CONTROLLED TRIAL OF HYPNOTHERAPY AS A TREATMENT FOR IRRITABLE BOWEL SYNDROME

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ABSTRACT

Nineteenth century philosophy and anatomy regarded the nervous system as the only pathway of communication between the brain and body but now, research in the field of psychoneuroimmunology (PNI) has provided evidence to prove the age-old belief that there is a connection between the mind (or mental/emotional states) and the body. Researchers in PNI have now shown that the communication between the nervous and immune systems is *bi-directional* – i.e. there is a psychological reaction to physical disease and a somatic presentation of psychological disorders - and that the immune system, the autonomic nervous system, the endocrine system and the neuropeptide systems all communicate with each other by means of chemicals called messenger molecules or ligands.

This paper outlines research into the treatment of Irritable Bowel Syndrome (IBS) with hypnotherapy, taking into account the mind-body connection and treating both the patient's physiological and emotional/psychological symptoms rather than treating the physiological symptoms only. In other words, using a more holistic approach to the treatment of IBS.

IBS is probably the most common functional gastrointestinal disorder encountered by both gastroenterologists and physicians in primary care. It is estimated that from 10% to 25% of the general population suffer from this condition and that it comprises about 30-50% of the gastroenterologists' workload, yet the aetiology of IBS is unknown and, so far, there is no cure.

Researchers are beginning to view IBS as a multi-faceted disorder in which there appears to be a disturbance in the interaction between the intestines,

brain, and autonomic nervous system, resulting in an alteration in the regulation of bowel motility and/or sensory function. Most researchers agree that a subset of IBS sufferers have a visceral hypersensitivity of the gut or, more specifically, an increased perception of sensations in the gut.

To date, studies of IBS have proposed previous gastroenteritis, small intestine bacterial overgrowth, psychosocial factors, a genetic contribution, and an imbalance of neurotransmitters as either possible causes or playing a part in the development of IBS. It is generally agreed that a patient's emotional response to stress can exacerbate the condition.

In section 1 of the thesis, the introduction, a detailed description and background appropriate to the study undertaken are provided, including aspects of epidemiology, diagnostic symptom criteria and clinical relevance of the Irritable Bowel Syndrome. Previous studies of various forms of treatment for IBS are discussed with the main emphasis being on treatment with hypnotherapy. All these therapies have concentrated on *either* mind or body treatments whereas this study demonstrates how hypnotherapy, and the use of imagery, addresses *both* mind and body. Finally, the rationale for the current study and the specific aims of the thesis are outlined.

In section 2, the methodology and assessment instruments used in the clinical trial are discussed, as well as recruitment processes, research plan and timetable, and treatment schedule. Statistical analyses are provided and the main outcomes measures of the clinical trial, its limitations and scientific implications are addressed.

STATEMENT OF ORIGINALITY

The study of this thesis represents original research undertaken by the author as a doctoral research student in the Department of Behavioural and Community Health Sciences, University of Sydney, Australia.

The author was responsible for the initiation and conduct of the work which was performed under the supervision of Dr. Gomathi Sitharthan and Professor Nick Talley.

The study was carried out by the author. Assessment of patients and their selection for study were also carried out personally.

This material has not been previously submitted either in whole or in part for a degree at the University of Sydney or any other university.

Signature: _____ Date_____

Candidate's Certificate.

I, Julie Phillips-Moore, hereby declare that the work contained within this thesis is my own and has not been submitted to any other university or institution as a part or whole requirement for any higher degree.

Student's Signature: _____

Supervisor's Certificate.

This is to certify that the thesis 'Controlled Trial of Hypnotherapy as a Treatment for Irritable Bowel Syndrome' submitted by Julie Phillips-Moore in fulfilment of the requirement for the degree of Doctor of Philosophy, is in a form ready for examination.

Supervisor's Signature:

STATEMENT OF ETHICS

All subjects who participated in these studies gave written informed consent. The protocols were approved by the Ethics Committee, University of Sydney, Australia.

PUBLICATIONS

- **The Australian Journal of Clinical Hypnotherapy & Hypnosis**. Vol 23 No.2 September 2002. *Psychoneuroimmunoligical background to a controlled trial of hypnotherapy as a treatment for irritable bowel syndrome* pp.101-113.

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ABSTRACTS

In addition, aspects of this work were delivered at:

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CHAPTER 1 INTRODUCTION

1.1 The Mind-Body Connection

Mind-body interaction (or psychoneuroimmunology) is a relatively new area of research and is best described as a scientific investigation of how the mind (or mental states) affects one's health and how one's health can be affected by behaviour (Solomon, 1987). Scientific evidence for the mind's influence on the body now comes from three diverging areas of research:

- physiological research, which investigates the biological and biochemical connections between the brain and the body's systems;
- epidemiological research, which shows correlations between certain psychological factors and certain illnesses in the population at large; and
- clinical research, which tests the effectiveness of mind-body approaches in preventing, alleviating, or treating specific diseases (Goleman & Gurin, 1995).

The area of focus for this thesis is in the area of clinical research. Rather than focusing on the *cause* of disease, the emphasis of this research (as in most clinical research) will be on the more positive aspect of *testing the effectiveness* of mind-body approaches on illnesses. The mind-body approach to be tested is hypnotherapy: the illness is Irritable Bowel Syndrome.

Interest in the mind-body connection has grown because research from studies on brain-immune-nervous system interactions and clinical results from both health professionals and researchers have substantiated not only the psychological effects on health and disease but also the effect of diseases on the psyche. As Achterberg so aptly states:

"There is little argument about the negative power of the imagination on health… Since nature creates few one-way passages, if we can become ill through our misbehaviours, even die from hexes and broken hearts, then we must also be able to make ourselves well" (Achterberg, 1985).

There is now a substantial amount of evidence from research in the field of psychoneuroimmunology which demonstrates how the mind and the neurological and immunological systems of the body communicate through the bi-directional flow of hormones, neuropeptides and cytokines (Martin, 1997; Watkins, 1997).

1.2 A Short History of the Mind-Body Connection

1.2.1 From Hippocrates to the Middle Ages

More than 4,000 years ago, Chinese physicians were aware of the fact that periods of emotional upset were often followed by physical illness and Egyptian physicians of the same period noted that by having an optimistic attitude, one could avoid poor health (Achterberg, 1985). Hippocrates taught his students to consider their patients' life circumstances and emotions as part of the treatment and Aristotle

believed that the soul was inseparable from the body and that all bodily systems worked together to serve the whole organism (Lyons & Petrucelli, 1987). This concept of a mind-body connection is also seen in the writings of the 2nd century Greek physician, Galen, who noted that melancholic women were more prone to malignancies of the breast than cheerful women (Locke & Colligan, 1986).

During the Middle Ages, there was no serious practice of medicine in most of the Western world except for that carried out by members of religious orders or folk medicine which was mainly practised by women and which included the use of imagination (Watson, 1971).

1.2.2 The Split in the Mind-Body Connection

In the 17th century, however, the holistic ancient medical beliefs (or mind-body connections) were discarded because of changes in the philosophy and technology of medicine – the most powerful influences of this period being Francis Bacon (who asserted that science should be used to gain mastery over nature) and the French philosopher-scientist, Rene Descartes. Descarte's view (which came to be known as the *reductionist method*) was that there were two separate substances in the world – *matter* (which behaved according to physical laws) and *spirit*: the body was matter, and the mind, spiritual. This split between the body and the mind came to dominate not only medical philosophy but religious philosophy as well (Lyons & Petrucelli, 1987).

Another theory, the *theory of specific aetiology*, came into being in France around the same time. This theory was strongly supported by research carried out by Robert Koch, whose experiments showed that only anthrax germs caused anthrax and no other disease and so he theorised that germs were the specific cause of every disease (Graham, 1995; Hafen, Karren, Frandsen, & Smith, 1996). Interestingly, Rudolf Virchow (a respected medical authority of the time), although agreeing that germs played a role in disease, disagreed with the simplicity of Koch's theory, arguing that there were other factors involved in disease such as heredity, pre-existing health, nutrition, environmental factors, stress, and the person's psychological state. His views, unfortunately, went unheeded and evidence for the theory that pathogens alone caused disease continued to grow (Locke & Colligan 1986).

1.2.3 A Renewed Interest in the Mind-Body Connection

However, even though this biomedical approach had been dominant for this period of medical history (and still is to a great extent, to this day), other forces were at work which would once again arouse interest in the mind and its influence on the body. At around the same time as the theory of specific aetiology was evolving out of the research of Pasteur and Koch, Sir William Osler, a Canadian physician who practised in Britain believed that it was much more important to know what sort of patient had the disease than what sort of disease the patient had (Dreher, 1995) and the French physiologist, Claude Bernard, talked of the *milieu interieur* or balance of the body which, when disturbed, resulted in sickness or death. Bernard believed that a person did not have a disease because germs managed to gain access to the body,

but instead, that the person became ill because the germs had found a hospitable home in a weakened terrain (Pelletier, 1995).

During the 1930s and 1940s, another physiologist, Walter Cannon, built on Bernard's concept and coined the term *homoeostasis* to describe the body's self-maintenance of health – the built-in mechanism that helps sustain a vital balance. Cannon also showed how stress can alter bodily functions via the nervous system and coined the term "fight or flight" response to explain the reaction of the sympathetic branch of the autonomic nervous system to threatening situations (Rice, 1992).

Hans Selye followed on Walter Cannon's concept of "fight or flight" with more investigations on the physical effects of psychological stress and how it is tranduced into psychosomatic problems by the hormones of the hypothalamic-pituitary-adrenal axis of the endocrine system (Rice, 1992).

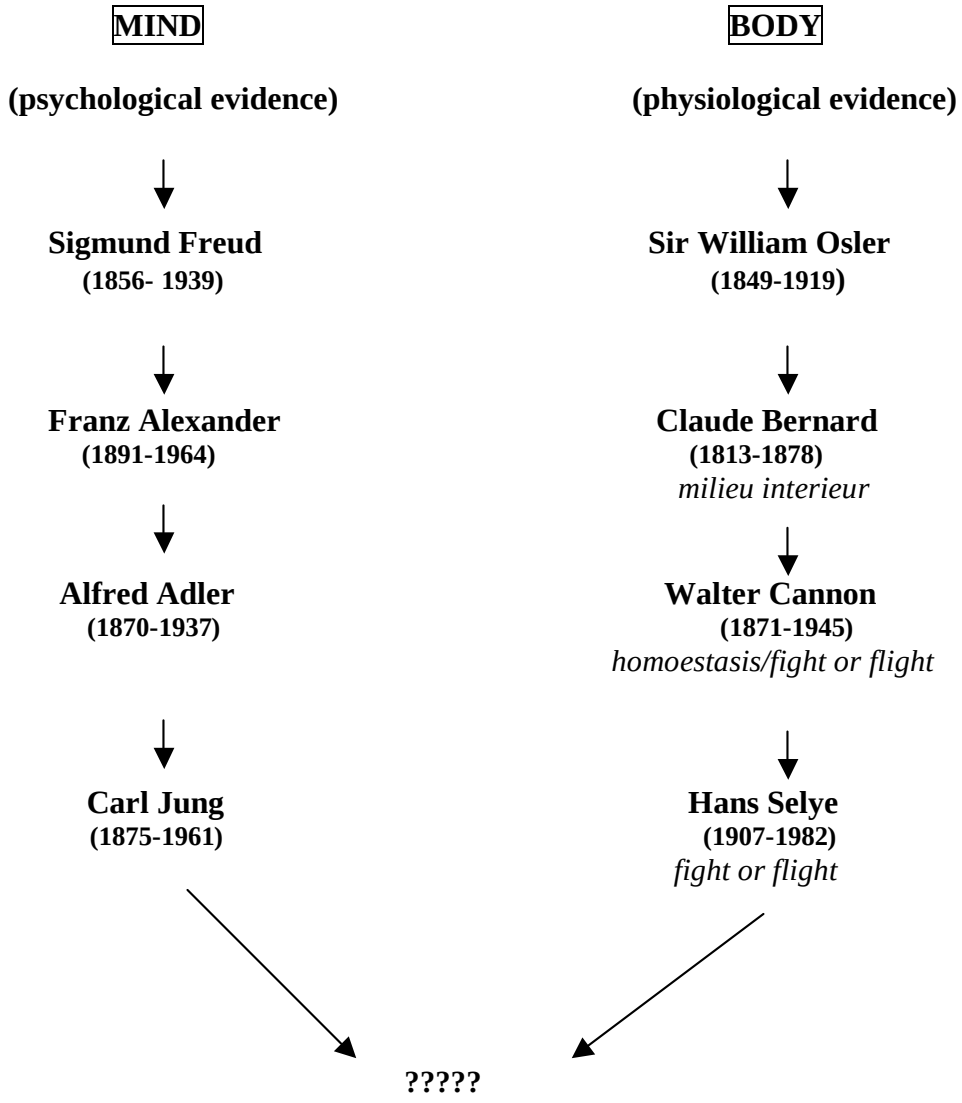
Sigmund Freud also brought the mind-body connection back to the fore with his concept of conversion neurosis, which he believed to be a result of repressed emotions resulting in physical problems (Hall & Lindzey, 1970). This concept was elaborated on in the 1940s by his student Franz Alexander, a Chicago psychiatrist whose ideas were to evolve into the discipline of psychosomatic medicine. Alexander believed that many chronic disturbances were not caused by external, mechanical, chemical factors or by micro-organisms, but by the continuous functional stress arising during the everyday life of the organism in its struggle for existence (Dreher, 1995).

Others such as Jung and Adler took up, and added to, this particular concept of a mind-body connection which was to become known as the theory of psychoanalysis (Hall & Lindzey, 1970).

It appears then that the reductionist method which began with Rene Descartes, and the theory of specific aetiology which resulted from the research of Pasteur and Koch, were beginning to lose ground as more research started to come up with evidence suggesting (as the ancient medical practitioners and philosophers had stated thousands of years before) that there was indeed some connection between the mind and the body.

Researchers such as Bernard, Cannon and Selye had come up with *physiological* evidence for this connection, and Freud and his followers had demonstrated a *psychological* connection. However, there was still a couple of missing links: there was no sound knowledge of either the immune system or the enteric nervous system. No-one as yet sufficiently understood the workings of these systems enough (nor had the scientific instruments) to prove how the fight and flight response, stress, or emotions could have reactions at a cellular level (*see Figure 1*).

Figure 1. **The Missing Links in the Mind-Body Connection.**



The Immune System & The Enteric Nervous System

Proof was needed of how the flight/fight response, stress, or emotions could have reactions at the cellular level.

1.3 The Immune System

1.3.1 Research & Anatomy

The first sustained programme of research in this area was on the classical conditioning of immune responses carried out by Russian researchers Metal'nikoff and Chorine, who were working at the Pasteur Institute in the 1920s and, since then, scientists have learnt that immune cells could attack microbes with the same efficiency in a test tube as in the body (giving rise to the belief that the immune system functioned independently), that the immune system could distinguish between cells belonging to its own body and those which were foreign, and that it had a biochemical memory that helped it recognise and destroy foreign cells (Ader, Felton & Cohen, 1991). But it wasn't until the late 1950s that finer details about the immune system were discovered.

In 1957, Aaron Frederick Rasmussen, a microbiologist, Norman Brill, a behavioural scientist, and an associate, J.T. Marsh carried out various animal studies which demonstrated the pathogenic effect of emotional stress; and research by a British biochemist, Rodney Porter and American immunologist, Gerald Edelman (1960/70s) resulted in the finding of the precise molecular structure of an antibody (Locke & Colligan 1986; Ader et al., 1991).

George Solomon, a Stanford psychiatrist, is considered the first to seriously consider the influence of mental states and traits on the immune system and began

research on the mind-body connection in the 1960s in collaboration with his colleague Rudolf Moos. Their research involved critical observations of the life histories and personality characteristics of the patients. Solomon became convinced that a connection between the brain and the immune system existed and, if this were so, it would conflict with the long-standing belief that the immune system network functioned independently of any other body system. Because his experiments indicated a link between the mind and the immune system, Solomon suggested the new science be called *psychoimmunology* (Locke & Colligan, 1986; Ader et al., 1991; Dreher, 1995).

Other evidence showing the effects of the mind on the body began accumulating in the 1960s. Lawrence LeShan (1960, 1966) suggested that mental states could have definite, physical repercussions on other diseases and, after interviews with a vast number of cancer patients, came to the conclusion that there was a "cancer personality." Also at this time Herbert Benson (Benson & Klipper, 1975; Benson et al., 1978), a cardiologist at Harvard Medical School was carrying out research on the relationship between stress and hypertension and reasoned that if stress could turn on hypertension, some other factor might be able to turn it off.

In 1969, radiation oncologist, Carl Simonton and Stephanie Matthews-Simonton (whose background was in motivational counselling), began looking at the possibilities of the influence of the mind to induce and enhance the "will to live" in cancer patients. They explored a number of psychological techniques and claimed to have achieved quite dramatic results through the use of visual imagery techniques

which, to them, indicated that patients had a much larger influence over the course of their disease than they were given credit for. These findings were considered to be purely anecdotal evidence as well as being methodologically flawed and were not published in mainstream journals (Simonton, Matthews-Simonton & Creighton, 1978; Kidman, 1983; Sheard, 1994).

However, even though experiments and research were suggesting there was a link between the mind and the body, the way to control or direct this influence had not as yet been discovered. A serendipitous observation on mortality in a conditioning study being carried out by Robert Ader in 1974 finally resulted in the hypothesis that classical conditioning could modify the immune system.

Ader and his colleague, Nicholas Cohen, had been conducting standard Pavlovian conditioning experiments with rats, instilling in the animals an aversion to saccharin-flavoured water by injecting them with cyclophosphamide after they had drunk the water. As was expected, the rats continued to experience the nausea caused by this drug even when the sweetened water alone was given to them. It was only after many of the animals had died during the experimental process, that Ader and Cohen realised that as well as causing nausea, cyclophosphamide was also a powerful immunosuppressant and that they had inadvertently taught the rats to suppress their immune system whenever they drank the sweetened water (Locke & Colligan, 1986; Ader et al., 1991). Their findings, however, did not make an impact on the biomedical community of that time because the belief still existed that there were no connections between the brain and the immune system.

Still more findings of a connection between the brain and the immune system began to appear in the 1970s. Edwin Blalock discovered that lymphocytes were a source of brain peptide neurotransmitters and pituitary hormones. Further studies revealed that supernatant fluids from human lymphocytes contained adrenocorticotropic hormone and endorphins, a result which, for the researchers at that time, was surprising since peptides were thought to exist in the brain and pituitary gland only. This discovery suggested that a relationship could exist between the brain and the immune system as they apparently spoke the same chemical language (Ader et al., 1991).

Karen Bulloch discovered that the thymus gland in the rat contained fibres of the vagus nerve which descends directly from the brain, and David Felten expanded on this finding by using fluorescent dyes to trace the pathways of these same nerve fibres. As well as finding connections to the thymus, he also found connections to the spleen, lymph nodes and bone marrow and networks of nerves near blood vessels through which the immune cells passed. This latter finding suggesting that nerve impulses could directly influence the behaviour of cells (Ader et al., 1991; Dreher, 1995).

However, even though researchers had found an anatomical connection between the lower brain and the immune and nervous systems, they had not fully explained how the immune cells in the blood and lymph nodes could be influenced by the central nervous system.

This breakthrough occurred in the early 1980s when Candace Pert and colleague, Michael Ruff, discovered that neuropeptides acted as messengers between the mind/brain and the immune system by way of receptors on the molecular surface of monocytes. These receptors are designed to receive substances which can change the growth patterns or activities of cells. Therefore, this discovery by Pert and Ruff indicated that brain chemicals present in the bloodstream could alter the behaviour of immune cells and, because these neuropeptides were believed to be the chemical carriers of emotions, it followed that changes in one's emotions could result in changes in one's immune system. Thus Pert's view that neuropeptides and their receptors are part of a psychosomatic network has brought about a new understanding of mind-body integration and has successfully challenged the commonly held assumption of an autonomous immune system (Pert, Ruff, Weber & Herkenham, 1986; Dreher; 1995; Pert, 1997).

Ader (1991) believed that the nervous system was also involved in the relationship between the brain and the immune system and changed Solomon's original name for this new science from *psychoimmunology* to *psycho-neuroimmunology*.

Research conducted over the past several years has substantiated these findings of a connection and interaction between the behavioural, neural, endocrine and immune systems and there now appears to be an attempt by more scientists to understand the workings of the mind-body function (Aziz & Thompson, 1998; Bunk, 1998; Theoharides, 2002).

1.3.2 The Immune System and Irritable Bowel Syndrome

IBS symptoms are widely accepted as being generated by abnormalities of the gut function – the major ones being abnormal gastrointestinal motility and increased sensitivity of the intestine (Camilleri, Coulie & Tack, 2001; Jarret et al., 2000). One of the reasons for this occurring is an involvement with the immune system. Research has now focused attention on the putative role of low-grade mucosal inflammation in IBS (Collins, Piche & Rampal, 2001). This inflammatory response is largely restricted to the colonic and ileal mucosa with evidence showing that patients with IBS have an increased number of inflammatory cells in this area - the result being disturbances in gut motility, myoelectricity and smooth muscle contractility as well as changes in the function of enteric nerves (Barbara, De Giorgio, Stanghellini, Cremon & Corinaldesi, 2002; Gui, 1998).

Research in this area points to a number of factors which may play a role in the development of this low-grade inflammatory process – the most prevalent being previous acute episodes of gastroenteritis (Gwee et al., 1999). Other possibilities include undiagnosed food sensitivities (Locke, Zinsmeister, Talley, Fett & Melton, 2000), changes in bacterial flora (Pimentel, Chow & Lin, 2000) and genetic factors (Gonsalkorale et al., 1999).

Collins et al. (2001) suggest two scenarios for the role of inflammation in the pathogenesis of IBS: the development of IBS in patients following gastroenteritis (post-infective IBS) and the observation that IBS-like symptoms occur with a higher

than expected frequency in patients in remission from inflammatory bowel disease (IBD).

On taking the history of patients with IBS, it is frequently found that they refer to a previous incidence of an enteric infection and that their IBS symptoms developed soon afterwards (Gwee et al. 1999; Neal, Hebden & Spiller, 1997). Neal et al. (1997) carried out a study in which patients who had had a laboratory-confirmed diagnosis of a bacterial gastrointestinal pathogen were given a questionnaire which included questions on the episode of food-poisoning, their bowel habit six months before it had occurred as well as questions about their current bowel habit. They were also asked about their general health, diet and allergies. At the completion of the trial it was found that 25% of the participants reported persistently altered bowel habits.

These findings have been confirmed by recent studies showing that persistent IBS symptoms develop in between 7% and 32% of subjects after enteritis caused by Salmonella (Mearin et al., 2005), Shigella (Wang, Fang & Pan, 2004), or Campylobactor (Garg et al., 2006). However, Marshall et al. (2004) contradicted these findings when the results of their study suggested that IBS symptoms were associated with a subtle increase in intestinal permeability *irrespective* of prior gastroenteritis.

Collins et al. (2001), suggest that it is the inflammatory response to these infections rather than the infective agent itself, which alters colonic physiology and

generates IBS symptoms. It has also been proposed that the inflammation associated with acute infection and subsequent chronic visceral hypersensitivity, results in the possibility of these sensitised immune cells being activated by psychological stress which increases intestinal permeability (Chang et al., 2000; Collins, 2001). Earlier studies by Solomon and Roos (Solomon, 1987) on rheumatoid arthritis also showed an apparent association between psychological factors (such as emotional states) with the onset or exacerbation of inflammation, indicating a link between the mind and the immune system (Ader et al., 1991).

The second scenario postulated by Collins et al. (2001) is that symptoms similar to IBS occur with higher than expected frequency in patients in remission from inflammatory bowel disease (IBD), in particular ulcerative colitis (Minderhoud, Oldenburg, Wismeijer, van Berge Henegouwen & Smout, 2004; Simren et al., 2002). Shahbazkhani et al. (2003) have also found that coeliac disease may easily mimic symptoms (such as diarrhoea, abdominal cramps, distension, and improvement by defecation) which are parts of the criteria used for diagnosing IBS.

Both IBS and IBD share symptoms of altered bowel motions associated with abdominal pain and discomfort – the difference proposed by the majority of researchers is that in IBS a characteristic cluster of symptoms occurs *in the absence of detectable structural abnormalities of the intestine* whereas in IBD the symptoms occur *in conjunction with* a chronic mucosal and/or transmural inflammation of the intestine (Bradesi, McRoberts, Anton & Meyer, 2003). Recent studies, however, have suggested that an on-going low-grade inflammatory/immune response may also

be part of the IBS symptomatology (Barbara et al., 2002; Collins et al., 2001; Quigley, 2005). It is proposed that similarities and differences between the two syndromes can best be addressed within the framework of interactions between the central nervous system and the gut immune system (Bradesi et al., 2003).

IBS patients have been shown to have an increase in the numbers of T lymphocytes and macrophages in the colonic mucosa. These immunocytes evoke changes in neuromuscular function in the intestinal tract and have been shown to result in abnormal intestinal permeability in subgroups of diarrhoea-predominant IBS (Collins, 1996; Dunlop, 2006).

Ohman, Isaksson, Lundgren, Simren & Siovall (2005) investigated the characteristics of colonic and peripheral blood lymphocytes in 71 patients (33 patients with IBS, 23 with ulcerative colitis and 15 control subjects) and found that all 33 patients with IBS exhibited an enhanced immune activity in the gut and an increased frequency of integrin beta7+ T lymphocytes in the peripheral blood – a result which further supports the hypothesis of an underlying inflammatory condition in IBS.

A study by Chadwick et al. (2002) also showed increased numbers of activated lymphocytes in the intestinal mucosa of all 77 IBS patients after immunohistologic studies on colonoscopic biopsy specimens had been taken from the participants. These results again implicating the mucosal immune system and possible mucosal barrier defects in the pathogenesis of IBS.

Studies have also demonstrated an increased number of mast cells in the colon or terminal ileum of IBS patients (O'Sullivan et al., 2000; Wood, 2006). Mast cells release heparin, serotonin, bradykinin and histamine in response to injury or infection – the most important effects of histamine and serotonin occurring early in the inflammatory process. Stimulation of mast cells and basophils also leads to the release of arachidonic acid metabolism, the products of which (leukotriene C4, D4 and E4) induce smooth muscle contraction and are important in delayed changes in vascular permeability at sites of inflammation (Rubin & Faber, 1988).

Histamine has been shown to be involved in the regulation of intestinal secretion and motility, processes that, when dysregulated, cause clinical symptoms such as diarrhoea and abdominal pain (Barbara et al., 2004). More specifically, Sander et al. (2004) have demonstrated that histamine receptor expression was altered in patients with gastrointestinal diseases. Biopsies were taken from the terminal ileum, caecum and rectum of 30 patients with IBS who fulfilled the Rome II criteria, and 14 control patients. In 19 of the IBS patients, a diagnosis of intestinal food allergies was confirmed - the remaining 11 patients were classified as having IBS according to the Rome II criteria. Both patients with IBS, and IBS + food allergy exhibited significantly higher levels of mRNA encoding for histamine receptors 1 and 2 compared with controls.

As well as being an important brain neurotransmitter, serotonin (5-hydroxy-tryptamine – 5HT) is involved in the local regulation of gastrointestinal motility, secretion, and perception of urge and pain (Kilkens, Honig, van Nieuwenhoven,

Riedel & Brummer, 2004). In the GI tract, 5-HT is found within the majority of enterochromaffin cells, as well as mast cells, smooth-muscle cells and neurons (Gershon, 1991; 1999). Animal studies have shown that 5-HT is implicated in enhancing inflammatory reactions in the gastrointestinal tract (Magro, Fraga, Azevedo & Soares-da-Silva, 2006; Oshima & Fujimora, 1999) and, in a study involving both mouse bone marrow-derived mast cells and human derived mast cells, Kushnire-Sukhov et al. (2006) found that 5-HT promoted inflammation by increasing mast cells at the site of tissue injury.

The extent to which inflammation contributes to the pathogenesis of some IBS patients remains under investigation but there are morphological data implicating immune activation in the myenteric plexus of patients with severe IBS. To take this one step further, Barbara et al. (2004) as well as identifying an increase of mast cells in the colonic mucosa of IBS patients compared to controls, also found that there was a closer anatomical proximity between nerve trunks and lymphocytes or mast cells, suggesting that abnormal neuroimmune interactions may contribute to the altered gastrointestinal physiology and hypersensitivity in the pathogenesis of IBS. Inflammatory neuropathy of the enteric nervous system is now emerging as an important research area in the field of neurogastroenterology.

1.4 The Enteric Nervous System

1.4.1 Research & Anatomy

The first differentiation of enteric neurons into three morphological types on the basis of the different shapes and lengths of their dendrites was done by the Russian histologist, A.S. Dogiel in the late 19th century (Brehmer, Schrodl & Neuhuber, 1999) and, in the 1860s, Auerbach found that the bowel contained a complex network (plexus) of cells and fibres (Wood, 1970), but the beginnings of serious research into neurogastroenterology is associated with two English investigators, Bayliss and Starling (1902), whose work with dogs resulted in a surprising discovering. Initially, they isolated a loop of intestine in anaesthetised dogs and found that, when the internal cavity of the bowel was stimulated and the internal pressure was raised sufficiently, the bowel would exhibit muscular movements which would propel the contents of the bowel in a one-way direction towards the anus.

The researchers then took this one step further and cut all nerves entering or leaving the loop of dog bowel, knowing that if this were done to nerves to other parts of the body, such as the limbs or other organs, all reflexes would be lost. Bayliss and Starling found, however, that when the internal pressure was increased, the bowel continued to exhibit muscular movements in exactly the same way as it had done before the nerves were cut. They came to the conclusion that nerves inside, rather than outside, the gastrointestinal tract were involved, as the reflex behaviour they had

observed had occurred after all input from the brain and spinal cord had been eliminated. Since this research, most of the knowledge about the functional features of enteric neurons has been derived from studies in the guinea-pig small intestine.

In 1958, Bulbring, Burnstock, & Holman carried out a series of experiments on isolated intestinal smooth muscle of the guinea-pig to find out whether responses to electrical stimulation were "all or none" and whether they were graded and, secondly, what the mechanism of conduction was. Their results showed that excitation appeared to be able to spread in two ways – by slow waves (where each cell might be stimulated by the contraction of the cell behind it) and by conducted response, thereby supporting the view that conduction takes place by electrical transmission from cell to cell.

No further substantial progress in the knowledge about the functional features of the enteric nervous system such as electrophysiological behaviour or neuronal connectivity of the neurons was made, however, until the early 1970s.

Wood (1970) published the first reports of single unit activity in the myenteric plexus and Nishi & North (1973) began intracellular recording from myenteric neurons with micro-electrodes. The study distinguished three types of cells and, with an intracellular injection of a fluorescent dye, discovered that the neurons had one to seven processes.

Hirst, Holman & McKirdy (1975) contributed to further understanding of the enteric nervous system by their findings that excitatory synaptic potentials could be evoked in most neurons by distension of the attached intestinal segment and that it was possible to distinguish two distinct firing patterns of synaptic potentials in response to distension. Their study suggests that distension may cause both descending inhibition and, after a delay, descending excitation of the guinea-pig small intestine.

In the 1990s research continued to identify enteric neurons that responded to physiological stimuli by using activity-dependent dyes. Furness, Johnson, Pompolo & Bornstein (1995) found evidence that enteric motility reflexes can be initiated through entirely intrinsic mechanisms in the guinea-pig small intestine by examining reflexes in segments of guinea-pig intestine in which extrinsic denervation, 9-11 days before the intestine was removed, and isolation of the intestine in vitro, were combined. They evoked both ascending and descending reflexes by distortion or distension of the mucosa and found that reflex responses recorded after denervation were no different to those recorded from control tissue. The researchers subsequently concluded that cell bodies of primary sensory neurons for mucosal reflexes in the small intestine of the guinea-pig were intrinsic to the organ.

In the same year, Kunze, Bornstein & Furness (1995) found direct evidence that some sensory neurons were contained entirely with the peripheral nervous system and, not as it was commonly believed, associated with the central nervous system or within the central nervous system itself. They recorded the response of

myenteric neurons in the guinea-pig small intestine to physiological stimuli applied to neighbouring mucosa and found that the myenteric plexus contained a population of chemosensitive sensory neurons and that these neurons corresponded to neurons with AH electrophysiological properties.

Chemical changes and distortion of the mucosa, however, are not sensed directly by the mucosal endings of the intrinsic primary afferent neurons but require the release of 5-HT from the entero-endocrine cells of the intestinal mucosa. Approximately 95% of 5-HT is located in the GI tract and enteric nervous system (the remaining 5% being in the central nervous system) and, in physiological studies of gut smooth muscle, 5-HT has made the bowel contract or relax through stimulating neurons to release acetylcholine or nitric oxide (Gershon, 1991, 1998).

Liu, Geddis, Wen, Setlik & Gershon (2005) carried out a study in the mouse enteric nervous system to identify the subtypes of 5-HT receptor that are expressed in the intestines, and to determine their locations and actions. As well as finding that transcripts encoding four 5-HT4 receptor isoforms were present in the mouse gut, the researchers observed that 5-HT4 agonists strengthened neurotransmission in excitatory pathways.

The two principal divisions of the nervous system are the central nervous system (CNS) and the peripheral nervous system (PNS) which is subdivided into three parts:

- the somatic nervous system;
- the autonomic nervous system (the motor portion is further subdivided into the sympathetic and parasympathetic divisions) and;
- the enteric nervous system -"the brain of the gut" (Costa, Brookes & Henning 2000). (*See Figure 2*).

The enteric nervous system (ENS) is often regarded as a displaced part of the central nervous system and communication between the two takes place via the sympathetic and parasympathetic afferent and efferent neurons, providing neural control of all functions of the gastrointestinal (GI) tract (Goyal & Hirano, 1996). The ENS extends the entire length of the GI tract and is composed of approximately 100 million neurons - approximately the number found in the spinal cord (Costa et al., 2000; Tortora, G.J. & Grabowski, S.R., 2000).

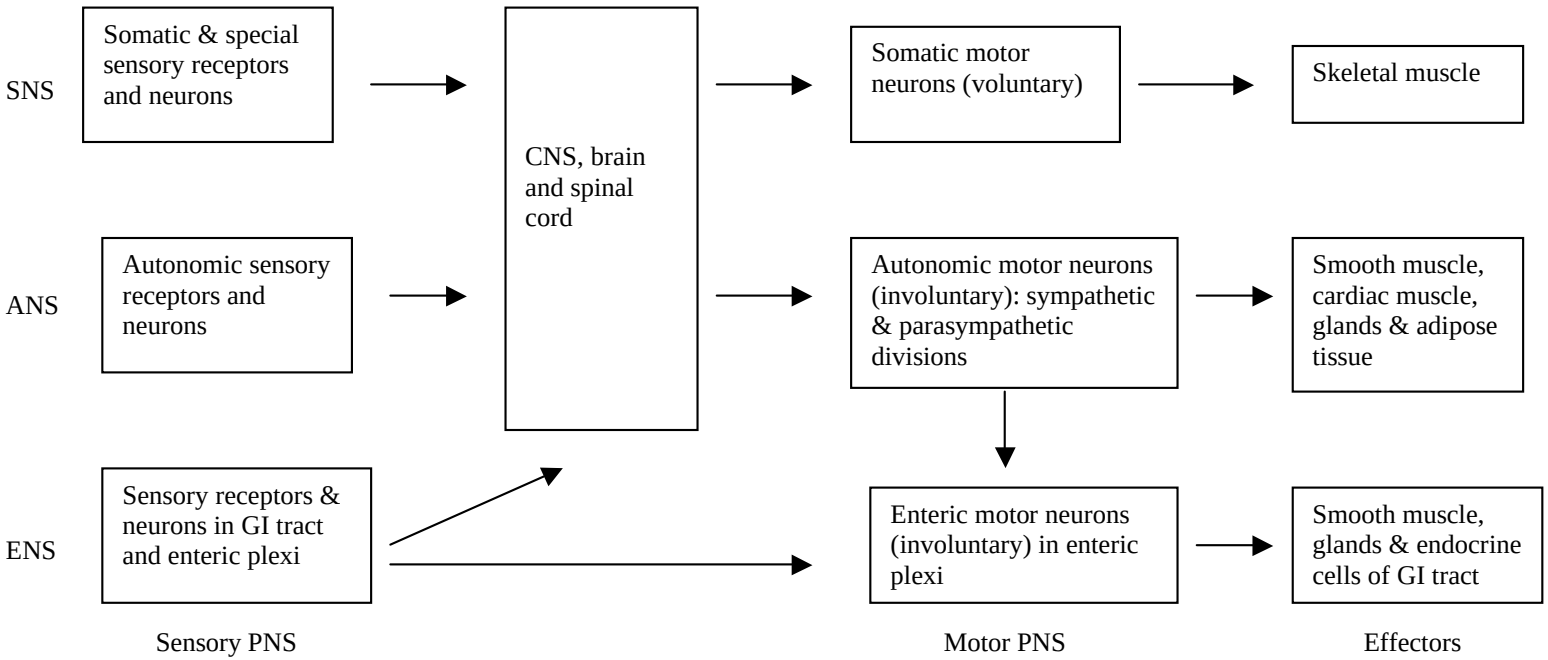
The ENS is a complex network of neurons and neuroglia (or glia) within the bowel wall that controls intestinal functions (such as motility, epithelial transport and secretion and blood flow) and modulates immune and endocrine functions. The movements of the intestine are determined by the interaction of the muscular apparatus, which consists of large collections of electrically interconnected layers of smooth muscle, and the neural apparatus which is composed of a large number of enteric neurons which can be identified according to their neurochemistry, electrophysiological properties, location, shape, proportions, connections, and function (Costa et al., 2000; Johnson, Alpers, Christensen, Jacobsen & Walsh, 1994).

Sensory neurons of the ENS monitor chemical changes within the GI tract and the stretching of its walls, and enteric motor neurons govern contraction of GI tract smooth muscle, secretions of the GI tract organs such as acid secretion by the stomach, and activity of GI tract endocrine cells (Goyal & Hirano, 1996; Gershon, 1999). Although the ENS communicates with the CNS via sympathetic and parasympathetic neurons, it can also perform many functions independently of both the autonomic and central nervous systems to some extent (Gariepy, 2001).

The four categories of nerves in the ENS are:

- extrinsic neurons - found primarily in the regions for the ingestion of food (mouth and oesophagus) and the expulsion of faeces (anal region);
- intrinsic motorneurons - release neurotransmitters (the main ones being substance P and acetylcholine) which cause contractions of both circular and longitudinal smooth muscles and secretion of water and electrolytes from the mucosa of the intestine;
- intrinsic interneurons - connect sensory neurons with motor and secretory neurons via synapses forming networks which process sensory information and control motor neurons; and
- sensory neurons - provide some intrinsic control of smooth muscle contractions and gastric juice secretion (Goyal & Hirano, 1996; Smith & Morton, 2001).

Figure 2. **Organisation of the Nervous System.**



Subdivisions of the PNS are the somatic nervous system (SNS), the autonomic nervous system (ANS), and the enteric nervous system (ENS).

In the ENS, neurons are grouped into small ganglia which are connected by bundles of nerve processes forming two major plexi (together with lesser plexi) in the wall of the GI tract. The major plexi are the myenteric plexus (Auerbach's plexus), which is situated between the layers of longitudinal and circular smooth muscle, and the sub-mucous plexus (Meissner's plexus), which lies in the mucosa. The myenteric plexus is involved mainly in the control of GI motility whereas the sub-mucous plexus is involved in the control of secretion and blood flow and also receives sensory information from the gut epithelium and from stretch receptors in the wall of the tract (Anderson et al. 1998; Smith & Morton, 2001).

An absence of intramural ganglion cells from a region of the myenteric plexus can result in symptoms of poor, or absent peristalsis and subsequent severe constipation as evidenced in Hirschsprung's disease (a congenital abnormality) and Chaga's disease (caused by parasitic toxins) (Gariepy, C.E. 2001). The ENS can also be damaged in intestinal pseudo-obstruction syndromes and in some forms of chronic disease such as diabetes (Heuckeroth & Pachnis, 2006), and recent evidence indicates that a subset of individuals with IBS may have primary defects within the ENS (Koszycki, Torres, Swain & Bradwein, 2005).

1.4.2 The Enteric Nervous System and Irritable Bowel Syndrome

The enteric nervous system (ENS) is a third division of the peripheral nervous system and has connections with both the central nervous system and the sympathetic and parasympathetic divisions of the autonomic nervous system. Gastrointestinal

function is controlled and co-ordinated by both extrinsic and intrinsic elements of the autonomic nervous system which can alter the activity of the GI tract via its influences on the ENS. In general, the sympathetic branch of the autonomic nervous system inhibits activity in the GI tract (e.g. movement of food through the GI tract can be completely blocked by strong activation of the sympathetic nervous system), whereas the parasympathetic branch stimulates secretion and motility (Costa et al., 2000; Smith & Morton 2001; Tortora & Grabowski, 2000).

The ENS is unique in that it is able to mediate reflex activity independently of input from the brain or spinal cord through sensory receptors, primary afferent neurons, interneurons and motor neurons. The ENS can control (at least in part), motor activity, secretion, absorption and blood flow, as well as interacting with the gallbladder and pancreas (Tack, 2000).

Disorders of the ENS, therefore, may result in motor, secretory, and inflammatory and immunologic dysfunction of the gut. Immune/inflammatory cells of the ENS are constantly changing during pathophysiological states, such as exposure to food antigens, bacteria, viruses and toxins, via information from both immune detection and signal transfer to the ENS. The signal is interpreted by the ENS and the gut attempts to clear the antigenic threat by co-ordinated mucous secretion and increased motility – the side-effects being symptoms of abdominal pain and diarrhoea (Spiller, 2002; Wood, Alpers & Andrews, 1999). Enteric mast cells may be responsible for functional gastrointestinal disorders, such as IBS, by

signalling the ENS and initiating inflammation that generates chemical mediators such as cytokines (Bueno, 2000; O'Sullivan et al., 2000).

Another system which may be responsible for functional GI disorders is the cholecystokinin (CCK) system of peptides and their receptors which are widely distributed in the GI tract and CNS. The CCKA receptors mediate pancreatic secretion, motility, and growth and are present in select nuclei of the CNS; and the CCKB receptors, found throughout the CNS, regulate anxiety, satiety, analgesia, and neuroleptic activity. Studies suggest that a dysfunction in this system may be involved in the pathophysiology of some enteric symptoms associated with IBS (Huppi, Siwarski, Pisegna & Wank, 1994*;* Koszycki et al., 2005).

Evidence of a relationship between emotional states and GI function has been reported by patients with functional bowel disorders, and studies in healthy volunteers have also shown alterations in GI function when they are subjected to experimental stressors (Mayer, E.A., 2000; Welgan & Meshkinpour, 2000). This, in part, can be explained by the fact that some afferent sensory fibres from the enteric nerves (which terminate in the sympathetic ganglia) and others from the GI tract (which have their cell bodies in the dorsal root ganglia of the spinal cord or in the cranial nerve ganglia) travel in the same nerve trunks as the autonomic nerves. These fibres transmit information to the medulla which transmits efferent signals back to the GI tract thereby influencing its functions (Costa et al., 2000; Smith & Morton, 2001).

1.5 The Mind-Body Connection in Irritable Bowel Syndrome: the Brain-Gut Axis

Studies have shown that emotions such as anger, fear, pain and anxiety can affect colonic motility more in IBS patients than in healthy controls (Welgan, Meshkinpour & Ma, 2000) and, for IBS, the most frequent comorbid psychiatric disorders are anxiety, depression and somatoform disorders (Drossman et al., 1999; Garakani et al., 2003).

The brain translates thoughts, feelings, beliefs and memories into complex patterns of nerve cell firing and chemical release which affect the physiology and biochemistry of the body (Salt & Neimark, 2002), and neuroimaging (functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scans) has provided evidence of physiological differences between healthy controls and subgroups of IBS patients in the way a visceral stimulus is processed in the brain (Wilder-Smith, Schindler, Lovblad, Redmond & Nirkko, 2004).

In non-IBS individuals undergoing balloon distension studies, PET scans show that when the bowel is stretched, certain areas of the brain that register pain respond and release neurotransmitters that suppress and lower the pain. In IBS patients another area of the brain responds which is associated with anxiety (Drossman, 2000).

Silverman et al. (2000) used PET scans to measure the changes in the pattern of blood flow in the brains of IBS patients in response to balloon distension of the rectum. When rectal stimuli were delivered, it was found that different areas of the brain were activated in IBS patients as compared to controls. This suggests that, as well as having a bowel problem, IBS sufferers may have some difficulty in terms of the way their brain regulates pain.

The brain's influence on GI function has also been demonstrated in reports of alteration in gut function after lesions of the CNS such as stroke and tumours. Dysphagia is common after a stroke and has been found to be more frequent in patients with haemorrhagic stroke than in patients with ischemic stroke (Mann, Hankey & Cameron, 1999). This condition is disabling to patients in that it compromises their diet, nutrition, and hydration as well as having the potential to cause serious complications such as dehydration and aspiration pneumonia (Paciaroni et al., 2004).

A case study by Wood, Camilleri, Low & Malagelada (1985) of an adult with a medullary glioma and unexplained vomiting documents the potential for brainstem lesions to present with symptoms of abnormal GI motor function, and Grant et al. (1999), using magnetic resonance imaging (MRI), detected an intra-axial mass lesion of the midbrain in children who presented with vomiting as well as other signs and symptoms of hydrocephalus.

Further evidence of a brain-gut connection is the existence of two major regulatory peptides, gastrin and CCK, which are synthesised (predominantly) in the human GI tract as a gut hormone, and in brain tissue as a neurotransmitter. They act on central and peripheral CCK receptors to mediate secretion and motility in the GI tract, and on receptors in the CNS where they contribute to the regulation of satiety, anxiety, and analgesia (Wank, 1995). Research also suggests that these peptides also play an important role in tumour growth regulation (Rehfeld & van Solinge, 1994; Schaer and Reubi, 1999).

Another mediator of the brain-gut axis is serotonin. As well as being involved in the local regulation of GI motility and secretion, it is an important neurotransmitter that is relevant to cognition, mood and depression (Kim & Camilleri, 2000; Kilkens et al., 2004).

Stress has been shown to exacerbate IBS symptoms (Levy, Cain, Jarrett & Heitkemper, 1997; Locke, Weaver, Melton & Talley, 2004). The initial step of the stress response activates the hypothalamus of the limbic system of the brain causing it to send chemicals and nerve signals (which can either activate or inhibit certain glands and organs) to the pituitary gland, which then communicates with the adrenal glands – a linkage called the hypothalamic-pituitary-adrenal (HPA) axis.

Two parallel pathways then emerge from the HPA axis – the epinephrine (adrenalin) and cortisol pathways. When epinephrine is released from the adrenal medulla, blood flows from the digestive tract to the muscles, the heart rate increases,

and blood pressure rises. The release of cortisol begins with the release of corticotropin releasing factor (CRF) from the hypothalamus which triggers the pituitary to release adrenocorticotropic hormone (ACTH) which stimulates the adrenal cortex to release cortisol. As well as increasing blood sugar for energy, cortisol causes the pituitary to turn off the release of CRF which then slows down the effects of epinephrine thereby lowering the heart rate and blood pressure, and sending blood back to the digestive system (Rice, 1992; Salt, 2002).

Research on interactions among neurotransmitters and neuromodulators in the brain is ongoing and recent studies have centred on the mast cell as being of interest because of its involvement in IBS (Bose & Farthing, 2001; Barbara et al., 2004). Stress is known to exacerbate many neuroinflammatory conditions and acute stress results in intestinal mast cell activation through the release of CRF (Theoharides, 2002). Studies have also shown an increased number of mast cells in the colon and terminal ileum of IBS patients **(**Rubin & Faber, 1988) and stimulation of these mast cells leads to the release of arachidonic acid metabolism which induces smooth muscle contraction (O'Sullivan et al., 2000).

The mast cell also appears to link emotional states to irritability of the GI tract as informational input processed by the enteric midbrain is not only derived from mast cells, but also by local sensory receptors and the CNS (Gui, 1998).

Degranulation of the mast cell and release of chemicals triggered by input from local sensory receptors and the CNS will have the same effect on motility and

secretory behaviour as degranulation triggered by antigen detection – i.e. bowel discomfort and diarrhoea. This may explain the similarity of bowel symptoms between patients whose symptoms are the result of noxious insults in the lumen of the bowel and those whose symptoms are associated with stress (Wood et al., 1999).

Another interesting brain-gut connection is that scientific data using neuroimaging (PET scans or fMRI) has shown that the same parts of the brain are activated whether participants were experiencing certain events or recalling them from memory. In other words, visual imagery and visual perception draw on the same neural machinery (Kosslyn et al., 1993, 1996). Following on this then, one can understand how stressful thoughts and feelings, as well as perceived stressful situations, can lead to disturbances in the GI tract.

1.6 Summary

It is evident from the above information that the brain and the GI tract are intricately connected to one another by pathways that are continuously monitoring and modulating gut function through complex patterns of nerve cell firing and chemical release (Salt & Neimark, 2002; Wank, 1995). Non-invasive techniques such as fMRI and PET scans have allowed researchers to study brain-gut pathways and assess interactions between the two (Kosslyn et al., 1993, 1996; Wilder Smith et al., 2004).

The immune system has long been regarded as operating, to a large degree, independently of the mind and behaviour, but it is now known that the body's three main regulatory systems – the nervous system, the endocrine system and the immune system – are intimately connected and interact with each other in a bi-directional flow along the various biological pathways (Martin, 1997; Watkins, 1997). Activity within the immune system can therefore influence the brain, mental state and behaviour.

There is also a greater understanding of the enteric nervous system of the GI tract and how it can function more or less independently of the CNS (Gariepy, 2001; Tack, 2000). Increasing knowledge of how the ENS controls or modulates motility, exocrine and endocrine secretions, and immune and inflammatory processes is contributing to the creation of new approaches in treatment (Goleman & Gurin, 1995; Rossi & Cheek, 1998). However, more research is needed in this area to reduce human morbidity and mortality associated with chronic dysfunctioning in the ENS structure such as that observed in functional bowel disorders such as IBS.

CHAPTER 2

IRRITABLE BOWEL SYNDROME

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2.1 Irritable Bowel Syndrome

Irritable Bowel Syndrome (IBS) which is sometimes referred to as spastic colon, mucous colitis, spastic colitis, nervous stomach or irritable colon, is probably the most common disorder encountered by both gastroenterologists and physicians in primary care (Everhart & Renault, 1991; Lee et al., 1999). Depending on the criteria used to define the disease, it is estimated that from 10% to 25% of the general population suffer from this condition and that it comprises about 30-50% of the gastroenterologists' workload (Farthing, 1995; Camilleri & Choi, 1997). Several conditions can masquerade as IBS and require a proper diagnosis (*see Table 1*).

After a complete history has been taken, patients usually undergo a complete physical examination and a series of tests which can include blood tests, blood-chemistry tests, liver-function tests, barium enema + flexible sigmoidoscopy or colonoscopy, and measurement of thyrotropin. In patients with diarrhoea, a biopsy from the mucosa of the descending colon is often carried out to rule out colitis. The diagnosis of IBS is suggested when a patient's symptoms meet the Rome II criteria (*see Table 6*).

Table 1 **Differential Diagnosis of IBS**

- **inflammatory bowel disease**
- **diverticulitis**
- **mechanical obstruction of the colon or small intestine**
- **enteric infection**
- **bacterial overgrowth**
- **ischaemia**
- **lactose intolerance**
- **gluten intolerance**
- **food intolerances**
- **malabsorption syndromes (e.g coeliac disease)**
- **endocrine disorders (e.g. thyroid)**
- **endometriosis**
- **medications which affect bowel pattern**
- **overuse of antibiotics**
- **colorectal cancer**

IBS is generally classified as a functional disorder where the primary abnormality is not an identifiable structural or biochemical cause such as an inflammatory, infectious or structural abnormality but rather an altered physiological function (Bradesi et al., 2003; Van Vorous, 2000). All routine investigations are found to be normal. Unfortunately, this form of diagnosis – one of exclusion of organic disease – often resulted in having negative connotations for both patients and clinicians (Bose & Farthing, 2001; Letson & Dancey, 1996).

Nowadays, there is a better understanding of IBS (and other functional gastrointestinal disorders) with a subsequent moving away from a disease-based model to a biopsychosocial one. This model takes into account not only the numerous physiological symptoms (e.g. altered motility, hypersensitivity of the gut and brain-gut dysfunction) but also the effects that sociocultural and psychosocial influences have on these symptoms. This has come about because of the growth in investigative techniques that support the conception of interactions between the brain and the enteric nervous system of the gut (Bennett et al., 1998; Drossman et al., 1999; Farhadi, Bruninga, Fields & Keshavarzian, 2001).

Symptoms of IBS can range from a slight annoyance to extreme cases where a person's social life can be severely affected and it can also disrupt a person's career because of numerous days off work (Dean et al., 2005; Drossman et al., 1993). As well as these restrictions in recreational and work-related activities, studies have demonstrated that IBS patients report lower overall quality of life compared to controls (Creed et al., 2000; Hahn, Yan & Strassels, 1999). Patients with IBS have

also been found to have higher levels of depression and anxiety relative to the general population (Garakani et al., 2003; Sykes, Blanchard, Lackner, Keefer & Krasner, 2003).

IBS is characterised by a group of symptoms in which abdominal pain or discomfort and bloating is associated with disturbances in bowel pattern. The common symptoms are diarrhoea, constipation or alternating diarrhoea and constipation (*see Table 2*). The stool form is often altered - lumpy and hard or loose and watery, and stool passage can be affected with straining, urgency, or a feeling of incomplete evacuation. The presence of mucus in the stool may be observed and the symptoms are typically continuous or intermittent (Drossman, 2000; Lynn, 1993). IBS symptoms are often accompanied by a number of extra-colonic symptoms which include nausea, vomiting, dysphagia, lethargy, backache and urinary symptoms (Whorwell, McCallum, Creed & Roberts, 1986). (*See Table 2*).

Researchers are beginning to view IBS as a multi-faceted disorder - one in which there appears to be a disturbance in the interaction between the intestines, the brain, and the autonomic nervous system resulting in an alteration in the regulation of bowel motility and/or sensory function (Smith & Morton 2001; Tortora & Grabowski, 2000). Triggering factors in this brain-gut condition may be responsible for causing symptoms of diarrhoea in some IBS sufferers, constipation in others, and alternating diarrhoea and constipation in the remainder (Wood et al., 1999; Zar, Benson & Kumar, 2006).

Table 2 **Symptoms of IBS**

- **constipation**
- **diarrhoea**
- **variation in bowel habit from constipation to diarrhoea**
- **pain associated with constipation, diarrhoea**
- **excessive flatulence**
- **ineffectual urging**
- **abdominal pain relieved by passage of bowel motion**
- **more/less frequent bowel motions when pain begins**
- **looser/harder bowel motions when pain begins**
- **abdominal bloating/distension**

CURRENT THEORIES.

- **hypersensitivity of the GI tract**
- **previous gastroenteritis/bacterial infection**
- **imbalance in microflora**
- **imbalance in neurotransmitters**
- **stress (inability to cope with stress) exacerbates the condition**

Although many people have IBS symptoms, only a small portion (25-30%) ever seek medical attention (Schuster, Crowell & Talley, 2000). Some research suggests that psychological factors rather than symptoms drive IBS sufferers to seek medical advice (Blomhoff, Spetalen, Jacobsen & Malt, 2001; Whitehead, Bosmajian, Zonderman, Costa & Schuster, 1988) but when Talley, Zinsmeister, Van Dyke & Melton (1991) carried out a survey of 1021 local residents in Minnesota, U.S.A. and measured presentation for medical care, they found that even though only a minority had presented for medical evaluation, it was the duration and severity of the abdominal pain that were among the factors that prompted IBS patients to seek medical attention. It appeared that psychological problems or a history of abuse did not increase the chance of IBS patients to seek medical attention. Other studies have also shown that abdominal pain and diarrhoea instigated consultation (Drossman et al., 1988; Heaton et al., 1992).

Increasing evidence appears to suggest that the pathology of IBS is not only limited to the gut, brain, or autonomic nervous system but that all three systems may be involved (Costa et al., 2000). Therefore, any potential new therapy should be aimed at addressing all three.

2.2 Epidemiology of Irritable Bowel Syndrome

2.2.1 Prevalence

IBS is the most common disease diagnosed by gastroenterologists and affects about 20% of all people at any one time, accounting for 10% of visits to primary care doctors and at least 50% of visits to gastroenterologists (Camilleri, 1997; Salt, 2002; Drossman, 2000).

IBS affects nearly one out of five people in the US including children, teenagers, young adults, the middle-aged and the elderly - the average age of onset of IBS being between 20 and 29 years of age with the majority of sufferers being young and middle-aged (Salt, 2002; Ruigomez, Wallander, Johansson & Rodriguez, 1999). About half of those affected have alternating diarrhoea and constipation, about 30% will usually have only diarrhoea, and about 20% usually only constipation (Thompson et al., 1999; Drossman, 2000). However, in two studies carried out in Asian populations in Singapore and Hong Kong (Gwee et al., 2004; Lau et al., 2002), results showed that chronic constipation was more common than chronic diarrhoea in the IBS subjects. The majority of sufferers were similar to Caucasians in that they were also young and middle-aged.

As mentioned previously, a high percentage of people are known to be affected with this disorder but most of them (60-75%) do not consult a physician (Jones & Lydeard, 1992; Farthing, 1995). In terms of severity, therefore, IBS appears

to be a relatively minor health problem but when the effects that sociocultural and psychosocial influences have on these symptoms are taken into account, it can be a major one to some patients who suffer major distress on a daily basis.

2.2.2 Gender

In many clinical and population studies, women report symptoms of IBS more than men (Farthing 1995; Horwitz & Fisher, 2001). This difference is unexplained but may be due to a hormonal (Houghton, Lea, Jackson & Whorwell, 2002; Palsson & Whitehead, 2002), genetic (Camilleri, 2004; Pata et al., 2004; Yeo et al., 2004), or physiological difference between women and men that influences their IBS symptoms. Moreover, women seek medical care more often than men (Camilleri & Choi, 1997; Heitkemper et al., 2001). Thompson (2001) agrees with the latter statement but also suggests that the reason for the difference might also be a misperception about IBS and/or a "macho" attitude among men.

Gwee et al. (2004) suggest that the difference might be because the Manning criteria have a greater diagnostic sensitivity for women in that they include non-pain-related bowel symptoms (cf Rome I and II criteria) thus Heaton et al. (1992) and Thompson (2001) observed, non-pain-related bowel symptoms were more common in female than male subjects. In India, however, it appears that men with IBS are more likely than women to consult doctors (Camilleri, 1997; Kang, 2005) suggesting that there must be cultural and other reasons for the healthcare-seeking behaviour of men and women who have IBS symptoms.

Houghton, Jackson, Whorwell & Morris (1999) looked at gender difference from a different perspective when they investigated the possibility that male sex hormones could be protective from IBS. In this study, the investigators measured a series of male sex hormone levels in men with IBS compared to the hormone levels of men without IBS. They found that luteinising hormone was lower in men with IBS and that the men's pain threshold decreased with higher testosterone levels even though testosterone levels were the same in both groups. Yet another dimension to the role of gender in IBS was added when the results of a study by Miller, Whitaker, Morris & Whorwell (2004) indicated that men with IBS exhibited fewer male characteristics compared with controls.

There are conflicting data regarding the effect of menstrual hormones on IBS symptoms. Female patients with IBS often report more pain and exacerbation of their symptoms with menses (Houghton, Lea, Jackson & Whorwell, 2002; Drossman, 2000) yet a study by Meier et al. (1995) showed that menstrual hormones influenced colonic transit times and that more pain was experienced at the time of menstruation in non-IBS sufferers.

Another study by Degen & Phillips (1996), which was also carried out on healthy women, concluded that there were doubtful clinical significances of the influence of menstrual hormones. This conflicting data could be confounded by misdiagnosis as it is sometimes difficult to ascertain whether the discomfort is coming from the pelvic organs or from the GI tract (Thompson, 2001; Williams, Hartman, Sandler, Miller & Steege, 2004).

Some studies suggest that men have different responses to pain than women (Naliboff et al., 2003; Pedersen, 2004) but, according to Thompson (2002), the answer is more likely to be found in the psychosocial, cultural, and other characteristics of the affected person rather than in the nature of the symptoms themselves.

2.3 Aetiology

The aetiology of IBS is unknown and, as yet, there is no cure. Most researchers agree that a subset of IBS sufferers have a visceral hypersensitivity of the gut or, more specifically, an increased perception of sensations in the gut (Bouchoucha, Choufa, Faye, Berger & Arsac, 1999; Camilleri, Coulie & Tack, 2001). There is also altered bowel motility that may cause symptoms like cramping abdominal pain, diarrhoea and constipation (Spiller, 2002). However, previous gastroenteritis, small intestine bacterial over-growth, psychosocial factors, a genetic contribution, and an imbalance of neurotransmitters have all been proposed as either possible causes or playing a part in the development of IBS (Gershon, 2004; Neal, Hebden & Spiller, 1997; Pimentel, Chow & Lin, 2000). It is generally agreed that a patient's emotional response to stress can exacerbate the condition (Gorard, Gomborone, Libby & Farthing, 1996; Salt, 2002).

2.3.1 Visceral hypersensitivity

When the colon is stimulated by eating, the secretion of cholecystokinin, or by balloon distension, the colon of patients with IBS is more likely to be hypersensitive and hyperreactive. Anorectal manometry is widely used to investigate the physiology of continence and defecation and gives data on anal pressure, rectal sensitivity and anorectal co-ordination. Bouchoucha et al. (1999) and Hammonds et al. (1998) found that anal pressure waves of patients with IBS have altered organisation and respond differently to distension as compared to controls.

In the study by Hammond et al. (1998), no difference was found in patients with constipation-predominant and diarrhoea-predominant IBS. Both appeared to have increased sensitivity to balloon distension throughout the GI tract with the jejunum being the site most likely to exhibit this phenomenon.

Camilleri (1997) on the other hand, found that there was excessive sensitivity at several sites (ileum, rectosigmoid and anorectum) in IBS patients and that there *was* a difference between constipation-predominant and diarrhoea-predominant IBS patients. The diarrhoea-predominant IBS patients exhibited lower thresholds for sensation of gas, stool and discomfort in the anorectum, and urgency was developed at lower volumes of distension of an intrarectal balloon. Patients with constipation-predominant IBS, however, developed discomfort at greater distension volumes than healthy controls.

His observations suggest that since the increased sensitivity of the anorectum was accompanied by the development of excessive reflex motor activity in the rectum, there could be possible interactions between excessive sensation and motor responsiveness. This being so, Camilleri suggests that the symptoms of pain before bowel movement, and the sense of incomplete evacuation may be explained by increased anorectal sensitivity, and that increased motor response to these stimuli may result in the increased frequency of bowel movements.

The different outcomes in the above-mentioned studies appear to illustrate why there is disagreement among researchers as to whether or not visceral hypersensitivity can be considered a biological marker for IBS.

Measurements. Two different types of measurements are generally used to evaluate visceral sensations. The first uses standardised symptom-based questionnaires (visual analogue scale or adjectival scale) to determine thresholds or severity of symptoms which are induced by balloon distension or electrical stimuli within the gut. During distensions, the individual is asked to complete a questionnaire pertaining to the symptoms that are of interest (e.g. pain and gas in the colon, pain and urgency in the rectum; or bloating, nausea and pain in the stomach).

The second method uses PET scans and fMRI during visceral stimulation to measure changes in cerebral blood flow.

In an fMRI study using a validated method of counter-irritation during rectal distension pain, Wilder-Smith et al. (2004) found that there were differences in activation of endogenous noxious inhibitory pathways between healthy controls and subgroups of IBS patients.

The results suggest impaired activation of inhibitory controls in both subgroups as there was an absence of a significant inhibitory effect on visceral pain. The researchers found that not only were brain activation patterns in IBS patients markedly different from healthy controls but that there were differences between IBS subgroups as well.

In non-IBS individuals undergoing balloon distension studies, PET scans show that when the bowel is stretched, certain areas of the brain that register pain respond and release neurotransmitters that suppress and lower the pain. In IBS patients, another area of the brain responds which is associated with anxiety (Drossman, 2000).

Silverman et al. (2000) used PET scans to measure the changes in the pattern of blood flow in the brains of IBS patients in response to balloon distension of the rectum. When rectal stimuli were delivered, it was found that different areas of the brain were activated in IBS patients as compared to controls. This suggests that, as well as having a bowel problem, IBS sufferers may have some difficulty in terms of the way their brain regulates pain.

Studies have also shown two other aspects of heightened visceral sensation in functional gastrointestinal disease. Firstly, it is not site-specific as patients presenting with one functional gastrointestinal syndrome often have additional symptoms in other parts of the gut (Trimble, Farouk, Pryde, Douglas & Heading, 1995; Constantini et al., 1993). Secondly, patients with IBS who have enhanced sensation and perception of bowel function were found to exhibit disturbed visceral nociception in other areas of the body.

A large proportion of IBS patients also complain of other functional disorders such as headaches, dysuria and non-cardiac chest pain (Azpiroz et al., 2000; Botoman, 2002; Scott et al., 1993), suggesting that internal pain thresholds are lower in patients with IBS (and other functional GI disorders).

Francis et al. (1997) found that a higher proportion of patients seen in the urology clinic have IBS compared to patients seen at other clinics (e.g. dermatology/ear, nose & throat) and a high prevalence of IBS (and upper GI symptoms) has been found in patients with chronic renal failure (Cukier, 1997; Kahvecioglu et al., 2005).

As mentioned previously, there are conflicting data regarding the effect of menstrual hormones on IBS symptoms. Women with IBS often report more significant exacerbation of their symptoms with menses, often making it difficult to determine whether the pain is coming from the pelvic organs or from the GI tract.

This can sometimes result in an incorrect diagnosis of endometriosis when the complaint is actually IBS (Kumar, 2004; Houghton et al., 2002).

Houghton et al. (2002) carried out a study where the data appeared to confirm that IBS symptomatology is exacerbated at menses and showed that, in contrast to healthy women, rectal sensitivity changes with the menstrual cycle. They measured rectal response to balloon distension during the follicular, luteal and premenstrual phases and found that there was a worsening of abdominal pain and bloating during menses, bowel habits also became more frequent, and patients tended to have a lower general well-being. Rectal sensitivity also increased at menses compared with all other phases of the cycle. These findings suggest that compared to healthy females, women with IBS respond differently to sex hormone fluctuations.

2.3.2 Previous Gastroenteritis

Gastrointestinal infection has also been implicated in the pathophysiology of IBS but, to date, no virus, bacteria, or parasite has been found to directly cause IBS. It has, however, been hypothesised that these microbes may indirectly cause IBS or at least exacerbate its symptoms.

Studies have shown that there is a subgroup of patients presenting with IBS who can relate the start of their symptoms to a previous episode of infective diarrhoea (Neal et al., 1997; Rodriguez & Ruigomez, 1999; Spiller et al., 2000). One explanation for this is that these patients may have been unable to down-regulate the

mucosal inflammation associated with the acute infection efficiently, and that this might have induced visceral hypersensitivity. This hypersensitivity may have come about because of neuroplastic changes in visceral afferent pathways because of low-grade inflammatory infiltration and activation of mast cells in proximity to nerves in the colonic mucosa (Bose & Farthing, 2001; Barbara et al., 2004). Psychological stress may later activate sensitised immune cells which may possibly induce a chronic low-grade or pre-inflammatory state which then modulates on visceral afferents in a chronic manner (Chang et al., 2000).

Mucosal evidence of an activated immune response in patients who develop IBS as a result of acute gastroenteritis has also been reported by Gwee et al. (1996; 2003) who found evidence of an increased number of intraepithelial lymphocytes in post-infectious IBS patients.

2.3.3 Microflora

In most IBS sufferers, abdominal bloating, distension and diarrhoea are extremely common complaints regarded by some researchers as possibly being caused by an overgrowth of small intestinal bacteria (Dapoigny et al., 2004; Salt & Neimark, 2002; Chang, Lee, Naliboff, Schmulson & Mayer, 2001).

A study of 202 patients meeting the Rome criteria for IBS by Pimentel et al. (2000) showed an apparent association between the increased prevalence of small

intestine bacterial overgrowth with IBS. As a testing procedure, the researchers used the lactulose hydrogen breath test.

This test is based on the fact that bacteria are usually only found in very high concentration in the large intestine with the production of gas occurring about 90 minutes after the ingestion of lactose. When there is bacterial overgrowth in the small intestine, the bacteria will digest the lactose sooner and produce an earlier excretion of hydrogen (and methane) in the lungs which is then measured. Patients may also develop symptoms of gas, bloating and diarrhoea.

The lactulose hydrogen breath test (as well as the glucose breath test) for the diagnosis of small intestine bacterial overgrowth is controversial. Obtaining a direct culture is limited because bacterial overgrowth occurs in the more distal portions of the small intestine making access difficult.

In this study by Pimental et al. (2000), the lactulose hydrogen breath test was used for both assessment of overgrowth and as a follow-up test to confirm eradication, and those participants with a positive breath test were treated with a 10-day course of antibiotics. The results showed that 78% of the participants had overgrowth and on the follow-up testing, 48% had eradication of small intestine bacterial overgrowth. However, there were limitations to the study. One issue was the small number of subjects returning for follow-up lactulose hydrogen breath test. Of the 202 IBS patients, 157 had overgrowth and only 47 of these had follow-up testing.

Parisi (2003) questioned the use of the lactulose hydrogen breath test as a diagnostic tool for small intestine bacterial overgrowth as the sensitivity can be as low as 16% and was of the opinion that the glucose breath test was more reliable. Whereas the results of a study by Wang, Bei & Pan (1995) found that the lactulose hydrogen breath test had a sensitivity of 71.4% and regarded it as a simple, non-invasive and relatively reliable method of diagnosis of small intestine bacterial overgrowth.

Parisi also queried the use of antibiotics in the treatment as they could be detrimental to intestinal bacteria and perhaps influence the development of functional bowel syndromes. This was demonstrated in a study by Noverr, Noggle, Toews & Huffnagle (2004) which showed that the use of antibiotics resulted in increases in GI enteric bacteria and GI Candida albicans in mice. Mishkin & Mishkin (2001), on the other hand, were of the opinion that a subgroup of IBS patients who had small intestine bacterial overgrowth would benefit from a course of antibiotics. This was also the conclusion reached by Attar et al. (1999) who found the antibiotics Norfloxacin and Amoxicillin-clavulanic acid to be effective in the treatment of bacterial overgrowth-related diarrhoea.

Mishkin & Mishkin (2001) found that their experience and data did not support the very high prevalence of small intestine bacterial overgrowth stated in the research by Pimentel et al., and pointed out the fact that patients with abnormal small intestine bacterial overgrowth could possibly have other disorders such as diabetes mellitus with complications, as well as a history of previous GI infections. They also

drew attention to the premise that if, on routine testing, IBS patients have no organic pathology, a positive lactulose hydrogen breath test or glucose breath test which indicated small intestine bacterial overgrowth would, in their view, be pathological.

Other researchers agreed that Pimentel et al. had ignored the fact that the diagnosis of IBS always presumes the absence of a structural or biochemical explanation for the symptoms (Jones, Craig & Olinger, 2001; Cuoco, Cammarota, Jorizzo & Gasbarrini, 2001). Jones et al. also criticised the fact that Pimentel et al. did not also evaluate for other recognised risk factors for bacterial overgrowth such as hypo- or achlorhydria, diabetes with neuropathy, small bowel dysmotility, malnutrition and immuno-deficiency states, and alcoholism.

Pimental et al. corroborated their findings of an apparent association between the increased prevalence of small intestine bacterial overgrowth with IBS in a further study in 2003 where they set out to evaluate whether hydrogen and methane patterns on lactulose breath testing coincided with diarrhoea and constipation symptoms in IBS and IBD. The 551 participants in the study - 296 (53.7%) of whom fulfilled Rome I criteria for IBS - were referred for a lactulose breath test (LBT). The researchers found that methane secretion among subjects with small intestinal bacterial overgrowth and IBS was associated with higher constipation severity scores and lower diarrhoea severity scores. They also found that diarrhoea, and conditions that produce this symptom such as IBD, are associated with hydrogen production on LBT.

Lin (2004) takes the apparent link between small intestine bacterial overgrowth and IBS a little further. He suggests that the GI and immune effects which small intestine bacterial overgrowth has on the patient may explain not only bloating, distension and abdominal pain but other symptoms of IBS such as altered motility, visceral hypersensitivity and immune activation, as well.

2.3.4 Neurotransmitter Imbalance

The enteric nervous system modulates GI function via the action of neurotransmitters and neuromodulators including serotonin, norepinephrine, dopamine and melatonin and that dysfunction of these can lead to gastrointestinal disorders. Of these, serotonin is generally considered to be the main candidate in the modulation of motor and sensory function in the GI tract and its involvement in the pathogenesis of IBS is being supported by accumulating evidence (Wade, Tamir, Kirchgessner & Gershon, 1994; Gershon, 1999; Crowell, 2001). Serotonin is involved in the local regulation of GI motility, secretion, and perception (of urge and pain) as well as being an important brain neurotransmitter that is relevant to cognition, mood, depression, and other neuropsychiatric illnesses. It is hence a key denominator of the brain-gut axis (Kim & Camilleri, 2000; Kilkens et al., 2004).

It has been estimated that approximately 95% of serotonin is located in the GI tract and enteric nervous system - the remaining 5% being in the central nervous system. In the GI tract, serotonin is found within the majority of enterochromaffin cells, as well as neurons, mast cells, and smooth-muscle cells. When

enterochromaffin cells release serotonin, vagal afferent nerve fibres and intrinsic enteric afferent nerve fibres are stimulated resulting in intestinal secretion and the peristaltic reflex.

In physiological studies of gut smooth muscle, serotonin can make the bowel contract or relax by stimulating cholinergic neurons to release acetylcholine, which results in smooth muscle contraction, or by stimulating inhibitory nitrergic neurons to release nitric oxide, which results in smooth muscle relaxation (Gershon, 1991; 1998). Any alterations to enterochromaffin cells and/or serotonin signalling can potentially result in GI dysmotility, visceral hypersensitivity and secretomotor abnormalities in the gut (Kim & Camilleri, 2000; Howitz & Fisher, 2001; Houghton, Atkinson, Whitaker, Whorwell & Rimmer, 2003).

Evidence is beginning to link disturbed serotonin physiology with the pathophysiology of diarrhoea. Studies have found a significantly higher postprandial serotonin concentrations and a longer duration of serotonin in diarrhoea-predominant IBS (dIBS) patients than in healthy volunteers. These findings indicated that there might be a difference in the way that serotonin is released in dIBS patients (Bearcroft, Perrett & Farthing, 1998; Houghton et al., 2003; Singh, Pandey & Singh, 2003). Houghton et al. (2003) also suggested that increased stores of platelet depleted plasma serotonin may act as a useful marker for the diagnosis and management of dIBS.

Melatonin (5-methoxy-*N*-acetyltryptamine) is a pineal gland neurohormone and a close derivative of serotonin. It is synthesised from the amino acid, tryptophan and secreted from the pineal gland into the blood in a circadian rhythm. Melatonin is known to modulate gut motility and alleviate stress as well as having an effect on many physiological and pathophysiological functions, including sleep, analagesia and anti-inflammation (Harlow & Weekley, 1986; Song, Gwee, Moochhala & Ho, 2005). It is thought to alleviate stress by exerting both excitatory and inhibitory effects on gut smooth muscle although, in an animal study by Harlow & Weekley (1986), the researchers suggested that the action may not be directly on smooth muscle contraction but, instead, be the result of an indirect action which inhibits the contractile response of serotonin. Bubenik (2002) suggested that this may occur via the central nervous system and the sympathetic and parasympathetic nerves.

In his research on the GI tract of vertebrate species, Bubenik (2002; Bubenik & Brown, 1997) found that the concentration of melatonin in GI tissues surpassed blood levels by 10-100 times and that there was at least 400 times more melatonin in the GI tract than in the pineal gland. These findings add to the evidence that melatonin may play an important role in modulating the digestive system. He also proposed that melatonin may serve as an endocrine, paracrine, or autocrine hormone which influences the regeneration and function of epithelium and which may also reduce the tone of GI muscle and enhance the immune system of the gut.

Messner, Huether, Lorf, Ramadori & Schworer (2001) studied the distribution of melatonin in the human hepatobiliary-gastrointestinal tract by measuring

melatonin concentrations in human bile, GI and liver tissue and in portal blood samples, and comparing them with plasma concentrations.

They found that, compared to concentrations of melatonin in the whole colon, the mucosal concentration of melatonin in the GI tissues was about five times higher - a similar concentration to that found by Bubenik (1997, 2002) in his studies on the GI tract of vertebrate species. The findings of Messner et al. (2001) also suggest that melatonin may act as a mediator of inter-organ communication between the GI tract and the liver.

Other neurotransmitters such as calcitonin gene-related peptide, acetylcholine, substance P, pituitary adenylate cyclase – activating polypeptide, nitric oxide, and vasoactive intestinal peptide, may also play an important role in functional gastrointestinal disorders. Horwitz & Fisher (2001) suggest that these neuro-transmitters may provide links not only between bowel contractility and visceral sensitivity, but also between the enteric and central nervous systems.

2.3.5 Genetic Influences

Researchers have found that IBS clusters in families (Kalartar, Locke, Zinsmeister, Beighley & Talley, 2003; Morris-Yates, Talley, Boyce, Nandurkar & Andrews, 1998) but Levy, Whitehead, von Korff & Field (2000) suggest that part of this may be due to parental reinforcement and modelling which eventually results in learnt illness behaviour. Their study compared 631 children whose parents were

diagnosed with IBS during one calendar year with a control group of 646 children whose parents did not receive a diagnosis of IBS during the same year.

They found that the case children had significantly more healthcare visits for all causes and more visits for GI symptoms than controls, and that outpatient health care costs were also significantly higher for case than control children. They also found that IBS parents made more health care visits than control parents for non-GI complaints and also incurred substantially higher health care costs than control parents. The gender of the IBS parent was not related to children's GI visits – both mothers and fathers appeared to be as effective at modelling GI-related illness behaviour.

The researchers came to the conclusion that perhaps IBS parents might not be specifically modelling *GI illness* behaviour to their children but modelling a *general* pattern of illness behaviour instead. Unfortunately, this study did not examine whether the health complaints of the parents were the same as those exhibited by their children.

A study on twins, however, suggests that a proportion of the liability for functional bowel disorders (FBD) may be under genetic control. Morris-Yates et al. (1998) carried out a study on 686 individual twins from same-sex pairs enrolled in the Australian Twin Registry. In this study the participants completed a structured interview that included questions related to symptoms consistent with FBD: abdominal pain, diarrhoea, constipation, excessive gas or bloating, and nausea.

Thirty-three of the participants (4.8%) had one or more symptoms diagnosed by a medical practitioner as FBD.

Other studies suggesting a genetic tendency have been carried out by Gonsalkorale, Miller, Afzal & Whorwell, (2003) and Yeo et al., (2004). Research has shown that inflammation may play a role in the pathogenesis of IBS (Bose & Farthing, 2001; Barbara et al., 2004). Persistent inflammation is thought to result from an imbalance of cytokines, and the elaboration of cytokines is under genetic control.

Gonsalkorale et al. (2003) designed a study to establish whether there might be a genetic predisposition to an altered pattern of anti-inflammatory cytokine production in patients with IBS. Their results showed that patients with IBS had significantly reduced frequencies of the high producer genotype for the anti-inflammatory cytokine, interleukin 10, than controls. This suggests that at least some IBS patients may be genetically predisposed to produce lower amounts of this cytokine and that there may then be an increased inflammatory component in some cases of IBS.

Yeo et al. (2004) carried out a study on 194 North American Causasian female diarrhoea-predominant IBS (dIBS) patients and 448 female Caucasian controls to assess the potential association between the serotonin reuptake transporter (SERT) polymorphisms and the dIBS phenotype.

As mentioned previously, serotonin plays in important part in gut functions such as intestinal peristalsis and secretion, and in the sensory signalling in the brain-gut axis (Gershon, 1999; Kim & Camilleri, 2000). SERT is a specific protein which mediates removal from the synapse. Polymorphisms in the SERT gene affect transcriptional activity which results in altered serotonin reuptake efficiency, indicating that the SERT polymorphism may play a role in the development of IBS. The researchers observed a strong genotypic association between the SERT-P deletion/deletion genotype and the dIBS phenotype, suggesting that the serotonin transporter was a potential candidate gene for dIBS in women.

2.4 Symptom Criteria

IBS is a functional disorder which can exhibit symptoms (especially in older people) similar to those of serious organic illness such as weight loss, rectal bleeding, recent changes in bowel pattern, and pain or bowel movements that wake the patient – a symptom which is often considered a warning sign of organic disease, yet can occur with functional disorders as well. In patients with IBS, weight loss may be due to depression, and rectal bleeding is commonly attributed to haemorrhoids or anal fissure caused by straining with a hard bowel movement (Manning, Thompson, Heaton & Morris, 1978).

Food allergies, gluten intolerance disorders such as coeliac disease, inflammatory bowel diseases such as Crohn's disease and ulcerative colitis, colon cancer, endometriosis, can all mimic the symptoms of IBS and must be conclusively

ruled out (Van Vorous, 2000). Because of the similarity of IBS and organic illness, a thorough evaluation is necessary applying both suitable criteria and laboratory and clinical testing to arrive at a conclusive diagnosis (Licht, 2000; Talley et al., 1990).

2.4.1 Manning Criteria

Diagnostic criteria for IBS were first developed by a study by Manning et al. in 1978 (Manning criteria) and later by a consensus meeting in Rome in 1988 (Rome criteria). Both criteria consist of a set of symptoms that, in the absence of structural or biochemical disorders of the GI tract, are consistent with IBS.

Between August 1975 and May 1976, Manning et al. (1978) recruited 109 patients who were complaining of abdominal pain, constipation, or diarrhoea. Each participant was given a questionnaire containing 15 symptoms thought to be characteristic of IBS (*see Table 3*).

Seventeen to twenty-six months later, 106 of the participants were reviewed independently by two gastroenterologists to establish a final diagnosis of the original complaints and a definite diagnosis was reached in 79 patients. Fourteen of these had diverticular disease of the colon and were excluded because their symptoms might be regarded as either organic or functional, leaving 32 patients with IBS and 33 with organic disease.

Table 3 **Symptoms Believed to be Characteristic of IBS**

Looser stools at onset of pain	Nocturnal bowel movement
More frequent bowel mvts at onset of pain	Urgency of defecation
Pain eased after bowel movement (often)	Pain worse after bowel movement
Visible distension	Pain eased with flatus
Feeling of distension	$\geq$ 2 bowel movements between meals
Mucus per rectum	Harder stools at onset of pain
Feeling of incomplete emptying (often)	Less frequent bowel movements at onset of pain
Bowel movement before breakfast	

Adapted from Manning et al. 1978

None of the 15 symptoms tested was more common in patients with organic disease but four were more common in patients with IBS: abdominal distension, pain relief with bowel action, more frequent stools with onset of pain, looser stools with onset of pain. Two further symptoms – passage of mucus and the sensation of incomplete evacuation – were more common in the patients with IBS and when these two symptoms were added to the four listed above, the discrimination between the two groups was increased (*see Table 4*).

Table 4 **Manning Criteria**

1. pain eased after bowel movement
2. looser stools at onset of pain
3. more frequent bowel movements at onset of pain
4. abdominal distension or bloating
5. mucus per rectum
6. feeling of incomplete rectal emptying

Adapted from Manning et al. 1978

2.4.2 Rome Criteria

Following the 12th International Congress of Gastroenterology in 1984, the need for further guidelines for the diagnosis and study of IBS was discussed and a working team was set up in 1986 to develop these guidelines. The ensuing draft was sent to 16 colleagues (in seven different countries) who were noted for their research. The document was revised in light of their comments and presented at the 13th International Congress in Rome in 1988 (Thompson, Dotevall, Drossman, Heaton & Kruis, 1989).

Table 5 **Rome I Criteria**

Continuous or recurrent symptoms of:

1. abdominal pain, relieved with defecation, or associated with a change in frequency or consistency of stool;

AND/OR

2. disturbed defecation (two or more of):

a) altered stool frequency
b) altered stool form (hard or loose/watery)
c) altered stool passage (straining of urgency, feeling of incomplete evacuation)
d) passage of mucus

USUALLY WITH

3. bloating or feeling of abdominal distension.

Adapted from Thompson et al., 1989.

Rome I

A committee was set up in the same year to look at subgroups of IBS and, as a result, the project was expanded to include all of the functional GI disorders. The members of the committee then developed a system to classify the functional GI disorders into 21 entities in five anatomical regions of the gut (oesophageal, gastroduodenal, bowel, biliary, and anorectal). From 1990-1995, further committees were formed to work on the classification system and the third revision, which included the IBS criteria (which now required pain for the diagnosis), was published in 1992 and is now known as Rome I criteria (Drossman, 2000; Thompson, 2000). (*See Table 5*).

Table 6 **Rome II Criteria**

IBS can be diagnosed based on at least 3 months continuous or recurrent symptoms in the preceding 12 months of:

a. abdominal discomfort or pain that has two out of three of these features:

    a. relieved with defecation; and/or

    b. onset associated with a change in frequency of stool; and/or

    c. onset associated with a change in consistency of stool; and

2. two or more of the following, at least a quarter of occasions or days:

    a. altered stool frequency (either more than 3 bowel movements per day or fewer than 3 bowel movements per week;

    b. altered stool form (lumpy/hard or loose/watery stool);

    c. altered stool passage (straining, urgency, or feeling of incomplete evacuation);

    d. passage of mucus;

    e. bloating or feeling of abdominal distension.

Rome II

New committees were set up (including basic science, physiology, psycho-social and paediatric committees) and a series of articles was produced as a supplement in Gut 4: 16-26, 1999. The expanded information from the work of these committees was then published in the Rome II book in 2000 (Drossman, 2000; Thompson, 2000). (*See Table 6*).

Rome III

A co-ordinating committee was set up in 2001 for Rome III. Most of the Rome II committees were retained and additional ones (pharmacology, gender, culture, society and the patient, two paediatric committees, functional abdominal pain) added. By December 2002, all committee members were selected and the publication was released in 2006 (Drossman, 2000; Thompson, 2000).

2.5 Impact on Quality of Life and Economic Cost

IBS typically affects those of working age and imposes a substantial economic burden in both direct medical costs and in indirect social costs. It poses a financial burden on the patient both through loss of pay and the added cost of healthcare (such as physician visits, investigations and treatments) and is also costly to the employer because of absenteeism, lost productivity, and medical, pharmaceutical and disability claims from employees (Cash, Sullivan & Barghout, 2005; Leong et al., 2003). There is also the less-measurable costs of decreased quality of life (Hulisz, 2004; Drossman et al., 2007).

In a 12-month study, Zacker, Chawla, Wang & Albers (2004) compared patterns of illness or disability-related absence from work in participants in the U.S. who had been diagnosed with IBS with a sample of patients with no GI disorders, and estimated that the absences were 3.27% greater for participants with IBS once they had been diagnosed with the disorder.

Dean et al. (2005) found IBS to be associated with a 21% reduction in work productivity in the U.S. (equivalent to working less than 4 days in a 5-day work week) and Hahn et al. (1999), in a study involving the U.S. and the U.K., found that in both countries, nearly 1/3 of those surveyed missed at least one day of work due to IBS in the previous 4 weeks and a greater percentage cut back in their work or activities due to IBS. More people in the UK experienced changes in jobs or declined opportunities for promotion or advancement due to IBS.

Leong et al. (2003) carried out a study to measure both the direct and indirect costs of treating IBS by analysing all medical, pharmaceutical, and disability claims for a U.S. company's employees and their dependents during 1998. They found that the average total cost per patient with IBS was $4,527 compared with $3,276 for controls, the average physician visit costs were $524 and $345 for patients with IBS and controls, respectively, and that the average out-patient care costs to the employer were $1,258 and $742 for patients with IBS and controls, respectively. On average, each employee with IBS cost the employer $901 as a result of absenteeism compared to $528 for those employees not suffering for IBS, indicating a significant financial burden on the employer. These costs were attributed to more visits to medical

practitioners and hospital out-patients care, a greater use of prescription medications and a subsequent increase in work absenteeism.

Current research shows a substantial economic burden on society as a result of IBS but the true economic burden is still unclear. Direct healthcare costs are clearly defined but, apart from absenteeism from work and lost productivity, there is insufficient data on indirect social costs because, even though a high percentage of people is known to be affected with this disorder, most IBS sufferers (60-75%) do not consult a physician (Jones & Lydeard, 1992; Farthing, 1995).

Suggested strategies to reduce direct costs include physician/patient education, avoidance of unnecessary investigations, the setting-up of support groups and the early consideration of psychosocial issues and psychological treatments (Camilleri & Williams, 2000).

Diminished quality of life (QOL) is another aspect of IBS. As well as having a possible financial impact on employers through reduced productivity, it affects the day-to-day functioning of the employee. Employees with IBS were found to have significantly lower scores on all domains of the SF-36 health survey, indicating poorer functional outcomes (Akehurst et al., 2002; Dean et al., 2005).

Hahn et al. (1999) compared health-related QOL of IBS sufferers in the U.S. and the U.K. and found that the general health status of participants with IBS in both countries was poorer compared to that of the general populations and that the effect

on QOL appeared to be greater in the U.K. They also found that healthcare utilisation was similar in both countries, as was the percentage of IBS patients using prescription drugs – approximately 75% in each group.

Badia et al. (2002) carried out a cross-sectional study on a representative sample of the Spanish population to compare health-related QOL in 146 participants meeting the Rome I criteria and 65 meeting the Rome II criteria, and found that participants meeting Rome II criteria reported worse health-related QOL scores than those meeting exclusively Rome I criteria. Of the Rome II individuals, 67.7% had consulted some type of healthcare professional in the previous 12 months (Rome I group 41.8%); drug consumption was 70.8% (Rome I group 45.2%) and reduced performance in main activity was 60% (Rome I group 27.4%). Overall, the study sample reported significantly worse health-related QOL scores than the general population in four dimensions of the SF-36 (bodily pain, vitality, social functioning and role-emotional).

IBS imposes a large medical burden on society in terms of consultations, investigations, treatments and drug consumption and the burden is further increased by social costs such as absenteeism from work and loss of productivity. As well as healthcare costs, there is a significant reduction in the quality of life of IBS sufferers and, since the number of people with this condition and the burden of illness appear to be so large, IBS should be looked upon more seriously by the medical community and society.

2.6 Psychosocial Factors and Irritable Bowel Syndrome

2.6.1 Life Stress

Studies have shown that life stress contributes to the onset and exacerbation of symptoms for the majority of patients with IBS and other functional disorders such as functional dyspepsia (FD) (Levy et al., 1997; Locke et al., 2004).

Bennett et al. (1998) recruited 117 IBS/FD outpatients to test the relation of chronic life stress the participants had experienced during the six months or more prior to the trial, to subsequent symptom intensity over time. To determine life stress and symptom intensity measures, patients were interviewed and asked to complete a self-report which was collected at the commencement of the two-week trial, and again at 6 and 16 months.

Stressors included divorce, relationship difficulties, serious illness (of self or others), lawsuits, business failures, housing difficulties, forced redundancies, and caring for a family member with significant physical and/or emotional problems. The results suggested that chronic life stress was a powerful predictor of subsequent symptom intensity and that the relation was not influenced by personality, age, sex, anxiety, or depression.

In a stress management trial, Corney and Stanton (1990) measured psychiatric symptoms, psychosocial distress and symptom severity over a period of a week in 42

patients suffering from IBS. The researchers found that 52% of patients had had symptoms continuously and the remainder had had symptom-free periods. Of the latter group, 45% felt that reoccurrence of symptoms was related to life stress and 55% of all the participants linked the initial onset of illness with stressful events such as employment difficulties, a family death, a medical operation, and marital stress.

Creed's research (1992; 1994) also suggested a strong association between IBS and psychological disorder. The findings showed that about half the IBS patients in a hospital clinic had a psychiatric disorder. This was two or three times greater than the prevalence among patients with organic GI conditions such as peptic ulcers or IBD, and healthy controls. Also, two-thirds of patients with IBS had experienced stressful events such as bereavement, marital separation or major argument leading to a broken family relationship, before the onset of abdominal symptoms.

Herschbach, Henrich & Von Rad (1999) carried out a study on a representative sample of the German population (2,201 volunteers – 52.9% women/47.1% men) with IBS or FD or both, to elucidate the role of psychological factors in the frequency of physician consultations by individuals with functional GI disorders. Of the volunteers, 288 (13.1%) suffered with IBS and/or FD. The subjects with IBS or FD, with and without physician visits, were compared with each other and with the general population.

The participants completed a questionnaire on physical symptoms, illness behaviour, living conditions, personality features, and sociodemographic status, and

were assigned to one of two groups – those with IBS and FD (FGD group), and the general population.

Those in the FGD group had significantly higher scores for depression, emotionality, and physical symptoms, were more worried about their health, and had more negative life stress in the previous twelve months than the general population. The study also showed that those participants who consulted a physician for their GI disorders (59.6%), and those who did not (40.4%), differed on psychological measures. Those participants who had not consulted a physician had higher scores for somatisation, emotionality, quality of life, health rating, and social support, but they did not differ from the general population on depression, concerns about health, and life events. Those participants who consulted a physician differed from the non-consulters with respect to somatisation, depression, emotionality, life events, and health rating.

The researchers suggest that, in view of the results of their trial, gastroenterologists, when seeing patients with functional GI disorders, should be aware that there may be a psychological component.

2.6.2 Anxiety and Depression

Hazlett-Stevens, Craske, Mayer, Chang & Naliboff (2003) examined the relationships between the presence of IBS and generalised anxiety disorder, chronic worry, neuroticism, anxiety sensitivity and anxiety about visceral sensations in a

sample of 905 university students. The participants completed a questionnaire containing measures of the afore-mentioned psychological symptoms, and IBS diagnostic status was determined according to the Rome II criteria.

The researchers found that there was a significant association of IBS and anxiety-related measures, especially anxiety about visceral sensations and that the prevalence of IBS reported by the university students was similar to that reported by adult population surveys.

In a Japanese study, Masanori, Hideyuki, Katsumi & Chiharu (2004) focused on functional pain in 128 outpatients with IBS. The participants were assigned to two groups: the first group of 99 patients whose main symptom was abdominal pain, and the second group of 29 patients in which the main symptom was abdominal discomfort, not pain. All participants completed a validated self-report questionnaire for anxiety (STAI-I) and depression (Zung's Self-rating Depression Scale – ZSDS).

According to the DSM III-R criteria, psychiatric disorders (depression, anxiety, conversion disorder, eating disorder, and pain disorder) were diagnosed in 51 (51.5%) of the 99 pain IBS patients and 13 (44.8%) of the 29 discomfort IBS patients. Anxiety disorder was diagnosed in 22.7%, and depressive disorder in 25% of all IBS patients. The rate of anxiety disorder in pain IBS patients was found to be higher than that in the discomfort IBS patients.

Studies have shown that treatment-seeking patients have higher levels of depressive symptoms than normal controls (Herschbach et al., 1999; Latimer, 1983) but, although IBS is often accompanied by depression, the mechanism underlying the relationship is not known. Also unknown is the nature of any influence pain catastrophising has on IBS symptoms (Drossman et al., 2003).

Lackner, Quigley & Blanchard (2004) carried out a study on 244 participants (196 (80.3%) female and 48 (19.7%) males) who satisfied the Rome II criteria for IBS and had undergone a medical examination and laboratory tests (when necessary) to exclude those volunteers who had inflammatory bowel disease or lactose malabsorption syndrome. Volunteers were also excluded if they had a history of current or past psychiatric disorders.

The purpose of the study was to test the mediational role of catastrophising (i.e. the patients' beliefs regarding pain) in the link between depression and pain severity. Catastrophising was measured using the subscale of the Coping Strategies Questionnaire (Rosenstiel & Keefe, 1983) and participants were asked to rate the frequency in which they engage in various beliefs during an episode of pain (0= never do to 6= always do) on the six items of the subscale. The severity of pain was measured on the Bodily Pain subscale of the SF-36 Health Survey (Ware & Sherbourne, 1992), trait anxiety by using the Trait subscale of the State-Trait Anxiety Inventory (Speilberger et al., 1970), and depression was measured using the Beck Depression Inventory (Beck et al., 1961).

The results showed that patients with IBS who experience higher levels of depression engage in more catastrophic thinking and, partly through this thinking style, experience more intense pain and greater activity limitations due to pain severity.

Gorard et al. (1996) carried out a study to determine whether patients with anxiety and depression had objective evidence of abnormal intestinal transit irrespective of any bowel symptoms. The participants for the study were 21 psychiatric outpatients, who fulfilled the criteria for generalised anxiety disorder and/or major depression, and 21 healthy controls. Orocaecal transit time was measured by the lactulose hydrogen breath test and whole gut transit time by abdominal radiography. Median range whole gut transit time was shorter in patients with anxiety (14 hours) than in patients with depression (49 hours) and controls (42 hours); and orocaecal transit time was shorter in patients with anxiety (60 minutes) than in patients with depression (110 minutes) and controls (75 minutes). The results indicated that anxiety was associated with diarrhoea and depression with constipation: mood has an effect on intestinal motor function.

2.6.3 Sexual and Physical Abuse

Researchers have also examined the relationship between a history of sexual or physical abuse and functional bowel disorders (Longstreth & Wolde-Tsakik, 1993; Reilly, Baker, Rhodes & Salmon 1999; Ross, 2005).

Dill, Sibcy, Dill & Brende (1997) designed a study to determine the percentage of patients in a medical practice who had both IBS and a history of sexual abuse. Sixty-five patients aged from 24 to 84 years participated in the study, 79% of whom were women. The participants were assigned to one of three groups: a) no reported history of sexual abuse; b) reported history of sexual abuse without history of being threatened with sexual abuse; and c) reported history of sexual abuse with history of being threatened with sexual abuse. Sixty-eight percent of the patients who had a history of childhood or adult sexual abuse also reported that they had been exposed to the threat of abuse, and had much higher symptoms scores than those exposed to abuse alone.

The results of the study suggest that threat combined with abuse is more likely to affect IBS symptom severity, and is a more significant predictor of IBS symptomatology.

Drossman et al. (1990) recruited 206 female patients from a university-based GI practice over a 2-month period. On completion of a questionnaire (which requested information about demographics, functional GI symptoms, health-care utilisation, and a history of abuse), 89 participants (43.2%) reported a history of sexual or physical abuse in childhood or adulthood. All but one of the physically abused patients had been sexually abused. The study also found that almost one third of the abused patients had never discussed their experiences with anyone and only 17% had informed their doctors.

The results indicated that patients with functional disorders were more likely than those with organic disease diagnoses to report a history of sexual and physical abuse, chronic or recurrent abdominal pain, and more surgical intervention; and that abused patients were more likely than non-abused patients to report pelvic pain, multiple somatic symptoms and more surgical intervention.

Ali et al. (2000) were interested in determining whether the experience of emotional abuse (which includes various forms of psychological maltreatment, trauma, and non-physical aggression) was associated with IBS beyond the syndrome's association with a history of physical and/or sexual abuse.

The researchers investigated the presence of emotional abuse, self-blame, and self-sacrificing, in a sample of 25 women who had been diagnosed with IBS to a comparison sample of 25 women who had been diagnosed with IBD.

Emotional abuse was assessed using a psychometrically validated measure, the Abusive Behaviour Inventory (Shepard & Campbell, 1992), self-blame was assessed through a series of validated self-blame scenarios (Janoff-Bulman, 1979), and self-silencing was measured with the Silencing the Self Scale (Jack, 1991). Physical/sexual abuse was assessed using questions previously used with a female GI population (Drossman et al., 1990).

The results showed that women in the IBS sample scored significantly higher physical/sexual abuse (IBS–mean=2.24, SD=1.85; IBD–mean=0.360, SD=0.810),

emotional abuse (IBS–mean=39.5, SD=12.4; IBD–mean=29.4, SD=6.94), self-blame (IBS–mean=24.6, SD=7.92; IBD–14.2, SD=5.47), and self-silencing (IBS–mean=77.2, SD=20.5; IBD–mean=64.7, SD=13.8) than the women in the IBD sample, suggesting that this difference went beyond the differences accounted for by physical and/or sexual abuse history.

Psychological variables such as anxiety, anxiety sensitivity, depression, and physical and/or sexual abuse, have been shown to play a substantial role in the IBS condition of many patients and should be carefully assessed in order to achieve satisfactory clinical outcomes with these patients. Gastroenterologists would also benefit through this assessment by increasing work satisfaction and reducing the difficulty and frustration in working with IBS patients (Norton, Norton, Asmundson, Thompson & Larson, 1999; Palsson & Drossman, 2005).

2.7 Current Management of Irritable Bowel Syndrome

There is no single pathophysiological marker and, therefore, no effective treatment for the whole symptom complex in IBS patients but there are some treatment options which have been shown to be successful in treating the various symptoms of IBS. These treatments include pharmacological treatments (Baker, 2005; De Ponti & Malagelada, 1998; Mertz, 2003), dietary modification (Dainese, Galliani, De Lazzari, Di Leo & Naccarato, 1999; Shanahan, & Whorwell, 2005; Van Vorous, 2000), relaxation training (Blanchard, Greene, Scarff & Schwarz-McMorris, 1993; Boyce, Talley, Balaam, Koloski & Truman, 2003), cognitive-behavioural

therapy (Boyce et al., 2003; Hutton, 2005; Read. 1999), psychotherapy (Kohutis, 1998; Spiller, 2005), and hypnotherapy (Gonsalkorale**,** Houghton & Whorwell, 2002; Palsson, Turner, Johnson, Burnett & Whitehead, 2002; Palsson, Turner & Whitehead, 2006; Whorwell 1984, 1987, 2006). (*See Table 7*).

2.7.1 Pharmocological Treatments

Medications mainly include antidepressants, anticholinergics/antispasmodic agents, antidiarrhoeal and laxative agents, serotonin-receptor agonists for contipation-predominant IBS, serotonin-receptor antagonists for diarrhoea-predominant IBS, and selective serotonin reuptake inhibitors (SRRIs) for associated psychological disorders such as anxiety, depression, and obsessive-compulsive behaviour (Foxx-Orenstein, 2006; McGuire & Towers, 2006).

2.7.1.1 Antidepressants

Tricyclic antidepressants such as amitriptyline (Endep), paroxetine (Aropax), desipramine (Norpramin), clomipramine (Anafranil), doxepin, (Sinequan) and trimipramine (Surmontil), and selective serotonin reuptake inhibitors (SSRIs) such as sertraline (Zoloft), have been shown to decrease IBS symptoms and are recommended (in low-dosage) for moderate-to-severe IBS syndrome in which pain is predominant or when other therapies have failed (Jackson et al., 2000; Morgan, Pickens, Gautam, Kessler & Mertz, 2005). Side-effects include constipation, urinary

retention, fatigue, somnolence, weight gain, cardiac toxicity and haematological abnormalities (Mertz, 2003; Talley, 2003).

Serotonin is an important neurotransmitter in both the brain and the GI tract, where it plays a key role in the regulation of sensory and motor functions. As patients with IBS (and other functional GI disorders) often have comorbid psychiatric diagnoses such as anxiety, depression, and somatoform disorders (Drossman et al., 1999), selective serotonin-reuptake inhibitors (SSRIs) (such as Buspirone, and Paroxetine), and serotonin and noradrenaline reuptake inhibitors (SNRIs) (such as Vanlafaxine-XR) may be useful when IBS is accompanied and exacerbated by mood disorder. Some SSRIs (Prozac, Celexa, Zoloft, and Paxil), however, can trigger severe IBS attacks in diarrhoea-predominant patients. Other side-effects include nausea, headache, restlessness, anxiety, perspiring, and sexual dysfunction (Chial et al., 2003; Kim & Camilleri, 2000).

2.7.1.2 Antispasmodic agents

Abdominal pain is a major symptom in IBS and, therefore, the most frequently prescribed drugs for IBS are antispasmodics, the most common ones being dicyclomine (Bentyl), belladonna/phenobarbital (Donnatal), mebeverine (Colofac), propantheline, and hyoscyamine (Levsin, Anaspaz). These drugs affect gut motor activity and reduce the colon's response to both eating and stress. Antispasmodic agents may reduce abdominal pain or bloating through anticholinergic pathways (by blocking the effects of acetylcholine, the chemical transmitter that nerves release in

order to cause muscles to contract) and, in refractory cases, nitrates are occasionally useful for direct relaxation of smooth muscles (Horwitz, 2001; Poynard, Regimbeau & Benhamou, 2001).

2.7.1.3 Antidiarrhoeal agents

Loperamide (Imodium) and diphenoxylate (Lomotil) are the classic anti-diarrhoeal agents for predominant-IBS patients for whom diarrhoea is the predominant symptom. They enhance intestinal water and ion absorption, increase resting anal sphincter tone, and slow GI transit time by acting on the circular and longitudinal muscle of the intestine, thereby increasing stool consistency and reducing frequency (Camilleri, 1999; Efskind, Bernklev & Vatn, 1996).

Alosetron (Lotronex), the serotonin-3-receptor antagonist, prescribed for women with diarrhoea, was withdrawn from the market in November, 2000 because of serious, life-threatening, GI side-effects. In June, 2002 it was approved again by FDA for marketing but in a restricted manner (Chang et al., 2006).

2.7.1.4 Laxative Agents

The most common pharmacological treatments are serotonergic agents such as Mosapride, Renzapride, and Tegaserod (Zelnorm) which enhance the upper GI motility; opioid agonists and antagonists (e.g. Asimadoline), which reduce sensation responses to gastric and colonic extension, and chloride-channel activators such as

Lubriprostone (Amitiza) which accelerate small intestinal and colonic transit (Camilleri et al., 2006; Delgado-Aros et al., 2003; Harris, Hansel, DiBaise & Crowell, 2006). Chemical laxatives such as Milk of Magnesia or ExLax tend to stimulate the bowel by causing irritation of the intestinal lining and can easily lead to dependency. Constipation-predominant IBS patients with mild constipation may benefit from non-prescription soluble fibre supplements such as Metamucil, Citrucel, Fibercon, or Psyllium (Fernandez-Banares, 2006; Hadley & Gaarder, 2005).

2.7.1.5 Other Agents

Antibiotics. Antibiotics have been suggested as a treatment of refractory diarrhoea where there is evidence of overgrowth by enteric bacteria in the small bowel and bacterial infection is suspected. Antibiotics are not indicated for long-term use because they may increase diarrhoea through changes in the bowel flora (Hadley & Gaarder, 2005; Viera, Hoag & Shaughnessy, 2002), or may result in short-term inflammatory response in the colon which may produce a hypersensitive state similar to that of post-infective IBS (Collins, Barbara & Vallance, 1999).

In a study on antibiotics by Maxwell, Rink, Kumar & Mendall (2002), the researchers found that antibiotics increased functional abdominal symptoms in subjects (recruited from the general population) who had been given a course of antibiotics by their general practitioners, and that the subjects, when compared to controls, were more than three times as likely to report more bowel symptoms four months later.

Prebiotics. Prebiotics are non-digestible food ingredients such as non-digestible carbohydrates (oligo- and polysaccharides), some peptides and proteins, and certain lipids (both ethers and esters). They beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the colon (Gibson & Roberfroid, 1995; Ouwehand, Derrien, de Vos, Tiihonen & Rautonen, 2005). Among the colonic bacterial capable of metabolising prebiotic oligosaccharides, and whose growth is stimulated, are species of Lactobacillus and Bifodobacterium (Santos, San Mauro & Diaz, 2006; Shoaf, Mulvey, Armstrong & Hutkins, 2006).

A study by Shoaf et al. (2006) has suggested that some prebiotic oligo-saccharides may have anti-adhesive activity and directly inhibit the adherence of enteric pathogens to the host epithelial cell surface, thereby preventing infection; and Furrie et al. (2005) carried out a pilot study in which they showed a reduction in inflammation, and regeneration of epithelial tissue, in patients with ulcerative colitis by using a synbiotic (a combination of a prebiotic and a probiotic).

Probiotics. Probiotics consist of a preparation containing a single or mixed culture of live microbes that are presumed to restore normal bowel microflora, and studies indicate that they may be beneficial to IBS (Gill & Guarner, 2003; Nanda, James, Smith, Dudley & Jewell, 1999).

Table 7 Examples of Pharmacological & Other Agents in the Therapeutic Management of IBS

Antidepressants.

- Amitriptyline (Elavil)
- Sertraline (Zoloft)
- Paroxetine (Aropax)
- Desipramine (Norpramin)
- Clomipramine (Anafranil)
- Doxepin (Sinequan)
- Trimipramine (Surmontil)
- Selective serotonin-reuptake inhibitors (SSRIs)

Anti-spasmodic Agents.

- Dicyclomine (Bentyl)
- Propantheline
- Belladonna/Phenobarbital (Donnatal)
- Hyoscyamine (Levsin, Anaspaz)
- Mebeverine (Colofac)

Antidiarrhoeal agents.

- Loperamide (Imodium)
- Diphenoxylate (Lomotil)
- Alosetron (Lotronex) – with caution

Laxative Agents.

- Milk of Magnesia/ExLax
- Lactulose
- Polyethylene glycol solution
- Tegaserod (Zelnorm) (5-HT4 agonist) – with caution
- Mosapride (5-HT4 agonist, 5-HT3 antagonist)
- Renzapride (5-HT4 agonist, 5-HT3 antagonist)
- Lubiprostone (Amitiza) (chloride channel activator)
- Methylnaltrezone (opioid receptor agent)
- Alvimopan (opioid receptor agent)

Other Agents.

- Antibiotics
- Prebiotics/Probiotics
- Fibre
- Bulking agents (Psyllium, Metamucil, Guar Gum)
- Peppermint Oil
- Herbal Medicine

In a double-blind, randomised, crossover design, Bifidobacterium animalis reduced the colonic transit time in a group of healthy women aged 18-45 years (Marteau et al., 2002), and a study by Koebnick, Wagner, Leitzmann, Stern & Zunft, (2003) indicated a significant improvement in severity of constipation and stool consistency in a group of 70 patients with chronic constipation who had ingested a probiotic beverage containing Lactobacillus casei Shirota.

Probiotics may also be useful in the prevention and treatment of antibiotic-associated diarrhoea (D'Sousa, Rajkumar, Cooke & Bulpitt, 2002) and in modulating inflammation and the immune system in the gut (Bradesi, et al., 2003; Harris et al., 2006).

Fibre. The administration of fibre to the diets of IBS patients has had mixed results with the type of fibre (soluble or insoluble) rarely being considered. The proposed mechanism of action of fibre is the enhancement of the stool's water-holding properties, gel formation to provide lubrication, bulking of the stool, and binding of agents such as bile (Friedman, 1991).

In a study of 100 IBS patients by Miller, Lea, Agrawal & Whorwell (2006), participants were asked to consume bran and then complete a self-report questionnaire. The assessment showed that 27% of the participants said that bran had improved their symptoms compared with 22% who claimed it made them worse, and 51% reported that bran had had no positive or negative effect on their symptoms. Forty-eight of the participants had previously tried one or more commercial fibre

products and of these, 56% reported no change in symptoms, 25% reported an improvement, and 19% a deterioration in symptoms.

In a six-month trial of 72 IBS patients by Lambert et al. (1991), patients with constipation, mucus, urgency or watery stools at the beginning of the study, and who were consuming more than 30g of fibre by the end of the trial, reported an improvement in symptoms.

However, in a study by Francis & Whorwell (1994) 55% of the 100 participants were made worse by consuming bran and only 10% found it to be helpful. All symptoms of IBS were exacerbated by bran, with bowel disturbance most often adversely affected.

Most researchers appear to carry out trials on insoluble fibre and not soluble fibre or a combination of both. Van Vorous, (2000) has suggested that both soluble and insoluble fibre should be part of the diet for an IBS sufferer and that insoluble fibre should not be eaten alone or on an empty stomach but should be eaten with a larger quantity of soluble fibre. This hypothesis, however, has not been tested in clinical trials.

Bulking agents. Bulking agents are a concentrated form of non-starch polysaccharides useful for patients who cannot take adequate dietary fibre. Available bulking agents include psyllium (Ispaghula husk), wheat bran, calcium polycarbophil, methylcellulose, guar gum, and sterculia (Indian tragacan or karaya) (Fernandes-

Banares, 2006). Placebo-controlled trials using psyllium as a bulking agent have demonstrated increases in stool frequency and improved stool consistency in patients with idiopathic constipation (Ashraf, Park, Lof & Quigley, 1995; Jalihal & Kurian, 1990).

Guar gum has been shown to be effective for GI problems, functional status, and psychological distress, after just one month of administration (Parisi et al., 2005). In a trial comparison between wheat bran and partially hydrolysed guar gum (PHGG), both bran and PHGG improved abdominal pain and bowel motions but PHGG was better tolerated by the participants (Parisi et al., 2002).

Peppermint Oil. Clinical trials have demonstrated the variable efficacy of peppermint oil to act as a smooth muscle relaxation in patients with IBS. Kline, Kline, Di Palma & Barbero (2001) carried out a two-week study on 42 children with IBS to investigate the efficacy and clinical usefulness of pH-dependent, enteric-coated, peppermint oil capsules. Their results showed that the peppermint oil capsules reduced the pain the children experienced during acute phases of IBS but did not alter heartburn, gas, urgency of stools, belching, stool pattern or stool consistency.

In a previous study on 101 adults with symptoms of IBS by Liu, Chen, Yeh, Huang & Poon (1997) the experimental group (n=52), taking an enteric-coated peppermint oil formulation (Colpermin), showed significant improvement over the placebo group (n=49). In the experimental group, 79% experienced reduced

abdominal pain (placebo, 43%), 83% had less abdominal distension (placebo, 29%), 83% had reduced stool frequency (placebo, 32%), and 79% had less flatulence (placebo, 22%).

Herbal Medicine. The most frequently used complementary medicine is herbal medicine which also includes a variety of Western herbal supplements such as peppermint oil, aloe and ginger (Spanier, Howden & Jones, 2003; Kline, 2001). Trials on herbal medicine have shown varying results and consist of either studies on specific herbs, combinations of herbs, or herbs in combination with either a pharmacological agent or bulking agent.

Brinkhaus et al. (2005) carried out a trial on 106 IBS patients using two herbs, curcuma (part of the ginger family) and fumitory (part of the poppy-seed family) and found that neither herb showed any therapeutic benefit over placebo.

Vejdani et al. (2006) carried out a study on 28 IBS patients to evaluate the effectiveness of adding the herbal medicine Carmint, or its placebo, to either loperamide (for participants with diarrhoea-predominant IBS) or psyllium (for participants with constipation-predominant or alternating IBS) for the relief of abdominal pain/discomfort and bloating in IBS patients. The results of the study showed a decrease in the severity of abdominal pain/discomfort, and significantly less bloating in the Carmint group compared to the placebo group.

In a trial by Bensoussan et al. (1998), 116 patients were randomly allocated to one of three treatment groups: individualised Chinese herbal formulations, a standard Chinese herbal formulation, and placebo, to determine whether Chinese herbal medicine was of any benefit in the treatment of IBS. Compared to patients in the placebo group, patients in both treatment groups (standard and individualised Chinese herbal medicine) had significant improvement in bowel severity symptom scores. On follow-up (14 weeks after completion of treatment), only the individualised treatment group had maintained improvement.

However, the results of a trial by Leung et al. (2006), using standardised Chinese herbal medicine only on IBS patients with predominant diarrhoea symptoms, were not as effective. One hundred and nineteen participants were randomly assigned to two groups: 60 who received standardised Chinese herbal medicine, and 59 who received a placebo. The researchers found that the herbal formulation for diarrhoea-predominant IBS did not lead to global symptom improvement.

2.7.2 Dietary Modifications

Initial recommendations to the IBS patient generally focus on modifying the diet by excluding trigger foods to lessen symptoms, and often by placing emphasis on a more fibre-enriched diet. Food diaries are recommended to help patients identify and avoid dietary triggers (Fernandez-Banares, 2006; Lynn & Friedman, 1993). However, a complicating factor is that patients may experience symptoms as a generalised effect to eating *any* foods (Hadley & Gaarder, 2005).

There are few studies to substantiate exact diets for IBS sufferers, so broad dietary plans are recommended for the different symptoms of IBS. A precise dietary history should be taken and a 7-day prospective dietary analysis. The food diary should include the type of food consumed, chronological sequence and nature of symptoms, and the nature and frequency of bowel movements (Floch & Narayan, 2002; Friedman, 1991).

The perception of adverse reactions to food is much higher in IBS with 20-65% of patients attributing their symptoms to food hypersensitivity (Bischoff, Herrmann & Manns, 1996; Young, Stoneham, Petruckevitch, Barton & Rona, 1994). (*See Table 8*). Studies have shown positive skin prick tests for food to be higher in IBS patients than controls (Jun et al., 2006) and Serum IgG4 antibodies to common foods like wheat, beef, pork, and lamb are elevated in IBS patients (Zar, Benson & Kumar, 2005). Food intolerance may also be related to an abnormal intestinal microflora (Drisko, Bischoff, Hall & McCallum, 2006; King, Bia & Hunter, 1998) and recent studies have shown the benefit of bacterial manipulation by probiotics as a therapeutic approach (Gill & Guamer, 2003; Madden & Hunter, 2002).

Table 8. Suspected Trigger Foods For IBS.

red/dark meat	**dairy products**
citrus juices	**egg yolks**
fried foods	**coconut milk**
oils	**shortening**
butter	**fats**
solid chocolate	**coffee**
caffeine	**alcohol**
carbonated beverages	**artificial sweeteners**
refined sugar	**processed foods**

Some vitamin and mineral supplements are also known to cause GI problems for people with IBS. Vitamin C can cause gas, abdominal cramps and diarrhoea; calcium can have a constipating effect; and magnesium a laxative effect. Iron can also cause stomach upsets and constipation, especially in the form of ferrous sulphate (Mahan & Stump, 2000).

Lactose malabsorption could be a dietary cause for some IBS patients. Without the enzyme lactase, lactose cannot be hydrolysed in the small intestine and thus could be fermented in the colon causing diarrhoea, gas, bloating and abdominal cramps (Tortora & Grabowski, 1993). An association between lactose or fructose malabsorption and early signs of mental depression has been shown in trials by Ledochowski, Sperner-Unterweger & Fuchs (1998) and Ledochowski, Sperner-Unterweger, Propst, Vogel & Fuchs (2000). Another trial by the same researchers suggests that non-absorbed carbohydrates may interfere with tryptophan metabolism, which may explain the development of anxiety, mental depression, and other signs of serotonin deficiency (Ledochowski, Widner, Murr, Sperner-Unterweger & Fuchs, 2001).

Other causes in the development of IBS in lactose-intolerant patients might include alterations to colonic microflora, low-grade inflammation of the colon, and the effects of post-infective enteritis (Barbara et al., 2002; McGuire & Towers, 2006).

2.7.3 Psychological Approaches

Conventional medical treatment of IBS has left a large proportion of patients without significant relief and, therefore, studies have been carried out on alternative therapies to identify those that can complement current medical care and improve clinical outcomes (Poitras et al., 2002; Tillisch, 2006).

Studies also indicate that psychological disorders (especially depression and generalised anxiety disorder) are present in the majority of IBS patients who actively seek medical care (American College of Gastroenterology Functional Gastrointestinal Disorders Task Force, 2002) and, because of this overlap between psychological disorders and IBS, numerous studies have been done to evaluate the benefits of behavioural therapies such as cognitive-behavioural therapy, psychotherapy, relaxation therapy, and hypnotherapy, to reduce IBS symptoms (Drossman et al, 2003; Guthrie, Creed, Dawson & Tomenson, 1993; Blanchard et al., 1993; Whorwell, Prior & Faragher, 1984; Whorwell, 2006).

The most studied psychological/behaviours interventions in IBS have been cognitive-behavioural therapy and hypnotherapy with most of these studies demonstrating that individual IBS symptoms improved and that this improvement frequently correlated with improvement in anxiety symptoms and depression symptoms (Harris & Chang, 2006).

2.7.3.1 Cognitive-Behavioural Therapy

Cognitive-behavioural therapy (CBT) addresses misinterpretations patients may have in their responses to life events. These responses are cognitive (what the patient thinks), behavioural (how the patient reacts), and physiological (what the patient feels). In IBS, patients might misinterpret the visceral sensations and reactions that are brought on by their response to stress, and respond with illness behaviour (Read, 1999). Treatment involves problem identification and solving which gives patients a sense of confidence and control over their condition (Van Dulmen, Fennis & Bleijenberg, 1996).

In a study by Drossman et al. (2003), 215 female patients with IBS were randomly assigned to treatment with either CBT or education (where patients reviewed symptom diaries, read educational material on functional bowel disorders, and discussed the information with a therapist). Results showed a highly significant response in the CBT group (70%) compared to those patients receiving education only (30%). The least beneficial effect was found for IBS patients with depression.

Two studies by Boyce, Gilchrist, Talley & Rose (2000) and Boyce et al., (2003), however, showed different results when treating IBS patients with CBT. In the first study, eight participants with a diagnosis of IBS underwent eight sessions of CBT and maintained daily records of symptom severity. CBT appeared to reduce the distress and disability associated with IBS (but not the frequency of bowel symptoms)

and, after treatment, five of the eight patients no longer met the Rome diagnostic criteria for IBS.

In the second study, however, where 105 patients with IBS were randomly assigned to three treatment groups (routine clinical care, relaxation training, and CBT) there were no significant differences among the treatment groups, suggesting that CBT does not have an advantage over relaxation training or routine clinical care. All subjects in the study improved significantly over the course of the study in terms of their self-reported bowel symptoms (frequency, distress and impairment), psychological symptoms (particularly anxiety and depression) as well as quality of life, irrespective of the treatment received.

Van Dulmen et al. (1996) carried out a study with 25 patients receiving CBT treatment in a group (rather than as individual patients) and 20 patients in a waiting-list control condition. The results showed that cognitive-behavioural group treatment was as effective in alleviating IBS, in stimulating coping strategies, and in reducing avoidance behaviour, as was individual treatment, thereby making the treatment more cost-effective.

Some researchers have combined CBT with other treatments and obtained positive results (Heymann-Monnikes et al., 2000; Gonsalkorales, Toner & Whorwell, 2004).

Heymann-Monnikes et al. (2000) compared a combination of standardised multicomponent behavioural therapy plus standard medical treatment with standard medical treatment only. The multicomponent behavioural therapy included IBS information and education, progressive muscle relaxation, training in illness-related cognitive coping strategies, problem-solving, and assertiveness training. Twenty-four patients were randomly allocated to one of the two groups for 10 weekly sessions.

The results showed significantly greater IBS symptom reduction and significant improvement in overall well-being in the multicomponent behavioural therapy group than in the standard medical group, suggesting that the combination of medical treatment plus CBT was superior to medical treatment alone in the therapy of IBS.

Gonsalkorale et al. (2004) designed a study to determine whether the improvement in treating IBS with hypnotherapy was associated with cognitive change. The study supported the findings shown in previous research (Whorwell et al., 1984, 1987; Houghton, 1996) – i.e. that hypnotherapy reduced both IBS symptoms and associated extra-colonic manifestations, and improved the patients' quality of life and psychological well-being. More specifically, it showed that symptom improvement with hypnotherapy was associated with a change in cognitions (*see Chapter 4*).

2.7.3.2 Psychotherapy

Psychotherapy attempts to help both therapist and patient understand the reason why the patient has developed psychological symptoms and what the symptoms might mean, so that the patient might gain insight and view the problem realistically. The expectation is that the insight gained will cause changes in attitudes and behavioural patterns within the patient thereby alleviating the symptoms (Read, 1999). In various studies, psychotherapy has been compared to other modalities including supportive listing (Guthrie et al., 1993) and medical treatment (Corney, Stanton, Newell, Clare & Fairclough, 1991), and patients have been treated either individually or in groups.

One hundred and two patients with refractory IBS took part in a randomised trial comparing psychotherapy with supportive listening (Guthrie et al., 1993) in which psychotherapy was found to be superior to supportive listening in terms of an improvement in both physical and psychological symptoms. The control group were offered psychotherapy on completion of the trial; 33 accepted treatment and, after therapy, demonstrated a marked improvement in their symptoms. The researchers suggested that these results showed that psychotherapy was effective in the majority of IBS patients with chronic symptoms that were unresponsive to standard medical treatment.

A group psychotherapy programme was carried out on 47 patients who were suffering from functional gastrointestinal disorder (FGID) as defined by Rome I

criteria – 40 of whom were suffering from IBS (Poitras et al., 2002). The treatment programme combined patient education (diet, medical or psychiatric management) and counselling intervention.

The programme consisted of ten two-hour sessions over 10-12 weeks (10-12 patients in each group) and the main aim of the study was to facilitate and emphasise recognition of the influence of emotions on the biopsychosocial attitude including GI symptoms. The control group consisted of 17 patients who were on a waiting list before starting the group psychotherapy programme. Researchers monitored the natural evolution of the disease during this period where participants weren't receiving treatment.

Patients showed significant improvement in GI symptoms and quality of life with psychotherapeutic intervention compared to controls. The data showed the relationship between GI symptomatology and quality of life in patients with FGID and also demonstrated that both criteria could be improved by psychotherapy.

However in a trial by Corney et al. (1991) where 42 IBS patients were randomly assigned to receiving either medical treatment or psychotherapy, no significant differences were found between treatment groups, but a significant correlation was found between improvement in stomach pain and diarrhoea and improvement in psychological symptoms, suggesting a close interrelationship between the two.

2.7.3.4 Relaxation Training

As stress is thought to be a major factor in the aetiology of IBS (Levy et al., 1997; Locke et al., 2004), the rationale behind relaxation training is that reducing the emotional tension by relaxation will help reduce symptoms (Deckro et al., 2002; Nakao et al., 2001).

Blanchard et al. (1993) carried out a study on 16 patients with IBS who were assigned to two groups – eight participants in each group. One group received training in muscle relaxation over 10 sessions (plus regular home practice), the other merely monitored GI symptoms. All patients started on a daily GI symptoms diary on which they rated the severity of seven GI symptoms – abdominal pain, abdominal tenderness, diarrhoea, constipation, bloating, flatulence, and nausea. Based on these daily GI symptom diaries (which were collected for 4 weeks before and 4 weeks after treatment), participants in the relaxation group showed significantly more improvement than those participants who were only monitoring symptoms. Fifty percent of the relaxation group were clinically improved at the end of treatment compared to controls.

In a later study consisting of 13 participants, Keefer & Blanchard (2001) compared relaxation response meditation (RRM) plus symptom monitoring, with symptom monitoring alone. The participants receiving RRM were asked to keep a record of their relaxation practice, to rate the level of relaxation before and after practice, and to note the length of practice time. After six weeks, patients in the

symptom monitoring only group were crossed over into the treatment plus symptom-monitoring group and received six weeks of treatment.

The relaxation training protocol proved to be superior (67% clinically improved) to the waiting-list symptom monitoring condition in the reduction of flatulence, belching, diarrhoea, constipation, and bloating; and those who crossed over into the treatment after being on the waiting-list improved significantly (86% clinically improved), suggesting that the improvement was due to the relaxation training.

A one-year follow-up of this study (Keefer & Blanchard, 2002) was carried out to determine whether the effects of relaxation training on IBS symptom reduction had been maintained over the long-term, and significant reductions were noted for the symptoms of abdominal pain, diarrhoea, flatulence, and bloating.

2.7.3.5 Hypnotherapy

The first controlled trial in the field of gastroenterology using hypnotherapy as a treatment for IBS (Whorwell et al., 1984) showed significant improvement in both the patients' symptoms and well-being. The trial generated more interest in hypnosis as a treatment option for this condition and further research and hypnotherapy trials were carried out with similar outcomes (Gonsalkorale et al., 1999, Gonsalkorale et al., 2002, Gonsalkorale, Miller, Afzal & Whorwell, 2003,

Gonsalkorale et al., 2004; Palsson, 1998, 2002, 2006; Whorwell, 1987, 1991, 2006) (*see Chapter 3*).

Imagery is a major component of hypnosis, and research has provided numerous examples of the physiological effects imagery has on the body. In two separate studies, Gemignani et al. (2000) and Gemignani, Sebastiani, Simoni, Santarcangelo & Ghelarducci (2006) observed changes in autonomic and EEG patterns induced by hypnotic imagination of aversive stimuli; Hunt et al. (2006) showed the positive effect of imagery in the treatment of snake phobia; and Zitman (1992) demonstrated the use of imagery in hypnosis as a treatment to alleviate tension headaches. These findings suggest the possibility that physiological functions usually regarded as autonomic or involuntary may be controlled by imagery, and that this link between the conscious intent and the autonomic function could be used in the treatment of illness.

There are a number of different treatments for IBS, most of which appear to fall into two distinct categories: those that deal with the mind and those that deal with the body. It appears, then, that once again the mind-body connection has become detached to some extent.

Compared to the various treatment options for IBS, which focus on either the psychological or physiological aspects of an illness, hypnotherapy is a more holistic treatment in that it addresses both. When one takes into account that both psychological and abdominal symptoms are associated with impaired health-related

quality of life in patients with IBS, and that hypnosis can change both psychological and physiological symptoms through the use of imagery, hypnotherapy then, has the potential of being the optimal treatment for IBS sufferers.

2.8 Summary

IBS affects approximately 20% of all people at any one time and is probably the most common disorder encountered by both gastro-enterologists and physicians in primary care (Farthing, 1995; Camilleri & Choi, 1997). The disorder typically affects those of working age and imposes an economic burden on the patient through healthcare costs and loss of income through illness (Dean et al., 2005). There is also the less-measurable cost of decreased quality of life (Creed et al., 2000).

The aetiology of IBS is yet unknown but most researchers agree that a subset of IBS sufferers have a visceral hypersensitivity of the gut (Bouchoucha et al., 1999; Camilleri et al., 2001). Other possible causes that have been proposed include previous gastroenteritis, small intestine bacterial overgrowth, psychosocial factors such as life stress, a genetic contribution, and an imbalance of neurotransmitters (Gershon, 2004; Neal et al., 1997; Pimentel et al., 2000).

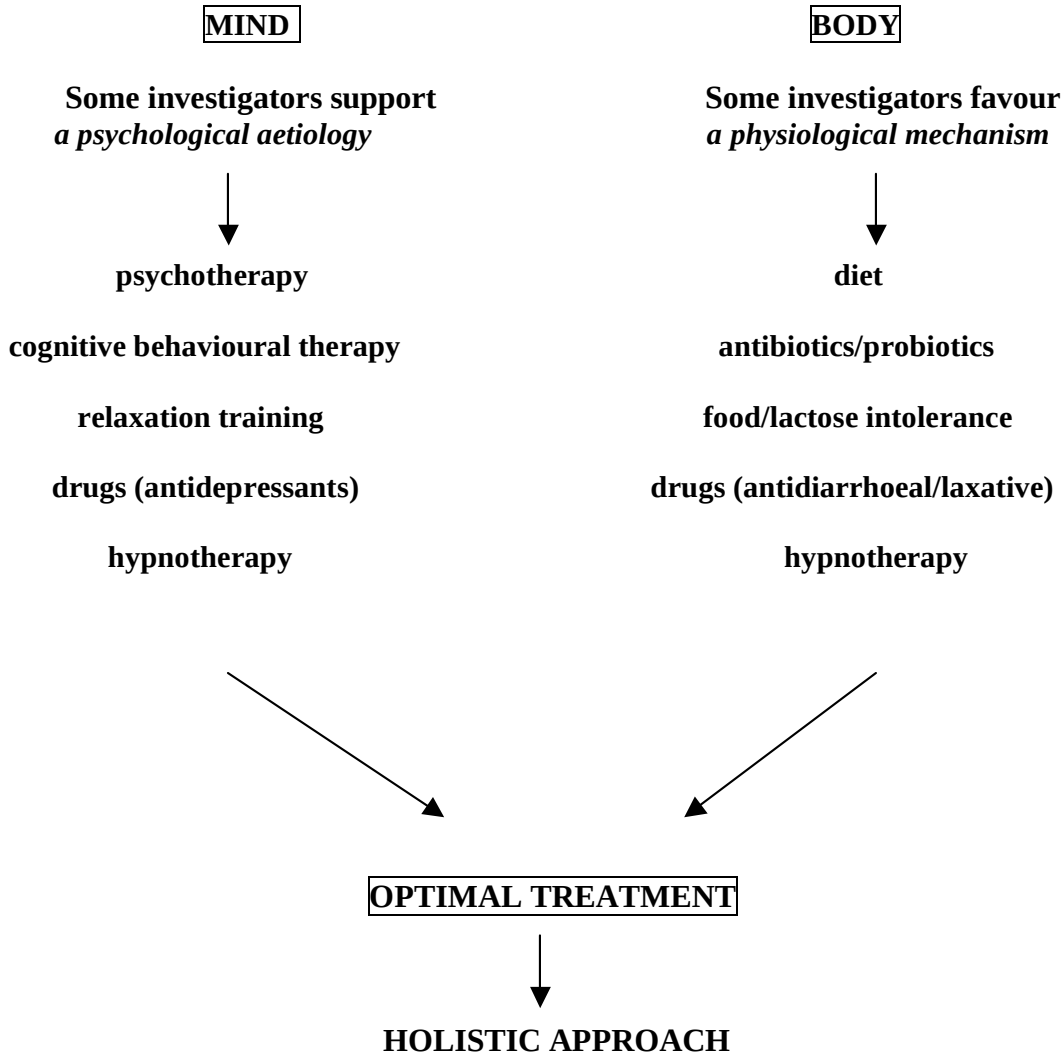
Researchers are beginning to view IBS as a multi-faceted disorder in which there appears to be a disturbance in the interaction between the intestines, brain, and autonomic nervous system, resulting in an alteration in the regulation of bowel

motility and/or sensory function (Smith. & Morton, 2001; Tortora & Grabowski, 2000). Studies have shown that emotions such as anger, fear, pain and anxiety can affect colonic motility more in IBS patients than in healthy controls and, for IBS, the most frequent comorbid psychiatric disorders are anxiety, depression and somatoform disorders (Creed, 1992, 1994).

IBS continues to be a therapeutic challenge both because of its diverse symptomatology and because there is no effective treatment for the whole symptom complex - less than half of IBS patients are satisfied with the outcome of standard medical treatments (Schuster et al., 2000).

There are, however, some treatment options which have been successful in treating the various symptoms of IBS. These treatments include pharmacological treatments (Baker, 2005), prebiotics (Ouwehand et al., 2005), probiotics (Gill & Guarner, 2003), fibre supplements (Lambert et al., 1991), bulking agents (Ashraf et al., 1995), peppermint oil (Kline et al., 2001), herbal medicine (Bensoussan et al., 1998), dietary modification (Shanahan & Whorwell, 2005), cognitive-behavioural therapy (Boyce et al., 2003), psychotherapy (Spiller, 2005), relaxation training (Blanchard et al., 1993), and hypnotherapy (Gonsalkorale et al., 2002). (*See Figure 3*).

Figure 3 **Treatment Options for IBS**



Both abdominal & psychological symptoms are associated with impaired health-related quality of life in patients with IBS.

Increasing evidence appears to suggest that the pathology of IBS is not only limited to the gut, brain, or autonomic nervous system but that all three systems may be involved. The links between mind and body and the influence of the mind on the body is becoming more widely acknowledged, therefore, any potential new therapy should be aiming at addressing all three (Costa et al., 2000). Successful interventions aimed at breaking cycles within the brain-gut axis include antidepressants, behavioural therapy, relaxation therapy and hypnotherapy.

The mechanisms responsible for the therapeutic success of hypnotherapy are largely unknown, but research has shown that it may act affecting visceral sensitivity, GI motor function and psychological distress. As mentioned previously, imagery is a major component of hypnosis, and research has provided numerous examples of the physiological effects imagery has on the body. Unlike other treatment options which separate the mind/body connection by focusing on either the psychological or the physiological aspects of IBS, hypnotherapy addresses both via the brain-gut axis.

CHAPTER 3

HYPNOSIS AND HYPNOTHERAPY

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3.1 Imagery in Healing

The mind's power to affect the body has long been known in medicine in the form of the placebo effect – the power for healing that can stem simply from a patient's belief that a treatment will be effective (Macedo, Farre & Banos, 2003). Physicians have been using this for centuries and the power of the placebo is still very real – not only is it acknowledged in medical journals but scientific method now requires a placebo to be used in drug trials (Papakostas & Daras, 2001). Medical researchers have long been puzzled by the fact that a substantial portion of symptoms improve when patients are given a placebo, but what is more puzzling is that they often regard the result as an interference or something that has to be controlled rather than investigating it and identifying how it could best be used in health care (Achterberg, 1985; Goleman & Gurin, 1995).

Research has shown that different feelings, emotions, or states of mind produce different and quite specific chemicals in the brain which travel via the blood to the cells of the immune system and attach to specific receptor sites on the outer membranes of those cells thereby altering their function (Pert, 1997; Pert, Ruff, Weber & Herkenham, 1986). Furthermore, lymphocytes also produce their own specific chemicals which travel via the bloodstream to the brain, giving feedback and thereby completing the bidirectional communication between the brain and the immune system (Ader et al., 1991; Pert, 1997).

Research also suggests that immune functioning may be influenced by imagery. Graham (1995) cites numerous examples of the physiological effects of imagery including: the ability of the mnemonist Shereshevskii (1920) to increase his heart-rate by imagining himself running, and alter the size of his pupils and his cochlear reflex by imagining sights and sounds; experiments by Jacobsen (1929) and Shaw (1946) demonstrating the increase in muscle tension when subjects imagine lifting progressively heavy weights. The use of imagery can also elicit changes in blood sugar levels (Weller, Linder, Nuland & Kline, 1961), GI activity (Barabasz & Barabasz, 2006), and blister formation (Paul, 1963) as well as demonstrate the physiological effect of phobic imagery (Brown, 1993).

These findings suggest the possibility that physiological functions that are usually regarded as autonomic or involuntary may be controlled by imagery. In other words, imagery may provide a link between the conscious intent and the autonomic function and could, in fact, be used in the treatment of illness.

In history, the healers with the most experience in dealing with the inner world are the shaman and the Buddhist monk. According to Achterberg (1985), shamanism is the older of the two and is the most widespread method of healing with the imagination with archaeological evidence suggesting that imagery (the process of the imagination) is the product of what is now known as the "subconscious mind" and, inner conditions that are usually hidden to ordinary consciousness, are often revealed. They used either a person's spontaneous imagery or instructed the patient

in the use of deliberate imagery, sometimes working directly on both the psychological and the physical aspects of the disease.

The monks, on the other hand, used their imagery of a deity to achieve spiritual growth or enlightenment but found that by practising exercises that have been perfected over thousands of years, they could also exert powerful effects on the body's physiology thereby healing illness (Achterberg, 1985; Graham, 1995; Samuels & Samuels, 1990).

Other healing systems using imagery include Ayurveda, a health system which is believed to be some 3,000 years old and which includes yoga as its central practice. Many different forms of yoga are practised but one of these, Mantra yoga, is based on the inherent healing power of sound and vibration which is achieved through repetition of divine names or phrases (mantras). Mantras can be used alone but more often than not are combined with other techniques including imagery such as imagining a healing light or visualising a mandala - a geometric pattern representing wholeness (one's relationship to the infinite) which is used to aid in meditation and trance induction (Cunningham, 2000).

Healing practices in Tibetan Buddhism also incorporate visualisation such as one in the form of the mandala of the medicine Buddha. As the visualisation of light is an important part of Tibetan medicine, light is imagined as radiating from a deity and flowing through a person's body, cleansing and healing it both mentally and physically. The light can be directed by the person to a diseased area of his or her

body, or outwards into the universe if healing others – this is still used in meditation and healing today (Gawler, 1984, 1997; Hay, 1991).

In Chinese medicine a similar technique is used. Chi (vital energy or breath) is directed and redirected around the body in various ways through the use of imagery. In Chinese martial arts, for example, a common exercise is to imagine breathing in light and directing it to various parts of the body (Graham, 1995).

It appears then that in the East the mind is considered a very important, if not the primary, consideration in the treatment of disease, whereas in the West, mind and body are still generally regarded as two distinct entities, the mind (and especially the imagination) having little, if anything, to do with health and illness.

Ironically, the Hippocratic Oath begins with a dedication to mythical figures – one of whom, Asclepius, was the founder of a famous healing family whose treatment involved the use of imagination and, more specifically, the use of dreams as a diagnostic and therapeutic tool. Both Aristotle and Hippocrates were trained in this tradition and the staff with the snake curled around it, that Asclepius is said to have carried, is still the emblem used by physicians today (Achterberg, 1985; Graham, 1995).

Freud (1856-1939) and Jung (1875-1961) recognised the mind's role in illness and health and, in particular, the role of imagery – Freud in his dream analysis which was the core of his psychotherapy and Jung in his belief that the subconscious can

only be known indirectly through images and symbols encountered in dreams, fantasies and visions.

Others at this time who used imagery were Carl Happich, who was influenced by Freud and Jung and viewed the symbolic subconscious as fundamental to all creative production and the healing process; Walter Frederking, who encouraged patients to engage in fantasy during progressive relaxation and describe their experiences; and Roberto Assagioli, who used guided imagery, daydreams or symbols to assist his patients in mediating between conscious and subconscious material (Achterberg, 1985; Graham, 1995; Samuels, 1990).

During the late 1960s Carl and Stephanie Simonton approached the mind-body connection from a different angle. Their research involved looking at the possibilities of the influence of the mind to induce the will to live in cancer patients – in other words, to give the patients more control over their illness. They experimented with a number of techniques and claimed to have achieved quite dramatic results through the use of imagery techniques (Kidman, 1983; Simonton, Matthews-Simonton & Creighton, 1978).

At the same time in Australia, Ainslie Meares was also experimenting with the effect of mind on disease (especially that of cancer) and, following this line of exploration, developed a form of meditation which he called Mental Ataraxis. He believed that the natural restorative activities of the mind and body, including the

immune system, were regenerated if a state of inner stillness could be achieved (Meares, 1977; 1978).

Today, there are numerous health professionals both overseas and in Australia who have incorporated into their various treatments the use of imagery for the healing and prevention of a number of diseases. One such profession is that of hypnotherapy where imagery – either guided or spontaneous – is often used in the treatment of both psychological and physiological illnesses while the patient is in a hypnotic trance.

3.2 A Brief History of Hypnosis and Hypnotism

One of the oldest forms of medicine is healing by trance state (hypnosis). Early man believed that the gods were responsible for curing the patient and the 'sleep temples' of the ancient Egyptians and Greeks, where patients were supposedly healed by sleep and incantations, are well-documented (Cunningham, 1980). Sleep temples appeared a hundred years later in Rome and continued functioning during the golden period of the Roman Empire. Hippocrates and Hippocratic medicine were descendants of this form of medicine (Heap, 1996).

The beginnings of modern hypnosis is associated with two men: the Austrian physician Anton Mesmer from whom the term *mesmerism* came and the Scottish surgeon, James Braid, who was responsible for changing the term *mesmerism* to *hypnotism.* Their early work was tested and expanded by various practitioners such as James Esdaile, Ambroise Liebeault, Hippolyte-Marie Bernheim, Jean Charcot, Josef

Breuer, Sigmund Freud, Carl Jung, Milton Erickson, and John Grinder and Richard Bandler (Frank & Mooney, 2002).

Franz Anton Mesmer (1734-1815) believed that illness resulted from an imbalance or blockage of 'ethereal fluid' within the patient and that healing could be effected by restoring the balance and releasing the blockages by the use of magnetic forces. He used various techniques such as passing his hands over a patient's body, 'magnetising' inanimate objects or trees which the patients had to touch or embrace and, in his practice in Paris, treating people in groups gathered around large tubs (*baquets*) filled with 'magnetised' substances and protruding iron rods which patients applied to the affected parts (Heap, 1996; Manusov, 1990). The results were often quite dramatic, as many patients experienced hysterical reactions and then went into a state of drowsiness or stupor, and also surprising, as patients with numerous ailments appeared to have been cured.

His reputation grew throughout Europe until he was first forced to leave Vienna by his medical colleagues, and then was struck off the medical register in Paris when a commission appointed by King Louis XVI to investigate mesmerism failed to discover any concrete evidence of either animal magnetism or of the invisible fluid. This resulted in the practice of animal magnetism being made illegal and, although Mesmer's ideas continued to spread throughout Europe and North America, many of his followers dispensed with both the hysterical aspect of his treatment and the notion that an 'ethereal fluid' existed (Best, Neuhauser & Slavin, 2006; Waterfield, 2002).

James Braid (1795-1860), who popularised the term ‘hypnosis’ and introduced the technique of visual fixation and eye fatigue to induce hypnosis, first became interested in mesmerism in 1841. He did not believe that the trance had anything to do with magnetic fluids nor the theatrical performances Mesmer was renowned for, but that it was instead due to suggestion acting on the subject whose suggestibility had been increased by having the patient fixate on an object. Braid maintained that the trance state was a form of sleep brought about by tiring the eyes and possibly paralysing the optic-nerve centres, causing a condition that resembled sleep (Frank & Mooney, 2002; Rossi & Cheek, 1988). However, James Esdaile, a Scottish physician who practised in India in the 1840s and performed operations such as amputations on his patients using hypnosis instead of anaesthetic, did so without using either verbal suggestion or eye contact (Forest, 1999; Zahourek, 2001).

The concept of the subconscious was not in existence in the time of Braid or his contemporaries, but he appeared to sense intuitively what researchers and practitioners in the field of hypnosis now know today – that the trance is a combination of the effects and influence of the hypnotist and the subconscious reactions of the subject. In 1843 Braid published a book entitled Neurypnology, (also known as the Rationale of Nervous Sleep Considered in Relation to Animal Magnetism), in which he introduced the terms: hypnotism, hypnotise, and hypnotic (Zilboord, 1969).

Ambroise August Liebeault (1823-1904) tested Braid’s method of fixed attention in his clinic in Nancy, France, and is said to have been the first to

demonstrate the value of hypnosis as a means of cure on thousands of patients. Professor Hippolyte-Marie Bernheim from the University of Nancy Medical School, who was a famous neurologist at the time, tried to discredit Liebeault but on learning more about his work, Bernheim both accepted and put into practice Liebeault's views (Watson, 1971; Zilboorg, 1969).

Jean Martin Charcot (1825-1893) and his colleagues in Paris used hypnosis for treating patients who were suffering from epilepsy and hysteria. He still believed in the idea of magnetism and was convinced that only hysterical patients could be hypnotised and that the hypnotic state, itself, was a form of hysteria. These views, which put him at odds with the Bernheim school of thought, were finally exposed as being unscientific **(**Watson, 1971**).** Charcot did, however, suggest the existence of what is now known as post-traumatic stress disorder and, through his investigations, dispelled the idea that hysteria only occurred in women – he showed that the condition could manifest itself in both sexes (Goetz, 1999).

Josef Breuer (1842-1925), one of Freud's colleagues, suggested that these "hysterical" symptoms were in fact suppressed emotions or memories buried within the subconscious and that these symptoms could be eliminated or relieved by having the patient talk about them while under hypnosis (Temes, 2000).

Sigmund Freud (1856-1939) visited Charcot in Paris to study neurology and also the clinic of Liebeault and Bernheim in Nancy where, through observing post-hypnotic suggestions being carried out by the patients after they had been hypnotised,

he gained insight into the idea of there being hidden memories and emotions in the subconscious which determined human behaviour (Hall & Lindzey, 1970). Freud, at first, used hypnosis to uncover these hidden memories and emotions but later found that he had more success in getting patients to talk about these forgotten memories without formally hypnotising them – a talking cure which he called psychoanalysis (Waterfield, 2002).

After Freud abandoned hypnosis, it started to lose favour in the medical world and was instead mainly practised by lay practitioners and stage entertainers, until a brief resurgence during World Wars I and II where, because of a shortage of psychiatrists, it was used both for direct symptom removal and the treatment of post-traumatic stress disorder **(**Frank & Mooney, 2002; Zahourek, 2001**).**

Milton H. Erickson (1901-1980), the founding president of the American Society of Clinical Hypnosis, is considered as probably being the most famous American hypnotherapist of the second half of the 20th century. Like Freud, Erickson achieved various levels of hypnosis in patients, often without formally hypnotising them and, through giving suggestions, could bring the patients into a very light trance-state known as a hypnoidal state, without the usual signs of relaxation (Gorton, 2005; Kirmayer, 1988).

He had an acute observation of non-verbal behaviour and, during the trance state, used language in a deliberately vague way so that his patients could choose the meaning that was appropriate for them. He also used the technique of pacing – i.e. to

use language in such a way as to tune into the patients' world by describing what they must be feeling, hearing and seeing at the time – and then, through suggestions, gradually lead them into hypnosis (Rosen, 1984).

By using this technique, he could both induce and maintain a trance state in order to uncover hidden memories and emotions that may be affecting the patients' health and, at the same time, help patients discover and utilise their own inner resources (which he believed all individuals had) in order to make the necessary changes in their lives (Gorton, 2005). Erickson's approach eventually came to be the basis of a therapy known as Neuro-linguistic Programming (O'Connor & Seymour, 1990).

Neuro-Linguistic Programming (NLP) began in the early 1970s as a collaboration between John Grinder and Richard Bandler as a result of their studying three well-known therapists; Fritz Perls (originator of Gestalt therapy), family therapist, Virginia Satir, and Milton Erickson. The principal basis of this therapy was Erickson's unique approach to hypnotherapy. In NLP (as in Freud's psychoanalysis) the word "hypnosis" is not used, but NLP practitioners still communicate with their patients on the subconscious level, therefore having something in common with practitioners such as Erickson in the hypnotherapeutic field (Bandler & Grinder, 1982; Barnett, 1990).

The number of practitioners using hypnosis has dropped considerably since the late nineteenth century, mainly because of the rise of therapies such as

psychoanalysis and behaviourism, the stage shows, and the controversy as to whether its application was based on a sound scientific theory. Fortunately, interest has been increasing in the therapeutic use of hypnosis as its application is becoming more and more acceptable because of supportive evidence achieved through academic research (Heap, 1996; Manusov, 1990). Its potential and place in modern medicine, however, has yet to be realised.

3.3 What is Hypnosis?

Many definitions and theories that have been put forward by both researchers and practitioners in the field of hypnotherapy as to what hypnosis is. It is generally defined as a state of mind or altered state of consciousness (trance) which is enhanced through relaxation and the use of imagery. Through the use of therapeutic hypnosis, patients are able to be freed from limiting inhibitions and opinions that may have been brought about by social conditioning (Frank & Mooney, 2002; Waterfield, 2002). The hyper-suggestibility of the individual appears to be an important component of the hypnotic state.

Hypnotherapists use the trance state to enable the subconscious mind to communicate with the conscious mind, through a heightened and focused concentration, and through the use of suggestion to maximise the potential, or change the cognition, of the patient (Francis & Houghton, 1996; Manusov, 1990).

In hypnosis, the patient first achieves a meditative state and then, through the use of imagery and/or suggestion, works on changing a thought, idea, or behaviour. The difference between hypnosis and meditation is that in meditation, one simply stays in that meditative state (Temes, 2000). (*See table 9*).

Table 9 **Comparison of Meditation and Hypnosis**

	Meditation	**Hypnosis**
1. Motivation	To focus on yourself	To focus on something outside yourself
2. Goal	No goal	To change your behaviour
3. Process	Enter an altered state and then focus on yourself	Enter an altered state and then receive suggestions

(Table with kind permission of Temes, R. 2000).

The word "hypnosis" comes from the Greek word, *hypnos*, meaning sleep, as it was believed that patients were supposedly healed by sleep and incantations, both in the 'sleep temples' of the ancient Egyptians and Greeks and, a hundred years later, in sleep temples which existed during the Rome Empire (Cunningham, 1980; Heap, M., 1996).

During hypnosis, a patient may appear to be asleep because the eyes are closed and the person is often sitting motionless but EEG studies show that the mind is extremely alert – in hypnosis the brain waves have high alpha activity (indicative

of alertness) whereas in sleep, the brain waves show little alpha activity (Esposito, Nielsen & Paquette, 2004; Kawano, 1994). (*See Table 10*).

Williams & Gruzelier (2001) also demonstrated that high-hypnotically susceptible participants had greater alpha power than low-hypnotically susceptible participants - both preceding and during hypnosis, indicating an association of alpha with hypnotic susceptibility.

Table 10 **Comparison of Sleep and Hypnosis**

Sleep	Hypnosis
Eyes closed	Eyes may be closed, but can remain open
Body relaxed	Body usually relaxed, but can be instructed to become tense
No attention paid to surrounding environment	No attention paid to surrounding environment
Will not hear conversations	Will hear the therapist's voice
Usually moves around	Remains still; too much effort to move
No ability to concentrate	Extremely high ability to concentrate
EEG studies show brain waves of sleep have little alpha activity	EEG studies show brain waves during hypnosis have high alpha activity, indicative of alertness

(Table with kind permission of Temes, R. 2000)

EEG studies have also shown that greater theta power in the more frontal areas of the cortex is displayed by high-hypnotic suggestible participants during the baseline period and that in the periods preceding and following a hypnotic induction, low-susceptible participants displayed an increase in theta activity and high-susceptible participants displayed a decrease (Graffin, Ray & Lundy, 1995). During the hypnotic induction itself, theta power significantly increased for both groups in the more posterior areas of the cortex, whereas alpha activity increased across all sites (De Pascalis, Ray, Tranquillo & D'Amico, 1997).

Research has also indicated that brain wave changes associated with hypnosis can also be triggered by other methods of deep concentration, such as the relaxation response - the difference being that there is higher theta activity in relaxation and higher alpha activity in the hypnotic experience (Jacobs & Friedman, 2004; Williams & Gruzelier, 2001).

A hypnotic state is a natural-occurring experience and can spontaneously occur many times a day. Daydreaming, not being aware of the passage of time, "automatic" driving, being absorbed in a book or movie, listening to music, being able to shut out one's surroundings by concentrating very hard on something else, are all examples of a hypnotic state, and people often recognise this difference (Olness, 1995; Roet, 1986). (*See Table 11*). What separates hypnotherapy from the above activities is how the practitioner uses the hypnotic state.

Table 11 **Naturally-occurring Hypnotic Experiences**

1. Being in a room full of people, supposedly taking part in the group yet mentally being far away from it.

2. Being unsure whether you did something or just thought about having to do it (e.g. not knowing whether you either mailed a certain letter or just thought about mailing it).

3. Being so lost in thought that you did not understand what people said to you, even when they were talking directly to you and even when you nodded in agreement.

4. Staring off into space, actually thinking of nothing and hardly being aware of the passage of time.

5. Driving somewhere and not remembering part of the journey or which route you took because you were thinking of something else.

6. Being able to shut out your surroundings from your mind by concentrating very hard on something else.

7. Being lulled into a groggy state or put to sleep by a lecture or a concert, even though you were not otherwise fatigued or tired.

8. Wandering off in your own thoughts while doing a routine task so that you actually forgot you were doing the task and then found, a few minutes later, that you had completed it without even being aware that you were doing it.

As mentioned previously, hypnosis is an altered state of high suggestibility (Francis & Houghton, 1996; Manusov, 1990), and the hypnotherapist makes use of this quality by offering suggestions to the patient whilst under hypnosis to improve/change a sensation, belief, or behaviour, or some other aspect of his or her mental or physical functioning (Palsson, 2002). The theory is that in the hypnotic state, the power of criticism (which is restricted largely to the conscious mind), is either fully or partially suppressed, enabling the suggestions to by-pass the conscious

mind and enter the subconscious mind which has little or no power of criticism - the patient, being unable to reject suggestions, will usually act upon them. The effect the suggestions have on the patient depends on how much criticism is suppressed and how much rejection from the conscious mind is removed (Hartland, 1979; McGill, 1996).

Suggestions are usually given in the form of imagery which can be any perception that comes through any of the senses – the patient may see, hear, smell, taste, or touch something while under hypnosis (McGill, 1996; Olness, 1995). The body is thought to be unable to discriminate between sensory images in the mind and reality, and interprets these images as almost real events. While in this altered state, the patient's attention is focused on, and has a heightened sensitivity to, one particular thing (or closely-related things) and, at the same time, a decreased awareness of other activities or sounds going on around (Gindes, 1976; Naparstek, 1994).

Suggestions can also be given to the patient, post-hypnotically. These suggestions are given during the trance state and take effect either immediately after the patient has come out of hypnosis or at a future date with little or no interference from the conscious mind. They are usually in the form of therapeutic suggestions to help patients overcome difficulties or problems but can also be used in facilitating future trance induction (Hartland, 1979; Roet, 1986).

The success of suggestions used in hypnosis depends on the careful selection of the words used. Words can make one feel better, more confident, and strengthen one's will but they can also have the opposite effect and make one feel belittled or embarrassed. The success of the hypnotherapy sessions and of the goal the patient wishes to achieve is very much dependent on the words used (Cunningham & Ralph, 1980).

3.4 Misconceptions about hypnosis

There is nothing supernatural about hypnosis. As mentioned previously (*see Table 11*), it is a natural-occurring phenomena, in tune with the natural suggestive behaviour of humans. Unfortunately, the use of hypnosis for entertainment – both stage hypnosis and in horror movies - has trivialised a serious therapeutic tool and promoted misconceptions which range from the belief that it is a stunt or some form or magic, to the notion that it is a panacea for all illnesses (mental and physical) and that one visit to a hypnotist is all that is needed to cure even a chronic condition (Olness, 1995; Van Pelt, 1979).

The most common misconceptions are: that it is dangerous; that the person is under the hypnotist's control and could be hypnotised to say or do something against one's will; the person loses control in hypnosis; or that the person will be unconscious while in the trance.

3.4.1 Hypnosis is dangerous

Practitioners and researchers have become more sophisticated in their understanding of the hypnotic process and there is a developing conviction that the hypnotic state is not considered dangerous when under the guidance of a qualified hypnotherapist but, as in any counselling or therapeutic method, therapy carried out by an unqualified therapist could result in a distressful situation for the patient (Barber, 1994; Yapko, 1994).

One example of this is the self-reports of childhood trauma that may be "uncovered" during the hypnotherapy treatment sessions which, although considered by the patient as being real are, more often than not, "false memories" (Barber, 1995; Brandon, Boakes, Glaser & Green, 1998; Lyle & Johnson, 2006).

Another possible danger of hypnosis is posed by Gindes (1976) who is of the opinion that an unethical person could, with adequate conditioning, strong suggestion, and an adaptable mind, facilitate criminal acts through the use of hypnosis. This view, however, is hypothetical.

3.4.2 While in a hypnotic state, the person is under the hypnotist's control and can say or do something against his/her will

The capacity to influence people to do things against their will does exist in certain conditions such as brainwashing, but this necessitates very powerful

influences (hypnosis being only one of them) which rarely surface in a therapeutic session involving clinical hypnotherapy (Yapko, 1995).

In clinical hypnosis the patient does not surrender his or her will - the relationship between the hypnotherapist and patient is one of mutual responsiveness rather than one of control – the hypnotherapist acts as a guide and uses communications skills in such a way as to make the patient more likely to accept suggestions.

The only control is the *degree* of control the patient gives the hypnotherapist. Through suggestions, the hypnotherapist may direct the patient's experience under hypnosis, but only to the degree that the patient permits. If the suggestions conflict with the person's tendencies or moral nature, he or she will either refuse to respond to them and/or will come out of hypnosis (Cunningham, 1980; McGill, 1996; Yapko, 1995).

Wall, (2000) regards the mutual responsiveness between hypnotherapist and patient as more of a process which depends on an agreed transfer of authority – the patient handing over to the practitioner the responsibility for deciding how the session will ensue – and, since this is done voluntarily, there is no conflict of the patient's standards. The successful outcome of the session, however, still depends on the relationship the patient has with the hypnotherapist.

Roet (1986), Borysenko & Borysenko, (1994) and Naparstek (1994), however, are of the opinion that all hypnosis is *self-hypnosis* and, even though the patient is being guided by the practitioner, he or she is actually being *instructed* on how to achieve an altered state and may subsequently be able to do it either alone or with the help of a self-hypnosis CD. In other words, the patient is both the subject and the hypnotist or, as Borysenko & Borysenko (1994) view it, the hypnotist who controls the patient is within the patient, himself.

3.4.3 People lose control in hypnosis and will be unconscious

This misconception has unfortunately come about because of stage shows involving hypnosis where people appear to be under the control of the hypnotist. Most jokes played on people during these shows are similar and the volunteers have quite a good idea of what will happen. So, by volunteering, the person is actually giving permission for what is about to take place - an agreed transfer of authority - the person handing over to the hypnotist the responsibility for deciding what will ensue (Shinkarovsky, 1996; Wall, 2000).

A person under hypnosis remains in full control. He/she is aware of what is happening, is able to talk (Frank & Mooney, 2002; Mongan, 2005) and, as mentioned previously (Cunningham, 1980; McGill, 1996; Yapko, 1995), is quite able to refuse to respond to any conflicting or amoral suggestions, will often come out of hypnosis, and can get up and walk away.

The idea that the person is unconscious during hypnosis is an erroneous one. Although in a trance state, the person is aware of what is happening around them but may choose not to focus on it (Olness, 1995). In the HypnoBirthing programme (Mongan, 2005) for example, where expectant mothers learn self-hypnosis, they are taught to narrow their field of attention and focus on internal images during the birthing process so as not to be distracted by what might be going on around them or by other people in the room. However, if their partner, the midwife or obstetrician instruct them to do something, they will respond by either remaining under hypnosis or by bringing themselves out, doing what is necessary, and then often putting themselves back under hypnosis again.

3.4.4 Only a few people can undergo hypnosis

Research suggests that about 60% of the population can be hypnotised (Frank & Mooney, 2002; Waterfield, 2002) and most people naturally enter hypnosis countless times every day without realising it (*see Table11*). In general, those with normal learning skills can learn self-hypnosis - some have a greater ability to focus their attention than others but this ability can be achieved through practice (Olness, 1995). Research has also shown that subjects who were considered to have a low susceptibility for hypnosis could be trained to achieve a much higher hypnotic responsivity (Gfeller et al., 1987; Spanos et al., 1986).

Some people are more difficult to put under hypnosis than others mainly because of their misconceptions and fears about hypnosis (which the hypnotherapist

should recognise and resolve in the first hypnosis session) and also because of their personality. The practitioner needs to take into account various facets of the patient's personality in order to choose the appropriate hypnotic induction (Gindes, 1976; Yapko, 1995).

Hypnosis then, may be regarded as the means of inducing a subconsciously responsive state of mind where, through suggestions given by the hypnotherapist, there is a narrowing of attention (or focus) on a small range of stimuli, and sensory perceptions appear to be more enhanced (McGill, 1996). Misconceptions about hypnosis are gradually being dispelled and hypnotherapy has now become more widely accepted in various areas of clinical medicine such as psychology, psychiatry, dentistry and social work, and shown to be successful in the treatment of pain control, habit disorders and many other medical problems (Burrows & Stanley, 1995; Lynn, Kirsch & Rhue, 1996).

3.5 Clinical Studies in Hypnotherapy

Research on hypnotherapy moved slowly until World War II when it was found to alleviate pain and help in the treatment of post-traumatic stress disorder. Since then, more scientific investigation has been undertaken with the result that more health-care professionals now regard hypnosis as a legitimate form of treatment (Shinkarovsky, 1996; Zahourek, 2001).

Unfortunately, hypnosis is still sometimes misunderstood and undervalued. Although mostly known because of stage shows and as a treatment for giving up smoking and losing weight, hypnosis has cured or alleviated a wide range of illnesses and ailments such as tension headaches and migraines (Zitman, van Dyck, Spinhoven, Corrie & Linssen, 1992; Matthews & Flatt, 1999), dermatological disorders (Rucklidge & Saunders, 1999; Shenefelt, 2000; Willemson, Vanderlinden, Deconinck & Roseeuw, 2006) and gynaecological and obstetrical problems (Simon & Schwartz, 1999; Younus, Simpson, Collins & Wang, 2003).

It has primarily shown, however, to be effective in the alleviation of pain, addressing stress-related and psychological problems, boosting the immune system and, more recently, as a treatment option for GI problems (Handel, 2000; Waterfield, 2002; Gonsalkorale et al., 2003).

3.5.1 Hypnosis in the treatment of pain

One of the widest applications of hypnosis is that of pain control – the pain response referring to both physical (somatogenic) and psychological variables such as anxiety and expectation (Manusov, 1990) – and a number of studies has been undertaken to examine changes in pain perception in hypnotised subjects.

Arendt-Nielsen, Zachariae & Bjerring (1990) induced both analgesia and hyperaesthesia in eight highly hypnotisable subjects in the same experimental trial in order to study aspects of hypnotic-suggested analgesia. Brief and well-defined argon

laser pulses were used to elicit pain after sensory and pain thresholds to laser stimulation had been determined, and the laser-evoked brain potentials had been measured in three conditions: the waking state, with suggestion of hyperaesthesia, and with suggestion of analgesia. They found that pain thresholds were reduced during induced hyperaesthesia and increased during analgesia, and that the amplitude of the evoked brain potentials increased during hyperaesthesia and decreased during analgesia. Their results showed that both analgesia and hyperaesthesia could be hypnotically induced.

In another study by Sharav & Tal (2004), hypnotic analgesia was also induced and two different types of hypnotic suggestion - generalised relaxation and focused analgesia - were examined.

Hypnotic susceptibility was tested and the 15 subjects were assigned to low- and high-susceptibility groups – eight subjects and seven subjects respectively. Each subject was tested twice, once under generalised relaxation and once under focused analgesia. Both groups were initially given suggestions of physical relaxation, relaxing guided imagery, and a feeling of tranquillity and restfulness before being given more specific suggestions of either feeling relaxed at the time of the stimuli (generalised relaxation) or suggestions creating focused analgesia. Painful electrical stimuli were randomly delivered in five ascending intensities and rated on visual analogue scales by the participants.

The researchers found that both focused analgesia and generalised relaxation decreased pain intensity significantly but that as stimulus intensity became higher, pain reduction was enhanced under focused analgesia, while a constant reduction occurred under generalised relaxation. Pain reduction was also found to be significantly higher in the highly-hypnotisable subjects.

3.5.1.1 Surgery and Invasive Medical Procedures

Hypnosis can help patients overcome pre-operative anxiety and fear (Saadat et al., 2006); can be a means of managing adverse surgical side-effects such as pain, nausea and distress (Faymonville et al., 1997); has been shown to accelerate post-surgical wound healing (Ginandes, Brooke, Sando, Jones & Aker, 2003); and is very often considered as an adjunctive therapy to help ameliorate pain during invasive medical procedures (Astin, 2004).

Research supports the use of hypnosis as an adjunctive approach to surgery (hypnosedation) where patients receive standard surgical and anaesthesia procedures as well as hypnosis (Lang et al., 2000; Astin, 2004). Hypnosis is usually established by an induction where the patients are given suggestions of physical relaxation followed by guided imagery which focuses on creating a feeling of peacefulness. This both distracts the patient from aversive stimuli and makes them more open to therapeutic suggestions such as reduced pain or stress (Montgomery, David, Winkel, Silverstein & Bovbjerg, 2002; Sharav & Tal, 2004).

In 1995, after successfully performing more than 1,000 procedures under hypnosedation, Meurisse et al. (1999) decided to apply this procedure in endocrine cervical surgery. Thirty-one subjects agreed to hypnosedation for hyper-parathyroidism and the hypnotic state was induced by eye-fixation and progressive muscle relaxation. Suggestions of well-being were given by the anaesthetist with the exact words of the induction and suggestions varying according to patient behaviour.

During hypnosis, the patients appeared mobile and relaxed and experienced increased pain thresholds and intense subjective well-being. Hypnosis was induced within 10 minutes and, at the completion of the procedure, a fully conscious state was obtained in several seconds. All patients reported altered perception of time during the operation (the length of the operation appeared to be shorter) and all had pleasant experiences involving recollections of past events. None regretted choosing hypnosis for the operation and would request the same again, if necessary. No conversion to general anaesthesia was needed and no complications were observed.

The researchers found that hypnosedation provided excellent perioperative pain and anxiety relief, reduced the incidence of side-effects associated with general anaesthesia and allowed rapid post-operative recovery.

Hypnosis has also been found to be beneficial for children both in reducing distress in invasive medical procedures, and lessening pain and anxiety during examinations. In a study by Butler, Symons, Henderson, Shortliffe & Spiegel (2005) children undergoing voiding cystourethrography for bladder abnormalities such as

urinary tract infections and vesicoureteral reflux were randomised to receive either hypnosis (21 children) or routine care (23 children). The children in the hypnosis group were given a one-hour session in self-hypnosis and visual imagery by a trained therapist and then instructed to practise (with their parents) several times daily in preparation for the procedure. The children in the routine care group participated in a programme which included relaxation and breathing techniques as well as demonstration of the procedure on dolls.

Results of the study indicated hypnosis to be more beneficial than routine care in that, compared to the routine care group, children in the hypnosis group were reported as being less traumatised by this procedure than by the previous one; their distress levels were significantly lower; medical staff reported less difficulty in conducting the procedure; and the total procedural time was significantly shorter by almost 14 minutes.

After observing children in the emergency department of a Mexican hospital having forearm fractures set without any form of sedation or anaesthesia (because of lack of equipment and personnel), Iserson (1999) suggested trying hypnosis prior to the procedure. Over a five-week period, four children presented with forearm fractures while the author was on duty and were hypnotised prior to the manipulation. The children were asked to concentrate on their toes and imagine sensations of heaviness or warmth flowing up the body. They were then given suggestions of relaxation and sleep and told to travel in their mind to a pleasant place followed by

the suggestion that they would not remember the process or the pain during the fracture reduction.

All four children appeared to be awake at the height of the fracture manipulation and seemed to experience pain and three of the four appeared to fall asleep immediately afterwards. Two hours post reduction, the children were questioned about their memory of the procedure and whether they had experienced pain. All of the children appeared confused about what had happened and none of them remembered the procedure or the cast being applied. They all denied having any pain.

3.5.1.2 Dental Surgery

The main advantages of using hypnosis in dental surgery are to lessen anxiety, pain and discomfort, minimise blood loss, and achieve rapid healing. An added advantage is that the facial muscles can be relaxed and held in position for long periods without pain or fatigue (Ambrose & Newbold, 1980; Yapko, 1995).

In a controlled trial using hypnosis as an adjunct treatment for the surgical removal of third mandibular molars, Enqvist & Fischer (1997) had the 33 patients in the experimental group listen to an audiotape containing a hypnotic relaxation induction followed by suggestions of healing and recovery and ways of achieving control over stress and pain. The control group of 36 patients received no hypnotic intervention. Their findings showed that preoperative anxiety remained at baseline

level in the experimental group but increased significantly in the control group. They also found that postoperative consumption of analgesics was significantly reduced in the patients using hypnosis and that there was also reduced nausea and vomiting.

Ghoneim, Block, Sarasin, Davis & Marchman (2000) also carried out a study on the use of hypnosis in third molar surgery in which the experimental group of 24 patients used a similar self-hypnosis tape, supplied by Enqvist, which included suggestions on enhancement of perioperative well-being such as control of bleeding and healing and alleviation of pain. Once again, the control group (22 participants) did not receive hypnotic intervention. As in the study by Enqvist & Fischer, Ghoneim et al. found that anxiety in the experimental group was reduced but they also found an increase in the incidence of postoperative vomiting and no improvement in the severity of postoperative pain or reduction in postoperative consumption of analgesics.

There were two limitations to this study cited by the researchers. The first was that whereas Enqvist, a clinical hypnotherapist, personally introduced hypnosis to the patients before presenting them with the tape, Ghoneim et al., (2000) because of a busy hospital setting, considered it impractical to introduce hypnosis separately to each patient and induced self-hypnosis by means of the audiotape alone. Secondly, Ghoneim et al. (2000) could not ascertain whether hypnosis had actually occurred in each patient as there had been no observer present to recognise a trance state when the patients listened to the tape.

Another possible flaw in the study is that on the tape the patients were also given suggestions that they would feel hunger, thirst, and a desire to eat and drink after surgery - the researchers assumed that these sensations would be incompatible to vomiting. However, there is a possibility that no specific time was given as to when these suggestions would take effect, with the result that the patients ate and drank too soon after surgery when they had not fully recovered from sedation and anaesthesia.

3.5.1.3 Burns

As well as suffering anxiety and disfigurement, patients with burn injuries often have to endure intense pain during burn care procedures which typically include washing wound sites, debridement, topical application of medication and dressing changes (Frenay et al., 2001; Wright & Drummond, 2000). As medication is not always efficient in diminishing the discomfort of burn dressing changes (Perry & Heidrich, 1982), and burn patients can also develop some degree of tolerance to analgesic drugs (Patterson, Everett, Burns & Marvin, 1992), hypnosis has been trialled as a viable adjunct treatment for burn pain.

Frenay et al. (2001) conducted a trial designed to compare hypnosis and stress-reducing strategies (SRS) for anxiety and pain management during burn care procedures. The 11 patients in the hypnosis group were asked to choose a pleasant life experience to recall during the dressing change and a hypnotic state was then induced using eye fixation and muscle relaxation. Positive suggestions to transform sensations and to dissociate the patient from his or her pain were then given. The

word ‘hypnosis’ was not used in order to avoid any positive or negative bias based on preconceived notions the patient may have – instead, the hypnotic state was explained as being a state in which patients could distract themselves by thinking about the pleasant life experience they had chosen. The 15 patients in the SRS group were given instruction in deep breathing and relaxation by the burn unit psychologist who also focused the patients on a pleasant memory as well as using any coping strategies the patients were naturally using.

The results showed that in the hypnosis group, anxiety levels were significantly lower during wound care than in the SRS group, and that pain perception before, during and after wound care was also consistently lower in the hypnosis group - although these results did not reach statistical significance.

In their studies, both Patterson et al., (1992) and Wright & Drummond (2000) used a technique called “rapid induction analgesia’ (RIA) for the treatment of pain in burn care. This technique includes suggestions which aim to reduce tension, anxiety and sensations of pain. In the study by Patterson et al. (1992), 87 participants were randomly assigned to three groups with both patients and nursing staff remaining blind to group assignment throughout the study.

Group one participants underwent their first dressing change (Day 1) with pain medication only and then before their second dressing change (Day 2), they received the hypnotic intervention using the RIA procedure. The subjects were asked to imagine walking down a staircase with 20 steps while the psychologist gave them

indirect suggestions of increasing comfort and relaxation. When they had reached the bottom of the staircase, they were given further suggestions which were designed to elicit confusion and amnesia. This was followed by a post-hypnotic suggestion that when either the psychologist or the nurse touched the patients' shoulder during the dressing change, they would experience a deep level of comfort.

Group two participants also underwent their first dressing change (Day 1) with pain medication only and, before their second dressing change (Day 2), were told they would undergo a hypnotic intervention but instead, were given information regarding the emotional effects of burn injuries and the nature of burn pain. They were also informed that their pain (described as 'sensation') was a positive sign of healing. Towards the end of the session the subjects were told that, prior to the dressing change, it would be useful for them to close their eyes, count to 20 and imagine themselves in a relaxing place. They were also told that the nurse would prompt them to begin 'hypnosis' by giving some instructions followed by a touch on the shoulder. None of the subjects questioned whether they had been actually hypnotised. The control group (group three), received medication only for both Day 1 and Day 2.

The results indicated that patients in the hypnosis group (group one) gave significantly lower pain ratings than patients in both the control group (group three) and participants of group two who had equivalent time and attention from the burn psychologist and believed they had undergone hypnosis. Staff ratings were consistent with those of the patients.

Wright (2000) investigated sensory and affective pain ratings before, during and after dressing changes in patients who received RIA and whether RIA had a cumulative effect on pain ratings and anticipatory anxiety over two consecutive sessions. They also evaluated the effect of RIA on analgesic intake.

The 30 participants were randomly assigned to two groups – the experimental group and the control group. No changes were made to normal pain-relieving medication during the study and all patients were free to request additional analgesic medication. Staff were asked to leave the room while the participants in the experimental group were administered a 15-minute hypnotic induction (RIA) followed by suggestions for progressive deepening of comfort and relaxation as well as suggestions for analgesia. They were told to imagine a staircase and when they had reached to the count of 20 (indicating the bottom of the staircase), they were requested to enjoy their state of relaxation and comfort, with their eyes remaining closed if they wished.

Throughout the burn care session, the investigator repeated the suggestions for analgesia and relaxation. Patients remained aware of the activities undertaken but were observed to be in a calm, relaxed and comfortable state. Dressing changes proceeded as usual for patients in the control group.

The major finding of the study was that the experimental group experienced decreased pain perception and anticipatory anxiety during and after burn care compared to the control group. In addition, analgesic requirements in the

experimental group were also decreased, suggesting that the therapeutic effects of RIA persisted for at least several hours after treatment. The study appears to confirm RIA as a viable adjunct to medication for pain control during burn care.

3.5.1.4 Childbirth

The management of labour pain is one of the main goals of maternity care but the two models of care - the medical model, whose focus is mainly the elimination of pain; and the midwifery model, where the emphasis is largely on the prevention of suffering – have very different goals.

The medical model involves pain (and other) medications, interventions and complex technology which places the burden of pain control solely on medical professionals. This results in the woman's role becomings one of passive compliance, dependency and powerlessness because she views the control and management of pain relief (as well as other aspects of labour and birth) to be held by others.

The midwifery model, on the other hand, takes into account the psychological elements – such as the feeling of helplessness, distress, and loss of control - as well as the management of labour pain (Simkin & Bolding, 2004).

The latter model has been addressed in programmes such as HypnoBirthing in which the mother and her partner learn about the physiology of the birth process, the

'fear-tension-pain' syndrome and the fight-or-flight response, both of which usually accompany labour.

They then learn how to break this response, feel less anxious and more in control of the birthing process, and how to achieve a reduction in pain through hypnotic anaesthesia, breathing techniques and visualisation (Mongan, 2005). As well as facilitating autonomy and giving the patient a sense of control, hypnosis has also been shown to reduce the need for analgesia requirements during labour which could result in minimising the need for epidural analgesia (Cyna, McAuliffe & Andrew, 2004; Harmon, Hynan & Tyre, 1990).

This is reflected in a study by Jensen & Karoly (1991) where their findings showed that the patients' belief in personal control over pain and the strategies they used to manage pain had a direct impact on well-being and medication use.

Harmon et al. (1990) conducted a trial to ascertain the benefits of hypnotic analgesia as an adjunct to childbirth education in 60 nulliparous women. Subjects were divided into two groups with half the subjects in each group receiving a hypnotic induction at the beginning of each session and the other half receiving relaxation and breathing exercises typically used in childbirth education. The results showed that hypnosis resulted in shorter Stage 1 labours, less medication, more spontaneous deliveries and higher Apgar scores.

In an Australian study by Cyna, Andrew & McAuliffe (2005), 77 women, who had undergone antenatal self-hypnosis preparation for labour analgesia at 37 weeks' gestation between August 2002 and August 2004, were compared to women matched for parity and gestation who had given birth at the Women's and Children's hospital in Adelaide in 2003 but had received no hypnosis preparation. The researchers found that women who had used hypnosis had fewer epidurals than controls and required less augmentation with oxytocics - these data being consistent with those of a previous systematic review carried out by the same researchers in 2004.

While more research is needed to understand in more detail the effects of hypnosis on labouring women and their infants, it has been shown to be a powerful intervention for women to use during childbirth with both positive physical and psychological maternal outcomes.

Chronic pain can lead to emotions such as anxiety, fear, frustration, depression, hopelessness and desperation in patients and can reduce their quality of life, especially if there appears to be no logical reason for its existence (Roet, 1986). Hypnosis can be of benefit in many cases by using distraction (where the patient recalls a pleasant place or event while in a trance thereby replacing pain from top priority); removing negative emotions that are connected with the pain and which may play a role in causing or maintaining the pain; and producing analgesia in the affected part (Mongan, 2005; Sharav & Tal 2004).

3.5.2 Stress-related/psychological problems

3.5.2.1 Phobias/Anxiety

A phobia is an irrational, persistent fear of some specific object or circumstance (Brown, 1993). Among the common simple phobias are animal phobias (e.g. snakes, spiders, dogs), fear of heights or flying, fear of painful medical procedures and fear of lifts.

The most prevalent however, is agoraphobia, the fear of open, public places such as shops, stores and restaurants, or enclosed or confined places such as bridges, tunnels and public transport. The main feature of agoraphobia is anxiety about being far away from home (or from a 'safe' person) for fear of having panic attacks, and people with this phobia will eventually begin to avoid these anxiety-provoking situations, thereby restricting their activities and lifestyle, which in turn may lead to depression because of their feeling of lack of control over the condition (Bourne, 2000).

The most severe anxiety reactions are panic attacks in which the person experiences a feeling of apprehension or terror together with physiological symptoms such as dyspnoea, perspiring, trembling, dizziness, nausea, rapid pulse, chest pain or palpitations (Anderson et al., 1998).

In a case study by Harris (1991), hypnosis was used to eliminate panic attacks and agoraphobia in a 34 year-old woman. The patient, who was taught desensitising techniques and self-hypnosis, was able to obtained long-term relief from her symptoms, thus providing evidence for the efficacy of hypnosis in eliminating panic attacks.

Social phobia is one of the more common anxiety disorders where there is an irrational fear of situations that expose the person to public observation and possible embarrassment – the most common one being fear public-speaking or performing in public. Fear of blushing, using public toilets and taking examinations are also common social phobias all of which can eventually cause the person to avoid the situation altogether (Rice, 1992).

Studies show social phobia to be frequently comorbid with major depression. Stein et al. (2001) carried out a prospective, longitudinal epidemiological study of adolescents and young adults (aged 14-24 years) with social phobia for a period of 34-50 months. A total of 3,021 participants were available at baseline with 2,548 participants at the second follow-up. Results indicated that social phobia during adolescence or young adulthood was an important predictor of more serious depression in adulthood, with an increased risk of subsequent depressive episodes and an amplified risk of suicide.

3.5.2.2 Managing specific fears with desensitisation

Anxiety can affect a person on a physiological, behavioural, and psychological level. Therefore, in order for recovery to take place, a programme must be set in place which addresses all three levels - reducing physiological reactivity, eliminating avoidance behaviour and changing subjective interpretations or "self-talk" (Bourne, 2000). This can be achieved through imagery desensitisation, a process where anxiety can be replaced by feelings of relaxation and calmness while visualising a phobic situation in a hypnotic trance.

As anxiety and relaxation are incompatible responses, the goal of desensitisation is to learn to remain in the phobic situation and be relaxed at the same time. The person first constructs a hierarchy which begins, through a sequence of steps, from a mild instance of the phobia to the most challenging scene relating to the phobia. Each step of the hierarchy is visualised repeatedly while under hypnosis until the person can view the phobic situation in a relaxed state. If the person begins to feel anxious at any time, he or she leaves the phobic situation, imagines being in a peaceful scene until the anxiety has subsided, and then returns to the phobic situation again. Being in control and allowing the situation or object to approach at a steady rate while in a relaxed state helps desensitise the fear (Bourne, 2000; Roet, 1986).

Hypnosis is an alternative to drug therapy in the treatment of performance anxiety. The therapist can either help undo a conditioned physiological response such as hyperventilation or nausea, or guide the patient through a desensitisation exercise

or mental rehearsal of the upcoming event whether it be public speaking, a sporting event or exams (Cunningham, 1980; Olness, 1995). Gruzelier, Smith, Nagy & Henderson (2001) and Naito et al. (2003) found hypnosis to have both beneficial effects on mood and sizeable influences on cell-mediated immunity in their studies on the use of self-hypnosis in stress-reduction training before exams.

3.5.3 Stress and the Immune System

The adverse effect of emotions on physical health is not a new idea. Hippocrates taught his students to consider their patients' life circumstances and emotions as part of the treatment (Lyons & Petrucelli, 1987) and the 2nd century Greek physician, Galen, noted that melancholic women were more prone to malignancies of the breast than cheerful women (Locke & Colligan, 1986). This in turn, has led to the recognition by modern-day health practitioners of the comorbidity of psychological and physical disorders and the belief that negative emotional states are associated with unhealthy patterns of physiological functioning such as increasing the susceptibility to infectious agents and influencing the severity of infectious disease (Glaser & Kiecolt-Glaser, 2005; Salovey, Detweiler, Stewart & Rothman, 2000).

Researchers in the field of psychoneuroimmunology are providing evidence about the ways in which negative emotions generated by stressors can be translated into physiological changes (Webster et al., 2002; Padgett & Glaser, 2003). There is now compelling evidence that: ligands (peptide hormones, peptide neurotransmitters

and cytokines) and their receptors form a bi-directional, biochemical information circuit between, and within, the immune and neuroendocrine systems; the hypothalamic-pituitary-adrenal axis and the autonomic nervous system provide the key pathways for immune system dysregulation; and that stressors can activate both the hypothalamic-pituitary-adrenal axis and the sympathetic-adrenal-medullary axis, releasing both the pituitary and adrenal hormones – commonly known as "stress" hormones (Blalock, 1994; Pert, 1997; Glaser & Kiecolt-Glaser, 2005).

Significant alteration of the immune response as measured by B-cells and helper T-cells has also been demonstrated in highly hypnotisable subjects exposed to hypnosis (Ruzyla-Smith et al., in Evans & Burrows 1998).

Hypnosis is commonly used in the treatment of stress disorders as it is thought to be able to strengthen the body's immunological functions and assist in fighting off disease (Rossi, 1993; Wickramasekera, 1999). Research has been carried out on medical students prior to exams to assess the influence of hypnosis on cellular immune function during a stressful event and to examine the effect of self-hypnosis on stress reduction before exams.

In a study by Glaser & Kiecolt-Glaser (2001), 42 medical students were randomly assigned to one of three protocols during the exam period: hypnosis, social contact, or no intervention. The experimental group receiving hypnotic intervention began their sessions with a series of deepening exercises, plus imagery exercises and suggestions of greater relaxation during the day and enhanced comprehension and

retention of academic material. The sessions lasted 25-30 minutes and, prior to the sessions, students were asked to rate how they felt from 0 (extremely tense and anxious) to 10 (extremely calm and relaxed) and how often they had practised their self-hypnosis. Blood samples were also taken: the first at the beginning of the semester and the second three days before the first major academic exam of the semester.

The researchers found that, although all three groups started at comparable levels at the lower stress baseline, control participants' lymphocyte proliferation decreased prior to the exams and, in contrast, the proliferative responses of hypnotic participants remained relatively stable or increased slightly. The data from this study provide encouraging evidence that hypnosis may reduce the immunological dysregulation associated with acute stressors.

Gruzelier et al. (2001) carried out a similar study on 28 pre-clinical medical students (17 males and 11 females). As a condition for participation, students agreed to practise self-hypnosis three times a week and were monitored with a diary, so that frequency of practice was controlled. Total white blood cell and lymphocyte counts were assessed. Blood samples were taken four weeks prior to the exams (baseline sample) and again during the exam period. Participants who were assigned to the hypnosis group attended a group hypnosis session three weeks prior to exams and were given an audiotape of the same hypnotic induction to practise at home for the remaining three weeks.

The researchers' findings showed that hypnosis moderated aspects of immune down-regulation induced by the stress of examinations. The self-hypnosis training was effective in buffering the decline of natural killer cells (which have antiviral and anti-tumour functions) and increased the number of helper cells which positively correlated to increased feelings of calmness. Energy levels were also higher in the hypnosis group and the energy level was positively correlated with natural killer cell count.

Naito et al. (2003) also carried out a study using self-hypnosis as stress-reduction training prior to exams and achieved similar results. Forty-eight participants were recruited and randomly assigned to three groups – self-hypnosis, Johrei (a Japanese philosophy and healing method) or a mock neurofeedback relaxation control, and were instructed to attend weekly training sessions for a period of one month before their exams. The hypnosis group was taught a relaxation induction combined with immune imagery together with breathing control for acute anxiety and the Interrupt Distraction Procedure for worries and belief change to be used when appropriate. Participants were provided with a taped relaxation induction that included imagery description and were asked to practise the self-hypnosis three times a day for the first fortnight and once a day after that. Absolute number and percentages of lymphocytes, natural killer cells and natural killer cell cytotoxic activity were measured by means of venous blood samples taken at baseline, post-training and during the exam period. Results were in keeping with the beneficial effects of hypnosis and also suggested Johrei as being a possible procedure for stress reduction.

Hypnotic-guided imagery has also been shown to be effective on immune function and psychological parameters in patients during stressful illnesses. In a study by Bakke, Purtzer & Newton (2002), 25 patients being treated for Stage I or Stage II breast cancer undertook an eight-week imagery-training programme in which psychological and immunological data were obtained at baseline, after an 8-week intervention, and at a 3-month follow-up.

Subjects received eight one-hour individual imagery sessions in hypnotic guided imagery: in the first session, current ideas about the negative influence of stress and depression on the immune system were discussed; in the first and second sessions a standard progressive relaxation was taught and subjects were encouraged to develop specific images of their immune system being effective; and in the subsequent six sessions the subjects focused on making the images as vivid as possible by focusing on the details of their activated killer cells and on how exactly they removed the cancer cells.

The results showed a significant increase in improvement of depression and an increase in absolute number of natural killer cells during the 8-week programme, however these changes were not retained after treatment.

In a pilot study by Fox et al. (1999), the researchers investigated the effect of hypnotherapy on a variety of immune parameters such as natural killer cells, lymphocyte counts, cortisol levels and specific cellular cytotoxicity in response to the herpes simplex virus (HSV) on twenty subjects recruited from a clinic for the

treatment of frequently recurrent genital HSV-2. Psychological and immunological parameters were measured 6 weeks prior to, and 6 weeks after sessions of hypnotherapy during which patients kept a diary of symptoms.

Following hypnotherapy, subjects who showed improvement demonstrated significant rises in natural killer cell counts, HSV specific lymphokine-activated killer activity, and reduced levels of anxiety when compared to non-improvers and there was also a significant increase in CD3 and CD8 lymphocytes in all subjects. The study showed hypnotherapy as having the potential to produce significant immune changes, suggesting that it could have wider application as an investigative tool.

3.5.4 Gastrointestinal disorders

Numerous early studies have reported on gastric function during hypnosis and the therapeutic effects of hypnosis on GI disorders (Hall, Herb, Brady & Brooks, 1967; Kehoe, M., 1970) but it wasn't until the first controlled trial in the field of gastroenterology by Whorwell et al. (1984) - where results showed a significant improvement in both symptoms and well-being in the patients receiving hypnosis - that more interest in hypnosis as a treatment option was generated. Since then, more controlled trials have been carried out in this area with encouraging results.

Gastrointestinal disorders such as nausea and vomiting problems related to chemotherapy (Marchioro et al., 2000), after medication (Desdames, Marchand &

Moulin, 2002) and during pregnancy (Buckwater & Simpson, 2002) have been shown to improve with hypnosis, and Whorwell et al. (1992) demonstrated that hypnosis was also effective in suppressing or increasing gastric muscle activity depending on the patients' emotions.

A study by Calvert, Houghton, Cooper, Morris & Whorwell (2002) successfully used hypnotherapy for the treatment of functional dyspepsia. The 126 participants were randomly assigned to hypnotherapy, supportive therapy plus placebo medication, or medical treatment for a period of sixteen weeks.

The results indicated that in the hypnotherapy group both short-term and long-term symptom scores improved more than in the other two groups, there was an improvement in quality of life, and no participant in the hypnotherapy group commenced medication during follow-up compared to 82% of participants in the supportive therapy group and 90% in the medical treatment group.

Hypnosis has also been trialled as a treatment option for children with functional abdominal pain (Anbar, 2001). Five children (aged from 8 to 16) with a primary diagnosis of functional abdominal pain (recurrent abdominal pain in the absence of an identifiable physiological cause) and whose medical therapy provided no significant relief, were taught self-hypnosis. The imagery used for hypnosis was developed with input from each patient and instruction in self-hypnosis included imagining a relaxing place of the patients' choice, progressive relaxation, choosing an anchor (a post-hypnotic sign as a reminder of how to relax) and pain control.

Following the first session of hypnotherapy, the abdominal complaints of four of the patients were resolved within three weeks. The fifth patient was sceptical about hypnosis, refused to practise on a regular basis and there was very little rapport with the therapist. The researcher suggested that, under different circumstances, this patient may also have responded to hypnotherapy.

Most research in the use of hypnosis in the field of gastroenterology, however, has been in its application as a treatment for IBS (Barabasz & Barabasz, 2006; Francis & Houghton, 1996; Gonsalkorale et al., 2002; Whorwell 1984, 1987, 2006).

The use of hypnosis as an adjunct to the treatment of IBS was pioneered by Whorwell et al. in 1984 and this approach has continued to develop within the Department of Medicine at the University Hospital of South Manchester in the U.K. The 1984 trial showed improvement in symptoms of pain, abdominal bloating, bowel disturbances and general well-being in the participants in the hypnosis group compared to those in the control group.

Further research and hypnotherapy trials (Whorwell (1987, 1991, 1992; Gonsalkorale et al., 1999, 2002, 2003, 2004) were carried out with similar outcomes. As a result, hypnosis was adopted as an additional treatment modality for IBS patients (especially for those who had failed to respond to the usual medical interventions for this condition) and a hypnotherapy unit was set up within the hospital in 1995.

Palsson and Whitehead, from the University of North Carolina followed on from Whorwell's findings and Palsson designed a seven-session hypnosis protocol to address the problems of IBS, which, after preliminary testing on co-workers, was further tested in two published research studies (Palsson et al., 2002). As with the Manchester Modal, application of the North Carolina protocol also showed improvement in IBS symptoms and was of benefit to patients who did not experience adequate relief of symptoms from standard medical interventions.

Numerous other studies on the therapeutic effects of hypnosis in the treatment of gastrointestinal symptoms and IBS have been carried out since Whorwell's initial trial in 1984 (Forbes, Macauley & Chiotakakou-Faliakou, 2000; Ran, 2001; Galovski & Blanchard, 2002; Houghton et al., 2002; Simren et al., 2004; Barabasz & Barabaz, 2006; Whitehead, 2006) and research in this specific area of medicine is ongoing.

Summary

In the history of hypnotism, the word "hypnosis" has a long been associated with the occult and power control where the hypnotist appeared to have complete dominance over the subject – a concept which instilled fear, distrust, and avoidance of the situation altogether (Waterfield, 2002).

More recently, through research and clinical trials, hypnotherapy has now come to be regarded as a situation which involves co-operation and trust between the hypnotherapist and the patient – a form of therapeutic communication – where the

therapist recognises changes in states of awareness and makes a positive intervention to either initiate a change in the patient's behaviour or alleviate symptoms while he or she is in a hypnotic trance (McGill, 1996; Roet, 1986).

Hypnosis is neither magical nor mysterious, it is a natural phenomenon. It is a dream-like state which can occur numerous times a day - a change in the level of awareness in which suggestibility is heightened and the resources of the subconscious mind can be accessed (Olness, 1995; Zahourek, 2001).

Hypnotherapy is a complementary treatment which is effective over a wide range of disorders such as phobias (Harris, 1991), anxiety (Bourne, 2000), depression (Stein et al., 2001), cancer (Kidman, 1983; Syrjala, Cummings & Donaldson, 1992), gastrointestinal disorders (Gonsalkorale et al., 2003; Whorwell et al., 1984, 2006), and the alleviation of pain (Frenay et al., 2001; Manusov, 1990).

The involvement of hypnosis with immune function has been illustrated in studies in the field of cancer research where women with metastatic breast cancer receiving hypnosis training for pain relief lived 18 months longer on average than the control group (Bakke et al., 2002), and in exam stress (Gruzelier, et al., 2001; Naito et al., 2003) where practising hypnosis prior to exams resulted in high T-cell percentages over baseline.

Studies on the effect of emotions such as anger, fear, pain and anxiety have been shown to affect the enteric nervous system in the colon by increasing motility

more in IBS sufferers than in healthy controls (Blomhoff et al., 2001; Welgan & Meshkinpour, 2000), and evidence also suggests the entire GI tract to be involved (Whorwell, 1992).

Unfortunately, hypnosis is often recognised by the public as the treatment of choice for only a small range of problems and it is usually considered as a last resort. However, successful outcomes from both anecdotal evidence and clinical trials have shown hypnosis to be a genuine and useful treatment which is slowly becoming acknowledged by medical authorities (Waterfield, 2002).

This change in attitude towards the application of hypnotherapy for a wider range of disorders is considered to be due to more information coming to light about the complexities of the brain systems and also to a more rigorous application of scientific methodology and experimental design (Gruzelier, 1996).

The links between mind and body and the influence of the mind on the body, in both psychosomatic disorders and conditions such as infections and inflammation (which can be influenced by stress and other emotional factors), are becoming more widely acknowledged (Gonsalkorale, 1996, 2003). The mind-body link also has resources for self-healing and hypnosis can unlock them (Waterfield, 2002).

CHAPTER 4

RATIONALE FOR CURRENT STUDY AND SPECIFIC AIMS OF THESIS

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4.1 Clinical Studies in the Use of Hypnotherapy with Irritable Bowel Syndrome

Previous studies have demonstrated the effects and use of hypnosis on gastric motor and secretory function (Eichorn & Tracktir, 1955*;* Hall, Herb, Brady & Brooks, 1967) but the use of hypnosis as an adjunct to the treatment of IBS wasn't really addressed until a trial was carried out by Whorwell et al. in 1984. As a result, hypnosis was adopted as an additional treatment modality for IBS patients in the U.K. (especially for those who had failed to respond to the usual medical interventions for this condition) and, in 1995, a hypnotherapy unit was set up within the Department of Medicine at the University Hospital of South Manchester.

Following on from Whorwell's findings, Palsson and Whitehead from the University of North Carolina designed a seven-session hypnosis protocol (between 1994 and 1996) which was based on the Manchester model. This protocol also showed improvement in IBS symptoms and was of benefit to patients who did not experience adequate relief of symptoms from standard medical interventions.

In Whorwell's 1984 trial, thirty patients with severe refractory IBS were randomly allocated to two groups for treatment with either hypnotherapy, or psychotherapy plus placebo. Patients in the hypnotherapy group were given a simple account of intestinal smooth muscle physiology before hypnosis was induced and,

after the third session, were given a tape for daily autohypnosis. All hypnotherapy sessions concluded with standard ego-strengthening suggestions.

The psychotherapy group showed a small but significant improvement in abdominal pain and distension, and in general well-being but not bowel activity pattern, whereas the hypnotherapy patients showed a dramatic improvement in all symptoms (pain, abdominal bloating, bowel disturbances and general well-being). There was a three-month follow-up period in which the participants continued to receive hypnosis sessions on a monthly basis and were asked to telephone if they experienced a relapse so that a further session of hypnotherapy could be arranged.

The study also showed that patients with evidence of psychopathology appeared to do less well than those without - the researchers suggesting that this might be the result of their techniques being much more directed towards the physiological symptoms rather than psychological ones.

In a follow-up study by Whorwell et al. in 1987, thirty-five patients with severe IBS symptoms who had proved refractory to conventional forms of therapy and who had received hypnotherapy for IBS, were added to the fifteen patients who had already been treated with hynotherapy in the 1984 trial. The fifty participants were divided into three groups:

i) classical cases of IBS exhibiting abdominal pain, abdominal distension, and an abnormal bowel habit (n=38);

ii) atypical cases lacking one of two of the three criteria necessary for group 1 (n=7) and;

iii) patients with classical IBS plus significant psychopathology (n=5).

As in the 1984 trial, patients were given a simple account of intestinal smooth muscle physiology before hypnosis was induced, a tape for daily autohypnosis after the third session, and all sessions concluded with standard ego-strengthening suggestions. A control group for this study was considered inappropriate by the researchers as the previous controlled trial had shown a clear-cut advantage for hypnotherapy. Patients were judged as having improved only if their symptoms became mild or absent and they required no medication for IBS (with the exception of bulking agents).

The study showed an 84% success rate with classical cases responding best (95%). As in the 1984 trial, the researchers found that the response to hypnotherapy appeared to be dependent on the subject's age and that patients with atypical symptoms (i.e. those with abdominal pain but without distension or bowel disturbance), and those with psychological problems, were less likely to respond. All non-responders were women. After completing the ten weekly sessions, the subjects were encouraged to continue with regular autohypnosis but also received three monthly hypnotherapy sessions to maintain remission.

Harvey, Hinton, Gunary & Barry (1989) suggested that the success of the study by Whorwell et al. (1987) may have depended on the skill of a particular hypnotherapist and set out to compare the results obtained by two different hypnotherapists in the treatment of refractory IBS. The researchers also compared group hypnotherapy with individual treatment.

Of the thirty-three patients treated, twenty reported an improvement in symptoms and thirteen found no benefit. No significant difference was found in the response rate between men and women, hypnotherapists, or patients treated in groups or individually. Hypnotherapy in groups of up to eight patients was shown to be as effective as individual therapy. As in the Whorwell studies, Harvey et al. also found that patients with psychological problems were less likely to improve with hypnotherapy.

In addition to relieving the symptoms of IBS, hypnotherapy has been shown to profoundly improve the patient's quality of life and reduce absenteeism from work.

In a study by Houghton, Heyman & Whorwell (1996), fifty patients with IBS were administered a validated quality of life questionnaire (SBQOL) and assigned to two groups of twenty-five patients each – one group receiving hypnotherapy and the other (the control), were patients on a waiting-list. Patients treated with hypnotherapy reported less severe abdominal pain, bloating, bowel habit, nausea, flatulence, urinary symptoms, backache, and dyspareunia compared with controls.

Quality of life such as well-being (psychic and physical), mood, and work attitude were also favourably influenced by hypnotherapy.

In order to compare hypnotherapy and therapeutic audiotape, Forbes et al. (2000) carried out a randomised controlled trial in which subjects were assigned to either a course of gut-directed hypnotherapy (plus an audiotape of (usually) the third session which was to be listened to daily), or to receive a special audiotape recorded by the same therapist who carried out the hypnotherapy. The latter tape consisted of structured relaxation, suggestions on ways of reducing life stresses, and encouraged acceptance of symptoms. There were pauses on the tape but no background music or other sounds. The patients in this group were also advised to listen to the tape daily. Twenty-five patients were randomised to hypnotherapy and twenty-seven to the tape. The recruitment period extended over three years and there was a high "drop-out" rate after the initial consultation.

The researchers found that both procedures proved valuable in a modest majority of patients with resistant IBS and that, although a slightly smaller proportion responded to the audiotape, they suggested that, as hypnotherapy was time-consuming and labour-intensive, the ease and economy of the tape should be considered as a second-line option in the treatment of IBS. The results of neither group, however, approached statistical significance.

Anbar (2001) used self-hypnosis rather than recorded tapes in a trial on five paediatric patients with a primary diagnosis of functional abdominal pain. The

imagery used was developed with input from each patient – i.e. imagination of what might be perceived by all five senses in a relaxing place of the patients' choice. Each child was also asked to choose a sign (such as pressing index finger and thumb together) as a reminder of how to relax when not in a state of hypnosis and was complimented on his/her hypnotic abilities.

Following the first session of hypnotherapy instruction, the abdominal complaints of four of the patients resolved within three weeks. The fifth patient was sceptical about hypnosis and, although being able to relax with the aid of hypnosis, refused to practise on a regular basis.

The researchers were aware that the study involved a very small number of participants and, as all the patients were referred for hypnotherapy, they represented a potentially non-representative sample. However, the relatively high success rate in this report suggests that children with functional abdominal pain might respond well to a brief hypnotherapeutic intervention. This is especially so considering that abdominal pain is thought to be the most common recurrent physical symptom attributable to psychological factors among children and adolescents (Fekkes, Pijpers & Verloove-Vanhorick, 2004; Stein, Crow, Abbott & Tanner, 2003).

Although only a single case, the study by Galovski & Blanchard (2002) continued to provide support for the efficacy of hypnotherapy in a very refractory IBS patient. The patient suffered from refractory IBS and Generalised Anxiety Disorder and had suffered from IBS for thirty years. After six treatment sessions

using hypnosis, his IBS symptoms had improved (53%). He then continued treatment by listening to audiotapes provided by his therapist.

At the six-month follow-up, the subject rated his level of IBS symptom improvement on a visual analogue scale to be 70% and the two-year follow-up showed an improvement of 38% in IBS symptoms. The subject's levels of depression and anxiety also showed significant improvement. The patient's levels of depression (as measured by the Beck Depression Inventory - BDI) had decreased from a pre-treatment score of 13 to 10 at the six-month follow-up, and 6 at the two-year follow-up. His levels of anxiety (measured by the State Trait Anxiety Inventory - STAI) had decreased from a pre-treatment score of 49 to 38 at the six-month follow-up and 36 at the two-year follow-up, and he was also able to substantially decrease his medication regimen.

Ongoing research has been carried out by practitioners at the hypnotherapy unit of the University Hospital of South Manchester, U.K., the largest of which was a large-scale audit of hypnotherapy carried out by Gonsalkorale, Houghton & Whorwell (2002) in which 250 patients (aged 19-79 years) with IBS of at least two years' duration and refractory to previous treatment, received a course of hypnotherapy.

At the first visit, participants completed questionnaires to measure the severity of IBS symptoms and psychological status over the preceding month. This was followed by twelve weekly sessions of hypnotherapy using previous techniques

(Whorwell et al., 1984) over a period of three months, plus daily home practice between sessions. At each session, interventions were reinforced or modified according to the patients' needs and, after the last session, patients were asked to contact the unit if they needed any additional help.

A marked improvement was seen in IBS symptoms (abdominal pain, bloating and bowel habit disturbance), extra-colonic score (nausea/vomiting, headaches, backaches, lethargy, body aches, excess wind, heartburn, thigh pain, urinary symptoms), quality of life, and anxiety and depression, in all sub-groups with the exception of males with diarrhoea-predominant bowel habit who improved far less than the other participants for no known reason.

The outcome of therapy was measured after the last session and no long-term follow-up was pursued because of difficulties in obtaining date on such a large scale. No control group was included for comparison because this research was not a clinical trial, and previous studies that had included control groups had already demonstrated that hypnotherapy was superior to placebo or non-treatment.

The previous audit by Gonsalkorale et al. (2002) confirmed the beneficial effects of hypnotherapy in a large number of patients but outcome was only measured immediately after patients had completed the course of hypnotherapy. In order to determine the longer-term effects of therapy in terms of symptoms improvement, consultation rates, and use of medication, Gonsalkorale et al. (2003) carried out a

study to establish follow-up on a large group of patients who had previously been treated with hypnotherapy.

Two hundred and four patients, who had undergone a course of gut-directed hypnotherapy at least one year previously, completed questionnaires rating IBS symptoms, extra-colonic features, quality of life, anxiety, and depression before, immediately after, and up to six years following hypnotherapy treatment. Immediately after hypnotherapy, 71% of patients considered their symptoms very much or moderately better, and of these participants, 81% maintained benefit of treatment or reported further improvement over the follow-up period. The remaining 19% of these participants had only slight or no improvement with hypnotherapy and little or no change in the follow-up period.

The study demonstrated that the beneficial effects of hypnotherapy for the majority of patients appear to last at least five years, thus making hypnosis a viable therapeutic option for the treatment of IBS, both because of its sustained effect and because of the possible ensuing reduction in the cost of medications and other healthcare demands.

Studies using cognitive and/or behavioural interventions have also reported reduction in IBS and psychological stress (symptoms (Boyce et al., 2000; Greene & Blanchard, 1994; Murray et al., 2004) but few have integrated cognitive-behavioural therapy (CBT) *with* hypnotherapy. The combination of these two modalities has been shown to be successful in trials other than those concerning IBS. In a meta-analysis

of 18 studies by Kirsch, Montgomery & Sapirstein (1995) in which CBT was compared to CBT plus hypnosis, it was concluded that hypnosis enhanced the effectives of CBT, and research by Bryant, Moulds, Guthrie & Nixon (2005) indicated that the addition of hypnosis to CBT substantially increased outcome in the treatment of acute stress disorder.

Gonsalkorale, Toner & Whorwell (2004) designed a study to determine whether the improvement in treating IBS with hypnotherapy was associated with cognitive change. The specific aims of the study were to establish whether patients' cognitions were related to the severity of the IBS symptoms, whether these cognitions changed after hypnotherapy, and if so, whether this change was related to improvements in symptoms.

Seventy-eight patients attended twelve sessions of hypnotherapy over a three-month period. Before and after the treatment period, the participants completed questionnaires to measure severity of IBS symptoms, extra-colonic features and psychological status as well as IBS-related cognitions. The Cognitive Scale for Functional Bowel Disorders (Toner et al., 1998) which was designed specifically for use in this group of patients, was used to measure the IBS-related cognitions. It contains statements, derived from typical thoughts of IBS patients, and is subdivided into themes relating to bowel function and personal characteristics relevant to IBS.

The study supported the findings shown in previous research (Whorwell et al., 1984, 1987; Houghton, 1996) – i.e. that hypnotherapy reduced both IBS symptoms

and associated extra-colonic manifestations, and improved the patients' quality of life and psychological well-being. More specifically, it showed that symptom improvement with hypnotherapy was associated with a change in cognitions. In particular, the results showed that IBS-related cognitions were associated with symptom severity and quality of life and that these cognitions improved with hypnotherapy and this improvement correlated with improvement in symptoms.

The researchers also indicated the importance for healthcare professionals to consider functional disorders in the way that patients think about these symptoms rather than thinking about them in terms of symptomatology only.

As mentioned previously, Palsson and Whitehead from the University of North Carolina continued research on IBS and hypnosis, based on the Manchester model of Whorwell et al. (1984). Their initial investigations consisted of two studies (1997; 2000) in which hypnosis, as demonstrated in the Manchester study, was shown to substantially improve all the central symptoms of IBS in the majority of patients.

Previous to these two studies Palsson (in consultation with Whitehead), had written a seven-session hypnosis protocol (The North Carolina Protocol) designed to address the problems of IBS, plus a shorter session script for an audio recording for patients to use daily at home between clinic sessions. The nature of the protocol was that it had to be usable without customisation with all patients, regardless of their ability to visualise, their pace of hypnotic response, or their need for direct instruction.

In their first study, Palsson, Burnett, Meyer & Whitehead (1997) evaluated the effects on rectal pain thresholds and muscle tone by having therapists read identical scripts to 18 patients with severe IBS symptoms while they were under hypnosis. Seventeen out of the eighteen patients showed significant improvement in their clinical symptoms however, as in the Manchester study, the gut pain thresholds and muscle tension remained unchanged after treatment.

In the second study, Palsson, Turner, & Johnson (2000) used the same treatment protocol and, in addition, measured the functioning of the autonomic nervous system and the blood levels of the gut hormone, vasoactive intestinal peptide. Twenty-one out of the twenty-four patients with severe IBS symptoms showed improvement in their clinical symptoms as well as improvement in their psychological well-being, but again, no changes in the physical measurements were evident after treatment.

Both studies demonstrated the verbatim delivery of hypnosis using written script. Most patients showed an improvement in clinical symptoms which lasted for at least ten months. Palsson et al. also intimated that suggestions or imagery specifically directed at reducing intestinal pain sensitivity seemed to be unnecessary, as they appeared to have had no measurable effect on bowel pain threshold or the degree of clinical pain improvement.

Research on hypnosis as a treatment for IBS to date has shown consistent IBS symptom reduction as well as an improvement in patients' psychosocial well-being and quality of life.

4.2 Limitations of Previous Studies

Hypnotherapy, or more specifically, 'gut-directed' hypnotherapy, is the most frequently reported therapy shown to have a beneficial therapeutic impact on IBS symptoms (Francis & Houghton 1996; Locke et al., 1999). The first evaluation of "gut-directed" hypnotherapy in the management of IBS (published by Whorwell et al. in 1984) indicated a significant benefit over placebo, and in 2003, Gonsalkorale et al. reported long-term benefits of the effect of hypnotherapy on IBS sufferers as well as a reduction in consultation rates and medication.

More recent reviews of studies on hypnotherapy as a treatment for IBS have found that published evidence still suggests that 'gut-directed' hypnotherapy is very effective in the management of IBS (Gholamrezael et al., 2006; Wilson, Maddison, Roberts, Greenfield & Singh, 2006). In these reviews, the authors observed some methodological inadequacies in the studies such as lack of a control group and/or long-term follow-up, too small a sample size, and other aspects such as hypnotisability and expectancy of the patient not being taken into account.

For the purpose of the study in hand, however, one inadequacy the reviewers did not address was that the therapists in the various studies *failed to specifically*

target the patients' psychological symptoms in the hypnosis sessions. The effect that hypnosis has on the direct control of gut function, the reduction of visceral pain sensitivity, and somatisation, was acknowledged, and Gholamrezael et al. did suggest that one cannot rule out that hypnosis also partially reduces anxiety and depression, thereby improving symptomatology, but the importance of addressing this component of the IBS symptom picture was not identified.

Researchers have acknowledged that psychological factors play some part in the amelioration of IBS symptoms and, therefore, cannot be ignored (Whorwell et al., 1987; Chapman, 2005) but, as yet, imagery specifically addressing the mental, psychological and emotional aspects of IBS, has not been part of the hypnosis sessions in these studies.

Psychological distress, which can trigger or exacerbate symptoms (Jarret et al., 1998; Koloski, Talley & Boyce, 2003), has been shown to be an important component of IBS symptoms (*see Chapter 2*) and should be considered when treatment strategies are designed. To date, none of the researchers who have carried out studies on hypnotherapy as a treatment for IBS has taken this into account. By using scripts that specifically target each individual patient's emotional/psychological symptoms (in conjunction with scripts for the physiological aspects of the disease), the therapist addresses the whole patient profile. The following studies highlight the absence of individual scripts pertaining to the psychological component of IBS in the researchers' treatment protocol.

Whorwell (1987) observed that IBS patients with evidence of psychopathology who were undergoing his treatment with hypnosis, appeared to do less well than those without, and attributes this to that fact that his techniques are much more directed towards physiology than psychology. The hypnotherapy treatment Whorwell used was targeted at the gut and, although he admits that psychological factors cannot be ignored entirely, in his view, they very much take second place.

Hypnosis, according to Whorwell, can be used as *either* a predominantly physical, or a predominantly psychological treatment, and suggests that physicians would be more comfortable with the former approach (Whorwell, 1991).

Treatment by Whorwell et al. consisted of half-hour sessions of decreasing frequency over a three-month period, with hypnotherapy solely directed at general relaxation and control of intestinal motility. After a hypnotic induction, suggestions on improvement of health and well-being were given to patients. To control gut function, they were asked to place a hand on the abdomen and feel the sense of warmth while imagining the gut as a river – the aim being to make the river flow smoothly. The patients were also provided with an audiotape, which contained suggestions similar to those given in the session, for daily autohypnosis.

The imagery used in the sessions was the same for each patient and, although all hypnotherapy sessions concluded with standard ego-strengthening suggestions,

psychological problems such as anxiety and depression were not specifically addressed.

Both Harvey et al. (1989) and Forbes et al. (2000) utilised a specifically gut-directed hypnotherapy technique which was closely derived from that of Whorwell et al. (1984) in which the patient placed a hand over the abdomen, was asked to imagine a river and relate it to the smooth rhythm action of their own GI tract, and was given an audiotape containing similar suggestions as those used in the sessions.

Again, all suggestions and visualisations in the sessions were targeted at the physiological symptoms of IBS, were the same for each patient, and no specific suggestions or imagery relating to psychological problems were given. Forbes et al. also used an audiotape for the control group, which contained background information about IBS, structured relaxation, and suggestions on ways of reducing life stresses and accepting symptoms. However, the tape was the same for all participants and contained no specific suggestions regarding psychological symptoms.

Physical symptoms attributable to psychological stress are known to be present in children and adolescents, and functional abdominal pain is an example of a symptom that can respond to psychological intervention (Chapman, 2005; Egger, Costello, Alaattin & Angold, 1999).

Anbar (2001) used self-hypnosis in a trial on five paediatric patients with a primary diagnosis of functional abdominal pain. The patients were taught how to go into hypnosis themselves rather than relying on the therapist, and practised the self-hypnosis at home rather than relying on an audiotape. There was also more flexibility in the use of imagery in both the deepening segment of the hypnotherapy session and in the gut-directed therapy.

In the deepening segment of the hypnotherapy session, instead of using the same imagery for each patient, the imagery used was developed with input from each individual patient – i.e. imagination of what might be perceived by all five senses in a relaxing place of the patients' choice. The therapy was still directed by the therapist but each patient was able to visualise the specific problem (e.g. pain in the stomach) as he/she wished and then imagine a way of resolving it.

As all five patients attended only a one-hour session and four returned for only one or two follow-up sessions, Anbar suggested that, because of the brief time involved, psychopathology that may be associated with functional abdominal pain might not be identified and that the practitioner should remain vigilant for psychological problems including anxiety and depression.

In two studies by Gonsalkorale et al. (2002; 2004), hypnotherapy was carried out based on gut-directed techniques used in previously-mentioned trials (Whorwell et al., 1984; Harvey et al. 1989; Forbes et al. 2000) once again

demonstrating that hypnotherapy remains an extremely effective treatment for IBS and that symptomatic improvement is long-lasting.

Neither trial directly targeted psychological symptoms in the hypnotherapy sessions although the latter trial indicated a possible change in direction towards considering a more psychological approach to treatment. It showed that symptom improvement with hypnotherapy was associated with a change in cognitions and that IBS-related cognitions were associated with symptom severity and quality of life. The researchers suggested that practitioners should take into account the way patients think about these symptoms rather than thinking about them in terms of symptomatology only.

Following on his doctoral research where he tested a scripted hypnosis protocol designed to treat chronic stress problems, Palsson (1998) designed a standardised hypnosis intervention for physical problems which eventually led to a seven-session hypnosis protocol to address the problems of IBS. The entire course was designed for verbatim delivery both for scientific rigor and to make generalisation of the treatment easier.

His seven-session treatment consists of a therapist reading a script, verbatim, to each IBS patient at each session. The seven scripts are basically the same format: induction, progressive relaxation, a deepening technique (e.g. therapist counting from 1-20 while the patient imagines going down a staircase or lift), followed by visualisation and suggestions.

The suggestions are mainly directed towards the physiology of IBS (in particular the pain and discomfort in the stomach and intestines) and, in each session, patients are told that their bowel sensations no longer bother them and that they are becoming less sensitive to pain and discomfort. Visualisations to this effect include imagining that there is a protective coating on their intestines, or that the thick walls of the log cabin they are visualising, protect them from the ice and wind outside in the same way as they are protected from pain or discomfort in the stomach and bowels. Other suggestions are targeted at getting away from troubles and cares by visualising a garden or a place in nature. The audiotape, given to patients at the completion of the second session, contains suggestions of the body learning how to maintain the feeling of comfort inside.

Although part of Palsson's treatment involved visualising calm, relaxing places away from the tension of the day which could lessen anxiety, no other psychological issues such as depression, panic (Creed et al., 2005; Sykes et al., 2003), perceived stigma, or abnormal illness attitudes in IBS patients (Dancey et al., 2002; Gomborone et al., 1995) were addressed.

Psychological influences may act as predisposing or precipitating factors which eventually lead to symptoms that exacerbate or maintain the problem the IBS patient is suffering (Toner, Garfinkel & Jeejeebhoy, 1990; Whitehead & Palsson, 1998). In addition, these symptoms may be a source of psychological distress (such as the patient feeling out of control, helpless and anxious) which, because of the

patients' automatic thoughts or cognitions, may in turn exacerbate symptoms (Gonsalkorale et al., 2004).

4.3 Rationale for Current Study and Hypotheses

The current interest in the mind-body connection has grown because current research has substantiated how the brain and the nervous system and immune systems of the body communicate through the bi-directional flow of hormones, neuropeptides and cytokines (Heitkemper et al., 2001; Leahy et al., 1999; Pert, 1997). Nerve endings have been found in the thymus, lymph nodes, spleen and bone marrow, and immune cells respond directly to chemical signals produced by the nervous system and released into the bloodstream (Ader, 1991; Dreher, 1995).

For decades, health professionals have focused solely on the causes of disease rather than on the psychological effects on health and disease, and the effects of disease on the psyche. In other words, emphasis has been more on pathology than on factors which promote health (Dreher, 1995).

There is now a great body of evidence suggesting that direct connections exist between parts of the body that had previously been thought of as being independent, and greater credibility is now being given to the notion that the mind is able to influence the body (Hannigan, 1999; Pelletier, 1995). Interest is being shown in the effects of imagery and hypnosis on the immune and nervous systems and research in

that area indicates that hypnotic intervention can moderate immune and nervous system functioning (Glaser & Kiecolt-Glaser, 2001; Whorwell et al., 1992).

Ernest Rossi (1993) suggests that hypnosis acts on the brain's structures and chemistry to facilitate the communication process and aid healing by acting on the limbic-hypothalamic part of the brain. This area of the brain can alter mind-body interactions by normalising the body's ultradian rhythms which, when disrupted is a major cause of stress-related illnesses.

The nervous system is constantly maintaining homeostasis which can be disrupted by stressors. Stressors can be either physical such as temperature extremes, accident, injury, inflammation, infection, toxins, and surgery; or psychological such as major life events, trauma, abuse, loss, anxiety, and depression (Salt, 2002).

The stress-response is the body's attempt at restoring equilibrium by secreting certain hormones, inhibiting others, and activating particular parts of the nervous system and the immune system. However, when these protective hormones are produced repeatedly, they create harmful physiological changes leading to an imbalance and disturbance of homeostasis, which in turn results in functional symptoms. Collections of these symptoms commonly lead to the diagnosis of IBS and other functional syndromes (Rice, 1992; Wood, Alpers & Andrews, 1999).

The brain translates a person's perceptions, thoughts, beliefs, memories and emotions into patterns of nerve cell firing and chemical release. The system works in

reverse as well - pain that originates in the body can affect a patient's mood and behaviour. The pathways connecting mind and body integrate responses to threats (behavioural, physiological or immunological) and enable homeostasis to be maintained (Pert, 1997; Watkins, 1997).

Studies have shown that hypnotherapy can normalise abnormal visceral sensitivity and lessen pain (Prior, Colgan & Whorwell, 1990; Houghton et al., 1999) suggesting, once again, the possible role the nervous system may play in this abnormality. Both PET scans (Silverman et al., 1997) and fMRI (Mertz et al., 2000) appear to support this by demonstrating the presence of abnormal cerebral processing of visceral stimuli.

A study by Whorwell, Houghton, Taylor & Maxton (1992) showed that hypnosis could be used to induce various emotions, and that different emotions could have different effects on colonic motility. The researchers suggested that these observations might explain, for example, the frequency of defaecation and cramping during stressful events as well as their amelioration when the stressful event was over; and therefore, awareness of the emotional state of the patient should be taken into account when treating IBS. However, even though the researchers made this observation, the emotional state of the patient was not specifically addressed in their hypnotherapy sessions.

IBS has a considerably negative impact on sufferers' lives and is associated with psychological distress. Strong evidence exists that IBS has an important

psychological component. In an interview and questionnaire involving 180 outpatients, Bennett et al. (1998) found that psychosocial disturbance was strongly related to the overall severity and extent of functional gut disturbance, and that 98% of patients had been exposed to at least one chronic social stressor for more than a year. They found significant relationships between IBS, somatic symptoms, and severity of emotional distress such as anxiety, depression, anger, and goal frustration. They also found a relationship between IBS and absent or inadequate emotional support, and increasing age.

Two thirds of patients with IBS have been shown to have experienced a severe social stress before the onset of the abdominal symptoms, compared to a quarter of patients with organic disease and healthy controls (Creed et al., 1988; Dancey et al, 1997) and relationships between the presence of IBS and generalised anxiety disorder, chronic worry, neuroticism and anxiety about visceral sensations have been documented (Hazlett-Stevens, Craske, Mayer, Chang & Naliboff, 2003).

Psychological factors may be involved in both the onset and maintenance of GI symptoms and IBS patients with a lifetime psychopathology were significantly more likely to have developed psychiatric disorders before the onset of IBS (Sykes, Blanchard, Lackner, Keefer & Krasner, 2003).

Psychological treatments, such as hypnotherapy, are rarely suggested to IBS patients as, up until now, medication (such as antispasmodics, antidepressants, anti-diarrhoeal and laxatives) has been the treatment of choice (Baker, 2005; De Ponti &

Malagelada, 1998). Considering the high cost of medication, repeated visits to medical practitioners (Cash, Sullivan & Barghout, 2005; Hahn et al., 1999), and the high prevalence of stress, IBS sufferers would obtain a great deal of benefit from programmes such as hypnotherapy.

To date, trials using hypnosis as a treatment for IBS have focused on the physiological symptoms of IBS and, although some researchers have used imagery of calm places away from the tension of the day (usually the same imagery for each patient) and/or concluded the hypnotherapy sessions with standard ego-strengthening suggestions, *they have not addressed specific psychological disorders* (such as anxiety and depression) that patients often present with at their first session.

4.4 Specific Aims of the Trial

The primary aim of this trial was to achieve a more holistic approach when attending to IBS patients and to evaluate the effectiveness of hypnosis and imagery in the treatment of IBS in an Australian population. More specifically, the study aimed at comparing the use of "gut-directed" imagery used in previous hypnosis trials (Gonsalkorale et al., 2002, 2003; Whorwell et al., 1984, 1987, 1991) with imagery that reflected the patients' complete symptom picture – i.e. imagery addressing not only physiological symptoms but psychological/emotional symptoms as well. The main hypothesis being that patients who were treated holistically would have a better outcome in the improvement of their IBS symptoms than those whose physiological symptoms alone were treated.

As previous clinical trials in IBS had noted that a variety of psychological conditions often co-existed with IBS (*see Chapter 2*), patients were asked to complete the Symptom Checklist-90-R (SCL-90-R) before commencement of treatment. This questionnaire helps evaluate a broad range of psychological problems and symptoms of psychopathology, and is also useful in measuring patient progress or treatment outcomes (*see Chapter 5*).

For the purpose of this trial, four of the nine primary symptom dimensions of the SCL-90-R (anxiety, depression, interpersonal sensitivity, and obsessive-compulsive) which most reflected the psychological symptoms of the majority of the participants, were measured, and scripts targeting these four symptoms were compiled and read to relevant participants during the hypnosis sessions.

Secondary aims of the trial were to test the following hypnotheses:

a) participants who had been diagnosed with IBS would present with not only physiological symptoms but psychological ones as well; and that, at the end of the study, participants who underwent individualised hypnotherapy (using imagery which addressed both the psychological/emotional aspects and the physiological symptoms of the syndrome), would have a better outcome in the improvement of their IBS symptoms than participants who underwent standard "gut-directed" hypnotherapy in which physiological symptoms alone were treated. Specific psychological symptoms were highlighted through administration of the SCL-90-R questionnaire to trial participants;

b) participants' IBS symptoms would improve during the trial period and, as a result, their quality of life would subsequently improve. To measure their general health status, participants completed the SF-36 both throughout the trial and during the follow-up period;

c) participants who had a support system in place would improve more quickly than those who hadn't. To outline which functions or behaviours, if any, had produced a beneficial effect on their health and well-being, trial participants were administered the Duke-UNC Functional Social Support Questionnaire at the screening session;

d) participants who were experiencing, or who had recently experienced, stressful episodes in their life would be more likely to have more severe and more frequent IBS symptoms. The Survey of Recent Life Experiences (SRLE) was administered to participants at the screening session to examine their emotional responses to life stress and how this may have influenced their GI function via the brain-gut connection.

4.5 Summary

Medical practitioners have long focused solely on the agent causing disease rather than on the effects psychological problems can have on health and disease (and the effects disease can have on the psyche) via the immune and nervous systems of the body. This practice dates back to Pasteur who played a major role in the

development of the germ theory and spent most of his life finding substances that would kill the infecting organisms (*see Chapter 1*).

However, another nineteenth-century scientist, Claude Bernard, believed that the patient's internal environment or "terrain" was more important than the pathogen and that physicians should focus more on enhancing the body's own defences (Pelletier, 1995). Unfortunately, modern medicine has mostly forgotten the importance of the "terrain."

Medical practitioners often attend only to the physical condition and ignore how the patients are reacting emotionally to their illness, but there is now a growing body of evidence to support the role emotional states have on a patient's vulnerability to disease (Goleman, 1996).

IBS symptoms have been shown to be generated by abnormalities of the GI function such as abnormal GI motility and increased sensitivity of the intestine (Camilleri et al, 2001; Jarret et al., 2000) - one of the reasons being an involvement with the immune system.

Research has shown that IBS patients have an increased number of inflammatory cells in the colonic and ileal mucosa, resulting in disturbances of gut motility, smooth muscle contractility, and changes in the function of enteric nerves (Barbara et al., 2002; Gui, 1998). IBS patients also have an increase in the numbers of T lymphocytes and macrophages in the colonic mucosa which result in abnormal

intestinal permeability in subgroups of diarrhoea-predominant IBS (Collins, 1996; Dunlop, 2006).

Evidence about the ways in which negative emotions, such as anxiety and depression, are generated by stressors and can be translated into physiological changes, are being provided by researchers in the field of psychoneuroimmunology (Webster, Tonelli & Sternberg, 2002; Padgett & Glaser, 2003).

Studies on the effect of emotions such as anger, fear, pain and anxiety have been shown to effect the enteric nervous system in the colon by increasing motility more in IBS sufferers than in healthy controls (Welgan & Meshkinpour, 2000; Blomhoff, Spetalen, Jacobsen & Malt, 2001) and evidence also suggests the entire GI tract to be involved (Whorwell et al., 1992).

Hypnosis has been shown to be effective in alleviating pain, boosting the immune system, addressing stress-related and psychological problems and, more recently, as a treatment option for GI problems (Handel, 2000; Waterfield, 2002; Gonsalkorale et al., 2003).

SECTION 2

A CONTROLLED TRIAL OF HYPNOTHERAPY AS A TREATMENT FOR IRRITABLE BOWEL SYNDROME

CHAPTER 5

METHODOLOGY AND INSTRUMENTS

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5.1 Introduction

Classic IBS symptoms are pain and alteration of bowel habit. However, there are many different patterns or combinations of symptoms that can be caused by the gut failing to function properly. Common complaints include a variation in bowel habit from diarrhoea to constipation (or both), excessive flatulence, abdominal bloating and abdominal pain and often a feeling of an incomplete evacuation of the bowel after defecation (Barbara et al., 2004; Blanchard & Galovski, 1999). High levels of comorbidity with psychiatric illness, especially anxiety, anger and depression, have also been reported (Garakani et al., 2003; Sykes et al., 2003).

Even though the high prevalence of IBS accounts for a high percentage of the gastroenterologists' workload, its aetiology and pathogenesis are still unknown. Several lines of evidence suggest that the cause of IBS is a result of a hypersensitive GI system which is exacerbated by stressful or emotional states (Bouchoucha et al., 1999; Camilleri et al., 1999; Prior et al., 1990; Whitehead et al., 1990). It has also been suggested that IBS could be the result of a previous viral or bacterial infection (Neal et al., 1997; Rodriguez & Ruigomez, 1999).

5.2 Scientific Aims of the Trial

This research proposed to evaluate the use of hypnosis and imagery in the treatment of IBS in an Australian population and, more specifically, to compare the use of "gut-directed" imagery used in previous hypnosis trials (Gonsalkorale et al., 2002, 2003; Whorwell et al., 1984, 1987, 1991) which addressed the patients' physiological symptoms only, with imagery that reflected the patients' complete symptom picture.

The latter took into account the patients' psychological and emotional symptoms as well as the physiological ones - the main hypothesis being that patients who were treated holistically would have a better outcome in the improvement of their IBS symptoms than those whose physiological symptoms alone were treated.

The progress of participants through the study is shown in *Figure 4*, as per the Consort statement (*Appendix 13*).

5.3 Recruitment Processes, Inclusion and Exclusion Criteria

5.3.1 Subject Selection

Patient Population. Fifty-one symptomatic volunteers aged between seventeen and seventy-five were recruited from the general public and medical and naturopathic clinics, and were invited to undergo screening tests. The participants were deemed suitable for the study after having met the Rome II criteria for IBS.

Non-compliance and Discontinuations. Characteristics of patients who discontinued or showed non-compliance were omitted from the statistical analyses.

Inclusion Criteria. Participants who had been diagnosed with IBS by a primary care physician or gastroenterologist; who had been symptomatic for at least six months prior to the trial; had failed to respond adequately to conventional medicines; and, who had experienced at least four days with at least moderate pain over a two-week period after screening.

Exclusion Criteria. Participants who were not free of organic disease and who did not fit the inclusion criteria.

5.3.2 Gastroenterological Screening of Study Population

During the initial screening visit, participants completed the Irritable Bowel Symptom Questionnaire (IBSQ) (*Appendix 4*) to establish diagnosis and exclude other differential diagnoses, and the Bowel Symptom Severity Scale (BSSS-VI) (*Appendix 5*) to measure the severity of IBS symptoms.

At the commencement of each of the five visits to the clinic, participants were asked to complete a short IBS symptom scale (BSS 1-5) (*Appendix 6*) and the Bowel Symptom Severity Scale and hand them in to the receptionist who sealed them in an envelope and filed them. Two weeks after completion of the trial, and again three

months after completion, participants were asked to complete the Bowel Symptom Severity Scale and forward it to the clinic.

Patients were required to attend one initial screening visit which included completing the following questionnaires:

Irritable Bowel Syndrome Questionnaire (IBSQ) (*Appendix 4*)

Bowel Symptom Severity Scale (BSSS) (*Appendix 5*)

SCL-90-R (*Appendix 7*)

SF-36 Health Survey (*Appendix 8*)

Duke-UNC Functional Social Support Questionnaire (*Appendix 9*)

Survey of Recent Life Experiences (SRLE) (*Appendix 10*)

They were then given a daily diary *(Appendix 3)* in which to record their symptoms and requested to hand it in at the beginning of their first treatment session in two weeks' time. The diary helped subcategorise the IBS participants into one of three main subtypes: diarrhoea-predominant, constipation-predominant, and mixed (diarrhoea and constipation).

Using a linear scale, the participants were asked to rate daily the overall severity of symptoms, as well as the severity and degree of distress caused by the following GI symptoms:

- pain or discomfort in the stomach or abdomen
- feeling as if the stomach or abdomen were bloated (excluding bloating due to a menstrual period)
- constipation
- diarrhoea.

Participants were then asked to attend a further five treatment sessions which were conducted fortnightly by the same practitioner at the same clinic location.

Before the commencement of each of these sessions they were asked to fill in a short Bowel Symptom Scale (BSS 1-5) (*Appendix 6*), the Bowel Symptom Severity Scale (*Appendix 5*) and the SF-36 General Health Questionnaire (*Appendix 8*) and, after the second and fourth sessions, they were also asked to complete the Credibility Scale (*Appendix 11*). These were handed in at reception where they were sealed in an envelope and filed. After the second session, each participant was given a CD/cassette of the script used in the session (see *Appendix 12*) and asked to practise it daily until the end of the trial.

5.3.3 Ethical Considerations, Confidentiality and Privacy

All subjects who participated in these studies read the Subject Information Statement (*Appendix 1*), gave written, informed consent (*Appendix 2*) and were free to withdraw from the trial at any time. The protocols were approved by the Ethics Committee, University of Sydney, Australia. The confidentiality and privacy of

participants were taken into account by allocating all patients an identification code from the commencement of the trial. All questionnaires, documentation and data referred to patients by their identification code only. All clinical notes and questionnaires were sealed in an envelope and stored in a locked filing cabinet at the clinic and access was only possible by the investigator.

5.4 Research Plan and Timetable

Randomisation. After screening, and after exclusion criteria were met, 51 subjects were randomly allocated by means of random number tables (Boyer, 1968) to one of the three groups (2 experimental & 1 control).

Blinding. Participants were randomly allocated to 3 groups by a random number table (Boyer [Ed.] 1968) and were unaware of which treatment group they were assigned to. They were also unaware of other participants in their treatment group, or in the other two groups. Each participant was treated individually by the same therapist with a quarter of an hour's break between his or her consultation and that of the next patient to minimise possible contact between patients. The waiting-room was a common one for patients of all twelve practitioners working at the clinic, so participants would be unaware of which practitioner other patients were waiting to see. Also, consultations for private patients of the author were interspersed between those for IBS trial participants, again minimising contact between subjects.

The success in blinding was evaluated using a treatment credibility scale which was administered before the second and fourth sessions (*Appendix 11*).

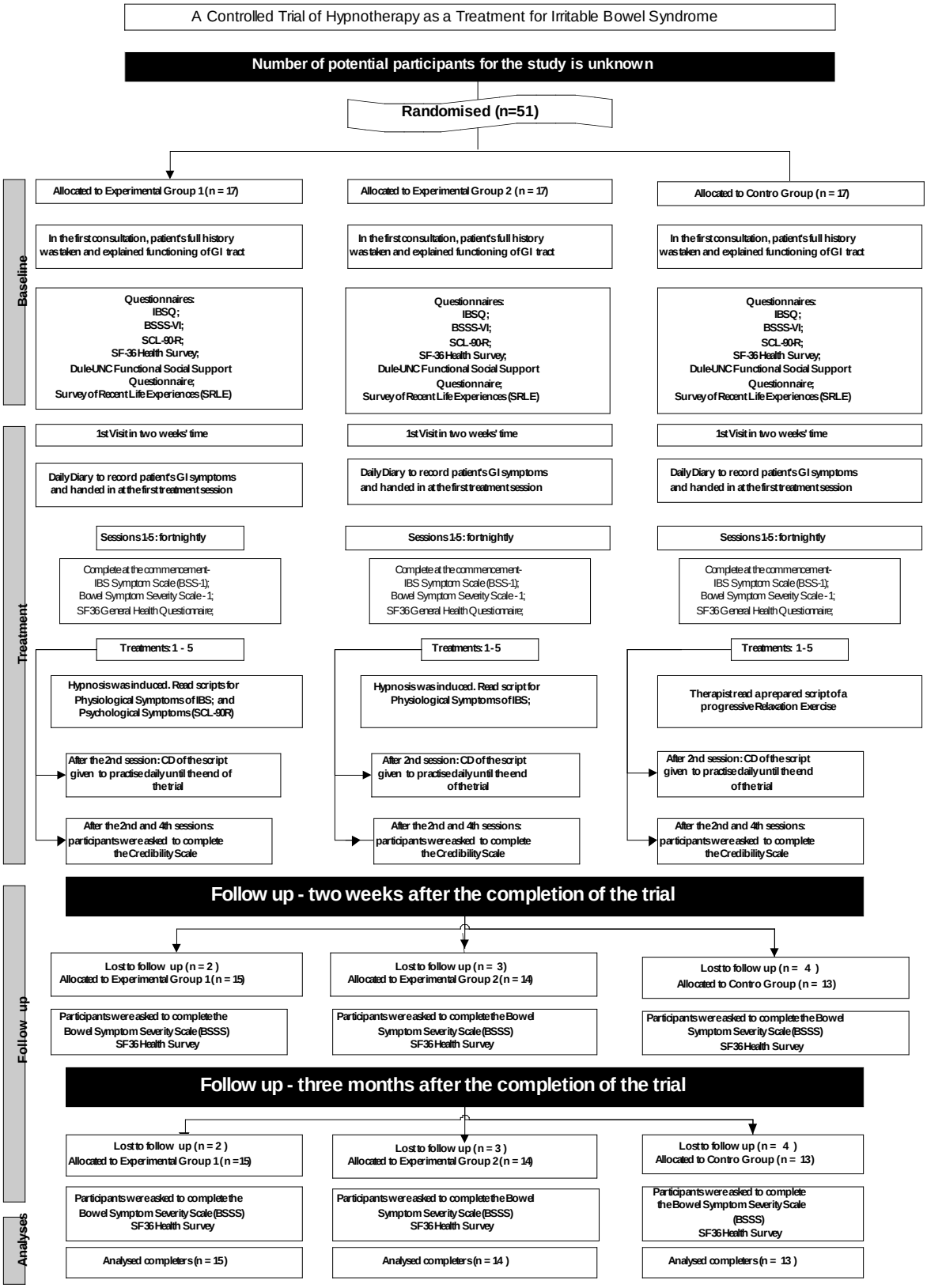
Baseline Period. Each participant was screened by means of the IBSQ to ensure that symptom frequency and severity were adequate before randomisation, and participants were each given a daily diary two weeks before treatment in which to record symptoms.

Follow-up. At the end of the trial, two questionnaires (the Bowel Symptom Severity Scale and the SF-36 Health Survey) were completed (at two weeks and again at 3 months) by each participant to assess whether IBS symptoms had significantly changed, compared with baseline, after hypnotherapy or relaxation treatment. Unlike previous trials (Whorwell et al., 1987; Gonsalkorale et al., 2002) no further treatment was given during the follow-up period, nor were participants invited to return for further treatment if symptoms returned.

Compliance: daily diaries were completed during the two weeks prior to the commencement of treatment sessions and handed in at the first consultation. At each session, participants were asked how often they had practised their relaxation or hypnosis techniques since the last session.

Drugs: concurrent medication could have an impact on outcome so patients were asked what drugs they are on before the trial and were asked to continue them for the duration of the trial.

Figure 4: Flow diagram of subject's progress through the phases of the trial



5.5 Treatment schedule

The three groups consisted of two experimental (hypnosis) groups and one control group. At the end of the trial, participants in the control group were offered two complementary sessions in hypnosis. The assessment instruments completed by all participants prior to each consultation are shown in *Table 12*.

The first experimental group was read a script using "gut-related" imagery (physiological symptoms of IBS) while under hypnosis plus a further script containing the patient's individual psychological symptoms (as evidenced by the SCL-90-R); the second experimental group was read the same script using "gut-related" imagery while under hypnosis, (but no script pertaining to psychological symptoms); and the third group (the control group) was given a relaxation session in which no scripts pertaining to either physiological or psychological symptoms were presented.

There were six scripts in all – one for the "gut-related" imagery which related to physiological symptoms only, one script for the control (relaxation) group, and one script each for the four of the nine dimensions of the SCL-90-R which most reflected the psychological symptoms of the majority of the participants. The four dimensions were: obsessive-compulsive, interpersonal sensitivity, depression, and anxiety. The appropriate script(s) was read to the participant during each treatment session. The script(s) for each group of participants was identical (see *Appendix 12*) and participants were blinded as to which script was being read to them.

Contact time. For all three groups: an initial consultation of a one-hour screening session plus five follow-up sessions of a half an hour each was the same for all randomised strata.

- Experimental group 1. In the first consultation, the patient's full history was taken and the functioning of the GI tract was explained. The following procedure was then strictly adhered to for the remaining sessions in the trial. Hypnosis was induced, after which the therapist read two prepared scripts (*Appendix 12*) – one containing "gut-directed" imagery (physiological symptoms of IBS), plus a further script containing the patient's individual psychological symptoms as evidenced by the SCL-90-R (*Appendix 7*). At the end of the second session a CD/cassette of the scripts used in this session was given to each patient to be taken home and practised daily.

- Experimental group 2. The patient's full history was taken in the first consultation followed by an explanation of the functioning of the GI tract. The following procedure was then strictly adhered to for the remainder of the trial. Hypnosis was induced in the same manner as for group 1, after which the therapist read the same prepared script containing "gut-directed" imagery (physiological symptoms of IBS) as for experimental group 1 (*Appendix 12*) but *no script containing the patients' psychological symptoms.* At the end of the second session a CD/cassette of the "gut-directed" imagery script was given to each patient to be taken home and practised daily.

- Control group. The patient's full history was taken in the first consultation and an explanation of the functioning of the GI tract was given. The following procedure was then strictly adhered to for the remainder of the trial. *No hypnosis was induced.* The therapist read a prepared script of a progressive relaxation exercise (*Appendix 12*) which contained neither the aforementioned "gut-related" imagery nor addressed the patients' individual psychological symptoms. At the end of the second session a CD/cassette of the relaxation exercise was given to each patient to be taken home and practised daily.

  Trial Length: The trial length was 23 weeks to allow for placebo response to settle and to control for the fluctuating nature of IBS.

5.6 Assessment Instruments

5.6.1 The Irritable Bowel Symptom Questionnaire (IBSQ)

The Irritable Bowel Symptom Questionnaire (IBSQ), a modified version of the previously validated Bowel Symptom Questionnaire (BSQ) (Talley, Boyce, Owen, Newman & Paterson, 1995), was utilised in order to verify the diagnosis of IBS and to acquire general data on patients participating in the trial. The IBSQ addressed aspects such as pain/discomfort, bloating, frequency and type of bowel movements, urgency, frequency of visits to doctor or alternative therapist, and daily amount of alcohol and coffee ingested.

Table 12 **Assessment Instruments Completed Prior to Each Session**

Session 1	IBS Symptom Scale (BSS1)
	Bowel Symptom Severity Scale (BSSS)
	SF-36 Health Survey
Session 2	IBS Symptom Scale (BSS2)
	Bowel Symptom Severity Scale (BSSS)
	SF-36 Health Survey
	Credibility Scale
Session 3	IBS Symptom Scale (BSS3)
	Bowel Symptom Severity Scale (BSSS)
	SF-36 Health Survey
Session 4	IBS Symptom Scale (BSS4)
	Bowel Symptom Severity Scale (BSSS)
	SF-36 Health Survey
	Credibility Scale
Session 5	IBS Symptom Scale (BSS5)
	Bowel Symptom Severity Scale (BSSS)
	SF-36 Health Survey

The IBSQ was a shorter form of questionnaire than the BSQ and therefore was more appropriate for use in this clinical trial as participants were required to complete several other instruments during the screening process and follow-up period, and on a regular basis prior to each treatment session.

5.6.2 The Bowel Symptom Scales (BSS1-5)

The Bowel Symptom Scales (BSS) (Boyce et al., 2003) were used to assess change in IBS symptoms during the course of treatment. The first item of all five BSS consists of five 100mm visual analogue scales (VAS) which refer to each of the principal symptoms of IBS (pain/discomfort, bloating, constipation, and diarrhoea), plus an overall symptom severity rating. Each of the 100mm lines is marked *very extreme* at the extreme right, and *symptoms not present* at the extreme left. Visual analogue scales are widely used and appear sufficiently sensitive to change (Agreus, 1993).

All five of the BSS also assess stool form (which, to an extent, reflects bowel transit time – a concept that had previously been validated by Heaton et al., 1991), the degree to which IBS symptoms interfered with the patient's life and activities, medication usage and fibre consumption. BSS 2-5 compares the participants' IBS symptoms to the previous time they had completed the questionnaire, and BSS 4 and 5 also compares the participants' symptoms to those stated in the questionnaire completed at the commencement of the trial. The participants' compliance is assessed in BSS 3 and 4.

5.6.3 The Bowel Symptom Severity Scale (BSSS)

The validated Bowel Symptom Severity Scale (BSSS) was developed in the Nepean Hospital research unit by Boyce et al. (2000) and was based in part on the previously validated Bowel Symptom Questionnaire (BSQ) by Talley et al., (1995). The BSQ provides a measure of the frequency and duration of symptoms according to Rome 1 criteria. It has been found to have good validity, and test retest scores of two weeks have shown it to have good internal consistency (Talley et al., 1995).

Patients completed the BSSS at the initial screening, at the beginning of every treatment session, and as follow-up two weeks and three months after the completion of the trial.

The scale consists of eight questions relating to possible symptoms the patient may have endured between treatment sessions. The symptoms specific to this questionnaire were: stool formation (loose and watery/hard or lumpy), abdominal pain, frequency of bowel motions, bloating, urgency, inability to have a bowel motion, and a general feeling of discomfort in the abdomen.

Each question also had two sub-questions which asked how distressed the patient had been during this period and how much the specific symptom had interfered with his or her daily life.

5.6.4 **The SCL-90-R** (Hopkins Symptom Checklist 90-Revised)

Clinical trials in IBS have noted that a variety of psychological conditions often co-exist with IBS and that a person's psychological state may impact on symptom reporting (see *Chapter 2*).

The Symptom Checklist-90-R (SCL-90-R) instrument from Pearson Assessments (Derogatis, Yevzeroff & Wittelsberger, 1975; Derogatis, 1994) is a widely used psychological status symptom inventory used by psychiatrists, clinical psychologists, medical practitioners, professionals involved in mental health, and for research purposes (Peveler & Fairburn, 1990; Schmitz et al., 2000).

The SCL-90-R helps evaluate a broad range of psychological problems and symptoms of psychopathology (Coelho et al., 1999; Kaplan et al., 1998), and is also useful in measuring patient progress or treatment outcomes. It provides an overview of the patients' symptoms and their intensity.

The questionnaire consists of 90 items which measure nine primary symptom dimensions:

somatisation	hostility
obsessive-compulsive	phobic anxiety
interpersonal sensitivity	paranoid ideation
depression	psychoticism
anxiety	

For the purpose of this trial, four of the nine primary symptom dimensions (anxiety, depression, interpersonal sensitivity, and obsessive-compulsive) which reflected the psychological symptoms of the majority of the participants, were measured, and relevant scripts were compiled and read to participants during treatment sessions. The SCL-90-R is seen as a useful instrument in both measuring psychological status and screening for mental disorders (Schauenburg, 1999; Schmitz et al., 2000).

5.6.5 The SF-36 General Health Survey

The Short Form (SF-36) General Health Questionnaire (Stewart, Hays & Ware, 1988) is a validated measure of general health status in IBS patients designed for use in clinical practice and research, health policy evaluations, and general population surveys. It was constructed for use in the Medical Outcomes Study (MOS) to broaden the health concepts measured, and improve measurement precision for each concept over that achieved by the previous short-form questionnaire, the SF-20.

The main improvements in the SF-36, compared to the SF-20, were the addition of items which addressed the patients' vitality and their perception of their general health, and those that distinguished between the physical and mental causes of role limitations and increased measurement precision for physical, role, social, and bodily pain scales (McHorney & Ware, 1995; Ware & Sherbourne, 1992).

The SF-36 has been applied widely to clinical trials and is capable of discriminating between healthy patients and those with moderate levels of psychiatric or physical illness (McHorney, Ware & Raczek, 1993; McHorney, Ware, Lu & Sherbourne, 1994; Russo et al., 1998).

The SF-36 is a 36-item questionnaire consisting of eight health concepts or sub-scales broadly related to quality of life, mental health and social activities:

physical functioning;

role functioning (physical health);

role-functioning (emotional health);

bodily pain;

general health perceptions;

vitality/fatigue;

social functioning;

general mental health; and

reported health transition

Each health concept is comprised of a number of specific questionnaire items and the SF-36 also includes a single item that provides an indication of the participants' perceived change in health over the past week. The health concepts are summarised in *Appendix 8*.

The sensitivity of the SF-36 to change in health status of IBS patients was tested by examining changes in SF-36 sub-scale scores throughout the treatment period and as follow-up two weeks and three months after the completion of the trial.

5.6.6 The Duke-UNC Functional Social Support Questionnaire

Social support encompasses a number of functions or behaviours which can produce a beneficial effect on the health and well-being of people. Functions are usually grouped into one of two types: a health-facilitating function (gratifying human needs for affection, approval, identity) and a stress-reducing function (practical help, problem-solving, advice, information, education) (Suurmeijer et al., 1995).

The Duke-UNC Functional Social Support Questionnaire (Duke-UNC) used in this trial was adapted, with permission, from Broadhead, Gehlbach, De Gruy, & Kaplan (1988).

The 8-item instrument (*Appendix 9*) contains questions in two content areas: confidant support (items 1,3,4,5,7) which reflects a confidant relationship where important matters in life such as social contact and personal/work/financial problems are discussed and shared; and affective support (items 2,6,8) which reflects a more emotional form of support or caring.

Broadhead, Gehlbach, De Gruy & Kaplan (1988) view the Duke-UNC as a short, easy-to-complete questionnaire that should be a cost-effective measurement tool, but acknowledge that it does not cover all the dimensions of social support.

5.6.7 The Survey of Recent Life Experiences (SRLE)

Emotional responses to life stress can influence gastrointestinal function via the brain-gut connection and produce symptoms such as pain and altered bowel function (Lundberg, 2005; Mayer, 2000). In IBS sufferers, however, symptoms are more likely to be more severe and to occur more frequently (Drossman et al. 1999; Salt, 2002). (See *Chapter 2*).

The Survey of Recent Life Experiences (SRLE) was developed by Kohn and McDonald (1992) to measure daily hassles and to eliminate confusion between them and psychological distress that had existed in previous measurements of this kind.

The SRLE consists of 51 items, covering six concepts which are summarised in *Appendix 10.*

The six concepts are:

social and cultural difficulties	finances
work	social acceptability
time pressure	social victimisation

Each of the 51 items has a possible score of from one to four and participants were asked to rate them accordingly.

The possible scores were:

1. *not at all* part of my life
2. *only slightly* part of my life
3. *distinctly* part of my life
4. *very much* part of my life

5.6.8 The Credibility Scale

Research has shown that patient expectancy for improvement is an important variable affecting the outcome of clinical trials (Linde et al. 2007; O'Malley, Roddey, Gartsman & Cook, 2004). The Credibility Scale (Borkovec & Nau, 1972) has been successfully used in the evaluation of blinding and has been shown to have a good internal consistency and test-retest reliability (Vincent, 1989). The Credibility Scale (*Appendix 11*) was issued to subjects on two occasions throughout the trial (week two and week four) to assess the credibility of treatment as perceived by the participants and to test the success of patient blinding.

The 4-item assessment contains questions on how confident the patients are in the treatment they are receiving, how confident they are in recommending the treatment to a friend suffering a similar complaint, how logical the treatment seems to

them, and how successful they think this form of treatment would be in alleviating other complaints.

Each participant was asked to circle the number which most represented their credibility on each of the four questions. The numbers range from one to six - number one, at the extreme left, is marked *not at all confident* and number six is at the extreme right is marked *extremely confident*.

5.7 Summary

The methodological design of this trial was planned to accommodate results of previous trials of hypnotherapy and IBS and to extend them by taking into account the holistic view of a patient's medical profile rather than the physiological aspects only.

Important trial characteristics include:

- a standardised population with defined baseline features
- randomisation
- verification of blinding
- a parallel design with a placebo control group
- an appropriate trial length with a baseline observation phase and extended follow-up
- assessment of compliance

- outcome measures that are disease specific, symptom specific, and also included psychological aspects, degree of stress, quality of life and evidence of a support system
- appropriate data handling and statistical analysis

CHAPTER 6

HYPNOTHERAPY AS A TREATMENT FOR IRRITABLE BOWEL SYNDROME: RESULTS OF A RANDOMISED CONTROLLED TRIAL

CHAPTER 6

HYPNOTHERAPY AS A TREATMENT FOR IRRITABLE BOWEL SYNDROME: RESULTS OF A RANDOMISED CONTROLLED TRIAL

CHAPTER 6 HYPNOTHERAPY AS A TREATMENT FOR IBS: RESULTS OF A RANDOMISED CONTROLLED TRIAL

6.1 Introduction

This chapter reports the results of a clinical trial comparing the use of standard "gut-directed" imagery (which addressed the participants' physiological symptoms only) used in previous hypnosis trials, with individualised imagery that reflected the participants' complete symptom picture (i.e. physiological, psychological, and emotional symptoms). The scientific aims of the trial and the methodology were described in detail in *Chapter 5*.

A total of 51 subjects diagnosed with IBS (44 females and 7 males) aged from 17 to 75 years (mean age 40 years) were recruited over a period of twelve months. The participants were randomised into one of three groups: 17 into the individualised treatment group, 17 into the standard ("gut-directed") group, and 17 into the control group.

Three participants withdrew during the three-month course of the trial - one participant from each group. Participant 2 withdrew in week 2 due to her daughter's illness; participant 15 in week 1 as her medical practitioner advised her against participating in the trial (her scores on the SCL-90-R were high in all four categories - anxiety, depression, interpersonal sensitivity, and obsessive-compulsive disorder - indicating possible major psychological problems); and participant 14 in week 4 with no reason given. Six participants were excluded due to incomplete records, bringing

the total of participants completing the trial to 42 – 14 in each group (*Table 13*). Participants' data on study entry are shown in *Table 14*.

Table 13 **Number of Participants Completed Bowel Symptom Severity Scores at Each Session in the Study by Treatment Group**

Treatment	Baseline	Week 1	Week 2	Week 3	Week 4	Week 5	2 wks	3 mths	Completed all sessions
Group 1	17	17	17	16	16	16	16	15	14
Group 2	17	16	16	15	15	15	15	17	14
Group 3	17	17	17	17	16	16	15	14	14

Note: ID# (Respondents) 2,9,10,14,15,21,31,45,51 (9) have been excluded due to incomplete or missing records (Baseline – End of Treatment periods).

At the commencement of the trial period (as per the IBSQ), the majority of participants (81.6%) suffered abdominal pain most of the time (of these, 59.2% had mild to moderate pain and 40.8% had severe to very severe pain) with 61.2% of participants experiencing pain several times a week or daily. Three months prior to treatment, 98.0% of participants experienced bloating and 78.4% of participants had visual abdominal swelling. Of the 51 participants, 51% were diarrhoea-predominant, 44.9% constipation-dominant, and 4.1% had alternating diarrhoea and constipation. As evidenced in previous research (Chang & Heitkemper, 2002; Salt, 2002), the majority of participants in this study were women (86.3%), and the majority of sufferers were aged between 20-40 (82.3%).

BASELINE DATA – IRRITABLE BOWEL SYMPTOMS

Table 14 Demographic and Baseline Data for Subjects Randomised to the Three Treatment Groups

Variables	Group 1 'Individualised' Group (n=17)		Group 2 Standard 'gut-directed' Group (n=17)		Group 3 Relaxation Group (n=17)		Total (n=51)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Age in year	47.8	38.6-57.1	37.4	31.1-43.6	34.9	27.5-42.4	40.0	35.6-44.5
% Female	88.2	-	82.4		88.2	-	86.3	-
Bowel symptom severity scale								
Distress	18.7	14.9-22.5	17.8	15.0-20.6	21.8	17.9-25.6	19.3	17.4-21.3
Frequency	20.0	17.0-23.0	19.3	17.5-21.1	22.0	19.2-24.8	20.4	19.0-21.8
Interference	16.4	12.2-20.6	16.6	13.5-19.6	20.2	16.2-24.1	17.6	15.6-19.7
SCL-R								
Total								
Depression	19.3	12.8-25.8	15.5	9.9-21.2	17.2	10.9-23.4	17.3	14.0-20.7
Anxiety	8.7	5.8-11.7	9.2	5.1-13.3	10.5	4.8-16.1	9.5	7.1-11.8
Obsessive-Compulsive	11.4	8.0-14.8	11.1	6.9-15.4	11.8	6.7-16.9	11.4	9.1-13.7
Interpersonal Sensitivity	10.5	6.0-15.1	8.8	4.9-12.6	8.5	4.9-12.1	9.3	7.1-11.4
SF - 36								
Physical functioning	75.7	64.0-87.4	92.3	87.3-97.3	79.6	68.8-90.4	82.9	77.4-88.3
Role-physical	53.6	28.3-78.8	63.3	40.6-86.1	55.8	34.3-77.3	57.7	45.4-70.1
Pain	53.0	38.8-67.2	65.3	55.9-74.7	54.7	42.4-67.0	57.9	51.4-64.5
General health	51.6	38.8-64.3	62.7	50.4-75.1	60.0	45.7-73.7	58.1	51.1-65.1
Vitality	45.4	32.4-58.3	49.3	41.7-56.9	35.8	26.3-45.2	43.8	38.2-49.5
Social functioning	55.4	36.274.5	73.3	59.5-87.1	59.6	47.2-72.0	63.1	54.6-71.6
Role-emotional	54.8	32.6-76.9	55.6	30.7-80.4	61.5	38.5-84.6	57.1	44.7-69.6
Mental health	56.0	44.9-67.1	64.0	56.1-71.9	61.5	50.2-72.9	60.6	55.2-66.0

Data are means +- and 95% CI unless otherwise specified.

6.2 Results

6.2.1 Reliability and Validity Testing

For the BSS, analysis of variance (ANOVA) was used to determine the differences among groups at baseline, end of treatment, and follow-up, and repeated measures for trend over time were also determined. All *P* values were 2-tailed, unless otherwise indicated, and the alpha level of significance was set at 0.05. Missing scale and item scores were not replaced. Data for all other outcome measures are presented as per protocol analysis.

6.2.2 Statistical Analysis

Bowel Symptom Severity Scale

Changes on the BSSS for the participants in the study were examined. The BSSS produces three separate scores: symptom frequency, distress, and interference associated with each symptom. The results for each of the three groups, from baseline to the final session, are shown in *Table 15;* and changes over time in the Bowel Symptom Severity scores, tests of within subjects effects, linear trend, and treatment effect are shown in *Table 16.*

Table 15 Bowel Symptom Severity Scale: Mean Scores and Standard Deviation at Each Session from Randomisation

	Baseline		Week-1		Week-2		Week-3		Week-4		Week5	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Frequency												
Group 1	20.0	5.4	21.3	5.3	19.6	4.8	18.7	6.1	17.7	6.0	17.5	6.3
Group 2	19.3	3.2	22.3	4.0	20.1	3.1	20.8	4.7	18.8	4.9	18.5	5.1
Group 3	22.0	4.6	23.2	4.9	21.9	4.2	20.3	4.8	20.2	5.8	17.5	4.9
Distress												
Group 1	18.7	6.8	17.1	6.1	14.9	6.5	14.7	7.1	14.3	6.0	12.9	5.1
Group 2	17.8	4.8	18.6	3.1	16.4	3.7	17.6	4.6	14.6	4.3	14.2	4.2
Group 3	21.8	6.3	21.7	6.9	17.2	4.6	16.1	4.6	15.3	6.0	14.2	4.3
Interference												
Group 1	16.4	7.6	14.5	7.1	13.4	6.3	13.3	7.5	12.5	6.4	11.8	5.0
Group 2	16.6	5.3	16.4	3.2	14.4	2.9	15.4	4.8	13.4	4.1	13.1	4.8
Group 3	20.2	6.5	18.8	6.7	14.7	5.1	13.2	3.8	13.9	5.3	11.6	4.1

Note: ID# (Respondents) 2,9,10,14,15, 21,31,45,51 (9) have been excluded due to incomplete or missing records (Baseline – End of Treatment periods).

Table 16 Bowel Symptom Severity Scores changes over time: Tests of Within-Subjects Effects, Linear Trend, and Treatment Effect

BSSS	**df**	*F*	*p - value*
Frequency			
Main effect of scores over time	5	9.65	.000**
Linear trend of scores to change over time	1	15.94	.000**
Treatment effect	2	.628	n.s.
Distress			
Main effect of scores over time	5	18.34	.000**
Linear trend of scores to change over time	1	44.65	.000**
Treatment effect	2	.924	n.s.
Interference			
Main effect of scores over time	5	16.20	.000**
Linear trend of scores to change over time	1	36.95	.000**
Treatment effect	2	.545	n.s.

** $p < 0.01$. * $p < 0.05$.

Frequency

The mean score for the total sample showed an improvement in symptoms from commencement of treatment (22.2) to the end of treatment (17.8) but the symptom frequency score increased at the two-week follow-up for Group 1 (individualised group) and Group 3 (control group), with a further increase at the three-month follow-up for all 3 groups (*see Table 17*). There was a highly significant fall in the scores on the frequency subscale over time and a highly significant linear trend for scores to change over time.

Table 17 Frequency of Bowel Symptom Severity: Mean Scores and Standard Deviation at Each Session from Randomisation

	Bowel Symptoms Severity - Frequency										
Treatment Groups/	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	20.0	5.4	19.3	3.2	22.0	4.6	20.4	4.5			
Week 1	21.3	5.3	22.3	4.0	23.2	4.9	22.2	4.7			
Week 2	19.6	4.8	20.1	3.1	21.8	4.2	20.5	4.1	8.89**	4.06*	n.s.
Week 3	18.7	6.1	20.8	4.7	20.3	4.8	19.9	5.2			
Week 4	17.7	6.0	18.8	4.9	20.2	5.8	18.8	5.6			
Week 5	17.5	6.3	18.5	5.1	17.5	4.9	17.8	5.4			
2-week Follow-up	19.6	6.4	18.2	4.8	18.8	5.6	18.9	5.6			
3-month Follow-up	22.0	5.3	20.9	5.1	21.5	5.0	21.5	5.0			
Total	19.5	5.7	19.9	4.5	20.7	5.1	20.0	5.2			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Distress

A similar pattern emerged for the scores on the distress subscale with scores for the total sample falling from commencement of treatment (19.0) to the end of treatment (13.7) but a rise for Group 1 (individualised group) and Group 3 (control group) at the two-week follow-up and a further rise for all three groups at the three-

month follow-up (*see Table 18*). There was a highly significant fall in the scores on the distress subscale over time with a highly significant linear trend for scores to change over time.

Table 18 Distress due to Bowel Symptom Severity: Mean Scores and Standard Deviation at Each Session from Randomisation

	Bowel Symptoms Severity - Distress										
Treatment Groups/	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	18.7	6.8	17.8	4.8	21.8	6.3	19.3	6.2			
Week 1	17.1	6.1	18.6	3.1	21.7	6.9	19.0	5.8			
Week 2	14.9	6.5	16.4	3.7	17.2	4.6	16.1	5.1			
Week 3	14.7	7.1	17.6	4.6	16.1	4.6	16.1	5.6	13.50**	23.26**	n.s.
Week 4	14.3	6.0	14.6	4.3	15.3	6.0	14.7	5.4			
Week 5	12.9	5.1	14.2	4.2	14.2	4.3	13.7	4.5			
2-week Follow-up	15.6	7.8	14.1	4.5	15.5	5.9	15.1	6.1			
3-month Follow-up	16.5	7.0	20.9	15.0	16.9	5.6	16.1	5.7			
Total	15.6	6.6	16.0	4.4	17.3	6.0	16.3	5.8			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Interference

A similar pattern emerged for the scores on the interference subscale with symptoms for the total sample improving from commencement of treatment (16.5) to the end of treatment (12.2). There was a rise in symptoms in Group 1 (individualised group) and Group 3 (control group) at the two-week follow-up and a further rise for all three groups at the three-month follow-up (*see Table 19).*

Table 19 **Interference due to Bowel Symptom Severity: Mean Scores and Standard Deviation at Each Session from Randomisation**

	Bowel Symptoms Severity - Interference										
Treatment Groups/	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	16.4	7.6	16.6	5.3	20.2	6.5	17.6	6.6			
Week 1	14.5	7.1	16.4	3.2	18.8	6.7	16.5	6.1			
Week 2	13.4	6.3	14.4	2.9	14.7	5.1	14.1	4.9	11.37***	14.89***	n.s.
Week 3	13.3	7.5	15.4	4.8	13.2	3.7	14.0	5.6			
Week 4	12.5	6.4	13.4	4.1	13.9	5.3	13.2	5.3			
Week 5	11.8	4.9	13.1	4.8	11.6	4.1	12.2	4.6			
2-week Follow-up	13.7	7.5	12.0	4.3	14.2	5.9	13.3	6.0			
3-month Follow-up	15.3	8.3	13.8	4.7	15.5	5.4	14.8	6.3			
Total	13.9	7.0	14.4	4.5	15.3	5.9	14.5	5.9			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

The main effect and linear trend in all three symptom categories (frequency, distress, and interference) for all three treatment groups were significant.

Abdominal Pain

Abdominal pain for all three groups was then compared (*see Table 20 and Figure 5*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had less abdominal pain than the other two groups in week 1 of treatment. Pain was slightly less in week 2 of treatment, increased slightly in week 3, lessened a little in week 4, and lessened more in week 5. At the end of treatment, Group 1 still had less abdominal pain than the other two groups.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had more abdominal pain at baseline and in week 1 than Group 1, but less than Group 3 (control group). The pain lessened in week 2 at the same rate as Group 1 then worsened in week 3 before lessening in weeks 4 and 5. At the end of the treatment period, Group 2 had more abdominal pain than the other two groups.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had more abdominal pain than the other two groups in the first week of treatment. However, the pain lessened gradually over the remaining four weeks of treatment - weeks 2 to 5. At the end of treatment, Group 3 had less pain than Group 2 but more than Group 1.

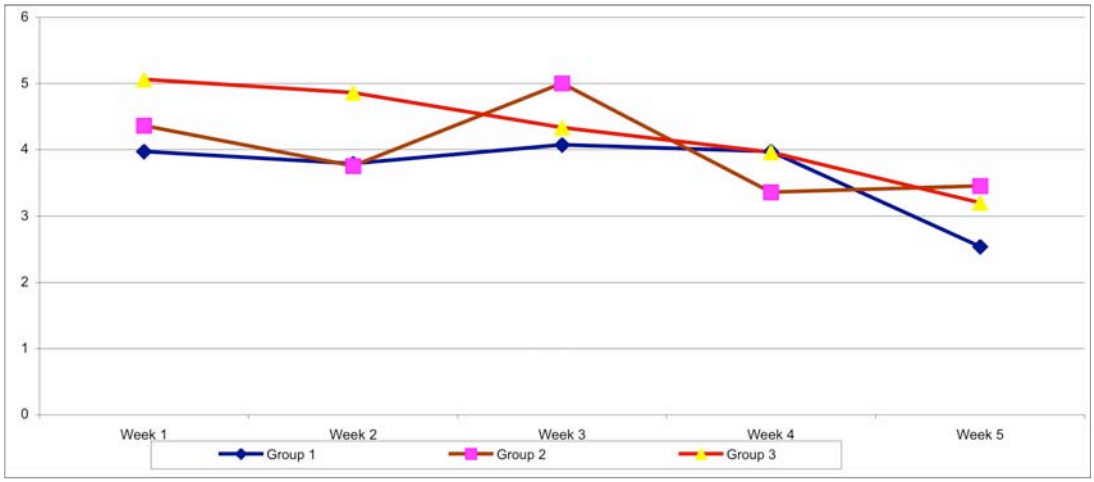
The mean score for the total sample showed a lessening of pain from commencement of treatment (4.5) to the end of treatment (3.1). The main effect and linear trend were highly significant.

Table 20 Irritable Bowel Syndrome: Abdominal Pain: Mean Scores and Standard Deviation at Each Session from Randomisation

Treatment Groups/	Group 1		Group 2		Group 3		Total		F1	F2	F3
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Week 1	4.0	2.2	4.4	2.1	5.1	2.8	4.5	2.4			
Week 2	3.8	2.8	3.8	2.0	4.9	2.6	4.2	2.5	5.54**	17.90**	n.s.
Week 3	4.1	3.3	5.0	2.8	4.3	3.0	4.5	3.0			
Week 4	4.0	2.7	3.4	2.4	4.0	2.5	3.8	2.5			
Week 5	2.5	2.2	3.5	2.8	3.2	2.0	3.1	2.3			
Total	3.7	2.6	4.0	2.4	4.3	2.6	4.0	2.6			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 5 **Irritable Bowel Syndrome - Abdominal Pain by Treatment Groups and Control Group**



Bloating

Bloating was compared for all three groups (*see Table 21 and Figure 6*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had less bloating overall at the commencement of treatment than the other two groups. From week 2 to week 5 the bloating continued to lessen (with a slight rise in week 4) and, at the end of treatment, Group 1 still had less bloating overall than the other two groups.

Comparison of Group 2 to Groups 1&3

At the commencement of treatment, Group 2 (standard 'gut-directed' group) had more bloating than Group 1, but less than Group 3. In week 2, the bloating was less but the score was still higher than Group 1 and less than Group 3. Bloating was more than the other two groups in week 3, and in week 4 the symptoms were the

same as group 1 but still more than group 3. At the end of treatment, bloating was still more than Group 1 and slightly less than Group 3.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had the highest score for bloating overall than the other two groups at commencement of treatment. Bloating lessened gradually over weeks 2 to 5 but, at the end of treatment, Group 3 still had higher scores for bloating than the other two groups.

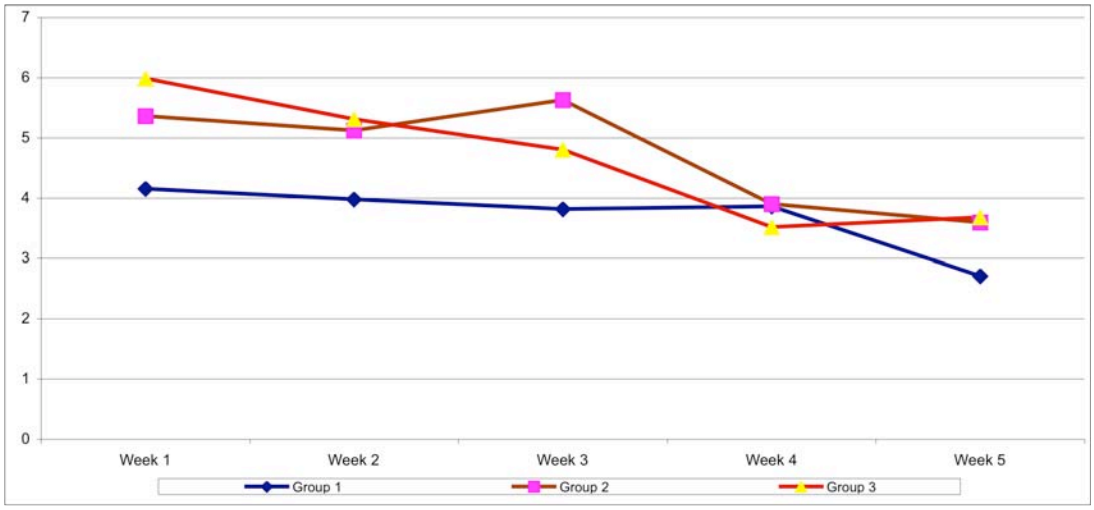
The mean score for the total sample showed an improvement in bloating from commencement of treatment (5.2) to the end of treatment (3.3). The main effect and linear trend were highly significant.

Table 21 Irritable Bowel Syndrome - Bloating: Mean Scores and Standard Deviation at Each Session from Randomisation

	Irritable Bowel Syndrome - Bloating										
Treatment Groups/ *Sessions*	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Week 1	4.2	2.5	5.4	2.5	6.0	2.4	5.2	2.5			
Week 2	4.0	3.0	5.1	2.6	5.3	2.4	4.8	2.7	9.23**	33.40**	n.s.
Week 3	3.8	2.4	5.6	3.0	4.8	3.2	4.7	2.9			
Week 4	3.9	2.6	3.9	2.8	3.5	2.6	3.8	2.7			
Week 5	2.7	2.5	3.6	3.2	3.7	2.2	3.3	2.6			
Total	3.7	2.6	4.7	2.9	4.7	2.7	4.4	2.8			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 6 **Irritable Bowel Syndrome - Bloating by Treatment Groups and Control Group**



Constipation

The scores for constipation were then compared for all three groups (*see Table 22 and Figure 7*).

Comparison of Group 1 to Groups 2&3

At week 1, the score for Group 1 (individualised group) was slightly higher than Group 2 but less than Group 3. From week 2 to 4 constipation lessened, and in week 5 it rose slightly. At the end of treatment, Group 1 had less constipation than the other two groups.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had less constipation at the commencement of treatment than the other two groups but the scores rose in weeks 2 and 3. In weeks 4 and 5 the scores for constipation dropped and, at the end of

treatment, Group 2 had a slightly higher score than Group 1 and a slightly lower score than Group 3.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had the highest score for constipation compared to the other two groups. During weeks 2 to 4 constipation gradually lessened but increased in week 5. At the end of treatment, Group 3 still had the highest score for constipation.

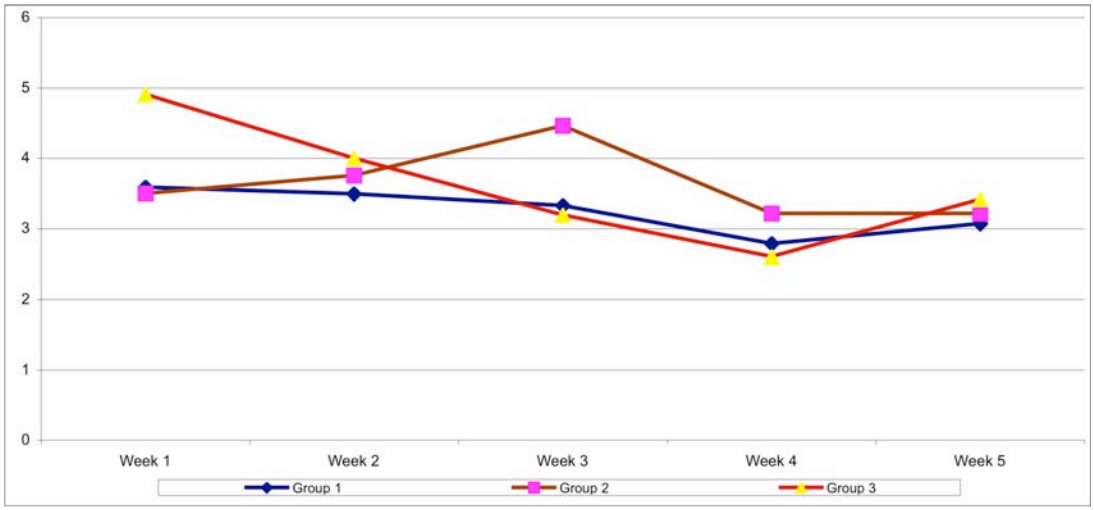
The mean score for the total sample showed an improvement in symptoms from the commencement of treatment (4.0) to the end of treatment (3.2). The main effect and linear trend were significant.

Table 22 Irritable Bowel Syndrome - Constipation: Mean Scores and Standard Deviation at Each Session from Randomisation

	Irritable Bowel Syndrome - Constipation										
Treatment Groups/ *Sessions*	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Week 1	3.6	3.0	3.5	2.9	4.9	2.6	4.0	2.9			
Week 2	3.5	3.5	3.8	3.1	4.0	2.9	3.8	3.1			
Week 3	3.3	2.8	4.5	3.2	3.2	2.7	3.6	2.9	2.66*	5.43*	n.s.
Week 4	2.8	2.4	3.2	2.5	2.6	2.4	2.9	2.4			
Week 5	3.1	2.5	3.2	3.2	3.4	3.0	3.2	2.8			
Total	3.3	2.8	3.6	3.0	3.6	2.8	3.5	2.8			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 7 **Irritable Bowel Syndrome - Constipation by Treatment Groups and Control Group**



Diarrhoea

Scores for diarrhoea were then examined for the three treatment groups (*see Table 23 and Figure 8*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had higher scores than both Group 2 and Group 3 at the commencement of treatment. Improvement was gradual through weeks 2 to 4 (with a slight rise in week 5), the final score being lower than the other two groups.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had a lower score than Group 1 but a higher score than Group 3 at the commencement of treatment. Symptoms improved

in week 2, worsened in week 3, improved in week 4, and worsened again in week 5. At the end of treatment, Group 2 had higher scores than both the other two groups.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had the lowest score for diarrhoea at the commencement of treatment. Symptoms lessened in week 2, worsened in weeks 3 and 4, and then lessened again in week 5. At the end of treatment, Group 3 had a higher score than Group 1 but a lower score than Group 2.

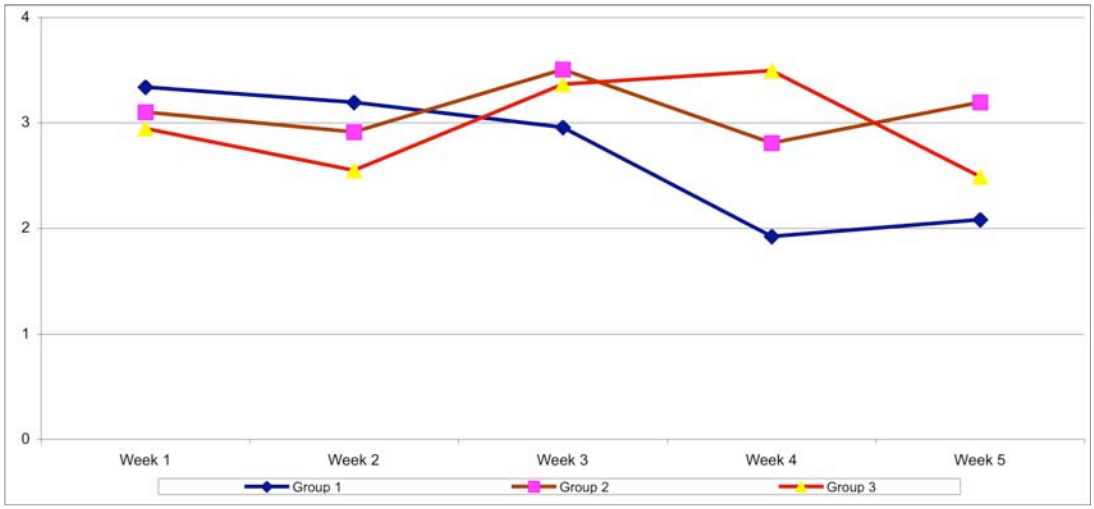
The mean score for the total sample showed a lessening of symptoms from commencement of treatment (3.1) to the end of treatment (2.6). The main effect and linear trend were not significant.

Table 23 **Irritable Bowel Syndrome - Diarrhoea: Mean Scores and Standard Deviation at Each Session from Randomisation**

	Irritable Bowel Syndrome - Diarrhoea										
Treatment Groups/	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Week 1	3.3	2.7	3.1	3.1	2.9	2.6	3.1	2.7			
Week 2	3.2	2.7	2.9	2.1	2.5	3.0	2.9	2.6	n.s.	n.s.	n.s.
Week 3	3.0	2.9	3.5	3.1	3.4	2.9	3.3	2.9			
Week 4	1.9	2.4	2.8	2.8	3.5	3.1	2.7	2.8			
Week 5	2.1	2.5	3.2	2.8	2.5	2.4	2.6	2.6			
Total	2.7	2.6	3.1	2.8	3.0	2.7	2.9	2.7			

F1=main effect; F2=linear trend; F3=treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 8 **Irritable Bowel Syndrome - Diarrhoea by Treatment Groups and Control Group**



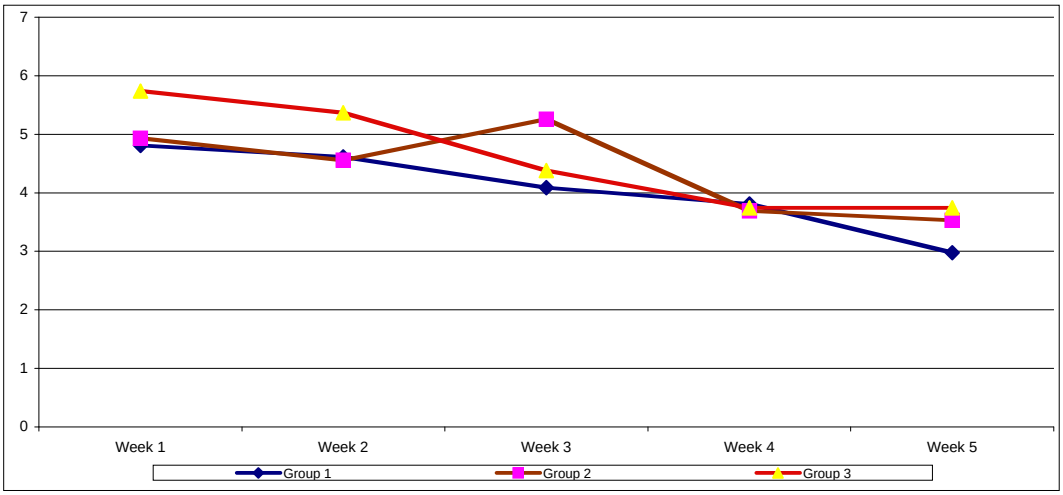
The overall severity of symptoms (pain, bloating, constipation, and diarrhoea) had gradually decreased in all three groups from commencement of treatment (5.2) to the end of treatment (3.4) with Group 2 having a worsening of symptoms in week 3 (*see Table 24 and Figure 9*). The main effect and linear trend were highly significant.

Table 24 **Irritable Bowel Syndrome - Overall Severity: Mean Scores and Standard Deviation at Each Session from Randomisation**

	Irritable Bowel Syndrome - Overall Severity										
Treatment Groups/ *Sessions*	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Week 1	4.8	2.0	4.9	1.9	5.7	2.0	5.2	2.0	8.67**	28.96**	n.s.
Week 2	4.6	2.8	4.6	1.8	5.4	1.9	4.9	2.2			
Week 3	4.1	2.6	5.3	2.7	4.4	2.5	4.6	2.6			
Week 4	3.8	2.2	3.7	2.5	3.7	2.6	3.7	2.4			
Week 5	3.0	2.1	3.5	3.0	3.7	1.8	3.4	2.3			
Total	4.1	2.4	4.4	2.4	4.6	2.3	4.4	2.4			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 9 **Irritable Bowel Syndrome - Overall Severity by Treatment Groups and Control Group**



SF-36 General Health Survey

Table 25 **General Health Outcomes Short Form 36 (SF-36): Mean Scores and Standard Deviations, by Treatment Group, by Health Concepts at Each Session from Randomisation**

	Baseline		Week-1		Week-2		Week-3		Week-4		Week5	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Physical Functioning												
Group 1	75.7	20.3	81.8	14.9	81.8	17.5	84.6	12.6	84.6	14.6	84.3	17.9
Group 2	92.3	9.0	91.3	12.2	92.0	10.1	89.3	12.8	96.0	7.6	94.7	6.1
Group 3	79.6	17.9	78.1	22.6	80.4	22.2	80.8	24.7	80.8	24.5	82.7	25.3
Role-Physical												
Group 1	53.6	43.7	58.9	42.3	60.7	41.3	51.8	46.5	50.0	40.4	60.7	45.7
Group 2	63.3	41.0	65.0	40.0	68.3	36.0	63.3	35.2	75.0	37.8	81.7	29.1
Group 3	55.8	35.6	51.9	45.2	51.9	37.5	65.4	31.5	51.9	42.7	51.9	45.0
Pain												
Group 1	53.0	24.6	60.2	18.8	54.1	21.0	62.2	23.1	61.0	24.9	67.2	17.9
Group 2	65.3	20.0	67.7	15.5	70.1	17.5	66.8	25.6	78.3	19.4	77.1	24.6
Group 3	54.7	20.3	52.9	18.8	54.5	21.5	65.5	19.7	68.8	19.4	67.9	18.2
General health												
Group 1	51.6	22.1	52.5	19.4	52.4	20.4	54.3	21.4	56.4	20.8	59.9	21.4
Group 2	62.3	22.4	62.5	23.5	62.1	23.9	62.1	20.6	63.5	25.1	65.3	25.3
Group 3	60.0	23.2	62.4	24.6	60.9	20.8	63.5	21.8	64.5	21.3	63.3	24.4
Vitality												
Group 1	45.4	22.5	42.1	21.6	43.2	26.0	41.8	26.6	43.6	29.6	48.9	27.8
Group 2	49.3	13.7	50.0	21.8	48.0	21.3	51.3	18.0	58.0	20.7	59.7	23.3

Note: ID# (Respondents) 2,9,10,14,15,21,31,45,51 (9) have been excluded due to incomplete or missing records.

Table 26 Medical Outcomes Index Mean Changes Over Time: Tests of Within-Subjects Effects, Linear Trend, and Treatment Effect

SF-36	**df**	*F*	*p - value*
Physical functioning			
Main effect of scores over time		2.7	.022*
Linear trend of scores to change over time		6.48	.015*
Treatment effect		2.57	n.s.
Role-physical			
Main effect of scores over time	5	.35	n.s.
Linear trend of scores to change over time	1	.66	n.s.
Treatment effect	2	.99	n.s.
Pain			
Main effect of scores over time	5	6.23	.000**
Linear trend of scores to change over time	1	23.99	.000**
Treatment effect	2	2.15	n.s.
General health			
Main effect of scores over time	5	2.27	.049*
Linear trend of scores to change over time	1	6.00	.019*
Treatment effect	2	.704	n.s.
Vitality			
Main effect of scores over time	5	3.20	.008**
Linear trend of scores to change over time	1	5.68	.022*
Treatment effect	2	2.20	n.s.
Social functioning			
Main effect of scores over time	5	5.13	.000**
Linear trend of scores to change over time	1	11.77	.001**
Treatment effect	2	1.164	n.s.
Role-emotional			
Main effect of scores over time	5	1.63	.153
Linear trend of scores to change over time	1	4.45	.041*
Treatment effect	2	.586	n.s.
Mental health			
Main effect of scores over time	5	5.99	.000**
Linear trend of scores to change over time	1	15.61	.000**
Treatment effect	2	.488	n.s.

**p <0.01.*p <0.05. Note: ID# (Respondents) 2,9,10,14,15,21,31,45,51 (9) have been excluded due to incomplete or missing records during sessions (Baseline – End of treatment periods).

The effects of the treatment on the subscales on the SF-36 (a measure of quality of life) were examined over the five treatment sessions; the results are shown in *Table 25*. Within-subjects effects, linear trend, and treatment effect are shown in

Table 26. The SF-36 has eight subscales: physical functioning, role-physical, pain, general health, vitality, social functioning, role-emotional, and mental health.

Physical Functioning

The scores relating to physical functioning indicate the extent to which health limits physical activities such as self-care, walking, climbing stairs, bending, lifting, and moderate and vigorous exercise. A high score indicates that participants perform all types of physical activities without limitations due to health. A low score indicates that participants are greatly limited in performing all physical activities.

All three groups had above average scores, indicating that there were few limitations in performing physical activities due to health (*see Table 27 and Figure 10*), and all three groups showed improvement in physical functioning at the end of the follow-up period compared to baseline.

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had lower scores at baseline than both Groups 2 and 3 but, at the commencement of treatment, had lower scores than Group 2 and higher scores than Group 3. Improvement was gradual during weeks 2 to 4 with a slight decline at week 5; lower at the two-week follow-up; then slightly higher than week 5, and higher than baseline, at the three-month follow-up.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had the highest score of the three groups both at baseline and at commencement of treatment. There was a slight improvement in week 2; a slight decline in week 3; a greater improvement in week 4; and, although there was a slight decline again in week 5, the score for that week was higher than scores at both week 1 and baseline. There was an improvement in symptoms during both the two-week follow-up and the three-month follow-up (with a slightly lower score at the two-week follow–up). The scores for the follow-up period were higher than baseline and at the commencement of treatment.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had a higher baseline score than Group 1 and a lower baseline score than Group 2, but had the lowest score of all three groups at the commencement of treatment. There was a gradual improvement in symptoms during the remainder of the treatment sessions and during the follow-up period (with a slightly lower score at the three-month follow-up), with both scores at follow-up higher than those at baseline.

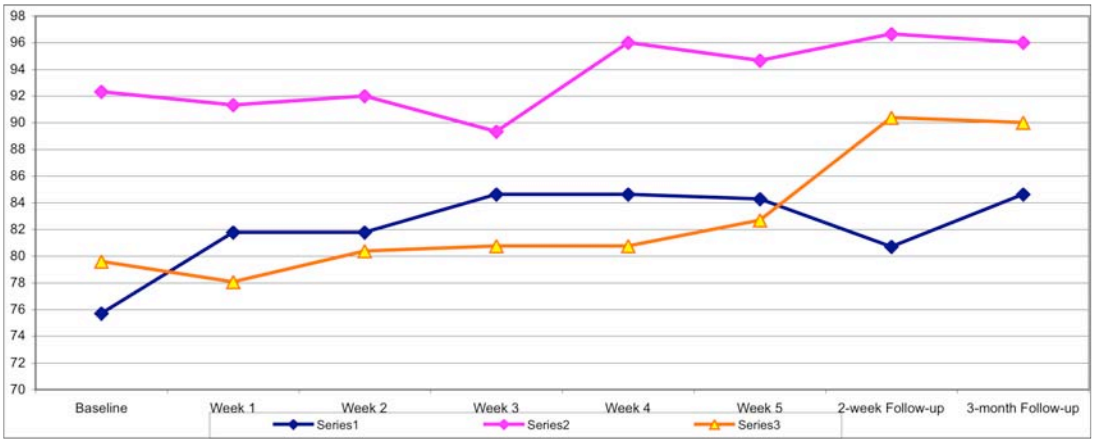
The mean score for the total sample showed improvement in physical functioning from commencement of treatment (84.0) to the end of treatment (87.5). The main effect and the linear trend were highly significant.

Table 27 **Secondary Health Outcome – Physical Functioning**

Treatment Groups/ *Sessions*	Group 1		Group 2		Group 3		Total		F1	F2	F3
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	75.7	20.3	92.3	9.0	79.6	17.8	82.9	17.5			
Week 1	81.8	14.9	91.3	12.2	78.1	22.6	84.0	17.4			
Week 2	81.8	17.5	92.0	10.1	80.4	22.2	85.0	17.5			
Week 3	84.6	12.6	89.3	12.8	80.8	24.7	85.1	17.2			
Week 4	84.6	14.6	96.0	7.6	80.8	24.5	87.5	17.5	3.05**	9.99**	n.s.
Week 5	84.3	17.9	94.7	6.1	82.7	25.3	87.5	18.2			
2-week Follow-up	80.7	26.0	96.7	5.2	90.4	14.2	89.4	18.1			
3-month Follow-up	84.6	18.5	96.0	5.4	90.0	13.1	90.4	13.9			
Total	82.3	17.9	93.5	9.1	82.8	20.8	86.5	17.2			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 10 **Secondary Health Outcome - Physical Functioning by Treatment Groups and Control Group**



Role Functioning – physical

Role functioning – physical is the extent to which physical health interferes with work or daily activities, such as accomplishing less than wanted, and limitations or difficulty in performing activities. A high score indicates that there are no limits due to physical health. A low score indicates that there are limits with work and daily activities due to physical health.

At baseline, all three groups had only slightly above average scores which showed some indication of interference in their work or daily activities due to physical health. The scores for all three groups at the 3-month follow-up were higher than at baseline (*see Table 28 and Figure 11*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had the lowest scores of the three groups at baseline and lower scores than Group 2, but higher scores than Group 3 at the commencement of treatment. The participants' physical health improved slightly in week 2, lessened in weeks 3 and 4, and then improved to the same score as in week 2. Interference with work or activities worsened slightly during the 2-week follow-up and then, in the 3-month follow-up, the participants' physical health improved to the same score as in week 1 and higher than baseline.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had higher scores than the other two groups at baseline and at the commencement of treatment, with a gradual improvement in symptoms (with the exception of week 3) through to week 5. There was a slight decline during the follow-up period but the follow-up scores were higher than at baseline and at the commencement of treatment.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had higher scores than Group 1 and lower scores than Group 2 at baseline, but lower scores than the other two groups at the commencement

of treatment. There was an improvement in week 3 and then the scores for weeks 4 and 5 were the same as at the commencement of treatment. However, symptoms improved during the follow-up period, both scores for the 2-week follow-up and the 3-month follow-up being higher than the scores at baseline and at the commencement of treatment.

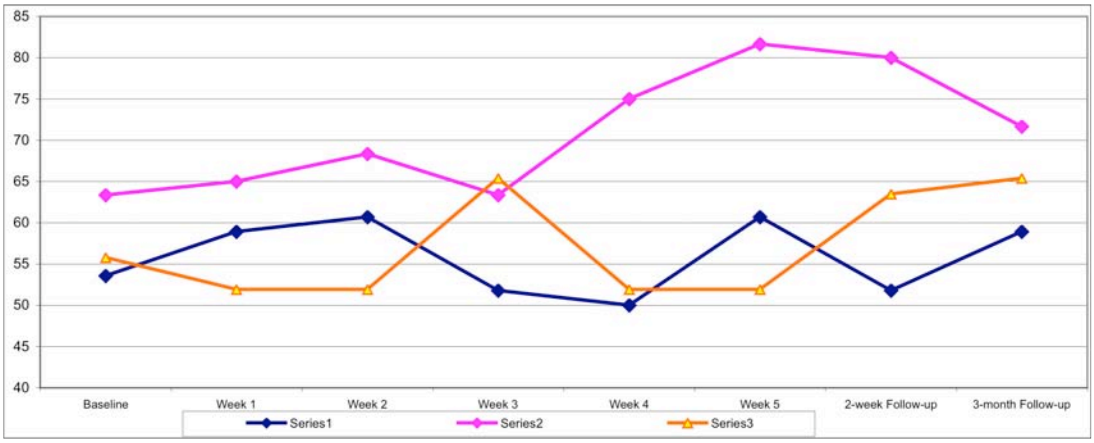
The mean score for the total sample showed improvement in participants' limitations due to physical health from commencement of treatment (58.9) to the end of treatment (65.5). The main effect and linear trend were not significant.

Table 28 **Secondary Health Outcome – Role Physical**

Treatment Groups/	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	53.6	43.7	63.3	41.0	55.8	35.6	57.7	39.6			
Week 1	58.9	42.3	65.0	39.9	51.9	45.0	58.9	41.6			
Week 2	60.7	41.3	68.3	35.9	51.9	37.4	60.7	37.9			
Week 3	51.8	46.5	63.3	35.2	65.4	31.5	60.1	37.9			
Week 4	50.0	40.4	75.0	37.8	51.9	42.6	59.5	40.9	0.6	2.15	n.s.
Week 5	60.7	45.7	81.7	29.1	51.9	45.0	65.5	41.3			
2-week Follow-up	51.8	46.5	80.0	35.6	63.5	44.0	65.5	42.8			
3-month Follow-up	58.9	40.0	71.7	41.0	65.4	38.9	65.5	39.4			
Total	55.8	42.2	71.0	36.7	57.2	39.4	61.7	39.9			

F1 = main effect; F2 = linear trend; F3 = treatment effect ; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 11 **Secondary Health Outcome - Role Physical -Treatment Groups and Control Group**



Bodily Pain

Bodily pain is the intensity of pain and effect of pain on normal work, both inside and outside the home. A high score indicates that there was no pain or limits in the week before the completion of the questionnaire. A low score indicates severe and extremely limiting pain.

The scores for all three groups indicated that pain had an effect on the participants' normal work, and all three groups showed improvement in symptoms from the commencement of treatment (60.6) to the end of the treatment sessions (71.0) (*see Table 29 and Figure 12*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had the lowest score of the three groups at baseline, and a lower score than Group 2, and a higher score than Group 3 at the commencement of treatment. Pain increased in week 2, lessened in week 3, increased

slightly again in week 4 and then lessened in week 5 to a higher score than at baseline and at the commencement of treatment. During the 2-week follow-up, symptoms worsened slightly but improved in the three-week follow-up to higher scores than at baseline and at the commencement of treatment.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had higher scores than the other two groups both at baseline and at the commencement of treatment - improvement in symptoms was also higher than the other two groups at the end of treatment. Apart from a slight worsening of symptoms in week 3, symptoms gradually improved up until week 5. There was a slight worsening of symptoms during the follow-up period, but the scores during both the 2-week follow-up and the 3-month follow-up were higher than the scores at baseline and at the commencement of treatment.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had higher scores than Group 1 and lower scores than Group 2 at baseline, but lower scores than either of the other two groups at the commencement of treatment, indicating that pain had more of an effect on their normal work than on participants in the other two groups. Except for a slight decline in week 5, symptoms improved gradually over the treatment period with the scores in week 5 being higher than the scores for the group at baseline and at commencement of treatment. Symptoms continued to improve at the 2-week follow-up but declined at the 3-month follow-up. The follow-up scores were higher than the scores both at baseline and at the commencement of treatment.

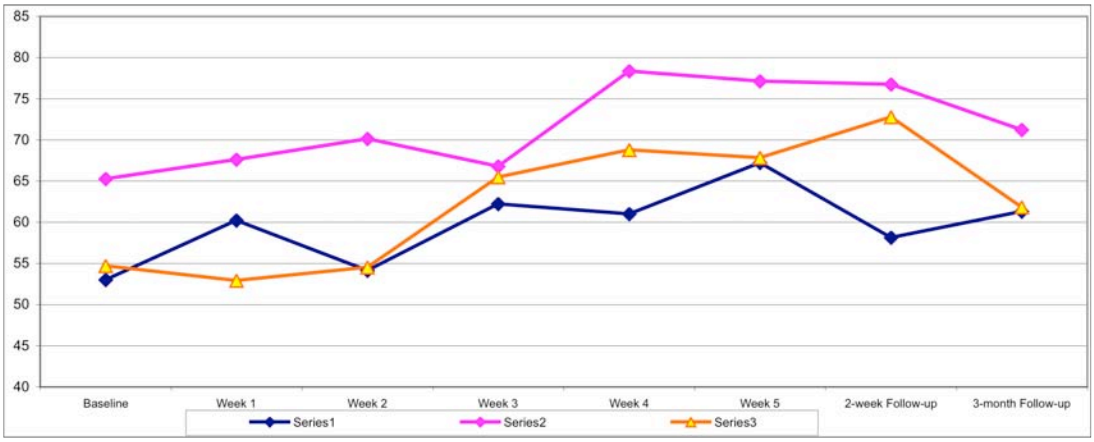
The main effect and the linear trend were highly significant.

Table 29 **Secondary Health Outcome – Pain**

Treatment Groups/ *Sessions*	Group 1		Group 2		Group 3		Total		F1	F2	F 3
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	53.0	24.6	65.3	16.9	54.7	20.3	57.9	21.0			
Week 1	60.2	18.8	67.6	15.5	52.9	18.8	60.6	18.3			
Week 2	54.1	21.0	70.1	17.5	54.5	21.5	60.0	21.0			
Week 3	62.2	23.1	66.8	25.5	65.5	19.7	64.9	22.6			
Week 4	61.0	24.9	78.3	19.4	68.8	19.4	69.6	22.1	5.22**	13.05**	n.s
Week 5	67.2	17.9	77.1	24.6	67.8	18.2	71.0	20.7			.
2-week Follow-up	58.1	23.5	76.7	22.8	72.8	20.3	69.3	23.2			
3-month Follow-up	61.3	23.6	71.2	17.7	61.8	19.8	65.0	20.5			
Total	59.7	22.0	71.7	20.3	62.4	20.4	64.8	21.5			

F1 = main effect; F2 = linear trend; F3 = treatment effect ; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 12 **Secondary Health Outcome - Pain by Treatment Groups and Control Group**



General Health Perceptions

General Health Perceptions are the personal evaluations of health by the participants. A high score indicates that the participants perceive their health as excellent. A low score indicates that participants perceive their health as poor.

All participants rated their health as slightly above average at baseline (58.1) and at the commencement of treatment (59.1), and all felt they had improved a little by the end of the five weeks of treatment (62.9) (*see Table 30 and Figure 13*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had lower scores than the other two groups at baseline and at the commencement of treatment but their perception of health continued to improve through to week 5. During the follow-up period, scores dropped slightly in the 2-week follow-up but increased at the 3-month follow-up, with the final scores being higher than those in week 1 and at baseline.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had higher scores than the other two groups at baseline and at the commencement of treatment and, apart from slightly lower scores in weeks 2 and 3, continued to improve both throughout the treatment period and the follow-up period. Scores at the end of both the treatment and follow-up periods were slightly higher than at baseline and at the commencement of treatment.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had higher scores than Group 1 and lower scores than Group 2 at baseline, and slightly lower scores than group 2 and higher scores than group 1 at the commencement of treatment. Even though there was a slight variation in scores throughout treatment, perception in health continued to improve overall

compared to baseline. At the two-week follow-up the scores were slightly higher than at the commencement of the treatment but at the 3-month follow-up the scores were slightly lower. The follow-up scores were higher than at baseline.

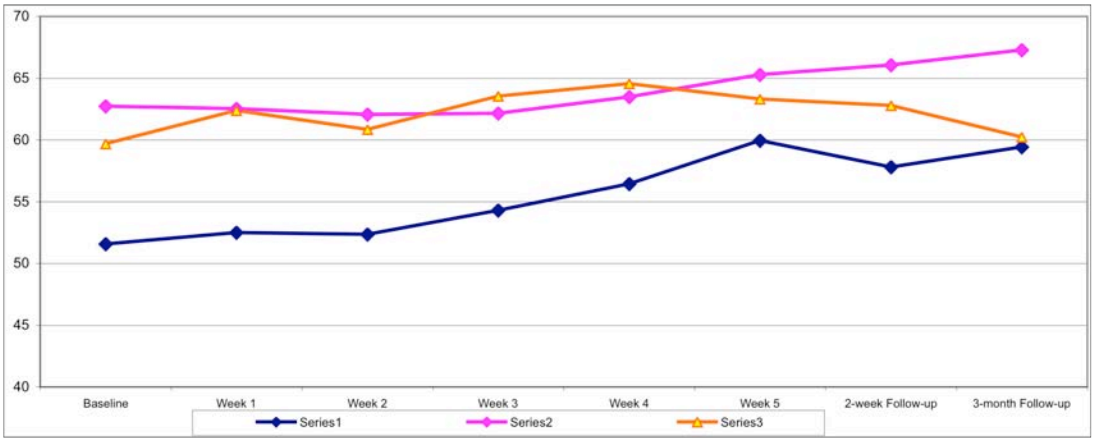
The main effect and linear trend were significant.

Table 30 **Secondary Health Outcome – General Health Perceptions**

Treatment Groups/	Group 1		Group 2		Group 3		Total		F1	F2	F3
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	51.6	22.1	62.7	22.4	59.7	23.2	58.1	22.5			
Week 1	52.5	19.4	62.5	23.5	62.4	24.6	59.1	22.5			
Week 2	52.4	20.3	62.1	23.9	60.8	20.8	58.5	21.7			
Week 3	54.3	21.4	62.1	20.6	63.5	21.8	60.0	21.1	2.33*	5.73*	n.s.
Week 4	56.4	20.8	63.5	25.1	64.5	21.3	61.5	22.4			
Week 5	59.9	21.3	65.3	25.3	63.3	24.4	62.9	23.3			
2-week Follow-up	57.8	18.7	66.1	23.8	62.8	26.8	62.3	22.9			
3-month Follow-up	59.4	20.4	67.3	23.4	60.2	24.9	62.5	22.7			
Total	55.5	20.2	63.9	22.9	62.2	22.8	60.6	22.2			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 13 **Secondary Health Outcome - General Health Perceptions by Treatment Groups and Control Group**



Vitality

Vitality indicates how energetic or tired participants are. A high score indicates that the participants felt full of energy during the week prior to their treatment session. A low score on this health measure indicated that the participants felt tired and worn out all the time. The energy level increased in all three groups – the mean score for the total sample was 42.7 at the commencement of treatment and 52.0 at the end of treatment (*see Table 31 and Figure 14*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had lower scores than Group 2 but higher scores than Group 3 at both baseline and at the commencement of treatment sessions. The participants showed a gradual improvement in energy levels throughout the treatment period with the exception of a slight decrease in week 3. Scores decreased during the follow-up period. At the two-week follow-up, scores were higher than those at baseline and at the commencement of treatment, and at the three-month follow-up, scores were higher than at baseline but lower than at the commencement of treatment.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had higher scores than the other two groups at baseline and at the commencement of treatment and, except for a slight drop in week 2, continued to improve throughout the treatment period. During the 2-week follow-up period, energy levels continued to rise but dropped slightly in the 3-

month follow-up. Once again, the scores at the 3-month follow-up were higher than those at baseline and at the commencement of treatment.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had the lowest scores on vitality at baseline and at the commencement of treatment, and except for a slight decline in energy in week 4, participants continued to improve during the treatment period. Symptoms worsened slightly during both the 2-week follow-up and the 3-month follow-up but the scores were still above those at baseline and at the commencement of treatment.

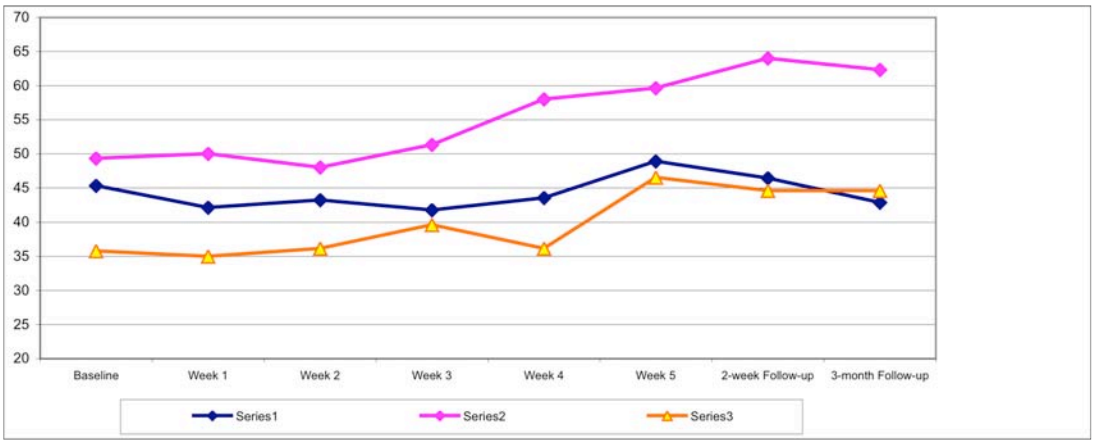
The main effect and linear trend were highly significant.

Table 31 **Secondary Health Outcome – Vitality**

Treatment Groups/	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	45.4	22.5	49.3	13.7	35.8	15.7	43.8	18.1			
Week 1	42.1	21.6	50.0	21.8	35.0	16.2	42.7	20.6			
Week 2	43.2	26.0	48.0	21.3	36.2	17.5	42.7	22.0			
Week 3	41.8	26.6	51.3	18.0	39.6	21.9	44.5	22.4			
Week 4	43.6	29.6	58.0	20.7	36.2	21.1	46.4	25.3	4.66**	15.57**	n.s.
Week 5	48.9	27.7	59.7	23.3	46.5	20.0	52.0	24.1			
2-week Follow-up	46.4	26.6	64.0	20.6	44.6	19.9	52.1	23.8			
3-month Follow-up	42.9	25.2	62.3	16.2	44.6	21.6	50.4	22.6			
Total	44.3	25.1	55.3	20.0	39.8	19.2	46.8	22.6			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 14 **Secondary Health Outcome - Vitality by Treatment Groups and Control Group**



Social Functioning

Social functioning is the extent to which physical health or emotional problems interfere with normal social activities. A high score indicates that there is no interference from health in social activities. A low score indicates extreme interference with social activities.

The scores of all three groups indicated that the participants' physical health or emotional problems interfered to some degree with their social activities. All three groups showed improvement from commencement of treatment (72.3) to the end of treatment (80.4). (*See Table 32 and Figure 15*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had lower scores than both Group 2 and Group 3 at baseline, and lower scores than Group 2 and slightly higher scores than Group 3 at the commencement of treatment. The participants showed a gradual

improvement in the extent to which physical health or emotional problems interfere with normal social activities throughout the treatment period with the exception of a slight decrease in weeks 3 and 4. Scores decreased during the follow-up period to below those in week 1, but above the scores at baseline.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) showed the least interference from health in their social activities at baseline and at the commencement of treatment compared to the other two groups. Except for a slight decrease in week 3, the group continued to improve throughout the treatment period with a decrease during the follow-up period. The follow-up scores, however, were higher than those at baseline and in the first week of treatment, indicating that their social functioning had improved.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had higher scores than Group 1 and lower scores than Group 2 at baseline and the lowest scores of the three groups at the commencement of treatment. Scores declined slightly in week 2, rose sharply in week 3, decreased in weeks 4 and 5 with the scores at the end of treatment higher than those in week 1. Scores declined during the follow-up period but were higher than at baseline and in the first week of the treatment period.

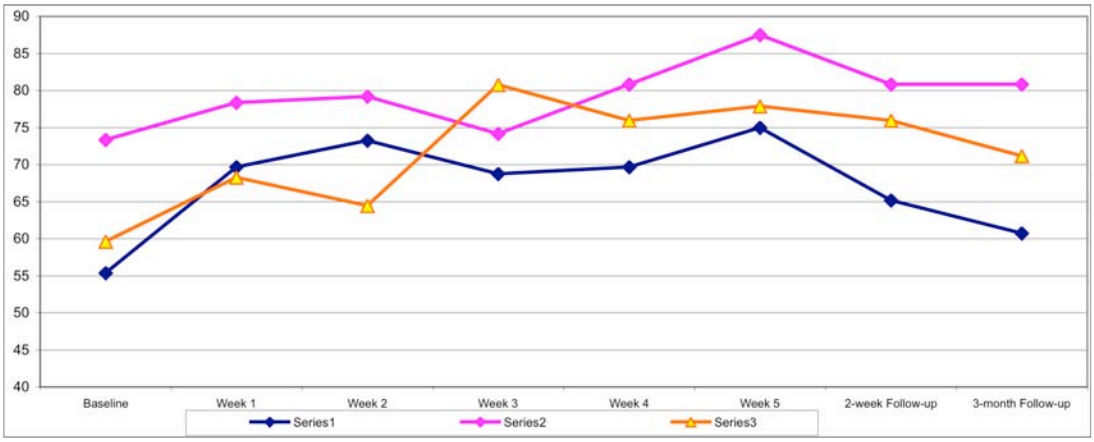
The main effect was highly significant but the linear effect was not significant.

Table 32 **Secondary Health Outcome – Social Functioning**

Treatment Groups/ *Sessions*	Group 1		Group 2		Group 3		Total		F1	F2	F3
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	55.4	33.1	73.3	24.9	59.6	20.5	63.1	27.3			
Week 1	69.6	28.9	78.3	21.4	68.3	23.2	72.3	24.5			
Week 2	73.2	25.9	79.2	19.9	64.4	22.7	72.6	23.1			
Week 3	68.8	25.4	74.2	20.3	80.8	18.8	74.4	21.7			
Week 4	69.6	28.0	80.8	21.1	76.0	20.1	75.6	23.3	3.75**	3.91	n.s.
Week 5	75.0	29.0	87.5	23.1	77.9	22.9	80.4	25.2			
2-week Follow-up	65.2	26.5	80.8	20.0	76.0	23.6	74.1	23.8			
3-month Follow-up	60.7	30.2	80.8	18.2	71.2	21.3	71.1	24.6			
Total	67.2	28.2	79.4	21.0	71.8	22.0	73.0	24.4			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 15 **Secondary Health Outcome - Social Functioning by Treatment Groups and Control Group**



Role Functioning-emotional

Role-functioning-emotional is the extent to which emotional problems interfere with work or other daily activities, including decreased time spent on activities, accomplishing less, and not working as carefully as usual. A high score indicates no limits due to emotional problems. A low score indicates that there are limits due to emotional problems.

At baseline, and in the first week of treatment, the scores for all three groups indicated that emotional problems were part of the patients' symptom picture (*see Table 33 and Figure 16*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had lower scores than the other two groups at baseline, and lower scores than Group 2, and higher scores than Group 3 at the commencement of treatment. There was a decline in scores in week 2, a gradual improvement through to week 5, and then a further decline during the follow-up period. The scores in the 2-week follow-up period were the same as at baseline with the scores in the 3-month follow-up lower than scores both at baseline and in the first week of treatment.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had a higher score than Group 1 and a lower score than Group 3 at baseline with higher scores than the other two groups at the commencement of treatment. Group 2 showed improvement in emotional functioning with identical scores from week 3 to the 2-week follow-up. The scores then increased further in the 3-month follow-up to a higher level than scores both at baseline and in week 1.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had the highest scores at baseline and the lowest scores of the three groups at the commencement of treatment. Scores for weeks 1 and

2 were the same with an improvement in week 3. Symptoms worsened slightly in week 4 and then improved in week 5. There was a slight decline in scores during the 2-week follow-up and an improvement in the 3-month follow-up, with scores for the two-week follow-up period being both lower, and scores for the three-month follow-up being higher than at baseline and at the commencement of treatment.

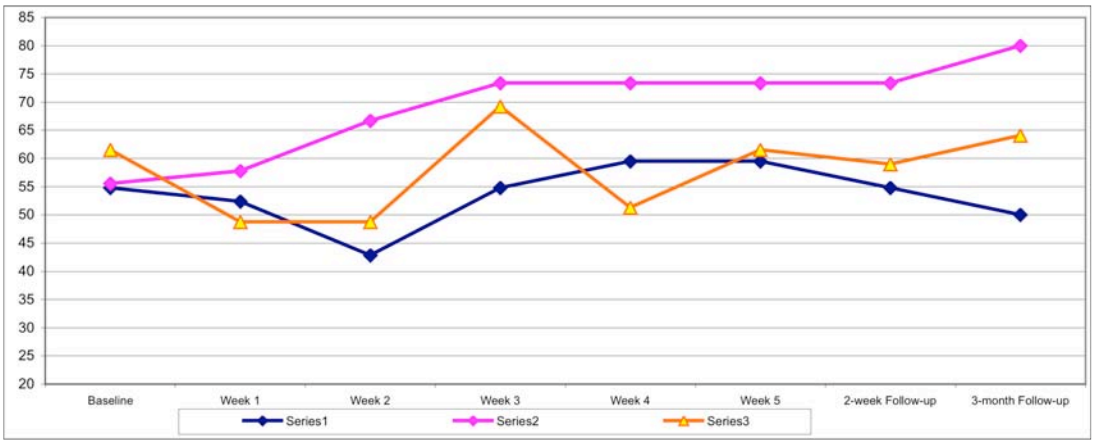
The mean score for the total sample showed an improvement in limits due to emotional problems from the commencement of the treatment (53.2) to the end of treatment (65.1). The main effect and linear effect were not significant.

Table 33 **Secondary Health Outcome – Role Emotional**

Treatment Groups/	**Group 1**		**Group 2**		**Group 3**		**Total**		**F1**	**F2**	**F3**
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	54.8	38.4	55.6	44.8	61.5	38.1	57.1	39.8			
Week 1	52.4	44.7	57.8	38.8	48.7	44.3	53.2	41.7			
Week 2	42.9	42.2	66.7	43.6	48.7	46.4	53.2	44.2			
Week 3	54.8	50.0	73.3	36.1	69.2	37.2	65.9	41.3			
Week 4	59.5	41.7	73.3	40.2	51.3	44.3	61.9	42.0	1.53	3.86	n.s.
Week 5	59.5	39.6	73.3	45.8	61.5	44.8	65.1	42.9			
2-week Follow-up	54.8	40.5	73.3	42.2	59.0	47.4	62.7	43.1			
3-month Follow-up	50.0	40.8	80.0	35.2	64.1	44.0	65.1	41.0			
Total	53.6	41.3	69.2	40.6	58.0	42.6	60.5	41.9			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 16 **Secondary Health Outcome - Role Emotional by Treatment Groups and Control Group**



Mental Health

Mental health includes depression and anxiety. A high score indicates that participants felt peaceful, happy and calm during the week prior to the treatment session. A low score indicates that the participants had felt nervous or depressed.

The scores at baseline and at the commencement of treatment for all three groups showed that participants had experienced some level of depression or anxiety (*see Table 34 and Figure 17*).

Comparison of Group 1 to Groups 2&3

Group 1 (individualised group) had lower scores than Groups 2 and 3 at baseline and lower scores than Group 2 and slightly higher scores than Group 3 at the commencement of treatment. Symptoms improved throughout the treatment period and declined slightly in weeks 4 and 5 and during the follow-up period, with the

scores at the 3-month follow-up being higher than scores at baseline and only slightly above those in the first week of treatment.

Comparison of Group 2 to Groups 1&3

Group 2 (standard 'gut-directed' group) had higher scores than Groups 1 and 3 both at baseline and at the commencement of treatment. Symptoms continued to gradually improve until a decline in week 5, with a further improvement in symptoms during the follow-up period. The follow-up scores were higher than at baseline and at week 1 of treatment.

Comparison of Group 3 to Groups 1&2

Group 3 (control group) had higher scores than Group 1 and lower scores than Group 2 at baseline, and lower scores than the other two groups at commencement of treatment. With the exception of a slight decline in scores in week 4, the participants continued to gradually improve during the treatment period. Scores declined during the follow-up period but were higher than those at baseline and in the first week of treatment.

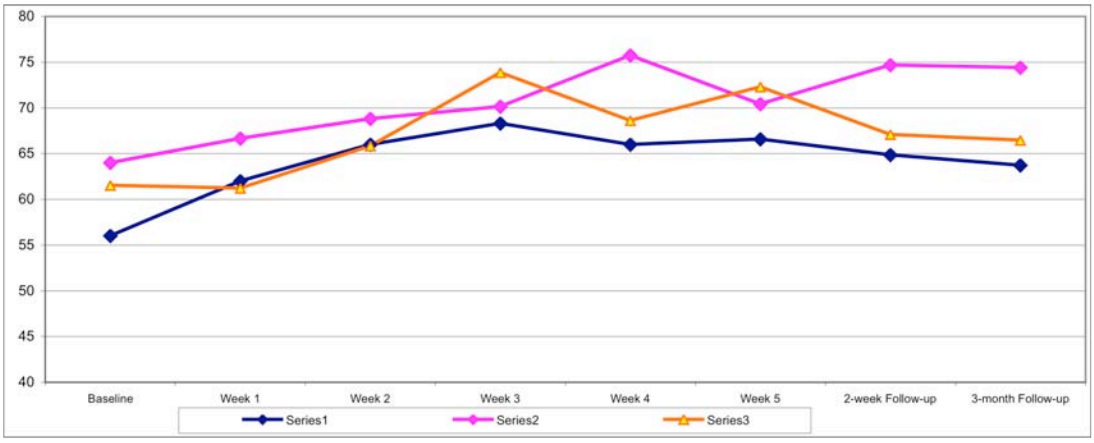
The mean score for the total sample showed improvement in mental health from the commencement of treatment (63.4) to the end of treatment (69.7). The main effect and linear trend were highly significant.

Table 34 **Secondary Health Outcome – Mental Health**

Treatment Groups/	Group 1		Group 2		Group 3		Total		F1	F2	F3
Sessions	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Baseline	56.0	19.2	64.0	14.3	61.5	18.8	60.6	17.4			
Week 1	62.0	15.8	66.7	15.9	61.2	20.0	63.4	17.0			
Week 2	66.0	14.6	68.8	16.2	65.8	25.5	67.0	18.7			
Week 3	68.3	17.9	70.1	13.5	73.8	14.9	70.7	15.3	4.89**	15.91**	n.s.
Week 4	66.0	16.9	75.7	12.9	68.6	17.0	70.3	15.8			
Week 5	66.6	17.8	70.4	20.8	72.3	16.7	69.7	18.3			
2-week Follow-up	64.9	17.1	74.7	13.8	67.1	22.0	69.0	17.9			
3-month Follow-up	63.7	21.0	74.4	12.7	66.5	19.5	68.4	18.1			
Total	64.2	17.4	70.6	15.3	67.1	19.3	67.4	17.5			

F1 = main effect; F2 = linear trend; F3 = treatment effect; n.s. = not significant. ***P <0.01; *P <0.05*

Figure 17 **Secondary Health Outcome - Mental Health by Treatment Groups and Control Group**



All participants demonstrated improvement in the overall severity of their individual IBS symptoms and functioning at the end of the treatment period (week 5), with the 'individualised' group (Group 1) having a numerically better outcome than the other two groups.

The main effect and linear trend for all three treatment groups were significant but the treatment effect between groups was not significant. The differences in response between the groups, therefore, might be attributable to random factors.

Improvement in IBS symptoms and general health outcomes did not continue during the 3-month follow-up period. This increase in symptoms during the follow-up period was possibly due to both non-compliance and to no further contact with the therapist.

Intercorrelations Among the Four Dimensions of the SCL-90-R at Baseline and the SF-36 Health Concepts at the End of Treatment

Some of the general health measures of degree of improvement in SF-36 at the end of the treatment sessions, and the SCL-90-R measures at baseline, are significantly correlated, indicating a better quality of life for the patients. For example, as the pain level lessened, the extent to which the patients' health limited their physical activities and interfered with their work or daily activities improved (*see Table 35*).

A higher index (0-100) on the SF-36 scale indicates better quality of life, and a higher score on the four dimensions of the SCL-90-R scale indicates more psychological problems. The General Health Perceptions concept in SF-36 measure at the end of the treatment sessions is significantly related to all four dimensions of SCL-90-R ($p < 0.01$). A negative value indicates fewer psychological problems and better quality of life.

Table 35. **Intercorrelations among four dimensions of the SCL-90-R at baseline and the SF-36 health concepts at the end of treatment.**

	Physical Functioning	Role - physical	Pain	General Health Perceptions	Vitality	Social Functioning	Role-emotional	Mental Health	Depression	Obsessive-Compulsive	Anxiety	Interpersonal Sensitivity
Physical Functioning	1											
Role-physical	.495(**)	1										
Pain	.431(**)	.697(**)	1									
General Health Perceptions	.199	.479(**)	.603(**)	1								
Vitality	.312(*)	.559(**)	.703(**)	.491(**)	1							
Social Functioning	.303	.681(**)	.688(**)	.374(*)	.633(**)	1						
Role-emotional	.141	.657(**)	.579(**)	.575(**)	.538(**)	.582(**)	1					
Mental Health	.098	.248	.349(*)	.462(**)	.450(**)	.260	.629(**)	1				
Depression	-.081	-.329(*)	-.389(*)	-.572(**)	-.429(**)	-.366(*)	-.619(**)	-.521(**)	1			
Obsessive-Compulsive	.058	-.287	-.334(*)	-.408(**)	-.192	-.234	-.601(**)	-.456(**)	.795(**)	1		
Anxiety	-.067	-.328(*)	-.193	-.571(**)	-.094	-.150	-.539(**)	-.384(*)	.695(**)	.725(**)	1	
Interpersonal Sensitivity	.044	-.306	-.267	-.467(**)	-.200	-.198	-.484(**)	-.391(*)	.814(**)	.741(**)	.805(**)	1

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

Intercorrelations: SCL-90R Duke-UNC, BSSS and the Overall Severity of IBS at the end of treatment sessions,

Intercorrelations among the four dimensions of the SCL-90-R, the Duke-UNC Functional Support Scores at baseline, the BSSS, and the overall severity of IBS (BSS-5) at the end of the treatment sessions were then examined.

BSSS measures which are specific to the frequency of bowel motions, distress, and interference with daily life at the end of the treatment sessions; and the SCL-90-R measures including depression, obsessive-compulsive, and interpersonal sensitivity at baseline, are all significantly correlated ($p<0.01$), but anxiety was found to be unrelated. At the end of the treatment sessions, the overall severity of IBS is significantly correlated with all SCL-90-R scores, except for anxiety ($p<0.05$). A positive value indicates that patients with more bowel symptoms had more psychological distress (*see Table 36*).

The confident social support score (Duke-UNC) is negatively correlated with all SCL-90-R scores as well as bowel symptom severity scores. The only significant correlation ($p<0.05$) was found between the confident support score and the depression score. A negative value indicates that patients with less social support had more psychological distress (*see Table 36*).

Table 36. Intercorrelations among four dimensions of the Symptom Checklist-90 R (SCL-90-R), the Duke-UNC Functional Social Support Scores at Baseline, the Bowel Symptom Severity Scale (BSSS), and the Overall Severity of IBS (BSS-5) at the end of treatment sessions.

	Depression	Obsessive-Compulsive	Anxiety	Interpersonal Sensitivity	Frequency	Distress	Interference	Overall severity of IBS	Confident Support	Affective Support
Depression	1									
Obsessive-Compulsive	.794(**)	1								
Anxiety	.699(**)	.731(**)	1							
Interpersonal Sensitivity	.816(**)	.746(**)	.809(**)	1						
Frequency	.546(**)	.588(**)	.390(*)	.543(**)	1					
Distress	.421(**)	.431(**)	.264	.425(**)	.675(**)	1				
Interference	.464(**)	.490(**)	.270	.444(**)	.684(**)	.916(**)	1			
Overall severity of IBS	.351(*)	.483(**)	.285	.344(*)	.613(**)	.728(**)	.730(**)	1		
Confident Support	-.322(*)	-.242	-.091	-.270	-.150	-.044	-.041	-.163	1	
Affective Support	-.223	-.029	-.073	-.225	-.014	.096	.061	.028	.686(**)	1

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

The Survey of Recent Life Experiences

The SRLE covers six concepts which are considered to be stressful – social and cultural difficulties, work, time pressure, finances, social acceptability, and social victimisation (*see Appendix 10*).

The baseline data on the SRLE demonstrates that, for this particular sample of IBS patients, the emotional responses to life stress were more evident in relation to time pressure (e.g. having too many things to do at once, a lot of responsibilities, not enough leisure time); work (e.g. dissatisfaction with work, bored with work, conflicts at work); and social and cultural difficulties (e.g. conflicts with friends/family members, having trust betrayed by a friend, ethnic or racial conflicts).

The three groups showed similar responses to stress but, compared to the other two groups, Group 1 (individualised group) had higher scores on social acceptability and social victimisation; and Group 3 (control group) had higher scores on stress that was related to work, time pressure, and finances. See *Table 37*.

When correlations between the SRLE and the BSSS at baseline were examined, there were highly significant correlations between bowel frequency, and the distress and interference in the participants' everyday lives. There were also significant correlations between social and cultural difficulties and interference from the severity of bowel symptoms from which participants were suffering (*see Table 38*).

Table 37 Baseline Data on Survey of Recent Life Experiences (SRLE)

		Mean	Std. Deviation	95% Confidence Interval for Mean	
				Lower Bound	Upper Bound
Social & Cultural Difficulties	Group 1	16.1	4.1	14.0	18.2
	Group 2	15.6	4.5	13.3	17.9
	Control Group	16.1	3.0	14.5	17.6
	Total	**15.9**	**3.9**	**14.8**	**17.0**
Work	Group 1	10.6	4.8	8.1	13.1
	Group 2	11.8	4.2	10.0	14.0
	Control Group	12.2	4.3	10.0	14.4
	Total	**11.5**	**4.4**	**10.3**	**12.8**
Time Pressure	Group 1	15.9	6.3	12.7	19.1
	Group 2	17.1	6.5	13.8	20.4
	Control Group	17.2	4.9	14.7	19.8
	Total	**16.8**	**5.8**	**15.1**	**18.4**
Finances	Group 1	8.4	2.7	7.0	9.8
	Group 2	9.8	4.3	7.6	12.0
	Control Group	10.2	3.7	8.3	12.1
	Total	**9.5**	**3.7**	**8.5**	**10.5**
Social Acceptability	Group 1	9.4	3.6	7.6	11.3
	Group 2	8.8	3.3	7.1	10.5
	Control Group	8.3	2.0	7.3	9.3
	Total	**8.8**	**3.0**	**8.0**	**9.7**
Social Victimisation	Group 1	6.8	2.2	5.7	8.0
	Group 2	6.5	2.8	5.1	8.0
	Control Group	6.5	2.0	5.5	7.6
	Total	**6.6**	**2.3**	**6.0**	**7.3**

Table 38 Correlations: SRLE & Bowel Symptom Severity Scale (BSSS) at Baseline

	Frequency	Distress	Interference	Social & Cultural Difficult.	Work	Time Pressure	Finance	Social Accept-ability	Social Victim
Freq.	1								
Distr.	.829**	1							
Interf.	.731**	.917**	1						
Social & Cult. Diff.	.226	.278	.322*	1					
Work	.293	.342*	.342*	.194	1				
Time Press.	.121	.079	.168	.077	.380*	1			
Fin.	.216	.258	.321*	.370*	.463**	.400**	1		
Social Accept	.192	.200	.250	.472**	.411**	.422**	.431**	1	
Social Victim	.078	.105	.200	.420**	.352*	.436**	.606**	.590**	1

** Correlation is significant at the 0.01 level (2-tailed); * Correlation is significant at the 0.05 level (2-tailed)

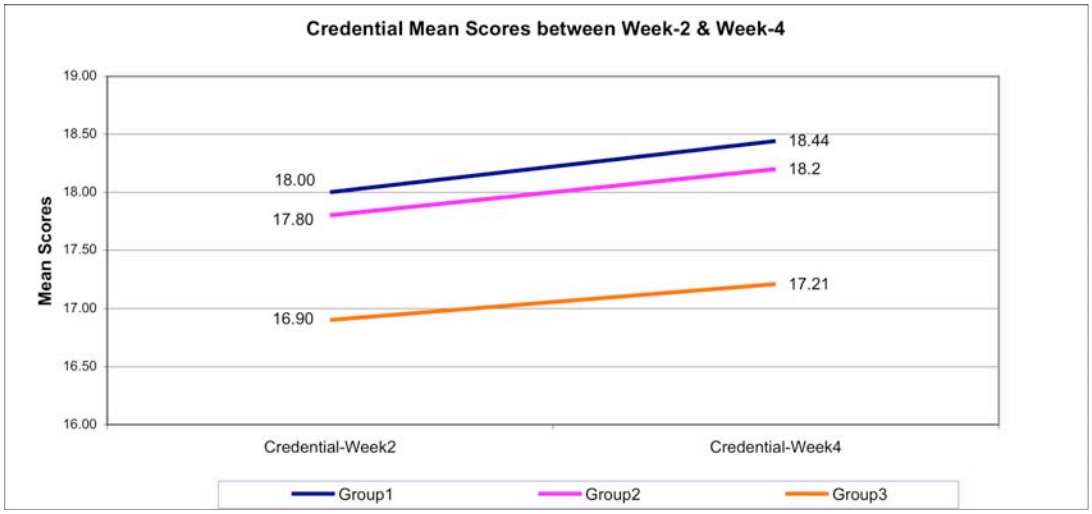
Credibility Scale

Participants' expectancy for improvement is an important variable affecting the outcome of clinical trials (Linde et al. 2007; O'Malley et al. 2004) and, in this trial, the Credibility Scale (*Appendix 6*) was used for both measurement of this variable and to test the success of participant blinding. The scale was issued to participants twice throughout the trial (in week 2 and week 4).

The participants were asked to indicate on the form how confident they felt that the treatment could alleviate their complaint; if they would be confident in recommending the treatment to a friend suffering a similar complaint; how logical the treatment seemed to them; and how successful they thought the treatment would be in alleviating other complaints (*see Appendix 11*). All participants were blinded to both the treatment they were receiving, and to other participants in the study (*see Chapter 5*).

Although the results do not show statistically significant differences among the three treatment groups, the participants in all three groups showed that their expectancy for improvement increased from the commencement of their treatment to the end of treatment (*see Figure 18*).

Figure 18 **Credibility Scale: Mean Scores between Week 2 and Week 4 by Treatment Groups and Control Group**



6.2.3 Follow-up Assessment

Follow-up on all participants was performed at both two weeks and three months after completion of the initial trial. The BSSS and the SF-36 General Health Survey, which had been administered to participants at the screening session and throughout the treatment periods, were also administered throughout the follow-up period. The results of the BSSS during this period are shown in Tables 17-19, and the results of the SF-36 are shown in Tables 27-34.

CHAPTER 7

DISCUSSION

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Research has demonstrated the consequences of IBS as being both an individual and economic burden to sufferers. Studies have repeatedly shown that patients with IBS are often restricted in recreational and work-related activities (Dean et al., 2005; Drossman et al., 1993), have reported a lower quality of life compared to controls (Creed et al., 2000; Hahn et al., 1999), and have been found to have higher levels of depression and anxiety relative to the general population (Garakani et al., 2003; Sykes et al., 2003). Life stress contributes to symptom onset and exacerbation of symptoms in the majority of IBS patients, and the level of chronic life stress threat can predict the clinical outcome in most patients (Bennett et al., 1998).

7.1 Hypotheses

Based on previous research and consistent with the aims of the study, the present research sought to empirically investigate four main hypotheses.

The first hypothesis was that participants who had been diagnosed with IBS would present with not only physiological symptoms but psychological ones as well and that, at the end of the study, participants who underwent individualised hypnotherapy (using imagery which addressed both the psychological/emotional aspects and the physiological symptoms of the syndrome), would have a better outcome in the improvement of their IBS symptoms than participants who underwent standard gut-directed hypnotherapy in which

physiological symptoms alone were treated. The group of participants whose treatment incorporated both psychological and physiological aspects of IBS, had a better outcome than the other two groups.

The second hypothesis was that participants' IBS symptoms would improve during the trial period and, as a result, their quality of life would subsequently improve. Participants in all three groups demonstrated an improvement of overall severity in their IBS symptoms during the treatment period and a subsequent improvement in their quality of life.

The third hypothesis was that participants who had a support system in place would improve more quickly than those who hadn't. The only significant correlation found was between the confident support score and the depression score.

The final hypothesis was that participants who were experiencing, or who had recently experienced, stressful episodes in their lives would be more likely to have more severe and more frequent IBS symptoms. Participants in all three groups demonstrated similar emotional responses to life stress and there were highly significant correlations between bowel frequency and its interference in the patients' everyday lives.

7.2 'Individualised' Imagery vs 'Gut-directed' Imagery

This study supports previous research that has shown that psychological disorders (especially depression and generalised anxiety disorder) are present in the majority of IBS patients who actively seek medical care (American College of Gastroenterology Functional Gastrointestinal Disorders Task Force, 2002; Blanchard, 1993; Blanchard et al., 1990).

This overlap between psychological disorders and IBS has led to research which has found that there was a significant association of IBS with anxiety and depression (Gorard et al., 1996; Harris & Chang, 2006; Hazlett-Stevens et al., 2003) and also to studies which have been carried out to evaluate the benefits of hypnotherapy in reducing IBS symptoms (Gonsalkorale, 2002, 2006; Palsson, 1997, 2006; Whorwell, 2006; Whorwell et al., 1992).

Most of these studies demonstrated that individual physiological IBS symptoms improved and that this improvement frequently correlated with improvement in anxiety symptoms and depression symptoms. To date, however, there appears to be an absence of studies which target this apparent link between the physiological symptoms and the psychological/emotional symptoms of IBS.

The present study aimed at achieving a more holistic approach in the treatment of IBS patients by designing hypnotherapy sessions for the 'individualised' group (Group 1) which incorporated imagery for psychological as well as

physiological symptoms into the treatment plan. Scripts for the participants in this group were based on the results of the SCL-90-R which each participant was asked to complete before commencement of treatment to evaluate psychological problems and symptoms of psychopathology.

At baseline, the 51 participants in this study presented with depression, anxiety, obsessive-compulsive disorder, and interpersonal sensitivity – depression being the most prevalent psychological disorder. Thirty participants presented with depression, four with anxiety, two with obsessive-compulsive disorder and one with interpersonal sensitivity. Of the remainder, five had both depression and anxiety, five had depression and obsessive-compulsive disorder, and four presented with depression and interpersonal sensitivity.

The original 17 participants in the 'individualised" group (Group 1) presented with all four primary symptom dimensions of the SCL-90-R – depression, anxiety, obsessive-compulsive disorder, and interpersonal sensitivity, and, as indicated in previous research, depression was the most prevalent psychological disorder. Nine participants presented with depression, two with anxiety, two with anxiety and depression, three with depression and obsessive-compulsive disorder, and one with interpersonal sensitivity.

At the end of the treatment sessions, all participants in this study demonstrated improvement in their IBS symptoms with the 'individualised' group, whose hypnotherapy sessions included scripts which incorporated both their

psychological and physiological aspects of IBS, having a better outcome than the other two groups.

7.3 Quality of Life

Previous research has demonstrated that diminished QOL is another aspect of IBS which needs to be addressed when treating the disorder. Studies have shown that IBS poses a financial burden on the patient through medical expenses such as investigations, treatments and medications, and loss of pay through illness (Cash et al., 2005; Leong et al., 2003).

Research has also shown that diminished QOL also affects the day-to-day functioning of the IBS sufferer, and patients with IBS were found to have significantly lower scores in all domains of the SF-36 questionnaire, indicating poorer functioning outcomes (Akehurst et al., 2002; Dean et al., 2005).

In the present study, participants in all three groups completed the SF-36 questionnaire prior to commencement of treatment sessions. The SF-36 is a 36-item questionnaire consisting of 8 health concepts or subscales broadly related to quality of life, mental health and social activities.

The results supported those of previous research in that all IBS patients in this trial had low scores in the SF-36 questionnaire. With the exception of physical

functioning, in which all participants indicated few limitations in performing physical activities, scores for the other seven health concepts were low.

Results of all three groups demonstrated that participants showed some indication of interference in their work or daily activities due to physical health, that pain had an effect on the participants' normal work, and vitality was low. Scores also indicated that participants viewed their health as only slightly above average and that all participants found that physical health or emotional problems interfered to some extent with their social activities and that emotional problems interfered with work or daily activities. All participants experienced some level of depression or anxiety.

Participants in all three groups demonstrated an improvement of overall severity in their IBS symptoms during the treatment period and a subsequent improvement in their quality of life. There was a highly significant decrease in the level of pain, and also a highly significant improvement in the patients' vitality, social functioning, and mental health. There was also significant improvement in physical functioning, general health, and the extent to which emotional problems interfered with the patients' work or daily activities.

7.4 Social Support

Social support encompasses a number of functions or behaviours which can produce a beneficial effect on the health and well-being of people. Functions are usually grouped into one of two types: a health-facilitating function (gratifying

human needs for affection, approval, identity) and a stress-reducing function (practical help, problem-solving, advice, information, education) (Suurmeijer et al., 1995).

In previous studies on IBS, the data suggested a need for support groups, opportunities for patients, medical health-care professionals, and supportive others to share experiences and concerns, and informational support within the areas of symptom interpretation and illness management (Coulson, 2005; Meadows et al., 1997).

Participants in the present study were asked to complete the Duke-UNC questionnaire prior to commencement of treatment. This 8-item instrument contains questions in two content areas: confidant support, which reflects a confidant relationship where important matters in life such as social contact and personal/work/financial problems are discussed and shared; and affective support which reflects a more emotional form of support or caring.

In this trial, there was no significant correlation between support and improvement in the overall severity of IBS symptoms. The only significant correlation found was between the confident support score and the depression score indicating that patients with less social support had more psychological distress.

7.5 Stress

Researchers in the field of psychoneuroimmunology are providing evidence about the ways in which negative emotions generated by stressors can be translated into physiological changes (Webster et al., 2002; Padgett & Glaser, 2003). Research has shown that ligands and their receptors communicate biochemically between, and within, the immune and endocrine systems and that stressors can activate the HPA axis releasing pituitary and adrenal hormones, commonly know as “stress” hormones (Blalock, 1994; Pert, 1997; Glaser & Kiecolt-Glaser, 2005). Studies have also shown that stressful episodes can influence GI function (Lundberg, 2005) and that, in IBS sufferers, the symptoms are more likely to be more severe (Drossman et al., 1999).

Further studies have shown that patients who confronted stress with problem-solving, active behavioural approaches, and self-management programmes, had significantly better quality of life, a decrease in pain and depression, and had fewer visits to medical practitioners (Blixen & Kippes, 1999; Swindells et al., 1999). This aspect was not investigated in the present study.

Prior to the treatment sessions in the present study, participants were asked to complete the SRLE questionnaire which consists of 51 items covering six concepts: social & cultural difficulties, work, time pressure, finances, social acceptability, and social victimisation.

Participants in all three groups demonstrated similar emotional responses to life stress (such as time pressure, work, and social and cultural difficulties) and there were highly significant correlations between bowel frequency and its interference in the patients' everyday lives. There were also significant correlations between social and cultural difficulties and interference from the severity of bowel symptoms from which patients were suffering.

Hypnosis is thought to be able to strengthen the body's immunological functions and assist in fighting off disease and is therefore commonly used in the treatment of stress disorders (Rossi, 1993; Wickramasekera, 1999).

7.6 Hypnotherapy

Numerous studies have been done to evaluate the benefits of complementary therapies such as hypnotherapy to reduce IBS symptoms because of the overlap between psychological disorders and IBS (Drossman et al, 2003; Guthrie, Creed, Dawson & Tomenson, 1993; Blanchard et al., 1993; Whorwell, Prior & Faragher, 1984; Whorwell, 2006). Research has also been carried out on complementary therapies to identify those that can complement current medical care and improve clinical outcomes. This has been considered necessary because of the lack of significant relief in a large proportion of patients using only conventional medical treatment for IBS (Poitras et al., 2002; Tillisch, 2006).

Research has suggested that the brain, gut, and the autonomic nervous system are involved in the pathology of IBS, and researchers are more widely acknowledging the link between the mind and body (Salt & Neimark, 2002; Smith & Morton, 2001). One of the successful interventions aimed at breaking cycles within the brain-gut axis is hypnotherapy (Gonsalkorale, 2006; Palsson & Drossman 2005; Whorwell, 2006).

The mechanisms responsible for the therapeutic success of hypnotherapy are largely unknown, but research has shown that it may act by modulating visceral sensitivity, motor function and psychological distress (Guzelier et al., 2001; Houghton et al., 1999; Marchioro et al., 2000). Research in the area of the effects of imagery and hypnosis on the immune and nervous systems indicates that hypnotic intervention can moderate the functioning of these two systems (Glaser et al. 2001; Whorwell et al., 1992).

Imagery is a major component of hypnosis, and research has provided numerous examples of the physiological effects imagery has on the body (Graham, 1995). In hypnosis, suggestions are usually given in the form of imagery, which can be any perception that comes through any of the senses (McGill, 1996; Olness, 1995), and, as the body is thought to be unable to discriminate between sensory images in the mind and reality, these images are interpreted as almost real events (Gindes, 1976; Naparstek, 1994).

Participants in the two hypnosis groups in this trial were asked to imagine themselves in a peaceful, safe, place, and suggestions given during the trance state

were in the form of therapeutic suggestions to help patients overcome the difficulties or problems associated with their IBS symptoms.

Suggestions which related to the participants' physiological IBS symptoms, and which aimed at modulating visceral sensitivity and motor function, were given to both hypnosis groups (Group 1 - "individualised" imagery, and Group 2 – standard "gut-related" imagery). After suggestions of relaxation and safety, participants were guided through a visualisation of drinking a liquid that would heal and soothe the digestive tract, make the muscles strong and give them tone, allow the correct processing and absorption of food, and regulate peristalsis.

In addition, participants in Group 1 ("individualised" imagery) were given suggestions relating to each participant's individual psychological IBS symptoms, as evidenced by the SCL-90-R (*Appendix 7*), with the aim of reducing psychological distress. Depending on each participant's specific need, suggestions were given to reduce anxiety, depression, obsessive-compulsive behaviour, or interpersonal sensitivity.

The success of the hypnotherapy sessions and of the goal the patient wishes to achieve is very much dependent on the words used (Cunningham & Ralph, 1980) and so, the words in the scripts that were read to patients in the hypnosis groups were carefully selected to help target each patient's symptoms (whether psychological and/or physiological) in order to improve/change a sensation, belief or behaviour.

7.7 Reflections on the Study

This study follows on previous research which has shown hypnotherapy to be of benefit to patients with IBS and, as far as the author is aware, is the first clinical trial in Australia using hypnotherapy as a treatment for IBS, and the first to incorporate *both* physiological and specific psychological imagery into the hypnotherapy scripts.

In the present study, participants presented with high scores in psychological ratings and there were correlations between three of the four subgroups (anxiety, depression, and obsessive-compulsive symptoms) indicating a non-specific psychological characteristic of IBS patients, which was consistent with previous studies.

As mentioned in Chapter 4, the aim of the present trial was to examine whether hypnosis using imagery which combined *both* this psychological characteristic of IBS as well as the physiological aspects of the illness, would benefit IBS sufferers more than either hypnosis with imagery which only addressed the physiological symptoms, or relaxation therapy.

The study found that the group which combined both psychological and physiological aspects of the IBS symptom picture (Group 1), improved more than the other two groups (Group 2 - hypnosis targeting physiological symptoms only; and Group 3 - relaxation therapy).

The participants' improvements in abdominal complaints related to improvements in quality of life. The mean bowel scores for the whole sample for all physiological IBS symptoms had fallen by the end of the treatment period with a significant linear trend for scores to change over time. Significant changes over time were found for physical functioning, general health, vitality, and the social functioning scales on the SF-36; with all three arms showing similar improvement.

The results of this trial in the use of hypnosis as a treatment for IBS, indicate a significant difference *within* groups on both physiological and psychological symptoms of IBS. However, there was no significant difference among the three treatment groups which suggests that neither individualised hypnosis nor relaxation therapy were superior to the standard "gut-related" hypnotherapy, and that all three treatment options were of benefit to participants.

7.8 Limitations

One limitation of the study was that it was insufficiently powered. Due to time limits and the fact that the therapist was the only person recruiting, the sample size was small. A much larger sample size would have been required to detect such a small effect size difference among the groups, but such a difference would possibly not have been clinically significant.

It was hypothesised a priori that, with respect to the abdominal pain subscale of the SCL-90, the control group would not change on average, the standard therapy group

would improve by one point and the individualised therapy by two points. Under these conditions and with an assumed SD=2.0 n=25 subjects per study group would have yielded statistical power >0.85 at the 0.05 (two-tailed) level of statistical significance. Due to difficulty with recruitment, n=17 subjects were actually recruited per group and this yields statistical power of approximately 0.72 under the same conditions. While this power is less than the desired 0.8 it is unlikely to have materially affected the statistical analysis.

Also, although participants demonstrated improvements in their IBS symptoms at the end of the treatment sessions, these improvements did not persist at the three-month follow-up. One possible explanation for this could be that, again, the study was insufficiently powered to detect differences.

During the follow-up period in previous trials in hypnotherapy (Whorwell et al., 1984, 1987; Gonsalkorale et al., 2002, 2003), participants continued to receive hypnosis sessions on a monthly basis and were asked to telephone if they experienced a relapse so that a further session of hypnotherapy could be arranged.

In this study, there was no further contact with the therapist by the participants, adherence to treatment protocols during the follow-up period was not checked, and participants were not given further hypnosis sessions (either on a regular basis or in case of relapse) to maintain remission. This could be another possible explanation for the lack of improvement in IBS symptoms during the follow-up period. With continued checking of adherence to autohypnotic practice and

ongoing hypnosis sessions with the therapist, improvement in scores may have increased but, in the author's view, to do so would not have constituted a pure trial.

Another limitation in this study was an absence of data on eligible subjects who did not complete all the questionnaires.

Research has indicated that brain wave changes associated with hypnosis can also be triggered by other methods of deep concentration, such as the relaxation response - the difference being that there is higher theta activity in relaxation and higher alpha activity in the hypnotic experience (Jacobs & Friedman, 2004; Williams & Gruzelier, 2001).

The control group in this trial underwent sessions in relaxation as a treatment for their IBS symptoms, whereas treatment for the other two experimental groups (the individualised group and the standard 'gut-directed' group) involved sessions in hypnosis. Considering that the relaxation response can trigger brain wave changes associated with hypnosis, and that the hypnosis sessions themselves involved deep relaxation, participants in the control group could have easily lapsed into hypnosis.

In other words, the treatment for the control group was too similar to the treatment for the other two groups. This could account for the similarities in treatment outcome and the small effect size difference between the groups. Other possibilities for the control group could have been to have patients on a waiting-list;

receiving education on IBS to allay concerns; or discussing their problems within their group under the guidance of a counsellor.

7.9 Strengths

The present study also has a number of strengths. All of the participants were provided with information on IBS, and the functioning of the gastrointestinal tract was explained. Careful attention was given to blinding throughout the trial and the therapist (the author) who administered the therapy was an experienced and qualified hypnotherapist.

Further strengths of the study lie in the fact that participants were recruited prospectively; participants with other pre-existing functional gastrointestinal diseases were carefully excluded; and validated, standardised questionnaires to define the outcomes measures of IBS, and strict criteria for diagnosing IBS were utilised. Also, the drop-out rate during the trial period was small.

Anecdotally, one of the participants in the 'gut-directed' experimental group reported as being symptom-free for the first time in twenty years. Eighteen months later, she was still symptom-free. Another, also from the same experimental group was symptom-free a year after the trial.

Notwithstanding the limitations of this clinical trial, and that the findings need further confirmation, this study appears to support a psychophysiological hypothesis

that successful treatment of the psychological aspects is accompanied by improvement in IBS symptoms.

7.10 Future Research

Research has been slowly moving away from the biomedical approach that has been dominant for the greater part of medical history since the 17th century and interest in the mind-body connection is becoming more and more prevalent.

There is no single pathophysiological marker and, therefore, no effective treatment for the whole symptom complex in IBS patients, so further research needs to increase the knowledge of how the ENS controls or modulates motility, exocrine and endocrine secretions and immune and inflammatory processes, and how this knowledge can contribute to the creation of new approaches in treatment.

Future research also needs to continue the investigation of the brain-gut axis in IBS and the role of hypnosis (which addresses both the psychological and physiological aspects of this disorder) as an effective and viable treatment option. There is also a possible need to identify the types of patients, as early as possible in their treatment, who are most likely to respond positively to hypnotherapeutic intervention to help them cope with their symptoms, and also reduce healthcare use and cost in the long term.

More well-designed and executed studies with adequate sample sizes are needed to examine the effect of hypnosis on IBS and to compare the different ways of implementing the treatment (e.g. groups, one-to-one, or CDs of the sessions for home use). Also, the methods of hypnotic induction and scripts used should be reported in detail so that they can easily be reproduced by others both in future research and in the clinical setting.

7.11 Conclusions

Despite ongoing research as to its aetiology and pathophysiology, IBS remains a poorly understood condition. Many recent findings add to a growing body of evidence that a subset of IBS sufferers have a visceral hypersensitivity or an increased perception of sensations of the gut (Bouchoucha et al., 1999; Camilleri et al., 2001), and that IBS, at least in part, may result from previous gastroenteritis, small intestine bacterial over-growth, psychosocial factors, a genetic contribution, or an imbalance of neurotransmitters (Gershon, 2004; Neal et al., 1997; Pimentel et al., 2000). It is generally agreed that a patient's emotional response to stress can exacerbate the condition (Gorard et al., 1996; Salt, 2002).

Diminished quality of life affects the day-to-day functioning of the IBS sufferer, and patients with IBS were found to have significantly lower scores on all domains in the SF-36 questionnaire, indicating poorer functioning outcomes (Akehurst et al., 2002; Dean et al., 2005). IBS also poses a financial burden on the patient through loss of pay through illness and the cost of healthcare such as visits to

primary care physicians and gastroenterologists, plus the added cost of investigations, treatments and medications (Cash et al., 2005; Leong et al., 2003). Suggested strategies to reduce direct costs include physician/patient education, avoidance of unnecessary investigations, the setting-up of support groups and the early consideration of psychosocial issues and psychological treatments (Camilleri & Williams, 2000).

Nowadays there is a better understanding of IBS (and other functional GI disorders) with a subsequent moving away from a disease-based model to a biopsychosocial one which takes into account not only the numerous physiological symptoms of IBS but also the effects that sociocultural and psychosocial influences have on these symptoms (Bennett et al., 1998; Farhadi et al., 2001).

This study highlighted the use of hypnosis as a treatment for IBS. Previous studies have demonstrated the beneficial effects of hypnosis in the treatment of IBS and its sustained effect (Gonsalkorale et al., 2002; Palsson et al., 2000). Studies have been carried out to investigate the differences, if any, between individual sessions versus group sessions, and audiotape versus therapist, with the results showing little difference in outcome. All of these trials were considered as having a relatively high success rate in alleviating IBS symptoms.

Through research and clinical trials, hypnosis is beginning to lose its association with the occult and power control, and has come to be regarded as a situation which involves co-operation and trust between the hypnotherapist and the

patient. It is now being considered as a genuine and useful treatment which is gradually becoming acknowledged by medical authorities (Waterfield, 2002).

This change in attitude towards the application of hypnotherapy is considered to be due to more information coming to light about the complexities of the brain systems and also to a more rigorous application of scientific methodology and experimental design (Gruzelier, 1996).

The influences the mind has on the body (and the body has on the mind), in both psychosomatic disorders and physiological conditions such as IBS, are becoming more widely acknowledged; and the use of imagery in hypnotherapy, in which the therapist can address both the physiological and the psychological aspects of IBS symptomatology, is an important link.

This paper also discussed research into psychoneuroimmunology and the role of the brain-gut-axis in disease. Studies have shown that emotions can affect colonic motility more in IBS patients than in healthy controls (Drossman et al., 1999; Garakani et al., 2003) and that stress can exacerbate IBS symptoms (Levy et al., 1997; Locke et al., 2004).

The mind and the neurological and immunological systems of the body communicate through the bi-directional flow of hormones, neuropeptides and cytokines (Martin, 1997; Watkins, 1997). The brain translates thoughts, feelings, beliefs and memories into complex patterns of nerve cell firing and chemical release

which affect both the physiology and biochemistry of the body. This is clearly evidenced in the symptomatology of IBS (Salt & Neimark, 2002).

A better understanding of the neural regulation of the enteric nervous system and how action by the sympathetic branch of the autonomic nervous system can inhibit or stimulate activity in the GI tract, makes it easier to understand the interrelationship between emotions, GI function, and pain, in IBS (and other functional disorders), and subsequently, how mind-body treatments such as hypnotherapy can be of benefit.

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APPENDICES

APPENDIX 1

SUBJECT INFORMATION STATEMENT

THE UNIVERSITY OF SYDNEY

FACULTY OF HEALTH SCIENCES
School of Behavioural & Community Health Sciences

SUBJECT INFORMATION STATEMENT

Irritable Bowel Syndrome: clinical trial in relaxation therapies.

The purpose of this study is to investigate the use of progressive relaxation and hypnosis to help in the treatment of irritable bowel syndrome.

Irritable bowel syndrome (IBS), which can affect up to one in four people, can be extremely debilitating yet tests to investigate the cause of these symptoms are always normal and the reasons why people suffer from the symptoms of IBS are still unknown. As the various symptomatic treatments given to patients with IBS are not always successful, this study aims to trial the effects of relaxation/hypnosis techniques in relieving the symptoms of IBS.

After being randomly allocated to one of three groups, all you need to do in this study is to attend an initial one hour consultation in which you will be asked to complete questionnaires, regularly practise the relaxation or hypnosis technique which will be taught to you, present for a further five ½ hour sessions, and keep a daily diary for the two weeks prior to your first session. The sessions will take place at a private clinic located at 31 Rowe Street Woollahra. Please be assured that you may withdraw from the study at any time. All data collected will be kept confidential, and your name, address and other identifying details will not be stored in the computer database.

Should you wish to discuss the study or its outcomes, please contact the researcher (see below for address). Any person with concerns or complaints about the conduct of the study can contact the Secretary of the Human Ethics Committee, University of Sydney on (02) 9351 4811.

Researcher:
Julie Phillips-Moore - doctoral student
School of Behavioural & Community Health Sciences
Faculty of Health Sciences
University of Sydney
P.O. Box 170, Lidcombe N.S.W., 1825
Ph. (02) 9351 9228
Supervisors: Dr. Gomathi Sitharthan, Prof. Nick Talley.

APPENDIX 2

CONSENT FORM

THE UNIVERSITY OF SYDNEY

FACULTY OF HEALTH SCIENCES
School of Behavioural & Community Health Sciences

CONSENT FORM

Irritable Bowel Syndrome: clinical trial in relaxation therapies.

Researcher: Julie Phillips-Moore - doctoral student
School of Behavioural & Community Health Sciences
Faculty of Health Sciences
University of Sydney
P.O. Box 170, Lidcombe, N.S.W., 1825
Ph. (02) 9351 9228

Supervisors: Dr. Gomathi Sitharthan, Prof. Nick Talley.

I, _____ (name)

of _____ (address)

hereby consent to taking part in the research project about the efficacy of progressive relaxation and hypnosis in the treatment of irritable bowel syndrome. I understand that this will involve six consultations, the first of which will take approximately one hour – the remaining five, approximately ½ an hour.

1. The study and the procedure of the study have been explained to me by Julie Phillips-Moore.

2. I have read and understood the SUBJECT INFORMATION STATEMENT and am aware of the general purpose and methods.

3. I understand that I am free to withdraw from this study at any time without penalty or prejudice.

4. I understand that all the information I provide to the study will be kept completely confidential.

Signature_____ Date_____

APPENDIX 3

DAILY DIARY

DAY OF THE WEEK: **DATE:**
Patient's ID:

PLEASE RATE THE SEVERITY OF YOUR SYMPTOMS **today** by marking a cross on the line (_____) at the appropriate place:

1. Pain or discomfort in your stomach or abdomen (*do not include chest pain or period pain)*

_____

not present — very severe

2. Feeling as if your stomach or abdomen were bloated (*do not include bloating due to a menstrual period)*:

_____

not present — very severe

3. Constipation (*very hard or lumpy stools or straining to pass stool)*:

_____

not present — very severe

4. Diarrhoea (*very soft or watery stools or very urgent need to pass stool)*:

_____

not present — very severe

5. Please rate the **overall severity** of your IBS symptoms **today**:

_____

not present — very severe

APPENDIX 4

IRRITABLE BOWEL SYNDROME QUESTIONNAIRE (IBSQ)

IRRITABLE BOWEL SYNDROME QUESTIONNAIRE – IBSQ

Date: __/__/__ Patient ID No.: _____
Patient Initials: _____

Thank you for participating in this important research. All you need to do is tick the answers. Some of the questions are of a sensitive nature. You do not have to answer any question that you don't want to, but please remember all answers are kept totally confidential. If you are NOT SURE or CAN'T REMEMBER the answer to a question, just tick your best guess.

1. How old are you? _____ years

2. Are you *(tick answer)*:

1 ☐ FEMALE
2 ☐ MALE

FIRST, WE WOULD LIKE TO GET SOME DETAILS ABOUT ONLY THE PAST 3 MONTHS. Stomach, abdominal or stomach pain or discomfort can be difficult to describe and sometimes more than one type of pain can occur. We would like to ask you some questions only about the usual or primary pain or discomfort in your stomach or abdomen in the past year.

3. IN THE PAST 3 MONTHS has there been a time when you KEPT GETTING pains or discomfort in your stomach or abdomen? (Please do NOT count cramps or pain with menstrual periods, and do NOT count pain in your chest). *(Tick answer).*

1 ☐ YES
0 ☐ NO

IF NO, PLEASE GO TO QUESTION 11

IF YES, PLEASE ANSWER THE FOLLOWING QUESTIONS:

4. Over MOST of the PAST 3 MONTHS, have you KEPT GETTING this pain or discomfort? *(Tick answer)*

1 ☐ YES
0 ☐ NO

5. IN THE PAST 3 MONTHS, how bad has the pain or discomfort been, usually? *(Tick one answer)*

1	☐	VERY MILD: can usually be ignored
2	☐	MILD: can be ignored if you don't think about it
3	☐	MODERATE: cannot be ignored but does not affect your lifestyle
4	☐	SEVERE: affects your lifestyle
5	☐	VERY SEVERE: markedly affects your lifestyle

6. IN THE PAST 3 MONTHS, ON AVERAGE, how often have you had this pain or discomfort? *(Tick one answer)*

1	☐	LESS THAN ONCE A MONTH
2	☐	ABOUT ONCE A MONTH
3	☐	ABOUT TWO OR THREE TIMES A MONTH
4	☐	ABOUT ONCE A WEEK
5	☐	SEVERAL TIMES A WEEK
6	☐	DAILY

7. Please look at Diagram 1 (below). IN THE PAST 3 MONTHS, has this pain or discomfort in your abdomen usually been: *(tick one answer)*

1	☐	IN THE AREA MARKED A
2	☐	IN THE AREA MARKED B
3	☐	IN BOTH AREAS (A AND B)

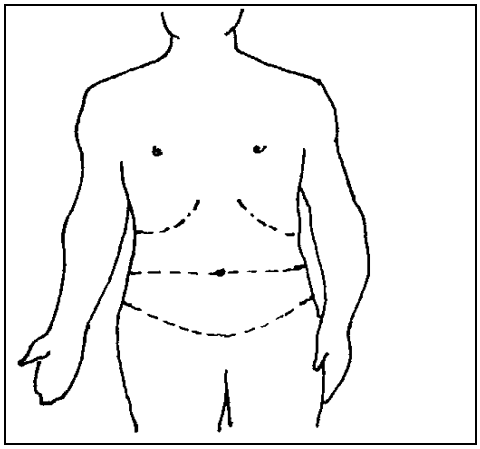
8. IN THE PAST 3 MONTHS, has your pain or discomfort EVER WOKEN YOU from your sleep at night? *(Tick one answer)*

1	☐	YES
0	☐	NO

9. Does this pain or discomfort COME AND GO PERIODICALLY? Periodically here means periods of at least a month with no pain or discomfort, with periods in-between of weeks to months when there is pain or discomfort. *(Tick answer)*

1	☐	YES
0	☐	NO

PLEASE NOTE: WHEN WE SAY **OFTEN** WE MEAN MORE THAN 25% (ONE QUARTER) OF THE TIME.



10. IN THE PAST 3 MONTHS, WOULD YOU SAY THAT: *(tick YES or NO for each item)*

	Yes	*No*
This pain or discomfort was OFTEN made BETTER by having a bowel movement (passing stool)?	☐	☐
You OFTEN had MORE bowel movements than usual when this pain or discomfort began?	☐	☐
You OFTEN had FEWER bowel movements than usual when this pain or discomfort began?	☐	☐
You OFTEN had LOOSER bowel movements (stools) than usual when this pain or discomfort began?	☐	☐
You OFTEN had HARDER bowel movements (stools) than usual when this pain or discomfort began?	☐	☐
This pain or discomfort OFTEN occurred AFTER meals?	☐	☐

11. IN THE PAST 3 MONTHS, WOULD YOU SAY THAT: *(tick YES or NO for each item)*

	Yes	*No*
You OFTEN had MORE than 3 bowel movements each DAY?	☐	☐
You OFTEN had FEWER than 3 bowel movements each WEEK?	☐	☐
Your stools were OFTEN VERY LUMPY or HARD?	☐	☐
After finishing a bowel movement, you OFTEN felt there was still stool needed to be passed?	☐	☐
You OFTEN experienced an URGENT need to have a bowel movement that made you rush or hurry to a toilet?	☐	☐
You OFTEN felt FULL soon after starting to eat so that you could not finish a normal meal?	☐	☐
You OFTEN needed to STRAIN a lot to have a bowel movement?	☐	☐

PLEASE CHECK THAT YOU HAVE ANSWERED ALL THE ITEMS IN QUESTIONS 10 AND 11.

12. IN THE PAST 3 MONTHS, have you OFTEN been troubled by feeling as if you stomach or abdomen were swollen (BLOATED)? *(Tick answer)*

1 ☐ YES
0 ☐ NO

IF **YES**, PLEASE ANSWER QUESTION 13.	IF **NO,** PLEASE GO TO **QUESTION 14.**

13. Please look at Diagram 1 *(page 2)*. IN THE PAST 3 MONTHS, has your bloated feeling usually been *(tick one answer)*:

1 ☐ IN THE AREA MARKED A
2 ☐ IN THE AREA MARKED B
3 ☐ IN THE BOTH AREAS (A AND B)

14. IN THE PAST 3 MONTHS, have you OFTEN seen your stomach or abdomen swell up, or had to loosen your belt or clothes because of swelling? *(Tick answer)*.

1 ☐ YES
0 ☐ NO

15. IN THE PAST 3 MONTHS, have your stools been VERY LOOSE or WATERY? *(Tick one answer)*.

0 ☐ SOMETIMES (LESS THAN ONE QUARTER OF THE TIME) OR NEVER
1 ☐ OFTEN (MORE THAN ONE QUARTER OF THE TIME)
2 ☐ USUALLY (MORE THAN THREE QUARTERS OF THE TIME)

16. IN THE PAST 3 MONTHS, have you EVER seen MUCUS (white or green slimy material) in your stools? *(Tick one answer)*.

1 ☐ YES
0 ☐ NO

WE WOULD LIKE TO ASK YOU ABOUT PAIN OR DISCOMFORT IN YOUR STOMACH OR ABDOMEN DURING YOUR WHOLE LIFETIME, EXCEPT FOR THE PAST YEAR.

17. IN YOUR LIFETIME BEFORE THE PAST 3 MONTHS, was there ever a time when you KEPT GETTING pains or discomfort in your stomach or abdomen? (Please do NOT count cramps or pain with menstrual periods, and do NOT count pain in your chest). *(Tick one answer)*.

1 ☐ YES
0 ☐ NO

IF **YES**, PLEASE ANSWER THE FOLLOWING QUESTIONS.	IF **NO**, PLEASE GO TO QUESTION 22.

18. When in your life did this pain or discomfort FIRST begin, as close as you can recall? *(Tick one answer)*.

1	☐	UP TO 2 YEARS AGO
2	☐	MORE THAN 2 YEARS TO 5 YEARS AGO
3	☐	MORE THAN 5 YEARS TO 10 YEARS AGO
4	☐	MORE THAN 10 YEARS TO 20 YEARS AGO
5	☐	MORE THAN 20 YEARS AGO

19. IN YOUR LIFETIME BEFORE THE LAST 3 MONTHS, were you ever TROUBLED by pain or discomfort in your stomach or abdomen over a period of THREE MONTHS OR LONGER? *(Tick one answer).*

1	☐	YES
0	☐	NO

20. Please look at Diagram 1 (page 2). IN YOUR LIFETIME BEFORE THE PAST 3 MONTHS, was that pain or discomfort in your stomach or abdomen USUALLY: *(tick one answer)*

1	☐	IN THE AREA MARKED A
2	☐	IN THE AREA MARKED B
3	☐	IN BOTH AREAS (A AND B)

21. IN YOUR LIFETIME BEFORE THE PAST 3 MONTHS, when you were TROUBLED BY that pain or discomfort, were you also TROUBLED BY BOWEL DISTURBANCES (such as CONSTIPATION and/or DIARRHOEA)? *(Tick one answer)*.

0	☐	YES
1	☐	NO

NOW WE NEED TO KNOW ABOUT YOUR GENERAL HEALTH AND LIFESTYLE

22. IN THE PAST **12** MONTHS, how frequently have you visited a doctor for any reason (for yourself)? *(Tick one answer).*

0 ☐ NEVER
1 ☐ OCCASIONALLY
2 ☐ SOMETIMES
3 ☐ OFTEN

23. IN THE PAST **12** MONTHS, how frequently have you sought alternative therapy of any kind (acupuncture, naturopathy, homoeopathy, herbal medicine etc.) for any reason (for yourself)? *(Tick one answer).*

0 ☐ NEVER
1 ☐ OCCASIONALLY
2 ☐ SOMETIMES
3 ☐ OFTEN

24. IN THE PAST **12** MONTHS, how frequently were your visits to a doctor or alternative therapist for pain or discomfort in your stomach or abdomen? *(Tick one answer).*

0 ☐ NEVER
1 ☐ OCCASIONALLY
2 ☐ SOMETIMES
3 ☐ OFTEN

25. IN YOUR LIFETIME **BEFORE** THE PAST 12 MONTHS, about how frequently have you visited any doctor or alternative therapist for pain or discomfort in your stomach or abdomen? *(Tick one answer).*

0 ☐ NEVER
1 ☐ OCCASIONALLY
2 ☐ SOMETIMES
3 ☐ OFTEN

26. What is your CURRENT marital status: *(tick one answer)*

1 ☐ MARRIED
2 ☐ DE FACTO/LIVING WITH
3 ☐ NEVER MARRIED
4 ☐ WIDOWED
5 ☐ DIVORCED
6 ☐ SEPARATED

27. Please indicate your HIGHEST level of EDUCATIONAL training, or equivalent: *(tick one answer)*

1	☐ POSTGRADUATE QUALIFICATIONS
2	☐ UNIVERSITY GRADUATE (3 YEARS OR MORE)
3	☐ COMPLETED TAFE CERTIFICATE/ASSOCIATE DIPLOMA, TRADES APPRENTICESHIP, OR 2 YEARS UNIVERSITY
4	☐ H.S.C. (HIGHER SCHOOL CERTIFICATE)
5	☐ COMPLETEDYEAR10 (FOURTHFORM/SCHOOL CERTIFICATE)
6	☐ SOME YEARS AT HIGH SCHOOL
7	☐ PRIMARY SCHOOL ONLY

28. Please indicate how much coffee or alcohol you have ON AVERAGE EACH DAY.

Number of cups of coffee per day _____

Number of alcoholic drinks per day _____

29. **If relevant**, please indicate whether you are taking hormonal pills including oral contraception or hormone replacement therapy.

1	YES
0	NO

Please specify the date of your last menstrual period: _____

PLEASE CHECK THAT YOU HAVE ANSWERED ALL THE QUESTIONS.

Thank you for your participation in this research – it is very much appreciated. You are welcome to make any comments or ask any questions.

APPENDIX 5

BOWEL SYMPTOM SEVERITY SCALE

BOWEL SYMPTOM SEVERITY SCALE (VI)

Subject No. ☐☐☐ **Date** ☐☐ ☐☐ ☐☐

General Instructions.

Please indicate below, how often you may have had each symptom of bowel disease **over the past 2 weeks.** Do this by placing a cross neatly in the small box. If you do not have the symptom, place a cross in the "not at all" box. Please ensure you answer all of the questions.

1a. Over the **past two weeks**, how often have you had **loose or watery bowel motions**?

Not at all	Every other day	Every day	1-3 times a day	More than 3 times a day
☐	☐	☐	☐	☐

1b. How **distressed** were you by this?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

1c. How much did this **interfere** with your everyday life?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

2a. Over the **past two weeks**, on how many occasions did you have **hard or lumpy stools** when you had a bowel motion?

Not at all	Occasionally	Sometimes	Most times	Every time
☐	☐	☐	☐	☐

2b. How **distressed** were you by this?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

2c. How much did this **interfere** with your everyday life?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

3a. Over the **past two weeks**, how often have you had **abdominal (tummy) pain**?

Not at all	Once or twice	3-5 times	Every day	More than once a day
☐	☐	☐	☐	☐

3b. How **distressed** were you by this?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

3c. How much did this **interfere** with your everyday life?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

4a. Over the **past two weeks**, on how many days have you had **more than 3 bowel motions a day**?

Not at all	1	2-3	4-5	6-7
☐	☐	☐	☐	☐

4b. How **distressed** were you by this?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

4c. How much did this **interfere** with your everyday life?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

5a. Over the **past two weeks**, how often have you felt **bloated** or had an **uncomfortable fullness in your abdomen?**

Not at all	Once or twice	3-5 times	Every day	More than once a day
☐	☐	☐	☐	☐

5b. How **distressed** were you by this?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

5c. How much did this **interfere** with your everyday life?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

6a. Over the **past two weeks**, how often have you had **an urgent need to have a bowel motion**?

Not at all	Once or twice	3-5 times	Every day	More than once a day
☐	☐	☐	☐	☐

6b. How **distressed** were you by this?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

6c. How much did this **interfere** with your everyday life?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

7a. Over the **past two weeks**, how many days have there been when you were **unable to have a bowel motion**?

Not at all	1	2-3	4-5	6-7
☐	☐	☐	☐	☐

7b. How **distressed** were you by this?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

7c. How much did this **interfere** with your everyday life?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

8a. Over the **past two weeks**, how often have you had a **general feeling of discomfort in your abdomen (tummy)**?

Not at all	Once or twice	3-5 times	Every day	More than once a day
☐	☐	☐	☐	☐

8b. How **distressed** were you by this?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

8c. How much did this **interfere** with your everyday life?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

APPENDIX 6

IRRITABLE BOWEL SYNDROME SYMPTOM SCALES 1-5

BSS1

IRRITABLE BOWEL SYNDROME – SYMPTOM SCALE (BSS1)

Date: ___/___/___ Patient ID: _____
Patient Initials:_____

INSTRUCTIONS. This questionnaire asks for your views about your health, how you feel, and how well you are able to do your usual activities. If you are unsure about how to answer any question, please give the best answer you can.

1. PLEASE RATE THE SEVERITY OF YOUR SYMPTOMS **over the last two weeks** by marking a cross on the line (_____) at the appropriate place:

   Pain or discomfort in your stomach or abdomen (*do not include chest pain or period pain):*

   _____

   Not present — Very severe

   Feeling as if your stomach or abdomen were bloated or swollen (*do not include bloating due to a menstrual period*):

   _____

   Not present — Very severe

   Constipation (very hard **or** lumpy stools **or** fewer than 3 bowel movements a week **or** straining to pass stool):

   _____

   Not present — Very severe

   Diarrhoea (very soft or watery stools **or** more than 3 bowel movements a day **or** very urgent need to pass stool):

   _____

   Not present — Very severe

   Please rate the **overall severity** of your IBS symptoms over **THE LAST TWO WEEKS:**

   _____

   Not present — Very severe

2. Please TICK the description below which BEST FITS YOUR BOWEL MOVEMENTS **in the last two weeks:**

- ❑ Separate hard lumps
- ❑ Sausage-shaped but lumpy
- ❑ Like a sausage or snake, but with cracks in its surface
- ❑ Like a sausage or snake, smooth and soft
- ❑ Soft blobs with clear-cut edges
- ❑ Fluffy pieces with ragged edges, a mushy stool
- ❑ Watery, no solid pieces

3. **Over the last two weeks**, how much has your irritable bowel syndrome INTERFERED WITH YOUR LIFE AND ACTIVITIES? (*tick one answer*):

- ❑ Not at all
- ❑ A little
- ❑ Some
- ❑ A lot
- ❑ Extreme interference

4. Please WRITE THE NAMES of any MEDICATIONS you have taken **in the last two weeks,** and how often you took them (e.g. "once only", "twice a day for four days", etc.). Include ALL medications, even headache tablets, antacids and other digestion medication, contraceptive pills, high doses of vitamins, sedatives, and any herbal or homoeopathic medications. If you cannot remember exactly, please write your best guess.

MEDICATION	HOW OFTEN?
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

5. **In the last two weeks**, have you eaten MORE FIBRE (e.g. wholemeal bread, high-fibre breakfast cereals, fruit and vegetables, fibre supplements, etc.) than you USUALLY eat?

- ❑ No
- ❑ A little more
- ❑ A lot more

BSS2

IRRITABLE BOWEL SYNDROME – SYMPTOM SCALE (BSS2)

Date: ___/___/___ Patient ID: _____
Patient Initials: _____

INSTRUCTIONS. This questionnaire asks for your views about your health, how you feel, and how well you are able to do your usual activities. If you are unsure about how to answer any question, please give the best answer you can.

1. PLEASE RATE THE SEVERITY OF YOUR SYMPTOMS **over the last week** by marking a cross on the line (_____) at the appropriate place:

Pain or discomfort in your stomach or abdomen (*do not include chest pain or period pain):*

_____

Not present — Very severe

Feeling as if your stomach or abdomen were bloated or swollen (*do not include bloating due to a menstrual period*):

_____

Not present — Very severe

Constipation (very hard **or** lumpy stools **or** fewer than 3 bowel movements a week **or** straining to pass stool):

_____

Not present — Very severe

Diarrhoea (very soft or watery stools **or** more than 3 bowel movements a day **or** very urgent need to pass stool):

_____

Not present — Very severe

Please rate the **overall severity** of your IBS symptoms over **THE LAST WEEK:**

_____

Not present — Very severe

2. Please TICK the description below which BEST FITS YOUR BOWEL MOVEMENTS **in the last week:**

- ❑ Separate hard lumps
- ❑ Sausage-shaped but lumpy
- ❑ Like a sausage or snake, but with cracks in its surface
- ❑ Like a sausage or snake, smooth and soft
- ❑ Soft blobs with clear-cut edges
- ❑ Fluffy pieces with ragged edges, a mushy stool
- ❑ Watery, no solid pieces

3. **Over the last week**, how much has your irritable bowel syndrome INTERFERED WITH YOUR LIFE AND ACTIVITIES? (*tick one answer*):

- ❑ Not at all
- ❑ A little
- ❑ Some
- ❑ A lot
- ❑ Extreme interference

4. COMPARED TO LAST TIME you filled in this questionnaire (**a week ago**), do you feel that your irritable bowel syndrome symptoms have: (*tick one answer*)

- ❑ Improved ----------> **If improved**, are your symptoms: (*tick one answer*):
- ❑ Stayed the same
- ❑ Worsened

- ☐ A little better
- ☐ Moderately better
- ☐ A lot better

5. Please WRITE THE NAMES of any MEDICATIONS you have taken **in the last week** and how often you took them (e.g. "once only", "twice a day for four days", etc.). Include ALL medications, even headache tablets, antacids and other digestion medication, contraceptive pills, high doses of vitamins, sedatives, and any herbal or homoeopathic medications. If you cannot remember exactly, please write your best guess. If your medications have not changed since you last filled in this form, just write "same as before".

MEDICATION	HOW OFTEN?
_____	_____
_____	_____
_____	_____
_____	_____

6. **In the last week**, have you eaten MORE FIBRE (e.g. wholemeal bread, high-fibre breakfast cereals, fruit and vegetables, fibre supplements, etc.) than you USUALLY eat?

☐ No ☐ A little more ☐ A lot more

BSS3

IRRITABLE BOWEL SYNDROME – SYMPTOM SCALE (BSS3)

Date: ___/___/___ Patient ID: _____
Patient Initials: _____

INSTRUCTIONS. This questionnaire asks for your views about your health, how you feel, and how well you are able to do your usual activities. If you are unsure about how to answer any question, please give the best answer you can.

1. PLEASE RATE THE SEVERITY OF YOUR SYMPTOMS **over the last two weeks** by marking a cross on the line (_____) at the appropriate place:

Pain or discomfort in your stomach or abdomen (*do not include chest pain or period pain):*

_____

Not present — Very severe

Feeling as if your stomach or abdomen were bloated or swollen (*do not include bloating due to a menstrual period*):

_____

Not present — Very severe

Constipation (very hard **or** lumpy stools **or** fewer than 3 bowel movements a week **or** straining to pass stool):

_____

Not present — Very severe

Diarrhoea (very soft or watery stools **or** more than 3 bowel movements a day **or** very urgent need to pass stool):

_____

Not present — Very severe

Please rate the **overall severity** of your IBS symptoms over **THE LAST TWO WEEKS:**

_____

Not present — Very severe

2. Please TICK the description below which BEST FITS YOUR BOWEL MOVEMENTS **in the last two weeks:**

- ❑ Separate hard lumps
- ❑ Sausage-shaped but lumpy
- ❑ Like a sausage or snake, but with cracks in its surface
- ❑ Like a sausage or snake, smooth and soft
- ❑ Soft blobs with clear-cut edges
- ❑ Fluffy pieces with ragged edges, a mushy stool
- ❑ Watery, no solid pieces

3. **Over the last two weeks**, how much has your irritable bowel syndrome INTERFERED WITH YOUR LIFE AND ACTIVITIES? (*tick one answer*):

- ❑ Not at all
- ❑ A little
- ❑ Some
- ❑ A lot
- ❑ Extreme interference

4. COMPARED TO LAST TIME you filled in this questionnaire (**two weeks ago**), do you feel that your irritable bowel syndrome symptoms have: (*tick one answer*)

- ❑ Improved ----------> **If improved**, are your symptoms: (*tick one answer*):
  - ☐ A little better
  - ☐ Moderately better
  - ☐ A lot better
- ❑ Stayed the same
- ❑ Worsened

5. Please WRITE THE NAMES of any MEDICATIONS you have taken **in the last two weeks,** and how often you took them (e.g. "once only", "twice a day for four days", etc.). Include <u>ALL</u> medications, even headache tablets, antacids and other digestion medication, contraceptive pills, high doses of vitamins, sedatives, and any herbal or homoeopathic medications. If you cannot remember exactly, please write your best guess. If your medications have not changed since you last filled in this form, just write "same as before".

MEDICATION	HOW OFTEN?
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

6. **In the last two weeks,** how many times did you COMPLETELY MISS doing your relaxation exercise?
   (*Please write the number of times*) ☐

7. **In the last two weeks**, have you eaten MORE FIBRE (e.g. wholemeal bread, high-fibre breakfast cereals, fruit and vegetables, fibre supplements, etc.) than you USUALLY eat?

   ☐ No ☐ A little more ☐ A lot more

BSS4

IRRITABLE BOWEL SYNDROME – SYMPTOM SCALE (BSS4)

Date: ___/___/___ Patient ID: _____
Patient Initials: _____
_____

INSTRUCTIONS. This questionnaire asks for your views about your health, how you feel, and how well you are able to do your usual activities. If you are unsure about how to answer any question, please give the best answer you can.

1. PLEASE RATE THE SEVERITY OF YOUR SYMPTOMS **over the last two weeks** by marking a cross on the line (_____) at the appropriate place:

Pain or discomfort in your stomach or abdomen (*do not include chest pain or period pain*):

_____

Not present — Very severe

Feeling as if your stomach or abdomen were bloated or swollen (*do not include bloating due to a menstrual period*):

_____

Not present — Very severe

Constipation (very hard **or** lumpy stools **or** fewer than 3 bowel movements a week **or** straining to pass stool):

_____

Not present — Very severe

Diarrhoea (very soft or watery stools **or** more than 3 bowel movements a day **or** very urgent need to pass stool):

_____

Not present — Very severe

Please rate the **overall severity** of your IBS symptoms over **THE LAST TWO WEEKS:**

_____

Not present — Very severe

2. Please TICK the description below which BEST FITS YOUR BOWEL MOVEMENTS **in the last two weeks:**

- ❑ Separate hard lumps
- ❑ Sausage-shaped but lumpy
- ❑ Like a sausage or snake, but with cracks in its surface
- ❑ Like a sausage or snake, smooth and soft
- ❑ Soft blobs with clear-cut edges
- ❑ Fluffy pieces with ragged edges, a mushy stool
- ❑ Watery, no solid pieces

3. **Over the last two weeks**, how much has your irritable bowel syndrome INTERFERED WITH YOUR LIFE AND ACTIVITIES? (*tick one answer*):

- ❑ Not at all
- ❑ A little
- ❑ Some
- ❑ A lot
- ❑ Extreme interference

4. COMPARED TO LAST TIME you filled in this questionnaire (**two weeks ago**), do you feel that your irritable bowel syndrome symptoms have: (*tick one answer*)

- ❑ Improved ----------> **If improved**, are your symptoms: (*tick one answer*):
- ❑ Stayed the same
- ❑ Worsened

☐ A little better
☐ Moderately better
☐ A lot better

5. COMPARED TO BEFORE YOU COMMENCED THE TRIAL, do you feel that your irritable bowel syndrome symptoms have: (*tick one answer*)

- ❑ Improved ----------> **If improved**, are your symptoms: (*tick one answer*):
- ❑ Stayed the same
- ❑ Worsened

☐ A little better
☐ Moderately better
☐ A lot better

6. Please WRITE THE NAMES of any MEDICATIONS you have taken **in the last two weeks,** and how often you took them (e.g. "once only", "twice a day for four days", etc.). Include <u>ALL</u> medications, even headache tablets, antacids and other digestion medication, contraceptive pills, high doses of vitamins, sedatives, and any herbal or homoeopathic medications. If you cannot remember exactly, please write your best guess. If your medications have not changed since you last filled in this form, just write "same as before".

MEDICATION	HOW OFTEN?
_____	_____
_____	_____
_____	_____
_____	_____

7. **In the last two weeks,** how many times did you COMPLETELY MISS doing your relaxation exercise? (*Please write the number of times*) ☐

8. **In the last two weeks**, have you eaten MORE FIBRE (e.g. wholemeal bread, high-fibre breakfast cereals, fruit and vegetables, fibre supplements, etc.) than you USUALLY eat?

☐ No ☐ A little more ☐ A lot more

BSS5

IRRITABLE BOWEL SYNDROME – SYMPTOM SCALE (BSS5)

Date: ___/___/___ Patient ID: _____
Patient Initials: _____

INSTRUCTIONS. This questionnaire asks for your views about your health, how you feel, and how well you are able to do your usual activities. If you are unsure about how to answer any question, please give the best answer you can.

1. PLEASE RATE THE SEVERITY OF YOUR SYMPTOMS **over the last two weeks** by marking a cross on the line (_____) at the appropriate place:

Pain or discomfort in your stomach or abdomen (*do not include chest pain or period pain*):

_____

Not present — Very severe

Feeling as if your stomach or abdomen were bloated or swollen (*do not include bloating due to a menstrual period*):

_____

Not present — Very severe

Constipation (very hard **or** lumpy stools **or** fewer than 3 bowel movements a week **or** straining to pass stool):

_____

Not present — Very severe

Diarrhoea (very soft or watery stools **or** more than 3 bowel movements a day **or** very urgent need to pass stool):

_____

Not present — Very severe

Please rate the **overall severity** of your IBS symptoms over **THE LAST TWO WEEKS:**

_____

Not present — Very severe

2. Please TICK the description below which BEST FITS YOUR BOWEL MOVEMENTS **in the last two weeks:**

- ❑ Separate hard lumps
- ❑ Sausage-shaped but lumpy
- ❑ Like a sausage or snake, but with cracks in its surface
- ❑ Like a sausage or snake, smooth and soft
- ❑ Soft blobs with clear-cut edges
- ❑ Fluffy pieces with ragged edges, a mushy stool
- ❑ Watery, no solid pieces

3. **Over the last two weeks**, how much has your irritable bowel syndrome INTERFERED WITH YOUR LIFE AND ACTIVITIES? (*tick one answer*):

- ❑ Not at all
- ❑ A little
- ❑ Some
- ❑ A lot
- ❑ Extreme interference

4. COMPARED TO LAST TIME you filled in this questionnaire (**two weeks ago**), do you feel that your irritable bowel syndrome symptoms have: (*tick one answer*)

- ❑ Improved ----------> **If improved**, are your symptoms: (*tick one answer*):
- ❑ Stayed the same
- ❑ Worsened

- ☐ A little better
- ☐ Moderately better
- ☐ A lot better

5. COMPARED TO BEFORE YOU COMMENCED THE TRIAL, do you feel that your irritable bowel syndrome symptoms have: (*tick one answer*)

- ❑ Improved ----------> **If improved**, are your symptoms: (*tick one answer*):
- ❑ Stayed the same
- ❑ Worsened

- ☐ A little better
- ☐ Moderately better
- ☐ A lot better

6. Please WRITE THE NAMES of any MEDICATIONS you have taken **in the last two weeks,** and how often you took them (e.g. "once only", "twice a day for four days", etc.). Include ALL medications, even headache tablets, antacids and other digestion medication, contraceptive pills, high doses of vitamins, sedatives, and any herbal or homoeopathic medications. If you cannot remember exactly, please write your best guess. If your medications have not changed since you last filled in this form, just write "same as before".

MEDICATION	HOW OFTEN?
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

7. **In the last two weeks**, have you eaten MORE FIBRE (e.g. wholemeal bread, high-fibre breakfast cereals, fruit and vegetables, fibre supplements, etc.) than you USUALLY eat?

☐ No ☐ A little more ☐ A lot more

APPENDIX 7

SCL-90-R

SCL-R

Below is a list of problems people sometimes have. Please read each one carefully, and circle HOW MUCH THAT PROBLEM HAS DISTRESSED OR BOTHERED YOU DURING THE PAST THREE (3) MONTHS.

Blacken the circle for only one number for each problem and do not skip any items. Read the example below before beginning, and if you have any questions please ask about them.

	NOT AT ALL	A LITTLE BIT	MODERATELY	QUITE A BIT	EXTREMELY	EXAMPLE HOW MUCH WERE YOU DISTRESSED BY:
1	0	1	2	●	4	Bodyaches

	NOT AT ALL	A LITTLE BIT	MODERATELY	QUITE A BIT	EXTREMELY	HOW MUCH WERE YOU DISTRESSED BY:
1	0	1	2	3	4	Headaches
2	0	1	2	3	4	Nervousness or shakiness inside
3	0	1	2	3	4	Repeated unpleasant thoughts that won't leave your mind
4	0	1	2	3	4	Faintness or dizziness
5	0	1	2	3	4	Loss of sexual interest or pleasure
6	0	1	2	3	4	Feeling critical of others
7	0	1	2	3	4	The idea that someone else can control your thoughts
8	0	1	2	3	4	Feeling others are to blame for most of your troubles
9	0	1	2	3	4	Trouble remembering things
10	0	1	2	3	4	Worried about sloppiness or carelessness
11	0	1	2	3	4	Feeling easily annoyed or irritated
12	0	1	2	3	4	Pains in heart or chest
13	0	1	2	3	4	Feeling afraid in open spaces or on the streets
14	0	1	2	3	4	Feeling low in energy or slowed down
15	0	1	2	3	4	Thoughts of ending your life
16	0	1	2	3	4	Hearing voices that other people do not hear
17	0	1	2	3	4	Trembling
18	0	1	2	3	4	Feeling that most people cannot be trusted
19	0	1	2	3	4	Poor appetite
20	0	1	2	3	4	Crying easily
21	0	1	2	3	4	Feeling shy or uneasy with the opposite sex
22	0	1	2	3	4	Feelings of being trapped or caught
23	0	1	2	3	4	Suddenly scared for no reason
24	0	1	2	3	4	Temper outbursts that you could not control
25	0	1	2	3	4	Feeling afraid to go out of your house alone
26	0	1	2	3	4	Blaming yourself for things
27	0	1	2	3	4	Pains in lower back
28	0	1	2	3	4	Feeling blocked in getting things done
29	0	1	2	3	4	Feeling lonely
30	0	1	2	3	4	Feeling blue
31	0	1	2	3	4	Worrying too much about things
32	0	1	2	3	4	Feeling no interest in things
33	0	1	2	3	4	Feeling fearful
34	0	1	2	3	4	Your feelings being easily hurt
35	0	1	2	3	4	Other people being aware of your private thoughts
36	0	1	2	3	4	Feeling others do not understand you or are unsympathetic
37	0	1	2	3	4	Feeling that people are unfriendly or dislike you

CONTINUED OVER PAGE

	NOT AT ALL	A LITTLE BIT	MODERATELY	QUITE A BIT	EXTREMELY	HOW MUCH WERE YOU DISTRESSED BY:
38	0	1	2	3	4	Having to do things very slowly to insure correctness
39	0	1	2	3	4	Heart pounding or racing
40	0	1	2	3	4	Nausea or upset stomach
41	0	1	2	3	4	Feeling inferior to others
42	0	1	2	3	4	Soreness of your muscles
43	0	1	2	3	4	Feeling that you are watched or talked about by others
44	0	1	2	3	4	Trouble falling asleep
45	0	1	2	3	4	Having to check and double-check what you do
46	0	1	2	3	4	Difficulty making decisions
47	0	1	2	3	4	Feeling afraid to travel on buses, subways, or trains
48	0	1	2	3	4	Trouble getting your breath
49	0	1	2	3	4	Hot or cold spells
50	0	1	2	3	4	Having to avoid certain things, places, or activities because they frighten you
51	0	1	2	3	4	Your mind going blank
52	0	1	2	3	4	Numbness or tingling in parts of your body
53	0	1	2	3	4	A lump in your throat
54	0	1	2	3	4	Feeling hopeless about the future
55	0	1	2	3	4	Trouble concentrating
56	0	1	2	3	4	Feeling weak in parts of your body
57	0	1	2	3	4	Feeling tense or keyed up
58	0	1	2	3	4	Heavy feelings in your arms or legs
59	0	1	2	3	4	Thoughts of death or dying
60	0	1	2	3	4	Overeating
61	0	1	2	3	4	Feeling uneasy when people are watching or talking about you
62	0	1	2	3	4	Having thoughts that are not your own
63	0	1	2	3	4	Having urges to beat, injure, or harm someone
64	0	1	2	3	4	Awakening in the early morning
65	0	1	2	3	4	Having to repeat the same actions such as touching, counting, or washing
66	0	1	2	3	4	Sleep that is restless or disturbed
67	0	1	2	3	4	Having urges to break or smash things
68	0	1	2	3	4	Having ideas or beliefs that others do not share
69	0	1	2	3	4	Feeling very self-conscious with others
70	0	1	2	3	4	Feeling uneasy in crowds, such as shopping or at a movie
71	0	1	2	3	4	Feeling everything is an effort
72	0	1	2	3	4	Spells of terror or panic
73	0	1	2	3	4	Feeling uncomfortable about eating or drinking in public
74	0	1	2	3	4	Getting into frequent arguments
75	0	1	2	3	4	Feeling nervous when you are left alone
76	0	1	2	3	4	Others not giving you proper credit for your achievements
77	0	1	2	3	4	Feeling lonely even when you are with people
78	0	1	2	3	4	Feeling so restless you couldn't sit still
79	0	1	2	3	4	Feelings of worthlessness
80	0	1	2	3	4	The feeling that something bad is going to happen to you
81	0	1	2	3	4	Shouting or throwing things
82	0	1	2	3	4	Feeling afraid you will faint in public
83	0	1	2	3	4	Feeling that people will take advantage of you if you let them
84	0	1	2	3	4	Having thoughts about sex that bother you a lot
85	0	1	2	3	4	The idea that you should be punished for your sins
86	0	1	2	3	4	Thoughts and images of a frightening nature
87	0	1	2	3	4	The idea that something serious is wrong with your body
88	0	1	2	3	4	Never feeling close to another person
89	0	1	2	3	4	Feelings of guilt
90	0	1	2	3	4	The idea that something is wrong with your mind

Table 15 - Procrustes and Varimax Loadings on the Nine Dimensions of the SCL-90-R

SOMATIZATION	P	V
1. HEADACHES	.42	.40
4. FAINTNESS OR DIZZINESS	.49	.49
12. PAINS IN HEART OR CHEST	.53	.51
27. PAINS IN LOWER BACK	.62	.64
40. NAUSEA OR UPSET STOMACH	.52	.50
42. SORENESS OF YOUR MUSCLES	.64	.67
48. TROUBLE GETTING YOUR BREATH	.54	.52
49. HOT OR COLD SPELLS	.60	.61
52. NUMBNESS OR TINGLING IN PARTS OF YOUR BODY	.61	.61
53. A LUMP IN YOUR THROAT	.43	.40
56. FEELING WEAK IN PARTS OF YOUR BODY	.62	.66
58. HEAVY FEELINGS IN YOUR ARMS OR LEGS	.61	.65

OBSESSIVE-COMPULSIVE	P	V
3. REPEATED UNPLEASANT THOUGHTS THAT WON'T LEAVE YOUR MIND	-	-
9. TROUBLE REMEMBERING THINGS	.62	.61
10. WORRIED ABOUT SLOPPINESS OR CARELESSNESS [2]	.44	.43
28. FEELING BLOCKED IN GETTING THINGS DONE	.49	.50
38. HAVING TO DO THINGS VERY SLOWLY TO ENSURE CORRECTNESS	.72	.72
45. HAVING TO CHECK AND DOUBLE CHECK WHAT YOU DO	.70	.68
46. DIFFICULTY MAKING DECISIONS	.50	.47
51. YOUR MIND GOING BLANK	.58	.56
55. TROUBLE CONCENTRATING	.58	.57
65. HAVING TO REPEAT THE SAME ACTIONS SUCH AS TOUCHING, COUNTING, WASHING	.50	.48

INTERPERSONAL SENSITIVITY	P	V
6. FEELING CRITICAL OF OTHERS	-	-
21. FEELING SHY OR UNEASY WITH THE OPPOSITE SEX	.56	.5
34. YOUR FEELINGS BEING EASILY HURT	.35	
36. FEELING OTHERS DO NOT UNDERSTAND YOU OR ARE UNSYMPATHETIC [1]	.30	
37. FEELING THAT PEOPLE ARE UNFRIENDLY OR DISLIKE YOU	.58	.5
41. FEELING INFERIOR TO OTHERS	.46	.4
61. FEELING UNEASY WHEN PEOPLE ARE WATCHING OR TALKING ABOUT YOU	.69	.6
69. FEELING VERY SELF-CONSCIOUS WITH OTHERS	.67	.6
73. FEELING UNCOMFORTABLE ABOUT EATING OR DRINKING IN PUBLIC [4]	.51	.5

DEPRESSION	P	V
5. LOSS OF SEXUAL INTEREST OR PLEASURE	.35	-
14. FEELING LOW IN ENERGY OR SLOWED DOWN	.50	.44
15. THOUGHTS OF ENDING YOUR LIFE	.42	.52
20. CRYING EASILY	.42	.44
22. FEELING OF BEING CAUGHT OR TRAPPED	.48	.51
26. BLAMING YOURSELF FOR THINGS	.53	.63
29. FEELING LONELY	.62	.69
30. FEELING BLUE	.70	.77
31. WORRYING TOO MUCH ABOUT THINGS	.55	.60
32. FEELING NO INTEREST IN THINGS	.58	.60
54. FEELING HOPELESS ABOUT THE FUTURE	.60	.67
71. FEELING EVERYTHING IS AN EFFORT	.52	.51
79. FEELINGS OF WORTHLESSNESS	.61	.71

ANXIETY	P	V
2. NERVOUSNESS OR SHAKINESS INSIDE	.63	.57
17. TREMBLING	.54	.50
23. SUDDENLY SCARED FOR NO REASON [4]	.48	-
33. FEELING FEARFUL [4]	.51	.31
39. HEART POUNDING OR RACING	.55	.54
57. FEELING TENSE OR KEYED UP	.54	.44
72. SPELLS OF TERROR OR PANIC [4]	.49	-
78. FEELING SO RESTLESS YOU COULDN'T SIT STILL	.36	-
80. FEELING THAT SOMETHING BAD IS GOING TO HAPPEN TO YOU	.61	.56
86. THOUGHTS AND IMAGES OF A FRIGHTENING NATURE	.60	.57

HOSTILITY	P	V
11. FEELING EASILY ANNOYED OR IRRITATED	.41	.4
24. TEMPER OUTBURSTS THAT YOU COULD NOT CONTROL	.70	.7
63. HAVING URGES TO BEAT, INJURE OR HARM SOMEONE	.60	.6
67. HAVING URGES TO BREAK OR SMASH THINGS	.68	.7
74. GETTING INTO FREQUENT ARGUMENTS	.62	.6
81. SHOUTING OR THROWING THINGS	.75	.8

PHOBIC ANXIETY	P	V
13. FEELING AFRAID IN OPEN SPACES OR IN THE STREETS	.64	.67
25. FEELING AFRAID TO GO OUT OF YOUR HOUSE ALONE	.59	.61
47. FEELING AFRAID TO TRAVEL ON BUSES, SUBWAYS, OR TRAINS	.70	.70
50. HAVING TO AVOID CERTAIN THINGS, PLACES, OR ACTIVITIES BECAUSE THEY FRIGHTEN YOU	.51	.54
70. FEELING UNEASY IN CROWDS, SUCH AS SHOPPING OR AT A MOVIE	.57	.58
75. FEELING NERVOUS WHEN YOU ARE LEFT ALONE	.35	-
82. FEELING AFRAID YOU WILL FAINT IN PUBLIC	.40	.44

PARANOID IDEATION	P	V
8. FEELING OTHERS ARE TO BLAME FOR MOST OF YOUR TROUBLES	.54	.54
18. FEELING THAT MOST PEOPLE CAN NOT BE TRUSTED	.55	.58
43. FEELING THAT YOU ARE WATCHED OR TALKED ABOUT BY OTHERS [3]	.35	.40
68. HAVING IDEAS OR BELIEFS THAT OTHERS DO NOT SHARE	.30	.30
76. OTHERS NOT GIVING YOU PROPER CREDIT FOR YOUR ACHIEVEMENTS	.47	.47
83. FEELING THAT PEOPLE WILL TAKE ADVANTAGE OF YOU IF YOU LET THEM	.58	.60

PSYCHOTICISM	P	V
7. THE IDEA THAT SOMEONE ELSE CAN CONTROL YOUR THOUGHTS	.49	.6
16. HEARING VOICES THAT OTHER PEOPLE DO NOT HEAR	.35	.4
35. OTHER PEOPLE BEING AWARE OF YOUR PRIVATE THOUGHTS	.39	.4
62. HAVING THOUGHTS THAT ARE NOT YOUR OWN	.57	.6
77. FEELING LONELY EVEN WHEN YOU ARE WITH PEOPLE [3]	.34	
84. HAVING THOUGHTS ABOUT SEX THAT BOTHER YOU A LOT	.45	
85. THE IDEA THAT YOU SHOULD BE PUNISHED FOR YOUR SINS	.46	.3
87. THE IDEA THAT SOMETHING SERIOUS IS WRONG WITH YOUR BODY [1]	.31	
88. NEVER FEELING CLOSE TO ANOTHER PERSON	.36	
90. THE IDEA THAT SOMETHING IS WRONG WITH YOUR MIND	.38	

1 - ALSO LOADS ON THE SOMATIZATION DIMENSION
2 - ALSO LOADS ON THE INTERPERSONAL SENSITIVITY DIMENSION
3 - ALSO LOADS ON THE DEPRESSION DIMENSION
4 - ALSO LOADS ON THE PHOBIC ANXIETY DIMENSION
5 - ALSO LOADS ON THE PARANOID IDEATION DIMENSION

APPENDIX 8

SF-36 HEALTH SURVEY (VI)

SF-36 HEALTH SURVEY(VI)

Subject No. ☐☐☐ **Date** ☐☐ ☐☐ ☐☐

INSTRUCTIONS: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is: (cross one)

Excellent..... ☐

Very Good ..... ☐

Good ..... ☐

Fair ..... ☐

Poor ..... ☐

2. Compared to <u>two weeks ago</u>, how would you rate your health now?

(*cross* one)

Excellent ..... ☐

Very Good ..... ☐

Good ..... ☐

Fair ..... ☐

Poor ..... ☐

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Activities	Yes. Limited a lot.	Yes. Limited a little.	No. Not limited at all.
a. Vigorous activities such as running, lifting heavy objects, participating in strenuous sports	☐	☐	☐
b. Moderate activities such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
c. Lifting or carrying groceries	☐	☐	☐
d. Climbing several flights of stairs	☐	☐	☐
e. Climbing one flight of stairs	☐	☐	☐
f. Bending, kneeling or stooping	☐	☐	☐
g. Walking more than a mile	☐	☐	☐
h. Walking several blocks	☐	☐	☐
i. Walking one block	☐	☐	☐
j. Bathing or dressing yourself	☐	☐	☐

4. During the <u>past two weeks</u>, have you had any of the following problems with your work or other regular daily activities as a result of your physical health? (cross one box on each line)

	YES	NO
a. Cut down on the amount of time you spent on work or other activities	☐	☐
b. Accomplished less than you would like	☐	☐
c. Were limited in the kind of work or other activities	☐	☐
d. Had difficulty performing the work or other activities (e.g. it took extra effort)	☐	☐

5. During the past two weeks, have you had any of the following emotional problems with your work or other daily activities as a result of any emotional problems (such as feeling depressed or anxious)? (cross one box on each line)

	YES	NO
a. Cut down on the amount of time you spent on work or other activities	☐	☐
b. Accomplished less than you would like	☐	☐
c. Didn't do work or other activities as carefully as usual	☐	☐

6. During the past two weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

(cross one)

Not at all..... ☐

Slightly ..... ☐

Moderately ..... ☐

Quite a bit ..... ☐

Extremely ..... ☐

7. How much bodily pain have you had during the past two weeks? (cross one)

None ..... ☐

Very Mild ..... ☐

Mild ..... ☐

Moderate ..... ☐

Severe ..... ☐

Very Severe ..... ☐

8. During the past two weeks, how much did the pain interfere with your normal work (including both work outside the home and housework)? (cross one)

Not at all ..... ☐

A little bit ..... ☐

Moderately ..... ☐

Quite a bit ..... ☐

Extremely ..... ☐

9. These questions are about how you feel and about how things have been with you during the past two weeks. For each question, please give the answer that comes closest to the way you have been feeling.

How much of the time during the last two weeks ... (cross one box on each line)

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of pep?	☐	☐	☐	☐	☐	☐
b. Have you been a very nervous person?	☐	☐	☐	☐	☐	☐
c. Have you felt so down in the dumps that nothing could cheer you up?	☐	☐	☐	☐	☐	☐
d. Have you felt calm and peaceful?	☐	☐	☐	☐	☐	☐
e. Did you have a lot of energy?	☐	☐	☐	☐	☐	☐
f. Have you felt downhearted and blue?	☐	☐	☐	☐	☐	☐
g. Did you feel worn out?	☐	☐	☐	☐	☐	☐
h. Have you been a happy person?	☐	☐	☐	☐	☐	☐
i. Did you feel tired?	☐	☐	☐	☐	☐	☐

10. During the past two weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

(cross one)

All of the time ..... ☐

Most of the time ..... ☐

Some of the time ..... ☐

A little of the time ..... ☐

None of the time ..... ☐

11. How TRUE or FALSE is each of the following statements for you? (cross one box on each line)

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people.	☐	☐	☐	☐	☐
b. I am as healthy as anybody I know.	☐	☐	☐	☐	☐
c. I expect my health to get worse.	☐	☐	☐	☐	☐
d. My health is excellent.	☐	☐	☐	☐	☐

SF-36 Health Survey

Concepts	No. of items	Meaning of low score	Meaning of high score	Summary of content
Physical functioning	10	Limited a lot in performing all physical activities	Performs all types of physical activities without limitations due to health	Extent to which health limits physical activities such as self-care, walking, climbing stairs, bending, lifting, and moderate and vigorous exercises
Role functioning - physical	4	Limits with work & daily activities due to physical health	No limits due to physical health	Extent to which physical health interferes with work or other daily activities, including accomplishing less than wanted, limitations in the kind of activities, or difficulty in performing activities
Bodily pain	2	Severe, extremely limiting pain	No pain or limits in the past week	Intensity of pain and effect of pain on normal work, both inside and outside the home
General health	5	Perceives health as poor	Perceives health as excellent	Personal evaluation of health
Vitality	4	Feeling tired, worn out all the time	Feeling full of energy during the past week	How energetic or tired
Social functioning	2	Extreme interference with social activities	No interference from health in social activities	Extent to which physical health or emotional problems interfere with normal social activities
Role functioning - emotional	3	Limits due to emotional problems	No limits due to emotional problems	Extent to which emotional problems interfere with work or other daily activities, including decreased time spent on activities, accomplishing less, and not working as carefully as usual
Mental health	5	Feeling nervous or depressed in the past week	Feeling peaceful, happy and calm in the past week	General mental health including depression, anxiety
Reported health transition	1	Health poor and likely to get worse	Believes health is excellent	Evaluation of health compared to a week ago

Health concepts, items, levels and summary of content for SF36 sub-scales

APPENDIX 9

DUKE-UNC FUNCTIONAL SOCIAL SUPPORT QUESTIONNAIRE

Duke-UNC Functional Social Support Questionnaire

(Adapted from Broadhead, W.E., Gehlbach,S.H., De Gruy, F.V. & Kaplan, BB.H.(1988). The Duke-UNC Functional Social Support Questionnaire: measurement of social support in family medicine patients. *Medical Care, 26, 709-723).*

Here is a list of some things that other people do for us or give us that may be helpful or supportive. Please read each statement carefully and place a tick ( ) in the blank that is closest to your situation.

Here is an example:

I get ….	As much as I would like	Much less than I would like
holiday time	l_____l_____l_____l_____l_____l	

If you put a tick where we have, it means that you get almost as much holiday time as you would like, but not quite as much as you would like.

Answer each item as best you can. There are NO right or wrong answers.

I get ….	As much as I would like	Much less than I would like
1. invitations to go out and so things with other people	l_____l_____l_____l_____l_____l	
2. love and affection	l_____l_____l_____l_____l_____l	
3. chances to talk to someone about problems at work or with my house-work	l_____l_____l_____l_____l_____l	
4. chances to talk to someone I trust about my personal and family problems	l_____l_____l_____l_____l_____l	
5. chances to talk about money matters	l_____l_____l_____l_____l_____l	
6. people who care what happens to me	l_____l_____l_____l_____l_____l	
7. useful advice about important things in life	l_____l_____l_____l_____l_____l	
8. help when I'm sick in bed	l_____l_____l_____l_____l_____l	

Scoring: Each item is scored on a five point scale (1= As much as I would like, 5= Much less than I would like). Item scores are summed for confidant support (Items 1,3,4,5,7) and affective support (Items 2,6,8)

APPENDIX 10

SURVEY OF RECENT LIFE EXPERIENCES (SRLE)

SURVEY OF RECENT LIFE EXPERIENCES.
(SRLE)

Following is a list of experiences which many people have some time or other. Please indicate for each experience how much it has been a part of your life *over the past month*. Put a "1" in the space provided next to an experience if it was *not at all* part of your life over the past month; "2" for an experience which was *only slightly* part of your life over that time; "3" for an experience which was *distinctly* part of your life; and "4" for an experience which was *very much* part of your life over the past month.

Intensity of Experience over the Past Month.

1. *not at all* part of my life
2. *only slightly* part of my life
3. *distinctly* part of my life
4. *very much* part of my life

---

1. Disliking your daily activities _____
2. Lack of privacy _____
3. Disliking your work _____
4. Ethnic or racial conflict _____
5. Conflicts with in-laws or boyfriend's/girlfriend's family _____
6. Being let down or disappointed by friends _____
7. Conflict with supervisor(s) at work _____
8. Social rejection _____
9. Too many things to do at once _____
10. Being taken for granted _____
11. Financial conflicts with family members _____
12. Having your trust betrayed by a friend _____
13. Separation from people you care about _____
14. Having your contributions overlooked _____
15. Struggling to meet your own standards of performance & accomplishment _____
16. Being taken advantage of _____
17. Not enough leisure time _____
18. Financial conflict with friends or fellow workers _____

19. Struggling to meet other people's standards of performance & accomplishment _____

20. Having your actions misunderstood by others _____

21. Cash-flow difficulties _____

22. A lot of responsibilities _____

23. Dissatisfaction with work _____

24. Decisions about intimate relationship(s) _____

25. Not enough time to meet your obligations _____

26. Dissatisfaction with your mathematical ability _____

27. Financial burdens _____

28. Lower evaluation of your work than you think you deserve _____

29. Experiencing high levels of noise _____

30. Adjustments to living with unrelated person(s) (e.g. roommate) _____

31. Lower evaluation of your work than you hoped for _____

32. Conflicts with family member(s) _____

33. Finding your work too demanding _____

34. Conflict with friend(s) _____

35. Hard effort to get ahead _____

36. Trying to secure loan(s) _____

37. Getting "ripped off" or cheated in the purchase of goods _____

38. Dissatisfaction with your ability at written expression _____

39. Unwanted interruptions of your work _____

40. Social isolation _____

41. Being ignored _____

42. Dissatisfaction with your physical appearance _____

43. Unsatisfactory housing conditions _____

44. Finding work uninteresting _____

45. Failing to get money you expected _____

46. Gossip about someone you care about _____

47. Dissatisfaction with your physical fitness _____

48. Gossip about yourself _____

49. Difficulty dealing with modern technology (e.g. computers) _____

50. Car problems _____

51. Hard work to look after and maintain home _____

The Six Concepts of the SRLE.

Social and Cultural Difficulties.

Gossip about someone you care about
Being let down or disappointed by friends
Having your trust betrayed by a friend
Conflict with friend(s)
Gossip about yourself
Decisions about intimate relationship(s)
Conflicts with family member(s)
Experiencing high levels of noise
Ethnic or racial conflict
Difficulty dealing with modern technology (e.g. computers)
Conflicts with in-laws or boyfriend's/girlfriend's family

Work.

Dissatisfaction with work
Disliking your work
Finding work uninteresting
Disliking your daily activities
Conflict with supervisor(s) at work
Lower evaluation of your work than you think you deserve
Lower evaluation of your work than you hoped for

Time Pressure.

Too many things to do at once
Not enough time to meet your obligations
A lot of responsibilities
Not enough leisure time
Finding your work too demanding
Hard work to look after and maintain home
Unwanted interruptions of your work
Struggling to meet your own standards of performance and accomplishment

Finances.

Cash-flow difficulties
Financial burdens
Trying to secure loan(s)
Failing to get money you expected
Unsatisfactory housing conditions
Financial conflicts with family members

Social Acceptability.

Dissatisfaction with your physical fitness
Being ignored
Social isolation
Dissatisfaction with your physical appearance
Social rejection

Social Victimisation.

Being taken for granted
Being taken advantage of
Getting “ripped off” or cheated in the purchase of goods
Having your contributions overlooked

APPENDIX 11

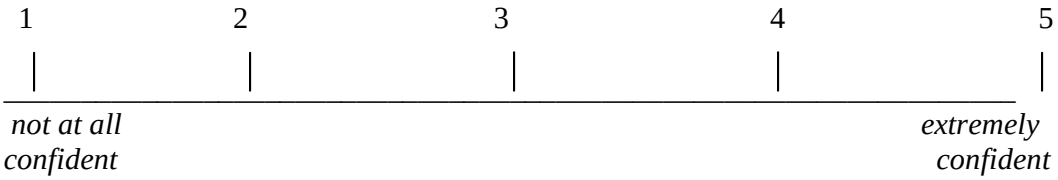
IRRITABLE BOWEL CREDIBILITY SCALE

IRRITABLE BOWEL SYNDROME – CREDIBILITY SCALE.

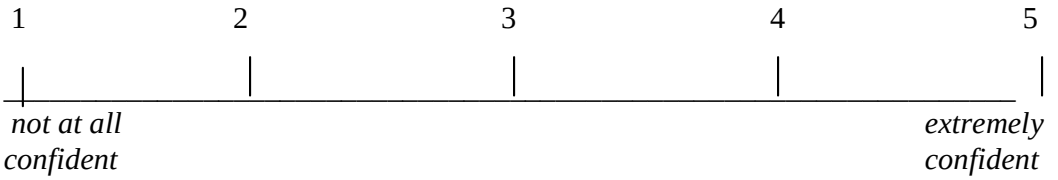
Date: __/__/__ Patient ID: _____
Patient Initials _____

Please answer the following additional questions. Circle the number which best expresses your answer.

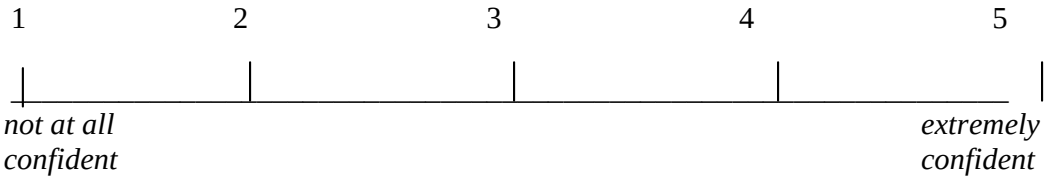
A. How confident do you feel that the treatment you are receiving can alleviate your complaint?



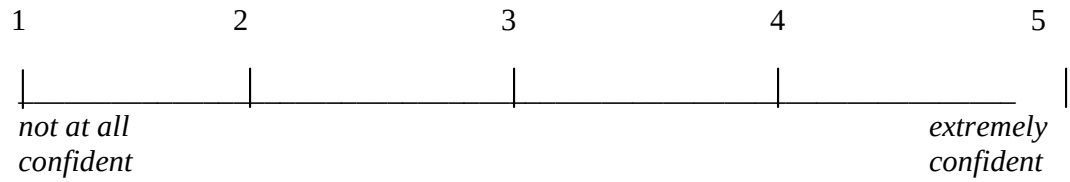
B. How confident would you be in recommending this form of treatment to a friend who suffers from similar complaints?



C. How logical does the treatment you are receiving seem to you?



D. How successful do you think this form of treatment would be in alleviating other complaints?



APPENDIX 12

SCRIPTS

GUT-RELATED IMAGERY

THE GOLDEN WATER.

Imagine that you are in your special place. The sun is shining and the breeze is soft and gentle. It feels warm against your skin. It is such a lovely day. Next to you is a table. On the table is a clear glass jug of sparkling water. Look at the water and see that it contains tiny gold flecks. They sparkle and glimmer in the sun. The flecks in the water are very good for you. You feel and know this. In this place it seems that you are fearless and courageous. You realise that life is a process of give and take, and you are in control of this process.

You feel free in this place and you trust that everything is really okay. You are filled with positive energy and you pick up the jug and pour yourself a glass of this special water. Drink the water. The water goes down your throat and into your digestive tract. Feel how the golden flecks in the water sparkle in your body. The flecks are healing you as it goes throughout your digestive tract. Now feel the golden-flecked water reach your intestines and colon. Soothing the sides, healing everything that needs to be healed. Feel the healing taking place.

Feel the water absorbing into all the muscles in your digestive tract, making them strong and giving them good tone. Feel this now. The golden-flecked water is throughout your digestive tract, making you able to process and absorb food correctly. Making you regular in elimination. Making everything in perfect working order. You know this is happening right now. Feel the healing.

If you need more water, keep drinking as much as you need. After each drink, feel how the gold-flecked water is healing you. Giving you what you need. Empowering you and repairing your body at the same time. You know that everything inside and outside your body is perfect in every way. You desire to eat only the right foods for your body. You desire to drink the right amount of liquids for your body every day. Everything in your body is working correctly and properly. You feel balanced, centred, and happy. These feelings will stay with you.

ANXIETY

ANXIETY.

Imagine that you are standing in a room. Look up over your head. See a light. …. It is the most beautiful light you have ever seen. Look at it shine ... sparkle ... glimmer. Watch as this light starts to surround the right side of your body. Watch as it forms an outline around you. It feels so safe. It feels so comfortable.

You feel this light absorbing all the stress, all the tension from your body. Watch as it goes down the right side of your body down to your right foot. Watch and feel all the stress and all the tension being absorbed by this light as it goes underneath your foot and outlines your inner right leg. See the light go down your inner left leg and under your left foot. So soothing. So comforting. Now feel the light go up your left leg and up your torso, your arm, your shoulder. Outlining the body. Drawing away all the tension all the stress. Making you feel so calm, so centred.

Watch as this light attaches to where it started. Fully outlining your body. Feel the glow of the light around you. Feel it absorbing any stress or tension that is left in your body. Making you feel calm and safe right here, in this time, in this place. You feel peaceful in this light. You are centred. This is your protective light. You are safe within this light. You can imagine this light whenever you need it. Whenever you feel anxious, this light will surround your body. Absorbing the tension. Absorbing the stress. Making you feel centred and safe. This feeling will stay with you.

DEPRESSION

DEPRESSION.

With peace of mind, calm, and at ease, being able to look out at every part of the universe, at every person around you, at every flower and tree and plant, grass and children, and in a new way, as you begin, starting now, to see the world in a new way, with a freshness, and wonder, and awe of a little child.

You begin now to see the world again as you once did when you were an unspoilt child, and you can regain that capacity again to see and appreciate everything freshly, and naively, in a simple way as you can begin once again to see things anew, fresh, wonderful, clean.

Now you can begin to look at every sunrise as if it's the first sunrise you've ever seen, and every sunset, and you will see the colours, and the wonder, and the beauty surrounding you again, as if it's the first time you've ever seen it.

Starting now, every bird that you see will be as if you've never seen a bird before, as if you're a new child, and you're beginning again to look with wonder and amazement at the world around you. You see every bird in a new way, and every tree, and the leaves of the tree, and the seeds on the tree, and the bark on the tree, and the green leaves and the sun shining, and the grass around you, you'll be able to see it in a new way, fresh, with wonder and awe. As you again the capacity to appreciated everything as you once did.

Everything that's become stale over the years will no longer be stale for you, as you become aware again that we can be the way we once were, looking at each thing as miraculous, as beautiful, as wonderful as the first time we saw them, when we were children.

As if we're here now, again, for the first time. As if we're here from another planet. We've just landed and we see the wonders of the Earth, and we see the people on the Earth, and we see their hair, and their faces, and their noses, and their skin, and the wonders of their being and their minds. And we see each person as if we've never seen this person before.. We see them fresh and new, and we see all the wonderful aspects of their being.

And we look again at every cloud and we feel every breeze. And we begin to feel the air around us, and we become more aware of the oxygen we breathe, and we become more aware of the colours and the details of the flowers and the trees, and the people, and the buildings, and the grass, and the books, and everything that surrounds us, every day, every person, every child, every adult, every animal, every plant – we see it anew.

Experiencing every moment in a new way, starting now, as if a fog has been lifted, as if everything is becoming sparkling clean, as if we've come from another planet and we look around, and we see, and we feel, and we experience in a new way, starting now, and every day.

And this feeling will grow more and more as time goes on – you will be able to feel more and more at ease and calm and peaceful with vibrant energy, enjoying every aspect of your being, feeling strong, healthy, with peace of mind, calm mind, body at

ease, and yet very vibrant and energetic, looking at everything in a new way, as if you've been here now, just a short time.

You're beginning to experience the world again, fresh, clean, sparkling new, new perceptions, aware of everything around you freshly, once again. And this will grow every day.

With this new way of looking at life, you'll find every day that your energy will increase and you'll feel so healthy, and you feel healthy and free, you'll feel all the tensions will leave. You'll feel at ease and calm, and free as you become more aware of the blood circulating in your body, and the strength in your muscles, and the wonders of your strong, healthy being.

You begin to feel that you're living, you're beginning to live more and more, growing every day, becoming more aware, more filled with energy, more vibrant.

Starting today, you'll begin to feel that life is just beginning, that your potential for living a very good life is there, and it will increase and you'll become more aware of the potential, and you'll become aware of how you can enjoy life more and more every day.

And you'll look forward to every coming day as another exciting day that you can live fully, growing, changing, maturing, healthy, strong, vibrant, and energetic. You will realise that you have the potential to be happy, strong and much greater than you thought. That you have vibrant energy, that you're able to flow and move with every person, every individual you meet. You'll be able to feel with them, be able to feel with every animal, and every plant, and every part of the Earth.

From this day on, you'll begin to live fully, moment by moment, every day. You'll get so much out of every day, more and more, starting now, every day, every hour, every second, will become more and more exciting, full, enthralling, amazing. You'll become more and more aware of the wonders of your being, yourself, the Earth, and everything around you. You'll become more and more deeply involved in everything that is happening around you, the people you meet, the tasks you meet, and the children that you see, and everything that comes into your life.

You'll be aware, and become more and more involved, like a child, living fully, enjoying every moment, being unselfconscious, feeling free. You'll be able to enjoy more and more activities, and your activities will be the way they were when you were a child, free and unspoilt, at ease, enjoying, able to get into things, more and more, as you were once able to be creative, ingenious, able to make everything into a fun game. You'll again remember how to play and have fun, by your own creativity and imagination, using your own ingenuity, able to regain your lost spontaneity, your naturalness, your freshness – it will come out and you will feel at ease with it.

OBSESSIVE-COMPULSIVE

OBSESSIVE COMPULSIVE.

Look above your head and see a light … it's a colour you really like. It's the most beautiful light you've ever seen. Look at it shine … sparkle … glimmer. Watch as this light starts to surround your head. It feels so safe. It feels so comfortable. You feel this light absorbing any repeated, unpleasant thoughts that may occur in your head … clearing your mind so that you no longer have difficulty remembering things … from now on you can remember things easily. Feel the healing. Feel the light clearing your mind and allowing you to concentrate more easily … allowing you to make decisions more easily. From now, on concentrating and making decisions will be easy for you.

Watch as this light goes down the right side of your body from your head down to your right foot. You feel this light absorbing all the stress, all the tension from your body. Watch and feel all the stress and all the tension being absorbed by this light as it goes underneath your foot and outlines your inner right leg. See the light go down your inner left leg and under your left foot. So soothing. So comforting. Now feel the light go up your left leg and up your torso, your arm, your shoulder. Outlining the body. Drawing away all the tension, all the stress. Making you feel so calm, so centred.

Watch as this light attaches to where it started. Fully outlining your body. Feel the glow of the light around you. Feel it absorbing any stress or tension that is left in your body. Making you feel calm and safe right here, in this time, in this place. As the stress and tension leave your body, you are calm and peaceful … calm and peaceful … able to carry out any action without unnecessarily repeating it.

You are peaceful in this special light. You are centred. This is your protective light. You are safe within this light. You can imagine this light whenever you need it. Whenever you feel the need, this light will surround your body. Absorbing the tension … absorbing the stress. Making you able to concentrate more easily … making you able to make decisions … taking away any anxiety, any unnecessary, repetitive actions. Making you feel centred and safe. Any outside negative actions, words or thoughts will just bounce off this protective shield … bounce off and away. Leaving you protected, calm and peaceful. These feelings will stay with you.

INTERPERSONAL SENSITIVITY

INTERPERSONAL SENSITIVITY.

Feel each breath lead you into deeper relaxation as if the very air surrounding your body were a vast ocean of peace. Each inward and outward breath like a wave on the shore of that ocean, softly in, softly out. As you breathe quietly, send a wave of relaxation from the top of your head all the way down to the tips of your toes. If you have an area of tension in your body, bring your awareness to that area now and breathe quietly into that tension, allowing it to soften and relax. Devote the next little while to nurturing yourself. A special time that is just for you.

If there is any tightness in your solar plexus, just above your navel, visualise that area as a pool of water and see a pebble dropped right into its centre … spreading ripples of relaxation out from its centre.. Let your heart be cradled in peace, visualising it as a flower bud, that in the presence of peace, opens to its full blossom, revealing deep in the heart of that flower all its beauty and simplicity. Allow these qualities to spread like a perfume all throughout your body … easing all the tension. Imagine feeling two hands resting on those shoulders, hands of a loved one or an angel … absorbing all the tension … sending ripples of healing and love into your body.

From now on, you'll always be aware of your surroundings, you're not going to be asleep. You'll always hear those sounds around you that are perfectly normal for where you are … any sounds you hear will not affect or disturb you in any way … those sounds will actually help you to relax even more deeply.

Now visualise yourself standing on a cliff top, above a rainforest that stretches out endlessly. Feel the spaciousness around your body, the touch of the sun against your skin, the vast dome of the sky stretching above. Deep within the heart of this forest there is a special place just for you … a place of nurturing, of understanding … a place where you receive replenishment. The sky is clear after recent rain. You can walk down into the forest via a path or you can simply let yourself drift like a feather … easily and softly floating down in the air … a feather supported … carried gently down … floating soft and light.

As you near the canopy of the leaves you see they open to allow you to float down into the forest until you come to rest on the forest floor. Allow your eyes to become accustomed to the colours … the greens and brown of the forest … perhaps there are brightly-coloured birds. Feel the peace of the forest … its ancientness … the strength of the earth beneath your feet. And as you begin to walk along the path towards the pool in the centre of the forest, feel yourself become part of the forest … not so much a visitor but as an expression of the forest … all of its beauty and peace. With each step, your body is becoming more relaxed, your mind at peace, until you see a little way ahead a pool that sparkles in the sunshine … its surface too bright to look at.

On the far side of the pool there's a waterfall … and as you stand at the edge of the pool, looking into the water, you see that it is crystal clear and the waterfall is splashing, creating rainbows all around you. You may want to test the water with your foot, finding it just the right temperature for you … and you let yourself enter into the water … feeling it wash over your skin … refreshing, revitalising every cell in your body. You may like to swim over to the waterfall … feeling the joy of having all your needs met right now. Let yourself stand under that waterfall … feeling it cascade down onto your head, your shoulders … every cell in your body sparkling

and alive … the water so fine it passes right through the centre of your body. Every cell sparkling like a rainbow within your body.

Allow all the anxieties and fears, old attitudes and beliefs, to wash away … washed out through the sole of your feet. Allow yourself the pleasure of being free … releasing the past … and the future. Feel the vitality flow freely within you. Breathing in the sunshine as soft, golden, sparkling light that flows into your body with each inward breath, filling the chest with its light and spreading beyond … flowing out to every fibre of your being. You deserve to be happy … allow that light to flow freely. Feel yourself worthy of your own love. Allow appreciation and gratitude for your body … mind at peace … full of joy.

Allow an image of yourself to arise in your mind's eye. See yourself at peace with others and with yourself … look into your own eyes and see the peace that's there … see the joy that sparkles there … a confidence in yourself and in your own abilities. See yourself able to accomplish whatever you set your heart to … full of enthusiasm for life … brimmed full of vitality. See yourself worthy of your own love … deserving to be happy … giving value to yourself. Allow that image to become strong in your mind's eye and see it become small enough to place inside your heart … put it there … breathing in the qualities that would bring that image to life. Breathing in vitality and love to yourself … breath in compassion for yourself … and see the image within your heart grow strong … so strong that your heart can no longer contain it … and see it spill over as light that radiates throughout the whole of your being … every cell bathed in the light of your own confidence … your peace and love … spreading beyond your body to form a cocoon of light that surrounds and heals and nourished you. A light that you can draw on always … breathe that light in, allowing it to flow out from yourself to touch others.

Then allow your breathing to deepen … and as it deepens, feel the energy flooding back into your body as if again you are standing under that waterfall of light … its vitality showering down onto your head and shoulders … energising ever cell within your body … energising your mind.

Feel the muscle tone returning to your arms and legs … begin moving your hands and feet just a little … and, keeping your eyes closed, let yourself stretch the way a cat stretches after a sleep. Feel the refreshment and relaxation in all the tissues of your body … the mind at peace and confident … full of joy … enjoying the stretch. And when you're ready, allow your eyes to open gently and easily … no need to hurry … just take your time.

RELAXATION

RELAXATION.

I'd like you to begin by just resting back, very comfortably, and closing your eyes. Just rest back in the way that is most comfortable for you right now, just resting your hands on your thighs, or on the arms of the chair. And as you just settle back comfortably, this will be an opportunity for you to become even more comfortable, and to experience a hypnotic state, very easily, and very gently, and very comfortably.

And as you rest back, you can begin noticing the feelings, and sensations in your body right now. Just notice some of the sensations, that you can be aware of right now. For instance, you may become aware of the feel of the shoes on your feet; or you may notice the sensations in your hands as they rest there; or perhaps you may be aware of how the chair supports your body. And as you continue to listen to me, and breathing easily and comfortably, and deeply, you may become aware of the sensations as you breathe, noticing for example that the sensations are different when you breathe in..... and when you breathe out..... Just notice those feelings as you breathe in .... and fill your lungs; and then notice the sense of release, as you breathe out .....

And now I'd like you to concentrate particularly on the feelings in your toes and feet. Just allow all the muscles and fibres in your toes and feet, to become very deeply relaxed. Perhaps even picturing in your mind's eye what they would look like, for all those little muscles and tissues to relax, loosely and deeply. Allowing yourself to get that kind of feeling you have when you take off a pair of tight shoes that you've had on for a long time. And you can just let go of all the tension in your toes and feet and feel the relaxation spread.....

And now imagine that this comfort and relaxation, is beginning to spread and flow, like a gentle river of relaxation, upward, through your ankles and all through your calves. Letting go of all the tension in your calves, allowing them to deeply, and restfully, and comfortably relax.

And allow that comfort to continue, flowing upward, into your knees, and behind your knees and through your knees, and into your thighs, letting go of all the tension in your thighs. Perhaps once again imagining what they might look like, for all those large muscles and tissues, to become soft and loose, and deeply relaxed. Perhaps already noticing that sense of gentle heaviness in your legs, as they just sink down, limply and comfortably.

And continue to allow that comfort, to flow and spread upward, at its own pace and speed, into the middle part of your body. Flowing into your pelvis and abdomen and stomach..... through your hips and into your lower back. Letting that soothing, deep comfort spread, inch by inch, up through your body, spreading from muscle group to muscle group. Gradually, progressively flowing into your chest.... into your back.... between your shoulder blades, and into your shoulders. Just allow all the tension to loosen, and flow away. As if somehow, just the act of breathing is increasing your comfort. As if somehow, every breath you take, is just draining the tension out of your body, taking you deeper ... and deeper, into comfort, with every breath you take. And allow that comfort to flow into your neck and throat. Perhaps imagining once again what that would look like, for all the little fibres and muscles in your neck and throat, to deeply, softly, comfortably relax. Let that relaxation sink deep into your

neck. and it can gradually flow up your neck, up into your scalp, and all out across your scalp, as if it's just bathing your head, with waves of comfort and relaxation. And that relaxation can flow down, into your forehead, and like a gentle wave, down across your face, into your eyes, your cheeks, your mouth and jaw. Just let go of all the tension in your face, your mouth, your jaw, allowing those tissues and muscles to sag down, slack and relaxed.

And now allow that comfort to flow back down your neck, and across your shoulders, and down into your arms, through your elbows....through your wrists, through your hands and fingers, right down through your fingertips. Letting go of all the tension, and tightness, letting go of all the stress, and strain, all through your body. Just allowing your body to rest, and relax.

Now remain for a few moments in this relaxed, comfortable state and then gently, gradually, bring yourself back to awareness … to the present … to where you are now … and open your eyes.

APPENDIX 13

CONSORT CHECKLIST

		Consort Checklist.	
Paper Section and Topic	**Item**	**Description**	**Page Number**
TITLE Abstract	1	Controlled Trial of Hypnotherapy as a Treatment for Irritable Bowel Syndrome.	i-ii
Introduction and Background	2	Introduction. Scientific background and explanation of rationale.	2-35 161-188
Methods Participants	3	Treatment Schedule and Assessment Instruments. Eligibility criteria for participants. Trial carried out and data collected at Phoenix Holistic Centre – 31 Rowe Street, Woollahra, Sydney.	198-210 191
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	198-200
Objectives	5	Specific objectives and hypotheses.	184-186
Outcomes	6	Clearly defined primary and secondary outcome measures.	213-258
Sample size	7	Sample size was determined through time and funding restraints.	191-192
Randomisation – sequence generation	8	Random number tables were used to generate the random allocation sequence.	195
Randomisation – Allocation concealment	9	Random number table (Boyer, 1968) was used to implement the random allocation sequence. Concealment.	195 195
Randomisation - Implementation	10	Receptionists at the clinic generated the allocation sequence, enrolled participants, and assigned participants to their groups.	195
Blinding (masking)	11	Blinding. Success of blinding was evaluated by means of the Irritable Bowel Syndrome Credibility Scale.	195 209&390
Statistical methods	12	Statistical methods used to compare groups for primary outcomes.	211
RESULTS Participant flow	13	Flowchart of participants through each stage showing each group,numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analysed for the primary outcome.	197
Recruitment	14	Dates defining the periods of recruitment and follow-up.	196
Baseline	15	Chart showing baseline demographic and clinical characteristics of each group.	215
Numbers analysed	16	14 participants in each group were included in each analysis and analysis was by “intention-to-treat”.	214
Outcomes and estimation	17	Summary of results for each group for each primary and secondary outcome, and the estimated effect size and its precision.	216-258
Ancillary analyses	18	Other analyses performed.	216-258
Adverse events	19	All important adverse events or side-effects in each intervention group.	None
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	260-280
Generalisability	21	Generalisability (external validity) of the trial findings.	260-280
Overall evidence	22	General interpretation of the results in the context of current evidence.	260-280