

Literature Review on Stress and Psychosocial Determinants of Irritable Bowel Syndrome

Michael Galanakis¹, Theoni Grammatikou², Sofia Kalogridi², P. George Chrousos^{2,3*}, Christina Darviri^{2*#}

¹Panteion University of Social and Political Sciences, Athens, Greece

²Postgraduate Course Science of Stress and Health Promotion, School of Medicine, University of Athens, Athens, Greece

³First Department of Pediatrics, Children's Hospital Aghia Sofia, School of Medicine, University of Athens, Athens, Greece

Email: [#]cdarviri@yahoo.com

Received 30 September 2015; accepted 12 February 2016; published 15 February 2016

Copyright © 2016 by authors and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

In recent years, the irritable bowel syndrome (IBS) has developed into a multi-factorial disease involving visceral hyperactivity, changes in the nervous and humoral communication between the enteric nervous system and the central nervous system, altered intestinal microflora, and increased intestinal permeability and minimal enteral inflammation. Psychological and social factors can affect the communication between the central and enteric nervous system, and there is evidence that is involved at the IBS and affect the response to treatment and outcome. There are indications that abuse history and stressful life events are implicated in initiation of functional gastrointestinal disorders. Genetic factors and social learning mechanisms have been proposed in order to explain grouping of IBS in families. The psychological characteristics, such as anxiety, depression, and comorbid psychiatric disorders, health beliefs have important role in the management of patients with IBS associated with both symptoms and results. This knowledge can be the trigger for a better and more holistic treatment of IBS, by giving to patient the opportunity for a better quality of life.

Keywords

Irritable Bowel Syndrome (IBS), Stress, Psychosocial Stressors, Psychiatric Disorders, Anxiety, Enteric Nervous System, Multi-Factorial Disease

*These authors contributed equally and shared last authorship.

#Corresponding author.

1. Introduction

IBS is a chronic intermittent functional gastrointestinal disorder, characterized by abdominal pain, swell and intestinal disorders (Clark & DeLegge, 2008). The Rome Committee for the Classification of Functional Gastrointestinal Disorders has determined IBS on the basis of abdominal and bowel symptoms that constantly occur in suffers. Specifically, should be abdominal pain for a minimum of 3 days, for 3 straight months. The pain must have at least two of the below characteristics:

- 1) Reprieve by evacuation
- 2) Commencement associated with changes in the incidence of the excreta
- 3) Commencement associated with changes in the form of the excreta

According to studies 1/3 of the population show similar symptoms to those of IBS. It seems that IBS is more common in lower social and economic groups, which is affected by environmental factors, while in contrast appears that there is a moderate reduction in prevalence with advancing age (Rey & Talley, 2009). IBS divided into two categories. Patients in the first category there is constipation as the predominant symptom, while in patients of the second, document diarrhea (Dorn, Morris et al., 2009). IBS has multifactorial reasoning. In the pathophysiology of IBS, the gut flora is altered by both psychosocial stressors and environmental factors.

Nowadays IBS is considered as a disorder of the brain-gut axis of deregulation, including abnormal function of the intestinal, autonomic and central nervous system (Posserud, Ersryd et al., 2006).

The aim of this manuscript is to present, Irritable Bowel System is not just a physical illness based on the brain gut axis dysfunction but affected by daily hassles (everyday stressors), major life events and health beliefs. For these reasons we firstly analyzed the pathophysiology of IBS in order to have a complete view of the function of Irritable Bowel System and afterwards to determine how the IBS affected by both psychologically stressful factors, the beliefs of health and coping with stress.

2. Pathophysiology

2.1. Pathophysiological Mechanisms

2.1.1. Visceral Hyperactivity

The most recent knowledge available show that the basic mechanism that provoke abdominal pain is the visceral hyperactivity (Bueno & Fioramonti, 2002). The dominant afferent neuron terminals of enteric nervous system (ENS) that are found in submucosal tunica of gastrointestinal tract (Meissner plexus) and between smooth muscle fibers (Auerbach plexus) forward stimuli to central nervous system (CNS) via sympathetic and parasympathetic autonomic nervous system (SANS and PANS). SNS conveys stimuli that are identified as abdominal pain, while PANS conveys stimuli starting off a variety of reflexes. The pain stimuli via thalamus induce the cerebral cortex and allows the acknowledgement of visceral pain. Then again, to achieve interoperation of visceral reflexes, the afferent stimuli via hypothalamus tripper efferent neural fibers which via PANS tripper or hinder the contraction of smooth muscle fibers and the excretion of enterocytes in the gastrointestinal tract altering the put motility and excretion (Bueno & Fioramonti, 2002). It is widely accepted that visceral sensitivity is controlled in a variety of levels. This regulation is especially intervened at the stage of enteric mucosa and submucosa, the stage of spinal cord, the stage of thalamus and the stage of cerebral cortex.

2.1.2. Visceral Sensitivity at the Level of Enteric Mucosa and Submucosa

When enteric mucosa suffers from an injury, this can result in the release of such chemical mediators as K⁺, ATP and bradykinin as well as inflammatory mediators such as prostaglandin E₂ (PGE₂) (Bueno, Fioramonti et al., 1997). All this matter can straightly stimulate the afferent neuron terminals but have also the capacity to tripper the release of algogenic matter (serotonin (5HT), histamine, prostaglandins and nerve growth factor (NGF)). This torrent results in the reinforcement of the stimulus which involves the visceral pain (Tracey & Walker, 1995).

The interconnection between afferent neuron terminals and mast cells has been greatly intriguing. The release of substance P from the neuron terminals trippers the formulation and release of histamine and NGF from mast cells. The release of substance P is reinforced by histamine, while NGF conveys the impression to be associated with neuron terminal's plasticity (Moss & Sanger, 1990). The latest evidence associate the enrichment of neural sensitivity for algogenic stimuli with elevated expression of sodium channels on basic afferent endings (Moss & Sanger, 1990).

The role of a few of the inflammatory mediators, which are discharged in enteric mucosa and submucosa appear to be more defined. Serotonin (5HT), is thought to tripper the prime afferent neuron terminals. Precent-day studies based on pseudo-affective (cardiovascular) reflex responses to gut distention have put forward an action via 5HT₃ receptor subtype conjoined with a sodium channel which exists on primary afferent endings. If a small dosage of 5HT₃ antagonists is administered through the views, it increase visceral analgesic results in response to gut distention in various rat models of abdominal pain (Zemlan, Murphy et al., 1994).

It is common knowledge that the signaling of bradykinin's affects visceral sensitivity in a variety of ways (Barthan & Proud, 1991). Two receptor types of bradykinin (BK) have been a knowledged. Some studies maintain that BK receptors undergo selective up regulation in the course of processes that follow some types of intestinal tissue injury and inflammation. With the help of various stimuli endogenous NGF are discharged from most cells, increasing the prime afferent sensitivity to BK by upregulating BK receptors. Studies conducted on experimental animals have concluded that pharmacological agents which perform as BK antagonists sooth the pain experienced in the abdominal which is caused by intraperitoneal administration of acetic acid and urate crystals (Sharkey, Coggins et al., 1990).

A number of mediators such as adenosine, tachykinin, calcitonin gene related peptide (CGRP) and neurokinins take part in a series of events. Some C afferent fibers have "silent receptors" for neurokinins which can be stimulated by inflammatory procedures in peripheral tissues. All in all if nerve remodeling occurs during inflammation, it can cause hypersensitivity in the submucosa and other intestinal structures (Millan, 1999). The aforementioned modification are composite, they depend on time and are affiliated to the kind of inflammation. The intense nature of *Nippostrongylus brasiliensis* infection is connected with a 2.5-fold rise in nerve content of the tissues, mainly an outcome of axonal dilatation. In the course of recovery when mast cell proliferation is ensured, the mean cross sectional area of the nerve is reduced yet the diameter of small fibers is on the increase.

3. Biopsychosocial Model of Irritable Bowel Syndrome

The advent of the 19th century saw the emerge of the idea that emotions probably affect the sensorimotor function of the gastrointestinal tract. Much of the evidence researched during that time is still worthy (Van Ouden-hove, Vandenbergh et al., 2010). This model includes all probable liable factors for the pathogenesis and clinical expression in IBS. According to the biopsychosocial approach symptoms can be regulated by psychological and social effects (Drossman et al., 2006). The connection between psychological elements and gastrointestinal function (sensation, motility, inflammation) is via the brain-gut axis. This entails a bidirectional association system between the gastrointestinal tract and the brain found in neural, neuroimmune and neuroendocrine pathways (Jones, Dilley et al., 2006).

Every part of the biopsychosocial model is affected by psychosocial factors. At the early stapes of one's life, genetics and environmental elements (e.g., family influences, abuse, major losses), can easily influence a person's psychosocial development (psychological state, coping skills) and the advancement of gut dysfunction. Gut dysfunction and dysregulation of the brain-gut axis may induce IBS. In a lifetime, psychosocial circumstance such as stressful incidents and psychological distress can affect digestive functions, symptom perception, illness behavior and therefore health daily function and quality of life (Drossman et al., 2006). On the other hand, visceral pain can influence central pain perception, mood and behavior (Creed, Levy et al., 2006).

4. Psychosocial Stressors

Lazarus (1990) divided stressors into life events and daily hassles. Life events refer to major events such as divorce, unemployment, or death of a close relative. Daily hassles are events which everybody experiences daily and frequently (Lazarus & Folkman, 1984). His assumption is that "(daily) hassles appear to be better predictors of health outcomes than life events". The results of a recent prospective study support this theory: there was a significant increase in stress or score (daily hassles) just before progression from IBS non-patient to IBS patient (Fujii & Nomura, 2008). The majority of the subjects in this study however, were young college students, so factors rated as relatively stressful life events, were not very common.

The current data regarding the role of life events in the onset of IBS are the result of observations from the 80 s. For example, Creed et al. (1988) showed that the most frequent events reported by patients with functional abdominal pain (FAP) (including IBS patients) during 38 wk prior to onset of symptoms, were a major disruption of close relationships, a marital separation, a family member leaving home, or break-up of a serious

girl/boyfriend relationship. In addition, marked personal relationship difficulties such as severe marital problems or extreme family or household tensions, were much more frequently recorded among the FAP patients than in the organic GI diseases group (such as ulcer disease) or community subjects.

Recent data support the role of major life events in IBS. Childhood trauma was associated with an increased vulnerability for multiple somatic symptoms of which IBS is one subset (Videlock, Mayer et al., 2010). The items reported significantly more frequently in IBS than in healthy controls were: seeing someone being murdered, death or illness of a parent, failing to be understood by parents and having someone in the family with a psychiatric illness.

Holocaust survivors are another example of the impact of stressful life events on the development of IBS. The prevalence of IBS, duration of suffering, and frequency of GI symptoms were significantly higher in Holocaust survivors (Stermer, Bar et al., 1991) when compared to controls with the same demographic background, but who had not been exposed to extreme mental and physical hardships during the war. From our personal experience (Dumitrascu & Baban, 1991) the stress developed by dramatic events presented live on television, during the uprising in Romania in 1989, led to an increased number of IBS symptoms within the first month.

Sometimes, what is considered to be a major life event is difficult to determine. For instance, a sudden cultural change (such as moving from a rural to an urban area) increased the prevalence of IBS in one study (Sperber & Friger, 2005).

The experience of stressful life events can also determine symptom exacerbation among adults with IBS and frequent health-care seeking (Creed, Levy et al., 2006; Palsson & Drossman, 2005). Thus, the severity of abdominal pain was higher in patients exposed to emotional stress (Devanarayana, Mettananda et al., 2011) and stress exacerbated abdominal distension in one third of IBS patients (Chang, Lee et al., 2001). In addition, recent data showed that environmental factors and psychosocial stressors (for example history of being psychologically abused, less than 6 h of sleep and irregular diet) influenced the progression from an IBS non-consulter to an IBS patient (Fujii & Nomura, 2008).

Based on these data we can say that psychosocial stressors, either during childhood or later in life are involved in the onset of IBS symptoms in susceptible individuals, and these factors influence the clinical course of IBS.

5. Health Beliefs and Coping with Stress

It is widely believed among patients with IBS that the chronic gut symptoms they encounter suggest a serious illness or even cancer. Furthermore, these patients acknowledge that IBS symptoms influence their everyday function, thought, emotions and attitude. They report to experience the sense of losing freedom, directness and social acquaintance along with feelings of apprehension, shame and self-consciousness. All these can easily change one's behavior for example by avoiding activities or by making adaptations in their routine while trying to gain control (Drossman, Chang et al., 2009).

The most severe kind of preoccupation with an illness is hypochondriasis, which is part of the group of somatoform disorders. Hypochondriasis is known as exaggerated fear of a serious illness, although the patients has been medically tested and reassured to the contrary (Widiger & Thomas, 1994). In a study dating from the 1990s, those patients who suffered from IBS tended to have more hypochondriacal behaviors when they were compared with patients suffering from organic healthy GI diseases. The scores on bodily preoccupation, hypochondriacal beliefs and disease phobia of the disease were really high among patients with IBS (Gomborone, Dewsnap et al., 1995). There is no other evidence available. Screening for hypochondriacal behavior is not recommended but on a daily basis we most likely deal with patients with sky-high illness-related fear. The Illness Attitudes Scales (IAS) questionnaire can be used to determine the presence of hypochondriacal attitudes. The specific questionnaire was established in 1986 (Kellner, 1986), but it is still a valuable tool to our days (Sirri, Grandi et al., 2008).

Having psychologically assessed IBS patients it is now known that there are dissimilarities about how people with IBS react to their condition. Strictly speaking, patients take up mixed kinds of coping strategies in comparison with patients who suffer from organic diseases or healthy controls. When we state "coping" we actually mean "steadily altering cognitive and behavioral attempts to deal with certain external and/or internal demands that are assessed as taxing or going beyond the resources of the individual" (Lazarus & Folkman, 1984). The authors have categorized coping strategies in two main groups: problem-orientated coping which focuses directly on the course of stress, like information seeking effective way of reducing/solving the problem and planning, and

Table 1. IBS in connection with health beliefs and coping with stress.

There can be irrational beliefs about health in IBS patients, leading to the hypochondriacal behaviors
Patients with Irritable Bowel Syndrome usually adopt incorrect coping strategies that are ineffective, such as catastrophizing
More severe pain referred by patients with a high degree of catastrophizing

emotion-orientated coping which is used to deal with emotions stirred by this situation (such as running away from feeling, trying to flee from the problem or putting the blame on oneself).

There are a lot of questionnaires that evaluate coping strategies, for example Coping Strategies Questionnaire (CSQ) (Rosenstiel & Keefe, 1983), the Ways of Coping Questionnaire (WCQ) (Folkman & Lazarus, 1988) and Coping Inventory for Stressful Situation (CISS) (Endler & Parker, 1999). The CISS has shown up to now to possess very good psychometric qualities and was confirmed in a lot of languages (Schwarzer & Schwarzer, 1996). All of these contain the aforementioned coping strategies.

According to WCQ, Drossman et al. (2000) we know that patients suffering from IBS and other FGIDs, did not make use of revaluation as frequently as patients with organic disorders (such as IBD, acid peptic disease, pancreato-biliary diseases). As reported in a Polish study, patients with IBS showed a high emotional-oriented coping style (Wrzeńska & Kocur, 2008).

The CSQ targets basically on coping as for as painful conditions are concerned. The focal point in using the CSQ in IBS patients is associated with the sub scale measuring catastrophizing (for example “When I am in pain, I feel I cannot stand it anymore” or “it’s awful and I feel it devours me”). Catastrophizing is a maladjusted coping tactic described as “a negative mental procedure consisting of negative reflection and concern” (Keogh & Asmundson, 2004). IBS sufferers are more inclined to catastrophize than those suffering from organic disorders (Drossman, Leserman et al., 2000). Furthermore, catastrophizing plays the role of a mediator in the relationship between depression and pain severity. The subsequent observation suggest this relationship: IBS patients and a high level of catastrophizing tend to report more intense pain; catastrophizing and depression are linked (Lackner, Quigley et al., 2004); depression did not predict symptom intensity (Drossman, 1999). IBS patients who encounter greater degree of depression are occupied with more catastrophic ideas, and to certain extent this kind of thinking involves more severe pain and larger-scale limitations in activity because of the pain (Lackner, Quigley et al., 2004).

The CSQ assesses, as well, the total success of coping tactics (the amount of control over symptoms and self-considered capability to minimize symptoms). Patients with IBS showed less tendency to feel in control of symptoms and to feel capable of reducing symptoms than patients with organic disorders (Drossman, Leserman et al., 2000) indicating that coping tactics are not very effective in IBS patients.

A general conclusion is hard to be drawn when talking about coping styles in IBS patients. All the work presented above made use of various questionnaires to evaluate coping strategies in IBS. The outcome is not conflicting, but simultaneously did not indicate a certain coping strategy in IBS patients (see also the summary in Table 1). Additional research is vital to show the role of coping in symptom understanding and control, and clinical result in IBS suffers.

6. Conclusions

An important part for biopsychosocial model of IBS are the psychosocial and environmental aspects, because they are participate in deregulation of the brain-gut axis, resulting in the appearance of IBS, insistence of symptoms or disease abnormal behavior. In human’s life there is a vast range of environmental and psychosocial stressors, acting in different times; nevertheless IBS will be appeared only in susceptible individuals.

Other important factors, like personality traits and psychiatric disorders, it is likely the elements that make someone sensitive to the development of IBS; accordance with the biopsychosocial model.

References

- Barthan, J. M., & Proud, D. (1991). Bradykinin Antagonists. *Annual Review of Pharmacology and Toxicology*, 31, 129-162. <http://dx.doi.org/10.1146/annurev.pa.31.040191.001021>
- Bueno, L., & Fioramonti, J. (2002). Visceral Perception: Inflammatory and Non-Inflammatory Mediators. *Gut*, 51, i19-i23.

- http://dx.doi.org/10.1136/gut.51.suppl_1.i19
- Bueno, L., Fioramonti, J., Delvaux, M. et al. (1997). Mediators and Pharmacology of Visceral Sensitivity: From Basic to Clinical Investigations. *Gastroenterology*, 112, 1714-1743. [http://dx.doi.org/10.1016/S0016-5085\(97\)70056-8](http://dx.doi.org/10.1016/S0016-5085(97)70056-8)
- Chang, L., Lee, O. Y., Naliboff, B., Schulson, M., & Mayer, E. A. (2001). Sensation of Bloating and Visible Abdominal Distension in Patients with Irritable Bowel Syndrome. *The American Journal of Gastroenterology*, 96, 3341-3347. <http://dx.doi.org/10.1111/j.1572-0241.2001.05336.x>
- Clark, C., & DeLegge, M. (2008). Irritable Bowel Syndrome: A Practical Approach. *Nutrition in Clinical Practice*, 23, 263-267. <http://dx.doi.org/10.1177/0884533608318107>
- Creed, F. H., Levy, R., Bradley, L., Drossman, D. A., Francisconi, C., Naliboff, B. D., & Olden, K. W. (2006). Psychosocial Aspects of Functional Gastrointestinal Disorders. In: D. A. Drossman, E. Corazziari, M. Delvaux, R. C. Spiller, N. J. Talley, W. G. Thompson, & W. E. Whitehead (Eds.), *Rome III: The Functional Gastrointestinal Disorders* (3rd ed., pp. 295-368). McLean, VA: Degnon Associates Inc.
- Creed, F., Craig, T., & Farmer, R. (1988). Functional Abdominal Pain, Psychiatric Illness, and Life Events. *Gut*, 29, 235-242. <http://dx.doi.org/10.1136/gut.29.2.235>
- Devanarayana, N. M., Mettananda, S., Liyanarachchi, C., Nanayakkara, N., Mendis, N., Perera, N., & Rajindrajith, S. (2011). Abdominal Pain-Predominant Functional Gastrointestinal Diseases in Children and Adolescents: Prevalence, Symptomatology, and Association with Emotional Stress. *Journal of Pediatric Gastroenterology and Nutrition*, 53, 659-665. <http://dx.doi.org/10.1097/mpg.0b013e3182296033>
- Dorn, S. D., Morris, C. B., Hu, Y., Toner, B. B., Diamant, N., Whitehead, W. E., Bangdiwala, S. I., & Drossman, D. A. (2009). Irritable Bowel Syndrome Subtypes Defined by Rome II and Rome III Criteria Are Similar. *Journal of Clinical Gastroenterology*, 43, 214-220. <http://dx.doi.org/10.1097/MCG.0b013e31815bd749>
- Drossman, D. A. (1999). Do Psychosocial Factors Define Symptom Severity and Patient Status in Irritable Bowel Syndrome? *American Journal of Medicine*, 107, 41S-50S.
- Drossman, D. A. (2006). The Functional Gastrointestinal Disorders and the Rome III Process. In D. A. Drossman, E. Corazziari, M. Delvaux, R. Spiller, N. J. Talley, W. G. Thompson, & W. E. Whitehead (Eds.), *Rome III: The Functional Gastrointestinal Disorders* (3rd ed., pp. 1-30). McLean, VA: Degnon Associates Inc.
- Drossman, D. A., Chang, L., Schneck, S., Blackman, C., Norton, W. F., & Norton, N. J. (2009). A Focus Group Assessment of Patient Perspectives on Irritable Bowel Syndrome and Illness Severity. *Digestive Diseases and Sciences*, 54, 1532-1541. <http://dx.doi.org/10.1007/s10620-009-0792-6>
- Drossman, D. A., Leserman, J., Li, Z., Keefe, F., Hu, Y. J., & Toomey, T. C. (2000). Effects of Coping on Health Outcome among Women with Gastrointestinal Disorders. *Psychosomatic Medicine*, 62, 309-317. <http://dx.doi.org/10.1097/00006842-200005000-00004>
- Dumitrascu, D. L., & Baban, A. (1991). Irritable Bowel Syndrome Complaints Following the Uprising of December 1989 in Romania. *Medicine and War*, 7, 100-104. <http://dx.doi.org/10.1080/07488009108408973>
- Endler, N. S., & Parker, J. D. A. (1999). *Coping Inventory for Stressful Situations (CISS): Manual* (2nd ed.). Toronto: Multi-Health Systems.
- Folkman, S., & Lazarus, R. S. (1988). *Ways of Coping Questionnaire Manual*. Palo Alto: Consulting Psychologists Press.
- Fujii, Y., & Nomura, S. (2008). A Prospective Study of the Psycho-Behavioral Factors Responsible for a Change from Non-Patient Irritable Bowel Syndrome to IBS Patient Status. *Biopsychosocial Medicine*, 2, 16. <http://dx.doi.org/10.1186/1751-0759-2-16>
- Gomborone, J., Dewsnap, P., Libby, G., & Farthing, M. (1995). Abnormal Illness Attitudes in Patients with Irritable Bowel Syndrome. *Journal of Psychosomatic Research*, 39, 227-230. [http://dx.doi.org/10.1016/0022-3999\(94\)00126-P](http://dx.doi.org/10.1016/0022-3999(94)00126-P)
- Jones, M. P., Dille, J. B., Drossman, D., & Crowell, M. D. (2006). Brain-Gut Connections in Functional GI Disorders: Anatomic and Physiologic Relationships. *Journal of Neurogastroenterology and Motility*, 18, 91-103. <http://dx.doi.org/10.1111/j.1365-2982.2005.00730.x>
- Kellner, R. (1986). *Somatization and Hypochondriasis*. New York: Praeger.
- Keogh, E., & Asmundson, G. J. G. (2004). Negative Affectivity, Catastrophizing and Anxiety Sensitivity. In G. J. G. Asmundson, J. W. S. Vlaeyen, & G. Crombez (Eds.), *Understanding and Treating Fear of Pain* (pp. 91-117). New York: Oxford University Press.
- Lackner, J. M., Quigley, B. M., & Blanchard, E. B. (2004). Depression and Abdominal Pain in IBS Patients: The Mediating Role of Catastrophizing. *Psychosomatic Medicine*, 66, 435-441.
- Lazarus, R. S. (1990). Theory-Based Stress Measurement. *Psychological Inquiry*, 1, 3-13. http://dx.doi.org/10.1207/s15327965pli0101_1
- Lazarus, R. S., & Folkman, S. (1984). *Stress, Appraisal and Coping* (pp. 141-327). New York: Springer.

- Millan, M. J. (1999). The Induction of Pain: An Integrative Review. *Progress in Neurobiology*, 57, 1-164.
- Moss, H. E., & Sanger, G. J. (1990). The Effects of Granisetron, ICS 205-930 and Ondansetron on the Visceral Pain Reflex Induced by Duodenal Distension. *British Journal of Pharmacology*, 100, 497-501.
- Palsson, O. S., & Drossman, D. A. (2005). Psychiatric and Psychological Dysfunction in Irritable Bowel Syndrome and the Role of Psychological Treatments. *Gastroenterology Clinics of North America*, 34, 281-303. <http://dx.doi.org/10.1016/j.gtc.2005.02.004>
- Posserud, I., Ersryd, A., & Simren, M. (2006). Functional Findings in Irritable Bowel Syndrome. *World Journal of Gastroenterology*, 12, 2830-2838.
- Rey, E., & Talley, N. J. (2009). Irritable Bowel Syndrome: Novel Views on the Epidemiology and Potential Risk Factors. *Digestive and Liver Disease*, 41, 772-780.
- Rosenstiel, A. K., & Keefe, F. J. (1983). The Use of Coping Strategies in Chronic Low Back Pain Patients: Relationship to Patient Characteristics and Current Adjustment. *Pain*, 17, 33-44. [http://dx.doi.org/10.1016/0304-3959\(83\)90125-2](http://dx.doi.org/10.1016/0304-3959(83)90125-2)
- Schwarzer, R., & Schwarzer, C. (1996). A Critical Survey of Coping Instruments. In M. Zeidner, & N. S. Endler (Eds.), *Handbook of Coping: Theory, Research, Applications* (pp. 107-133). New York: John Wiley and Sons.
- Sharkey, K. A., Coggins, P. J., Tetzlaff, W., Zwiers, H., Bisby, M. A., & Davison, J. S. (1990). Distribution of Growth-Associated Protein, B-50 (GAP-43) in the Mammalian Enteric Nervous System. *Neuroscience*, 38, 13-20.
- Sirri, L., Grandi, S., & Fava, G. A. (2008). The Illness Attitude Scales. A Clinimetric Index for Assessing Hypochondriacal Fears and Beliefs. *Psychotherapy and Psychosomatics*, 77, 337-350. <http://dx.doi.org/10.1159/000151387>
- Sperber, A. D., Friger, M., Shvartzman, P., Abu-Rabia, M., Abu-Rabia, R., Abu-Rashid, M., Albedour, K., Alkranawi, O., Eisenberg, A., Kazanoviz, A., Mazingar, L., & Fich, A. (2005). Rates of Functional Bowel Disorders among Israeli Bedouins in Rural Areas Compared with Those Who Moved to Permanent Towns. *Clinical Gastroenterology and Hepatology*, 3, 342-348. [http://dx.doi.org/10.1016/S1542-3565\(04\)00553-1](http://dx.doi.org/10.1016/S1542-3565(04)00553-1)
- Stermer, E., Bar, H., & Levy, N. (1991). Chronic Functional Gastrointestinal Symptoms in Holocaust Survivors. *American Journal of Gastroenterology*, 86, 417-422.
- Tracey, D. J., & Walker, J. S. (1995). Pain Due to Nerve Damage: Are Inflammatory Mediators Involved? *Inflammation Research*, 44, 407-411.
- Van Oudenhove, L., Vandenbergh, J., Demyttenaere, K., & Tack, J. (2010). Psychosocial Factors, Psychiatric Illness and Functional Gastrointestinal Disorders: A Historical Perspective. *Digestion*, 82, 201-210. <http://dx.doi.org/10.1159/000269822>
- Vidlock, E. J., Mayer, E. A., Naliboff, B. D., & Chang, L. (2010). The Effect of Childhood Trauma and Abuse on the Development of Irritable Bowel Syndrome Is Mediated by Somatization. *Gastroenterology*, 138, S-144.
- Widiger, T. A., & Thomas, A. (Eds.) (1994). *Diagnosis and Statistical Manual of Mental Disorders* (4th ed.). Washington DC: American Psychiatric Publishing.
- Wrzesińska, M. A., & Kocur, J. (2008). The Assessment of Personality Traits and Coping Style Level among the Patients with Functional Dyspepsia and Irritable Bowel Syndrome. *Psychiatria Polska*, 42, 709-717.
- Zemlan, F. P., Murphy, A. Z., & Behbehani, M. M. (1994). 5-HT1A Receptors Mediate the Effect of the Bulbospinal Serotonin System on Spinal Dorsal Horn Nociceptive Neurons. *Pharmacology*, 48, 1-10.