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The Application of Exposure Therapy and D-Cycloserine to the Treatment of Anorexia Nervosa: A Preliminary Trial

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Abstract

Objective—Novel approaches to the treatment of anorexia nervosa (AN) are needed. This preliminary study examined the utility and safety of an exposure therapy intervention and D-cycloserine (DCS) in a population of patients with AN.

Method—Eleven participants completed a series of 6 laboratory meals, including pre- and post-exposure test meals and four exposure sessions. Participants were randomly assigned to receive either DCS or placebo in double-blind fashion before each of the 4 exposure sessions. These results were compared to data from a previously studied group of patients who received treatment as usual.

Results—Total caloric intake increased significantly from the baseline meal session to the post-test meal session in the patients who received the exposure therapy intervention. In the comparison group, caloric intake did not increase significantly.

Conclusion—These data suggest that an exposure therapy intervention specifically focused on meal consumption may be helpful in increasing intake of a test meal.

Keywords

anorexia nervosa; exposure therapy; D-cycloserine; phobia; eating disorders

Anorexia nervosa (AN) is a serious mental illness with a chronic course and high rates of morbidity and mortality.¹ Treatment of AN can be difficult, and available randomized controlled studies of adults with AN have not yet shown substantial benefit from either psychological or pharmacological treatment modalities.^{2–5} There remains an urgent need to develop and test new, more effective treatments for this disorder.

A recently described model of AN⁶ posits that an abnormality in fear conditioning explains both the development of an irrationally intense fear of weight gain subsequent to the

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Results of this study were presented at the International Conference on Eating Disorders, June 9th, 2006, Barcelona, Spain, at the 158th meeting of the American Psychiatric Association, May 24th, 2005, Atlanta, Georgia and the 39th meeting of the Association of Cognitive and Behavioral Therapies, November 18th, 2005, Washington, D.C.

initiation of dieting behavior in AN, and the resistance of this fear to cognitive interventions. This model is supported by evidence of high rates of anxiety disorders and anxious temperaments preceding the onset of AN⁷ and possible shared additive genetic influences in anxiety and eating disorders.⁸ Moreover, many patients with AN behave as though they have a phobia of eating. Patients report anxiety specifically related to meals: anxiety in anticipation of a meal, concern about the contents of the food they eat, and fear of the effect of the food on their shape and weight. Such fears lead directly to an avoidance of food that is akin to the extreme forms of avoidance observed among individuals with specific phobias of feared objects or situations.⁹ Food intake has been quantified in a laboratory setting through eating behavior studies of patients with AN.¹⁰ A recent study by our group¹¹ found significant food avoidance among 12 inpatients with AN, tested before and after weight normalization, when the patients were presented with a test meal (strawberry yogurt shake) and allowed to consume as much or as little as they liked. Patients who were regularly eating between 850 and 1,000 kcal for lunch when it was prescribed in a behaviorally-oriented inpatient unit, with privileges contingent upon eating all their meal, ate an average of 185 kcal of the test meal, compared to 509 kcal for normal controls. Avoidance of food among patients with AN is highly maladaptive as it promotes perpetuation of the underweight state that is associated with high morbidity and mortality. Thus, if abnormal sensitivity to fear conditioning is an important component of AN, exposure therapy, which has been used effectively in the treatment of other anxiety disorders, may also be useful in ameliorating phobic avoidance behaviors in AN.

It has recently been shown that the addition of D-cycloserine (DCS), a glutamate partial agonist at the N-methyl-D-aspartate (NMDA) receptor, can augment behavioral treatment of phobic disorder. In rodents, DCS enhances learning of fear extinction, as an animal exposed to a previously feared stimulus in the presence of DCS will learn to tolerate the stimulus faster than in the absence of DCS.^{12,13} In an extension of this work to humans, Ressler et al.¹⁴ studied DCS in a clinical model of fear extinction by randomly assigning 27 patients with height phobia to receive DCS (50 or 500 mg) or placebo in conjunction with two sessions of virtual reality exposure therapy. Each of the groups receiving DCS showed greater improvement in avoidance symptoms compared to the group who received placebo. The authors suggest that DCS facilitated the extinction learning that occurs during exposure therapy, in a way similar to that in which fear extinction occurred in animals. The utility of DCS in clinical populations has been replicated in a study that demonstrated that DCS enhanced the effect of exposure therapy in patients with social phobia.¹⁵ Patients with social phobia ($N=27$) were randomly assigned to receive DCS (50 mg) or placebo prior to four exposure therapy sessions. The patients who received active medication had significantly greater decreases in their anxiety symptoms post-treatment and at 1 month follow-up.

Anxiety and phobic avoidance behaviors are central to the phenomenology of AN, yet treatments explicitly targeting the pathological aspects of fear behavior have not been developed and rigorously examined in this population. Exposure therapy modules for the treatment of bulimia nervosa have been developed^{16,17} and elements of behavior therapy have been found useful in the treatment of AN, but the specific utility of exposure therapy for AN has not been fully explored. As an initial stage in the development of exposure therapy augmented with DCS, a laboratory paradigm was used to examine the utility of this type of treatment for AN. In the current pilot study, our goal was to decrease food restriction in the laboratory through the use of an exposure therapy intervention. This intervention was augmented with DCS versus placebo, to assess the tolerability and feasibility of using DCS in this population.

METHODS

Participants

Fourteen women agreed to participate in the experiment, 11 of whom completed all study procedures. Of these 11 participants, 5 had anorexia nervosa, binge-purge subtype (AN-B/P), and 4 participants had anorexia nervosa, restricting subtype (AN-R) as defined by the Diagnostic and Statistical Manual of Mental Disorder, 4th edition, text revision¹⁸ and assessed using the Structured Clinical Interview for DSM-IV (SCID-IV).¹⁹ Two individuals had eating disorder not otherwise specified (EDNOS); these individuals met all DSM-IV diagnostic criteria for AN except for the presence of amenorrhea.²⁰ Three participants met SCID-IV criteria for comorbid psychiatric diagnoses, 1 on whom met criteria for obsessive-compulsive disorder (OCD) and posttraumatic stress disorder (PTSD); 1 for panic disorder and PTSD, and 1 for PTSD and substance abuse.

All patients were women between the ages of 18 and 45 years who were receiving treatment at the New York State Psychiatric Institute/Columbia University Medical Center in New York City as part of an inpatient or day treatment program. The treatment program is a structured, behaviorally oriented program which begins with a brief period of medical stabilization, followed by an active weight gain phase in which patients are expected to make minimum weight gains three times per week, with the goal of achieving 90% of ideal bodyweight as determined by the 1959 Metropolitan Life Tables.²¹ Privileges and behavioral incentives are contingent, in part, upon meeting weight expectations.

Exclusion criteria included psychotic disorders, active suicidal ideation, history of a seizure disorder, history of an adverse reaction to DCS, pregnancy, and abnormal liver function tests or renal insufficiency. Participants were not taking psychotropic medications (including antidepressants and benzodiazepines) for at least 2 weeks prior to participation, and at least 4 weeks prior to participation for fluoxetine, due to its longer half life. Because of symptom overlap between disorders, patients with AN often meet criteria for depressive or anxiety disorders, and subjects with these diagnoses were not excluded. All participants provided written informed consent. This study was reviewed and approved by the Institutional Review Board of the New York State Psychiatric Institute.

Test Meals

Patients completed two test meal sessions, one shortly after admission to the inpatient unit and another approximately 1 week after completing the four training meal sessions described below. The procedures were the same for both test meal sessions and were identical to those used in a previous study.¹¹ Patients consumed a standardized breakfast on the morning of the test meal, and did not consume any food or liquid, other than water, prior to the meal session 4 hours later. The test meals consisted of approximately 1500 grams (1.04 calories per gram, or approximately 1560 calories) of strawberry yogurt shake in a covered opaque container with a straw. Patients were informed that the meal consisted of a strawberry yogurt shake, but were not informed of the amount provided in the container. Tape recorded instructions before each test meal informed patients that they should eat as much of the shake as they would like, that the meal would serve as their lunch for the day, and that they should avoid touching or manipulating the container. Intake (in grams) was measured by the change in the weight of the container before and after the meal. Patients signaled completion of the meal by ringing a bell. For compliance and safety, patients were observed through a closed circuit video monitor during the meal.

Training Meals

Prior to initiation of the training sessions, patients were randomly assigned to receive DCS (50 mg orally) or placebo, which was administered in double-blind fashion before each training meal. Participants completed four training meal sessions, which began once patients entered the active weight gain phase of treatment. The training meals occurred twice-weekly on non-consecutive days.

The procedures were identical for each of the four training meal sessions. Patients were provided with their prescribed breakfast as well as any nutritional supplementation (e.g., Ensure) on the inpatient unit in the morning prior to the training meal; they then completed the training meals in place of lunch on the unit. Medication was administered approximately 3 hours prior to each training meal, for a total of 4 doses. The dosage of DCS used in this study was based on that used by Ressler et al.¹⁴ who found that 50 mg was an effective dose and that its effects did not differ from those at higher doses. Side effects were systematically assessed by a study psychiatrist. A calculation was made of the amount of shake (in calories) that each patient needed to consume for lunch based on their caloric prescription, and patients were signaled when they had consumed the amount of calories needed for lunch.

The training sessions were designed as a form of exposure therapy in which patients were repeatedly “exposed” to consuming an unfamiliar test meal (strawberry yogurt shake). A therapist was present with the patient during the meal, and the therapeutic intervention consisted of the following:

- Encouraging the patient to continue eating until the signal was given that she had consumed an adequate number of calories for lunch (“see if you can try one more sip”),
- Discussing goals of treatment and how the training meal session might assist in those goals. Specifically, patients were told that the purpose of this intervention was to confront, rather than avoid, the anxiety around eating.
- Focusing on sensations experienced during the test meal (“stay focused in the room”).

Measures

On the morning of the baseline and final test meal sessions, patients completed the Beck Depression Inventory (BDI)²² and the Beck Anxiety Inventory (BAI).²³ Before and after the test meals, patients also completed ratings on a 15 cm visual analog scale (VAS) anchored by the phrases “not at all” and “extremely” for the following: hunger, fullness, sickness, loss of control, preoccupation with food, fear of fat, anxiety, and fearfulness. Patients also indicated how much they liked what they had been eating in their VAS ratings after the test meals. Patients also completed VAS ratings for loss of control, anxiety, fearfulness, and liking of the shake after each 50 g increment during the test meals, or after a 5 minute interval if 50 g had not yet been consumed.

Before and after each of the training meal sessions, patients completed VAS ratings of loss of control, fearfulness, and anxiety. They also rated how difficult they felt the session was at the end of each training meal.

Statistical Analyses

Means and standard deviations were calculated for intake at the test meals, BDI, BAI, the pre- and post-meal VAS ratings of anxiety and fearfulness, and the post-meal ratings of liking. One-way analyses of variance (ANOVAs) of these variables were used to compare

patients with AN who received DCS with those who received placebo. Effect sizes (d) were calculated for intake and ratings in patients with AN who were randomized to DCS vs. placebo. One-way repeated-measures ANCOVAs were calculated for intake and pre- and post-meal VAS ratings of anxiety and fearfulness for the four training meals, with medication as the between-subjects factor and the value from the baseline test meal used as a covariate. For those variables on which there was no significant difference between patients receiving DCS and those receiving placebo, paired t -tests were calculated across all patients to compare changes in scores between the first and final test and training meal sessions.

All of the patients enrolled in the current study were receiving inpatient treatment. Therefore, it is possible that elements of treatment on the inpatient unit, or weight gain alone, could have affected the outcome of this study. We conducted a secondary analysis to determine whether inpatient treatment alone may have influenced intake during the final test meal session. We compared data from the current study with that of a previously published study by our group.¹¹ In that earlier study, 12 patients with AN who were receiving the same inpatient treatment as patients in the current protocol were compared with 12 normal controls. Patients participated in a baseline test meal session, identical to that used in the current study, shortly after admission to the hospital. Eleven of twelve patients completed a second meal after attaining at least 90% of ideal body weight. The controls participated in one test meal. The final test meal occurred 54.18 ± 14.48 days after the baseline meal, and outside of the usual inpatient treatment protocol, no additional interventions were provided.

All statistical calculations were performed using SPSS for Windows, version 11, and means are reported plus or minus standard deviations.

RESULTS

All of the 14 participants who were enrolled in the study completed a baseline test meal session an average of 6.9 ± 4.9 days (range 1-20 days) after admission to the hospital. One patient withdrew from the study prior to randomization and two additional patients withdrew after randomization, one after completing the first training meal, and the second after completing two training meals. Thus, 11 of 14 patients completed all portions of the study. Data from these patients are presented below. There were no statistically significant differences between completers and non-completers.

Of the 11 patients who completed the study, 9 participants were Caucasian and 2 were African American. The mean time between test meals was 27.8 ± 5.8 days (range 21-37). The means, standard deviations, and ranges for the demographic characteristics (age, duration of illness, body mass index [BMI]), psychological measures (BDI and BAI), and VAS ratings at the first (baseline) test meal and final (end of study) test meal are presented in Table 1.

There were two statistically significant differences in VAS ratings after the baseline test meal between patients assigned to receive DCS and patients assigned to receive placebo, before any medication had been administered. Patients assigned to DCS had significantly lower post-meal VAS scores for anxiety (9.73 ± 4.66 vs. 13.96 ± 1.68 , $p = 0.05$) and loss of control (6.25 ± 6.87 vs. 12.40 ± 2.49 , $p = 0.05$) than those who received placebo. A trend ($p = 0.06$) with a large effect size ($d = -1.33^{24}$) was observed for patients receiving DCS to experience a greater decrease in BDI scores from the baseline test meal to the final test meal (mean change in BDI = -10.67 for DCS patients vs. -2.60 for placebo patients). No other statistically significant differences were observed between the medication and placebo groups on demographic characteristics, psychological measures, or VAS ratings. None of

the patients reported side effects from the medication and no medication-related laboratory abnormalities were noted.

Figure 1 illustrates the average total meal intake (in grams) for the baseline test meal, four training meals, and final test session. As there were no differences in intake at any of the test or training meals between patients receiving DCS or placebo, the data was collapsed across medication groups. Total intake increased significantly from 163.26 g (169.79 kcal) at the baseline test meal session to 428.02 g (445.14 kcal) at the final test meal session [$t(10) = -4.87$, $p = 0.001$]. A bivariate correlation was calculated between the change in intake from the baseline to final test meal session and initial baseline BMI. There was a trend ($r = 0.589$, $p = 0.06$) for patients who had a lower BMI at the baseline test meal to show less of a change in intake from the baseline to final test meal. There was a trend toward significance in change in VAS report of “liking” of the shake, so that patients reported liking the shake less after the final test meal than after the baseline meal ($t(10) = 2.056$, $p = 0.07$). Subgroup analyses revealed no difference in intake by subtype ($n = 4$ restricting subtype, 5 binge/purge subtype) or presence of comorbid anxiety disorders ($n = 3$).

The increase in total intake from the first training session (626.16 g/651.21 kcal) to the fourth training session (742.10 g/771.78 kcal) was not significant [$F(1, 8) = 0.852$, $p = \text{NS}$], and there was no effect of the medication on intake during the training meals [$F(1, 8) = 0.015$, $p = \text{NS}$]. On average, patients consumed approximately 89.1% of the calories they needed for lunch at the first training meal and 92.1% of their prescribed calories at the fourth training session.

Figure 2 depicts the average VAS ratings for anxiety and fearfulness before and after each of the four training meals. Pre-meal anxiety was 9.67 ± 4.79 at the first training meal and 6.93 ± 4.54 at the fourth training session. Pre-meal fearfulness was 8.76 ± 4.63 at the first training meal versus 5.47 ± 4.03 at the fourth training session. There were no significant effects of the medication on pre-meal anxiety or fearfulness from the first to the fourth training meal, and paired t-tests collapsed across medication groups also did not find a significant decrease in pre-meal anxiety [$t(10) = 1.30$, $p = \text{NS}$] or fearfulness [$t(10) = 1.43$, $p = \text{NS}$]. Post-meal anxiety was 9.28 ± 5.06 at the first training meal versus 8.30 ± 3.94 at the fourth training session, and post-meal fearfulness decreased from 9.40 ± 4.08 at the first training meal to 6.02 ± 5.17 at the fourth training session. There were no significant effects of the medication on post-meal anxiety or fearfulness from the first to the fourth training meal. Paired t-tests collapsed across medication groups found a significant decrease in post-meal fearfulness [$t(10) = 2.53$, $p = 0.03$] but not post-meal anxiety [$t(10) = 0.251$, $p = \text{NS}$].

Figure 3 depicts the change in test meal intake from the baseline to the final test meal for the participants in this study, compared with the participants in the previous meal study.¹¹ After receiving 4 sessions of an exposure intervention in the current study, patients with AN increased their total intake from the baseline to the final test meal (**i.e., delta intake for each participant**) by **an average of 242.28 ± 165.04 grams**, while the comparison group increased their consumption from the baseline to the final test meal by an average of 65.60 ± 192.36 grams. The increase in intake in the comparison group was not statistically significant, although patients' weights increased substantially, with an average gain of 26.80 ± 10.60 pounds (range of 12.5–46.0 pounds) from the beginning to the end of the study. Total meal intake of patients with AN in the comparison group, both before and after weight restoration, was significantly less than that of normal controls.

DISCUSSION

In this pilot study, there was a significant increase in caloric intake in a test meal following four training meal sessions, which provides “proof of principle” that food exposure therapy may be a useful approach to the treatment of AN. These findings build on similar efforts to treat patients with AN using exposure-based approaches. Bergh et al.²⁵ trained patients with AN ($n = 10$) and bulimia nervosa (BN) ($n = 4$) to eat at a normal rate using computerized feedback, and found that patients improved in weight and psychological measures after receiving the intervention in comparison to a waitlist control group. However, this study involved several interventions in addition to the exposure-like sessions, including intensive behavioral inpatient treatment and the medication cisapride, making it difficult to determine the specific contribution of the feedback sessions. A pilot investigation of exposure for inpatients with AN found that a form of exposure therapy for body image produced a significant effect on anxiety related to body image.²⁶ Finally, one case report described exposure to high fat foods in an underweight male patient with AN,²⁷ with the intervention resulting in a subsequent decrease in reported anxiety and increased variety in the patient’s diet. These three studies and the current study were all small and their approaches varied, but collectively they serve as a consistent body of preliminary data that support a role for exposure therapy in the treatment of AN.

The data from this study suggest that the exposure intervention helped patients with AN increase their consumption from baseline to the final test meal. Although the patients were receiving concurrent inpatient treatment at the time of participation, comparison with the data from a previous study done by our group (Figure 3) indicates that inpatient treatment and/or weight gain alone is unlikely to account for the increase in intake observed in this study. Patients with AN in the comparison group did not receive the exposure intervention and did not show a **statistically significant** increase in intake from baseline to the final test meal session in spite of an average inpatient treatment duration between the two meals that was almost twice as long as that in the current study (54.2 days vs. 27.8 days) and a greater amount of weight gained (26.8 pounds vs. 12.8 pounds) between the two test meal sessions. Multiple factors have been shown to have an impact on food intake in people without eating disorders, including familiarity and palatability.^{28,29} Patients in this study reported liking the shake less after the final test meal; therefore, palatability is not a likely explanation for the increase in intake.

The absence of adverse events with DCS in this study was reassuring; however, DCS did not demonstrate any significant enhancing effect in this small study. However, our ability to detect a statistically significant effect of DCS was limited by the small sample size and possibly by the fact that participants assigned to receive DCS had significantly lower VAS scores on post-meal anxiety than those assigned to placebo at the baseline meal. In the study of DCS in the treatment of height phobia,¹⁴ only two exposure sessions were used, compared with the usual exposure therapy standard of 7 to 8 sessions. This “suboptimal dose” presumably allowed for detection of a medication effect that might otherwise have been masked by the effects of behavior therapy. It is notable that in the current study, subjects were able to consume approximately the amount needed for lunch during the training meals. Thus, it may be that any effect of medication during the training meals was masked. In that vein, the mean consumed in the final test meal was $445 \text{ kcal} \pm 175 \text{ kcal}$. While this amount is less than the amount consumed in the training meals, and less than the amount prescribed for lunch on the inpatient unit, it approaches the mean intake for controls reported in the eating behavior study by Sysko et al.¹¹ This raises the possibility that the intake in the test meal was sufficiently increased by the exposure intervention to obscure any effect of medication. No participant reported medication side effects, and no medication-

related laboratory abnormalities were detected, providing preliminary support for the safety of this medication in patients with AN.

The potential for exposure therapy as an adjunct in the treatment of AN is promising, but needs to be considered in the light of several limitations of the present study. The patients in the current study and the earlier study of Sysko et al.¹¹ were enrolled separately. Thus, caution is needed in drawing conclusions about the effectiveness of the exposure intervention based on this comparison group. On the other hand, both groups of patients were recruited in the same manner, were cared for on the inpatient unit using the same treatment protocol, and completed two identical test meal sessions.

In this study, the exposure intervention used several principles of standard exposure treatment, including following anxiety ratings during the session and assisting patients in tolerating moderate levels of anxiety. However, the food exposure therapy intervention warrants further development. Over the course of the four training sessions, patients' self-reported anxiety decreased; however, there was no statistically significant difference in VAS pre- or post-meal anxiety between the first and fourth training meal sessions. Unfortunately, anxiety and fearfulness appeared to increase between the final training session and the final test meal, suggesting that any decreases that occurred over the course of training did not generalize to the test meal and highlighting the need to refine the exposure intervention. The process of conducting this study suggested some particular areas to address in future investigations of exposure and/or D-cycloserine for the treatment of individuals with AN. Participants with AN enrolled in this study used numerous cognitive strategies to avoid anxiety while eating, suggesting that a refined exposure intervention should focus more on helping patients decrease avoidance during the training meal sessions. Further, although studies using D-cycloserine and exposure therapy for anxiety disorders are typically short in duration (2-4 sessions), a brief interventions for AN may not yield similar effects because the disorder is much more difficult to treat than either height phobia or social phobia.^{14,15} Thus, future studies could consider extending the length of the treatment or increasing the intensity of the exposure intervention. Additionally, an a priori power analysis should be conducted to determine the size of the sample needed to evaluate the effect of the intervention or the D-cycloserine on eating behavior and anxiety among patients with AN based on the improvements observed in the current study.

Several additional methodological limitations in the current study should be noted. The range in BMI among patients completing the protocol was wide, and there was a suggestion that patients beginning the protocol at lower weights exhibited smaller changes in intake. Also, the exposure training and testing occurred during the weight gain phase of the inpatient treatment program, a context in which there are complex incentives to motivate intake during meals. Thus, it may be useful to examine the effect of exposure treatment in patients at a more uniform level of BMI and at a stage of treatment when fewer behavioral incentives are present.

In conclusion, this study suggests that food avoidance in patients with AN, akin to phobic behavior, can be mitigated by an exposure therapy intervention, yielding an increase in food intake. Future research should include a larger sample of weight-restored patients with AN using a more robust exposure therapy intervention, and comparing exposure therapy to a control intervention in order to further investigate the potential value of exposure therapy and DCS in enhancing or accelerating the extinction of eating-related phobic avoidance behaviors.

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Figure 1. Total Intake During Test and Training Meals (n=11)

Figure 2. Mean Pre- and Post -Meal VAS Ratings of Anxiety and Fearfulness (n=11)

Figure 3. Intake at the Baseline and Final Test Meals for Patients with Anorexia Receiving an Exposure Intervention (N = 11), Patients with Anorexia Receiving Treatment as Usual (N = 11),¹¹ and Individuals Without an Eating Disorder (N = 12)¹¹

Table 1
Demographic Characteristics, Psychological Measures, and VAS ratings at the First (Baseline) Test Meal and Final (End of Study) Test Meal for Patients with AN Completing the Study (N = 11)

	Baseline	End of Study
	Mean $\pm$ SD (Range)	Mean $\pm$ SD (Range)
Age (years)	27.0 $\pm$ 7.4 (19.0-39.0)	---
Duration of Illness (years)	8.4 $\pm$ 6.1 (1.0-22.0)	---
Body Mass Index (kg/m ²)	16.5 $\pm$ 1.4 (14.3-18.6)	18.7 $\pm$ 1.1 (17.1-20.2)
Beck Depression Inventory	22.9 $\pm$ 10.6 (10.0-40.0)	15.8 $\pm$ 7.6 (3.0-30.0)
Beck Anxiety Inventory	18.8 $\pm$ 12.4 (0.0-40.0)	14.6 $\pm$ 7.5 (4.0-26.0)
VAS Pre-Meal Anxiety	10.4 $\pm$ 4.0 (3.8-14.9)	9.2 $\pm$ 4.1 (3.4-15.0)
VAS Post-Meal Anxiety	11.5 $\pm$ 4.0 (3.6-15.0)	10.9 $\pm$ 3.1 (4.2-15.0)
VAS Pre-Meal Fearfulness	8.6 $\pm$ 4.7 (0.6-14.9)	7.9 $\pm$ 4.3 (1.2-12.9)
VAS Post-Meal Fearfulness	9.3 $\pm$ 4.9 (1.1-15.0)	10.1 $\pm$ 3.7 (3.2-15.0)

Note. SD = standard deviation. VAS = visual analog scale