
CHAPTER 4 DISCUSSION

4.0 REVIEW OF AIMS

The primary objective of this thesis was to provide data on the nature of relations between psychosocial and functional GI disturbances in representative samples of outpatients with FGID. A series of studies using standardised diagnostic criteria and objective methods determined these relations in the context of functional gut symptoms or gastrointestinal motility (transit and motor/sensory activity) outcomes. Both *global* (quantitative) and *specific* aspects of relations were investigated throughout. The novel inclusion of assessments of the severity and extent of FGID (eg number of syndromes present, number of gut regions displaying delayed transit) was based on the tendency of certain FGID to occur concurrently.

In relation to *functional GI symptomatology*, specific hypotheses were tested using longitudinal methods. One objective was to determine the psychosocial and demographic factors that most strongly influence the process of change in symptoms over time. Another objective was to identify the primary risk indicators of a poor clinical outcome.

In relation to *motility dysfunction* in FGID, aims and hypotheses targeted issues such as whether there are distinct psychophysiological variants within these disorders and, if so, whether they represent different levels of psychophysiological dysfunction. Of importance also, was whether non-conformity to these general patterns has its own set of predictors. In combination, these findings will have implications (i) for an increased understanding of the mechanisms involved in the development and exacerbation of symptom and/or sensorimotor disturbances in FGID, and (ii) for the practical aspects of patient care.

4.1 STUDY 1: CROSS-SECTIONAL EVALUATION OF PSYCHOLOGICAL, SOCIAL AND EXTRAINTESTINAL FEATURES OF FGID

The findings of this study considerably extend and refine previous research concerning the coexistence of psychological, social and extraintestinal disturbances in FGID. These findings are the first to show, in patients with these disorders, that:

1. the overall severity and extent of functional gut disturbance eg the number of syndromes present, *increased in parallel with* the severity of psychological, social and extraintestinal disturbance, while relations within this general pattern were marked by a high degree of specificity
2. the *psychosocial profile* which predicted the number of concurrent FGID syndromes comprised a *broad range of psychological, social and demographic factors*, suggesting a multifaceted explanation for severe and extensive functional GI symptomatology
3. *the simple linear relations* between the total severity of chronic life stress threat and gastrointestinal, extraintestinal and emotional symptomatology suggest that the severity of *chronic life stress threat* may account, at least in part, for the coexistence of specific gut, emotional, extraintestinal and behavioural disturbances, and
4. these associations were *most specific for the IBS and FD group of syndromes* (ie the FGID syndromes defined specifically by the presence of abdominal pain and/or discomfort), and for particular emotions (eg. anxiety) and extraintestinal and behavioural factors (eg. fatigue, binge eating).
5. Relations were linear throughout.

4.1.1 PATTERNS OF ASSOCIATION BETWEEN PSYCHOSOCIAL, EXTRAIESTINAL AND FGID SYMPTOMATOLOGIES

Aspects of design

With respect to this thesis, these initial findings formed the basis for subsequent hypothesis testing in relation to various symptom outcomes over the research period - specifically, at entry, during the follow up period, and (long-term) at 16 months (Study 2). They also provided a baseline against which the effects of psychological and demographic factors on various aspects of sensory and/or motor disturbances (Studies 3, 4 and 5) could be compared. A positive feature of the research design, therefore, was that the data was obtained using standardized procedures, objective methods, and sensitive measures. In particular, the methodology employed - that is, comprehensive and detailed interview-based ratings of chronic stressors (Brown & Harris, 1978) and emotional support (Henderson, 1980), together with the classification of the FGID (Drossman et al, 1994), provides a high degree of objectivity. Also, by taking into account overlap among syndromes, and by assessing both the severity and frequency of each symptom, the sensitivity of the quantitative symptom-outcome measures - the number of syndromes present and symptom intensity, respectively - is increased. Taking into account overlap among syndromes also improves the precision of differentiating between them. That is, primary features of individual syndromes were identified, based on conditional probabilities, whilst simultaneously adjusting for the presence of other syndromes. Nevertheless, for all studies, interpretation of the findings should not exceed the limits set by the methodology.

Gastrointestinal, psychological and social diversity in FGID

In terms of sample characteristics, the patient sample was as expected. Most patients had two or more coexistent FGID syndromes, most had been exposed to uncommonly high levels of chronic life stress threat, and a large number were emotionally distressed (anxious and/or depressed). With respect to individual levels of disturbance however, patients differed markedly in the number and the type of syndromes present and in levels of disturbance across multiple psychosocial factors. From a research perspective, the variable severity of these disturbances within the patient sample was well suited for preliminary within-group investigations of relations between psychological, social, extraintestinal and functional GI disturbances.

The prominence of psychological and social disturbance within this group of FGID patients - especially elevated levels of current anxiety and/or depression but also the severity and extent of chronic life stress threat and goal-frustration - is consistent with an extensive literature (eg Chaudhary & Truelove, 1962; Whitehead, 1996; Creed et al, 1988; Bennett et al, 1991) but unusual in that *the total severity* of chronic life stress threat has not been assessed previously.

4.1.2 PREDICTORS OF NUMBER AND TYPE OF FGID

Psychological, social and demographic features

It was hypothesised that psychological, social and extraintestinal disturbance would coexist in FGID, such that: a) the overall severity and extent of functional GI

disturbance (ie the *number* of syndromes present) would correspond with the intensity of psychological, social and extraintestinal disturbance, and b) psychosocial and extraintestinal disturbance would be a prominent feature of certain *types* of FGID. These hypotheses were strongly supported by these data.

Number of syndromes

In extending previous findings (Drossman, 1996b), this study is the first to show a quantitative relation between the severity of psychosocial disturbance and the *number* of FGID syndromes present. It is clinically relevant that the highest levels of such psychosocial disturbance was among patients with the largest number of FGID and that, although the type of syndromes varied, clusters always included at least one FD syndrome (usually dysmotility-like or reflux-like dyspepsia); IBS was also frequently present. That is, the type of disorder most likely to be present was quite specific, the FD/IBS group of syndromes.

The best combination of factors to describe this psychosocial disturbance included: *anger reactivity* and *neuroticism* (both predispose to a more intense and prolonged stress response); *chronic life stress threat*; *increased coping*; *poor emotional support*; and *increased age*. This profile, which combines psychological, social and biological elements, is prototypic of the most comprehensive chronic stress scenario.

It is interesting that the particular combination of individual psychosocial variables that predicted the number of syndromes present in this study, supports the more subjective observation of Chaudhary and Truelove (1962) based on clinical

judgement, that IBS patients with 'psychological problems' had a worse outcome than those without such problems.

While the combination of *trait anger reactivity* and *neuroticism* as primary predictors of the number of coexistent syndromes is new, it is generally consistent with previous reports of higher levels of neuroticism (and trait anxiety) in patient and non-patient groups with IBS (eg Gick et al, 1997; Talley et al, 1997). Neuroticism and trait anxiety also have been linked to changes in the severity of functional GI symptoms. Longstreth (1993) found a significant relation between high levels of trait anxiety and specific changes in IBS symptoms, also between trait anxiety and reports of stress-related effects on symptom severity, relations which were observed more frequently by women than by men.

The relation of *trait anger reactivity to symptom severity* has not been assessed previously in the context of these disorders. Indeed, although anger is a powerful emotion with a large physiological component, its role in FGID has been assessed rarely. In these studies, strong relations were found between the trait anger variables - trait anger reactivity and trait anger temperament - and both the number and the type of FGID syndromes, strongly supporting early views concerning the somatic effects of anger (eg. Anderson, 1981).

The combination of high levels of *neuroticism* and *chronic life stress threat* strongly supports the early work of Esler and Goulston (1973), whose findings suggested that neuroticism and stressful circumstances may have more effect on the course of IBS than neuroticism alone.

Another prominent feature of the 'stress profile' is the *total severity of chronic life stress threat*. In previous research, the presence of one or more highly threatening chronic stressor has been strongly associated with the onset or exacerbation of FGID (Craig & Brown, 1984; Creed et al, 1988; Bennett et al, 1991) and with the presence of high levels of psychological disturbance in patients with these disorders (eg. Bennett et al, 1991). In this study, the presence of high levels of chronic life stress threat enhanced the relevance of the remaining predictors. The *frequent use of mature emotion-focussed coping strategies* reflects the individual's attempts to modify the overall impact of life stress while *inadequate or unavailable intimate emotional support* and *increasing age* can be expected to increase the potency of the emotional response in certain situations eg when support is withheld and when increased age reduces opportunities for a fresh start, to mend damaged relations, or to start a new career. Age also represents an important biological vulnerability factor.

Type of syndrome

Against the background of significant quantitative effects, the findings also show that relations were marked by a high degree of specificity. High levels of psychosocial disturbance were not distributed evenly across the FGID subgroups. Levels of life stress (exposure to chronic stressors) and emotional distress (anxiety and/or depression) were highest in patients with FD syndromes, while distress in the form of hypochondriacal concerns was more prevalent in patients with IBS. Despite substantial differences in experimental design, the relations found in this study between type of distress and type of FGID support previous associations (eg. depression with dysmotility-like dyspepsia (Kaneko et al, 1993); hypochondriasis with

IBS (Ford, 1986; Drossman et al, 1988; Gomborone et al,1995b); and emotional distress (anxiety and depression) with heartburn / reflux (Johnston et al, 1995).

The present findings shed further light also on how personality, chronic life stress threat and distress may differentially influence the development and/or exacerbation of FGID. From these data, it seems reasonable to hypothesise that certain psychophysiological inheritance factors (Eysenck & Eysenck, 1985) may predispose to certain types of FGID and/or to more severe and extensive gut symptomatology - in particular, trait anger with FD syndromes (especially ulcer-like and reflux-like dyspepsia), and anger reactivity and neuroticism with a greater number of FGID. From a 'systems' perspective, exposure to chronic and severe stressors may thus determine *when* FGID is triggered and/or exacerbated, while the anger-reactive stress profile suggests that it is the *combination of* personality and chronic social stress that determines the severity and extent of functional GI symptomatology over time. It is of interest that this particular combination of psychosocial factors also seems to be linked to intestinal sensorimotor dysfunction in patients with these syndromes (Study 5). It remains to be determined, however, whether chronic overactivity of the sympathetic nervous system (Heitkemper et al, 1996) is integral to this process.

In support of several previous studies (Nyhlin et al, 1993; Bennett et al, 1991) suppression of emotions was a significant feature of the IBS/FD group of disorders. Unlike these earlier findings, but in support of the impressions of Stockton and colleagues (1985) that many patients with upper abdominal pain admitted to 'bottling up their anger', patients with IBS/FD in this study attempted to hold anger in, and to suppress and control *angry feelings* significantly more frequently than patients with functional constipation (a non-painful FGID). Also in comparison to the functional

constipation group, suppression of *anxiety* and *depression* were not significant features of the IBS/FD group of syndromes as a whole.

The specificity of relations between type of psychosocial (and gender) feature and type of syndrome (despite considerable overlap among syndromes) diminish any notion that linear relations, such as those between anger suppression variables and the IBS/FD group of syndromes, simply reflect an indiscriminate increase in mind and gut disturbance. Rather, these and subsequent findings suggest that relations linking psychosocial, extraintestinal and chronic life stress factors with different symptom subgroups demonstrate considerable specificity.

Extraintestinal features

Similar to psychosocial disturbance, extraintestinal (somatic) symptoms were associated exclusively with the FD/IBS group of syndromes, especially with dysmotility-like and reflux-like dyspepsia. The prominence of fatigue and unpleasant taste to dysmotility-like dyspepsia, and to pairs of syndromes that include dysmotility-like dyspepsia (dysmotility-like dyspepsia and IBS and dysmotility-like and reflux-like dyspepsia, respectively), is of particular interest. In each case, type of syndrome was specified, and the effects were linear. While both sets of associations are consistent with clinical experience, the nature of the relation between fatigue and dysmotility-like symptomatology remains unclear. These findings indicate, however, that this association is independent of chronic life stress threat, depression, age, gender, the severity and constancy of pain and/or discomfort, and the number of FGID present.

The relation of binge-eating behaviour and dry (eczema-like) skin to a single syndrome, reflux-like dyspepsia, is strong and highly specific. Binge-eating behaviour has been associated previously with FGID symptoms (Drossman et al, 1990; Guthrie et al, 1990), delayed gastric emptying (in patients with eating disorders) (Inui et al, 1995), and anxiety/depressive disorders in patients with IBS (Kellner, 1991). Our findings extend these reports by identifying reflux-like dyspepsia as the most likely of the FGID assessed in this study to be associated with this behaviour. Further, although binge-eating behaviour appears to be provoked by anxiety (and frustration), the effects in this study of binge eating on reflux-like dyspepsia far exceeded the effects of anxiety alone. It appears therefore, that over and above the effects of anxiety and even in the absence of self-induced vomiting, habitual binge-eating behaviour substantially increases the likelihood of reflux-like dyspepsia. While the strong association found in this study between binge eating behaviour and an increased number of FD/IBS syndromes may suggest that the effects of binge eating behaviour on functional GI symptoms are more wide-ranging than the relation with reflux-like dyspepsia suggests, this remains to be determined. The clinical relevance of the relation between dry (eczema-like) skin and reflux-like dyspepsia is also unclear.

Chronic life stress threat and gastrointestinal, extraintestinal and emotional symptomatologies

Multisystem symptomatology is thought to be in part a response to stress that is quantitative and involves physiological changes, elements of somatization, or a mix of both (Kellner, 1991). Furthermore, the disturbance appears to be not simply a

characteristic of those who seek treatment (Kellner, 1991; Gomborone et al, 1995a), or a reflection of extreme illness behavior (Talley et al, 1991b). The findings of this study, among patients with FGID, are entirely consistent with these empirically-based concepts. A new finding, however, is that emotional distress (in particular anxiety) is not associated with a random selection of symptoms - rather, there is a high degree of specificity in terms of the particular functional GI syndrome (dysmotility-like and reflux-like dyspepsia and IBS), extraintestinal symptom (fatigue, unpleasant taste, dry skin) or behaviour (binge eating) that is involved. Moreover, the severity of emotional, gastrointestinal, and extraintestinal symptomatology correlated with the severity of severe chronic threat in the person's life during at least the previous 12 months suggesting a 'causal' association.

Gender effects

Relations between gender and the number and type of FGID syndromes present in this study were few and specific to type (not number) of syndromes - women were more likely to have dysmotility-like dyspepsia, and men to have ulcer-like dyspepsia. These associations are strengthened by the methods used to determine them, that is, by controlling for concurrent syndromes. They are consistent also with previous links between female gender and dysmotility-like disturbances in other gut regions (eg functional heartburn (Richter et al, 1994)) and between male gender and acid secretion disturbances (for example, duodenal ulcer disease (Richter et al, 1994)). In the absence of mediating psychosocial influences, this finding is most consistent with a biologically-based view of gender effects in FGID which draw attention to hormonal differences (Heitkemper, & Jarrett, 1992), the presence of female hormone receptor

sites in the gut (Singh et al, 1994) and differences in brain opioids (with reference to hyperalgesia) (Kepler et al, 1991).

Summary

New information includes evidence that, although the overall severity and extent of functional gut symptomatology increased in parallel with the severity of psychological, social and extraintestinal disturbance in this study, relations within this general pattern were marked by some degree of specificity. In particular, high levels of non-gut disturbance (featuring chronic life stress threat, together with concurrent extraintestinal and emotional symptomatology) were distinctive of FD and IBS syndromes alone, thereby identifying a clinically distinct subgrouping of FGID characterised by abdominal pain and/or discomfort. Furthermore, in patients with one or more of these disorders (usually a cluster of syndromes including FD and/or IBS), chronic life stress threat, unusual in the community (Brown & Harris, 1978) and yet highly prevalent in patients with FGID (Craig & Brown, 1984; Bennett et al, 1991), was strongly associated with both the nature and the extent of concurrent multisystem (gastrointestinal, extraintestinal and emotional) symptomatology.

These findings suggest that, in patients with FD and/or IBS, chronic life stress threat may account, at least in part, for the coexistence of specific functional gut, emotional, extraintestinal, and behavioural disturbances. Overall, the specificity found in relations between non-gut and gut disturbance within this group of disorders supports the presence of distinct pathophysiologies, manifesting distinct symptom clusters - the premise upon which the classification of these disorders is based.

At a global level, linear relations between the severity and extent of the psychosocial and symptom-related outcomes appear to place each individual IBS/FD patient on a continuum of intensity ranging from mild, to moderate and severe dysfunction. The psychosocial and demographic factors which together helped to explain the level of symptom intensity included exposure to chronic highly threatening stressors, the presence of an angry-anxious and reactive personality, limited personal resources to deal with life stress (inadequate coping strategies, inadequate intimate emotional support) and increasing age. Of these factors, it was the severity of chronic life stress threat that consistently correlated with levels of functional gastrointestinal, emotional and extraintestinal symptomatology in these disorders.

4.2 STUDY 2: LONGITUDINAL EVALUATION OF LIFE STRESS IN IBS

The purpose of the longitudinal study was to extend the cross-sectional findings by assessing for each individual, the relative effects of chronic stressors, personality, and coping style on subsequent symptomatology over time in patients with IBS, the most common of the FGID. In particular it was hypothesised that chronic and severe life stress threat would have large and consistent effects on subsequent symptom intensity over time. This premise was supported overwhelmingly in this study.

In this section, several core findings of the present study are discussed - the overall strength, consistency and direction of the association between chronic life stress threat and subsequent symptom intensity, the nature of the stressor that predicted major changes in functional GI symptomatology, and the stressor threshold that predicted clinical outcome for most patients with IBS. This is followed by a brief discussion of other effects on long-term outcome.

4.2.1 THE SPECIAL EFFECTS OF CHRONIC LIFE STRESS THREAT ON SYMPTOMS OVER TIME

Aspects of design

This longitudinal study is the first, the author believes, to assess the relation of chronic life stress threat to subsequent symptom intensity in patients with IBS (with and without concomitant FD).

The selection of IBS as the study population and the inclusion of the symptoms of FD syndromes as well as IBS symptoms in the symptom intensity measure was based on the premise (a) that IBS and FD are either variants of the same dysfunction or are so commonly associated to be treated as a 'notional' single dysfunction, and (b) because the baseline data suggested that psychosocial disturbance was most strongly associated with these particular FGID syndromes.

The selection of chronic threat as the type of life stress most likely to provoke significant long-term changes in IBS/FD was based in the first instance on the primacy of the highly threatening chronic stressor over all other stressors in our earlier work (Bennett et al, 1991), and supported by the significant unmediated relation between the intensity of chronic life stress threat and the number of FD/IBS present in the previous study (Study 1).

That is, the standardised research design takes into account the chronic, fluctuating and recurrent course of IBS (Waller & Misiewicz, 1969; Talley et al, 1992a; Locke et al, 1996; Agréus et al, 1995), the frequent concurrence of FD and IBS (Talley et al, 1992a; Agréus et al, 1995), and the minimum duration of a chronic stressor situation (six months or more).

Furthermore, the study sample was large and the methodology ensured reliable diagnoses, objective and independent life stress and symptom intensity assessments, and a sophisticated approach to the analysis of their interrelation over time (for example, by statistically adjusting for baseline conditions). Life stress ratings were also independent of psychological and gut influences. The rater was blind to personal perceptions such as how individuals felt or how they reacted to particular situations, and stressors confounded by IBS/FD symptomatology, or its life stress consequences,

were not included. The failure of psychological variables (for example, neuroticism, depression) to mediate the relation of life stress to symptom intensity over time or to predict subsequent life stress or symptom intensity significantly, statistically confirms that these life stress ratings are free of contamination from psychological influences.

In sum, the independence of life stress ratings, and the wide range of responses on all measures both within and between subjects over time indicates that the IBS/FD cohort identified for this study was ideally suited to the evaluation of the relative effects of stressful chronic situations versus stress proneness (personality style) and illness related (hypochondriacal) attitudes on subsequent symptom intensity. As noted earlier, however, these findings cannot be generalised to community (non-patient) IBS populations or to patients with more complex medical histories.

Strength, consistency and unequivocal direction of effects over time

The results overwhelmingly support the research hypothesis that in patients with these functional gastrointestinal disorders a component of life stress - severe and chronic threat - has large and consistent effects on symptom intensity over time. New information includes evidence that:

- 1) almost all (97%) of the within subject variance in symptom intensity (assessed at three time points over 16 months) was explained by the severity of chronic threat during the prior six months or more; and
- 2) the presence of one or more highly threatening chronic difficulty (over and above the effects of baseline symptomatology) strongly predicted high levels of symptom intensity even after a time lag of ten months, while

3) continuing high levels of life stress from six to sixteen months, significantly reduced the likelihood of any improvement in symptom intensity over the entire follow-up period. Indeed, no patient exposed to even one such stressor improved clinically (by at least 50%) over the follow-up period.

The strength, consistency and direction of relations found in this study strongly support the methods and measures used to determine them. The 97% of variance found in this study, taking into account all changes over time in symptom intensity and chronic life stress threat for each individual, contrasts with the largest variance previously found (ie 11%) by Whitehead and colleagues (1992) who assessed the relation of scores on a life event scale with subsequent bowel symptoms in patients with IBS over four consecutive contacts during a 12 month period. While both studies addressed the issue of independence (ie attempts were made to ensure that the life stress ratings were not confounded by either IBS symptoms or psychological factors), albeit with different degrees of precision, the strength and consistency of the present findings are due primarily to the superior *independence* and *reliability* of the chronic stressor ratings which at present can be achieved only by using the strict interview and rating procedures of the LEDS, the only measure designed to deal adequately with these methodological problems.

The strength of the association between life stress and changes in symptom intensity is enhanced further by the finding that one or more highly threatening chronic difficulty predicted high levels of symptom intensity even after a time gap of 10 months, and even after controlling statistically for the severity and chronicity of baseline symptomatology, emotional distress (anxiety and depression), age and gender.

Failure to improve symptomatically over the 16 months was most strongly predicted by proximal life stress ie, the presence of one or more highly threatening chronic difficulty during the previous 10 months. As the odds against symptom improvement in such a situation was thirty three to one (with a specificity of 85% and a sensitivity of 85%), continuing exposure to high levels of chronic life stress threat has important clinical implications. Also relevant to clinical management is the finding that symptoms only reduced to half their intensity in the absence of such a stressor.

The fact that the temporal relationship was unequivocally as hypothesised - that is, life stress predicted subsequent symptom intensity (and not the reverse), and also that the effects were highly significant over and above that expected from symptoms alone and were not influenced by systematic extraneous factors, personality or mood state, fully supports early reports (Chaudhary & Truelove, 1962) that life stress has a powerful effect on the course of the disorder for the majority of patients with IBS/FD.

The nature of the provoking stressor

The superiority of chronic highly threatening stressors over all other potential predictors in this study (age, gender, emotional distress, personality and illness related attitudes) suggests that the experience of the stressor, and efforts (cognitive and behavioural) to deal with the stressor situation, constitute the primary link between prolonged exposure to threat and changes in symptom intensity. The chronic stressor in this study is similar to the major life stress situations that seemed to provoke or aggravate IBS/FD (or by their absence to relieve IBS/FD) both in early studies (Chaudhary & Truelove, 1962; Waller & Misiewicz, 1969), and in more recent studies

(Craig & Brown, 1984; Bennett et al, 1991) using the more formal methods of the LEDES (Brown & Harris, 1978). Chronic life stress threat arose in circumstances that involved divorce, relationship difficulties, serious illness (of self or other), lawsuits, business failures, housing difficulties and forced redundancies; other difficulties arose within the context of caring for a family member with significant physical and/or emotional problems.

The strong finding that in individuals with IBS/FD, symptom intensity covaried over three time periods with antecedent threat, far more than with goal-frustration, is highly consistent with the strength and specificity of relations found in previous research - between threatening life events and a non inflamed appendix in patients who present with appendiceal type pain (Creed, 1981; Beaurepaire et al, 1992) and between threatening life events and FGID generally (Craig & Brown, 1984). In particular, the findings of this study support reports by both Craig & Brown (1984) and Beaurepaire and colleagues (1992), of significant relations between severe threatening events (but not goal frustration) and *functional* GI disorder which contrasts with relations they and others (Ellard et al, 1990) have found between goal-frustration (more than threat) and *organic* GI disorder.

Certainly, the relation of these highly threatening chronic stressors (previously unexplored in IBS over time) to GI symptomatology is stronger than the presence of negative (usually transient) life events which have either a small effect (Whitehead et al, 1992; Hui et al, 1991; Dinan et al, 1991; Haug et al, 1995), or no effect (Talley & Piper, 1986; Talley & Piper, 1987; Drossman et al, 1988), and are stronger than the presence of daily irritations or the most bothersome events of the day (Hui et al, 1991;

Suls et al, 1994; Dancey et al, 1995), which also have no effect, or the effect is unclear (Dancey et al, 1998).

Stressor threshold

Stressor threshold adds an important non-linear dimension to the relation of life stress to subsequent symptom intensity. A dichotomous life stress predictor variable divided the sample into two subgroups of patients irrespective of their initial symptomatology: the majority (76%), where the clinical outcome was highly sensitive to a specific threshold for stress (that is, the presence/absence of one or more chronic highly threatening stressor); and the remainder (24%), where failure to improve (at lower levels of stress) could not be explained by the psychological or demographic factors assessed in this study. This does not exclude the possibility that idiosyncratic effects from any of a number of biogenetic and/or cognitive-behavioural factors may have inhibited improvement, and/or the perception of improvement for some individuals. It is also possible that differences in management strategies, which were not assessed in this naturalistic study, might help to explain differences in clinical outcome, however, it seems reasonable to expect that clinical management protocols would have been most effective early in the follow-up period.

From a research design perspective, the findings of this study highlight the importance of considering baseline conditions and non-linear (threshold) as well as linear effects; they are also consistent with concepts of dynamic interplay within a biopsychosocial framework (Cassileth & Drossman, 1993) and the likelihood of diverse outcomes from even small differences in initial conditions (Mandel, 1995).

4.2.2 OTHER EFFECTS ON LONG-TERM OUTCOME

In this study, the severity and chronicity of baseline symptomatology and gender were the only factors, other than chronic life stress threat, to significantly predict the overall severity and extent of IBS/FD symptomatology at 16 months. These data suggest that each of these factors negatively influenced the long-term outcome in very different ways.

The severity of *baseline symptomatology* (symptom intensity, the chronicity of severity intensity, and the number and type of syndromes present) had significant prognostic value for symptom outcomes on each of these parameters. Therefore, the factors that are strongly associated with baseline symptomatology (eg. the ‘stress-response’ profile of the number of syndromes present at entry), and those that influence its course over time (in particular, life stress and gender) have considerable clinical relevance.

Baseline symptomatology, however, also reflects the extent of improvement required to achieve a ‘recovery’. For severe and extensive symptomatology (particularly if it is of long duration), an improvement of this magnitude may not be possible within the relatively short period of 16 months. For only 10% of the patients in this sample, GI symptomatology reduced to recovery levels - that is, to subclinical or asymptomatic levels. This supports previous reports eg, Bleijenberg and Fennis (1989) who found that only 9% became asymptomatic over two years.

Female gender was more specific in its effects on the number and type of syndromes present at 16 months. Being a woman, these data suggest, continues to contribute to functional GI disturbance over time. Female gender significantly

enhanced the likelihood of having a larger number of syndromes at 16 months (even after adjusting for the effects of life stress and the number of syndromes present at baseline). While it is possible that the presence of widespread dysmotility and of FD syndromes such as dysmotility-like and reflux-like dyspepsia may add to the likelihood of a poor long-term outcome in women with IBS, at present the extent to which dysfunctions such as dysmotility are reversible over time, or the time that may be required for such reversals, is unknown.

After taking into account the initial severity and chronicity of the disorder, the primary risk indicators of a poor outcome, according to the findings of this study, are continuing high levels of chronic life stress threat and being a woman.

Summary

This study incorporated novel design features to assess the relation of chronic life stress to subsequent symptom intensity in a large group of patients with IBS syndrome over three consecutive time periods. The results suggest that, for most subjects: (1) chronic highly threatening stressors determine the magnitude and direction of change in functional GI symptomatology during the course of the disorder; (2) these effects exceed the effects of baseline gut symptomatology; and (3) the relation is strong, consistent and unequivocally in one direction, is uninfluenced by personality, age, gender, anxiety and depression, and is largely independent of systematic exogenous influences. These findings also suggest that if a particular level of chronic threat is maintained over six months or more, a clinical improvement - that is, a halving of symptom intensity, is extremely unlikely. It is unlikely also that medical or psychological treatments, or psychological factors that may influence whether or not

these treatments are provided, influence changes in symptom intensity over time. First, for patients with these disorders, medical treatments are largely ineffectual and referral for psychological management is rare; second, Study 2 shows that factors other than chronic threat explained only 3% of the variance in symptom intensity over time; and third, this relation was independent of psychological and demographic factors.

In terms of the overall severity and extent of IBS/FD at follow-up, the prognosis was most unfavourable for women.

In sum, these findings have identified continuing high levels of chronic life stress threat, and being a woman, as key risk indicators of a poor outcome for patients with IBS/FD.

4.3 STUDY 3: EVALUATION OF GASTRIC EMPTYING IN FUNCTIONAL DYSPEPSIA

In this study the linear effects of psychosocial and demographic factors on gastric stasis were determined on four parameters of solid gastric emptying and two parameters of liquid emptying in patients with functional (non-ulcer) dyspepsia (with and without IBS). The methods employed to assess gastric emptying include dual-isotope scintigraphy and power exponential analysis.

4.3.1 CONTROL AND SUPPRESSION OF ANGER

A very particular response to life stress - attempts to resist, control, suppress, and hold in anger - dominated the prediction of the presence and the severity of gastric stasis in patients with FD. Specifically, frequent attempts to *control and resist angry feelings and anger-provoking situations* (Anger-control), was strongly associated with a more prolonged initial delay time before solid gastric emptying commenced, while *anger held in* (Anger-in) was related to a slower rate of emptying and a prolonged half-emptying time. For liquid gastric emptying, *suppression of anger* was associated with a prolonged lag time. These relations were linear and specific to type of outcome.

Failure to suppress unhappiness (that is, *manifest unhappiness or depression*), and adopting a fighting spirit (i.e. the tendency to deal with life stressors in a positive and optimistic manner), had small additional effects on gastric stasis. The remaining psychological state or trait variables were not significantly related to the rate of gastric emptying after allowing for the effects of suppressed anger.

The prominence of *anger control*, *anger held in* and *anger suppression* relative to all other psychological factors in this study, strongly supports the research premise that specific ways of coping with negative emotions, especially powerful emotions such as anger, may be important in the development of gastric stasis. It also supports the more global notion that the psychological disturbance coexisting with gastric stasis (poor gastric tone/ 'suppressed' gastric motor activity) reflects a coping style that employs cognitive-behavioural restraint to reduce stressful impact and to control emotional reactions e.g. by avoiding stress-provoking persons or situations and by controlling unwanted emotions such as anger. The coexistent unhappy and depressed state is also consistent with this predominantly 'suppressed' mood state.

The consistency of these relations across parameters which reflect the overall pattern of gastric emptying, namely the delay phase, rates of emptying at 45 and 70 minutes, and the half emptying time, further enhances the specificity and strength of these findings.

Of significance to the strength and consistency of these findings, is the fact that each anger subscale represents a different aspect of attempts to control and suppress anger, and do not necessarily reflect a generally hostile or angry personality. *Anger-in*, which is the tendency to suppress and hold in angry feelings when they were aroused (e.g. by not admitting to, or showing others, the intensity of angry feelings), is conceptually distinct from *state anger* (the intensity of the experience of anger as an emotional state), and *trait anger* (individual differences in anger-proneness as a disposition to experience anger, i.e. to perceive a wider range of situations as anger-provoking). The items of the subscale *anger-control* reflect the tendency to resist and control becoming angry e.g. being patient with others, trying to be tolerant and

understanding, 'keeping one's cool'. In fact anger control has consistently been shown to correlate with low trait anger (Greer & Morris, 1975; Rosenham, 1985), low trait anxiety (Greer & Morris, 1975; Watson & Greer, 1983) and low hostility (Riley et al, 1989) and to be reliably independent of anger held in. That is, although the frequency of dealing with anger-provocation is the feature common to all of the anger subscales linked to prolonged gastric emptying, each subscale reflects a slightly different aspect of the person's attempts to deal with anger.

It is interesting and somewhat intriguing that *overt unhappiness* (that is, not concealing a sad or depressed state) strengthened the relation of suppressed anger to gastric stasis. It is not possible to determine whether this reflected an overload of negative emotions (high levels of anger and unhappiness) such that attempts to suppress unhappiness failed, situational differences, the social mores of our culture, or a combination of these or other factors. The overall impression however, is that feelings were actively or passively suppressed. The association of an unhappy (depressed) state with gastric stasis in this study is consistent with decreases in gut motility found in association with withdrawn-inactive states - for example, sadness, withdrawal (Sadler & Orten, 1968), depression (Almy et al, 1949a; Chaudhary & Truelove, 1961) and deep relaxation (Kellow et al, 1992b). It also supports the view that gastric motor function alters in accordance with the on-going function of the whole individual, and is particularly sensitive to stress, emotional disturbance and unhappiness (Wingate, 1987).

While the prominence of anger suppression variables (and to a lesser extent, a generally sad and depressed state) over all other psychological dimensions strongly suggests that the physiology involved in cognitive-behavioural restraint may include

alterations in gastric motor function, these findings must be regarded as preliminary until other studies investigate the relation of psychological variables to gastric physiologic activity in patients with FD.

To conclude, these findings suggest that the frequent control and suppression of anger is implicated in the processes that determine the development of gastric stasis and FD symptoms over time. The enhanced potency of this relation in the presence of an unhappy or depressed state has particular relevance to the findings of the following study - that is, in relation to the predictors of widespread (more than one region of) impaired (delayed) transit.

4.4 STUDY 4: EVALUATION OF WHOLE GUT TRANSIT IN FGID

This study assessed delayed transit simultaneously in three regions of the digestive tract - the stomach, the small intestine, and the colon. A wholly scintigraphic technique was used; this enabled concurrent assessment in the entire upper and lower gut. The psychological and demographic features of three subgroups of patients (that is, patients with impaired transit in one region only, patients with impaired transit in two or more regions (widespread), and those with normal transit) were determined and comparisons made across subgroups.

4.4.1 GENDER AND PSYCHOLOGICAL FEATURES

The main finding of this study is that in patients with FGID the presence or absence of delayed gut transit, particularly widespread (multiple regions of) delayed transit, was associated with contrasting demographic and psychological features. The prominent feature of both groups of patients with delayed transit was *female gender and low levels of hypochondriasis*. *Depression* and *increased age* were special features of widespread delay in transit alone. *Anger control* was a significant factor for those patients with three regions delayed ie. in addition to high levels of depression and low levels of hypochondriasis.

The predictors of the presence and the extent of delay in transit did not include any particular type of FGID syndrome, any combination of syndromes, or the total number of syndromes present. Rather, these data support the existence of a discrete psychophysiological subgroup within the FGID (that is, those with a specific type of

impaired transit) which does not seem to be distinctive of any particular symptom-based subgroup.

Gender

Although this is the first study to link female gender to widespread impaired transit, the association itself is not without earlier reference. Women are more prevalent than men in patients with *gastric* (eg Wegener et al, 1989; Talley et al, 1989a; Cabellaro-Plasencia et al, 1995; Stanghellini et al, 1996) and *colonic motor dysfunctions* (Thompson et al, 1994; Devroede, 1989a) - at least in western cultures (Talley, 1991). Few women and no men in the healthy control sample in this study had abnormal transit. It appears therefore that the strong association of female gender to delayed transit, especially widespread delayed transit, in these FGID patients is not simply a reflection of a more global gender bias. Indeed, the increased strength of the relation of female gender to widespread impaired transit in this study (that is, relative to the whole sample, to patients with delayed transit in one region and to those with normal transit in all three regions), may help to explain the disproportionate representativeness of women in patient groups with FGID, in those with constipation (Devroede, 1989a), and especially in those whose symptoms are severe and refractory. It also runs counter to the notion that their referral for gastrointestinal investigation was provoked by illness concerns that were inappropriate. This likelihood is further supported by low scores on the general hypochondriasis scale ie. scores similar to those of general practice attenders.

Psychological features

The strength and nature of the relationship of a depressed mood state to slow transit has not been fully explored. A significant association has been reported in patients with FGID symptoms and predominant depression (Chaudhary, 1989), but not in psychiatric outpatients with a diagnosis of major depression (with and without symptoms compatible with a diagnosis of IBS) (Gorard et al, 1996). Only one study suggests that the relation of whole gut transit times to degree of depression (from questionnaire responses) may be quantitative (Gorard et al, 1996). Our findings support the specificity of the association, that is, depression (but not anxiety) with delayed transit, and expand and qualify quantitative aspects of this relationship.

The relation of a depressed mood state to slow transit, this study suggests, is sensitive to increases in the number of regions displaying delayed transit (perhaps also to type of region), occurs more often in women, and is accompanied by a restrained coping style that resists inappropriate illness concerns (that is, scores on the general hypochondriasis scale are low). Importantly, transit impairment is also sensitive to frequent attempts to control and suppress anger. The association is independent of type of FGID, personality and other aspects of coping. These results are consistent with the finding of the previous study - specifically, a strong positive association between the frequency of anger suppression and the extent of gastric stasis, a relationship that is enhanced in the presence of an overtly sad and depressed state. The similarity of the psychological (Study 3) and gender (Stanghellini et al, 1996) features of the severity of gastric stasis to those of widespread delayed transit suggests a correspondence between the *severity* and the *extent* (number of regions) of impaired gut function. To date, this has not been investigated.

4.4.2 FEATURES OF NORMAL TRANSIT

With the exception of gender, the psychological predictors of normal transit appear to explain more about influences on health care seeking and referral than about influences on gastrointestinal transit per se. Based on the higher prevalence of somatic concerns in patient groups with FGID in comparison with nonpatient groups (Drossman et al, 1988), it has been proposed that the primary precipitant of health care seeking and hence of patient status is an enhanced perception of the severity of symptoms and their potential seriousness (represented in this study by scores on the general hypochondriasis scale). Certainly, abnormal illness attitudes (Drossman et al, 1988; Gomborone et al, 1995) and generalised illness concerns (Study 1) - independent of depression - have been associated specifically with outpatient IBS relative to organic GI disease (Gomborone et al, 1995), and to other FGID (eg. functional diarrhoea, functional constipation) subgroups (Study 1). The contribution of this study is that health care seeking based on an increased somatic focus is not widespread, and when present, it is associated with a specific combination of factors.

Only a small but distinct subset of FGID patients in this study, approximately 15% of a mixed gender sample, were distinguished by an enhanced perception of the severity of symptoms and their potential seriousness. The defining feature of this subset of patients was the absence of impaired transit (delayed or accelerated) in the stomach, small intestine and colon, irrespective of the number or type of syndromes present. The feature that most clearly differentiated these patients from those with delayed transit is male gender, however, the specificity of male gender to normal transit is uncertain. In healthy individuals we know that *faster* transit also is associated with male gender (Lampe et al, 1993; Tucker et al, 1981), alcohol consumption

(Probert et al, 1995) and with extraversion more than with dietary fibre intake (Tucker et al, 1981) while in patients with IBS, male gender and anxiety have been associated with faster colonic transit (Devroede et al, 1989b). These findings suggest that the psychosocial features of men with normal and with accelerated transit may differ - supporting evidence, however, is currently unavailable. While it is premature to speculate concerning the psychophysiology of men with IBS/FD, the likelihood of a unitary pattern (similar to that in patients with widespread dysmotility) appears unlikely.

In summary, these findings identify for the first time a subset of FGID patients who are distinguished by a distinct psychophysiology, comprising delayed transit (especially widespread delayed transit), female gender, depression, controlled anger and increasing age. In contrast, male gender and high levels of hypochondriasis are features of an entirely different subset of FGID patients with normal transit in the entire upper and lower gut, who nevertheless do not seem to differ with respect to the type or number of syndromes present. Current evidence suggests that for men a homogeneous psychophysiology is unlikely. The more important finding is that among individuals who consult, men are significantly more likely than women to have normal gut transit function while the psychophysiology for women is more likely to be more clearly defined. The gender differences found here are not inconsistent with previously mentioned gender differences such as the greater likelihood for IBS symptoms to match the Rome criteria for women than for men.

4.5 STUDY 5: EVALUATION OF JEJUNAL SENSORIMOTOR FUNCTION IN IBS

In this study, three subgroups of female patients with three different and increasing levels of jejunal sensory and/or motor dysfunction were identified. Levels of severity ranged from mild - the fasting motor subgroup, to moderately severe - the motor (fasting and postprandial dysmotility) subgroup, to the most severe dysfunction - the sensorimotor subgroup. It is noteworthy that the psychosocial profiles of sensory and/or motor dysfunction at each level also increased in a linear fashion.

A number of strengths add to the reliability of these findings: 1) the patient sample comprised women only, in case gender affected enteric perceptive responses; 2) jejunal distension was performed after a day which included two standard meals; this avoided the confounding effects of different residual contents in the lumen of the small intestine; 3) the prolonged period of ambulant manometric recording ensured a high degree of reliability; and 4) psychometric measures completed at the time of testing demonstrated that enteric sensitivity was not sharpened by concurrent fears and anxieties associated with the procedure itself; few previous distention studies have attended to this latter aspect of research design. A weakness is the small number of subjects in each subgroup.

4.5.1 RELATIONS BETWEEN PSYCHOSOCIAL, SENSORY AND MOTOR DYSFUNCTION

Taken as a whole, these data indicate that the psychosocial profiles of patients with sensorimotor, motor (fasting and postprandial) and fasting motor dysfunction differ in quite specific and clinically important ways.

Sensorimotor dysfunction

A distinct cluster of psychosocial characteristics were prominent features of combined sensorimotor disturbance: a personality that is highly anger-reactive and anxious, a coping repertoire that is limited and inherently ineffectual to deal with most stressful circumstances (mature strategies are rarely used); behavioural responses that include frequent attempts to control angry feelings and anger-provoking situations; and the existential effects of unsuccessful coping - the belief that circumstances and one's own reactions are beyond personal control.

Motor (fasting and postprandial) dysfunction

In contrast, the psychosocial profile which distinguishes the combination of motor (only) dysfunction portrays a personality that is less anger reactive and more introverted than those with either more or less sensory and/or motor disturbance. The coping style is restrained and controlled, and anger is not expressed. These patients believed that they had little personal control, and positively attributed control to external factors.

Fasting motor (only) dysfunction

Compared with the sensorimotor and motor subgroups, the predispositions of patients with mild gut dysfunction - that is, fasting (only) dysmotility, are more moderate and there is no evidence that patients in this group have developed emotional extremes in the course of trying to cope. Although this group is no less anxious or depressed than those with sensorimotor and motor disturbances, a vulnerable personality is not a feature.

These findings suggest that increases in sensorimotor disturbance are inextricably linked to the severity and the nature of psychosocial disturbance. It is of particular interest that in all three studies (Studies 3,4,5) a restrained coping style that includes some aspect of control or suppression of angry feelings was associated with severe dysmotility, whether severity was reflected in multiple parameters of gastric emptying, multiple regions of delayed transit or, in this study, with fasting and fed motor dysfunction with or without sensory dysfunction. Importantly, this study also links a contrasting response to anger, *anger reactivity*, which is emotionally expressive and reactive, with an *enhanced sensitivity and reactivity* of the gut (i.e. with sensory as well as motor dysfunction). Anger reactivity, it will be recalled, was also associated with the most severe and extensive FGID symptomatology (i.e. the number of syndromes present (Study 1)).

Although no other study has assessed these relations in the small bowel, these findings are generally consistent with recent studies of other gut regions: rectal hypersensitivity and anorectal hyper-reactivity have been associated with anxiety (Prior et al, 1993) and poor vagal tone with neuroticism (hyper-responsiveness) (Haug et al, 1994a), while task-related state dysphoria was found by Haug and colleagues (1994a) to best explain antral hypomotility.

From the perspective of psychosocial contributions to FGID, the profiles of this study suggest that personality and coping style factors which predispose to a more severe and prolonged sympathetic response to stressors, may hasten the development of sensorimotor disturbance displayed in the jejunum. Moreover, they suggest that contrasting styles of coping with powerful emotions such as anger may contribute to differences in degrees of severity and overall pervasiveness of dysfunction. These

findings support the concept of a high degree of interrelatedness between psychosocial disturbance, jejunal perceptual hypersensitivity and dysmotility.

Pain sensitivity

Jejunal pain sensitivity did not appear to share in this unity of association. Among patients with pain sensitivity, psychosocial disturbance was prominent only among those with perceptual hypersensitivity (the sensorimotor group). In the absence of perceptual hypersensitivity no psychosocial dimension was characteristic of pain sensitivity. From these preliminary findings it seems that psychosocial dimensions, such as those assessed in this study, are unlikely to contribute directly to jejunal pain sensitivity. This does not, however, exclude indirect influences (through effects on visceral hypersensitivity) of specific personality and coping factors that are primary enhancers of the stress process. It is noted that other aspects of personality (neuroticism, extroversion, anxiety), current distress (anxiety, depression), hypochondriacal attitudes and behaviours, and the existential effects of ineffectual coping (poor self-efficacy) had no effect, direct or indirect, on perceptual or pain sensitivity. These findings run counter to what one would expect if the neuroticism hypothesis (Latimer et al, 1979) was true, that is, if a low threshold for pain among patients with IBS was due to abnormal 'neurotic' tendencies to misperceive or mislabel normal sensations as painful. In rejecting this notion these data lend further support to similar findings in relation to colonic pain sensitivity (Latimer et al, 1979; Whitehead et al, 1990; Kullman & Fielding, 1981).

In summary, the study has found a high degree of interrelatedness between intestinal perceptual hypersensitivity, intestinal dysmotility and psychosocial

disturbance in this group of women with IBS. Overall these data suggest a linear relation between the severity and type of psychological disturbance and the severity and type of sensorimotor dysfunction. In particular, these data highlight the importance of anger reactivity, anger control and suppression, and personal resources such as adequate coping strategies as important factors in the development of sensorimotor dysfunction in adults with IBS.

4.6 SYNOPSIS OF FINDINGS

For the majority of outpatients with FGID, psychosocial disturbance was closely associated with the level of severity of FGID symptoms (Study 1), and in women outpatients, with the level of physiological dysfunction (Studies 3, 4 & 5), such that differences within this graduated pattern may simply reflect different levels in the development / severity of the disorder. For men, psychophysiology within IBS/FD may be more generally heterogeneous, but this has not been determined. These gender-related differences in psychophysiology have important implications concerning the course of the disorder long-term; the prognosis being worse for women (Study 2). For all subjects, however, the emotion most strongly associated with the net severity and extent of the disorder was anger (Studies 1,3 and 4), and the most powerful predictor of change in IBS/FD symptoms over time was the presence of one (or more) highly threatening chronic stressor (Study 2).

4.7 CONCLUSIONS

The strength, consistency and direction of the findings of these studies, leave little doubt that psychosocial disturbance is inherently involved in the processes that determine the severity and extent (and perhaps the type) of syndromes present in outpatients with FGID. The results demonstrate for the first time that psychosocial disturbance influences FGID symptomatology in a quantitative manner, that chronic life stress threat is central to this process and this stress-related process is a prominent feature of a particular group of syndromes defined primarily by the presence of pain and discomfort ie IBS/FD. The results show that in the presence of chronic life stress, an angry, anxious and reactive personality (also ineffectual coping, inadequate emotional support and increasing age) increases the overall severity and extent of the disturbance. Moreover, individuals with this particular stress-response style experience more intense pain and discomfort and display more extensive sensorimotor disturbance.

Key risk indicators of a poor outcome long-term are chronic life stress threat, symptom intensity, and female gender - life stress because it alone determines the magnitude and direction of change in symptom intensity over time, symptom intensity because it reveals the extent of improvement required to achieve a recovery, and female gender because it predicts more widespread gut disturbance in women long-term. Widespread impairment of gut transit represents one factor that may inhibit improvement (or rate of improvement) for women over time. A gender-specific psychophysiological subgroup has been identified within the IBS/FD group of disorders, which if empirically confirmed, may hasten the search for more effective psychological and pharmacological management for most patients with these disorders. More research is needed to determine whether non-conformity to this unique pattern has its own set of psychophysiological features.

4.8 CLINICAL IMPLICATIONS

The findings of this study have special relevance with respect to the question: who would benefit most from psychological intervention? This question is important in the context of an unknown etiopathophysiology, a psychological therapeutic approach that has proven effectiveness (eg. Chaudhary & Truelove, 1962; Creed, 1994), especially long-term (Guthrie, 1996), but which is seldom used. Guthrie (1996) argues that although brief psychological therapies can be helpful for patients with mild symptoms, because they are time consuming and costly, they should be reserved for patients with chronic and relapsing symptoms.

In general, the findings from the current studies reach a similar conclusion. At consultation, patients with the most chronic, severe and extensive functional gastrointestinal symptoms, had been exposed to higher levels of chronic and severe life stress threat, and were more anxious and/or depressed, than those with mild symptoms. More frequently their personality was stress-enhancing, their coping ineffectual, they had inadequate emotional support, and were older. In addition to more severe and extensive GI pain and discomfort, many had stress-related extraintestinal symptoms. The long-term outcome was bleak, especially for women, in terms of the extent of their FGID disturbance, the presence of widespread dysmotility and severe sensorimotor dysfunction. For these patients, the benefits of brief psychological therapy are clear, especially if the therapist has experience working with patients with such complaints.

The special contribution of this study is that it has identified a single factor that helps to explain not only chronicity, relapses and failure to improve, but also clinical improvement. With a high degree of sensitivity and specificity, chronic life stress threat

determined whose symptoms would improve, and whose would not. For three quarters of patients with IBS, the presence or absence of one (or more) highly threatening chronic stressor predicted not only when symptoms would improve, but also the extent of the improvement. It is noteworthy that with regard to clinical management, these strong effects were evident over and above the effects of routine clinical management. Clearly, psychological intervention that helps to reduce the stress experienced by these patients would have major beneficial effects.

Another contribution of these findings is that they show with considerable precision how much stress-reduction is needed to achieve a significant reduction in IBS/FD symptomatology at least over a 16 month period. Prospective evidence that the presence of even one highly threatening chronic stressor inhibits improvement, while its reduction or absence may be a prerequisite for a significant improvement, sets clear goals for stress reduction management. Thus, whether the patient is exposed to one, or multiple such stressors, the therapeutic goal would be to reduce each stressor to below the high threat threshold and to maintain threat at a more manageable level over time and changing circumstances. Clearly the sustained success of psychologically based treatment programs over reassurance, placebo and drug treatment (Guthrie et al, 1991; Shaw et al, 1991; Rumsay, 1991) suggests that this may be a highly achievable goal.

In particular, the results suggest that psychological management which targets specific aspects of the chronic stressor and its sequelae would prove beneficial for most IBS/FD patients in several ways: first, by reducing the severity of the present episode; and second, by teaching coping skills that can be used in the future. It is hoped that the beneficial effects of early intervention in preventing the development of such severe and extensive disorder may be an available option in the future.

4.9 LIMITATIONS OF THE FINDINGS AND DIRECTIONS FOR FUTURE RESEARCH

Much of this work must be considered as preliminary, and replication is needed on many levels. Advantaged by a new symptom-based classification system for the FGID, together with new and more sophisticated techniques and procedures to assess normal and abnormal physiological function in the GI tract, hypotheses have been tested with greater precision and reliability than was possible in the past. Novel as well as standard measures have been used to determine within-group differences and within-subject changes over time, and many relations between psychosocial factors and physiological outcomes (eg. widespread dysmotility) have been investigated for the first time. Replication is necessary, therefore, before these findings can be generalised to the whole IBS/FD outpatient population.

The limited representativeness of the sample population from which all subjects were drawn, has been acknowledged. As emphasised earlier, findings derived from outpatients referred by their family doctor for endoscopic evaluation cannot be generalised to either community (non-referred) or hospitalised (more severe) FGID sufferers. The strength of using the same population for the entire work is that it ensured a high degree of internal consistency across study samples and adds credence to hypothesis generation with respect to relations within that population. Marked variability within the symptom and psychosocial data also suggests that this population is well suited for preliminary within-group investigations - that is, to test for degrees of disturbance and differences between subgroups. While it is anticipated that this work can be generalised to similar groups of individuals with these disorders, it remains for

future research in a variety of clinical settings to determine the general representativeness of these data.

The current findings also beg further investigation at multiple levels of inquiry. The pursuit of psychophysiological variants within this group of disorders is in its infancy, as is the relation of psychophysiology to symptom-based categories. Findings with clinical relevance from this naturalistic study, should now be tested in randomised controlled treatment studies eg to compare the efficacy of targeting the reduction of chronic stress to below threshold levels with various traditional psychological therapies (psychotherapeutic treatments and treatments based on muscle relaxation) vs routine clinical management without psychological therapies.

Overall, this work represents a further step in the process of accumulating sufficient information to establish good practice guidelines for the management of these chronic, poorly understood disorders.