Psychoneuroimmunoendocrinology
Review and Commentary

by Robert A. Anderson, MD
614 Daniels Drive NE
East Wenatchee, Washington 98802 USA

Psychoneuroimmunoendocrinology describes the unity of mental, neurological, hormonal and immunological functions with its many potential applications. PNIE addresses the impact of cognitive images of the mind (whatever its elusive definition) on the central nervous system and consequent interactions with endocrine and immune systems. It encompasses many arenas, including biofeedback and voluntary controls, impacts of thought and belief on physiology, past and present effects of stress on mental, emotional and physical function, placebo effects, effects of social relationships on health and disease, and impacts of "energy medicine" on personal function and that of others. This column highlights the impact of cogent studies from these arenas on the understanding of holistic medicine in the new millennium.

Food and chemical sensitivities and illness

Four-hundred ninety college students, mean age 19, were studied for symptom patterns and psychological profiles and self-reported reactions to several common foods (wheat, milk, eggs) and chemicals (pesticides, car exhaust, paint, perfume, new carpets). Those with greater reported food/chemical sensitivity had higher psychological symptom scores (defensiveness was most prominent), indigestion, headache and memory problems. The higher illness groups reported more limitations from foods that mobilize endogenous opioids such as sweets, fats and breads. Nasal symptoms were more common in those with chemical sensitivities than those with food sensitivities. Irritable bowel syndrome and premenstrual syndrome were more common in those with both chemical and food sensitivities.


Comment: Indigestion, headaches and memory problems may occur in addition to rather than as a part of, emotional stress resulting from sensitivity reactions. These data are consistent with a role for involvement of olfactory-limbic and hypothalamic pathways as an explanation for food and chemical sensitivity syndromes. The bi-directional nature of mind-body and body-mind interrelationships is demonstrated here: not only does the mind-brain entity have profound effects on the physical, but the bodily reactions described profoundly affected the mental functions.

Learning, emotional reactions and food elimination

Sixteen children age 5-15 referred for remedial reading and behavior modification were each placed on a diet to reduce sugars, refined foods and toxins and given an individually designed vitamin-mineral supplement. Nutritional intake of 16 matched-pair control children was not changed and they took an over-the-counter RDA-level vitamin-mineral supplement. After 22 weeks, mean IQ scores increased 17.9 points in the treated v. 8.4 in controls (2p=0.02). Reading age significantly improved (2p=0.05) in treated v. controls, almost doubling the expected gain based on normal age-related experience. Mean hair cadmium dropped from 1.9 to 1.4 ppm (still above the recommended upper limit commonly accepted as safe), mean lead fell from 29 to 15 ppm and mercury from 2.92 to 2.1 ppm.


Comment: Again, what is happening in the physical plane in regard to macro- and micro-nutrients is shown here to significantly affect mental function, even significantly changing IQ scores. Appropriate nutrient intake and adequate/normal gastrointestinal assimilation may profoundly affect mental and emotional functions.

Stress and irritable bowel syndrome

Colonic smooth muscle spike potentials and contractility were recorded by a bipolar electrode-perfused catheter apparatus placed in the rectosigmoid colon in 6 healthy volunteers and 11 patients with irritable bowel syndrome during periods of stress. The 3 standardized stressful conditions were: (1) forearm ice-water immersion, (2) the Stroop stimulus differentiation test (a challenging psychological experience), and (3) ball sorting, another challenging psychological test. In healthy controls, colonic motility and respiratory rate rose with the first exposure to ice-water immersion (p<0.05), Stroop test (p<0.05), or ball sorting, but repeat exposures to the stresses did not increase colonic motility. Increases in colonic motility response occurred in IBS patients after exposure to ice water (p<0.05), Stroop Test, or ball sorting (p<0.05) and continued with repeated exposures. After exposure to the stressful situations, IBS patients pretreated with chloridiazepoxide (Librium) had a diminished increase in colonic motility and respiratory rate.


Comment: These data suggest that in healthy controls habituation reduces the stress-related increase in colonic motility with repeated exposures. In patients with irritable bowel syndrome, this adaptation does not readily occur. Benzodiazepines (anti-anxiety agents), decrease the stress-related increase in colonic motility, indicating that the mechanism involves responses at the emotional level.

Stress and irritable bowel syndrome

Thirty-one subjects with chronic symptoms of irritable bowel syndrome were studied for the relationship of their symptoms to day-to-day stress; 28 women and 5 men completed daily logs for 7 IBS symptoms, as well as a daily hassles questionnaire: 14 showed significant same-day relationships between perceived hassles and symptoms (p<.05); and, for 13, symptoms could be significantly predicted (p<.05) by hassles from the previous 4 days. The strongest overall relationship for the group as a whole was the relation of symptoms to same day stress + two previous days’ hassles, which occurred in 67% of the subjects.

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Comment: The stress effects on bowel function in these IBS patients resulted from same-day hassles as well as the accumulated stress of the prior two days. Stress, which may be defined as the total sum of demands on self and others, affects different people differently. Two individuals experiencing the same potentially stressful event may have widely differing responses, depending on two factors: how they interpret the stressful event and its meaning for them; and the adaptive skills which have been learned and incorporated by the time the event occurs. Both these factors can be greatly modified by cognitive and behaviorally-oriented training.

Irritable bowel syndrome and emotions

Hypnosis can be used safely to induce specific emotional states of considerable intensity. In 18 irritable bowel syndrome patients age 20-48, the effect on distal colonic motility of three hypnotically-induced emotions (excitement, anger, and happiness) was studied. Colonic motility index was reduced by hypnosis alone (mean change 19.1, p<.05) which was accompanied by decreases in pulse rate of 12/min (p<.001) and respiratory rate 6/min (p<.001 for both). Anger and excitement increased the colonic motility index 50.8 and 30.4, respectively (p<.01 for both), pulse rate 26 and 28/min, respectively (p<.001 for both), and respiration rate 14 and 12/min, respectively (p<.001 for both). Happiness further nonsignificantly reduced colonic motility from that observed during hypnosis alone. Changes in motility were mainly due to alterations in rate rather than in amplitude of contractions. Whorwell PJ et al. Physiological effects of emotion: assessment via hypnosis. Lancet 1992 Jul 11; 340(8831):69-72

Comment: The observation that hypnosis strikingly reduces fasting colonic motility may partly explain the beneficial effects of this form of therapy in all functional bowel disorders. These marked effects would indicate that this approach could be useful in other organ systems as well. The gut appears to be very sensitively related to brain function, in part because of the concentration of neural elements in the submucosa (the so-called "GI brain"). The distinct changes in motility with three emotions seemed distinctive. There may also be a thin differentiation with even less concretely measured functions commonly referred to as "gut feelings," which some authorities relate to intuition. While the gut functions autonomously, it is acutely reactive to an enormous variety of stimuli including basic emotions.

Relaxation and biofeedback in irritable bowel syndrome

Eleven patients with irritable bowel syndrome were treated for 12 weeks with an integrated program including 6 thermal biofeedback sessions, education about normal intestinal function, teaching of progressive relaxation and cognitive stress-coping techniques. The patients met in groups of 3-6 persons following 12 weeks of baseline monitoring, recording
and observation. Diarrhea and abdominal pain improved significantly (p<.05), and 6 weeks later in followup, constipation and flatulence had also improved significantly (p<.05).

Comment: Behavioral relaxation approaches oriented toward equilibrating the control of the sympathetic nervous system have proven generally successful in mitigating IBS symptoms. In this study, symptoms of IBS significantly improved over a course of 18 weeks from baseline. Subjects learned these behaviorally-induced changes in autonomic nervous system controls in a group setting. Besides my enthusiasm for the technique itself, readers of this column are also aware that I strongly advocate working with patients in groups. This has advantages of the group support effect, which tends to entrain greater compliance and attendance. It extends the efficiency of the health practitioner whose valuable time to actually spend with patients is constantly being constricted. Functional problems such as IBS seem to respond especially well to biofeedback. The best advantage is perhaps its freedom from unwanted side effects.

Hypnosis in irritable bowel syndrome

Fifteen patients with severe irritable bowel syndrome unresponsive to conventional treatment improved with “gut-directed” hypnotherapy and maintained improvement for a mean duration of 18 months during which they were followed with one hypnotherapy session every 3 months. Two relapsed on one occasion, requiring an extra session. In a larger cohort of 50 patients, overall success rate was 84 percent. Those >50 years of age tended to be non-responders.


Comment: Hypnotherapy is also a successful approach to managing functional gastrointestinal problems, as demonstrated in this and the following studies. Many of these studies have been conducted on standard treatment failures, making success with the subjects even more impressive. Like biofeedback, the worst outcome is that it might not succeed. Significant negative effects are very rare. Practitioners who have studied and now use hypnosis in their medical practices find it an extremely successful addition to their therapeutic armamentarium.

More hypnosis

Thirty-three patients with irritable bowel syndrome refractory to conventional therapy were treated with four 40-minute hypnotherapy sessions over 7 weeks: 20 improved, 11 becoming virtually symptom-free. These improvements obtained for at least three months without additional treatment.

Comment: Most hypnosis/irritable bowel studies have found long-lasting improvement. A common experience is significant regressive in times when the patient comes under siege with additional stresses. And so it is with any conditioning experience. While most of us remember Pavlov’s conditioning of dogs to salivate with the ringing of a bell after pairing this stimulus with the presentation of meat powder, few recall the sequel. After Pavlov had trained numerous dogs, his laboratory in the Ukraine was nearly destroyed by a calamitous flood which inundated mud from a four-foot wall of water which inundated their facility. Some animals tragically died and survivors had to swim for their lives, sometimes for hours. After weeks of reconstruction, when returning to their experiments, Pavlov was dismayed to find that his animals had forgotten their acquired behavior and no longer salivated with the ringing of the bell. Ultimately, however, he established that some elements of training survived: the animals could be retrained in half the time it took originally. During the stressful experience of fighting for their lives, their recent conditioned behavior was lost. Perhaps the animals in the interval after the flood when they were no longer in training could have been given a No-bell prize? In any event, this extinction phenomenon under great stress is observed in patients treated with behavioral methods.

Irritable bowel syndrome and hypnosis

Compared to 25 IBS patients treated routinely (age 25-55, 23 women), 25 IBS patients (25-55, 21 women) treated with hypnosis reported on an analogue scale less severe abdominal pain (p<0.0001), bloating (p<0.02), diastolic bowel habit (p<0.0001), nausea (p<0.05), flatulence (p<0.05), urinary symptoms (p<0.01), lethargy (p<0.01), backache (p=0.05) and dyspareunia (p=0.05). Quality of life (psychic well being [p<0.0001], mood [p<0.001], locus of control [p<0.05], physical well being [p<0.001] and work attitude [p<0.001]) were also favorably influenced by hypnotherapy. For employed subjects, more of the controls were likely to take time off work (79% vs. 32%) (p=0.02) and visit their general practitioner (58% vs. 21% (p=0.056) vs. those treated with hypnotherapy. Three of 4 hypnotherapy patients out of work prior to treatment resumed employment vs. 0 of 6 controls.

Comment: In addition to relieving the symptoms of IBS, hypnotherapy profoundly improved quality of life and reduced absenteeism from work. Despite relatively high initial cost, hypnotherapy could well be a good long-term investment, since ongoing numbers of office visits are reduced and refills of pharmaceuticals which often do not work well in this condition are reduced or eliminated. There is great variability in the length of time and number of hypnosis sessions required to begin to obtain significant improvement. Additionally, patients benefit from a greater sense of control and accomplishment.

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Irritable bowel syndrome/psychological coherence and quality of life

The purpose of this study was to describe and compare sense of coherence (SOC) and holistic quality of life (QOL) of women with and without IBS. A two-group comparison design involved 235 women with IBS and 89 controls without IBS who completed four psychological instruments (Sense of Coherence Questionnaire, Flanagan QOL Scale, Bowel Disease Questionnaire, and Symptom-Checklist-90-R). Sense of coherence and holistic quality of life were lower in women with IBS (p<0.001). Correlations between SOC and global distress, depression, anxiety, and somatization without GI symptoms were moderately and inversely related (p<0.001). Relationships between holistic QOL and psychological distress indicators were universally of lower magnitude (p<0.001). The GI symptom most significantly related to SOC and holistic QOL was alternating constipation and diarrhea (p<0.001).


Comment: This study was not designed to determine whether interventions targeted at enhancing SOC and holistic QOL can impact the psychological distress associated with irritable bowel syndrome. Nor did it distinguish which is the cart and which is the horse: i.e. did a diminished sense of coherence contribute to or result from symptoms of IBS? The global research would seem to indicate that there are elements of bi-directional effects of both. My own experience would bear out the benefits of cognitive and behavioral interventions in reducing GI symptoms and improving quality of life.

Irritable bowel syndrome and mind-body interactions

Brain-gut interactions are increasingly recognized as underlying pathomechanisms of functional gastrointestinal disorders. Bi-directional communication between the central nervous system and the enteric nervous system occurs both in health and disease. Various central nervous system and gut-directed stressors stimulate the brain-gut axis, involving processes which modulate responsiveness to the stressors. Disturbances at every level of neural control of the gastrointestinal tract can affect modulation of gastrointestinal motility, secretion and immune functions, as well as perception and emotional response to visceral events. Gut neural function, CNS processing, and autonomic regulation play an important role in the brain-gut dialogue. Stress and emotions commonly trigger neuroimmune-endocrine reactions via the brain-gut axis. Various non-site-specific neuro-transmitters influence gastrointestinal, endocrinological and immunological function, as well as human behavior and emotional state, depending on their location. The physiology of the digestive tract, the subjective experience of symptom, health behavior, and treatment outcome are strongly affected by psychosocial factors. Recently, a biopsychosocial (holistic) model of IBS including physiological, emotional, cognitive and behavioral components has been proposed to explain a greater portion of observable phenomena.


Comment: I like this summary because it bears out my own experience and beliefs!! These authors are supportive of a holistic worldview, although they might not put it in these terms. Understanding the implications of the brain-gut axis are the quintessence of this entire topic. Rapid progress in neurogastroenterology, using new brain imaging techniques, should bring better understanding of this brain-gut axis and open new therapeutic perspectives.

Gastrointestinal disorders/psychosocial factors

It is widely accepted based on volunteer studies, that levels of psychological distress are similar in those with functional gastrointestinal (GI) disorders and those in good health, while increased psychological distress in outpatients is largely explained by health-care seeking. A case-control study recruited 103 subjects with functional GI disorders (irritable bowel syndrome and nonulcer dyspepsia) and 119 controls aged 20-50. Functional GI disorders were more likely to be reported by those with higher scores on each of the nine SCL-90-R (Symptom CheckList) scales used to measure psychological distress (except phobic anxiety), as well as in those with more negative and total life event stress. Somatization, interpersonal sensitivity, and total life event stress were independently associated with functional GI disorders.


Comment: Contrary to current dogma, psychosocial factors in this study were significantly associated with functional GI disorders in this community sample. This suggests that these factors may be involved in the etiopathogenesis rather than just being driven by health-care utilization. The preponderance of recent studies has tended to explain functional GI problems on a purely physical basis. With this study and those above, I rest my case: Gastrointestinal function affects mind-brain function and mind-brain function affects GI function.


Anderson was the founding president of the American Board of Holistic Medicine, past president of the American Holistic Medical Association, former Assistant Clinical Professor of Family Medicine at the University of Washington and currently Adjunct Instructor in Family Medicine at Bastyr University.