



Adrenal hormone response and psychophysiological correlates under psychosocial stress in individuals with irritable bowel syndrome

Nagisa Sugaya^{a,b,*}, Shuhei Izawa^c, Kenta Kimura^d, Namiko Ogawa^e, Kosuke C. Yamada^f, Kentaro Shirotaki^g, Ikuyo Mikami^e, Kanako Hirata^e, Yuichiro Nagano^h, Shinobu Nomuraⁱ, Hironori Shimadaⁱ

^a Tokyo Metropolitan Institute of Medical Science, 2-1-6 Kamikitazawa, Setagaya-ku, Tokyo 156-8506, Japan

^b Advanced Research Center for Human Sciences, Waseda University, 2-579-15 Mikajima, Tokorozawa, Saitama 359-1192, Japan

^c National Institute of Occupational Safety and Health, Japan, 6-21-1 Nagao, Tama-ku, Kawasaki-shi, Kanagawa 214-8585, Japan

^d Department of Psychological Science, Kwansai Gakuin University, 1-155 Uegahara-1bancho, Nishinomiya, Hyogo 662-8501, Japan

^e Graduate School of Human Sciences, Waseda University, 2-579-15 Mikajima, Tokorozawa, Saitama 359-1192, Japan

^f National Institute of Advanced Industrial Science and Technology, 2-3-26 Aomi, Koto-ku, Tokyo 135-0064, Japan

^g Faculty of Human Relations, Tokai Gakuin University, 5-68 Nakakirinocho, Kakamigahara-shi, Gifu 504-8511, Japan

^h Department of Human Studies, Bunkyo Gakuin University, 1196 Kamekubo, Fujimino-shi, Saitama 356-8533, Japan

ⁱ Faculty of Human Sciences, Waseda University, 2-579-15 Mikajima, Tokorozawa, Saitama 359-1192, Japan

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ABSTRACT

Objective: In this study, we investigated levels and relative ratios of adrenal hormones (including cortisol, dehydroepiandrosterone [DHEA], and DHEA-sulfate [DHEA-S]) and their psychophysiological correlates under acute psychosocial stress in individuals with irritable bowel syndrome (IBS).

Methods: Fifty-three college students participated in the study (male: 42, female: 11; mean age: 22.64 years), including 13 individuals with IBS (IBS group) and 40 individuals without IBS (control group). The participants were exposed to a standardized laboratory stressor, which included delivering a speech and performing a mental arithmetic task. We measured subjective stress levels and salivary cortisol, DHEA, and DHEA-S levels at relevant time points before, during, and after the tasks.

Results: DHEA-S level and the DHEA-S/DHEA ratio in the IBS group were significantly lower than those in the control group, and the cortisol/DHEA-S ratio in the IBS group was higher than that in the control group throughout the experiment. In the IBS group, the appraisal of a threat was positively correlated with cortisol levels ($r=0.61$), and the appraisal of controllability was negatively correlated with cortisol levels ($r=-0.64$) and with the cortisol/DHEA ratio ($r=-0.71$). The control group showed a significant positive correlation between the appraisal of threat and cortisol levels ($r=0.32$).

Conclusion: The present study indicates that individuals with IBS had lower DHEA-S levels, and that their stressful cognitive appraisals under acute psychosocial stress caused the effects of cortisol to dominate. This adrenal hormone response may be involved in exacerbating abdominal symptoms in individuals with IBS.

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1. Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder with persistent chronic abdominal pain and disturbance of bowel movements. It is a typical digestive system psychosomatic disorder that is exacerbated by stress. Recently, the brain–gut axis in IBS has attracted much attention, and a relationship between IBS symptoms and the hypothalamic–pituitary–adrenal (HPA) axis has frequently been suggested.

IBS patients experience an increase in bowel movements after the injection of corticotropin-releasing hormone (CRH) (Fukudo et al., 1998) and secrete more CRH than do healthy control individuals (Tache et al., 1999). IBS patients also have an accelerated rate of adrenocorticotrophic hormone (ACTH) secretion in response to CRH (Fukudo et al., 1998). These results indicate that there is an excessive response to CRH stimulation in the brain and gut of IBS patients. Moreover, levels of cortisol – a component of the HPA axis – are affected by psychological stress, and can be an important index in the relationship between psychological and physiological factors related to the onset and deterioration of IBS. Regarding cortisol secreted from the adrenal fasciculata by ACTH stimulation, a previous study reported that individuals with IBS had an increased cortisol response

* Corresponding author at: Tokyo Metropolitan Institute of Medical Science, 2-1-6 Kamikitazawa, Setagaya-ku, Tokyo 156-8506, Japan. Tel./fax: +81 3 6834 2390.

E-mail address: nagisa618@gmail.com (N. Sugaya).

under CRH stimulation (Dinan et al., 2006), while another study reported that there was no difference in cortisol secretion between IBS and control individuals (Fukudo et al., 1998). It has been suggested that there is no significant difference in the cortisol response to psychological stress in cases of IBS (Elsenbruch et al., 2001; Elsenbruch et al., 2006; Posserud et al., 2004). As shown by these examples, the results of previous studies on cortisol levels in IBS patients are inconsistent.

From the results of previous studies, Mayer and Collins (2002) suggested that complex interrelationships exist between gut-associated immune tissues, the central nervous system, and the enteric nervous system. Psychosocial stressors activate stress circuits within the emotional motor system, and the resulting peripheral output manifests in the form of cortisol, corticotropin-releasing factor, and autonomic responses. These induce the mucosal immune system to activate a Th2 response (Chrousos, 2000; Elenkov and Chrousos, 1999). Mast cell numbers were increased by alterations in the Th1/Th2 balance, and degranulated in the gut during the response to psychological stress (MacQueen et al., 1989; Santos et al., 1998). Mast cell degranulation products released in the gut (such as proteases or histamine) have the potential to activate and/or sensitize visceral afferent fibers (Vergnolle et al., 2001).

Dehydroepiandrosterone (DHEA) may also be a useful index of the HPA axis in IBS. DHEA is the most important androgen secreted by the adrenal medulla and is a precursor for sex steroids; ACTH is thought to be the main secretagogue for DHEA. DHEA is thought to affect immunological function in a manner opposite to that of cortisol; DHEA increases Th1 cytokines (Evans et al., 2000; Norbiato et al., 1997; Roger et al., 1998). DHEA levels are also reported to increase under acute psychological stress (Izawa et al., 2008). Moreover, the cortisol/DHEA ratio was found to be an important and useful index for studying the association between adrenal hormones and psychological problems; cortisol/DHEA ratio was correlated with the negative mood induced by acute psychological stress (Izawa et al., 2008), and a high cortisol/DHEA ratio was predictive of persistent major depression (Goodyer et al., 2003). It is therefore possible that not only cortisol but also DHEA or cortisol/DHEA ratios, may be important to the pathophysiology of IBS.

The cognitive appraisal of stressors may be an appropriate psychological index relevant to the physiological background of abdominal symptoms. Anticipatory cognitive appraisals (threat, challenge, and primary appraisal) and stress more strongly predict the cortisol response to acute stress than personality or retrospective cognitive appraisals (Gaab et al., 2005). Moreover, Gaab et al. (2003) reported that group-based cognitive-behavioral stress management training reduced the challenge, the perceived threat, perceived stress, and the cortisol response, and also elevated the patient's self-concept of their competence and control expectancy under the Trier Social Stress Test (TSST) (Kirschbaum et al., 1993). These results suggest that the increase of cortisol secretion by cognitive appraisal (e.g., higher appraisal of a threat or lower perceived ability to control a stressor) may affect abdominal symptoms via the Th1/Th2 balance in individuals with IBS.

As mentioned above, evidence from previous studies suggests that the increase in cortisol secretion by psychological stress may alter the immune response related to the abdominal symptoms in IBS. However, the following aspects must be addressed: first, DHEA levels in IBS have not been well characterized. The determination of both cortisol and DHEA levels and their ratio may be useful for understanding the relationship between adrenal hormones and IBS. Moreover, DHEA is converted into DHEA-sulfate (DHEA-S) by a sulfotransferase and accumulates within a relatively short time after secretion. Therefore, DHEA-S is the major circulating form and is further converted to DHEA by a steroid sulfatase in the tissue. Previous research suggests that lower DHEA-S concentrations in plasma or serum are related to higher ratings of perceived stress (Labbate et al., 1995), severe

depressed mood (Barrett-Connor et al., 1999), trait anxiety (Diamond et al., 1989), and other factors. Moreover, the cortisol/DHEA-S ratio and DHEA-S/DHEA ratio were also reported to be associated with psychological stress or psychiatric diseases (Jeckel et al., 2010; Ritsner et al., 2007; Yanase et al., 1996). DHEA-S, cortisol/DHEA-S ratio, and DHEA-S/DHEA ratio are therefore important parameters to investigate when considering psychological influence on IBS.

Second, the specific psychological indices appropriate for observing psychophysiological correlates in IBS are not yet sufficiently understood. The effect of the cognitive appraisal of stressors on the adrenal response in IBS has not yet been assessed. The effect of cognitive therapy on IBS symptoms warrants investigation of the relationship between the cognitive appraisal of a stressor and adrenal hormones in IBS. This may have important clinical implications.

In the present study, we have therefore investigated the levels and ratios of relevant adrenal hormones and psychophysiological correlates under acute psychosocial stress in individuals with IBS. The present study focused on the following issues: First, we determined the differences in the adrenal hormone response (cortisol, DHEA, DHEA-S, cortisol:DHEA ratio, cortisol:DHEA-S ratio, and DHEA-S:DHEA ratio) to acute psychosocial stress in individuals with and without IBS. Second, we determined the characteristics of correlations between these adrenal hormones and cognitive appraisals of stressors in individuals with IBS.

2. Methods

2.1. Participants

The participants were 53 college students (male: 42, female: 11; mean age: 22.64 years). Because most of the college students were not patients nor were they taking any prescription medication, as opposed to patients, studies in non-patients may be suitable for correctly evaluating characteristics of adrenal hormone levels. All of the participants were non-smokers. None of the participants had been diagnosed with a psychiatric disorder or had been prescribed any medications that affect the HPA axis. All female participants were investigated for several days before and 7 days after the start of menstruation (the late luteal and follicular first phases) in order to minimize the influence of sex hormones on HPA and autonomic nervous activities. Written informed consent was obtained, and the study was approved by the university's Ethical Committee.

2.2. Measures

2.2.1. Questionnaire prior to the experiment

2.2.1.1. Rome II modular questionnaire (only items related to IBS), Japanese version (Drossman et al., 2000; Shinozaki et al., 2006). The Rome II diagnostic criteria for gastrointestinal disorders are widely used to define IBS. Using the Rome II modular questionnaire (RMQ), the presence of IBS was determined if participants had abdominal pain or discomfort during at least 3 weeks (at least once per week) out of the previous 3 months and had 2 of the 3 following symptoms: [1] pain or discomfort that improves or stops after a bowel movement, [2] a change in the number of bowel movements when the pain or discomfort starts, and [3] either softer or harder stools than usual when the pain or discomfort starts. Participants meeting the above criteria and not reporting red-flag items (refer to later description) were assigned to the IBS group, and the others were assigned to control groups

2.2.1.2. Red-flag items. Seven red-flag items, based on the guidelines for IBS of the American Gastroenterological Association, were used to distinguish organic from functional gastrointestinal diseases.

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