *28*, 106–123.
178. Schneider, R.H.; Walton, K.G.; Salerno, J.W.; Nidich, S.I. Cardiovascular disease prevention and health promotion with the transcendental meditation program and maharishi consciousness-based health care. *Ethn. Dis.* **2006**, *16*, S4-15-26.
179. Anderson, J.; Liu, C.; Kryscio, R. Blood pressure response to transcendental meditation: A meta-analysis. *Am. J. Hypertens* **2008**, *21*, 310–316.

180. Kutz, I.; Borysenko, J.; Benson, H. Meditation and psychotherapy: A rationale for the integration of dynamic psychotherapy, the relaxation response, and mindfulness meditation. *Am. J. Psychiatry* **1985**, *142*, 1–8.
181. Garvin, A.W.; Trine, M.R.; Morgan, W.P. Affective and metabolic responses to hypnosis, autogenic relaxation, and quiet rest in the supine and seated positions. *Int. J. Clin. Exp. Hypn.* **2001**, *49*, 5–18.
182. Jorgensen, M. Autonomic and psychological responses to an acute psychological stressor and relaxation: The influence of hypnotizability and absorption. *Int. J. Clin. Exp. Hypn.* **2000**, *48*, 388–403.
183. Keefer, L.; Blanchard, E.B. The effects of relaxation response meditation on the symptoms of irritable bowel syndrome: Results of a controlled treatment study. *Behav. Res. Ther.* **2001**, *39*, 801–811.
184. Peters, R.K.; Benson, H.; Peters, J.M. Daily relaxation response breaks in a workig population. Ii. Effects on bloodpressure. *Am. J. Public Health* **1977**, *67*, 954–959.
185. Peters, R.K.; Benson, H.; Porter, D. Daily relaxation response breaks in a working population. I. Effects on self-reported measures of health, perfomrance and well-being. *Am. J. Public Health* **1977**, *67*, 946–953.
186. Mandle, C.L.; Jacobs, S.C.; Arcari, P.M.; Domar, A.D. The efficacy of relaxation response interventions with adult patients: A review of the literature. *J. Cardiovasc Nurs.* **1996**, *10*, 4–26.
187. Manzoni, G.; Pagnini, F.; Castelnuovo, G.; Molinari, E. Relaxation training for anxiety: A ten-years systematic review with meta-analysis. *BMC Psychiatry* **2008**, *8*, 41.
188. Sauer, S.; Lynch, S.; Walach, H.; Kohls, N. Dialectics of mindfulness: Implications for western medicine. *Philos. Ethics Humanit. Med.* **2011**, *6*, 10.
189. Kohls, N.; Sauer, S.; Walach, H. Facets of mindfulness—results of an online study investigating the freiburg mindfulness inventory. *Pers. Individ. Dif.* **2009**, *46*, 224–230.
190. Segal, Z.V.; Williams, J.M.G.; Teasdale, J.D. *Mindfulness-Based Cognitive Therapy for Depression: A New Approach to Preventive Relapse*; Guilford Press: New York, NY, USA, 2002.
191. Linehan, M.M. *Cognitive Behavioral Treatment of Borderline Personality Disorder*; Guilford Press: New York, NY, USA, 1993.
192. Baer, R.A. Mindfulness training as a clinical intervention: A conceptual and empirical review. *Clin. Psychol.* **2003**, *10*, 125–143.
193. Grossman, P.; Schmidt, S.; Niemann, L.; Walach, H. Mindfulness based stress reduction and health: A meta-analysis. *J. Psychosom. Res.* **2004**, *37*, 35–43.
194. Bohlmeijer, E.; Prenger, R.; Taal, E.; Cuijpers, P. The effects of mindfulness-based stress reduction therapy on mental health of adults with a chronic medical disease: A meta-analysis. *J. Psychosom. Res.* **2009**, *68*, 539–544.
195. Teasdale, J.D.; Segal, Z.V.; Williams, J.M.G.; Ridgeway, V.A.; Soulsby, J.M.; Lau, M.A. Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *J. Consult. Clin. Psychol.* **2000**, *68*, 615–623.
196. Fjorback, L.; Walach, H. Meditation based therapies: A systematic review and some critical observations. *Religions* **2012**, *3*, 1–18.

197. Keng, S.; Smoski, M.; Robins, C. Effects of mindfulness on psychological health: A review of empirical studies. *Clin. Psychol. Rev.* **2011**, *31*, 1041–1056.
198. Toneatto, T.; Nguyen, L. Does mindfulness meditation improve anxiety and mood symptoms? A review of the controlled research. *Can. J. Psychiatry* **2007**, *52*, 260–266.
199. Grossman, P.; Tiefenthaler-Gilmer, U.; Raysz, A.; Kesper, U. Mindfulness training as an intervention for fibromyalgia: Evidence of postintervention and 3-year follow-up benefits in well-being. *Psychother. Psychosom.* **2007**, *76*, 226–233.
200. Schmidt, S.; Grossman, P.; Schwarzer, B.; Jena, S.; Naumann, J.; Walach, H. Treating fibromyalgia with mindfulness-based stress reduction: Results from a 3-armed randomized controlled trial. *Pain* **2010**, *152*, 361–369.
201. Kohls, N.; Sauer, S.; Offenbacher, M.; Giordano, J. Spirituality: An overlooked predictor of placebo effects? *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **2011**, *366*, 1838–1848.
202. Fonnebo, V.; Grimsgaard, S.; Walach, H.; Ritenbaugh, C.; Norheim, A.J.; MacPherson, H.; Lewith, G.; Launso, L.; Koithan, M.; Falkenberg, T.; *et al.* Researching complementary and alternative treatments - the gatekeepers are not at home. *BMC Med. Res. Methodol.* **2007**, *7*.
203. Boon, H.; MacPherson, H.; Fleishman, S.; Grimsgaard, S.; Koithan, M.; Norheim, A.J.; Walach, H. Evaluating complex healthcare systems: A critique of four approaches. *Evid. Based Complement Alternat. Med.* **2007**, *4*, 279–286.

© 2012 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/3.0/>).