EDITORIALS

The Growing Case for Hypnosis as Adjunctive Therapy for Functional Gastrointestinal Disorders

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In 1984, Whorwell et al.[1] in Manchester, England, published a small but well-designed placebo-controlled trial of hypnosis as a treatment of irritable bowel syndrome (IBS). They randomized 30 patients with severe, refractory IBS to either 7 sessions of hypnotherapy or the same amount of psychotherapy plus placebo pills. The results indicated that hypnosis treatment had specific (nonplacebo) effects that substantially improved the central IBS symptoms of all the patients in that group (who showed far greater improvement than the control group). In a follow-up article,[2] the investigators reported that clinical improvement was maintained in all the hypnotherapy patients during a 2-year posttreatment period.

A dozen other hypnosis studies on IBS, by the same group[3–6] and by other investigators in several countries,[7–14] have followed this initial trial. The additional studies have largely confirmed the high efficacy of hypnosis in IBS treatment, although the 100% response rate in the first study has generally not been equaled. This body of research has made hypnosis the most investigated psychologic treatment of IBS. In that regard, it is rivaled only by cognitive-behavioral therapy, which also shows a high success rate and substantial impact on IBS symptoms in some trials.[15,16]

Although some of these studies have been small and inadequate in design, hypnotherapy has emerged from the cumulative experience of this work not only as effective in improving the gastrointestinal (GI) symptoms that define IBS but also as a potent way to counter the quality of life impairment, disability, and excess health care costs associated with the disorder.[3,4] This is most recently shown by the largest systematic assessment to date (250 consecutive patients) of the therapeutic impact of this treatment, reported in 2002 by the Manchester group.[3] Based on the more than 50% average reduction in IBS severity, substantial reduction in anxiety and depression, significantly reduced health care costs and improved quality of life noted in this report, and good maintenance of symptom improvement beyond 2 years after treatment, it might be argued that hypnotherapy is more effective than any other single treatment modality for severe IBS.

In the present issue of GASTROENTEROLOGY, the Manchester group again presents a controlled trial of hypnotherapy,[17] this time targeting functional dyspepsia (FD). The design closely parallels the group's 1984 controlled trial[1] for IBS. As in that study, patients were randomized to either hypnotherapy or to an equal amount of supportive psychotherapy combined with placebo medication. However, the present study added a second side-by-side control group of patients randomized to standard medical treatment.

The hypnosis intervention used in this study is also largely identical in form and in content to what the Manchester group has used for many years for IBS, with some relatively small modifications to address FD symptoms.

The impact on FD from the hypnotherapy reported in their article closely mirrors the benefits of hypnosis seen for IBS. The mean reductions in symptoms were about the same as for IBS[3] (59%) and continued to improve after treatment, reaching a remarkable average of 73% reduction in severity at 1-year follow-up (in contrast with the comparison groups). Greater decreases in medication use and improvement of quality of life after hypnotherapy were noted in this trial. As in the treatment of IBS, the therapeutic effects are generally well preserved at long-term follow-up.

Although replication of this first therapeutic trial for FD is needed, it expands considerably our knowledge of the potential for hypnotherapy as a treatment of functional GI problems. FD and IBS jointly account for more than half of the workload of gastroenterologists.[18] Up to half of these patients are dissatisfied with standard treatment,[19] which highlights a considerable unmet need for adjunctive or complementary treatments that can improve efficacy and patient satisfaction. With the present FD hypnotherapy study indicating that this treatment method may be as effective for FD as it is for IBS, it is becoming increasingly hard to ignore the notion that the skills of the hypnotherapist should be made routinely available to patients with functional GI disorders. The evidence consistently argues that wide availability of hypnotherapy would make management of these disor-

ders more effective and would add broad benefits in improved emotional well-being and functional status of these patient groups. It might also produce large savings in cost of care for health care systems because of reduction in medication use and health care visits.

These potential advantages of hypnotherapy as adjunct in the management of IBS and FD raise the question whether it would be possible to implement routine adjunctive hypnosis management in mainstream care for GI disorders. The short answer is that, although feasible, it would, at least in the United States, require overcoming substantial practical and systemic obstacles.

Psychologic treatment is currently used only rarely as a therapeutic modality for functional GI patients, offered to less than 10% of all patients in primary care and gastroenterology clinics. Furthermore, this option is probably exercised mostly with patients who either present with significant psychologic symptoms or have not responded to conventional treatment. Many health maintenance organizations dissuade primary care physicians from routinely making outside referrals for psychologic treatment of functional GI disorders because of the higher up-front cost of such care. Reimbursement for psychologic treatment of functional GI disorders is furthermore limited or nonexistent in many insurance plans. All of these aspects of the health care system would have to be addressed and corrected to make hypnosis for FD and IBS widely available.

Perhaps an even more serious hindrance to widespread application of hypnotherapy for functional GI disorders is the limited availability of suitably trained and experienced clinicians. Only a very small proportion of physicians and nursing staff have the training or experience to administer hypnotherapy. Because of time pressures on physicians, such work may be impractical, especially in primary care settings, in which a series of 30-minute sessions with any one patient is likely to seem an unattainable luxury. Close collaborative ties with hypnotherapists do not exist in most medical settings. In the United States, mental health professionals, many of whom have little knowledge of functional GI disorders and therefore are often reluctant to undertake treatment of these disorders, practice much of clinical hypnosis.

Finally, popular perception of hypnosis, which even today carries an unfortunate and erroneous legacy of mystery and coercive influence over people from popular media and stage shows, may make some patients and physicians less receptive to considering this treatment option.

In light of the growing evidence of the value of hypnotherapy in enhancing care for functional GI disorders, it would seem timely to make a concerted effort to examine ways to remove these barriers and facilitate the availability of such treatment; for example, by providing systematic training to health professionals specifically in hypnotherapy for functional GI disorders, integrating hypnotherapy services, and enhancing reimbursement and referral patterns for such treatment.

The Manchester group, the pioneers in the domain of GI hypnosis, represents 1 model of how hypnotherapy can be effectively integrated with clinical gastroenterology. They have established a unit dedicated to medical hypnotherapy, working hand-in-hand with the gastroenterology service, and using 6 hypnotherapists who treat a large numbers of functional GI patients with hypnotherapy.

Apart from practical hindrances that continue to keep hypnotherapy from broad use for GI disorders, a number of important research questions remain unanswered about such treatment:

1. The mechanism of the impact of hypnosis on functional GI disorders remains obscure. Unlike pharmaceutic agents for IBS and FD, which have a clearly delineated mechanism of action, it is largely unknown how hypnotherapy produces its effects on GI symptoms. It is well documented that hypnosis can modulate GI functioning. The hypnotic state seems by its own virtue to increase oro-cecal transit time[20] and quiet colonic motility.[21] Experimental application of specific hypnotic suggestions and imagery can also have demonstrable effects on gastric secretion[22] and transit time.[20] Tests performed during hypnosis show decreased perception of discomfort in patients with IBS[6] and FD.[23] However, the research to date on posttreatment changes associated with hypnotherapy have provided very little evidence[5,6,10,11] that overall changes in physiologic parameters such as pain thresholds, muscle tone, or autonomic functioning are central to the therapeutic effect, with the possible exception of increased pain thresholds for the most pain-sensitive subgroup of patients.[5] Further work is needed to elucidate the main mechanism of action that produces improvement in GI symptoms.
2. Side-by-side comparisons with other psychologic treatments are still lacking. Various other psychologic treatments have also been reported to have a positive impact on IBS symptoms, including cognitive-behavioral therapy,[15,16] interpersonal therapy,[24] stress-management training,[25,26] and psychodynamic therapy.[27] It remains uncertain at

this time whether hypnotherapy is superior to these alternative psychologic treatments because no side-by-side comparative studies have been conducted.

3. Combined effects with medications are unknown. To date, the research on hypnotherapy for FD has exclusively tested it as a monotherapy. The combination of this psychologic treatment with medications such as antidepressants and the 5-hydroxytryptamine modulating agents for IBS seems in order, if this type of treatment is to be considered as an adjunctive therapy in medical care. Such combination trials are also important because experience from non-GI trials of combined psychologic therapy and pharmacotherapy for headache[28] and depression,[29] for example, suggests that such a combined pharmacologic–psychologic approach is superior to either intervention alone.
4. It is unknown whether hypnotherapy for FD and IBS can be administered in an automated home-treatment format. Hypnosis is unlike most other psychologic treatments because it is largely a one-way talk therapy with very limited interactivity. For this reason, it can be used without a live therapist, and this is commonly done in the form of audiotaped home practice sessions that patients use between clinic visits. The availability and affordability of this therapy would be vastly increased if the same kind of face-to-face hypnosis treatment found effective for FD and IBS would also help patients when administered exclusively in a home-treatment audio format. No data have been presented to date to make it possible to conclude whether this is feasible.

In conclusion, although some of the studies to date on hypnotherapy for functional GI disorders have been small and lacking in methodological rigor, and many research questions remain unanswered, the cumulative and consistent evidence for efficacy of hypnotherapy for these disorders seems to warrant serious consideration of its use as a regular adjunct in primary care and gastroenterology treatment of patients with FD and IBS.

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0016-5085/02/$35.00
doi:10.1053/gast.2002.37286

Chemotherapy for Hepatitis B: New Treatment Options Necessitate Reappraisal of Traditional Endpoints

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Despite the availability of safe and effective vaccines, hepatitis B remains a global health problem, responsible for about 1.2 million deaths annually.[1] It has been estimated that more than 2 billion people either have been, or are currently infected, with hepatitis B virus (HBV) and that about 5% of the world's population are chronic carriers. This means that the global frequency of chronic infection with HBV is about 10 times higher than the frequency of infection with the human immunodeficiency virus (HIV). HBV infection is a complex and heterogeneous disease entity that may either resolve spontaneously or manifest itself in a variety of ways. Although HBV preferentially infects hepatocytes, infection of other cells including bile duct epithelium cells, mesangial cells of the kidney, pancreatic islet cells, and lymphoid cells have also been detected. Some or all of these extrahepatic sites may act as virus sanctuaries, protecting HBV from the antiviral activity of drugs and the immune system. HBV infection is rarely, if ever, directly cytopathic and it is believed that pathogenic sequelae of HBV infection are caused by deregulation of host cell gene expression and/or proinflammatory and cytotoxic effects secondary to abortive attempts by the host's own immune system to eliminate infected cells. These indirect effects, rather than viral integration or direct oncogenic potential, most likely account for the substantially increased risks for development of potentially fatal cirrhosis, liver failure, and/or primary hepatocellular carcinoma (HCC) that are associated with HBV infection. The heterogeneity of hepatitis B disease and its slow and variable progression to "real" endpoints (liver failure, cirrhosis, HCC, and death), together with limitations of available diagnostic technology, makes it difficult to define criteria by which the success of different therapeutic strategies can be judged. We can expect that a need to redefine treatment goals will become increasingly evident as the number of treatment options increases.

Detection of elevated levels of liver enzymes including aminotransferases (notably alanine aminotransferase [ALT]) in serum is regarded as a surrogate marker of liver damage and is often the first indicator of HBV infection. Diagnosis of hepatitis B is routinely based on interpretation of subsequent serological assays. During the course of infection, the viral core protein (HBcAg), surface antigens (HBsAg), and the secreted e antigen (HBeAg) all elicit immune responses in immunocompetent hosts, producing the corresponding antibodies (anti-HBc, anti-HBs, and anti-HBe). Assay for serum HBsAg, which is exposed on the surface of the virus envelope as a mosaic of glycoproteins, is a reliable and sensitive diagnostic test, because during infection an excess of