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Psychological adjustment and autonomic disturbances in inflammatory bowel diseases and irritable bowel syndrome

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Summary Psychological factors and the autonomic nervous system (ANS) are implicated in the pathogenesis of inflammatory bowel diseases (IBD) and irritable bowel syndrome (IBS). This study aimed to assess, firstly the way IBS and IBD patients cope with their pathology according to their affective adjustment and secondly the possible links between these affective adjustments and ANS reactivity. Patients with Crohn's disease (CD; $n = 26$), ulcerative colitis (UC; $n = 22$), or IBS ($n = 27$) were recruited and compared to 21 healthy subjects based on psychological variables (trait- and state anxiety, depressive symptomatology, negative mood, perceived stress, coping, health locus of control) and sympatho-vagal balance through heart-rate variability monitored at rest. A principal component analysis, performed on all affective variables, isolated a leading factor labelled as "affective adjustment". In each disease, patients were distributed into positive and negative affective adjustment. In all the diseases, a positive affect was associated with problem-focused coping, and a negative affect with emotion-focused coping and external health locus of control. Results show that the sympatho-vagal balance varied according to the disease. In CD presenting positive affectivity, an adapted high sympathetic activity was observed. In UC, a parasympathetic blunt was observed in the presence of negative affectivity and an equilibrated sympatho-vagal balance in the presence of positive affectivity. In contrast, in IBS, an

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important dysautonomia (with high sympathetic and low parasympathetic tone) was constantly observed whatever the affective adjustment. In conclusion, this study suggests that the equilibrium of the ANS is differentially adapted according to the disease. This equilibrium is conjugated with positive affective and cognitive adjustment in IBD (CD and UC) but not in IBS.

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1. Introduction

Inflammatory bowel diseases (IBD) are primarily comprised of 2 disorders: ulcerative colitis (UC) and Crohn's disease (CD). IBD are characterized by a chronic course in which phases of remission of variable length are interrupted by acute episodes. Irritable bowel syndrome (IBS) is a highly prevalent functional gastrointestinal disorder mainly characterized by abdominal pain and discomfort in association with altered bowel habits in the absence of any structural abnormalities (Schepper et al., 2008; Thompson et al., 2000, 1999). Despite differences in the aetiologies of IBD and IBS (Baumgart and Sandborn, 2007; Von Stein et al., 2008) stress represents a common risk factor in their pathogenesis. Patients often report stressful life events at the onset and/or during the time course of their disease (Collins, 2001; Li et al., 2004; Mawdsley and Rampton, 2005; Mönnikes et al., 2001; Reber et al., 2006; Tang et al., 2008). The burden of such chronic diseases adds undercurrents of psychological strain to the weight of the pathology. Most of the psychological disturbances reported in IBD and IBS are therefore principally related to the illness' time course (Jones et al., 2006). It results in high perceived stress levels (Rogala et al., 2008; Tang et al., 2008), impaired quality of life (Coffin et al., 2004) and affective co-morbidities such as worries, anxiety, negative mood or depression (Miehler et al., 2008; Mittermaier et al., 2004; Olden, 2008; Sugaya and Nomura, 2008). This forces the patients to develop coping strategies such as (i) problem-focused coping (i.e., where the individual faces the problem, seeks a solution, tries to resolve it), (ii) emotion-focused coping (i.e., where the individual changes by denying that there is a problem to be able to cope with) and (iii) search for social support (i.e., where the individual asks his family or health professionals for help, or counselling). These coping strategies may in turn influence the path of their disease: CD patients with low avoidance coping strategies were the least likely to relapse (Bitton et al., 2008). The individual coping style may therefore determine the outcome, which combines psychological (e.g., anxiety, depression), social (e.g., absenteeism, social withdrawal) and biological (e.g., evolution of the disease) dimensions. This is commonly observed in multiple chronic diseases (such as arthritis or heart disease) in which problem-focused coping or search for social support is usually more beneficial than emotion-focused coping (Martz and Livneh, 2007; Thompson and Gustafson, 1996). This point of view agrees with the Lazarus and Folkman's transactional model of stress in which stress is considered as the result of an "imbalance between demands and resources" occurring when "pressure exceeds one's perceived ability to cope" (Lazarus and Folkman, 1984). It could be speculation then, that the extent of positive affects influence coping in favour of beneficial ways (i.e., problem-focused and social support coping).

The interrelations between digestive diseases and psychological disturbances reflect the special link between the brain and the gut in what is called the "brain-gut axis". The

autonomic nervous system (ANS) is the neural interface relaying bottom-up and top-down informations. Visceral sensations are carried through vagal afferents. These informations directly modulate efferent premotor regions of the ANS (Craig, 2002; Mayer et al., 2006). More importantly, these efferent regions can also be negatively or positively modulated by a set of upper brain regions like amygdala, hippocampus and prefrontal cortex (Benarroch, 1993; Loewy and Spyer, 1990; Saper, 2002). These regions which can modulate gut function, are also involved in the regulation of emotional (e.g., mood, anxiety, negative affects, pain) and cognitive behaviours (e.g., decision making, planning, search for information), and therefore in the development of social behaviour, coping strategy and well-being (Gillanders et al., 2008; Seminowicz et al., 2004). Accordingly, a growing body of evidence suggests the existence of autonomic dysfunctions in patients with IBD and IBS (Ollsson et al., 2007; Spaziani et al., 2008; Spetalen et al., 2008; Taylor and Keely, 2007; Van Orshoven et al., 2006), whatever the severity of symptoms and even during remission in IBD or asymptomatic phase in IBS (Ganguli et al., 2007; Sharma et al., 2009). Despite these findings, little is known about the type of autonomic dysfunctions according to the way patients are psychologically adjusted with negative or positive affects. We speculate that the positive or negative affects observed in IBD and IBS patients are associated to specific coping strategies (more problem-centred in the positive affects cases or more emotion-centred in the negative affects cases) and to an adapted ANS activity (equilibrated autonomic balance in the positive affects cases and an imbalance in the negative affects cases). Since gut diseases are heterogeneous, we have studied these relations in three groups of patients (IBS, IBD with CD or IBD with UC) in comparison to healthy controls. In order to understand the links between emotion affects, coping strategies and ANS adaptations, each group of patients was subdivided into two subgroups according to their emotional adjustment. Differences in coping style and ANS balance were analyzed in these two subgroups.

2. Materials and methods

2.1. Subjects (Table 1, subject demographics)

Ninety-six subjects were prospectively recruited between January 1st, 2006 and December 31st, 2007. All patients were recruited in our Gastroenterology Department while age- and sex-matched healthy subjects were included from the Grenoble INSERM Clinical Investigation Centre. Subjects were distributed as (i) healthy volunteers (controls, $n = 21$), (ii) IBS patients ($n = 27$), and (iii) IBD patients (UC, $n = 22$; CD, $n = 26$). The study was conducted according to the Declaration of Helsinki and in accordance with the guidelines of Good Clinical Practice. The protocol was approved by the ethical committee of the Grenoble Faculty of Medicine and Hospital

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