Health Condition: Mental Health

"As a child, I grew up visiting my father's lab and my sister and I would play on the stairwell at the University of Montreal and between floors. We would occasionally wander onto the floor where Hans Selye's labs were. I describe in my book, recollections of this very imposing figure and I also went back and talked to Selye's former colleagues, very close friends of my family, and former students to try to piece together a picture of this man who was the person who brought the word 'stress' into the dictionary of virtually every language around the world. He borrowed it from the physicists and used it in the way that we understand it today, as the perturbation of the response of an organism to the various perturbations in the environment that we experience."
—Esther Sternberg, MD
Author of *The Balance Within: The Science Connecting Health and Emotions*
September, 2005

The Stress of Life

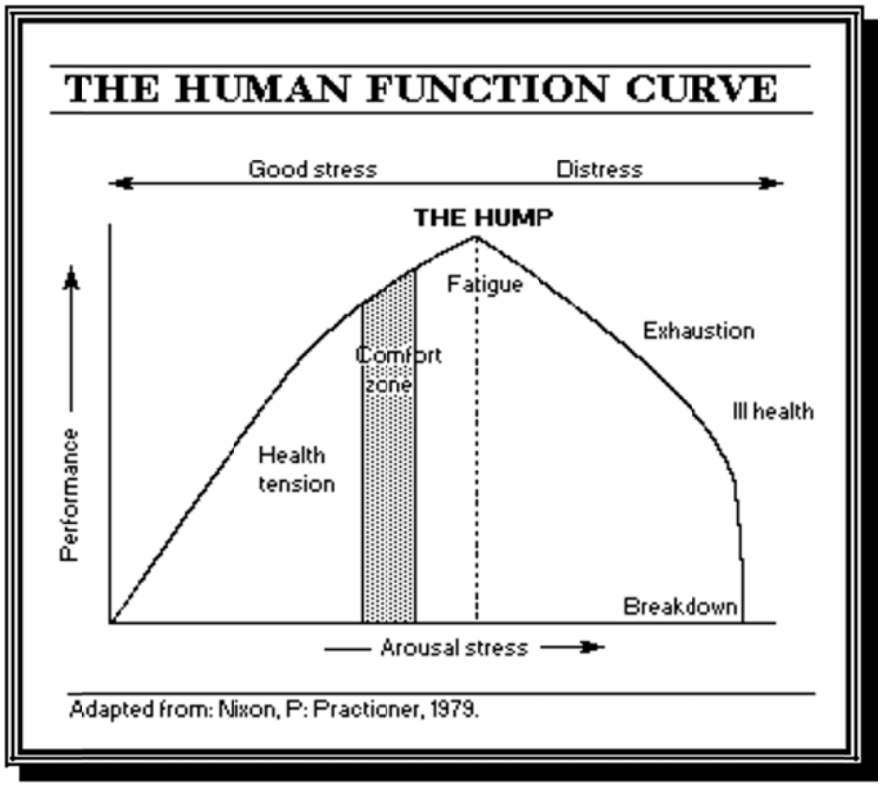
Stress is a word that has multiple meanings, similar to the word 'love.' In general, it is commonly used to refer to unpleasant phenomena, although it is related to a function necessary to our life. As the father of stress research, Hans Selye, MD, PhD, once commented, "Without stress, there is no life." Stress in itself is not a disease, but an adaptive response of our body to an outside demand. It gives rise to a mobilization of our body through the neuroendocrine system to succeed in a group of activities necessary to individual and social life. Under acute conditions, the body can produce the necessary stress hormones, and come back to its homeostatic state through subsequent restoration. However, in chronic stress, there is no significant recovery for the body, resulting in a multitude of symptoms, and, ultimately, any number of disease conditions. Many medical recommendations focus on 'reducing' stress, although it is probably more realistic to suggest that we can 'manage' stress more than reduce it. Dr. Mimi Guarneri, cardiologist and Medical Director of the Scripps Center for Integrative Medicine, has discussed the possibility of 'transforming' stress into positive outcomes.

It may come as a surprise that the word "stress," nowadays used to describe a physiological so common in 21st century life, has actually only been used with this definition since the 1950s. Hans Selye, MD, PhD (1907-1982), an Austrian endocrinologist based first at McGill University and later at the University of Montreal, is the father of our understanding of the word "stress," a concept he borrowed from physics and applied to physiology. Selye conducted research on animals and was able to make the connection between the adrenal glands, stress, and physiological function. He was obviously a keen observer who used his observations to put together a theme that is now a cornerstone of the way medicine is practiced in the 21st century: the endocrine/environmental interrelationship and how our nociceptor and propioreceptor systems respond to our environment through perceptions of stress or distress.

The hypothalamus/pituitary/adrenal (HPA) axis represents the antennae of our body that are out there sampling the energy of our world. The hypothalamus receives the signal of stress which leads to the production of corticotrophin releasing hormone, stimulating the pituitary gland to further engage the adrenal glands through its release of adrenocorticotrophin releasing hormone. These endocrine antennae are assessing our outer environment and matching it to our inner reserves. Is it harmonic

friendly energy, or dysfunctional energy that is outside the range of harmonic coordinated function that we call dis-energy or distress?

With his model of stress, Selye described the general adaptation syndrome (GAS). GAS has three stages. First is arousal, in which the adrenal glands are stimulated to action and pour out cortisol. After arousal, comes adaptation. The person says, "I'm not under stress; everything is fine." The adrenal glands are still hypertrophied, and they are in an altered state of physiological function, different messenger molecules. They are living in a state of hyperadrenaline and hypercortisol. Finally, if we push too hard, too long, and too intensely, we get what we used to call a nervous breakdown. Selye called it adrenal exhaustion. Exhaustion is the third stage of the GAS. We might say that people in our culture are running out of GAS in our physiological response to our lifestyle. Dr. Selye helped us understand how our environment and our perception of that environment through our sensory systems can be translated into physiological function.



In 1968, Bruce McEwen, PhD, found glucocorticoid receptors present in the brain. Glucocorticoids are a class of steroid hormones that can cross the blood/brain barrier. Once in the brain, glucocorticoids have an interesting preference for the hippocampus, which is the brain structure that is heavily involved in learning and memory. The work of Dr. McEwen led to the hypothesis that chronic stress could lead to memory impairment because of the action of these hormones. Dr. McEwen also developed the concept of allostatic load, meaning, what happens when you ask a body to adapt too often? You cannot always adapt. The allostatic load concept has been widely tested by the MacArthur Studies on Successful Aging

in the US, and what they have shown is that an allostatic load score (basically calculating the number of biological measures getting very high and dysregulated) is a good predictor of stress level. With allostasis, we adapt through changes, sometimes subtle shifts, in our environment over time. However, allostatic adjustments may come with a cost – for example, we may have had to adapt to a stressful environment for several years, resulting in progressively increasing elevations in blood pressure transitioning from normotension to prehypertension and on to Stage I hypertension. As author Peter Sterling writes, "But the allostasis model suggests that there is no defect - it proposes that hypertension emerges as the concerted response of multiple neural effectors to prediction of a need for vigilance." (Peter Sterling. Principles of allostasis: optimal design, predictive regulation, pathophysiology and rational therapeutics. IN: Allostasis, Homeostasis, and the Costs of Adaptation J. Schulkin; Cambridge University Press, 2004).

The work of pioneering researchers such as Selye and McEwen led, in the later part of the 20th century, to discoveries such as neuropeptides on the surface of white cell membrane binding sites, the substances secreted by our nervous system in response to perceptions of how our environment is influencing us. We now see that the immune system is a brain, and the brain is an immune system. An immune system and a brain travel through our cells. The mediators that come from our nervous system communicate with the immune system, and the immune system signals, through its release of mediators called cytokines and chemokines, messages that are communicated to and received by the nervous system. In turn, the immune system reacts to stressors in the environment. In his 2007 article in the *Journal of the American Medical Association*, Cohen et al. suggested the following:

- The effects of stress on the regulation of immune and inflammatory processes have the potential to influence depression; infectious, autoimmune, and coronary artery disease; and at least some (eg, virally mediated) cancers.
- Psychological stress might alter immune function through direct innervation of lymphatic tissue, through release of HPA and sympathetic-adrenal hormones that bind to and alter the functions of immunologically active cells, or through stress-induced behavioral changes such as increased smoking.[1]

How Stress Affects Brain Health

"…compelling evidence now suggests that mood disorders are characterized by reduced neuronal plasticity, which can be brought about by exposure to stress at different stages of life."

-Calabrese et al. Psychoneuroendocrinology. 2009 Dec;34 Suppl 1:S208-16. Neuronal plasticity: a link between stress and mood disorders.

How does the brain protect itself from certain kinds of adverse responses from long-term stress? This has been a topic of discussion within the basic sciences and the neurosciences for some time. Recently, we have begun to see some mechanistic understanding emerge as to how the brain has evolved the ability, over millennia, to protect itself from conditions that ultimately might result in altered

neurochemicals, neurotransmitters, and immune agents that could produce things ranging from depression to neuroinflammation.

The concept of coping is an important feature of living in the 21st century. We are on sensory overload most of the time dealing with time compression. The nervous system has to mobilize the neuroendocrine immune system's coping abilities. Obviously, there are psychological control processes that can buffer the adverse consequences of stress, but there are also neurophysiological or neuroendocrine immune processes. It has been suggested that the interaction occurs between the prefrontal cortex, one of the "executive centers" of the brain, and the serotonergic system, which projects diffusely around the dorsal raphe nucleus.

Built into our coping systems is the locus of control—the escape valve. There is a takeaway from this, not to focus so much now on neurochemistry, but on real-life clinical situations. How do we get a person to introduce a locus of control into his or her life when they have a runaway system of distress working within the neuroendocrine immune system and they have lost their ability to cope, both physiologically and psychologically?

The concept of establishing locus of control is a very important therapeutic guide, or potential tool. We cannot control everything in the universe as much as we might like to. The sun still rises in the east and sets in the west, and there are variables in our lives that we have to deal with as givens. What we can do in the face of those things that are dealt to us is to develop some guidelines as to a locus of control along the road of response; in other words, some sense that we are not out of control and just victims of circumstance. That has a dramatic impact upon altering the function of the neuroendocrine immune system. When we feel that our lives are out of control and there is no escape, there is a sense of hopelessness. We have a different neuroendocrine immune milieu of triggering or mediating molecules. The concept of locus of control not only has a psychological impact, but it has a neurophysiological impact on neuroendocrine immune system function. If that person is going to be confronted with long-term alterations in his or her environment that could produce adverse effects of distress over some period of time, developing these markers for a locus of control is a very important clinical objective.

Stress & Depression

According to Cohen et al. (2007), stressful life events have been linked to major depressive disorder (MDD) as well as to depressive symptoms. During the 3 to 6 months before the onset of depression, a significant majority - 50% to 80% - of depressed persons experience a major life event, compared with only 20% to 30% of non-depressed persons. About 20-25% of people who experience major stressful events develop depression. Significant research within the past decade has indicated that mood disorders are associated with deficits or impairment of neuronal plasticity (neuronal cell “responsiveness”) rather than just to abnormalities in monoaminergic neurotransmission. Because of reduced neuronal plasticity, depressed subjects may be unable to cope or adapt to the environment and may be more vulnerable to challenging experiences.

Neurotrophic factors within the brain such as brain-derived neurotrophic factor (BDNF) seem to be correlated with the incidence of depression as indicated by postmortem studies in brains of depressed

patients. Along the lines of neurotrophic factors, inflammation has been documented to contribute to the development of neuropsychiatric disorders like depression. Inflammatory cytokines and acute phase proteins have been found to be elevated in depressed patients, and the mere injection of inflammatory stimuli has been shown to be correlated with the development of depressive symptoms. Therefore, strategies to reduce inflammation and to promote neuronal plasticity should have favorable benefits for those with depression. There is some preliminary data to suggest that inflammatory cytokine production are associated with anxiety-related disorders, which ties into depression as alternating depression/anxiety is very common.

Stress and the Influence of Social Factors

Robert Sapolsky, PhD, is one of the leading neuroscientists in the world, a research associate with the Institute of Primate Research Museums of Kenya, and a recipient of a MacArthur Fellowship. Dr. Sapolsky is also a Professor of Biological Sciences and Professor of Neurology and Neurological Sciences at Stanford University. He is the author of several books, including *The Trouble with Testosterone*, *Why Zebra's Don't Get Ulcers*, and *A Primate's Memoir*.

In 2000, Dr. Jeffrey Bland had the opportunity to interview Dr. Sapolsky about his research, both his laboratory work and his field work in Kenya which has encompassed observing a baboon troop for several decades, with particular attention paid to social structure and stress response.

Dr. Sapolsky described his work this way:

"Some of what I do is field endocrinology on wild primates each year. It reflects the range of things I've been thinking about, which is broadly in three areas. The first one is how a neuron dies as a result of aging, as a result of neurological insults—acute insults like stroke or seizure, and prolonged insults like Alzheimer's disease. Thus, my lab asks, what are some of the common features of the cell biology of neuronal vulnerability? The second area I've been thinking about for a long time is the role of stress in potentially accelerating such neuron loss (basically bad news all around), and the possibility of designing gene therapy strategies to save a neuron during one of these neurological crises. The third area is the one that I concentrate more on in my East African research. Despite all the bad news about stress and its adverse effects on health, most of us have not collapsed into puddles of stress-related diseases. Most of us cope. The persistent mystery is why some individuals cope so much better than others. What I try to understand with these wild baboons I've been going back to year after year for 20 years now, is what do social rank, social behavior, and personality have to do with which baboons get the stress-related diseases and which don't?

On a certain level, the baboon work in the field is meant to counteract a common attitude in lab science. You study something or other in the lab and you're hoping for some nice effect as a result of the manipulation you've done. The bane of every lab scientist's existence is to have a lot of variability in the endpoint, a large standard error. The result is not clear; it's not significant. You've got to do the experiment over again. You're not going to get your grant. You're not going to get your tenure. Variability is a bad thing.

Field work is entirely built around the fact that variability is not only inevitable, it's a great thing. What that means is amid a general picture of the adverse effects of aging, of stress of that sort, there's no subset of individuals who are doing spectacularly. Lab science has finally formalized this in one area—gerontology. We now have this whole sub-field of successful aging, what used to be the irritating source of variability—oh, no—10 to 15 percent of subjects don't have renal filtration rates that get worse with age, don't have blood pressure rising with age, etc. Instead, they're doing just fine. They're even doing better. Instead of that being an irritant, it's now viewed as the most interesting thing to focus on. What are these successful agers doing right? Where can the rest of us sign up? So, the field work has left me with a taste for idiosyncratic individual differences, even in inbred lab mice and rats."

What can baboons teach us about stress in our society? Dr. Sapolsky explains:

"One theme I've had over the years is that if you're going to be a baboon in the Serengeti, if you've got a choice in the matter, you don't want to be a low-ranking baboon. One thing you find is that subordinate animals have elevated blood pressure and basal levels of corticosteroids. They have less optimal immune function and the insulin-like growth factors needed for wound repair. In short, they have an array of problems we now recognize as increasing the likelihood of their developing various stress-related diseases.

In a general way, this makes perfect sense. If you're a subordinate animal, you have a disproportionate burden of physical stressors. You have a lot of psychological stressors. You're working harder for your food. You don't have as much control or predictability over resources. So, seemingly, we've just learned something about rank and physiology. This sort of thing makes it very difficult to actually do a manipulative experiment out in the wild, but you begin to see, nonetheless, that having a certain rank means a very different thing in a different sort of primate society.

In primatology these days, a term we use, which is not anthropomorphic at all, is that different primate groups have different cultures. This is an absolutely seriously accepted term these days. In the realm of baboons, you find that in some troops, it's a lot more misery-making to be a low-ranking animal than in other troops. There's more displaced aggression. There's less control of resources. Food is more limited. You may have fewer outlets for your frustration. Fewer animals are willing to groom you—that sort of thing. One thing I've seen across a number of different baboon troops is that it's not just your rank that's important, but it's the sort of society in which that rank is occurring. That's the sort of correlative evidence that would be very tough to test out in the wild in a manipulative study, where you now generate a different sort of primate society. It's not only difficult to do, but it is also generally quite frowned upon. In a wild setting, you shouldn't go about removing individuals, removing food, and that sort of thing. Instead, you look at the variability that comes across and you begin to see something interesting.

In much the same way, a fascinating thing to me in terms of the gradient between socioeconomic status and health in humans is what was initially a story very much about healthcare access. There are major deficits if you are poor in a Westernized capitalist country. It's got to have something to do with healthcare access, because you can't afford to go to the doctor as readily. If you do the cross-cultural approach, suddenly you see the gradient is virtually as strong in socialist countries, in countries with universal healthcare access. If you look at 30 different societies with very different economic systems showing the same pattern, you've just learned some important stuff. It probably has nothing to do with healthcare access.

Locus of control is a major modifier of physiology. In classic experiments, you take two lab rats, and they both get electric shocks of the same intensity, same duration, same everything. Their bodies are being challenged to exactly

equivalent extents, but one of them has its psychological environment manipulated so that it has a sense of control. It can press a lever that it believes decreases the likelihood of a shock. Or perhaps that rat has predictive information. A warning light goes on 10 seconds before each shock, creating a manipulated psychological setting in which that physical stressor occurs. Studies show you can cause a ten-fold difference in the likelihood of an ulcer, the likelihood of hypertension, and things of that sort. This internal locus of control stuff, the psychological filters with which an external trauma occurs, can have an enormous impact on some health outcomes.

The second level is more societal. It shows that an internal locus of control is not always a good thing. There is a really interesting exception, a personality profile called John Henryism, which is very predictive of cardiovascular disease and hypertension.

John Henryism, basically, is an extreme version of an inner locus of control. These are individuals who, on personality profiles, endorse statements like: 'When the going gets tough, I just work harder.' '"There's no problem you can't solve just by applying yourself.' 'If some fellow disagrees with me, I will just talk to him and we should be able to see eye to eye after a while.' This sounds terrific, doesn't it? This is a very internal locus of control: Just by effort, you can overcome the problems thrown at you. It sounds like a wonderful thing. Why is it associated with an adverse health outcome? Because John Henryism is a marker of hypertension in working-class African Americans. You can't solve some societal problems just by working harder. You can't solve racism, for example, by just sitting down with a guy, realizing we're all the same, and finding common bonds. John Henrys are people dealing with uncontrollable external sources of stress with a coping style that assumes they can control the uncontrollable."

In terms of discoveries in brain chemistry, there is a call for optimism:

"There's a recent revolution of understanding that the adult brain, even the aged brain, still undergoes neurogenesis. This is overturning 100 years of dogma that you've got all the neurons you're ever going to have by age 3. All of these are areas of tremendous optimism in terms of being able to prevent the neuron loss in the aftermath of a neurological disaster. We may be able to replace the neurons by stimulating neurogenesis or neuronal transplants, and getting the remaining neurons to make more complex interconnections. There is tremendous optimism in the field at this point."

Scientific Abstracts on Stress

Autoimmun Rev. 2008 Jan;7(3):209-13. Epub 2007 Nov 29.

Stress as a trigger of autoimmune disease.

Stojanovich L, Marisavljevich D.

Source

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Abstract

The etiology of autoimmune diseases is multifactorial: genetic, environmental, hormonal, and immunological factors are all considered important in their development. Nevertheless, the onset of at least 50% of autoimmune disorders has been attributed to "unknown trigger factors". Physical and psychological stress has been implicated in the development of autoimmune disease, since numerous animal and human studies demonstrated the effect of sundry stressors on immune function. Moreover, many retrospective studies found that a high proportion (up to 80%) of patients reported uncommon emotional stress before disease onset. Unfortunately, not only does stress cause disease, but the disease itself also causes significant stress in the patients, creating a vicious cycle. Recent reviews discuss the possible role of psychological stress, and of the major stress-related hormones, in the pathogenesis of autoimmune disease. It is presumed that the stress-triggered neuroendocrine hormones lead to immune dysregulation, which ultimately results in autoimmune disease, by altering or amplifying cytokine production. The treatment of autoimmune disease should thus include stress management and behavioral intervention to prevent stress-related immune imbalance. Different stress reactions should be discussed with autoimmune patients, and obligatory questionnaires about trigger factors should include psychological stress in addition to infection, trauma, and other common triggers.

Age (Dordr). 2012 Dec;34(6):1421-33. doi: 10.1007/s11357-011-9319-0. Epub 2011 Oct 5.

Psychological stress and aging: role of glucocorticoids (GCs).

Hasan KM, Rahman MS, Arif KM, Sobhani ME.

Source

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Abstract

Psychological stress has extreme adverse consequences on health. However, the molecular mechanisms that mediate and accelerate the process of aging due to stress hormone are not well defined. This review has focused on diverse molecular paths that come out in response to chronic psychological stress via releasing of excessive glucocorticoids (GCs), involved in the aging process. GCs suppress transcription of nuclear cell adhesion molecules which impair synaptic plasticity, memory formation, and cognitive ability. Again, GCs promote muscle atrophy by means of motivating ubiquitin proteasome system and can repress muscle protein synthesis by inhibition of PI3-kinase/Akt pathway. GCs also inhibit interleukin-2 synthesis through suppressing T cell receptor signal that leads to loss of T cell activation, proliferation, and B-cell activation. Moreover, GCs increase the expression of collagenase-3, RANK ligand, and colony stimulating factor-1 that induce bone resorption. In general, stress-induced GCs can play causal role for aging and age-related disorders.

Adv Protein Chem Struct Biol. 2012;88:1-25. doi: 10.1016/B978-0-12-398314-5.00001-5.

Inflammation in anxiety.

Salim S, Chugh G, Asghar M.

Source

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Abstract

The idea of the existence of an interaction between the immune system and the central nervous system (CNS) has prompted extensive research interest into the subject of "Psychoneuroimmunology" taking the field to an interesting level where new hypotheses are being increasingly tested. Specifically, exactly how the cross talk of pathways and mechanisms enable immune system to influence our brain and behavior is a question of immense significance. Of particular relevance to this topic is the role of cytokines in regulating functions within the CNS that ultimately modulate behavior. Interestingly, psychological stress is reported to modulate cytokine production, suggesting potential relevance of this mediator to mental health. In fact, cytokine signaling in the brain is known to regulate important brain functions including neurotransmitter metabolism, neuroendocrine function, synaptic plasticity, as well as the neural circuitry of mood. It is rather obvious to expect an aberrant behavioral outcome as a result of a dysregulation in cytokine signaling which might lead to occurrence of depression, anxiety, and cognitive dysfunction. Thus, understanding the mechanisms by which the immune system influences behavior would reveal targets for potential therapeutic development as well as strategies for the prevention of neuropsychiatric diseases. To date, the presence of inflammatory responses and the crucial role of cytokines in depression have received most attention. However, considering a big socioeconomic impact due to an alarming increase in anxiety disorder patients, there is an urgent research need for a better understanding of the role of cytokines in anxiety. In this review, we discuss recent research on the role of neuroimmunology in anxiety. At the end, we offer an "oxidative stress theory," which we propose works perhaps as a "sensor of distress," the imbalance of which leads to neuroinflammation and causes anxiety disorders. Much research is needed to extensively test this theory keeping an open mind!

Hum Psychopharmacol. 2012 Jan;27(1):6-14. doi: 10.1002/hup.1259. Epub 2011 Dec 26.

A neuroimmunological perspective on anxiety disorders.

Hou R, Baldwin DS.

Source

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Abstract

OBJECTIVE:

Research into psychoneuroimmunology has led to substantial advances in our understanding of the reciprocal interactions between the central nervous system and the immune system in neuropsychiatric disorders. To date, the presence of inflammatory responses and the crucial role of cytokines in major depression have been addressed in numerous studies. However, neuroinflammatory hypotheses in anxiety disorders have been studied less extensively than in major depression. There is a high research need for better understanding of both the heterogeneous role of specific cytokines in the control of anxious states and in different anxiety disorders and of the immunomodulating effects of antidepressants on anxiety.

METHODS:

Relevant literature was identified through a search of MEDLINE via PubMed. We discuss recent research on neuroimmunology in anxiety and make methodological recommendations for future investigation of neuroinflammatory hypotheses in anxiety disorders.

RESULTS:

Some accumulating evidence has indicated modulatory effects of cytokines on neuronal communication and anxiety; however, research has not revealed consistent reproducible findings.

CONCLUSIONS:

The availability of inflammatory biomarkers may provide an opportunity to identify patients via specific pathophysiological processes and to monitor therapeutic responses within relevant pathways. Further understanding of the neuroimmunological mechanisms to untangle the reciprocal associations between inflammation and anxiety is warranted.

Personalized Lifestyle Medicine for Mental Health

Stress Management and "Transformation"

Managing stress positively involves a variety of lifestyle medicine approaches, including relaxation techniques, lifestyle strategies, exercise, sleep and targeted nutrients.

Relaxation therapy is one of the most common approaches to managing stress, and it appears that the more we do it, the more favorably our genes respond. Research by Dusek et al. at Harvard Medical School, published in 2008, showed that gene expression between people who were seasoned body-mind practitioners compared with those who had never practiced any mind-body technique differed by 2,209 genes.[2] Some genes were turned on and others turned off. When the novices were trained to do a twenty-minute mind-body technique (deep breathing, meditation, body scan, mantra, and ignoring thoughts) at home for 8 weeks, their gene pattern at baseline was dramatically altered compared to after 8 weeks with a shift in 1,561 genes (874 turned on and 687 turned off). Essentially, the changes in

their genes were related to more favorable patterns in how the cells deal with stress responses and inflammation.

Having an optimistic rather than a pessimistic attitude may also help to alleviate some stress. Studies have shown that people who have negative views and perceptions of the future (equated with greater pessimism) also have greater risk for the lifestyle-induced diseases associated with aging and early death as supported by elevated levels of inflammatory compounds in their bodies compared with people who are optimistic. Indeed, stress and pessimism have been shown to shorten telomeres and decrease telomerase, both indicators of rapid cell decline and aging. These stressed cells have lower amounts of protective antioxidants, more oxidative stress, and greater vulnerability to becoming diseased.

Listed below are some other studies indicating modalities that may be beneficial for stress.

Cochrane Database Syst Rev. 2009 Apr 15;(2):CD006577.

Music for stress and anxiety reduction in coronary heart disease patients.

Bradt J, Dileo C.

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Abstract

BACKGROUND: Individuals with coronary heart disease (CHD) often suffer from severe distress putting them at greater risk for complications. Music interventions have been used to reduce anxiety and distress and improve physiological functioning in medical patients, however its efficacy for CHD patients needs to be evaluated.

OBJECTIVES: To examine the effects of music interventions with standard care versus standard care alone on psychological and physiological responses in persons with CHD.

SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, CINAHL, EMBASE, PSYCINFO, LILACS, Science Citation Index, www.musictherapyworld.net, CAIRSS for Music, Proquest Digital Dissertations, ClinicalTrials.gov, Current Controlled Trials, and the National Research Register (all to May 2008). We handsearched music therapy journals and reference lists, and contacted relevant experts to identify unpublished manuscripts. There was no language restriction.

SELECTION CRITERIA: We included all randomized controlled trials that compared music interventions and standard care with standard care alone for persons with CHD.

DATA COLLECTION AND ANALYSIS: Data were extracted, and methodological quality was assessed, independently by the two reviewers. Additional information was sought from the trial researchers when necessary. Results are presented using weighted mean differences for outcomes measured by the same

scale and standardized mean differences for outcomes measured by different scales. Posttest scores were used. In cases of significant baseline difference, we used change scores.

MAIN RESULTS: Twenty-three trials (1461 participants) were included. Music listening was the main intervention used, and 21 of the studies did not include a trained music therapist.Results indicated that music listening has a moderate effect on anxiety in patients with CHD, however results were inconsistent across studies. This review did not find strong evidence for reduction of psychological distress. Findings indicated that listening to music reduces heart rate, respiratory rate and blood pressure. Studies that included two or more music sessions led to a small and consistent pain-reducing effect.No strong evidence was found for peripheral skin temperature. None of the studies considered hormone levels and only one study considered quality of life as an outcome variable.

AUTHORS' CONCLUSIONS: Music listening may have a beneficial effect on blood pressure, heart rate, respiratory rate, anxiety, and pain in persons with CHD. However, the quality of the evidence is not strong and the clinical significance unclear.Most studies examined the effects of listening to pre-recorded music. More research is needed on the effects of music offered by a trained music therapist.

J Psychosom Obstet Gynaecol. 1996 Dec;17(4):202-7.

The effects of relaxation response training on menopausal symptoms.

Irvin JH, Domar AD, Clark C, Zuttermeister PC, Friedman R.

Source

Mind/Body Medical Institute, New England Deaconess Hospital, Harvard Medical School, Boston, MA, USA.

Abstract

The specific aim of this study was to investigate the efficacy of elicitation of the relaxation response for the treatment of menopausal hot flashes and concurrent psychological symptoms. The volunteer sample consisted of 33 women, between the ages of 44 and 66 years, who were in general good health, with a minimum of 6 months without a menstrual period, experiencing at least five hot flashes per 24-h, and not using hormone replacement therapy. The setting was an outpatient clinic in a tertiary care teaching hospital. The interventions used were relaxation response training and an attention-control group and a daily symptom diary measuring both the frequency and intensity of hot flashes, the Spielberger State-Trait Anxiety Inventory (STAI), and the Profile of Mood Scale (POMS) were the measures used. This was a randomized, controlled, prospective study. Subjects were randomly assigned to one of three groups (relaxation response, reading, or control) for the 10-week study. The first 3 weeks of baseline measurement of frequency and intensity of hot flash symptoms, and the preintervention psychological scores were compared with the final 3 weeks measurement of frequency and intensity and the postintervention psychological scores for symptomatic improvement. The relaxation response group demonstrated significant reductions in hot flash intensity ($p < 0.05$), tension-anxiety ($p < 0.05$) and depression ($p < 0.05$). The reading group demonstrated significant reductions in trait-anxiety ($p < 0.05$)

and confusion-bewilderment ($p < 0.05$). There were no significant changes for the control group. Daily elicitation of the relaxation response leads to significant reductions in hot flash intensity and the concurrent psychological symptoms of tension-anxiety and depression.

Autoimmun Rev. 2006 Oct;5(8):523-7. Epub 2006 Mar 21.

The immune system and happiness.

Barak Y.

Source

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Abstract

Human ability to experience negative and positive emotions has an evolutionary perspective and the presence of feelings designed to influence behavior should thus be reflected in physiological and immune interactions. The complex interactions between the immune system and the central nervous system have been studied extensively in schizophrenia and depression. On the other hand, effects of positive human emotions, especially happiness, on physiological parameters and immunity have received very little attention. Emotions are intimately involved in the initiation or progression of cancer, HIV, cardiovascular disease, and autoimmune disorders. The specific physiological responses induced by pleasant stimuli were recently investigated with the immune and endocrine systems being monitored when pleasant stimuli such as odors and emotional pictures were presented to subjects. The results revealed that an increase in secretory immunoglobulin A and a decrease in salivary cortisol were induced by pleasant emotions. The mechanisms by which positive as opposed to negative states are instantiated in the brain and interact with the immune system are not yet understood. The present review investigates relations among physiological measures of affective style, psychological well-being, and immune function. There is data to support the hypothesis that individuals characterized by a more negative affective style poorly recruit their immune response and may be at risk for illness more so than those with a positive affective style. Future research is needed to expand our knowledge of the physiological and immune interactions of positive emotional states and their beneficial effects on health.

Brain Behav Immun. 2009 May;23(4):446-9. Epub 2008 Dec 11.

Pessimism correlates with leukocyte telomere shortness and elevated interleukin-6 in post-menopausal women.

O'Donovan A, Lin J, Tillie J, Dhabhar FS, Wolkowitz OM, Blackburn EH, Epel ES.

Source

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Erratum in

Brain Behav Immun. 2012 Aug;26(6):1017. Tillie, J M [corrected to Tillie, J]; Wolkowitz, O [corrected to Wolkowitz, O M]; Blackburn, E [corrected to Blackburn, E H]; Epel, E [corrected to Epel, E S].

Abstract

The combination of less positive and more negative expectations for the future (i.e., lower optimism and higher pessimism) increases risk for disease and early mortality. We tested the possibility that expectancies might influence health outcomes by altering the rate of biological aging, specifically of the immune system (immunosenescence). However, no studies to date have examined associations between optimism or pessimism and indicators of immunosenescence such as leukocyte telomere length (TL) and interleukin-6 (IL-6) levels. We investigated whether dispositional tendencies towards optimism and pessimism were associated with TL and IL-6 in a sample of 36 healthy post-menopausal women. Multiple regression analyses where optimism and pessimism were entered simultaneously, and chronological age and caregiver status were controlled, indicated that pessimism was independently associated with shorter TL (beta=-.68, p=.001) and higher IL-6 concentrations (beta=.50, p=.02). In contrast, optimism was not independently associated with either measure of immunosenescence. These findings suggest that dispositional pessimism may increase IL-6 and accelerate rate of telomere shortening. Mechanistic causal relationships between these parameters need to be investigated.

J Am Diet Assoc. 2009 Aug;109(8):1427-32.

Can relaxation training reduce emotional eating in women with obesity? An exploratory study with 3 months of follow-up.

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Abstract

Stress and negative emotions have been shown to be critical factors in inducing overeating as a form of maladaptive coping in some patients with obesity. We evaluated the efficacy of a 3-week relaxation protocol enhanced by virtual reality and portable mp3 players in reducing emotional eating in a sample of 60 female inpatients with obesity who report emotional eating, using a three-arm exploratory randomized controlled trial with 3 months of follow-up. The intervention included 12 individual relaxation training sessions provided traditionally (imagination condition) or supported by virtual reality (virtual reality condition). Control participants received only standard hospital-based care. Weight, behavior and psychological data were collected and analyzed. Relaxation training was effective in reducing emotional eating episodes, depressive and anxiety symptoms, and in improving perceived self-

efficacy for eating control at 3-month follow-up after discharge. The virtual reality condition proved better than the imagination condition in the reduction of emotional eating. Weight decreased in subjects in all three conditions without significant differences between them, probably due to the common treatment all inpatients received. We conclude that relaxation training supported by new technologies could be a useful tool for reducing emotional eating episodes and thereby reducing weight and obesity.

Depression

A number of lifestyle medicine strategies can be employed to address depression, including diet, activity, and social support. As an example, just a small percentage (17%) of Americans use mind-body medicine therapies such as prayer, meditation, and mindfulness practices to address depression, yet the science suggests that there could be some real benefit of these therapies, especially when used as adjuncts to other modalities. By engaging the relaxation response through mind-body techniques, the parasympathetic and sympathetic nervous systems become harmonized and regulated rather than the sympathetic activation and hypercortisolemia that typically comes with stress and subsequent depression. These techniques are easy to learn, can be done in many places, and simply require the time and attention to do them.

With respect to food, there is growing field connecting nutrition to mental health. With our diets changing to processed, low-nutrient-density foods, we are lacking the healthy components of food that protect the brain and reduce inflammation. Fat is one of the key nutrients that has the potential to significantly impact brain function and mood, largely because our brain matter is 60% lipid and the quality of that lipid will determine how the brain functions and how the neurons signal to each other. To date, good evidence exists that omega-3 fatty acids through the diet or via supplementation may assist with reducing behavioral/mood disorders such as depression and anger. Due to the omega-3 fatty acids being fluid and flowing, they allow for greater neuronal plasticity and cellular responsiveness in the brain. In addition to omega-3 fats, including anti-inflammatory foods into the diet, such as spices (e.g., curcumin), leafy, green vegetables, fruits high in protective polyphenols such as apples and dark-colored berries, may also be conducive to warding off inflammatory processes fueling depression.

A personalized approach to someone with mood imbalance would be to implement a combination of lifestyle medicine strategies to reduce the stress in one's life and, at the same time, provide the nutrients one needs to regulate brain function optimally.

Abstracts on Lifestyle Medicine Therapies for Depression

Psychosomatics. 2012 Sep-Oct;53(5):407-23. doi: 10.1016/j.psym.2012.04.006. Epub 2012 Aug 14.

Mind-body medicine therapies for a range of depression severity: a systematic review.

D'Silva S, Poscablo C, Habousha R, Kogan M, Kligler B.

Source

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Abstract

OBJECTIVE:

Of the 34 million adult Americans (17%) using mind-body medicine therapies, 8 million (24%) have anxiety/depression. The evidence for using mind-body therapies to address varying depressive symptoms in populations with and without other chronic comorbidities is reviewed.

METHODS:

Systematic literature searches of PubMed (Medline), Embase, CINAHL, and the seven databases encompassed by Current Contents, Web of Science, and Web of Knowledge were conducted. Studies designed as prospective control-comparison, adult population, English, at least 2 weeks long, sample size >30, and with primary or secondary outcome as depression measured on an established scale were included. Methodologic quality was evaluated using the modified scale for assessing scientific quality of investigations (SASQI) for Complementary and Alternative Medicine (CAM).

RESULTS:

Ninety papers of about 2900 met both inclusion and exclusion criteria; 60% of them scored a SASQI >9 and were deemed of sufficient quality to be included in the review; 74% of these selected quality papers demonstrated positive effects on the improvement of depressive symptoms. All mind-body modalities included in the study had at least one positive study. For cancer patients, several studies noted the positive effects of yoga and combination therapies on depression severity. For both diagnosed depression and fibromyalgia, several studies noted the positive effects of mindfulness on depression severity.

CONCLUSION:

The use of evidence-based mind-body therapies can alleviate depression severity. They could be used with established psychiatric treatments of therapy and medications. The likely long-term increased cost-effectiveness of integrating these therapies deserves further investigation.

Int J Psychiatry Med. 2012;43(1):85-98.

The effect of prayer on depression and anxiety: maintenance of positive influence one year after prayer intervention.

Boelens PA, Reeves RR, Replogle WH, Koenig HG.

Source

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Abstract

OBJECTIVE:

To investigate whether the effect of direct contact person-to-person prayer on depression, anxiety, and positive emotions is maintained after 1 year.

DESIGN, SETTING, AND PARTICIPANTS:

One-year follow-up of subjects with depression and anxiety who had undergone prayer intervention consisting of six weekly 1-hour prayer sessions conducted in an office setting. Subjects (44 women) completed Hamilton Rating Scales for Depression and Anxiety, Life Orientation Test, and Daily Spiritual Experiences Scale after finishing a series of six prayer sessions and then again a month later in an initial study. The current study reassessed those subjects with the same measures 1 year later. One-way repeated measures ANOVAs were used to compare findings pre-prayer, immediately following the six prayer sessions, and 1 month and again 1 year following prayer interventions.

RESULTS:

Evaluations post-prayer at 1 month and 1 year showed significantly less depression and anxiety, more optimism, and greater levels of spiritual experience than did the baseline (pre-prayer) measures ($p < 0.01$ in all cases).

CONCLUSIONS:

Subjects maintained significant improvements for a duration of at least 1 year after the final prayer session. Direct person-to-person prayer may be useful as an adjunct to standard medical care for patients with depression and anxiety. Further research in this area is indicated.

Brain Behav Immun. 2012 Feb;26(2):346-52. Epub 2011 Nov 18.

Maintenance of a positive outlook during acute stress protects against pro-inflammatory reactivity and future depressive symptoms.

Aschbacher K, Epel E, Wolkowitz OM, Prather AA, Puterman E, Dhabhar FS.

Source

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Abstract

Cognitive and affective responses to acute stress influence pro-inflammatory cytokine reactivity, and peripheral cytokines (particularly interleukin-1 beta (IL-1β)), can act on the brain to promote depressive symptoms. It is unknown whether acute stress-induced changes in positive affect and cognitions (POS) and pro-inflammatory reactivity predict future depressive symptoms. We examined acute stress

responses among women, to determine prospective predictors of depressive symptoms. Hypotheses: (1) Stress-induced decreases in POS will be associated with stress-related increases in circulating IL-1β. (2) Acute stress-induced decreases in POS and increases in IL-1β reactivity will predict increases in depressive symptoms 1 year later. Thirty-five post-menopausal women were exposed to acute stress with the Trier Social Stress Task (TSST) and provided blood samples under resting conditions and 30 min after the conclusion of the TSST, which were assayed for IL-1β. IL-1β reactivity was quantified as post minus pre-TSST. Failure to maintain POS was quantified as the decrease in POS during the TSST. Change in depressive symptoms from the study baseline to the following year was determined. Greater acute stress-induced declines in POS were significantly associated with increased IL-1β reactivity ($p \leq .02$), which significantly predicted increases in depressive symptoms over the following year ($p < .01$), controlling for age, body mass index, chronic stress, antidepressant use and baseline depressive symptoms. IL-1β reactivity was a significant mediator of the relationship between POS decline and future increases in depressive symptoms ($p = .04$). Difficulty maintaining positivity under stress and heightened pro-inflammatory reactivity may be markers and/or mechanisms of risk for future increases in depressive symptoms.

J Altern Complement Med. 2012 Jan;18(1):48-53.

Effects of an 8-week meditation program on mood and anxiety in patients with memory loss.

Moss AS, Wintering N, Roggenkamp H, Khalsa DS, Waldman MR, Monti D, Newberg AB.

Source

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Abstract

BACKGROUND:

This study assesses changes in mood and anxiety in a cohort of subjects with memory loss who participated in an 8-week Kirtan Kriya meditation program. Perceived spirituality also was assessed. Previous reports from this cohort showed changes in cognitive function and cerebral blood flow (CBF). The purpose of this analysis was to assess outcome measures of mood and affect, and also spirituality, and to determine whether or not results correlated with changes in CBF.

METHODS:

Fifteen (15) subjects (mean age 62±7 years) with memory problems were enrolled in an 8-week meditation program. Before and after the 8-week meditation, subjects were given a battery of neuropsychologic tests as well as measures of mood, anxiety, and spirituality. In addition, they underwent single photon emission computed tomography scans before and after the program. A region-of-interest template obtained counts in several brain structures that could also be compared to the results from the affect and spirituality measures.

RESULTS:

The meditation training program resulted in notable improvement trends in mood, anxiety, tension, and fatigue, with some parameters reaching statistical significance. All major trends correlated with changes in CBF. There were nonsignificant trends in spirituality scores that did not correlate with changes in CBF.

CONCLUSIONS:

An 8-week, 12 minute a day meditation program in patients with memory loss was associated with positive changes in mood, anxiety, and other neuropsychologic parameters, and these changes correlated with changes in CBF. A larger-scale study is needed to confirm these findings and better elucidate mechanisms of change.

J Altern Complement Med. 2010 Nov;16(11):1145-52. Epub 2010 Aug 19.

Effects of yoga versus walking on mood, anxiety, and brain GABA levels: a randomized controlled MRS study.

Streeter CC, Whitfield TH, Owen L, Rein T, Karri SK, Yakhkind A, Perlmutter R, Prescot A, Renshaw PF, Ciraulo DA, Jensen JE.

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Abstract

OBJECTIVES:

Yoga and exercise have beneficial effects on mood and anxiety. γ-Aminobutyric acid (GABA)-ergic activity is reduced in mood and anxiety disorders. The practice of yoga postures is associated with increased brain GABA levels. This study addresses the question of whether changes in mood, anxiety, and GABA levels are specific to yoga or related to physical activity.

METHODS:

Healthy subjects with no significant medical/psychiatric disorders were randomized to yoga or a metabolically matched walking intervention for 60 minutes 3 times a week for 12 weeks. Mood and anxiety scales were taken at weeks 0, 4, 8, 12, and before each magnetic resonance spectroscopy scan. Scan 1 was at baseline. Scan 2, obtained after the 12-week intervention, was followed by a 60-minute yoga or walking intervention, which was immediately followed by Scan 3.

RESULTS:

The yoga subjects (n = 19) reported greater improvement in mood and greater decreases in anxiety than the walking group (n = 15). There were positive correlations between improved mood and decreased

anxiety and thalamic GABA levels. The yoga group had positive correlations between changes in mood scales and changes in GABA levels.

CONCLUSIONS:

The 12-week yoga intervention was associated with greater improvements in mood and anxiety than a metabolically matched walking exercise. This is the first study to demonstrate that increased thalamic GABA levels are associated with improved mood and decreased anxiety. It is also the first time that a behavioral intervention (i.e., yoga postures) has been associated with a positive correlation between acute increases in thalamic GABA levels and improvements in mood and anxiety scales. Given that pharmacologic agents that increase the activity of the GABA system are prescribed to improve mood and decrease anxiety, the reported correlations are in the expected direction. The possible role of GABA in mediating the beneficial effects of yoga on mood and anxiety warrants further study.

J Consult Clin Psychol. 2010 Apr;78(2):169-83.

The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review.

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Source

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Abstract

OBJECTIVE:

Although mindfulness-based therapy has become a popular treatment, little is known about its efficacy. Therefore, our objective was to conduct an effect size analysis of this popular intervention for anxiety and mood symptoms in clinical samples.

METHOD:

We conducted a literature search using PubMed, PsycINFO, the Cochrane Library, and manual searches. Our meta-analysis was based on 39 studies totaling 1,140 participants receiving mindfulness-based therapy for a range of conditions, including cancer, generalized anxiety disorder, depression, and other psychiatric or medical conditions.

RESULTS:

Effect size estimates suggest that mindfulness-based therapy was moderately effective for improving anxiety (Hedges's g = 0.63) and mood symptoms (Hedges's g = 0.59) from pre- to posttreatment in the overall sample. In patients with anxiety and mood disorders, this intervention was associated with effect sizes (Hedges's g) of 0.97 and 0.95 for improving anxiety and mood symptoms, respectively. These effect sizes were robust, were unrelated to publication year or number of treatment sessions, and were maintained over follow-up.

CONCLUSIONS:

These results suggest that mindfulness-based therapy is a promising intervention for treating anxiety and mood problems in clinical populations.

References

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[2] Dusek JA, Out HH, Wohlhueter AL, Bhasin M, Zerbini LF, et al. Genomic counter-stress changes induced by the relaxation response. *PLoS One*. 2008;3(7):e2576.