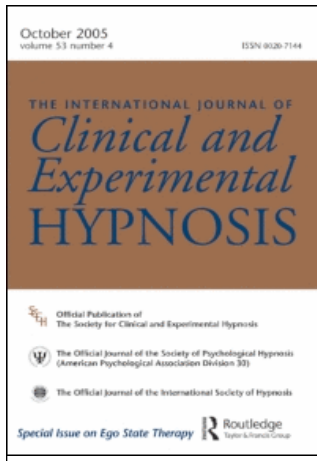


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International Journal of Clinical and Experimental Hypnosis

Publication details, including instructions for authors and subscription information:
<http://www.informaworld.com/smpp/title~content=t713657963>

Treatment of Inflammatory Bowel Disease: **A Role for Hypnotherapy?**

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Online Publication Date: 01 July 2008

To cite this Article: Miller, Vivien and Whorwell, Peter J. (2008) 'Treatment of Inflammatory Bowel Disease: **A Role for Hypnotherapy?**', International Journal of Clinical and Experimental Hypnosis, 56:3, 306 — 317

To link to this article: DOI: 10.1080/00207140802041884

URL: <http://dx.doi.org/10.1080/00207140802041884>

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TREATMENT OF INFLAMMATORY BOWEL DISEASE: *A Role for Hypnotherapy?*

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Abstract: Fifteen patients with severe or very severe inflammatory bowel disease on corticosteroids but not responding to medication received 12 sessions of “gut-focused hypnotherapy” and were followed up for a mean duration of 5.4 years with disease severity being graded as remission, mild, moderate, severe, or very severe. Two patients (13.4%) failed to respond and required surgery. At follow-up for the remaining 13 patients, 4 (26.6%) were in complete remission, 8 (53.3%) had mild severity, and 1 (6.7%) was moderately severe. Quality of life became good or excellent in 12 (79.9%). Corticosteroid requirements dramatically declined with 60% of patients stopping them completely and not requiring any during follow-up. Hypnotherapy appears to be a promising adjunctive treatment for inflammatory bowel disease and has steroid sparing effects. Controlled trials to clearly define its role in this disease area are justified.

Crohn’s disease and ulcerative colitis, collectively known as inflammatory bowel disease (IBD), are inflammatory conditions of the gastrointestinal tract that characteristically result in diarrhea often accompanied by bleeding, abdominal pain, and a variety of constitutional symptoms such as weight loss, anemia, or sometimes fever. Sufferers may also experience a series of extraintestinal features including mouth ulcers, arthralgia, iritis, erythema nodosum, and sclerosing cholangitis. Severity can range from mild to incapacitating and on occasions both diseases can be life threatening. The cause of these conditions has yet to be established, but a disorder of immune function or its regulation appears to be at least contributory (Bamias, Nyce, De La Rue, & Cominelli, 2005; Wen & Fiocchi, 2004; Young & Abreu, 2006). It is not even clear whether they represent polar ends of disease spectrum or are distinct entities that just share similar symptomatology. Whatever the cause, treatment approaches tend to be very similar, often involving the stepwise use of a range of

Manuscript submitted March 6, 2007; final revision accepted May 9, 2007.

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antiinflammatory or immunomodulatory medications. Fortunately, many patients respond to such a regimen, but, when they do not, surgery may have to be contemplated. It is in such individuals that an alternative solution to their problem would be useful in order to try and avoid an operation.

It is common for IBD patients to claim that stressful life events exacerbate their symptoms but research in this area has produced somewhat conflicting results, although the balance is in favor of an adverse effect (Maunder, 2005; Mawdsley & Rampton, 2005). In recent years, there has been a growing body of evidence that stress can have a significant effect on a whole range of measures of immunological function (Fleshner & Laudenslager, 2004; Maunder, 2005; Ray, 2004), and this could have significant effects in terms of disease expression. In addition, the potential for stress to affect the gut is a phenomenon that most individuals have experienced, and there is experimental evidence for an affect on secretory function, mucin release, and mucosal integrity (Bhatia & Tandon, 2005; Hart & Kamm, 2002). The latter can result in an increase in gut permeability to intraluminal antigens, which, at least theoretically, could play a part in initiating or perpetuating an inflammatory process within the gastrointestinal mucosa. Thus, stress reduction is a possible therapeutic target, and there is some evidence to suggest teaching patients to manage this aspect of their lives improves the course of their disease (Milne, Joachim, & Niedhardt, 1986). Traditionally, hypnosis is often regarded as a technique for managing stress and the psychological aspects of illness, although there has always been evidence indicating that it has effects that extend beyond these rather narrow confines. It is now becoming increasingly recognized that the technique appears to enable influence over a wide range of physiological parameters, including those of an immunological nature (Gruzelier, 2002), which could be of particular relevance to the treatment of IBD.

Our unit has been undertaking research into the application of hypnotherapy in gastroenterology for more than 20 years and has developed the technique of "gut-focused hypnosis," which is delivered on a weekly basis for 12 weeks with daily practice between sessions being encouraged and aided by the use of an audio recording (Whorwell, 2006). In clinical trials using this approach, we have shown benefit in irritable bowel syndrome (Whorwell, Prior, & Faragher, 1984), duodenal ulcer (Colgan, Faragher, & Whorwell, 1988), functional dyspepsia (Calvert, Houghton, Cooper, Morris, & Whorwell, 2002), and noncardiac chest pain (Jones, Cooper, Miller, Brooks, & Whorwell, 2006) with results not being dependent on the hypnotizability of the patient. Furthermore, the beneficial effects appear to be sustained over a number of years (Gonsalkorale, Miller, Afzal, & Whorwell, 2003). In addition

we have demonstrated effects on gastrointestinal physiology such as motility (Whorwell, Houghton, Taylor, & Maxton, 1992) as well as visceral sensation (Lea et al., 2003), and others have shown that gastric acid secretion (Klein & Spiegel, 1989), the gastrocolonic response to lipid infusion (Simren, Ringstrom, Bjornsson, & Abrahamsson, 2004), and gastric emptying (Chiarioni, Vantini, De Iorio, & Benini, 2006) can also be influenced. Given the potential for hypnosis to positively affect stress as well as gastrointestinal and immune function, it seemed reasonable to undertake a proof of principle study in IBD.

It was therefore the purpose of this study to assess the possible role of hypnotherapy in aiding the management of patients with severe Crohn's disease and ulcerative colitis who were not responding to conventional medication.

METHOD

Fifteen patients with inflammatory bowel disease, 12 with ulcerative colitis, and 3 with Crohn's disease, who were not responding to conventional treatment, were studied. Every patient with ulcerative colitis had at least a third of their colon affected by disease, and all cases of Crohn's disease were of the ileocolic variety. There were 12 females and 3 males ranging in age from 18 to 59 (mean = 43.9). They all had chronic active disease rather than being in an acute relapse and were of a severity where surgery was being contemplated in some for symptom-relief rather than being regarded as lifesaving. All patients were taking oral corticosteroids at or above 15 mg daily as well as oral 5 aminosalicylic acid preparations (mesalamine). Eight patients were also receiving azathioprine.

Disease severity was classified at the beginning of treatment as mild, moderate, severe, or very severe, and the same scale, with an additional category of remission, was used at the end of treatment as well as after follow-up. Quality of life was assessed as being excellent, good, moderate, poor, or very poor. In patients requiring surgery, the prehypnotherapy score was carried forward and used as the follow-up score in order not to overemphasize the effectiveness of hypnotherapy. Colonoscopy, sigmoidoscopy, and any other relevant gastrointestinal investigation was undertaken based on clinical need rather than any set time during the course of hypnotherapy treatment. However, the consumption of steroids was monitored closely and a reduction in dose was regarded as an important outcome measure. No attempt was made to withdraw mesalamine as not only is this drug effective in preventing relapse in ulcerative colitis but there is now accumulating evidence that in the same condition it may also help to protect from the development of colon cancer (Munkholm et al., 2006). Furthermore, it was not felt that it would be justified to withdraw azathioprine in any

hypnotherapy responders as this drug also helps to maintain remission, and the main purpose of this study was to ascertain whether disease severity could be reduced by hypnosis rather than assessing whether azathioprine could be withdrawn. Thus, the primary outcomes were symptom improvement, quality of life, and reduction of steroid dosage. The possible prevention of a surgical outcome was recorded.

All subjects had 12 sessions of gut-focused hypnosis, which utilized two main components, one tactile and the other utilizing visualization. The former involved the individual placing their hand on their abdomen, feeling warmth, and relating this to healing of the ulcerative process; a reduction of inflammation; decreasing discomfort; and a normalization of bowel function. It is self-evident that patients need to be given a simple tutorial on the pathophysiological concepts about IBD before embarking on all this. The visualization content of the technique involved asking the patient to imagine the state that their gut was in when affected by inflammation and then to envisage this being cleared away in whatever way was most meaningful for them. Suggestions such as healing of ulceration, color changes of the mucosa from red to pale pink, or the gut being bathed in soothing fluid were used, but patients were allowed to evolve their own visualization techniques and told it was perfectly reasonable to work with these. All patients were given an audio recording lasting approximately 30 minutes with content similar to that of a hypnotherapy session and encouraged to practice, preferably on a daily basis.

RESULTS

Figure 1 details the disease severity of the patients before, immediately after the course of hypnotherapy, and after a follow-up period ranging from 2 to 16 years (mean = 5.4 years). As can be seen, disease severity was classified as severe or very severe in all patients before hypnotherapy, and in 14 of the 15 patients it became either mild or moderate immediately following treatment. The remaining patient, who had ulcerative colitis, completely failed to respond to treatment and went on to have surgery. During follow-up, 1 patient with Crohn's disease relapsed and required surgery. In the remaining 13 patients, disease severity further improved with 4 ulcerative colitis patients (26.6%) going into complete remission, 2 Crohn's disease and 6 ulcerative colitis patients (53.3%) becoming mild, and 1 ulcerative colitis patient (6.7%) remaining moderately active. Other than the 2 patients who required surgery, no patient became worse following hypnotherapy. Ten (67%) of the patients said that they had attended the hospital outpatient department less often following treatment.

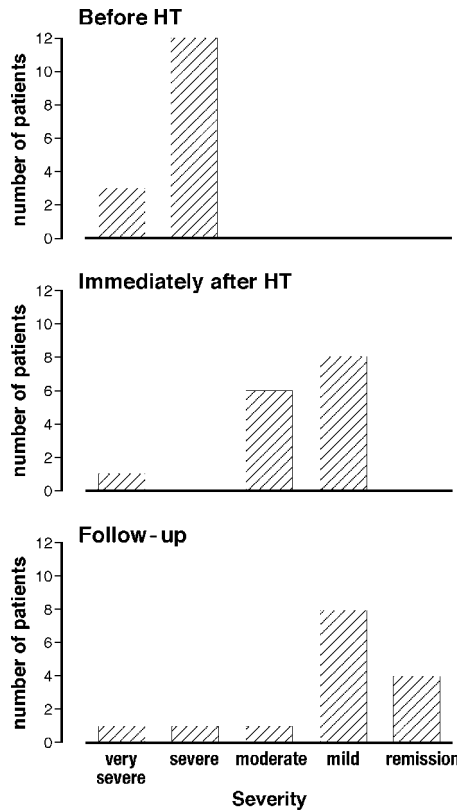


Figure 1. Effect of hypnotherapy on disease severity: numbers of patients in each severity category before, immediately after treatment, and at follow-up. Pre-hypnotherapy scores on the 2 patients requiring surgery carried forward as if unimproved.

Figure 2 shows quality of life before and after treatment, and, as can be seen, the changes generally reflected those observed in relation to disease severity. Initially, quality of life was very poor in 5 ulcerative colitis patients (33.3%), poor in 4 ulcerative colitis and 2 Crohn's disease patients (40%), moderate in 3 ulcerative colitis patients (20%), and good in 1 Crohn's disease patient (6.7%). At follow-up, in the 13 patients remaining after the 2 who required surgery, quality of life improved, becoming excellent or good in 10 ulcerative colitis patients and the 2 remaining Crohn's disease patients (79.9%). In the other ulcerative colitis patient, it was moderate. In the two patients requiring surgery one was initially classified as severe and the other very severe and therefore, because their data was carried forward, at follow-up they remained classified as severe and very severe respectively (Figure 1).

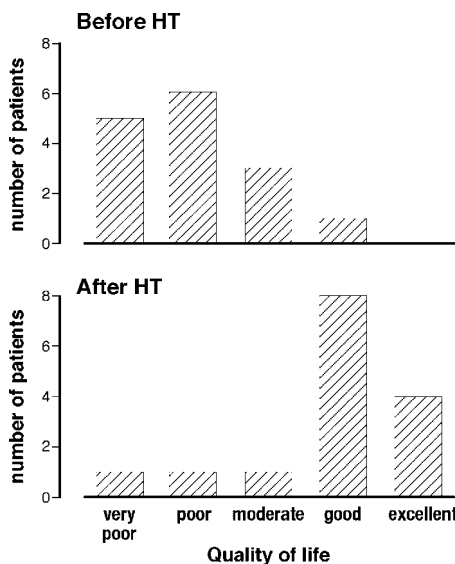


Figure 2. Effect of hypnotherapy on quality of life: numbers in each category before and after treatment. Pre-hypnotherapy scores on the 2 patients requiring surgery carried forward as if unimproved.

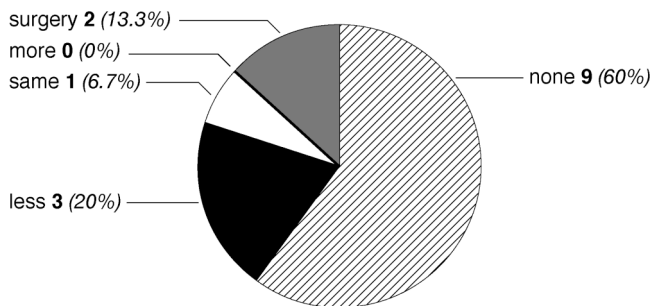


Figure 3. Corticosteroid consumption during follow-up compared with pre-hypnotherapy doses.

Figure 3 documents corticosteroid use in the patients during the follow-up period. Nine patients (60%) of the original group of 15, of whom 8 had ulcerative colitis and 1 had Crohn’s disease, have never required corticosteroids since their hypnotherapy. In the remainder, 1 Crohn’s disease and 2 ulcerative colitis patients were using less steroids, and in 1 ulcerative colitis patient it had remained the same. Not

one of these patients had required higher doses of steroids since treatment. Although only a subjective observation, it was considered that surgery had been avoided in at least 3 individuals. In the two patients requiring surgery one was initially classified as poor and the other very poor and therefore, because their data was carried forward, at follow-up they remained classified as poor and very poor respectively (Figure 2).

DISCUSSION

The results of this exploratory study suggest that hypnotherapy may well have utility in the management of IBD. This form of treatment will never replace pharmacological approaches but it could well help to enhance a patient's response to such measures, and this certainly seemed to be the case in this study. In addition, it appears to also have a steroid-sparing effect. Hopefully preliminary data such as this may help to persuade funding bodies, which have traditionally been reluctant to invest in hypnosis research, to underwrite the investigation of its application in this disease area so that its true role can be defined.

Although attitudes have now changed, in the mid-20th century ulcerative colitis in particular was considered to be a typical example of a psychosomatic disorder. In addition, patients not infrequently relate a relapse in their symptoms to stressful life events. It is therefore quite surprising that there have been relatively few studies investigating the beneficial effects of various psychologically orientated treatments in IBD. Not surprisingly, most of these are relatively old because, with the advent of the better understanding of immunological and inflammatory mechanisms, therapeutic approaches have concentrated more on these rather than psychological factors. Hopefully, as these artificial boundaries between systems become broken down, more integrated approaches to treatment will be forthcoming. Some, but not all, of these previous studies of psychologically orientated treatments (Freyberger, Kunsebeck, Lempa, Wellmann, & Avenarius, 1985; Jantschek et al., 1998; Karush, Daniels, O'Connor, & Stern, 1968, 1969; Milne et al., 1986; Schwarz & Blanchard, 1991) have suggested benefit, but it would be of interest to reassess them now that these techniques have become better documented and trial techniques more refined. With respect to hypnosis, there appear to be only two previous reports on the effects of hypnotherapy in inflammatory bowel disease, although one is in abstract form (Shetty et al., 2004), and the other describes just 3 patients (Schafer, 1997). However, both of these studies suggested that this approach might have potential, and certainly this is a treatment modality deserving further research (Abela, 2000; Anton, 1999).

It is interesting that in irritable bowel syndrome it has been shown that hypnotherapy brings about symptom improvement by a range of mechanisms, some physiological, some psychological, and there is also evidence from studies on healthy individuals that it can influence the way painful stimuli are processed by the brain (Rainville, Duncan, Price, Carrier, & Bushnell, 1997). Similarly, it seems likely that the technique might bring about improvement in inflammatory bowel disease by a range of mechanisms. Undoubtedly, it has direct beneficial psychological effects but these could also indirectly influence parameters such as intestinal permeability, which have already been referred to and are known to be adversely affected by stress. There is also experimental evidence that it can modulate immune function with effects on T-cell function, natural killer cell activity, and skin reactivity of the immediate type as well as the mantoux reaction (Fry, Mason, & Pearson, 1964; Gruzelier, Smith, Nagy, & Henderson, 2001; Kiecolt-Glaser, Marucha, Atkinson, & Glaser, 2001; Zachariae, Bjerring, & Arendt-Nielsen, 1989). Although the majority of published work is in favor of an immunological effect, not all studies have confirmed these observations (Locke et al., 1994), and it has to be born in mind that negative studies are less likely to be published. However, all these observations coupled with our results provide tantalizing evidence that hypnosis might be useful in inflammatory bowel disease.

These results obviously need to be confirmed in properly controlled clinical trials that should probably address issues such as induction of remission, steroid-sparing effects, symptom control, and maintenance of remission separately, because not all these aspects may necessarily respond to the same degree. Maintenance trials could be especially challenging, as they would take much longer to complete. It is frequently claimed that it is impossible to undertake good quality clinical trials assessing the efficacy of treatments such as hypnotherapy where issues arise especially in relation to blinding, expectation, and choice of suitable controls. However, these problems are not necessarily insurmountable, although it does have to be accepted that a truly double-blind study is impossible in a treatment where it is obvious to the recipient what modality they are receiving. Nevertheless, this should not dissuade researchers from undertaking trials and the scientific community accepting the results when all reasonable precautions have been taken. When considering the design of such studies, particular attention has to be given to what constitutes the most appropriate comparator group. Usual medical care would clearly not be an adequate control for a modality that involves so much attention and expectation. We have always felt that a session of "supportive" or "psychotherapy" of similar duration and frequency is mandatory (Calvert et al., 2002; Jones et al., 2006; Whorwell et al., 1984). In addition, we give the controls a placebo medication that serves two purposes. Primarily, its role

is to boost the therapeutic package being offered as much as possible, but it also helps to ensure that patients return for their sessions as further supplies of medication are only dispensed at the end of each appointment. There is no reason why a trial cannot be single blind, and we achieve this by using an independent assessor who is kept ignorant of the treatment allocation.

Thus, in conclusion, there is a considerable amount of experimental data to support the notion that hypnosis might have the capacity to positively influence some of the putative immunological and inflammatory mechanisms involved in the pathogenesis of inflammatory bowel disease as well as having useful psychological effects. This, coupled with our evidence of the possible clinical benefits, suggests that the potential use of hypnotherapy in this disease area deserves further research.

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Behandlung chronisch entzündlicher Darmerkrankung: Hypnosetherapie als mögliche Therapieform? Treatment of Inflammatory Bowel Disease: A Role for Hypnotherapy?

Vivien Miller und Peter J. Whorwell

Zusammenfassung: 15 Patienten mit schwerer entzündlicher Darmerkrankung und Kortikosteroidbehandlung, die jedoch nicht auf die medikamentöse Behandlung ansprachen, erhielten 12 Sitzungen von "darm-fokussierter Hypnosetherapie" und wurden im Durchschnitt über 5,4 Jahre weiter beobachtet. Die Schwere der Erkrankung wurde dabei als Remission, leicht, mittel, schwer oder sehr schwer klassifiziert. Bei zwei Patienten (13,4 %) schlug die Therapie nicht an und sie wurden chirurgisch behandelt. Bei der Folgeuntersuchung der verbleibenden 14 Patienten befanden sich 4 (26,6%) in Vollremission, 8 (53,3%) wurden als leicht und einer (6,7%) als mittelschwer klassifiziert. Die Lebensqualität verbesserte sich und wurde bei 12 (79,9%) als gut oder sehr gut eingestuft. Der Bedarf an Kortikosteroiden reduzierte sich drastisch, 60 % der Patienten konnten vollständig darauf verzichten und benötigten auch bei der Folgeuntersuchung keine Kortikosteroide. Hypnosetherapie stellt eine viel versprechende adjunktive Behandlungsform bei entzündlicher Darmerkrankung dar und reduziert den Bedarf an Steroiden. Kontrollierte Studien, welche helfen, die genaue Rolle von Hypnosetherapie bei der Behandlung dieser Krankheit festzulegen, sind gerechtfertigt.

RALF SCHMAELZLE

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**Le traitement de la maladie intestinale inflammatoire:
Un rôle possible pour l'hypnothérapie?**

Vivien Miller et Peter J. Whorwell

Résumé: Quinze patients souffrant de maladies intestinales inflammatoires graves ou très graves, chez qui la prise de corticostéroïdes demeurerait sans effet, ont bénéficié de 12 séances « d'hypnothérapie visant les intestins » et ont été suivis pendant une durée moyenne de 5,4 ans, à la suite de quoi leur maladie a été catégorisée selon les degrés de gravité suivants : en rémission, bénigne, modérée, grave ou très grave. Deux patients (13,4 %) n'ont retiré aucun bienfait de l'hypnothérapie et ont dû se faire opérer. Au moment du suivi, des 13 patients restants, 4 (26,6 %) étaient en rémission complète, 8 (53,3 %)

présentaient des symptômes bénins et 1 (6,7 %) montrait des symptômes modérément graves. La qualité de vie de 12 patients (79,9 %) était devenue de bonne à excellente. La nécessité de la prise de corticostéroïdes a diminué de façon radicale, alors que 60 % des patients ont complètement cessé de les prendre et n'en ont eu aucun besoin durant la période de suivi. L'hypnothérapie semble être un traitement adjuvant prometteur de la maladie intestinale inflammatoire et permet d'éviter l'usage des stéroïdes. Des essais contrôlés visant à définir clairement le rôle qu'elle pourrait jouer dans le soulagement de cette maladie sont maintenant justifiés.

JOHANNE REYNAULT
C. Tr. (STIBC)

El tratamiento de colon irritable: ¿Es útil la hipnoterapia?

Vivien Miller y Peter J. Whorwell

Resumen: Quince pacientes con colon irritable severo o muy severo que recibían corticoesteroides pero no respondían a la medicación recibieron 12 sesiones de "hipnoterapia enfocada en el estómago" y tuvieron seguimiento durante un intervalo promedio de 5.4 años. La gravedad de la enfermedad al final podía ser en remisión, leve, moderada, severa, o muy severa. Dos pacientes (13.4%) no respondieron y requirieron cirugía. En el seguimiento de los restante 13 pacientes, 4 (26.6%) estaban en remisión completa, 8 (53.3%) tenían un nivel de enfermedad leve, y 1 (6,7%) tenían un nivel medianamente severo. La calidad de vida llegó a ser buena u óptima en 12 (79,9%). La necesidad de corticoesteroides declinó dramáticamente, 60% de los pacientes dejaron de tomarla y no la requirieron durante el seguimiento. La hipnoterapia parece a ser un tratamiento adjunto prometedor para el colon irritable y disminuye los efectos de los esteroides. Diseños controlados para definir su papel claramente en esta enfermedad están justificados.

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