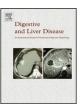
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#### **Alimentary Tract**

# Patients with irritable bowel syndrome and constipation are more depressed than patients with functional constipation



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#### ABSTRACT

Background: Psychosocial factors, such as depression, have been shown to be associated with gastrointestinal disorders like constipation.

Methods: We retrospectively compared the depression and anxiety profiles of patients with irritable bowel syndrome with constipation versus those of patients with functional constipation using validated questionnaires. Subjects rated the intensity of digestive symptoms experienced during the previous month using visual analogue scales. Colonic transit time measurements and anorectal manometry were performed.

Results: Of the 128 consecutive, constipated patients included (84% females, mean age  $49.7\pm15.5$  years) 66 suffered from irritable bowel syndrome with constipation and 62 from functional constipation. Demographic and physiological traits were similar in the two groups. Patients suffering from irritable bowel syndrome with constipation reported higher depression scores  $(18.8\pm1.4 \text{ vs } 12.7\pm1.3, P=0.002)$  and higher symptom intensity scores for constipation  $(6.2\pm0.3 \text{ vs } 4.3\pm0.4, P<0.001)$ , bloating  $(6.7\pm0.3 \text{ vs } 3.3\pm0.4, P<0.001)$  and abdominal pain  $(6.0\pm0.3 \text{ vs } 2.7\pm0.4, P<0.001)$  than patients with functional constipation. Multiple linear regression showed positive correlations between symptom intensity and depression and anxiety scores for functionally constipated patients only.

*Conclusions*: Our results support the integration of a psychosocial component to the traditional treatment of constipated patients; however, further research exploring causality between psychosocial factors and specific gastrointestinal disorders would contribute to developing a tailored therapeutic approach.

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#### 1. Introduction

The pathophysiology of all functional gastrointestinal disorders (FGID) combines interactions of the brain, spinal cord, enteric nervous system, and gut, translating to abdominal pain and disordered gastrointestinal function [1]. For the irritable bowel syndrome (IBS) a concept of the biopsychosocial model of illness and disease was developed [2]. This model integrates all possible accountable factors for the pathogenesis and clinical expression in IBS [3]. The biopsychosocial approach allows for symptoms to be both determined and modified by psychological and social influences [4]. IBS patients experience significant impairment in health-related

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quality of life [5], and have high levels of anxiety and mood disorders [6].

Most patients who seek medical advice for gastrointestinal problems have an associated affective disorder [7]. In fact, using grounded theory and comparing consulting and non-consulting IBS patients, Bourgault and colleagues identified as the major components of IBS, abdominal pain (long thought of as the main reason for consulting a physician), disordered bowel habits, and affective disorders [8,9].

Depression is frequently found in patients with constipation [10–13]. Nevertheless, the biopsychosocial approach allows for symptoms to be both determined and modified by psychological and social influences [3]. The link between psychosocial factors and gastrointestinal function (motility, sensation, inflammation) is through the brain–gut axis, implying a bidirectional connection system between the gastrointestinal tract and the brain, through neural, neuroimmune and neuroendocrine pathways [14]. Psychosocial factors (stressful life events, psychological

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distress) influence every component of the biopsychosocial model: digestive function, symptom perception, illness behaviour and, consequently, health outcome, daily function, and quality of life [15].

In patients complaining of constipation, two major functional diseases were described by the Rome III consensus conference [16]: functional constipation (FC) and IBS-constipation (IBS-C), a subtype of IBS. Nevertheless, there are few data comparing the psychological profile of these two types of constipated subjects [17]. The aim of the present study was to compare the psychological profile associated with these two types of constipation, in order to gain insight into the pathophysiology of these two disorders.

#### 2. Materials and methods

#### 2.1. Subjects

Between October 2008 and March 2011, 345 outpatients were referred to the Gastrointestinal unit of the Avicenne Hospital (Assistance Publique - Hôpitaux de Paris) for FGID and subsequently, referred to the CEFRED (Centre d'Exploration Fonctionnelle et de Reéducation Digestive, Functional and Re-education, GI unit). All patients meeting the criteria for constipation completed a psychological evaluation and were included in the present study. A full clinical evaluation failed to yield an organic cause for their complaint, including a morphological evaluation (endoscopy or radiology) and the ruling out of metabolic, endocrine, and neurological aetiologies. None of the patients were using narcotics, antidepressant drugs or calcium channel blockers, but they were allowed to continue thyroid replacement drugs, and contraceptive pills. None of the patients had been submitted to any previous surgery of the gastrointestinal tract. A single investigator (MB) confirmed, independently, the validity of the initial diagnosis of FGID.

#### 2.2. Experimental procedure

#### 2.2.1. Study design

The comparison of the two groups of constipated patients was performed using a retrospective observational study design.

#### 2.2.2. Questionnaires

A standard clinical questionnaire based on diagnostic questions for functional gastrointestinal disorders was filled individually [18,19]. The interpretation was based on the functional disorders as defined by the Rome III criteria. For all subjects constipation was defined by the presence of 2 or more of the following: (i) straining during at least 25% of defecations; (ii) lumpy or hard stools in at least 25% of defecations; (iii) sensation of incomplete evacuation for at least 25% of defecations; (iv) sensation of anorectal obstruction/blockage for at least 25% of defecations; (v) manual manoeuvres to facilitate at least 25% of defecations; (vi) fewer than 3 defecations per week, IBS was diagnosed when recurrent abdominal pain or discomfort at least 3 days per month in the last 3 months was associated with 2 or more of the following [16]: improvement with defecation; onset associated with a change in frequency of stool or with a change in form (appearance) of stool. IBS-C was defined according to the Rome III criteria by the presence of hard or lumpy stools in more than 25% of defecations and loose (mushy) or watery stools in less than 25% of bowel movements; other supportive symptoms included in the definition of constipation were not part of the criteria for the diagnosis of IBS-C, but were present in IBS-C patients. FC was defined when there were insufficient criteria for an IBS diagnosis.

In addition, functional anorectal pain (including the levator ani syndrome, proctalgia fugax, and others [20]), and difficult defecation (presence, in the preceding 6 months, of two or more of the

following: (i) straining in more than 25% of defecations; (ii) sensation of incomplete evacuation in more than 25% of defecations; (iii) sensation of anorectal obstruction/blockage in more than 25% of defecations; (iv) manual manoeuvres to facilitate more than 25% of defecations) were recorded.

Finally, a questionnaire about urinary (urinary incontinence, dysuria, urinary frequency) and sexual complaints (dyspareunia, impotence) was filled by all patients as previously described [19].

#### 2.2.3. Psychometric evaluation

Psychometric evaluation was focused on anxiety and depression

The level of depression was assessed by the Beck Depression Inventory (BDI-II). This test is frequently used in the evaluation of depression in gastrointestinal disorders [21–23]. It contains 21 multiple-choice items, each with a score from zero to three, so that the total point score varies from 0 to 63. All subjects completed the French validated translation of the BDI-II [24]. According to the score, the patients were grouped in 2 levels: high depression (15–63) and low depression (0–14). In addition, each item coded from 0 to 3 constituted the basis for a specific 4-level Likert scale used to characterize the psychological profile of the patient.

Anxiety was assessed by the French validated translation of the State and Trait Anxiety Inventory, composed of two axes (A1 for state anxiety and A2 for trait anxiety), both consisting of 20 multiple-choice items; each item has a score from one to four, so that the total point score of A1 and A2 axes can range from 20 to 80 [25]. In the general French population values of Trait anxiety and State Anxiety were  $50 \pm 10$ . This test was selected for its simplicity, validity, and reliability [26]; furthermore, it allowed to evaluate anxiety levels and to distinguish "state" anxiety from "trait" anxiety in gastrointestinal diseases [27,28]. The test is based on the conceptual distinction between anxiety as a transitory "state", expressed by emotional reactions of different degree, and anxiety as a relatively stable personality "trait". "State" anxiety is conceptualized as an emotive "state" characterized by subjective feelings perceived on a conscious level, such as apprehension and tension, which vary with time; anxiety as a "trait" refers to individuals with a continuous disposition towards anxiety [29].

#### 2.2.4. Visual Analogue scales

All subjects filled in 10-cm Visual Analogue Scales (VAS) to evaluate the intensity of four digestive symptoms: constipation, diarrhoea, abdominal bloating, and abdominal pain. VAS ranged from 0 ("absence of symptom") to 10 ("maximum intensity of symptoms"). Subjects were asked to score the symptoms experienced during the previous month.

Stool description was recorded using the Bristol Stool Form Scale [16].

#### 2.2.5. Physiological evaluation

In order to assess the physiological characteristics of the constipated subjects, two tests were performed: the measurement of colonic transit time and the evaluation of rectal sensitivity.

#### 2.3. Total and segmental colonic transit time

Colonic transit was measured using the technique we previously described [30]. Briefly, twelve radiopaque markers within a gelatin capsule (CT Transit, Plastimed, Le Plessis Bouchard, France) were ingested at 9:00 am from day 1 to day 6. A plain film of the abdomen was taken on the seventh day at 9:00 am. Markers were localized and counted in the different segments of the large bowel according to bony landmarks [30]. Three zones of interest were defined for the measurement of segmental colonic transit time: the right colon (ascending colon and right part of the transverse),

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