Psychological and sex features of delayed gut transit in functional gastrointestinal disorders

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Abstract
Background—The relation of demographic and psychological factors to the presence and extent of gut transit impairment in the functional gastrointestinal disorders has received little attention.

Aims—To compare the psychosocial and demographic features of patients with functional gastrointestinal disorders and delayed transit in one region of the gastrointestinal tract with those displaying more widespread delayed transit (that is, delay in two or three regions), and those with normal transit in all three regions.

Patients—Of 110 outpatient participants who satisfied standardised criteria for functional gastrointestinal disorders, 46 had delayed transit in one region, 32 had delay in two or three regions, and 17 exhibited normal transit in all regions.

Methods—Transit in the stomach, the small intestine, and the large intestine was assessed concurrently using a wholly scintigraphic technique; psychological status was assessed using established psychometric measures.

Results—Patients with delayed transit displayed demographic and psychological features that contrasted with patients with normal transit in all regions. In particular, widespread delayed transit featured female sex, a highly depressed mood state, increased age, frequent control of anger, and more severe gastric stasis, while the features distinguishing normal transit were male sex and high levels of hypochondriasis.

Conclusion—These data suggest the existence of a distinct psychophysiological subgroup, defined by the presence of delayed transit, in patients with functional gastrointestinal disorders.

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Keywords: delayed gut transit; psychophysiology; sex; mood

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A range of psychological factors, such as emotional distress, hypochondriasis, and an inadequate coping style, have been associated with the functional gastrointestinal disorders (FGID).[1–4] Female sex,[5] a depressed mood state,[6 7] anxiety,[8] and the control and suppression of anger,[9] have also been linked to inhibition of gut contractile activity in patients with these disorders. However, although impaired (delayed) gut transit is present in some patients with FGID, the demographic and psychological features of this pathophysiological condition remain poorly defined; in particular, whether more extensive disturbances in transit are associated with a greater degree of psychological distress than more localised disturbances is not known. Furthermore, the relation of impaired transit to type and number of coexistent FGID has received little attention.

Our first aim therefore, was to determine and compare, among patients with FGID, the demographic and psychological predictors of: (1) delayed gastrointestinal transit (in one region of the digestive tract, namely the stomach, the small intestine, or the large intestine); (2) widespread delayed transit (delay in two or three regions); and (3) normal transit in all three regions. Our second aim was to determine the relation of FGID syndromes to the extent of impaired transit. We employed a novel wholly scintigraphic technique for assessing transit, enabling assessment of all three regions of the gut concurrently.

Methods
PATIENTS

One hundred and ten consecutive outpatients (91 women, mean age 44 (15) years) with FGID were studied; FGID included irritable bowel syndrome (IBS), functional constipation (FC), unspecified functional bowel disorder, and functional dyspepsia (FD) syndromes (dysmotility-like, ulcer-like, reflux-like, and unspecified functional dyspepsia). All patients fulfilled the criteria for these FGID as elaborated by Drossman,[10] and organic disease had been excluded by appropriate diagnostic studies. All drugs known to affect gastrointestinal motility, including laxatives, were ceased at least 24 hours prior to scintigraphy. Premenopausal women were studied in the follicular phase of the menstrual cycle. Approval for the procedures was given by the Medical Research Ethics and Radiation Safety Committees of the Royal North Shore Hospital, and all subjects gave informed consent.

ASSESSMENT OF GASTROINTESTINAL TRANSIT
Gastric emptying and small intestinal transit
Evaluation of gastric emptying was carried out as described previously.[11] At 9 00 am on day 1, after an overnight fast, subjects consumed a

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Abbreviations used in this paper: DT1, delayed transit in one region only; DT2, delayed transit in two or more regions; FC, functional constipation; FD, functional dyspepsia; FGID, functional gastrointestinal disorder; IBS, irritable bowel syndrome; NT, normal transit in all three regions; ROI, region of interest; $t_{1/2}$, half emptying time.

standard meal (1.78 MJ; protein 14%, carbo-hydrate 27%, fat 58%); the solid phase was labelled with 20 MBq technetium-99m sulphur colloid, and the liquid phase with 4 MBq indium-111 DTPA.[11] For the assessment of small bowel transit, images were acquired at 15 minute intervals between one and four hours. A stomach region of interest (ROI) was used after realignment of the gastric emptying data, while caecal ROI or markers on the patient were used to reregister the small bowel data. In order to compensate for potential attenuation of counts as the meal traversed the end of the small bowel and arrived in the caecum and proximal colon, a normalising ROI including the caecum and all small bowel/gastric activity was used to define total activity for small bowel transit. Solid time-activity curves were generated by subtraction from the ^{99m}Tc curves of the product of down scatter fraction and ^{111}In curves. Attenuation corrected solid and liquid curves were generated from geometric means of anterior and posterior images, corrected for decay, and a power exponential function fitted. For gastric emptying, solid and liquid half emptying time ($t_{1/2}$) and solid lag time (time to 2% emptying) were calculated. Similar parameters of filling were generated for the small bowel curves. Small intestinal transit time for solid and liquid phases was calculated as the time from 50% gastric emptying to 50% caecal filling.[12 13]

Colonic transit

Anterior and posterior 10 minute images of the abdomen and pelvis were obtained at 6, 24, 48, 72, and 96 hours, with the subject in a supine position.[14] In order to obtain information which was as physiological as possible, subjects resumed their normal diet and activities following the six hour acquisition. Decay corrected time-activity points were obtained from geometric means of ^{111}In counts (maximum colon activity taken as 100%), and joined with a linear point to point fit. The resultant curve was used to derive the time to 50% colon emptying.

Scintigraphic data were compared with those obtained in 58 healthy asymptomatic subjects (43 women, mean age 39 (11) years). The sex composition of the patient and control groups was similar. For each region, abnormality was defined as one or more scintigraphic parameters outside the 5th to 95th percentiles of the control data for each sex with respect to delay and with respect to acceleration in transit. Four healthy females were outside the 5th to 95th percentiles for gastric emptying, and one for small bowel transit for the female group; no male control fell outside the control range for males. The accuracy of the scintigraphic method has been documented recently.[15 16]

PSYCHOSOCIAL ASSESSMENT

Psychometric measures assessed included demographic factors (age, sex, and marital, educational, and occupational status), and psychological variables including emotional distress/mood state, personality, coping style, and emotional expression/suppression.

Emotional distress/mood state

Depression—assessed by the Centre of Epidemiological Studies Depression Scale.[17]
State anxiety—items measure current levels of tension and apprehension (Spielberger State and Trait Anxiety Inventory (Form Y).[18]

Personality

Neuroticism—high scores reflect a tendency to over emotionality, and excessive worry.
Extroversion—to assess orientation to things external or internal (Eysenck Personality Inventory).[19]
Trait anxiety—to assess the tendency to anxious states (Form Y).[18]
Trait anger—anger temperament (the disposition to express anger), and anger reactivity (responses based on evaluations of situations as negative; Spielberger's State-Trait Anger Scale).[20]
General hypochondriasis—the tendency to be inappropriately concerned about one's health (nine item subscale of Illness Behaviour Questionnaire).[21]

Coping style

The tendency to use immature, neurotic, and/or mature defences (the Defence Style Questionnaire).[22]

Emotional expression/suppression

(1) To reflect the degree of suppression of unwanted emotions—anger, anxiety, and depression (Courtauld Emotional Control Scale).[23] (2) Anger in, anger out, anger control (Anger Expression (AX) Scale).[24]

DATA AND STATISTICAL ANALYSES

Patients were subdivided into three groups according to the presence or absence of delayed transit in each region: patients with delay in one region (DT1, n=46); patients with delay in two or more regions (DT2, n=32); or patients in whom all regions displayed normal transit (NT, n=17). Fifteen patients with accelerated transit were excluded because they had accelerated transit coexisting with delayed or normal transit. Age and sex distributions in transit subgroups were compared by analysis of variance for age, and the χ^2 test for sex. Analysis of variance was also used to assess differences with respect to scores on the hypochondriasis and depression scales. Stepwise multiple logistic regression analyses were performed to determine the psychological and demographic features, and in separate analyses, the FGID subgroup features, of the DT1 and DT2 subgroups, in contrast to patients with NT, and in comparison with each other. FGID predictor variables included: type of syndrome, combinations of FD syndromes with IBS and FC, and total number of syndromes present. Mann-Whitney U and Wilcoxon signed rank tests were performed to compare the severity of stasis in each gut region (stomach, small bowel, colon) of patients in the DT1 and DT2 groups. All probability values were two tailed with alpha set at 0.05.

Table 1   Parameters of gastrointestinal transit in the healthy control group (n=58)

	Median	5th centile	95th centile
Stomach			
Solid $t_{1/2}$	103	6.4	156
Solid lag	13	4	27
Liquid $t_{1/2}$	37	13	66
Small bowel			
Solid $t_{1/2}$	78	36	153
Liquid $t_{1/2}$	69	27	153
Colon $t_{1/2}$	38	18	73

Results

GASTROINTESTINAL TRANSIT

Of the 46 patients in the DT1 group, 16 (35%) displayed delay in the stomach, 10 (22%) in the small bowel, and 20 (43%) in the colon. The corresponding proportions for the 29 patients in the DT2 group (11 (34%), seven (21%), and 14 (45%), respectively) were similar (p<0.05).

Table 1 shows summary transit parameters for each region in the healthy control group. Table 2 shows the median (and centile) values for delayed transit (solid $t_{1/2}$) times according to the subgroups of DT1 and DT2. Gastric stasis was significantly increased in patients with multiple regions of delayed transit (DT2); the severity of small bowel and colonic stasis did not differ between groups.

Table 2   The severity of delayed transit in each gut region for patients with delayed transit in one region (DT1) and in multiple regions (DT2)

	DT1			DT2		
	25th centile	50th centile	75th centile	25th centile	50th centile	75th centile
Stomach*	163.9	170.1	200.1	164.1	231.1	253.3
Small bowel	161.8	255.6	381.2	170.8	206.4	371.4
Colon	86.4	94.3	95.1	82.5	93.6	95.3

$t_{1/2}$ times/values are shown (solid, for the stomach and small bowel).
*DT2 > DT1 (p<0.05).

Table 3   Summary of differences in age, sex, depression, and hypochondriasis between transit subgroups

	NT	DT1	DT2
Age (y); mean (SD)	38 (17)	42 (13)	49 (14)*
Female:male ratio	1.8:1	6.8:1†	9.7:1†
Depression scores; mean (SE)‡	13 (2.6)	11 (1.2)	16 (3.2)*
Hypochondriasis scores; mean (SE)§	2.6 (0.5)	1.4 (0.2)†	1.4 (0.3)†

*p<0.05 versus NT and DT1; † p<0.05 versus NT.
Normative data
‡The cut off score for depression of probable clinical significance is ⩾17.[25]
§The mean (SD) hypochondriasis scores are 1.44 (1.8) for general practice patients, and 2.69 (2.3) for psychiatric patients.[21]
NT, normal transit; DT1, delayed transit in one region; DT2, delayed transit in multiple regions.

Table 4   Frequency of functional gastrointestinal disorders (FGID) for each gut transit subgroup

Transit subgroup	IBS n (%)	FD* n (%)	UFBD† n (%)	UFD† n (%)	FC n (%)
NT (n=17)	13 (76)	2 (12)	0	0	2 (12)
DT1 (n=46)	36 (78)	4 (9)	1 (2)	2 (4)	3 (7)
DT2 (n=32)‡	23 (72)	4 (12.5)	3 (9)	0	4 (13)

*Functional dyspepsia (FD) subgroups: dysmotility-like, ulcer-like, and reflux-like dyspepsia.
†Unspecified functional bowel disorder (UFBD) and unspecified functional dyspepsia (UFD) occurred alone.
‡Row total exceeds 32 as two patients with functional constipation (FC) also had FD.
Note: no FGID subgroup, combination of subgroups, or total number of subgroups was significantly associated with gut transit status.
IBS, irritable bowel syndrome; NT, normal transit; DT1, delayed transit in one region; DT2, delayed transit in multiple regions.

DEMOGRAPHIC FACTORS

Table 3 summarises group differences in age and sex. The age of patients in the DT2 subgroup was significantly higher than in the DT1 or the NT subgroups; age did not differ, however, between the DT1 and the NT subgroups. With respect to sex, the female:male ratio was significantly greater in both subgroups with delayed transit. Sex was most discriminating of delayed versus normal transit for patients with delayed transit in two or more regions; the probability of being a female was almost eight to one for patients in this group (odds ratio = 7.6; 95% confidence interval = 1.44; p=0.02). There were no differences between transit subgroups with respect to marital, educational, or occupational status (data not shown).

PSYCHOLOGICAL AND DEMOGRAPHIC FACTORS

In comparison with normal transit, depression scores were significantly higher in the subgroup of patients with widespread delay in transit (DT2; table 3). In contrast, hypochondriasis scores were significantly lower in both delayed transit (DT1, DT2) subgroups (table 2). Normative data (table 3) for depression[25] and general hypochondriasis[21] show that mean depression scores are indeed high in the widespread delayed transit group (DT2), as are hypochondriasis scores in the NT group.

The psychological profile of widespread delayed transit (DT2) comprised increased depression, together with low levels of hypochondriasis (variance explained = 41.5%). A post hoc analysis revealed that for those patients with three regions delayed these same variables (depression and hypochondriasis) together with anger control strongly predicted delayed transit in all three regions (variance explained = 84%). In a separate analysis, female sex and increasing age together predicted DT2 relative to NT (variance explained = 45%).

The psychological profile of normal transit, after controlling for the effects of depression, included both male sex and high levels of hypochondriasis.

FGID FACTORS

Table 4 summarises the frequency of FGID syndromes for each transit subgroup. No FGID variable in the regression model (type of syndrome, combination of syndromes, or the number of syndromes present) predicted transit subgroup (NT, DT1, DT2).

Discussion

The main finding of the current study was 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 sex and low levels of hypochondriasis; both of these features, together with depression and age, increasingly discriminated delayed from normal transit as the number of regions displaying delay increased. For patients with three regions delayed, psychological

factors alone (low levels of hypochondriasis and high levels of depression and anger control) explained most (84%) of the variance in gut stasis. The predictors of delayed 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 subset within the FGID (those with a specific type of impaired transit) that seems to be independent of symptom based subgroups. An important clinical dimension of widespread delayed transit is the increased severity of gastric stasis in patients within the DT2 group; this strong relation between the severity of gastric stasis and the extent (number of regions) of gut stasis, previously unreported, is consistent with the observations of delayed gastric emptying in response to experimental rectal distension.[26]

Although this is the first study to link female sex to widespread impaired transit, the relation itself is not without earlier reference; whole gut transit time tends to be slower in women generally[27 28] and women are more prevalent than men among patients with gastric[5 29–31] and colonic motor dysfunctions,[8 32] at least in western cultures.[33] Few women and no men in the healthy control sample in this study had abnormal transit. It seems therefore that the strong association of female sex to delayed transit, especially widespread delayed transit, in these FGID patients is not simply a reflection of a more global sex bias. Indeed, the increased strength of the relation of female sex to widespread impaired transit (relative to the whole sample, to DT1 and NT) in this study, may help to explain the disproportionate representativeness of women in patient groups with FGID, in those with constipation,[8] and especially in those with severe and refractory FGID. 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 their very low scores on the general hypochondriasis scale.

The strength and nature of the relation of a depressed mood state to slow transit has not been fully explored. A significant association has been reported in patients with functional gastrointestinal symptoms and predominant depression,[7] but not in psychiatric outpatients with a diagnosis of major depression (with and without symptoms compatible with a diagnosis of IBS).[34] Only one study suggests that the relation of whole gut transit times to degree of depression (from questionnaire responses) may be quantitative.[34] Our findings support the specificity of the association (depression, but not anxiety, with delayed transit), and expand and qualify quantitative aspects of this relation. The association is sensitive to increases in the number of regions displaying delayed transit (perhaps also to type of region), occurs more often in women, is accompanied by a restrained coping style that resists inappropriate illness concerns (general hypochondriasis), and attempts to control and suppress anger; the relation is independent of type of FGID, personal-

ity, and other aspects of coping. These results are consistent with our earlier finding of a strong positive relation between the frequency of anger suppression and the extent of gastric stasis, a relation that was enhanced in the presence of an overtly sad and depressed state.[9] The similarity of the psychological[9] and sex[5] features of the severity of gastric stasis to those of widespread delayed transit supports the correspondence found in this study between the severity of gastric stasis and the extent (number of regions) of delayed gut function.

The association of depression and controlled anger with gut stasis identifies a distinct and recognisable psychophysiological subset of patients with FGID. The association is consistent with the view that gut motor function alters in accordance with the ongoing function of the whole individual.[35] While a contrasting psychophysiology (increased emotional and gastrointestinal expressiveness) that is distinctive for men is suggested by reports of extraversion in healthy male subjects with faster transit,[36] current evidence suggests that for men a homogeneous psychophysiology is unlikely. Male sex, which was so strongly associated with normal transit in this study of FGID patients, has been associated also with faster transit in healthy individuals.[27 28] A less clearly defined psychophysiology for men with FGID might be expected, however, given other reported sex differences such as the greater likelihood for IBS symptoms to match the Rome criteria for women than for men.[37]

With the exception of sex, the predictors of normal transit seem 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 non-patient groups,[38] it has been proposed that the primary precipitant of health care seeking, and hence of patient status in FGID, 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[38 39] and generalised illness concerns[4] (independent of depression) have been associated specifically with outpatient IBS relative to organic gastrointestinal disease,[39] and to other FGID (for example, FD, FC) subgroups.[4] This study suggests, however, 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.

In summary, these findings identify an important subset of FGID patients distinguished by a distinct psychophysiology that is most complete for patients with widespread delayed transit; specific features include female sex, more severe gastric stasis, a highly depressed mood state, the control of anger, and increasing age.

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