

The Physiology of Mind–Body Interactions: The Stress Response and the Relaxation Response

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ABSTRACT

There are key differences between mind–body medicine and alternative medicine. A central tenet of mind–body medicine is the recognition that the mind plays a key role in health and that any presumed separation of mind and body is false. Alternative medicine, however, does not focus on the role of thoughts and emotions in health and, therefore, is separate from mind–body medicine. Also, while there has been little scientific research on alternative medicine, the literature on mind–body medicine comprises more than 2000 peer-reviewed studies published in the past 25 years. The groundwork for understanding the physiology of mind–body interactions was established by pioneering studies in the 1930s by Walter Cannon, and in the 1950s by Walter Hess and by Hans Selye that led to an understanding of the fight-or-flight response. Later work by Holmes and Rahe documented measurable relationships between stressful life events and illness. Other research has shown clinical improvement in patients treated with a placebo for a variety of medical problems. The effectiveness of placebo treatment can be interpreted as compelling evidence that expectation and belief can affect physiological response. Recent studies using spectral analysis and topographic electroencephalographic (EEG) mapping of the relaxation response demonstrate that by changing mental activity we can demonstrate measurable changes in central nervous system activity. These, and other, studies demonstrate that mind–body interactions are real and can be measured.

It is an honor to be here to represent Harvard Medical School, Harvard Medical International, and the Mind–Body Medical Institute at Harvard Medical School. It is also an honor to address our friends, colleagues, and gracious hosts here at the Asan Medical Center. In my first talk, I'd like to talk about the physiology of mind–body interactions.

First of all, let me define mind–body medicine. Yesterday, mind–body medicine was described as part of complementary medicine. In fact, there are some key differences between mind–body medicine and complementary or

alternative medicine. First, one of the key definitions of mind–body medicine is that the mind—that is, thoughts and emotions—affects health. So one of the central tenets of mind–body medicine is the recognition that the mind plays a key role in health and that Cartesian dualism—that is, separation of mind and body—is false. The media, the public, and health care professionals, however, often conceptualize mind–body medicine as alternative medicine, and include mind–body medicine with therapies like acupuncture or herbal remedies. In fact, most alternative medicine

treatments, such as acupuncture or herbal remedies, have nothing to do with mind-body medicine because they do not focus on the role of thoughts and emotions in health.

A second difference between mind-body medicine and complementary or alternative medicine is that alternative medicine is not only young in terms of a science, but there is comparatively little research on alternative and complementary medicine relative to mind-body medicine. In fact, mind-body medicine is based on more than 2000 scientific studies that have been published in peer-reviewed journals in the last 25 years.

My contention is that, because mind-body medicine involves this kind of empirical research base, it should not be considered alternative and, in fact, should be considered mainstream. For example, in the United States, we have half a dozen journals—scientific peer-reviewed journals—that are specifically devoted to mind-body medicine. Some of the journals include biofeedback and self-regulation, behavioral medicine, psychosomatic medicine, and health psychology. There are dozens of other journals including the *Journal of the American Medical Association* and even the *New England Journal of Medicine* that publish studies on mind-body medicine.

Another difference between mind-body medicine and alternative medicine is the concept of self-care. In fact, Herbert Benson of the Harvard Medical School, who is one of the pioneers in mind-body medicine, uses the model of what he terms the “three-legged stool,” in which mind-body medicine is not intended to replace standard medical care, such as surgery and drugs, but should be used in conjunction with it. In Dr. Benson’s model of the three-legged stool, each leg—pharmaceuticals, surgery and procedures, and self-help techniques in the form of mind-body interventions—all work to support health (Benson, 1996). One of the pluses of mind-body medicine’s self-help techniques is that patients are actually given techniques that they learn and practice independently from an external agent or a health-care professional. Once they have learned the techniques, they can use the techniques on their own. That empowers the patient and increases the patient’s sense of self-control, which, as I

will talk about in my second lecture, is actually important for health maintenance. Developing a sense of control is an attitude and a belief that is associated with improved health and longevity.

I’d like to talk next about some of the scientific underpinnings of mind-body medicine by starting with what is called the fight-or-flight response, which, in a very real sense, formed the basis of the physiology of mind-body interactions. First, mind-body medicine is the result of a long history of research on the psychophysiological connections between the brain and the nervous, hormonal, and immune systems. This research initially focused on stress and its effects on the body.

The first person to conduct research in mind-body medicine, although they didn’t term it mind-body medicine then, and who studied the fight-or-flight response—or what we now term the stress response—was Walter Cannon, a physiologist at Harvard Medical School who conducted his research in the 1930s. Cannon documented the physiological effects of what he termed the “emergency reaction,” which he defined as an acute physiologic reaction that prepares the organism for fighting or fleeing. Cannon described the physiologic changes associated with the fight-or-flight response as being characterized by increased sympathetic nervous system activity, increased central nervous system arousal, and increased skeletal-muscle activity. He went on to define specific correlates of these physiologic changes, including reduced blood flow to the gut and extremities during fight or flight; increased blood flow to the muscles, heart, and lungs to aid in fighting or fleeing; and increased blood sugars among many other changes (Cannon, 1932).

Interestingly, Cannon also hypothesized that stress not only induces these physiologic changes, but he also believed that stress precipitates sudden death via ventricular fibrillation based on his studies on voodoo death. Later in the 1950s, the Swiss physiologist, Walter Hess, was awarded the Nobel Prize for his research on electrical stimulation of the hypothalamus in cats. Hess initially documented what he termed the “ergotropic responses,” which was his term for the emergency reaction.

He defined the ergotropic response as a hypothalamically mediated response. It is characterized by increased sympathetic, cortical, and skeletal muscle activation. Hess would also document an opposite response that we now term the “relaxation response,” which I will return to shortly (Hess, 1957).

The other key physiologist credited with the initial research on the effects of stress and emotions on the body is Hans Selye, who, in the 1950s, studied the neuroendocrine effects of the fight-or-flight response and the resulting general adaptation syndrome. Selye conceptualized stress and its effects on the body as consisting of three phases that make up the general adaptation syndrome. The first phase is an alarm phase in which the fight-or-flight response is elicited for mobilization and gearing up for fight or flight. A second phase is called a resistance phase in which the organism fights the stressor, but the acute fight-or-flight response ceases. And then, a third phase, which he termed the exhaustion phase, in which the organism can no longer adapt to the stressor. It is this third phase, the exhaustion phase, that Selye showed could result in illness, including shrinkage of thymus, the spleen, and the lymph nodes, also peptic ulcers, and, in some cases, death (Selye, 1956).

After or around the time that Hans Selye was conducting his research, two scientists developed a model in which they were able to begin to document the effects of stress, in particular, stressful life events, not just on the body, but on morbidity and mortality. This was the Holmes and Rahe Schedule of Recent Experiences, which is an inventory that assigns numerical ranking to various life events, from divorce to changing jobs, or moving, all the way down to a recent illness (Rahe, 1964). Holmes and Rahe and subsequent epidemiologic research on the relationship between stress and illness, documented consistent, measurable relationships between stressful life events and illness. For example, stressful life events have been linked to sudden cardiac death, pregnancy and birth complications, diabetes, and overall susceptibility to illness. In 1992, a review by two National Institutes of Health scientists in the *Journal of the American Medical Association* noted the role of stress in autoimmune diseases, coronary heart

disease, gastrointestinal disorders, chronic pain, and a range of other medical as well as psychiatric disorders (Chrousos and Gold, 1992). In all of these disorders it is believed that the effect of stressful life events on morbidity and mortality is mediated by overactivation of the fight-or-flight response.

The other research that supports the idea that the mind interacts with the body and affects health is research on the placebo effect. This research was done initially by Henry Beecher at the Harvard Medical School in the 1950s. Dr. Eisenberg discussed the placebo effect yesterday, and the fact that he educates his physicians and residents about the placebo effect. I would like to cover some of Beecher’s findings concerning the placebo effect, because these findings are powerful evidence of the effect that thoughts, beliefs, and expectations can have on the body and on health (Beecher, 1955).

Research on the placebo effect demonstrates that approximately one third of patients exhibit clinical improvement in response to a placebo pill for a variety of medical problems. Much of these findings come from randomized, double-blind trials. For example, curative placebo effects have been substantiated in illnesses ranging from headaches, angina pain, insomnia, hay fever, and arthritis. Evidence supports the efficacy of the placebo effect in yielding between 20% to 70% of relief of symptoms in controlled studies. Beecher’s studies at Harvard Medical School documented that 30% to 40% of pain patients report responding as well to a placebo pill as they do to 10 mg of morphine. In a review of more than 1000 patients, Beecher found that 35% of patients would be significantly relieved of severe pain by the double-blinded administration of a placebo.

Several researchers have found that a placebo is 50% as effective as any analgesic, including morphine, and that placebos can actually reverse the action of potent drugs. In fact, several researchers have argued that the history of medicine prior to the twentieth century was the history of the placebo effect. Instead of regarding the placebo effect as a nuisance variable, it should be viewed as providing powerful evidence of mind–body interactions—that is, the effects of expectation and belief on the body (Shapiro, 1971).

I ask you to imagine what it would be like if a drug was discovered today that had the same curative properties as the placebo effect. I think it would be an impressive drug.

The most recent research on the relationship between the mind and body involves research in the field of psychoneuroimmunology, which is the study of the relationship between the brain, thoughts and emotions, and the immune system. These studies demonstrate a connection between the central nervous system and the immune system that were until recently believed to act independently (Kiecolt-Glaser and Glaser, 1988). These studies, once again, disprove the notion of Cartesian dualism. For example, psychoneuroimmunology research over the past 10 to 15 years has shown that nerve endings can be found in the thymus, the spleen, and the lymph nodes (Ader et al., 1990). Additionally, the immune cells respond directly to chemical signals produced by the nervous system.

Robert Ader at the University of Rochester showed that immune responses can be conditioned through the central nervous system by pairing an immunosuppressing drug with saccharine (Ader et al., 1990). He eventually demonstrated that the administration of saccharine alone could cause an immunosuppressive effect and, ultimately, death. Around 1985, the *New England Journal of Medicine* published an editorial in which it characterized the effects of mental states on the body as folklore. Six years later, it published a landmark study that documented a direct link between the mind and the immune system by showing a relationship between levels of psychologic stress and susceptibility to infection by a common cold virus (Cohen et al., 1991).

It is perhaps ironic that the same fight-or-flight response that was designed to help us in our evolution can now actually harm us. Based on this large body of evidence, there is growing consensus that mind-body interactions in the form of excessive activation of the fight-or-flight response, in which it is not possible to fight or flee from modern day stressors, can cause or exacerbate many health problems via the central nervous system, the peripheral nervous system, and the immune system. For example, concerning cardiovascular disorders, stress has been repeatedly linked to hyperten-

sion, heart disease, heart attacks, and death, primarily in the areas of hostility, job strain, and lack of social support. Stress has also been linked to increased cholesterol, constriction of coronary arteries, and ischemia, as well as cardiac arrhythmias.

Recently, hostility has been associated with increased coronary blockage, increased risk of heart attack, and increased risk of dying from all causes. Redford Williams, in research at Duke University on the relationship between hostility and heart disease, has shown that hostile men are seven times more likely to die within 25 years from any cause compared to less hostile men (Williams and Williams, 1993). In numerous studies assessing stress in the laboratory, stress has been shown to result in increased blood pressure, heart rate, and reduced blood flow to the heart.

In the area of musculoskeletal disorders, stress has been linked to muscle contraction headaches and back pain (Budzynski et al., 1970; Caudill, 1994). For gastrointestinal disorders, stress has been implicated in irritable bowel syndrome, which is a syndrome characterized by abdominal pain, irregular bowel movements, constipation, and diarrhea. Stress has been shown to increase gastric secretion. It alters the contractions of the small intestine and colon, affects the time required for food to move through the gastrointestinal tract, and alters the balance of sympathetic and parasympathetic functioning in the gastrointestinal tract. In one study, two thirds of patients said that stress alters their bowel patterns, and 50% of patients reported abdominal pain from stress. In another study on patients with irritable bowel syndrome, stress caused pain or bowel pattern changes in 85% of those patients (Whitehead, 1993).

Concerning the central nervous system, stress has been linked to a variety of problems, including insomnia (Morin, 1993) and negative emotions, such as hostility, anxiety, and even depression (LeDoux, 1996). For example, Martin Seligman's work on learned helplessness shows that uncontrollable stressors can lead to a state of apathy and depression (Seligman, 1975). Stressful life events are also the primary precipitators of insomnia. And recent studies demonstrate that increased daytime stress is as-

sociated with increased nocturnal stress hormones, that is, catecholamines (Kiecolt-Glaser and Glaser, 1988). And these increased nocturnal stress hormones have been shown to be associated with reduced slow-wave sleep and increased complaints of insomnia.

In my research on insomnia, I also found that insomniacs exhibit elevated presleep cortical arousal, as measured by power spectral analysis, and that they not only demonstrate increased cortical arousal relative to good sleepers, but that this is consistent with central nervous system activation via the fight-or-flight response (Jacobs et al., 1993).

Concerning the immune system, stress has repeatedly been shown to cause immunosuppression. Particularly, the work of Ron Glaser and Janice Kiecolt-Glaser at Ohio State University has repeatedly shown that stress and immunosuppression can be measured through job loss, marital conflict, marital separation, divorce, loneliness, academic examinations, bereavement, and caring for family members with a debilitating illness such as Alzheimer's disease. Stress has also been shown to increase the risk of acute, infectious respiratory illness and herpes virus.

Most of the research on mind–body medicine

concerns the effects of stress on health. An impressive body of evidence has also been gathered suggesting that it is possible to, at least to some extent, control mind–body interactions. For example, Edmond Jacobson, in the 1930s in the United States, published research on progressive muscle relaxation (Jacobsen, 1938), and Schultz and Luthe in Germany in the 1950s, published their work on autogenic training (Schultz and Luthe, 1959), which are the two earliest mind–body techniques. In progressive muscle relaxation, patients learn to tense and relax various muscle groups throughout their body and to discriminate low levels of tension and relaxation as they progress in their training around the body, hence progressive muscle relaxation. In autogenic training—autogenic means self-induced—patients learn to self-induce relaxation by autosuggesting to themselves phrases of warmth and heaviness in the body. Numerous peer-reviewed scientific studies on these two techniques document that they are more effective than control conditions in reducing central nervous system and peripheral nervous system arousal (Lehrer and Woolfolk, 1984).

Another mind–body technique is biofeedback, which was researched extensively beginning in the 1970s in the United States. Biofeed-

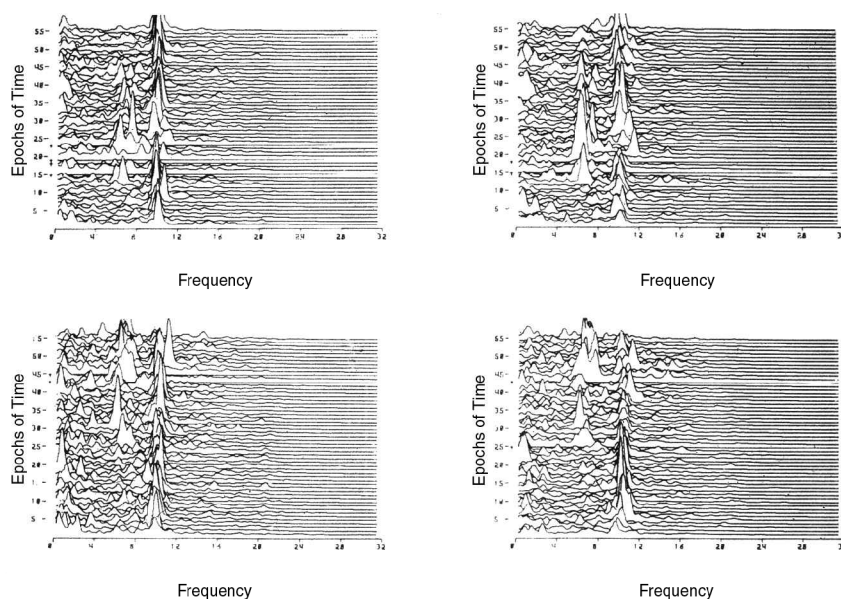


FIG. 1.

back is the use of electronic instrumentation to mirror, or feed back to individuals, information that they are normally not aware of, or information that is normally unconscious. Biofeedback was one of the first mind-body techniques in which a significant amount of scientific research documented that it was possible to achieve greater voluntary control over the autonomic nervous system and the central nervous system, including electroencephalograms (EEGs), heart rate, hand temperature, peripheral blood flow, galvanic skin response, and other physiologic parameters (Blanchard and Epstein, 1978).

In the 1970s, Dr. Herbert Benson at Harvard Medical School, who initially conducted research on blood pressure control in monkeys using biofeedback, later began to study meditation. He demonstrated that meditation, a classic Eastern mind-body technique, was another technique that allowed greater control over the peripheral and central nervous systems (Benson et al., 1974). His discoveries were made in the same laboratory that Walter Cannon used for his research 60 years earlier on the emergency reaction. It is perhaps ironic that two of the key researchers in mind-body medicine conducted their initial research in laboratories at Harvard Medical School.

When Walter Hess conducted his Nobel Prize-winning research on the cat hypothalamus, he also noted a contrasting set of responses characterized by reduced sympathetic nervous, cortical, and skeletal muscle activity, which Hess termed the "trophotropic response." Hess hypothesized that this parasympathetic response was a protective mechanism against overstress that promotes restorative processes. Benson drew heavily on Hess's work and proposed what he termed the "relaxation response" model, a model in which Benson suggested that all mind-body techniques, including biofeedback, meditation, progressive muscle relaxation, autogenic training, *tai chi*, *chigong*, *yoga*, and other techniques, elicit a common physiologic response that Benson termed the relaxation response.

Benson hypothesizes that the relaxation response is hypothalamically mediated and that it is an inborn counterbalancing mechanism to the stress response. Benson also suggested that

there are four elements necessary to elicit the relaxation response. They include relaxed musculature, a quiet environment, passive disregard of everyday thought, and the focus of attention on a repetitive mental stimulus, such as a word, a sound, a phrase, or even repetitive breathing.

Benson's relaxation response model is now widely used to explain the therapeutic effects of the relaxation response on various health problems. Literature reviews generally concur that all relaxation-response techniques are characterized by reduced stress hormones and reduced central nervous system activity in the form of measurable brain wave changes (West, 1980). In fact, a literature review by Michael West on the brain wave changes associated with relaxation response techniques indicates that, in the majority of scientific studies on the relaxation response, there is a measurable increase in alpha amplitude at the beginning of

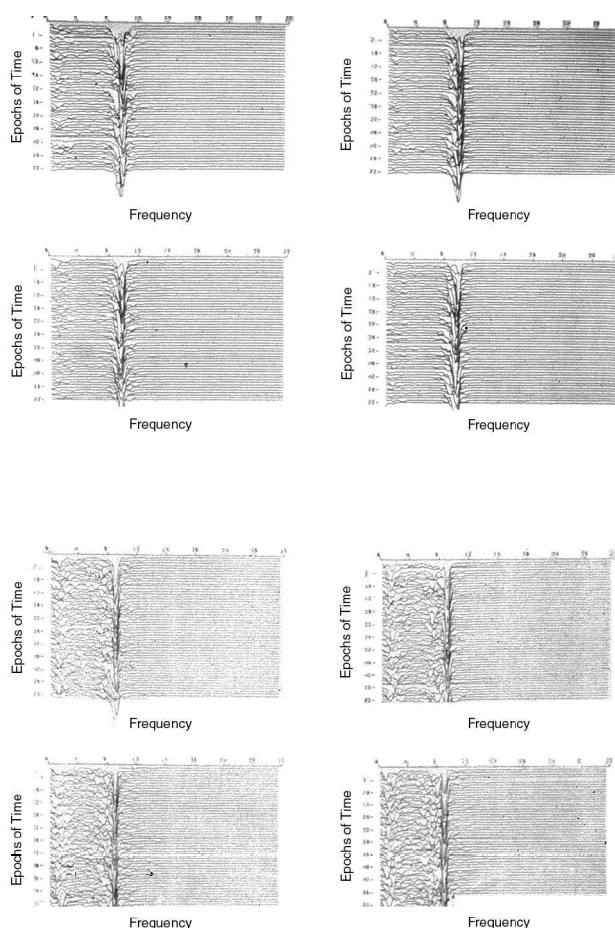


FIG. 2.

the relaxation response, a slowing of alpha frequency by one to three cycles per second and, later in meditation, theta trains or increased theta activity intermixed with alpha activity.

In my research, using power spectral analysis and topographic EEG mapping, I conducted a study in which I trained college students on the relaxation response, or an appropriate control condition, over an 8-week period (Jacobs and Lubar, 1989). Figure 1 shows compressed spectral arrays of EEG activity. On the horizontal axis are the various EEG frequency bands: Delta is 0 to 3, theta is 4 to 7, alpha is 8 to 12, and beta is 13 to 32 cycles per second. The vertical axes are epochs of time, with each epoch representing approximately 15 seconds of EEG activity. The area under each individual curve tells us about the amount of relative power in various EEG bands.

Figure 1 shows spectral plots of one channel of EEG activity in the left hemisphere and the right hemisphere in a control subject, in which the subject was sitting in a comfortable chair in a quiet room. Subjects were told to passively disregard everyday thought, but while listening to a control tape, which was taped novels. In this plot, you see that the typical EEG pattern for somebody who is very relaxed initially is the predominant alpha pat-

tern, both during the first 15 minutes of this trial and then during an additional 15 minutes. Figure 2 is also a plot of control subjects in which there is a very consistent alpha pattern. Figures 3 and 4 are plots of the relaxation response subjects; in the first 15-minute plot, they, too, listened to the taped novels. We again see a very predominant consistent alpha pattern. After 15 minutes, they were instructed to elicit the relaxation response and we see an immediate drop in alpha power followed by a significant increase in theta, and even delta, percent total power in both hemispheres. This is consistent across the majority of subjects.

This is a simple, but quantitative demonstration of the fact that, by altering mental activity in the form of a repetitive mental stimulus (in other words, changing cognitive activity), we can demonstrate measurable changes in central nervous system activity. Figure 5 depicts topographic EEG maps of subjects who came into our laboratory and had never elicited the relaxation response. We wanted to determine if there are measurable changes in central nervous system activity the first time somebody elicits the relaxation response (Jacobs et al., 1996). Figure 5 is a map of beta EEG activity, which is a measure of cortical activation.

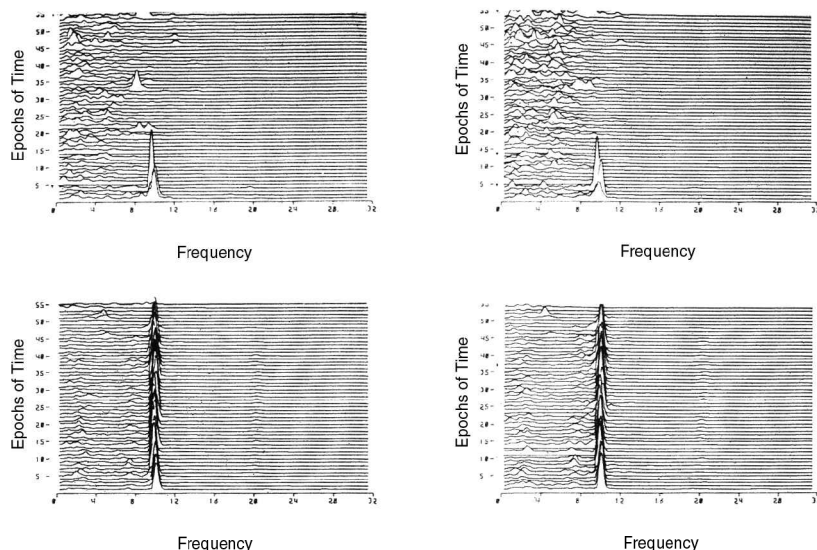
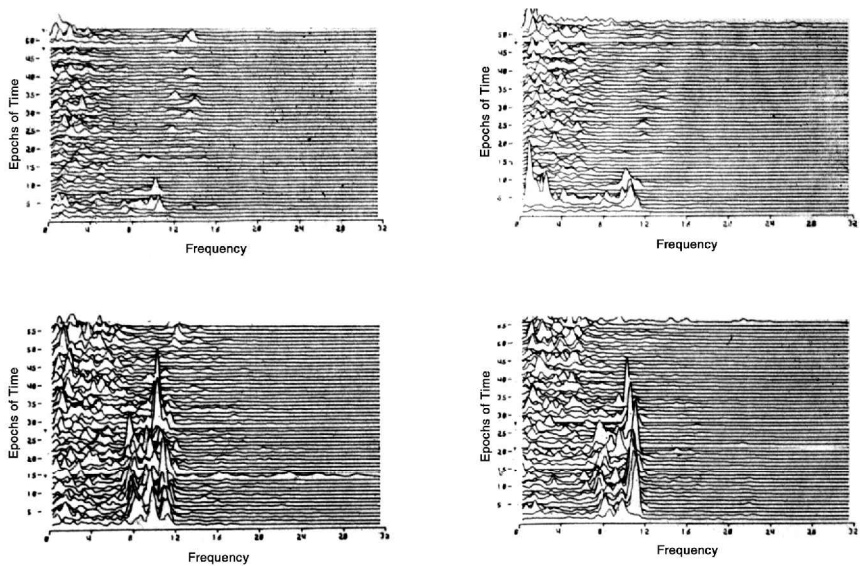
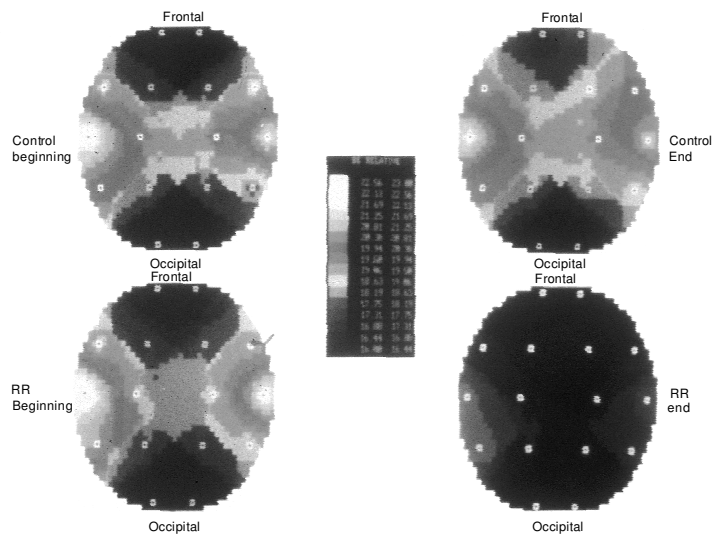


FIG. 3.



The map on the top left, labeled “Control Beginning,” is the first 5 minutes of a 15-minute control condition in which subjects listened to a tape of somebody describing the benefits of the relaxation response, but not actually instructing them on how to elicit the relaxation response. (The brighter the color, the more beta

activity.) The last 5 minutes of the control condition, labeled “Control End,” on the top right, show that, even when somebody sits in a quiet room, in a comfortable chair, beta activity remains relatively constant over 15 minutes. The experimental subjects exhibit a similar amount of beta activity during the first 5 min-



Vertical color bar indicates beta relative power (white highest, black lowest). Topographic maps are displayed in relative spectral power for greater resolution.

Note: at RR end (lower right), beta relative power is significantly ($p<.0164$) decreased in frontal areas.

FIG. 5.

utes of the relaxation response (labeled “RR Beginning,” on the lower left). However, during the last 5 minutes of the relaxation response (labeled “RR End,” on the lower right), they showed a significant reduction in anterior brain regions in beta activity, suggesting that even the first time that somebody elicits the relaxation response, we can observe measurable reductions in cortical arousal. In fact, this may explain why presurgical patients are able to use the relaxation response the very first time they practice it to reduce presurgical anxiety and to lessen the need for medication before, during, and after surgery (Mandle et al., 1990).

Regular elicitation of the relaxation response not only appears to mitigate the effects of the stress response. As I will discuss in my second lecture, the relaxation response has also been shown to be effective in the treatment of many health problems, which I will review in detail, including musculoskeletal disorders, gastrointestinal disorders, cardiovascular disorders, and others, including stabilizing blood sugars in diabetics, reducing nausea associated with chemotherapy, reducing the severity of arthritis, insomnia, and also reducing hostility and anxiety (Benson, 1996).

The research on the physiology of mind–body interactions, specifically the stress response and the relaxation response, demonstrate that mind–body interactions, that is, the effect of thoughts and emotions on the body, do exist and can be measured. Therefore, the question is not whether mind–body interactions are real, but rather, can the relaxation response and mind–body interactions be used to affect health outcome? This question will be the focus of my second talk. Thank you.

Question from the audience:

Thank you Dr. Jacobs. I have two questions. One, do you think mind–body technique is alternative medicine, or part of conventional medicine, if you had to put it in one or another category? Two, are mind–body techniques effective for pain management?

Dr. Jacobs:

I do not think that is an easy question to answer, as Dr. Eisenberg talked about yesterday. Part of the problem with this new field of alter-

native, complementary, and mind–body medicine, which I do not think is actually as new, as I pointed out, is a problem of semantics and definition. But based on my initial point—that mind–body medicine is not only defined differently in terms of its central focus on the relationship between thoughts and emotion and their effect on health and on the extensive research base that already exists, I do not think it is appropriate to describe it as alternative medicine, at least in the context of alternative and complementary therapies. And, in fact, it should be considered mainstream when the same guidelines that are used to evaluate traditional medical therapies, that is, controlled studies in peer-reviewed journals, have been applied to the field of mind–body medicine. I think it should be considered mainstream for that reason.

There has been extensive literature using mind–body techniques for back pain. Dennis Turk at the University of Pittsburgh and Margaret Caudill at Harvard Medical School have created programs to treat chronic pain conditions, including low-back pain. In these programs, mind–body therapies, including the relaxation response, and also what’s called cognitive therapy or cognitive restructuring, which I will be talking about later, have been found to be effective for various pain conditions, including low-back pain. In fact, mind–body therapies form some of the central components of those programs. So there is very good research to date, mainly in applied clinical studies but also in laboratory studies showing that mind–body techniques, in the form of the relaxation response and also cognitive restructuring techniques, are, in fact, effective for the treatment of pain.

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