Psychoneuroimmunoendocrinology
Review and Commentary

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Psychoneuroimmunoendocrinology describes the interrelationship of mental, neurological, hormonal, and immunological functions, addressing the impact of cognitive images of the mind (whatever its elusive definition) on the central nervous, endocrine and immune systems. It encompasses biofeedback and voluntary controls, impacts on physiology of thought, attitude and belief, past/present stress, placebos, social relationships, and "energy medicine." This column highlights clinical applications of cogent studies from these arenas of holistic medicine in the new millennium.

Brain Change and Childhood Abuse

Early stress is associated with lasting effects on the hypothalamic-pituitary-adrenal axis and norepinephrine systems, involving benzodiazepine, opiate, dopaminergic, and various neuropeptide systems. These neurochemical systems modulate function in the amygdala, hippocampus, and prefrontal cortex. Long-term alterations in these brain regions probably play a role in the maintenance of posttraumatic stress disorder, depression, and other psychiatric symptoms after childhood abuse.


Comment: Stress may be defined as the accumulated total of demands and expectations placed on oneself and others that cannot be comfortably met; it is a stimulus requiring adaptation, obliging an individual to be or do something different than s/he is at a given moment (See my book Stress Power! New York: Human Sciences Press; 1978). The effects of childhood stress are lasting. As physicians and counselors realize, the long shadow of this stress visited on children in the form of physical, verbal, emotional, or sexual abuse is related to a host of adult problems. The past abuse should come to mind when common treatments for these adult problems do not work. Two problems emerge: recognizing the source of the abuse (often repressed), and then dealing with it once it has surfaced. The case history at the end of this column deals with the first issue. The second issue involves encouraging the adult patient to recognize the dis-ease associated with the persisting powerful feelings that surround the memory of the childhood incident(s) and the potential relief deriving from invoking forgiveness, which is done purely for the benefit of the patient and has nothing to do with the perpetrator.

Posttraumatic Stress Disorder

Neuroimaging studies in posttraumatic stress disorder have shown decreased medial prefrontal cortical, inferior frontal gyrus, and hippocampal function; increased posterior cingulate function; and, in some behavioral paradigms, increased amygdala function. Several studies have shown smaller volume of the hippocampus in posttraumatic stress disorder.


Comment: Here the author discusses the evidence that chronic and repeated stress tends to leave its footprint as anatomical changes in the brain. He alludes to studies suggesting that servicemen with PTSD consequent to experiences in the Vietnam war have hippocampi up to 20% smaller than comparable-aged men without PTSD. Although it is not clear from the literature whether psychological work can allow the hippocampus to regenerate its full capacity, it is my experience that appropriate psychological work can improve functions attributed to the hippocampus.

Hepatitis C and Personality

This cross-sectional study examined the association between the severity of chronic hepatitis C and Grossarth-Maticiek's type 1 personality, which has been related to the incidence of cancer and mortality. Sixty-nine patients with chronic hepatitis C completing the Stress Inventory were classified into 3 groups: (1) with a normal serum alanine aminotransferase, (2) with an elevated ALT, and (3) with liver cirrhosis. Each of four scales related to the type 1 personality (low sense of control, object dependence of loss, unfulfilled need for acceptance, and altruism) was significantly and positively associated with hepatitis severity. The type 1 score, calculated as an average of
these four scales and adjusted for age, sex, education level, smoking, alcohol, and duration, was strongly related to hepatitis severity (p < 0.0001). Chronic psychosocial stress relevant to the type 1 personality may also influence the course of chronic hepatitis C.

Comment: Grossarth-Maticek and Eyesenck authored a series of papers about twenty years ago in following thousands of Central European adults for over twenty years. The worldview of their type 1 personality patients was characterized by feelings of helplessness, a belief that they had been abandoned, and that happiness depends on unattainable love. This group was particularly prone to cancer. This follow-up on the Matick-Eyseck work strongly links their type 1 personalities with hepatitis C of much greater severity. The theoretical link would be the already-demonstrated deterioration of immune function by short term stress.

Cancer Survival and Will to Live

In 189 patients with end-stage cancer, researchers found significant correlations between the will to live and existential, psychological, social, and, to a lesser degree, physical sources of distress. Existential variables proved to have the most influence, with hopelessness (p < .001), burden to others (p < .004), and dignity (p < .03) entering into the final model.

Comment: Whole-person care includes the importance of relating in the best way to the dying patient. As stated by these authors, paying attention to all the potential sources of distress – and primarily from existential issues – is part of the obligation of the attending physician. Health-care providers must learn to appreciate the importance of the existential issues and their ability to influence the will to live among patients nearing death. It is also incumbent upon the physician to cooperate with and reinforce the belief system of the patient and be comfortable in so doing.

Risk Factors for Myocardial Infarction

In 15,152 cases and 14,820 controls in a 52-nation case-control study, odds ratios for myocardial infarction were: smoking 2.9 for current vs. never (p < .0001), raised Apolipoprotein B/Apolipoprotein A1 ratio 3.3 for the highest vs. lowest quintile (p < .0001), history of hypertension 1.9 (p < .0001), diabetes 2.4 (p < .0001), truncal obesity 1.1 for highest vs. lowest tertile and 1.6 for middle vs. lowest tertile (p < .0001), psychosocial factors 2.7 (depression, stress, low locus of control) (p < .0001), daily consumption of fruits and vegetables 0.7 (p < .0001), regular alcohol consumption 0.9 (p = .03), and regular physical activity 0.9 (p < .0001). These associations were noted in men, women, old, young, and in all regions of the world. These nine risk factors accounted for 90% of the population attributable risk in men and 94% in women.


Comment: This nicely researched multinational study highlights the three contributions to lessened risk: regular physical activity, eating fruits and vegetables, and regular modest alcohol consumption. The latter is the most problematic of the three, because it is very difficult to separate the sociability factor that for many drinkers comes while imbibing. My point here is to emphasize the 2.7-fold increased risk from psychological factors, placing this just below smoking and third behind ApoB/ApoA1 ratio. Depression, stress, and low loci of control, then, provide greater risk than diabetes, hypertension, and obesity. In our medical teaching and public awareness, this is a relatively unknown factor. It needs greater awareness and emphasis in the halls of medicine. Practitioners would be well advised to ask the questions that bring these factors to light.

Cardiomyopathy and Stress

A clinical entity characterized by acute but rapidly reversible left ventricular (LV) systolic dysfunction and triggered by psychological stress is emerging, with reports largely confined to Japan. Over 32 months, 22 consecutive patients (all women, mean age 65) with this novel cardiomyopathy were prospectively identified in a community practice. The syndrome is characterized by (1) acute substernal chest pain with ST-segment elevation and/or T-wave inversion; (2) absence of significant coronary arterial narrowing by angiography; (3) systolic dysfunction (low ejection fraction – mean 29%), with abnormal wall motion of the mid and distal LV; and (4) profound psychological stress (for example, death of relatives, domestic abuse, arguments, catastrophic medical diagnoses, devastating financial or gambling losses) immediately preceding and triggering the cardiac events. Thirty-seven percent of patients had compromised hemodynamics and required vasopressor drugs and intra-aortic balloon counterpulsation. Each patient survived with normalized ejection fraction (mean 63%) (p < 0.001) and rapid restoration to previous functional cardiovascular status within 6 ± 3 days. In 95% of subjects, magnetic resonance imaging identified diffusely distributed segmental wall-motion abnormalities that encompassed LV myocardium in multiple coronary arterial vascular territories.


Comment: This study delineates a reversible cardiomyopathy triggered by psychologically stressful events that occurred for older women and that may mimic evolving acute myocardial infarction or the coronary syndrome. This condition is characterized by a distinctive form of systolic dysfunction that predominantly affects the distal LV chamber and a very favorable outcome with appropriate medical therapy. Texts describing cardiomyopathy refer to the majority of cases as stemming from unknown etiology. Based on these Japanese studies, older women appear to
be susceptible to an acute and sudden cardiomyopathy triggered by profound psychological stress and requiring aggressive treatment. Cardiac function was amazing restored in a mean of 6 days and in some cases within 3 days. This is a condition described only in biomedical terms. Based on these data, however, it is a biopsychosocial/holistic issue.

Legacies from Childhood – A Case History: Unexpected Wisdom from Within

Mildred, at 50, was in her sixth year of crisis. She experienced problems controlling weight gain; feelings of anxiety, panic, and depression; disappointment in her family and sex life; insomnia; fatigue; and confused thinking with elements of paranoia surfacing at times to be suggestive of psychotic illness. She had seen numerous counselors, psychiatrists, and physicians of various specialties. She had really not seemed to make many gains toward control over her many problems. Mildred was extremely bright; mother of four children; and a talented musician, playing expertly at the piano and the pipe organ.

I had seen Mildred for several medical problems and had agreed to help her work on some of her psychological issues as well. Her previous psychological work had enabled her to recall a childhood in which she was raised by parents of extremely rigid religious persuasion, with pervasive verbal abuse by her mother and acquiescence by her father. There was also physical abuse in the form of extreme spankings and hours of being confined to a chair.

In the context of working on some of her issues, we turned to her problem of insomnia and poor rest as a cause of much of her physical symptoms, including fatigue. While discussing her insomnia, she volunteered that if she went to bed early and was asleep by nine p.m., she rested well for the entire night. When my facial expression told her I was very curious but unsure what that meant, she volunteered further that if she stayed up to try to go to sleep past 11, she also had a sound night’s rest. Only if she lay down to sleep between 9 and 11 did she have a problem. I had never encountered a pattern such as this before, and it did not seem to have any rational cognitive explanation.

So, feeling stymied and uncertain about my next move, I turned to the use of guided imagery. With Mildred’s consent, I led her while seated in a chair through a three- or four-minute abbreviated relaxation exercise. Once she was breathing slowly and appeared quite relaxed with eyes closed, I asked her to imagine herself parked on a low-hanging cloud above her home. After she nodded in response to my question “Can you see your home clearly?” I suggested that she magically look down into her living quarters at 8:45 p.m. and describe what was happening. Still with eyes closed, she described seeing her husband finishing drying the dishes, while they discussed items she mentioned as she perused the day’s newspaper.

I then asked her to advance the clock to 9 p.m. and describe what she saw. Almost immediately, she inhaled a huge breath with a loud gasp. I said “Mildred, tell me what’s happening.” In a panicky voice, she sobbed that the scene had shifted to her childhood home when she was 12 and that her 16-year-old brother was entering her bedroom. She continued sobbing as she described her brother forcing his sexual attentions on her. I terminated the imagery, asked her to open her eyes, and talked with her for some time as she gradually calmed herself from this frightening insight. The scene had triggered the recall of a series of sexual assaults by her brother that extended across the greater part of three years. Her mother had dismissed Mildred’s vain attempts to get her intervention.

After weeks of intensive therapy, Mildred was able to deal with this tragic episode that foreshadowed many of her future relationship problems with her husband and family. Her psychological work gradually established a better self-image. The quintessential piece that enabled her to put the sexual abuse issue behind her involved forgiving her brother, in the sense of canceling the demand that things should not have happened that way. She was persuaded to move to forgiveness because she realized it was in her own self-interest.

As Mildred completed this process, her shoulders relaxed, the lines of strain disappeared from her face, she began to talk more slowly, and she began to make good eye contact. Her two powerful “aha” experiences were the insight into the memory of the event, and the feeling of relief and relaxation once she completed the forgiveness exercise.

The key to healing may be found already existing in the mindful awareness that programs the brain. In some situations, the act of forgiving may be the only path to reducing the stress with which we have been living. The wholly unexpected, spontaneous turn in her imagery taught me that sometimes the best thing that the physician or therapist can do is get out of the way.

Robert Anderson is a retired family physician who has authored several major books: Stress Power, Wellness Medicine, Clinician’s Guide to Holistic Medicine (2001), and The Scientific Basis for Holistic Medicine, (6th edition 2004), available from American Health Press, holos@charter.net. Anderson founded the American Board of Integrative Holistic Medicine, is a past president of the AHMA and former assistant clinical professor of family medicine at the University of Washington, and teaches The Art of Primary Care at Bastyr University.