Assessment and Treatment of Eating Disorders

Kazuhiro YOSHIUCHI1, Hisashi YAMADA2, Shu TAKAKURA3, Masanori ISOBÉ4, Koutatsu MARUYAMA5 and Toshihiko NAGATA6

1Department of Stress Sciences and Psychosomatic Medicine, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
2Department of Neuropsychiatry, Hyogo Medical University, Hyogo, Japan
3Department of Psychosomatic Medicine, Kyushu University Hospital, Fukuoka, Japan
4Department of Psychiatry, Kyoto University Hospital, Kyoto, Japan
5Laboratory of Community Health and Nutrition, Department of Bioscience, Graduate School of Agriculture, Ehime University, Ehime, Japan
6Mental Health Clinic of Dr. Nagata in Nanba, Osaka, Japan

Summary Eating disorders are serious psychiatric conditions in terms of chronicity and have the highest mortality rate among psychiatric disorders. The assessment and treatment of eating disorders are also challenging, due to patients’ denial of their illness and reluctance for change. Despite a large number of previous assessment and treatment studies, new strategies to overcome these difficulties are still needed. This study casts light on four aspects; involvement of the brain’s reward system, stages of change in relation to motivation, refeeding syndrome during renutrition, and gut microbiota changes relating to chronicity. Further studies relating to these aspects are encouraged.

Key Words anorexia nervosa, bulimia nervosa, reward system, stage of change, refeeding syndrome, gut microbiota

Eating disorders are serious psychiatric conditions that present with distinguishing psychological symptoms, as well as severe physical impairment. Eating disorders are mainly categorized into two conditions: anorexia nervosa and bulimia nervosa. Anorexia nervosa and bulimia nervosa share core symptomatology, such as a relentless pursuit for thinness and a morbid fear of obesity, but whereas patients with anorexia nervosa successfully restrict their food intake to stay underweight, patients with bulimia nervosa intermittently violate food-restricting rules with binge eating followed by purging behaviors (self-induced vomiting or laxative abuse). Eating disorder onset is usually in adolescence, and a considerable percentage of patients with eating disorders show a chronic course and have poor prognosis. Consequently, mortality rates with eating disorders are the highest among all psychiatric diseases.

This study focuses on four aspects, as new perspectives on the assessment and treatment of eating disorders: the brain’s reward system, stages of change theory as it relates to motivation, refeeding syndrome with inpatient treatment, and the gut microbiota as it relates to chronicity.

Reward system

It has been suggested that abnormalities in the reward system of the brain, which may explain patients’ clinical characteristics, are involved in symptom onset and maintenance in both anorexia nervosa and bulimia nervosa. Accordingly, not only the binge eating in bulimia nervosa, but also the restriction of food intake in anorexia nervosa, may be recognized as reward stimuli for the brain that lead to adverse behavior maintenance, and can be thought of as “behavioral addictions”. Against this background, the brain’s reward system has become a major target of research to elucidate the pathogenesis of eating disorders.

Impairment of the reward system is involved in the persistence of anorexia nervosa symptoms. Findings by structural brain imaging suggest that structural changes in brain regions involved in the reward system contribute to the pathogenesis of anorexia nervosa (1). Similarly, functional MRI studies have shown that the activity of reward system circuits in the brain of anorexia nervosa patients is distinctive, in response to presentations that may be rewarding, such as food stimuli, body image-related stimuli, and stimuli related to food intake restriction and overactivity. Furthermore, it is known that patients with anorexia nervosa, as well as those with mood and anxiety disorders, do not respond appropriately to many events that are conventionally perceived as rewarding, such as food and social interaction. On the other hand, these patients respond excessively to anorexia nervosa-related behaviors such as restricted food intake and excessive exercise. These characteristics of responses to rewarding stimuli likely contribute to the persistence of anorexia nervosa symptoms. An effect of increased responsiveness to punishing stimuli, as well as decreased responsiveness to rewarding stimuli have also been pointed out. Patients with anorexia nervosa show reward responses to weight loss behaviors and thinness-related stimuli, but strong aversions to weight gain, social situations, and financial loss. Such responses are easily influenced by context, and clarify-

E-mail: toshi@nanba-nagata.com
ing what information and stimuli patients with anorexia nervosa perceive as rewards or punishments provides not only crucial insights into their mechanisms of symptom maintenance, but also important knowledge for more effective practical support.

**Stage of change**

The treatment of eating disorders is challenging. One difficulty in the treatment of eating disorders is a high level of resistance to treatment, and high percentages of treatment dropout. One cause of treatment dropout on the part of the patient, is the issue of motivation. When introducing any treatment, it is necessary to evaluate the patient’s motivation for treatment, and to consider how best to motivate the patient for that treatment.

There are stages in any attempt to change one’s behavior in order to engage in treatment, and these are described in the Transtheoretical Model of the Stages of Change as a series of steps proposed by Prochaska and DiClemente, where people typically make progress in first thinking about, and then initiating and continuing new behaviors. These stages of change are structured in a cyclical model consisting of five steps: pre-contemplation, contemplation, preparation, action, and maintenance. Prochaska et al. showed that, in addictive behaviors, there is a relationship between these stages of change and the patient’s self-change awareness, dropout, and treatment efficacy. Such stages of change assessment have also been shown to be useful in patients with eating disorders. The stages of treatment motivation in patients with eating disorders follow five steps. First is the pre-contemplation stage, where the patient does not consider his or her eating behavior a problem, and does not think that he or she has a problem. Thus, there is no motivation to do anything about the eating behavior, nor will it improve. Second is the contemplation stage. In this stage, the person is aware that an abnormal eating behavior is a problem, and may want to do something about it. However, there are no positive attempts to change the abnormal eating behavior. The patient is torn between a desire for self-change and the desire to stay the same, and is unable to take any action. There is no strong will to change yet. Third is the preparation stage. Here there is a desire to change one’s current state, but one is not sure what will happen if that (anorexia or overeating) state stops. Factors that make it difficult to change oneself do not yet exist. Fourth is the action stage. Here there is a desire for self-change, and a show of determination, commitment, and promise to improve. The patient attempts to change his or her abnormal eating behavior, and actively seeks out a specialist on his or her own. The patient’s symptoms then show signs of improvement, but there is back and forth where the patient gets a little better, but relapses. Fifth is the persistent stage. The patient strives to maintain his or her improved status, and prevent any relapse of symptoms.

**Refeeding syndrome**

Inpatient treatment for patients with anorexia nervosa is another challenge. Refeeding syndrome (RFS) is a life-threatening complication of overzealous nutritional replenishment in the underweight patient with anorexia nervosa. Refeeding in a malnourished state is thought to serially induce hyperglycemia, hyperinsulinemia, and fluid and electrolyte shifts. It can also lead to refeeding hypophosphatemia (RH). Because phosphates are an essential component of adenosine triphosphate, RH can cause potentially fatal complications. Therefore, RH has been widely used as a criterion for assessing RFS in patients with anorexia nervosa. Risk factors for RH in patients with anorexia nervosa include lower prealbumin levels, lower body mass index (BMI), higher hemoglobin levels, older age, and higher blood urea nitrogen levels. Based on expert opinion, the NICE guidelines state that individuals with a BMI of <16 kg/m² are at risk for RFS, although the exact BMI cut-off point is not established.

Lower calorie refeeding has been previously investigated as a preventive strategy for RH. It may, however, be too conservative from the standpoint of poor weight gain. In addition, excessive low-calorie refeeding is sometimes life-threatening, and may result in hospital death. On the other hand, some experts have reported that, according to their clinical impression, low-carbohydrate diet administration in inpatients with anorexia nervosa may prevent RH occurrence.

Yamazaki et al. (3) examined the association between the ratio of carbohydrate to total energy consumption, and the occurrence of RH in inpatients with anorexia nervosa through data extracted from medical records, to identify the optimal BMI cut-off point for RH in patients with anorexia nervosa. They retrospectively reviewed medical charts of Japanese inpatients with
anorexia nervosa at the Department of Psychosomatic Medicine of the University of Tokyo Hospital. They determined the optimal BMI cut-off point for RH via receiver operating characteristic (ROC) analysis. ROC analysis was also performed, to determine the cut-off point for the percentage of carbohydrate content in diet for RH occurrence. Logistic regression analysis was then performed to assess the association between RH and the BMI cut-off point after adjusting for the propensity score, which was based on known risk factors for RH. Multivariate logistic regression analysis was also performed with RH occurrence as the dependent variable, and carbohydrate content at more than the identified cut-off point as the independent variable adjusted for RH risk factors. Logistic regression analysis was subsequently performed to assess the association between RH and the BMI cut-off point after adjusting for the propensity score, which was again based on known risk factors for RH. As a result, they identified the optimal BMI cut-off point as 12.6 kg/m². A BMI lower than the cut-off point significantly correlated with the occurrence of RH after adjusting for the propensity score. Carbohydrate content percentages higher than the cut-off point obtained from the ROC analysis were significantly correlated with the occurrence of RH, even after adjusting for variables associated with RH in univariate logistic regression analysis (age and BMI) as well as average daily calorie intake. Thus, the researchers concluded that the optimal BMI cut-off point for RH occurrence was 12.6 kg/m² in patients with anorexia nervosa. Diets with higher carbohydrate contents were associated with RH in inpatients with anorexia nervosa, even after adjusting for known risk factors. Early identification of patients who require prophylactic treatment for RH is essential, for inpatients with anorexia nervosa.

**Gut microbiota**

The treatment of patients with chronic eating disorders is challenging. With regards to psychological aspects, parental overprotection has been the only significant factor associated with longer duration of illness (>5 y) among chronic patients with anorexia nervosa. With regards to physiological aspects, although there are no significant differences in BMI, it has been observed that total protein, albumin, and potassium levels are significantly lower in patients with a longer duration of illness (>5 y) than in those with a shorter duration of illness (<5 y). In addition, it has been reported that hypoalbuminemia is observed at a high rate in patients with anorexia nervosa aged 40 y or older, suggesting that hypoalbuminemia is associated with aging. Therefore, serum albumin levels may be unsuitable for nutritional assessment, especially in younger patients with anorexia nervosa, which suggests that assessing albumin levels together with other nutritional biomarkers such as prealbumin is important.

Weight recovery is extremely important in the treatment of anorexia nervosa. Clinically, it is not uncommon for clinicians to observe poor weight regain in the early stages of nutritional recovery. Although various mechanisms, such as increased physical activity, are often assumed, definitive factors underlying poor weight regain remain unknown. In recent years, many studies have reported that the gut microbiota plays an important role in the regulation of weight regain. In other words, it is reasonable to assume a gut microbiota imbalance in patients with anorexia nervosa. Morita et al. (4) compared gut microbiota between 25 patients with anorexia nervosa and age-matched healthy women, using the Yakult Intestinal Flora-SCAN based on quantitatative RT-PCR technology targeting 16S or 23S rRNA. In the anorexia nervosa group, amounts of total bacteria (Clostridium cocoides group, C. leptum subgroup, Bacteroides fragilis, and Streptococcus) were significantly lower than those of the control group. Additionally, in a comparison of germ-free mice reconstituted with microbiota from restricting-type anorexia nervosa patients (gAN mice) and age-matched healthy control individuals (gHC mice), gAN mice had poor weight gain and showed higher levels of anxiety than their gHC mice. Furthermore, in a serum metabolomic analysis of patients with restricting subtype anorexia nervosa, amino acid levels were significantly lower than those of the healthy controls, levels of uremic toxins such as p-cresyl sulfate (PCS) were higher in the patients with restricting subtype anorexia nervosa, and serum PCS levels correlated positively with an abundance of the C. cocoides group or the C. leptum subgroup in the feces of patients, but not in those of the controls. These results suggest that “disbiosis” in some pathological conditions, such as decreased nutritional efficiency or the onset of psychiatric symptoms, are important findings to be considered in the treatment of anorexia nervosa.

**Conclusion**

The assessment and treatment of patients with eating disorders continue to be matters of the highest priority in psychiatric and psychosomatic fields. Further research is encouraged to overcome these difficulties.

**Disclosure of state of COI**

No conflicts of interest to be declared.

**REFERENCES**


