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Special Issue: Eating disorders

Cover image: "Lost Soul" – painting by Prof. Yael Latzer during special session with eating disorders patients

Editorial: New Horizons in the Classification, Biology and Management of Eating Disorders

INTRODUCTION

Over the past decade there has been a significant change in the mix of people seeking help in eating disorders (ED) centers in Israel. Populations that were previously relatively protected and observed with reduced morbidity joined the circle of patients. The penetration of Western culture into traditional cultures of minorities such as ultraorthodox religious Jews, Arabs, Bedouin and Druze has led to an increase in ED-related morbidity in these minorities, as has been observed in similar places in the world. The spread of EDs to new immigrants from Ethiopia and Russia resembles similar processes in other immigrant populations elsewhere. The recent increase in young female patients suffering from active EDs and getting pregnant is another challenge. These young women often lack adaptive coping strategies during pregnancy and, after the delivery, potentially showing worsening of their ED, alongside considerable difficulties in their experience of motherhood.

Nonetheless, major difficulties may be encountered in the study of EDs, first and foremost in the establishment of the diagnosis. As is the case with the general psychiatric taxonomy, the diagnosis of EDs is based mainly on subjective clinical symptoms reported the patients, who often may deny and hide their symptoms, and there are only a few objective signs (e.g., measured reduction in weight) that can confirm it. Second, the criteria of ED diagnoses have changed dramatically along the different versions of the DSM. Last, ED diagnoses are unstable over time, and patients may shift from one diagnostic entity to another, particularly from restrictive to binge/purge EDs. All these intricacies make the study of the clinical course and the treatment of EDs highly complex and challenging.

DSM-5: FROM EVOLUTION TO REVOLUTION

Major changes in the diagnosis of EDs have occurred with the publication of the new version of the DSM-5 (2013). Thus, the task force working on the diagnostic criteria of EDs has created an entirely new diagnostic entity, the avoidant/restrictive food intake disorder (ARFID), to describe restrictive childhood EDs that do not include symptoms of wanting to lose weight or body image disturbances characterizing the "classical" EDs. The ARFID diagnosis has replaced the DSM-IV "feeding disorder of infancy or early childhood," restricted to children six years of age or younger only. ARFID has no age limitations and can theoretically be applied also to adolescent and adult populations.

Nonetheless, the most important change from the DSM-IV to the DSM-5 is the reshaping of the DSM-IV waste basket category of eating disorder not otherwise specified (EDNOS), including up to 50% of all ED patients, and transforming it into two major specific diagnoses. One is the other specified feeding or eating disorder (OSFED), including ED patients who do not fit in the main clinical diagnoses, but who can be classified to subthreshold AN, BN and BED. The other is formation of new specific diagnoses such as binge-eating disorder (BED; patients who binge but do not purge, a provisional diagnosis in the DSM-IV), purging disorder (PD; normal weight patients who purge but do not binge), and night eating syndrome (NES; normal-weight patients whose ED symptoms occur in the late evening or at night). A relatively small waste basket diagnosis, the unspecified feeding or eating disorder, replaces the much larger DSM-IV EDNOS.

The recent change in the diagnostic criteria of EDs from the DSM-IV to the DSM-5 has resulted in a major change in the diagnostic criteria of AN. In the previous DSM editions (DSM-3, DSM-3R and DSM-IV), a precise reduction in weight has been specified (i.e., reduction of 75% of required weight in the DSM-3/DSM-3R, and 85% in the DSM-IV). By contrast, in the DSM-5, a clinically significant reduction in weight is sufficient (the increase from 75% to 85% of required weight has been found to have no effect on outcome). In addition, behaviors interfering with weight gain despite objective low weight suffice for another diagnostic criterion of AN, taking into consideration that these patients may often deny or hide their fear of gaining weight. Last, the amenorrhea criterion has been removed in the DSM-5 because in recent years a considerable proportion of patients may

develop AN before menarche, showing that the presence of amenorrhea does not largely affect outcome.

These changes have transitioned patients belonging in the DSM-IV to the NOS category to being diagnosed as AN in the DSM-5. As treatment is mainly investigated with respect to specific diagnoses, such a shift may have a favorable effect on the prognosis of the ED. Not surprisingly, these diagnostic changes have been accompanied by concomitant changes in the rates of several EDs in epidemiologic studies. Thus, the recent increase (1) in the rate of AN, alongside a concomitant decrease in the rate of EDNOS is associated, at least in part, with the broadening of the diagnostic criteria of AN from the DSM-IV to the DSM-5. This primary evidence supports the success in the aim of the DSM-5 task force to reduce and minimize the size of non-specific ED categories.

ATTEMPTS TO IMPROVE OUTCOME AND TREATMENT

AN is the most severe clinical entity in the ED category. Over the years, many attempts have been made to plan treatment protocols that would increase the chances for recovery and reduce the risk of mortality and chronicity. An illness staging model for AN seeking to find the right treatment along the developmental continuum of the illness has received increased attention in recent years. The overall concept is that psychiatric illnesses, including EDs, may follow a trajectory across the life course. High risk markers and prodromal features may already be present in childhood and adolescence. Partial subsyndromal disorders may develop during adolescence and can later transition to the full manifestation of the illness in early adulthood. Over time, the illness may become severe and enduring, resistant to treatment and associated with significant physical and psychiatric co-morbidity.

The use of the empirical Clinician Administered Staging Instrument for Anorexia Nervosa (CASIAN) has been recently found significantly to distinguish between earlier and milder clinical stages of AN vs. more severe and enduring stages of the illness. There is, however, currently only a preliminary support for a staging model in AN. Larger longitudinal studies with longer follow-up periods from the premorbid stage to recovery or chronicity are needed to evaluate the overall utility of the staging model in EDs (2).

Nonetheless, the staging model may have a specific importance in the study of severe and enduring (chronic) AN. The pattern of symptoms in the early phases of the illness (e.g., fasting, bingeing and/or purging) and the nutritional sequelae associated with protracted starvation may impact on brain plasticity and neuroadaptation in later stages. There is still uncertainty about how to manage patients with severe and enduring AN. A consensus, though, is emerging toward changing treatment priorities. Accordingly, obtaining the best quality of life for patients with severe and enduring AN and their families and minimizing discomfort may be prioritized to achieving significant restoration of weight and eating behaviors.

Last, severity specifiers were added in the DSM-5 to AN, BN and BED. Specifying the severity of the ED may have great impact on medical decisions and treatment priorities and facilities. Recent studies show limited support for the DSM-5 severity specifiers for BN and modest support for the DSM-5 severity specifiers for AN and BED (3-5). To conclude, the DSM-5 version seems to be a better diagnostic system for EDs than the earlier DSM editions, although the real test awaits its durability over time

THE ROLE OF DIETING IN PSYCHIATRY

A growing body of evidence suggests that the human diet is an important contributing factor in the development, management and prevention of several psychiatric illnesses. Tryptophan, an essential amino acid, is the sole precursor of 5-hydroxytryptamine (5-HT; serotonin). Administration of tryptophan can boost serotonin neurotransmission to produce therapeutically important effects in serotonin deficiency disorders, for example depression. Evidence suggests that excessive dieting and food restriction can decrease brain tryptophan and serotonin in patients with AN to precipitate depression, psychosis and hyperactivity.

NEUROIMAGING, NEUROMODULATORS AND NEUROSTIMULATION IN EATING DISORDERS

Anatomical and functional neuroimaging research in EDs has recently gained considerable momentum. Although important structural magnetic resonance imaging studies have been carried out in recent years, there are still no definite conclusions about the exact brain areas involved in ED-related pathology.

New functional MRI (fMRI) studies investigate network alterations potentially shared across different ED types. Findings on reward processing across both AN and BN point to the presence of altered sensitivity to salient food stimuli in striatal regions, and to the possibility of hypothalamic inputs being overridden by top-down cognitive control regions. Nevertheless, findings from functional network connectivity studies are still equivocal (6).

While the number of brain imaging studies in EDs has dramatically increased, there has been recent criticism that many of these studies have been too lenient in the control of statistical thresholds. Another major problem in human brain imaging research, including in the field of EDs, is the poor reproducibility of the results. It has been suggested recently that important factors should be considered when grouping together patients with EDs in neuroimaging studies to refine the findings. These include the development history, demographic details, illness condition, and effects of exercise, hydration, binge/purge behavior, malnutrition, hormone levels, psychiatric comorbidity and use of medications (7).

Whereas multimodal treatment is still considered the main approach for the management of patients with EDs, advances in etiological research call for the development of more targeted, brain-focused treatments. A range of neuro-stimulation approaches, most prominently repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS) and deep brain stimulation (DBS), are rapidly emerging as potential novel interventions for refractory patients. Indeed, new basic science research has looked for novel approaches to stimulate target areas in the brain that might be connected to EDs. Thus, investigation of DBS in the rat brain suggests that low-frequency prelimbic cortex stimulation might be useful for correcting prefrontal hypofunction, likely associated with bingeing and ED- and non-ED related addiction pathogenesis (8).

Additionally, brain circuits hypothesized to drive AN symptoms can be accessed using DBS. Initial results suggest that DBS of the subcallosal cingulate is safe, potentially associated with improvement in mood and anxiety. In patients with treatment-refractory AN, DBS has been found to be well tolerated and associated with significant and sustained improvement in affective symptoms, body mass index (BMI), and changes in neural circuitry, at 12 months post-treatment (9).

A meta-analysis of a total of 32 studies (526 participants) of brain stimulation was published recently (10). Whereas the findings are somewhat mixed for BN, neuro-stimulation techniques have shown favorable potential in the treatment of other EDs, in terms of reduction of ED and associated symptoms. Studies exploring cognitive, neural and hormonal correlates of these techniques have also been appearing recently. Nonetheless, despite the promise of neuro-stimulation approaches as potential treatment for EDs, large, well-conducted randomized controlled trials are required to assess treatment targets, stimulation parameters and mechanisms of action (10).

In contrast to DBS, rTMS is a less invasive technique, with less associated risk, and thus has greater potential to become a more widespread augmentation or add-on therapy for patients with refractory AN. The improvement of core ED symptoms with rTMS, however, is as yet only modest and limited (11). As the CNS-related pathophysiology of AN is still unclear, and since brain reactivity can be diminished overtime because of prolonged starvation, it is challenging to find the stimulation target area(s) and stimulation parameters proven beneficial for patients with severe and enduring AN.

NEW MEDICATIONS IN THE TREATMENT OF EATING DISORDERS

Drug therapy is a major component of integrated treatment for patients with EDs. Despite the extensive use of medications in these patients treatment options are relatively few, and limited mainly to symptomatic alleviation.

NEW MEDICATIONS IN ANOREXIA NERVOSA

There are currently no FDA approved pharmacological treatments for AN. In addition, APA and NICE guidelines state that currently there is a very limited evidence base for any pharmacological treatment in AN.

Antidepressant and antipsychotic medications are used in patients with AN mainly to treat associated psychiatric comorbidities such as depression, anxiety and obsessionality, and are not effective in increasing the patients' weight. This is despite the obesogenic effect of these medications in other psychiatric disorders. SSRIs may be ineffective in acutely-ill AN patients because of reduced absorption of tryptophan, the precursor of serotonin, compared to other essential amino acids, in malnourished conditions. Along these lines, tryptophan supplementation may enhance the therapeutic effect of SSRIs in AN patients (12). Last, some studies, although not all, suggest that antidepressants may reduce the risk of relapse in recovered weight-restored patients with AN.

The use of the atypical antipsychotic medication Olanzapine, a dopamine (D2), serotonin (5-HT2) and histamine antagonist, is associated with significant weight increase owing to its dopamine, serotonin and histamine blocking effects. This has led to the investigation of its weight enhancing effects in AN. Indeed, several open studies and four randomized control studies conducted in the past decade found that, in comparison to placebo, the use of Olanzapine may increase weight and reduce the severity of ED-related and obsessional symptomatology, anxiety and depression.

Lately, a randomized, double-blind, placebo-controlled design assessed the effect of the ghrelin agonist Relamorelin in AN. Indeed, treatment with a ghrelin agonist, significantly decreasing gastric emptying time, has been found to lead to a trend in weight gain after four weeks (13).

Additionally, since dopamine D2 receptor agonists may reduce anxiety, improve perceptual distortion, and increase appetite and weight gain, they may have a role in the treatment of AN. Thus, the use of the D2 receptor partial agonist Aripiprazole in patients with AN has been associated with an increase in BMI. Current knowledge is limited, though, and the effect of Aripiprazole in AN awaits further investigation (14).

Last, the endocannabinoid system may influence feeding behavior by acting on circuits located in the hypothalamus, on reward systems regulating and controlling feeding behavior by inducing pleasurable effects, and on the brain stem. Thus, the overall effect of the endocannabinoid tetra-hydro-cannabinol (THC) is anabolic, owing to an overall enhancement of food consumption. THC derivatives are FDA-approved for inducing appetite in cancer and HIV patients. Moreover, the cannabinoid receptor-1 antagonist Rimonabant has been studied for weight reduction in complicated obesity (although being associated with weight reduction, it had to be stopped because of significant adverse effects).

These findings have led to the investigation of the potential of THC to increase weight in patients with AN. However, two small scales studies have not found increase in weight in AN patients treated with THC vs. placebo/other medications. The patients treated in these studies, on the other hand, were chronic, perhaps resistant to any treatment. By contrast, Drobnabinol, a synthetic form of THC, showed greater weight gain vs. placebo in 25 patients with AN.

NEW MEDICATIONS IN BULIMIA NERVOSA AND BINGE EATING DISORDER

The use of Methylphenidate (MPH), particularly its long acting compounds, has been found useful in reducing bingeing behavior in case reports of patients with concomitant BN/BED and attention deficit hyperactivity disorder (ADHD). The rationale of MPH treatment in these patients is related to its potential to regulate reward-related activity, to reduce hyperactivity, impulsivity, affective instability, reactivity to food and stress, and obsessionality, and to enhance the organization of maladaptive eating behaviors. Nonetheless, the use of MPH in these patients has not been FDA approved yet, and is limited to BN/BED patients not responding to other treatments.

In 2015, McElroy and her associates published the first study showing the positive effect of another psychostimulant, Lisdexamfetamine, in reducing bingeing behavior in patients with BED (15). In later clinical trials, Lisdexamfetamine demonstrated statistical and clinical superiority over placebo in reducing binge eating (16, 17). These findings led the FDA to approve the use Lisdexamfetamine in the treatment of moderate to severe BED.

Altogether these studies suggest that although there are promising preliminary findings in EDs with the use of several new medications working on new mechanisms, their efficacy is mostly modest and limited. Future large-scale multicenter studies are required to support the effectiveness of these medications in the treatment of EDs and establish their indications and long-term safety.

THE CURRENT ISSUE

The aim of the current issue, the first of two publications, is to deepen our knowledge and broaden our understanding about clinical and biological aspects of EDs, to improve diagnostic methodology and to develop innovative treatments. We hereby present the summary of the seven studies included in this issue.

In the first study, Kreitler concludes that eating habits characterized by deviances from the common eating behaviors in one's family and culture that are not concerned with weight and physical appearance are not akin to classical EDs, but rather represent an independent manifestation of disordered eating

In the second study, Zohar and her associates show that the Hebrew translation of the Eating Disorders Examination Questionnaire (EDE-Q), the golden screening tool for EDs, has adequate structural validity, convergent validity, and screening properties and can safely be used in Israeli ED populations.

In the third study, Zohar and her associates show that the Hebrew translation of the Dresdner Körperbildfragebogen (DKB-35), a comprehensive self-report measure of the relationship with the body, has adequate structural validity, convergent validity, and screening properties, and can be used in the assessment of attitudes toward the body in Israeli patients with EDs.

In the fourth article, Hetman and her associates show that the percentage of the discharge weight relative to the recommended weight following inpatient treatment

may predict re-hospitalization in adolescents with AN. Accordingly, the recommendation to discharge adolescents with AN close to their recommended weight is of merit in reducing the risk for re-hospitalization.

In the fifth study, Nachum and his associates show that the neurocognitive search activity (SA) problem-solving ability – potentially related to the core ED-trait of ineffectiveness - is variously represented in different ED types. Thus, less adaptive SA strategies are found in acutely-ill patients with binge/purge EDs vs. controls but not in patients with restrictive-type AN (AN-R). Binge/purge, but not AN-R patients, show improvement in SA upon symptomatic stabilization.

In the sixth study, Avraham and her associates show that chronic patients with AN treated with low doses of oral Δ9-Tetrahydrocannabinol (Δ9-THC), the active compound of Cannabis Sativa with appetite-stimulating properties, show improvement in body care, ineffectiveness, asceticism and depression, but no increase in weight.

Last, in the seventh study, Israely and her associates show that adding Tyrosine, an essential amino acid that is the precursor of catecholamines to the diet of patients with AN, may shorten reaction time and test duration in memory tasks, and improve depressive mood.

We hope that the readers of the IJP will find this special issue a valuable and interesting read. We certainly do.

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Are Eccentric Eating Habits Eating Disorders?

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ABSTRACT

Background: The study deals with particular kinds of eating habits that are unusual, not focused on weight, different from eating disorders, and not pathological. They are characterized by features such as the kind, amount, manner and style of eating that deviate from the common ones in their family or culture. They would be included today under the DSM-5 categories of Avoidant restricting food intake disorder (AR-FID), and unspecified feeding or eating disorders (US-FED). The question was whether they are mild forms of eating disorders or an independent set of behaviors. The objective was to examine to which extent these atypical eating behaviors may be subsumed under the diagnostic category of eating disorders by testing their scores on the Cognitive Orientation Questionnaire of Eating Disorders (CO-ED), which is a measure of the general tendency for eating disorders.

Methods: The sample included 250 high school students (120 boys, 130 girls), 16-18 years old. They were administered the Eating Attitudes Test (EAT-26), the Eccentric Eating Habits (EEH) questionnaire and the Cognitive Orientation of Eating Disorders (CO-ED).

Results: EAT-26 and EEH were uncorrelated. High scorers on the EAT-26 scored higher than high and low scorers on EEH in several variables of the CO-ED. High and low scorers on EEH differed in most variables of the CO-ED.

Conclusions: EEH is manifestation of the general tendency for eating disorders but differs from eating disorders and may be considered as an independent manifestation of eating disorders.

INTRODUCTION

Food consumption or eating fulfils a very important role in our lives well beyond its function for survival. A great many habits and expectations grew around eating, many of which are supported by cultures, religions and specific community life (1). Some unusual eating habits have been organized in specific diets. At present there are several hundreds of diets including religious (e.g., Moslem, Buddhist, Jewish), vegetarian, medically-based, weight-control and healthy eating diets, etc. Over and beyond the particular diets adopted by many people all over the world, there are bizarre or abnormal eating habits devised and kept by particular individuals, some publicly and some rather in secrecy. Bizarre eating habits may refer to amounts of food, specific combinations of foods, narrowing down of food preferences to a highly limited number characterized by some feature (e.g., color, shape, place of origin), times of eating (e.g., only at a specific time), duration of eating (e.g., only during a certain number of seconds or minutes), conditions of eating (e.g., only when alone, or only when facing a certain direction), and swallowing and chewing abnormalities. Some of the abnormalities have earned a particular name, grazing (i.e., eating small amounts of food with short pauses), or hyperphagia (abnormally increased appetite). In the present study we chose the adjective eccentric because it has no specific clinical or judgmental connotation.

The present study deals with eating behaviors that fall short of clinical diagnosis and are yet reminiscent of disordered eating. These behaviors cannot be considered as secondary to a medical or psychiatric disorder, but contrary to eating disorders they are not intended to control weight and they do not significantly impair physical health or psychosocial functioning. Some time after conclusion of the present study, the new diagnostic categories of eating behaviors were published in the DSM-5 (2). These categories turned out to include most of the aberrant eating behaviors that have been noted and studied in the present context. Most prominent are pica, defined as eating of non-nutritive substances for a period of at least one month, with no cultural or medical support; rumination, defined as repeated regurgitation of food for a period of at least one month; avoidant/restrictive food

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intake disorder (ARFID), manifested in persistent failure to attain the required weight or energy, without a medical or explicit eating disorder basis; and unspecified feeding or eating disorder (UFED), which applies to behaviors causing distress or impaired functioning but do not meet the full criteria of any of the feeding or eating disorders.

Not much is known about unusual eating habits mainly because they have not been defined clearly enough or in a standard manner. There are no valid estimates of their frequency in the population (3). They seem to be more frequent in certain age groups (e.g., adolescents) (4) or the elderly (5), and individuals with particular diagnoses (e.g., autism, Asperger) (6, pp. 325-326).

There is disagreement about the nature and function of the deviant eating habits. In view of the many different cultural food norms and individual differences in regard to food and eating as well as the highly common tendency to diet it is admittedly difficult to differentiate between unusual eating behaviors and clinically significant eating disorders (7). Some investigators assume that unusual eating habits form a moderate kind of eating disorder on a subclinical level that is relatively frequent in adolescence and college age but tends to abate with time and growing maturity (8-11). Others assume that unusual eating habits constitute a precursor of more serious EDs (12-15). According to the first approach, follow-up is the only means that could be recommended in cases of serious disordered eating habits. In contrast, according to the second approach it is highly recommended to treat disordered eating habits even when not blatantly severe in order to prevent their development into serious clinical states of eating disorders.

Hence, it may be of benefit theoretically as well as from the viewpoint of clinical practice to examine whether tendencies for unusual eating habits are a manifestation of an underlying tendency for eating disorders. Accordingly, our hypothesis was that a high level of unusual eating habits will be related to high scores on the Cognitive Orientation Questionnaire of Eating Disorders, which is a measure of the underlying tendency for eating disorders (16). Confirmation of the hypothesis would support the assumption that unusual eating habits are a specific manifestation of a tendency toward eating disorders and may be considered as precursors or a risk factor of eating disorders.

METHOD

PARTICIPANTS

The participants were 250 high school students of both genders (130 girls, 120 boys), from three different schools in three parts of the country. The age range was 16-18 years. The mean was 16.8 (SD=0.5)

TOOLS

They were administered three questionnaires. One was the questionnaire of eccentric eating habits (EEH) (17) assessing tendencies for unusual eating habits and preferences (e.g., in regard to foods, diets, quantities). The items were collected in different groups of subjects ranging in age from 15 to 55. The original list included 95 items, of which 35 were deleted because in pretests (with two samples of high school students, with n=50, n=42) they got the score of 1 in over 20% of the responses. The EEH was validated by reports of teachers and instructors in regard to 20 respondents. The reliability of the EEH is satisfactory (Cronbach's alpha=.78).

The EEH consists of a list of 60 items to which the respondent is requested to respond by checking one of the following response alternatives: never, rarely, sometimes, often, scored as 1 to 4. The sum of the responses yielded a total score ranging from 60 to 240. The items of the EEH are listed in Supplement 1. A factor analysis of the EEH yielded three factors which were labelled characteristics of the kind of food, characteristics of food preparation and presentation, and external conditions of eating which accounted for 31%, 22% and % of the variance, respectively.

The second questionnaire was the Eating Attitudes Test (EAT-26) (18), which is a widely used screening measure of eating attitudes and concerns that may be indicative of eating disorder risk, as has been shown in regard to high school students (19). The EAT-26 has been shown to be a reliable and valid instrument in Hebrew (20). In the present study its reliability was in the acceptable range (Cronbach's alpha=.87). It includes 26 items, each with four response alternatives (often, sometimes, rarely, never), referring to three scales: Diet Scale assessing attention to calories ingested and burned doing physical exercise, desire to be thin, sense of guilt after eating; Bulimia Factor which is scale of bulimia and concern about food; and Oral Control which assesses food intake mode and its control. The EAT-26 was used mainly for identifying participants at high risk for eating disorders (the cut-off point of above 20 was used for this purpose).

The third questionnaire was the Cognitive Orientation Questionnaire of eating disorders (CO-ED) (16) that assesses the tendency towards eating disorders by means of beliefs defined in terms of formal features and contents.

The CO-ED was constructed in the framework of the cognitive orientation theory based on the assumption that

behaviors and disorders are a function of a motivational disposition, determining the directionality of behavior, and a behavioral program, determining the manner of performance of the motivational disposition (21, 22). The motivational disposition is neither conscious nor under voluntary control. It is defined by beliefs of four types – about the self, goals, norms and general beliefs – referring to specific themes, identified with a particular interviewing procedure, that represent meanings relevant for the particular disorder. A series of studies led to the identification of specific themes characteristic for anorexia, for bulimia, and for obesity, and enabling a significant differentiation between the groups and between each and healthy controls (23-26). Comparing the sets of themes for the three disorders (24-26, respectively) revealed 10 themes shared by all three disorders that have been suggested to constitute the "general CO-EDs core" (16).

The themes making up this "general CO-EDs core" are the following: 1) Avoiding emotional expression of all kinds; 2) Avoiding negative emotions, including anger and hostility; 3) Rejecting or down-playing one's gender role, which in the case of women relates to femininity, including the roles of mother and wife; 4) Fear of death, which might be amplified by the attraction towards death; 5) Persistent guilt; 6) Concealing one's inner self, including on the one hand, concealing from others one's feelings and weaknesses, and on the other hand, blurring of one's identity and the maintaining of a façade, so that a gap may arise between the inner and external self; 7) Dissociation from one's body; 8) Withdrawal from others, manifested as the avoiding of dependence on others and as withdrawing from contacts with others; 9) Not being in control over one's life, which may be manifested as outer-directedness and/or as feeling controlled by external forces, such as other people or biological factors; 10) Absence of enjoyment, manifested as anhedonia, and as a rejection of pain and suffering coupled with a strong tendency for enjoyment in the case of obesity.

The four types of beliefs form together with the 10 themes a matrix in which the beliefs are the columns and the themes in the rows. The four types of beliefs represent the direction and strength of the motivational disposition and the themes its contents.

Accordingly, the CO-ED questionnaire includes beliefs of four types – referring to the self, goals, norms and reality (others, situations, events) in regard to 10 themes which constitute the "general CO-ED core." Each theme appears in the form of each of the four belief types. Thus, the total number of items in the CO-ED is 40. The beliefs are presented as statements followed by four response alternatives: very true, true, not true, not at all true. The following are examples of beliefs, the first referring to the self and the second to norms: "I often feel as if my body does not quite belong to me," and "One should never feel anger or envy." The CO-ED yields four scores for the belief types and 10 scores for the themes. The CO-ED has been validated in several samples and its reliability has ranged from Cronbach's alpha=.77 to .82.

PROCEDURE

All three questionnaires were administered together, in random orders for different groups of respondents, in a classroom setup. An experimenter was present in order to answer questions that the participants may have. The study was approved by the Helsinki committee of ethics. Prior to responding to the questionnaires the parents' consent for participation in the study was obtained. All students signed an informed consent form before responding to the questionnaires. The questionnaires were anonymous. Full respondents' anonymity was preserved in all phases of the study.

RESULTS

Preliminary control analyses showed that the scores of the three questionnaires (EEH, EAT-26 and CO-ED) did not differ significantly in the three schools participating in the study. Further, the mean differences between the genders were of only borderline significance (p=.08 for CO-ED and p=.07 for EAT-26, with the girls scoring higher). Therefore the data for the whole sample were analyzed together.

The correlations between EEH and EAT-26 were positive but nonsignificant for the total score (r=.07), and the diet scale (r=.10), and bulimia factor (r=.11) and only for the scale of oral control the correlation was significant (r=.14, p<.05). These findings suggest that EEH assesses tendencies that are largely independent of eating disorders as commonly defined.

Out of the whole sample, 29 subjects (11.6%) of both genders (65.5% girls, 34.5% boys) scored in the EAT-26 above 20, which is indicative of possible eating disorders. Hence, they were defined as a separate group. The remaining subjects were split into two groups in line with the median score on EEH (=125): high in EEH versus low in EEH.

Table 1 presents the results of mean comparisons by ANOVA of the three groups of subjects (high in EAT-26, high in EEH and low in EEH) on the four belief types and the 10 themes of the CO-ED. The table shows that

in regard to the four belief types the mean differences between the three groups are significant except for general beliefs in which the differences are only of marginal significance. In regard to all belief types the highest means are in the group of high EAT-26, next in the group high in EEH and lowest in the group of low EEH.

The findings relate also to mean comparisons between the pairs of groups. Concerning the group high in EAT-26 the comparisons show that the means of EAT-26 are significantly higher than the means of the group high in EEH in regard to beliefs about self and goal beliefs. Further, the means of the group high in EAT-26 are significantly higher than the means of the group low in EEH in all four belief types. These findings suggest that the group high in EAT-26 tends to have higher scores on the four belief types than the groups with EEH, particularly the group with the low scorers on EEH.

Concerning the groups high and low in EEH, the mean comparisons show that the means of the group high in EEH are significantly higher than those of the group low in EEH in three belief types (about self, norms and goals) and of borderline significance in general beliefs.

Table 1 provides information also about the 10 themes of the CO-ED. The table shows that the three groups (EAT-26 high, EEH high, EEH low) differ significantly in eight of the 10 themes (all except TH 6 and TH 8). In eight of the 10 themes the highest mean is in the group of EAT-26, followed by the group of EEH high and then by the group of EEH low (the only deviations were in TH 6 where EEH high scored higher than EAT-26 high, and TH 7 where the highest mean was in EEH low).

Mean comparisons of pairs of groups show that the group scoring high in EAT-26 differed significantly from the group high in EEH in two themes (TH 1 and TH 10) and differed significantly from the group scoring low in EEH in five themes (TH 1, TH 3, TH 4, TH 5, TH 8).

Comparison of the two EEH groups showed that EEH high scored significantly higher than EEH low in seven of the 10 themes (all except TH 7, TH 8, TH 10).

Discriminant function analysis showed that correct group identification only on the basis of the CO-ED was correct in 55% which deviates significantly from the 33% expected by chance ($z=5.29$, $p<.001$). The highest percent of correct identifications was in the group of EAT-206 scorers (92%), next in the group of high EEH scorers (65%) and lowest in the group of low EEH scorers (59%).

Table 1. *Mean comparisons of the scores of the four belief types and the 10 themes of the CO-ED questionnaire between the three groups of high scorers on the EAT 26, high scorers on EEH and low scorers on EEH*

/Gr. Var.	(a) EAT-26 High		(b) EEH High		(c) EEH Low		F Value (df=2/276	Comp. group means
	Mean	Sd	Mean	Sd.	Mean	Sd		
CO scores[a]: The four belief types								
BS	2.51	0.36	2.45	0.29	1.70	0.30	3.147*	a>c** b>c*
GB	2.63	0.37	2.37	0.45	2.10	0.24	3.026 (p=.06)	a>c** a>b*
N	2.39	0.40	2.26	0.31	1.92	0.38	3.033*	a>c** b>c"
GO	2.69	0.35	2.48	0.39	2.05	0.30	3.057*	a>c** a>b* b>c**
CO scores[b]: The 10 themes of the CO-ED								
TH 1	2.79	0.40	2.44	0.24	2.03	0.34	3.802*	a>b* b>c* a>c*
TH 2	2.26	0.47	2.13	0.57	1.89	0.31	3.035*	b>c*
TH 3	2.88	0.58	2.62	0.50	2.32	0.44	3.968*	b>c* a>c*
TH 4	2.55	0.55	2.49	0.48	2.12	0.40	4.312*	a>c** b>c**
TH 5	2.29	0.44	2.05	0.67	1.76	0.45	3.831*	b>c* a>c*
TH 6	2.62	0.41	2.63	0.57	2.14	0.57	2.641	b>c**
TH 7	2.53	0.48	2.49	0.44	2.65	0.39	4.007*	
TH 8	2.73	0.43	2.55	0.60	2.00	0.46	3.010	a>c*
TH 9	2.68	0.40	2.46	0.34	2.20	0.48	3.469*	b>c* a>b*
TH 10	2.43	0.42	2.20	0.47	2.13	0.42	2.961	a>b*

*p<.05, **p<.01

[a]BS=Beliefs about self, N=Beliefs about norms, GB=General beliefs (about others and reality), GO=Beliefs about goals.

[b]TH 1=Avoiding emotional expression; TH 2=Avoiding negative emotions; TH 3=Rejecting gender role; TH 4= Fear of death; TH 5=Persistent guilt; TH 6=Concealing inner self; TH 7=Dissociation from body; TH 8 = Dissociation from others; TH 9=No control over oneself; TH 10=Anhedonia

[c]The comparisons in the last column refer to the three groups (a=EAT 26 high, b=EEH high, c=EEH low) are based on Scheffe post hoc analysis. All comparisons significant at the <.01 level pass also the Bonferroni criteria.

DISCUSSION

The present study focused on identifying the nature of EEH by answering the question to which extent it is a manifestation of the tendency for an eating disorder. The major tool for answering the question was the CO-ED which is a validated measure of the general tendency for eating disorders. The findings show that high EEH scorers score higher than low EEH scorers on all four belief types, significantly so in the three belief types about self, norms and goals. Previous studies showed

that high scores on at least three of the belief types suffice for predicting reliably the behavior in question (23). In addition, the findings show that high EEH scorers score significantly higher than low EEH scorers on seven of the 10 themes comprising the CO-ED. The sum total of these findings suggests strongly that EEH is related to the general tendency for eating disorders as assessed in term of the CO-ED questionnaire.

However, does this set of findings indicate that EEH is an eating disorder? This conclusion is possibly challenged by the findings concerning EAT-26, which assesses risk for the standard kinds of eating disorders. One relevant finding is that EEH was found not to be correlated with EAT-26. Further, the group of high scorers on EAT-26 has been found to score higher on two types of beliefs (about self and goals) than high EEH scorers and higher than low scorers on EEH in all four belief types. Similarly, in regard to themes, the high scorers on EAT-26 scored higher than the high EEH scorers on two themes and higher than the low EEH scorers on five themes. Also the findings based on the discriminant analysis indicate that EAT-26 is related to CO-ED much closer than EEH.

There are two sets of findings that need to be considered: the one concerning the differences in CO-ED variables between the high and low scorers in EEH and the other concerning the differences in CO-ED between the high scorers on EAT-26 and the high and low scorers on EEH. One possibility for interpreting the results is that both EAT-26 and EEH are manifestations of CO-ED. Both are indicative of eating disorders of the standard type that is assessed by EAT-26, namely the three syndromes of anorexia, bulimia and obesity. The only difference between EAT-26 and EEH would be in the strength or intensity of the manifestations of eating disorders, those of the high scorers of EAT-26 being stronger than those of EEH.

Another interpretation of the two sets of findings would emphasize the possibility of a difference between EAT-26 and EEH not only or not merely in the intensity of the manifestations of CO-ED but in the kind or nature of the manifestations. Those of EAT-26 seem apparently to be the standard three major eating disorders, while those of EEH are of a completely different order. This is the reason why EAT-26 and EEH are not correlated. If this interpretation is valid, it may be carried one step further and proceed to the hypothetical claim that perhaps manifestations of the standard eating disorders require a stronger and more complete grounding in the CO-ED than EEH. This may be the reason why high scorers on EAT-26 score significantly higher than high EEH scorers and particularly low EEH scorers on the belief types and the themes.

At present with the given findings it is not very possible to underscore the correct interpretation. It may suffice to state that according to the first interpretation, EEH are a weak form of eating disorders which has the potential of developing into full-fledged eating disorders. According to the second interpretation EEH are simply a different kind of eating disorder that does not resemble the standard disorders of anorexia, bulimia and obesity and does not have the potential to develop into such full fledged disorders. Those who score high or low on EEH may simply continue to maintain those behaviors on the same or a different level of intensity.

Both interpretations of the findings rely on the construct of the general CO-ED score. This construct represents a general motivational tendency toward eating disorders without specifying the particular kind of manifestation that this tendency will assume. In the case of EEH the particular manifestation is the unusual eating disorders. On the basis of the findings of the study there is no justification to reject the conclusion that EEHs are a particular manifestation of eating disorders, autonomous in its own right similarly to anorexia, bulimia and obesity. Further, it may even be hypothesized that there could be further types of eating disorders that differ from EEH as well as the standard eating disorders. Further support for the conclusion that EEH is an eating disorder in its own right could be obtained from a study that would provide proof for the existence of particular themes within the framework of the CO approach orienting toward EEH, just as is the case in regard to the specific standard eating disorders (16). Additionally, it would be advisable to examine whether all EEHs are of the same kind or whether they differ in their manifestations and in the particular CO variables orienting toward them.

Another issue that needs further clarification relates to the findings showing that EEH scorers, both high and low, score lower than EAT-26 high scorers on several of the CO measures. This suggests that the contribution or support of the CO-ED score for EEH is in general weaker than for the standard eating disorders or that it was weaker in the particular assessed sample.

The high correlations between the CO-ED variables and high scorers of EAT-26 provide further validation of the general CO-ED as a measure of the tendency toward eating disorders. The findings also indicate the relevance of the general CO-ED for detecting EEHs. Additionally, the identification of the motivational understructure

of EEH in terms of the CO variables provides a basis for intervention targeted at the treatment of EEH, if considered necessary and desirable.

The findings of the study contribute to strengthening the construct of a general tendency for eating disorders that may be used for identifying individuals at risk who have no particular manifestations of eating disorders and for defining possibly new forms of manifestations of the general CO tendency for eating disorders, which may develop as autonomous forms as well as preceding eating disorders or remaining after recovery from eating disorders.

The results need to be evaluated in light of the difference between the criteria applied for assessment in this context and the new diagnostic criteria of the DSM-5 which was published after the study was completed. It is likely that the matching between the two sets of criteria is not perfect. Further, there is another finding of a different order that needs to be considered. In the resent study the percent of subjects identified as at risk for eating disorders according to the EAT-26 (11.6%) was appreciably lower than in other studies: for example, 25% in (27) or 33.15% (28). One reason may be that high school students may have become aware of the significance of EAT-26 questions and responded in the lower scoring end of the scale, especially that the EAT-26 was administered together with two other questionnaires concerning eating. However, the hypothesis that the proximity of other relevant questionnaires may affect the responses as well as other possible hypotheses need to be studied in further research.

The limitations of the study focus mainly on the following two issues. First, the fact that the eccentric behaviors studied in the present context were not defined in terms of the new criteria of the updated diagnostic system DSM-5 that was published after the study was carried out. Second, the study examined individuals 16-18 years old. This age range is too limited in view of the fact that 95% of individuals with eating disorders are 12 to 25 years old (29) and that eccentric eating behaviors may be found also in adults and elder individuals (30).

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Supplement no. 1. *Items of the EEH*

All items start with the words "Eating only or mainly"

A specific number of times a day (e.g., once), in the morning, at noon, at night, at precise times (e.g., 13:10), dry things, foods with some kind of sauce, foods in a soup, foods that have been immersed in water before eating, one specific kind of food in each meal (e.g., 1 or 2), in each meal a specific number of varied food stuffs, in each meal only one kind of food substance (e.g., carbohydrates), drinking water after each mouthful, not drinking water before or after eating for at least one hour, when one is alone, when all windows are closed, outside the home, at home, things that have a specific color (e.g., green, white), with wooden cutlery, foods with a specific surface (e.g., smooth, rough), with the fingers, when it is possible to produce sounds during eating, in a completely silent environment, foods whose precise composition is known, foods prepared in one's presence, foods prepared only by oneself, vegetables, fruits, proteins, for a specified duration of time (e.g., 2 or 5 minutes), in a standing position, in dim light (raw food), things that have not been cooked in any way, things that have been cooked for at least one hour, on wooden plates, on plates of a certain shape, pauses of specific duration between different plates, a specific time after being outside, specific time after doing sport, fasting one or two days a week, foods without odor, foods with specific size on the plate, foods with specific form (e.g., round, long, grains), foods that have not been refrigerated, foods that have been cooked no more than 10 minutes prior to serving, after making relaxation for at least 15 minutes, after taking a bath or a shower, changing one's diet completely every two weeks, one specific kind of food (e.g., chicken legs, liver, sausage), without any sugar, tiny quantities, chewing each mouthful a specific number of times (e.g., 12), keeping the food in the mouth for a specific duration of time before swallowing it, spitting a specific number of times prior to putting food in one's mouth, keeping strange materials in the mouth before putting in food (e.g., matches, pebbles), meat that comes from herbivorous animals, food without any spices whatsoever, foods that have been consumed by the Neanderthals, powdery food.

The EDE-Q in Hebrew: Structural and Convergent/ Divergent Validity in a Population Sample

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ABSTRACT

Background: The Eating Disorders Examination Questionnaire (EDE-Q), originally written in English, is used to screen for and help diagnose eating disorders (EDs). The purpose of this study was to test a Hebrew version for structural validity, for convergent validity, and screening properties in a non-clinical community sample in Israel.

Method: The EDE-Q was translated into Hebrew, with permission, and administered online with other well-used self-report instruments to 292 community volunteers (18% male).

Results: Exploratory and confirmatory factor analyses largely confirmed the original factor structure, although weight and shape concerns converged into a single factor. Results indicate good convergent validity and screening properties.

Conclusions: The favorable psychometric properties of the EDE-Q found in this study add the Hebrew version to a growing list of EDE-Q translations valid in diverse cultures. This important instrument is now available to Israeli clinicians and researchers and should be used and further explored with larger and more diverse populations.

INTRODUCTION

The Eating Disorder Examination (EDE) was first formulated as a semi-structured clinical interview schedule (1) and has become widely referred to as the "gold standard" in detecting risk for eating disorders (EDs) and characterizing ED symptomatology. The EDE was then adapted to a self-report questionnaire, the Eating Disorders Examination – Questionnaire (EDE-Q) using the original items and response categories (2). The EDE-Q has been widely used to screen for EDs in population studies (3, 4), and assess symptom severity in clinical samples (5). Research has generally shown that the self-report instrument performs as well as, and sometimes even better than, the clinical interview (6). The EDE-Q is therefore an economical, effective, validated and widely-used tool for clinical use and for screening and research purposes.

The EDE-Q has been translated into many languages including Dutch (7); Spanish (8), Portuguese (9); Persian (10); Italian (11); Chinese (12); Finnish (13); German (14) and Norwegian (15). The EDE (16) and the EDE-Q (17) have been adapted for use with children. EDE-Q norms have been established for adolescents (18, 19), college students (20) and bariatric surgery candidates (21). The questionnaire is thus widely used across and within cultures for screening and diagnostic purposes, and to assess symptomatic change over time.

The original structure of the EDE had five subscales with good internal consistency, that discriminated between normal controls, AN and BN patients (22). The resultant EDE-Q included four factors: Dietary Restraint, Shape Over-evaluation, Weight Over-evaluation and Body Dissatisfaction (23). Subsequently, competing structures were found. A study using the EDE with obese patients, some with an ED, favored a two-factor solution (24). Wade, Byrne and Bryant-Waugh (25) followed a large sample of female twins over adolescence using the EDE, and found that only one factor, Shape and Weight Concerns, showed consistency and stability. Bryne, et al. (26) analyzed the responses of individuals with ED and healthy community volunteers and found that a single factor solution had the best fit. Grilo et al. (20), analyzing the EDE-Q responses of a large sample of male and female undergraduates in the

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USA, supported a three-factor solution, in which Weight and Shape Over-evaluation were combined.

The EDE-Q has also been used for screening for EDs in non-clinical samples. Quick and Byrd-Bredbenner (27) found different thresholds for men and women undergraduates, and Mond et al. (19) suggested thresholds for male and female adolescents in the community. Penelo et al. (8) found that Mexican adolescents differed by gender as well as by urban and rural locations; urban girls were significantly elevated in their EDE-Q scores relative to urban boys, and to rural girls and boys. Cutoff points appear to be affected by gender, age, ethnicity and sampling base.

The purpose of the current study was to test the EDE-Q in Hebrew for structural validity, as well as convergent validity, in a non-clinical community sample in Israel**.** An additional goal was to establish its screening properties for Israeli adults.

METHODS

PARTICIPANTS

Two hundred and ninety-two community volunteers, aged 19-74 and recruited via social networks (M=33.39, SD=14.52, 18%, or n=51 male), participated in the study. They came from diverse socioeconomic backgrounds, using housing density as a proxy for social economic status. They had a mean of 15.75 years of schooling (SD=3.64), and all but 40.1% had a college degree. Participants' BMIs ranged between 15.4 and 42.2 (M=23.4, SD=4.0). Most (65.1%) were in the BMI range generally defined as normal (18.5 < BMI<25).

PROCEDURE

The study protocol and informed consent procedure were approved by the IRB. The questionnaires detailed below were completed anonymously online by all participants, who provided consent in the opening screen. The researchers' contact details were published so they could be contacted in the event of queries or difficulties. The data were downloaded into SPSS without identifying personal information. The questionnaires took approximately 30 minutes to complete, and no queries were recorded.

INSTRUMENTS

1. EDE-Q (2) is a 28-item self-report questionnaire assessing the core symptoms of EDs and a wide range of associated pathology. It assesses the frequency of different forms of inappropriate eating behaviors like undereating, overeating, dysregulation and compensation. The EDE-Q has four subscales, Dietary Restraint, Eating Concern, Weight Concern, and Shape Concern, each containing five to eight items. The responses to 22 items are rated using a 7-point forced-choice format (0–6), with higher scores reflecting greater severity. The remaining six items about the frequency of weight, shape and use of purging techniques during the past 28 days require open, numerical responses. These are used diagnostically and excluded from factor analysis. The suggested clinical cut-off score for the EDE-Q is four, as calculated by the average of each of the sub-scales and of the global score, for men and women (28). For the screening of non-patient samples, the thresholds suggested for the purpose of identifying caseness vary for different groups. In particular, the cut-off points for the EDE-Q sub-scales tend to be higher for women than for men (27). The EDE-Q was translated into Hebrew with permission from its authors by three bi-lingual English-Hebrew psychologists. A native Hebrew speaker translated it into Hebrew, and a native English speaker independently back-translated it into English. A bi-lingual psychologist identified disparities between the original and the back-translation, which were discussed and resolved. The Hebrew translation is available from the authors on request. Internal consistency for the original subscales was good, with Cronbach's alphas between α=.78 and α=.93.
2. The Satisfaction with Life Scale (SWLS) (29) includes five items assessing how satisfied the responder feels in general with his or her life. Scores correlate positively with measures of social support, positive affect, resilient personality characteristics and subjective assessments of health (30). Its brevity makes it user-friendly. In the current study the Cronbach's α was 0.89.
3. The EAT-26 (31) assesses maladaptive eating attitudes and behaviors. It contains 26 items rated on a six-point Likert scale. The three least frequent categories ("never," "rarely," and "sometimes") are given a score of 0, "often" is scored as 1, "usually" is scored as 2, and "always" a score of 3. Its three subscales are Dieting, Bulimia and Oral Control. For screening purposes, the EAT-26 global score of 20 is often used as a cutoff point for putative caseness (32, 33). We used a validated Hebrew translation (34) that has been used widely in Israel for both research and clinical purposes (e.g., 35). In the current study for the EAT-26 global score, Cronbach's α was 0.89.
4. The DKB-35 (Dresdner Körperbildfragebogen-35 or Dresden Body Image Questionnaire-35; 36) has

recently been translated from German into Hebrew by our research group (37). This instrument assesses body image not only in terms of the thin ideal but also in terms of function, positive enjoyment, and expressiveness. It has 35 items that load onto five subscales: Vitality, Physical Contact, Sexual Fulfillment, Body-Narcissism, and Body Acceptance, with internal consistency estimates ranging from α=.73 to α=.90.

5. The Figure Rating Scale (FRS) contains an array of seven hand-drawn silhouettes of women that increase linearly in body fat (38). The first silhouette presents a slender woman with little body fat and the seventh an obese woman. Respondents enter a number corresponding to (1) their current body size, (2) their ideal body size, (3) their perception of the most aesthetic woman, and (4) their perception of the healthiest woman. The discrepancies between the current figure and ideal, healthy, and best looking figures are then calculated and serve of measures of body dissatisfaction. Positive scores indicate a desire to be thinner, negative scores indicate a desire to be larger, and 0 indicates satisfaction with body size. The reliability of figure drawings in assessing current and ideal body size has been shown to be satisfactory (39).

The EAT-26, the FRS, the DKB-35 and the SWLS were included to test for convergent validity.

RESULTS

EXPLORATORY FACTOR ANALYSIS OF THE EDE-Q

We studied the structural validity of the EDE-Q by performing exploratory factor analysis (EFA), and then confirmatory factor analysis (CFA). The EFA was performed with Varimax rotation, as in the original analysis of the EDE-Q in English (5).

We entered into the EFA 22 of the 28 items, excluding the open-ended items dealing with eating pathology severity, following the original EDE-Q (2).

EFA was first performed restricting the factors to four. The four-factors had Eigen values of 11.2, 1.7, 1.5 and 1.3, respectively, cumulatively explaining 71.6% of the variance. Although statistically the four-factor solution was satisfactory, we decided against it because the items did not group onto the factors in a coherent and interpretable manner.

We then restricted the number of factors to three, requiring items to have a loading of 0.1 or more. When restricted to three factors, the factors had Eigen values of 11.24, 1.71, and 1.52, respectively, with cumulative

Table 1. *Exploratory Factor Analysis for the EDE-Q – Hebrew version (N=292)*

No.	Item	Factor		
		SWC	EC	R
27.	How uncomfortable have you felt seeing your body (for example, seeing your shape in the mirror, in a shop window reflection, while undressing or taking a bath or shower)?	.88		
26.	How dissatisfied have you been with your shape?	.84		
28.	How uncomfortable have you felt about others seeing your shape or figure (for example, in communal changing rooms, when swimming, or wearing tight clothes)?	.81		
25.	How dissatisfied have you been with your weight?	.81		
11.	Have you felt fat?	.77		
12.	Have you had a strong desire to lose weight?	.71		
22.	Has your weight influenced how you think about (judge) yourself as a person?	.70		
23.	Has your shape influenced how you think about (judge) yourself as a person?	.67		
10.	Have you had a definite fear that you might gain weight?	.57		
24.	How much would it have upset you if you had been asked to weigh yourself once a week (no more, or less, often) for the next four weeks?	.52		
6.	Have you had a definite desire to have a totally flat stomach?	.42		
7.	Has thinking about food, eating, or calories made it very difficult to concentrate on things you are interested in (for example, working, following a conversation, or reading)?		.79	
8.	Has thinking about shape or weight made it very difficult to concentrate on things you are interested in (for example, working, following a conversation, or reading)?		.78	
9.	Have you had a definite fear of losing control over eating?		.58	
21.	Over the past 28 days, how concerned have you been about other people seeing you eat?		.55	
20.	On what proportion of the times that you have eaten have you felt guilty (felt that you've done wrong) because of its effect on your shape or weight?		.54	
4.	Have you tried to follow definite rules regarding your eating (for example, a calorie limit) in order to influence your shape or weight (whether or not you have succeeded)?			.87
3.	Have you tried to exclude from your diet any foods that you like in order to influence your shape or weight (whether or not you have succeeded)?			.87
1.	Have you been deliberately trying to limit the amount of food you eat to influence your shape or weight (whether or not you have succeeded)?			.81
5.	Have you had a definite desire to have any empty stomach with the aim of influencing your shape or weight?			.55
Cronbach's alpha		.95	.83	.89

WC: Shape & weight concerns; EC: Eating concerns; R; Restraint
Note: Only factor loadings of over .40 are shown

explained variance of 65.77% (see Table 1). Of the 22 items entered into the EFA, two (items 2 and 19) did not load onto any of the factors, and 20 items are therefore shown in Table 1 below.

CONFIRMATORY FACTOR ANALYSIS (CFA) OF THE EDE-Q

CFA is the current golden standard for testing whether measures of a construct are consistent with their theoretically or empirically hypothesized structure and for comparing competing structures. We ran CFA in AMOS-23 using the maximum likelihood estimation method. We compared the four-factor CFA model with the three-factor model and found a better fit for the latter (see Table 2). According to CFA, the three-factor solution (see Figure 1) had adequate Goodness of Fit indices.

CONVERGENT VALIDITY

To test for convergent validity, we calculated Pearson correlations between the EDE-Q global and subscale scores and reported BMI, with measures of disordered eating, and body dissatisfaction, as well as with the SWLS scores and the five DKB-35 subscale scores that assess dimensions of body satisfaction. As can be seen in Table 3, the correlations between BMI and EDE-Q scores were positive and significant, as they were with two of the three EAT-26 sub-scales and total EAT-26 score, the FRS body dissatisfaction discrepancy scores for ideal body size, perceived body aesthetics, and perceived health. EDE-Q scores (total and subscales) correlated negatively with SWLS scores and four of the five DKB-35 subscale scores that assess dimensions of body satisfaction. These significant correlations support the convergent validity of the Hebrew version of the EDE-Q. The Physical Contact subscale of the DKB-35 was not correlated with the EDE-Q subscales or global score, supporting divergent validity.

CASENESS IDENTIFICATION BY THE EDE-Q

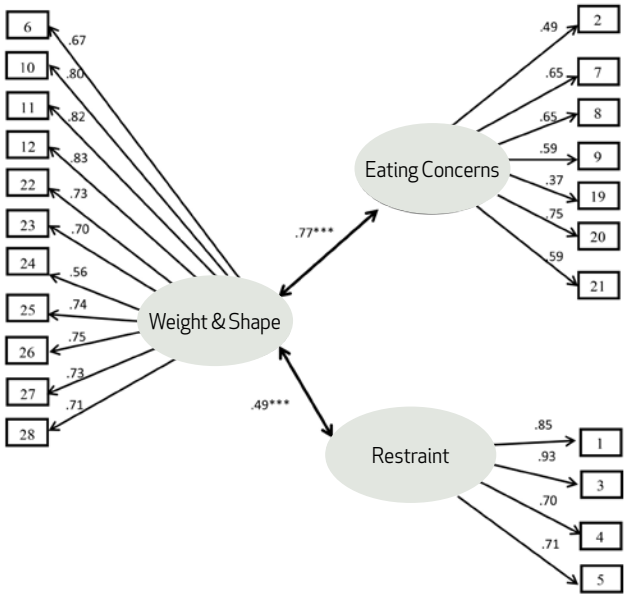
To identify potential ED cases, we used the cutoff point of 20 for global EAT-26 scores, and compared it to the

Table 2. *CFA: Comparison between the goodness of fit measures for the three- versus the four-factor model of the Hebrew EDE-Q (N=292)*

Model	Chi Square (df)	p	SRMR	RMSEA	CFI	TLI
Four factors	1306.8 (170)	.000	.32	.15	.77	.66
Three factors	457.51 (173)	.000	.16	.075	.94	.92

Note: SRMR= Standardized Root Mean Squared Residual; RMSEA = Root Mean Square Error of Approximation; CFI= Chi-square/df; TLI=Tucker Lewis index

Figure 1. *CFA for the three factor model: EDE-Q – Hebrew version (N=292)*



Note: Ellipses represent latent variables. Rectangles represent items in the Hebrew translation of the EDE-Q. All correlations between latent and observed variables were significant at p<.05.

Table 3. *Pearson correlations between the EDE-Q and body dissatisfaction subscales (Hebrew versions, N=292)*

EDE-Q	Restraint	Eating Concerns	Shape & Weight Concerns	Global score
BMI	.29**	.21**	.37**	.34**
EAT-26 Dieting	.72**	.70**	.73**	.81**
EAT-26 Bulimia	.51**	.73**	.62**	.67**
EAT-26 Oral Control	-.053	.13*	-.07	-.03
EAT-26 global score	.58**	.73**	.63**	.71**
FRS – ideal	.45**	.53**	.70**	.64**
FRS – aesthetic	.46**	.50**	.66**	.62**
FRS – healthy	.43**	.41**	.59**	.55**
DKB-35 Vitality	-.19**	-.37**	-.42**	-.36**
DKB-35 Body Acceptance	-.46**	-.58**	-.79**	-.69**
DKB-35 Body Narcissism	-.09	-.01	-.21**	-.15*
DKB-35 Physical Contact	.07	-.08	-.05	-.01
DKB-35 Sexual Fulfillment	-.16**	-.33**	-.41**	-.33**
SWLS	-.10	-.34**	-.31**	-.26**

Note: *p<.05; **p<.01 two tailed significance test
EDE-Q – Eating Disorders Examination Questionnaire; EAT-26 – Eating Attitudes Test-26; FRS – Figure Rating Scale; DKB-35 – Dresden Body Image Questionnaire-35; SWLS – Satisfaction With Life Scale.

threshold score of 4 on the EDE-Q total score as suggested by Quick and Byrd-Bredbenner (27) for undergraduates in the United States.

Using the EAT-26 cutoff point of 20, 27 of the 256 (10.6%) participants who completed both questionnaires had a suspected ED. Using the EDE-Q cutoff point of 4 for the global score, there were more, with 44 (17.2%) seemingly at-risk. Twenty of the 27 cases identified as at-risk by the EAT-26 (74.1%) were also identified as being at-risk by the EDE-Q. Only 20 (45.5%) of the 44 EDE-Q cases identified as being at-risk were also identified by the EAT-26. The test of association between the EAT-26 and the EDE-Q putative cases was χ^2=68.6 p<0.0001. The Sensitivity of the EDE-Q versus the EAT-26 criterion was therefore 20/27=74.07% and the Specificity of the EDE-Q versus the EAT-26 was 205/229=89.5%; Accuracy was 225/256 or 87.89%.

DISCUSSION

The purpose of this study was to validate the Hebrew version of the EDE-Q and investigate its psychometric properties. On the whole, the goals of the study were achieved. A three-factor structure that yielded interpretable and reliable subscales was found and confirmed. The EDE-Q total and subscale scores correlated positively with other measures of disordered eating and body dissatisfaction, and negatively with measures of well-being and body satisfaction, indicating convergent validity. The EDE-Q in Hebrew showed good screening properties, identifying more cases at-risk than the EAT-26.

The study is limited by the fact that all participants were adults, since children and adolescents tend to score differently on the EDE-Q. The sample size was adequate for the study goals, but participants included only community volunteers, with a limited number of probable ED cases, and only a small number of males. The EDE-Q in this study was compared to other self-reported measures and there was no diagnostic interview or clinical assessment available as an external criterion. Therefore, whereas we can state that the EDE-Q identified more individuals than the EAT-26 as being at-risk of having an ED, we do not really know which of these instruments is more accurately identifying individuals with a clinically diagnosable ED in accordance with the DSM-5.

The three-factor solution reported in this study was derived by EFA and confirmed by CFA with Goodness to Fit indices. While it does not fully correspond to the factor structure of the English version, this three-factor structure was found for college students, both athletes and non-athletes, in the United States (20, 40). It is very similar to the four-factor solution put forward by Cooper, Cooper and Fairburn (22) in their original presentation of the EDE-Q, except that the two assessing Shape Concerns and Weight Concerns are merged into a single factor. It is reassuring that the factors are easily interpretable and conform, in the main, to those found for the original EDE-Q. The factors derived in the current analyses have excellent internal consistency, ranging from 0.83 to 0.95, so constitute reliable sub-scales of the EDE-Q (41).

The merging of shape and weight concerns into one factor has been frequently found in studies of EDE-Q structure. Grilo et al. (20) followed American female and male college students and found that shape and weight concerns merged into a single factor; this was also found in a study of Mexican high school youth (8)

Convergent validity was tested by calculating the correlations between the EDE-Q global and subscale scores with those of the EAT-26 (31), the FRS (38) the five subscales of the DKB-35 that indicate body satisfaction (36), and between the EDE-Q and the SWLS (29). Positive and significant correlations were found between global and subscale EDE-Q scores and the EAT-26 total and subscales, the FRS discrepancy measures indicating body dissatisfaction, as well as reported BMI. Negative and significant correlations were found between the EDE-Q scale scores and four of the five subscales of the DKB-35 that indicate body satisfaction (36), and between the EDE-Q and the SWLS (29)

In addition, we tested the association between at-risk status using the threshold of 20 for the EAT-26 and at-risk status using the threshold score of 4 for the EDE-Q total score. The probability of being in both putative "case" groups was very high, and the EDE-Q detected more individuals with a suspected ED than did the EAT-26.

The pattern of correlations between the EDE-Q total and subscale scores and the Dresden Body Image Questionnaire subscales broadens our understanding of the connection between eating symptomatology and several body-related concepts previously not examined in this context. First, Vitality, as measured by the DKB-35, correlated negatively and significantly yet weakly with Restraint, and moderately with Eating Concerns, and with Weight and Shape Concerns. Vitality taps into a feeling of having a healthy, fit and zestful body, rather than a thin one, which is negatively associated with eating pathology. Second, our results show that Sexual Fulfillment has significant, negative associations with eating pathology. Our results support the fact that people who are free and flexible with their food and

eating tend, in general, to be more sexually fulfilled. Third, Body Narcissism, was negatively associated with Shape and Weight Concerns. Body Narcissism is the DKB-35 subscale that measures individuals' enjoyment of showing off their body and being admired for it. Not surprisingly, our enjoyment in having other people look at our bodies is negatively associated with our weight and shape concerns as measured by the EDE-Q. Physical Contact, a subscale of the DKB-35 that measures our use of physical contact and our ease of touching others in a non-sexual social context was the only DKB-35 subscale that was not related to the EDE-Q total or subscales. Thus tendencies to restrict food intake, to be concerned about eating, and to be preoccupied with weight and shape therefore are unrelated to the tendency to touch other people. As might be expected, there are significant gender differences in the EDE-Q subscales and global scores. Many community studies have found that adolescent and adult men in the community have lower scores on the EDE-Q relative to female adolescents and adults (e.g., 8, 20, respectively), and recently a large scale clinical study of male and female adult patients found lower scores for male patients in each diagnostic category and across all ED categories (42). It is reasonable to assume that such gender differences would also be found in the current EDE-Q version, although we did not analyze gender differences due to the relatively small number of male participants in the current study.

In summary, we present both an exploratory and a confirmatory factor analysis of a Hebrew translation of the EDE-Q in a non-clinical sample of Israeli adults, provide evidence of convergent validity, and demonstrate good screening properties. The factor structure of the English version was replicated overall, except that Weight and Shape concerns converged and formed a single factor. The favorable psychometric properties of Hebrew translation of the EDE-Q found in this study add this tool to the growing list of translations shown to be valid in diverse cultures. This useful and effective instrument is now available to Israeli clinicians and researchers and should be used and further explored with larger and more diverse populations.

• All three authors contributed to the conception and design of this study, the collection, analysis and interpretation of the data, and to the writing of the article submitted to the IJP.
• None of the authors have a conflict of interest.
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The Well Rounded Body Image: The Dresdner Körperbildfragebogen DKB-35 in Hebrew

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ABSTRACT

Background: The Dresdner Körperbildfragebogen (DKB-35) is a positive and comprehensive measure of the relationship with the body. Written and used in German the original has good psychometric qualities. The goal of the current study was to translate it into Hebrew and then test its psychometric qualities.

Method: 292 adult community volunteers self-reported online on the DKB-35 as well as on the Satisfaction with Life Scale and the Eat-26. The data were exported into and analyzed in SPSS 21.0.

Results: Structural validity, reliability and convergent and divergent validity of the Hebrew DKB-35 was demonstrated. All five original sub-scales: Body-Acceptance, Vitality, Body-Narcissism, Physical-Contact, and Sexual-Fulfillment were recovered.

Conclusions: The DKB-35 in Hebrew can be used in the context of mental health and the process of recovery from eating disorders.

INTRODUCTION

Most body image measures concentrate on weight and size. These measures reflect the criterion of anorexia nervosa that specifies a perceptual and/or cognitive distortion, ruling that smaller and lighter is better. The eating disordered individual's perception may be distorted so that she sees herself as much bigger and heavier than she is, in an extreme of rejecting her perceived body. Thus, for example, the Stunkard Figure Rating Scale (1) contains an array of nine hand-drawn silhouettes of women that increase linearly in body fat. The first silhouette presents a slender woman with very little body fat and the last one represents an obese woman. Participants are asked to identify their current body size as well as that of the ideal, best-looking and healthiest woman. The discrepancies between the current figure and ideal, healthy, and best looking figures are then calculated. Most women rate themselves as fatter than any of the other three alternatives, and thus are said to have a negative body image or high body dissatisfaction (e.g., 2). Most other measures are verbal rather than pictorial, and include items such as "my hips are too wide," i.e., quantify the dissatisfaction of the individual in not conforming to the thin ideal. These measures do a good job of predicting eating disorders (3), correlate negatively with BMI (4) and positively with disordered eating symptoms (5). Recovery from eating disorders is negatively correlated with these measures of body dissatisfaction (6).

The Dresdner Körperbildfragebogen (DKB-35) broadens this concept considerably. It was written by a team of German psychologists (7), and to the best of our knowledge has not yet been translated into other languages. The DKB-35 has a very positive and comprehensive conceptualization of body image. It includes five sub-scales, Bodily Acceptance, Vitality, Body Narcissism, Sexual Fulfillment and Physical Contact. **Bodily Acceptance** includes items such as: "There are many situations in which I feel satisfied with my body" (item 7); and "I consciously choose my clothing so that it hides my body" (item 12, reversed). This scale captures the reverse of what is measured by most extant body-image instruments. In addition the DKB-35 has four sub-scales that describe other positive and gratifying aspects of bodily experience. The **Vitality** subscale includes items such as: "I am physically fit" (item 8) and "I lack vigor and

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zest" (item 3, reversed). The **Body Narcissism** subscale includes items such as: "I find it pleasant and stimulating when somebody looks at me attentively" (item 13) and "I like to show my body off" (item 33). The **Sexual Fulfillment** subscale includes items such as: "I feel my body pleasantly and intensively in sexuality" (item 4) and "I am very satisfied with my sexual experience" (item 9). The **Physical Contact** subscale includes items such as: "Physical contact is important for me to express closeness" (item 5) and "I do not like being touched" (item 19, reversed). In addition, the DKB-35 includes supplementary items with "yes" or "no" response options pertaining to regular exercise, current dieting, body piercing and tattoos.

There is some research on the DKB-35 in the original German. In a large non-clinical sample of men and women, all subscales were negatively correlated with BMI (8). Those who exercised regularly scored higher on all subscales, as did those who were not currently on a diet. Men scored significantly higher than women for Vitality, Bodily Acceptance and Sexual Fulfillment. Validation on a clinical sample was reported by Pöhlmann et al. (9). The DKB-35 and other measures of body image were administered to 560 patients with psychosomatic complaints. The DKB-35 factor structure was replicated using confirmatory factor analysis, and the subscales showed very good internal reliability. In this clinical sample the DKB-35 subscale scores were strongly associated with BMI. The relationship between the DKB-35 scores and other measures of body image provided convergent and divergent validity for the instrument. Thus the DKB-35 in German has a robust factor structure, reliable subscales, and divergent and convergent validity, in non-clinical and in clinical samples.

The DKB-35 is a comprehensive measure of positive, healthy, even joyful body perception and experience. If mental health is defined to include body image, high scores on the DKB-35 would indicate better mental health. If recovery from eating disorders were to include not only an absence of symptoms and bodily rejection, but an exuberant physical, sexual, narcissistic enjoyment of the body, a rise in the DKB-35 score would be a good indicator of broadly conceived recovery.

It is in this spirit of measuring the positive that we wished to examine the properties of the DKB-35 in languages (and cultures) other than the original German. Because the focus of this study was to test the relationship of DKB-35 scores to mental health, we added the measure of Satisfaction with Life (SWLS, 10). Since we hope the DKB-35 will be adopted as part of the assessment of recovery from eating disorders, we also administered the EAT-26 (11).

The goals of the current study were to translate the DKB-35 into Hebrew, to examine its psychometric properties, and to make it available for use in Hebrew, not only in the context of psychopathology, but also of mental health and recovery.

METHODS

PARTICIPANTS

Participants were 292 community volunteers (57 or 19.1% male) recruited through social networks. Participants ranged in age from 19 to 74 with a mean of 33.39 (SD=14.52). The most frequently endorsed family status was single, 58.8%, followed by 35.1% married. Just less than one third, 31%, were parents. Using housing density as a proxy for social economic status, participants ranged from lower to higher middle class, like many on-line samples. Participants had on average a college education (15.76 $\pm$ 3.64 years of schooling), though 40.1% had only high school education. The self-reported height and weight of the participants showed a BMI ranging from 15.4 to 42.2, with a mean of 23.4 and a SD of 4.0. The majority of participants, 65.1%, were in the normal range (18.5 < BMI<25).

PROCEDURE

The IRB of the Ruppin Academic Center approved the study protocol and the informed consent procedure. Participants completed the self-report online, anonymously, and signed their consent in the opening screen of the electronic questionnaire, on which the researchers' contact details were available should questions or difficulties arise. The data were then downloaded into SPSS without any personal identifiers, to protect the privacy of the participants. The completion of the online questionnaire took about 30 minutes, and no queries or complaints were recorded.

INSTRUMENTS

1. DKB-35 (7): The instrument was downloaded in German from the internet site http://sportpaedagogik-sb.de/pdf/dkb-35.pdf in September 2014. The translation into Hebrew and English followed the star paradigm often used by the WHO (e.g., 12). A native German speaker translated it into English. A trilingual psychologist (RBM) independently back-translated it into German.

A bilingual psychologist (AHZ) translated the English version into Hebrew, and another bilingual psychologist (LLA) independently back-translated it into English. With the help of another trilingual psychologist (SK), the team then convened and discussed all disparities between the original German and the back-translation from English and corrected the English version accordingly; then the team did the same for the corrected English translation and the back-translation from Hebrew, correcting the Hebrew translation accordingly. The revised Hebrew version is available from the authors on request.

2. The Satisfaction with Life Scale (SWLS; 10) includes five items that measure the extent of the individual's satisfaction with his/her life and is a well-used scale of well-being. It correlates positively with measures of happiness, positivity, optimism, social support and subjective health, and negatively with depressive symptoms (13). Its brevity makes it user-friendly. In the current study the SWLS had internal reliability estimate of α=0.84.
3. The EAT-26 (11) has 26 items that assess eating attitudes. The Hebrew version has been used extensively for clinical (6) and nonclinical (14) samples. In the current study the EAT-26 had an internal reliability estimate of α=0.88.

RESULTS

After reversing 11 negatively framed items, the scales had good internal consistency, as measured by Cronbach's alpha. For **Vitality**, items: 2rev, 3rev, 6rev, 8, 14, 17, 26rev, and 32 α=.80; for **Body Acceptance** items: 7, 12, 15rev, 18rev, 23rev, 25, 28rev, and 33 α=.89; For **Body Narcissism** items: 1, 10, 13, 20, 29, 31, 33, and 34 α=.78; for **Sexual Fulfillment** items: 4, 9, 16, 21, 27, and 35 α=.89; for **Physical Contact** items: 5, 11, 19rev, 22, 24rev, and 30rev α=.73.

We studied the structural validity by first performing exploratory factor analysis (EFA), and then confirmatory factor analysis (CFA). The EFA was performed with Varimax rotation and Kaiser normalization, as in the original analysis of the DKB-35 in German (7). The factor analysis was restricted to five factors. The first five factors had Eigen values of 9.88, 3.33, 2.34, 2.01, and 1.82, respectively (see Table 1), with cumulative explained variance of 57.05%. There was a steep decline in Eigen values after the fifth factor. Item factor loading was restricted to >.10.

The resulting structure can be seen in Table 1. Three items do not conform satisfactorily to the expected structure: item 1 "I move gracefully" which should load onto the **Body Narcissism** subscale, loads instead onto the **Body Acceptance** subscale. On consideration of its content and behavior we decided to move item 1 to the Body Acceptance scale. Item 33 "I like to show my body off" that should load onto the **Body Acceptance** subscale, loads instead onto the **Body Narcissism** subscale. On consideration of its content and behavior we decided to move item 33 to the Body Narcissism scale. Doing so slightly improved the reliability of both scales: **Body Acceptance** to α=.90 and **Body Narcissism** to α=.78. A low but correct loading was observed for item 26rev: "I reach my physical limits easily" that loads onto the correct sub-scale **Vitality**, but has a factor loading of .15. Removing item 26rev from the **Vitality** subscale slightly raises the reliability to α=.82. Thus, item 26rev was totally subtracted from the structure. These three changes were introduced when performing the CFA.

CONFIRMATORY FACTOR ANALYSIS OF THE DKB-35

Confirmatory factor analysis (CFA) is the current golden standard for testing whether measures of a construct are consistent with their theoretically or empirically hypothesized structure. Thus if CFA confirms the structure of the translated questionnaire in the original language, it is additional reassurance that the translation has kept construct validity. In CFA the hypothesized structure is entered to constrain the analysis and then the equations are calculated to see how well the actual data fits the constraints of the hypothesized model. The CFA yields model-fit-indices; if they are good – the hypothesized structure is confirmed; if they are poor the model will be rejected.

Confirmatory Factor Analysis (CFA) shows that the five factor solution is a good one with sufficient Goodness of Fit indices: Chi square=306.89, p<0.001. NFI=.91; RMSEA=.07 (see Figure 1).

A comparison of the subscale means between those who exercised regularly with those who did not revealed a significant advantage to exercisers on **Vitality** (mean of 3.69 vs 3.27, $t_{(264)}$=-4.62, p<0.001), but not for the other four subscales. Comparison of subscale means between those who are currently on a diet (N=56) with those who are not showed significantly higher scores for the **Body Acceptance** for non-dieters (mean of 3.43 vs 2.90, $t_{(262)}$=4.15, p<0.001) and for **Sexual Fulfillment** (mean of 3.27 vs 3.51, $t_{(262)}$=1.71, p<.05). Men and women differed, women have significantly lower scores on **Vitality**

Table 1. *Exploratory Factor Analysis for DKB-35 – Hebrew version*

Item no.	Item	Factor				
		Body acceptance	Sexual fulfillment	Vitality	Body narcissism	Physical contact
23.	I wish I had a different body. (R)	.83				
25.	I am satisfied with how I look.	.79				
12.	I like my body.	.78				
28.	If I could change my body in some way, I would. (R)	.77				
18.	I often feel unwell in my body. (R)	.68				
7.	There are many situations in which I feel satisfied with my body.	.66				
15.	I consciously choose my clothing so that it hides my body. (R)	.57				
1.	I move gracefully.	.51				
9.	I am very satisfied with my sex life.		.78			
35.	My sexual experiences are satisfying for me.		.78			
27.	I can enjoy my sexuality.		.74			
21.	I can enjoy sexual situations without inhibition.		.69			
4.	While being engaged in sexual activity, I feel my body pleasantly and intensely.		.66			
16.	Sexuality is an important domain of my life.		.65			
17.	I am physically able to function well.			.74		
3.	I lack vigor and zest. (R)			.71		
14.	I have a lot of energy.			.69		
2.	I am often in poor physical state. (R)			.68		
32.	I am physically hardy and resilient.			.62		
8.	I am physically fit.			.57		
6.	I often feel physically run down. (R)	.50		.54		
33.	I like to show my body off.				.71	
31.	I make use of my body to attract attention.				.69	
34.	I like to be in the center.				.67	
20.	When somebody pays attention to my body, I feel appreciated.				.62	
13.	I find it pleasant and stimulating when somebody looks at me attentively.				.62	
29.	My body is expressive.				.40	
10.	Other people find me attractive.	.53			.37	
24.	I consciously avoid touching other people. (R)					.80
19.	I do not like being touched. (R)					.75
30.	I only allow a few people to touch me. (R)					.63
22.	I like it when someone takes my arm.					.49
5.	Physical contact is important for me to express closeness.		.57			.45
11.	I seek out physical closeness and tenderness.		.49			.42
Cronbach's alpha		.90	.89	.82	.78	.73

Note: Only factor loading of over .10 were chosen the analysis

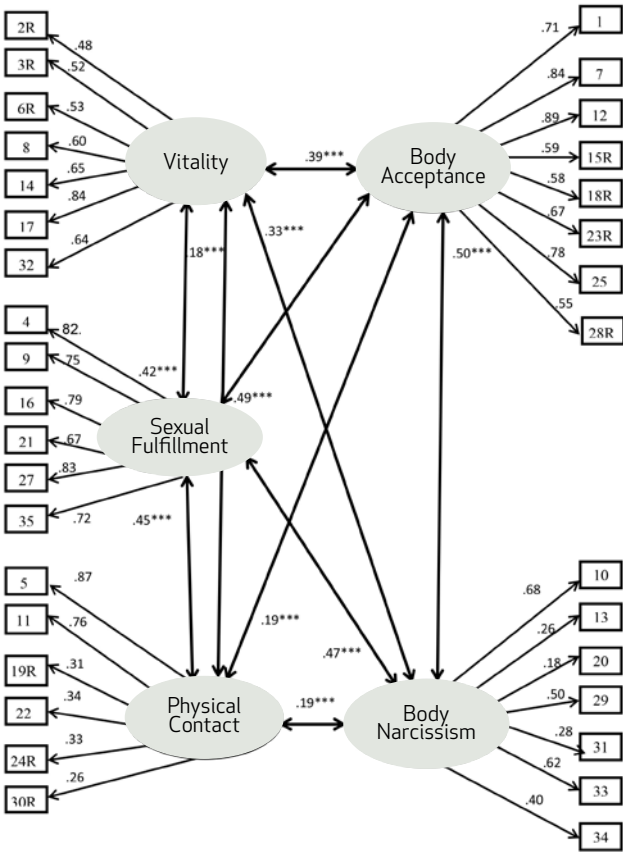
($t_{(260)}$=3.35; p<0.001); on **Physical Contact** ($t_{(259)}$=1.99; p<.05) and **Sexual Fulfillment** ($t_{(259)}$=3.58, p<.001).

The five subscale scores were inter-correlated; the inter-correlations are shown in Table 2. All subscale scores correlated positively with the Satisfaction with Life Scale (SWLS; 10) and negatively with the EAT-26 scale (11). These correlations are shown in Table 3, and they range from weak to moderate, showing convergent as well as divergent validity. The subscale scores are related to BMI; three out of five correlate negatively with BMI as shown in Table 3. The means for the subscale scores of different BMI intervals are different, in particular obese individuals have the lowest scores and the underweight individuals have the highest scores on all the subscales as shown in Table 4. It should be noted that the **Sexual Fulfillment** and the **Physical Contact** scale are more weakly related to BMI than the other three subscales.

DISCUSSION

The DKB-35 was written in German, and the original contained five subscales that describe a satisfaction with

Figure 1. *Confirmatory factor analysis for the five factor model: DKB-35 – Hebrew version*



Note: Ellipses signify latent variables. Rectangles signify questions in the Hebrew version. Rectangles between latent variables signify correlations between latent variables. All correlations between latent and observed variables were significant at p<.05.

Table 2. *Inter-correlations of the DKB-35 subscale-scores (N=267)*

	Physical Contact	Sexual Fulfillment	Body Narcissism	Body Acceptance
Vitality	.15*	.48***	.33***	.58***
Body Acceptance	.16***	.53***	.43***	
Body Narcissism	.27***	.47***		
Sexual Fulfillment	.41***			

Note: *** p<.001 (2-tailed). *p<.05 (2-tailed)

Table 3. *Correlations of the DKB-35 subscale-scores with other measures (N=267)*

	Eat26	SWLS	BMI
Vitality	-.25***	.39***	-.13*
Physical Contact	-.11	.14*	-.01
Sexual Fulfillment	-.23***	.35***	-.12
Body Narcissism	.02	.11	-.22***
Body Acceptance	-.49***	.41***	-.43***

Note: *** p<.001 (2-tailed); *p<.05 (2-tailed). Eat26 the Eating Attitudes scale (11); SWLS (10) Satisfaction with Life Scale

one's body's appearance (Body Acceptance), with the body's energy (Vitality) with its sexual function (Sexual Fulfillment), with its effect on others (Body Narcissism), and with touching and being touched (Physical Contact) (7). In the current study, the DKB-35 in Hebrew was administered to a community sample of adult volunteers.

The results presented here should be viewed with the study limitations in mind. The sample was a convenience sample and not representative of the general Israeli population. Because the self-report was administered online, the participants are younger and more educated on average than the general population. The distribution of BMI resulted in a small number of participants in the two extreme groups, the underweight and the obese, making comparisons of weight groups less potentially powerful.

Structural validity of the DKB-35 in Hebrew was shown in a number of different ways. The EFA recovered the five-factor structure shown in the German original, supplying high Eigen-values for the first five factors that together explained 57% of the variance. After minor changes suggested by the EFA, the CFA confirmed the factor structure and showed good fit indices. Thus the basic five-factor-structure shown in German is recovered in the Hebrew translation.

Convergent and divergent validity was examined by positive correlations with the Satisfaction with Life Scale (10) and negative correlations with the Eating Attitudes Test (11). Thus feeling good about one's life is correlated with feeling good about one's body, and feeling bad with one's body is correlated with disordered eating.

Reliability can be shown in a number of ways. In the current study we report on the internal reliability of the sub-scales, all showing moderately high reliability estimates, comparable to those found in the original German.

The negative correlations of the DKB-35 with BMI show the prominence of the thin ideal in Israeli culture, as in other Western cultures. Moreover, analysis of variance by BMI intervals result in the obese scoring lowest on all subscales and the underweight highest.

We see the DKB-35 as a promising instrument in the context of the process of recovery from eating disorders. Questionnaires used in the field of eating disorders traditionally emphasize the disappearance of negative attitudes towards the body ("body dissatisfaction") rather than the development of a positive connection. Such instruments are useful in assessing levels of psychopathology,

Table 4. *Analysis of variance of DKB-35 subscales for BMI intervals (N=267)*

	Underweight BMI<18.5 N=17	Normal Weight 18.5≤BMI<25 N=175	Overweight 25≤BMI<30 N=51	Obese BMI≤30 N=20	$F_{(df), p}$
Vitality	3.60 (.71)[d]	3.50 (.78)	3.53 (.69)	3.08 (.87)[a]	NS
Body Acc.	3.95 (.86)[d]	3.46 (.80)[c,d]	3.02 (.82)[a,b]	2.44 (.83)[a,b,c]	$F_{(3,258)}$=15.30, p<.001
Body Narc.	3.27 (.65)[b,c,d]	2.94 (.66)[c,d]	2.84 (.71)[a]	2.54 (.65)[a,b]	$F_{(3,256)}$=3.98, p<.01
Physical Con.	3.64 (.53)	3.74 (.75)	3.64 (.64)	3.69 (.65)	NS
Sexual Ful.	3.61 (1.01)	3.51 (.91)	3.29 (.96)	3.13 (1.03)	NS

Note: Body Acc.= Body Acceptance; Body Narc. = Body Narcissism; Physical Con.= Physical Contact; Sexual Ful.= Sexual Fulfillment. Superscript letters denote groups for which the comparison with the Bonferroni correction for multiple comparisons were significantly different, e.g., Body Acceptance of the Underweight (group a) is significantly higher than that of the Obese (group d) and the Obese are significantly lower in Body Acceptance than the Underweight (group a) the Normal weight (group b) and the Overweight (group c).

which obviously declines with the process of recovery. Yet measures that tap into elements of growth, vitality and joy in relation to one's body during the recovery process are sadly lacking. The development of positive body experience has been posited as an essential step in the eating disorder recovery process (13), and reconnection with the body characterizes full recovery from an eating disorder (15, 16). The DKB-35 may also be relevant to alleviation of other conditions, for example in assessing connection to the body as a result of growth following bodily trauma (17).

Further research is needed to extend our understanding of the DKB-35 in Hebrew. Clinical studies discriminating between patient groups and controls such as the study of psychosomatic patients (9) in German would be of value, as would longitudinal studies showing a rise in DKB-35 scores in patients recovering from eating disorders. Test-retest of non-clinical and clinical samples are needed to examine the stability over time of this promising measure of positive and accepting attitudes toward one's body.

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Percentage from Target Weight (PFTW) Predicts Re-hospitalization in Adolescent Anorexia Nervosa

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ABSTRACT

Background: The aim of the current study was to investigate whether the percentage of the discharge weight relative to recommended target weight (PFTW) during inpatient treatment predicts re-hospitalization in adolescent anorexia nervosa (AN).

Method: 51 hospitalized adolescents with AN were weighed and completed self-reports on admission and discharge. We examined reports regarding re-hospitalization within the first year after discharge.

Results: 19 patients (37.25%) required re-hospitalization. The proportion of the actual discharge weight relative to target weight (PFTW), previous re-hospitalizations and parental marital status were found to be significant predictors of re-hospitalization.

Conclusions: The study highlights the importance of discharge weight relative to target weight (PFTW) for long-term outcome. Failure to obtain discharge target weight is a significant predictor of re-hospitalization in adolescent AN.

INTRODUCTION

Among psychiatric illnesses, eating disorders are unique as patients have both physical and psychological disturbances (1). The restoration of healthy body weight is one of the key goals in the treatment of anorexia nervosa (AN) (1, 2). The role of inpatient hospitalization in the treatment of AN among adolescents has been a focus of debate (3-6). However, nutritional rehabilitation remained an essential component of inpatient treatment of adolescent AN (2). The goals of refeeding and weight restoration are often time consuming. Managed care companies frequently fail to provide approval for the ample length of stays required to provide proper care (7, 8).

On the one hand, recent studies support the use of a more rigid approach to nutritional rehabilitation in order to decrease hospital stays and improve social reintegration and post-hospitalization functioning (9-11). On the other hand, shorter hospitalizations do not appear to be effective for adolescent AN patients (8). There are higher rates of readmissions as the length of stays decreases (8). In addition, discharge at lower weights has been associated with increased relapse rates and poorer prognosis (12).

Alternative approaches to weight restoration are based on findings indicating that adolescent patients suffering from AN may also achieve target weight in less restrictive, less expensive settings (5, 13). For example, a recent study demonstrated that for adolescent patients with non-chronic AN, day-patient treatment (DP) (after short inpatient care) is not less effective than inpatient treatment (IP) – both for weight restoration and weight maintenance during the first year after admission. Thus, DP might be a safe and less costly alternative to IP (13).

However, common practice highlights weight restoration to be the gold standard of good clinical practice in adolescent AN. This is supported by findings indicating that weight gain during inpatient treatment as well as weight maintenance afterward are important prognostic factors (13). Studies have found that inpatients with AN who left treatment while still underweight had a poorer outcome

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and a higher risk for relapse than those who completed treatment and obtained target weight (12, 14-16).

A study by Kaplan et al. (17) conducted with a mixed sample of adolescents and young adults with AN indicated that body mass index (BMI) at discharge from an inpatient unit and the rate of weight loss within the following 28 days were the strongest predictors of BMI maintenance during the first 6 to 12 months following discharge. The authors defined discharge weight as BMI (kg/m2)>19.0. They concluded that weight maintenance after discharge may be improved by helping patients achieve a higher BMI during the weight-restoration phase of treatment.

Similarly, in a long-term multisite retrospective follow-up of 8.3 years, Steinhausen et al. (18) found that 44.8% of adolescent patients with AN required at least one re-hospitalization after inpatient treatment. The authors found that "insufficient weight gain" during first admission and the resulting lower BMI at discharge were risk factors for re-hospitalization. However, they provided no information regarding the definition of target weight at first admission. The retrospective design of the study and the lack of standardized treatment or discharge criteria are significant limitations of this study.

On the other hand, in a one-year follow-up Castro et al. (19) found that even after total weight restoration during first admission to inpatient treatment, 25 out of 101 (24.8%) adolescent patients with AN still required re-hospitalization. In this study, BMI at discharge did not emerge as a significant outcome predictor. In addition, there was no target weight definition (19). In another study investigating outcome within one year after inpatient treatment of adolescent AN, Salbach-Andrae et al. (20) found only BMI at admission and psychiatric comorbidities to be significant outcome predictors. BMI at discharge was not included as a predictor for future admissions. Moreover, no clear target weight criteria were included in the program description.

In this new era guided by principles of cost-effectiveness and featuring less coercive, less restrictive day-treatments for adolescent AN, there is a renewed interest to evaluate whether obtaining target weight within inpatient treatment is important. The current study had two main goals. The first was to investigate the impact of achieving target weight at discharge on re-hospitalization within the first year. For that purpose we used the variable PFTW (percent from target weight), which enabled us to examine the discharge weight percentage from the recommended target weight. The second aim was to identify demographic and psychological predictors of re-hospitalization. These questions were explored within the unique setting of a medical psychiatric unit, based on an open, voluntary, motivation-oriented intervention with high parental involvement and early community exposure (21).

METHOD

PARTICIPANTS

The sample consisted of 51 adolescent patients (males=5, females=46) between the ages of 11.8 to 18.8 years (Mean=14.98, SD=1.81). All were hospitalized between the years 2009-2013 in a child and adolescent medical psychiatric unit specializing in eating disorders. All were diagnosed with AN - restrictive (AN-R, n=44, 86.27%) or binge/ purging (AN-B/P, n=7, 13.73%) subtypes (1).

Due to the patients' young age, some of the diagnostic criteria for AN were not always relevant for diagnosis (especially the menstrual criterion). Thus, although evaluated using the DSM-IV, the patients' diagnoses are also congruent with the new criteria of DSM-5 (1). Patients arrived at the unit upon referrals from physicians or community psychiatrists. In other cases, they transferred from other pediatric units within the medical center (5)

Two patients were excluded from the original sample (N=53) after they were discharged because they required more restrictive psychiatric care due to serious psychological comorbidity and insufficient weight gain. Two of the participants included in the sample were admitted while they were minors but became adults during the follow up. Thirteen out of the 51 patients (25.5% of total sample) had not reached target weight upon discharge. Baseline characteristics of these patients were not significantly different from those who obtained target weight.

PROCEDURE

The protocol of the research project has been approved by the Ethics Committee of the Medical Center's Institutional Review Board (IRB). It conforms to the provisions of the Declaration of Helsinki. The patients and their parents received explanations regarding the aims and procedures of the study. A written consent was obtained from patients and parents and anonymity was guaranteed.

The unit's director (SF) assessed the patients for clinical diagnoses. Patients were diagnosed based on information from clinical interviews, observation, parents' reports and medical evaluations (5). In addition, the adolescents filled in self-report questionnaires at the beginning (first two weeks) and at the end (last two weeks) of their inpatient treatment. The questionnaires were an integral part of clinical assessment

and provided information about eating disorder symptoms, depression, anxiety and suicidal ideation. Re-hospitalization was defined as patient admission to a psychiatric or specialized eating disorder unit due to acute AN symptoms including weight loss within a year of discharge from the unit. Since patients could be hospitalized in any other hospital in Israel, re-hospitalization information was based on a combination of sources: The OFEK system (an official national computerized registry), family physicians' reports, reports from the admitting unit as well as parents' reports.

TREATMENT PROGRAM

The Child and Adolescent Medical Psychiatric Unit is an open, voluntary inpatient facility that specializes in the treatment of body-mind pathologies and eating disorders (22). Patients are mostly adolescents, with ages ranging from 6 to 18 years at admission. The treatment program has two phases: an intensive inpatient phase and a shorter phase of a half-day outpatient program. This two-phase structure exemplifies the community-based orientation of the program allowing patients reintegration into the community. A few weeks after admission a target weight is established. Target weight determination includes processing genetic, developmental and medical information. Parents and patients are informed about the final decision and from then on the exact individual "target weight" becomes the final weight goal that allows the discharge from the program (after two weeks of target weight maintenance). The target weight is defined as a range of 2 kg from a minimal recommended weight.

The unit clinical dietician sets the patients' target weight, taking into consideration different psychological and physical variables such as age, current weight and growth potential. Patients' goal is to gain a minimum of 500 grams per week. According to Golden et al. (11), setting target weight for adolescent patients must be an individualized process, taking into account pubertal stage, prior growth percentiles, growth potential, height and age. Treatment target weight is the weight at which the patient is well functioning medically. For girls, it is when menstruation and ovulation are restored. When patients attain target weight, they transfer into a half-day outpatient treatment format.

Treatment is voluntary and patients refusing hospitalization are referred to other psychiatric facilities with more restrictive programs, or discharged back into community settings according to their medical condition (fewer than 5%) (5). Patients requesting discharge prior to achieving the target weight are discharged against medical recommendation and are put under a social worker legal supervision.

The two-phase program integrates behavioral/motivational elements and focuses on weight restoration through structured group-supervised meals. The adolescents are under dietary supervision and are weighed twice a week (5). Individual therapy integrates Cognitive Behavioral Therapy (CBT) and dynamic principles and consists of twice-a-week sessions. The program includes weekly parental guidance and family-oriented therapy, as well as a variety of group therapies (e.g., psychodrama, nutrition, dynamic group therapy).

Weight restoration is the primary goal during the inpatient phase and secondary goals include active participation in the treatment program, and improvement of eating habits and communication skills. Patients who achieve their weekly goals move up in seven successive "functioning/therapeutic levels" that define the level of responsibility patients are prepared to assume, their privileges on the unit, and the degree of home and community exposure they can handle. The program includes no use of coercive measures (5).

During the second phase of the half-day outpatient program, the adolescents attend the unit twice a week for two weeks, with the same therapeutic components offered. The major aim of this phase is maintenance of target weight over time until final discharge (5).

INSTRUMENTS

Diagnostic information: We diagnosed patients based on clinical interviews, patients' observation, parental information and medical evaluations. The head of the unit (SF) performed all evaluations. We measured the patients' weight twice per week and height three times during hospitalization. BMI was calculated and we recorded BMI percentiles as well.

Demographic questionnaire: This self-report-questionnaire includes personal details such as gender, age, education, place of birth, nationality, religion, family status (i.e., intact family/ not intact family). In addition, the questionnaire includes items related to clinical features of the patient's eating disorder including weight, height, nutrition, minimal and maximal weight, previous hospitalizations, and onset and duration of eating problems.

Eating Disorders Examination Questionnaire (EDE-Q) (23): This self-report questionnaire assesses attitudes and behaviors related to eating disorders. It consists of 28 items that compose four subscales: weight concern, shape concern, eating concern and dietary restraint. Each item is rated on a scale of 0 (none) to 6 (every day). Higher scores reflect greater severity or higher frequency of symptoms during the previous 28 days. The sum of the subscales

provides the global score. The EDE-Q has been found to have good internal consistency and test retest reliability (24). In the current sample, Cronbach's Alpha measures of the total scale were 0.92 at admission and 0.93 at discharge.

The Beck Depression Inventory (BDI), version IA (25): The BDI is a self-report questionnaire consisting of 21 items that assess ongoing depressive symptomology. The scale covers mood, pessimism, sense of failure, lack of satisfaction, guilt feelings, sense of punishment, self-dislike, self-accusation, suicidal wishes, crying, irritability, social withdrawal, indecisiveness, distortion of body image, work inhibition, sleep disturbance, fatigability, loss of appetite, weight loss, somatic preoccupation and loss of libido. The symptoms are rated on a 0 (symptoms not present) to 3 (symptoms are severe) point Likert scale. Total scores of 0 to 9 are considered normal (i.e., non-depressed), 10 to 18 suggest mild depression, 19 to 25 – moderate depression, and above 26 – severe depression. In a meta-analysis, the estimated internal consistency in psychiatric samples was 0.86 (26). In the current sample, Cronbach's Alpha coefficients for the total scale were 0.87 at admission and 0.93 at discharge.

Suicide Ideation Questionnaire - Junior (SIQ-JR) (27): This 15-item self-report questionnaire assesses the extent of current suicidal ideation in participants as a component of suicide risk. Scores may range from 0 to 90. Items are phrased as thoughts and responses may range from 0 (I never had this thought) to 6 (almost every day). The test retest reliability is high and the internal consistency is 0.91 (28). In the current sample, Cronbach's Alpha coefficients for the total scale were 0.96 at admission and 0.95 at discharge.

STATISTICAL ANALYSIS

In order to analyze possible predictive variables, we divided the sample according to re-hospitalization (yes/no). We analyzed demographic data within these two categories (re-hospitalization – yes/no) using t-tests for independent samples for parametric variables and a chi-square test for nonparametric variables. We calculated the percentage of the weight obtained as the percent of the actual discharge weight from the Target Weight – Percent from Target Weight (PFTW). We used repeated measures analysis to compare the two groups at both time points (T1 - admission, T2 - discharge) with re-hospitalization as the independent variable.

In addition, we tested variables that significantly distinguished patients who were re-hospitalized and patients who were not re-hospitalized by using Hierarchical Binary Logistic Regressions. We entered a selection for each block in order to evaluate the relative predictive power of each significant predictor of re-hospitalization (19).

Nine out of the 51 patients did not complete the discharge assessment questionnaire (missing data). For the statistical analysis, we considered these patients as the intent-to-treat group. We used t-test for independent samples to analyze differences between those nine patients (intent-to-treat group) and the remainder of the sample. We found no significant differences between those groups in baseline characteristics, and therefore we report the full sample (N=51). In the intent-to-treat analysis, the admission scores of the nine patients who did not have the discharge assessment data were carried forward.

RESULTS

Of the 51 adolescents in the sample, 19 adolescents (37.25%) (males=1; females=18) were re-hospitalized during the first year after discharge. The average time between discharge and re-hospitalization was 5.4 months (SD= 3.8).

The percent from the target weight (PFTW) measure was found to significantly differ between the groups ($t=2.47$, $P<0.05$). In the re-hospitalization group, the PFTW was significantly lower (M=98.18%, SD=0.04%) in comparison to the non-re-hospitalization group (M=101.15%, SD=0.03%). Patients who had been hospitalized before the current hospitalization showed a higher rate of re-hospitalization relative to patients for whom the current hospitalization was their first one ($\chi^2 = 5.78$, $p < 0.05$).

In addition, patients whose parents were not married showed a higher rate of re-hospitalization ($\chi^2 = 4.401$, $p < 0.05$) relative to those whose parents were married. However, we found no significant differences between the re-hospitalization group and the non-re-hospitalization group in other demographic characteristics such as gender, age, education, weight, height, BMI at admission, onset and duration of the eating disorder (Table 1). Moreover, we found no significant differences in eating disorder symptomatology, depressive symptomology and suicidal ideation between these two groups (Table 2).

LOGISTIC REGRESSION PREDICTING RE-HOSPITALIZATION:

In a Logistic Regression, we examined the predictive power of the all variables that we found in the previous analysis to significantly differ between the groups. The block of variables included demographic characteristics such as PFTW, number of previous re-hospitalizations and parental marital status. The model and the specific variables were all significant. Taken together, these variables correctly predicted 36% of patients who were

Table 1. *Differences between Patients Who Were Re-hospitalized (N=19 (37.25%) and Patients Who Were Not (N=32 (62.74%)*

Re-hospitalization	Yes	No	Total	df	t	χ^2
Gender	Male -1 (5.2%) Female -18 (94.8%)	Male -4 (12.5%) Female -28 (87.5%)	Male -5 (9.8%) Female -46 (90.2%)	1		0.706
Age	14.60 (1.53) Range 12-17	15.21 (1.94) Range 11.8-18.8	14.98 (1.81) Range 11.8-18.8	49	1.17	
Type AN	Purging -4 (21.05%) Restrictive -15 (78.94%)	Purging -3 (9.37%) Restrictive -29 (90.62%)	Purging -7 (13.72%) Restrictive-44 (86.27%)	1		1.37
Social Economic Status	High - 0 (0%) Mid - 11 (57.89%) Low -0 (0%) Unknown -8 (42.10%)	High -2 (6.25%) Mid - 25 (78.12%) Low -1 (3.12%) Unknown -4 (12.5%)	High -2 (3.92%) Mid -36 (70.58%) Low -1 (1.96%) Unknown -12 (23.25%)	2		1.798
Place of birth	Israel - 17 (89.47%) Other - 2 (10.52%)	Israel - 30 (93.75%) Other -2 (6.25%)	Israel - 47(92.15%) Other - 4 (7.84%)	1		0.302
Family status of parents	Married -11 (57.89%) Not married -8 (42.10%)	Married -27(84.37%) Not married -5 (15.62%)	Married -38 (74.50%) Not married -13 (25.49%)	1		4.401*
Duration of illness (in years)	2.11 (3.09) Range 0-13.5	2.25 (3.3) Range 0-13.5	2.2 (3.19) Range 0-13.5	44	0.14	
Duration of Hospitalization (in days)	112 (69.58) Range -12-274	113.81 (34.83) Range -53-181	113.13 (49.96) Range -12-262	49	0.10	
Previous hospitalization	Yes -6 (31.57%) No -13 (68.42%)	Yes -2 (6.25%) No -30 (93.75%)	Yes -8 (15.68%) No-43 (84.31%)	1		5.78*
PFTW-percent from target weight	98.18% (0.04%) Range - 86.5%-104%	101.15% (0.03%) Range - 99%-109%	100% (0.04%) Range - 86%-109%	49	2.47*	
BMI admission	16.44 (1.80) Range - 12.3-19.6	16.39 (2.01) Range -13.11-22.7	16.41 (1.91) Range -12.3-22.7	49	-0.09	
BMI discharge	19.56 (1.05) Range - 16.9-21.2	19.89 (1.19) Range -17.5-23.41	19.77 (1.14) Range -16.9-23.41	49	1.01	
Weight loss (in kg)	10.55 (4.35) Range -3.5 - 22	15 (16.4) Range - 3.5 – 89	13.34 (13.34) Range -3.5 - 89	41	1.05	

*= p<0.05, **= p<0.01

Table 2. *Differences in Characteristics at Admission and Discharge between Patients with (N=19) and without (N=32) Re-hospitalization*

	T1 – Admission					T2 – Discharge				
	Yes		No		F	Yes		No		F
Re-hospitalization	M	(SD)	M	(SD)		M	(SD)	M	(SD)	
EDE total	3.66	(1.39)	3.11	(1.79)	1.11	3.13	(1.88)	2.58	(1.77)	0.80
EDE Subscales										
EDE- restraint	3.85	(1.74)	3.31	(2.30)	0.66	3.22	(2.14)	2.42	(2.10)	1.19
EDE- eating concern	2.89	(1.59)	2.58	(1.69)	0.36	2.31	(1.96)	1.84	(1.89)	0.50
EDE- weight concern	4.44	(1.77)	3.75	(2.21)	1.10	3.81	(2.52)	2.00	(1.90)	0.46
EDE- shape concern	4.83	(1.56)	3.99	(2.21)	1.76	4.37	(2.18)	3.97	(2.31)	0.26
BDI	21.00	(11.48)	19.62	(10.23)	0.17	16.46	(13.75)	13.46	(12.58)	0.45
SIQ	35.44	(23.43)	26.65	(17.41)	1.93	37.92	(19.36)	31.75	(21.22)	0.76

*= p<0.05, **= p<0.01

re-hospitalized (χ^2=15.84, p<0.01). Table 3 presents the Logistic Regression for prediction of re-hospitalization.

DISCUSSION

The aim of the current study was to examine whether the percentage of actual weight at discharge from the recommended target weight during inpatient intensive weight restoration predicts re-hospitalization among adolescent diagnosed with AN. The main finding of this study is that PFTW at discharge was significantly lower among patients who were later re-hospitalized (the re-hospitalization group) relative to patients who were not. Patients in the re-hospitalization group reached discharge in a weight that was lower than their recommended target weight.

Table 3. *Logistic Regression Predicting Re-hospitalization:*

	β	Var. Sig.	Chi-square	Model Sig.	Nagelkerke R Square
	block1 - demographic		15.84**	0.00	0.36
PFTW	-19.53	0.041*			
Parents Marital Status	-1.58	0.038*			
Previous Hospitalization	-1.97	0.038*			

*= p<0.05, **= p<0.01

This finding is in line with previous studies, conducted with adult samples, that highlighted the importance of full weight restoration during inpatient stays (15-17). A study on adults with AN found that patients who achieved 90% or less of their target weight at the time of transfer to a day hospital program were more likely to be re-hospitalized (16). The current study further demonstrates that reaching the target weight in full is also highly important among adolescents. It seems that even little less than 100% of target weight means a higher risk for re-hospitalization. This finding is in line with the recommendation by Howard et al. (16), who recommend a restoration of 100% of the target weight before transferring a patient to a less intensive level of care. They further claim that reaching less than normal body weight at discharge from inpatient settings is one of the most important predictors of short-term anorexic relapse.

Traditionally, the field of AN has focused on the significance of objectively low body weight, often measured by body mass index (BMI) (29). In contrast, we did not find BMI at admission and discharge to be variables with significant predictive power. This finding is consistent with a previous study (19) and partially consistent with Salbach-Andrae et al. (20), who found BMI at admission, but not at discharge, to be an important factor for outcome prediction. Based only on height and weight, without accounting for unique phenomena such as short stature or stunted linear growth due to malnutrition, BMI may be less sensitive of a measure (29), particularly with adolescents. It is also possible that a relative weight measure such as PFTW is more effective than BMI in measuring clinical outcomes such as re-hospitalization.

Our study also indicates that 37.25% of adolescent patients with AN were re-hospitalized during the first year following their discharge from inpatient treatment. This rate is higher than the rate found in the study by Castro et al. (19), which similarly examined re-hospitalization among adolescent patients within one-year follow-up. The higher re-hospitalization rate in our study may be explained by differences between our sample to the one used by Castro and colleagues. Castro et al.'s sample included patients who had their first inpatient stay and reached discharge after achieving a complete weight recovery. By contrast, in our sample eight patients (15.68%) had previous hospitalizations and 13 (25.5%) did not obtain target weight at discharge.

An additional finding of our study indicates the significant correlation between family status and re-hospitalization. This finding is consistent with findings from previous studies (30, 31). Perhaps single or divorced parents have fewer resources to prevent relapse. Perhaps such parents fit less well to deal with the specific demands characterizing the recovery process of anorexic patients (e.g., supervised home meals). However, it seems difficult to form any firm conclusions about the association between family status and re-hospitalization without a better understanding of variables such as perceptions of family relations and attachment style.

Unlike other studies, no significant demographic differences were found between patients in the different groups. For example, age predicted re-hospitalization in the study by Castro et al. (19), but in our study, we found only a non-significant trend toward a higher re-hospitalization rate among younger patients. AN subtype was also not found to have a predictive value. In this regard, it is noteworthy that only 13.71% of the patients in our sample were purging, a lower rate in comparison to the study by Castro-Fornieles et al. (32), in which 25% of patients were with AN, purging subtype. Due to the small number of purging patients in our sample, it is difficult to draw conclusions regarding the role of AN subtype.

The current study has several limitations. First, it included a small sample size that may preclude conclusions regarding negative findings. However, we conducted a retrospective power analysis which indicated that the effect size between re-hospitalization and non-hospitalization groups in PFTW was large (Cohen's d=5.99). Second, the study has a relatively short follow-up period. It is possible that a longer follow-up would yield different outcomes. Third, we measured psychological variables by using only self-report questionnaires, which are exposed to self-report biases. Fourth, we did not include measurement of perceptions of family relations and attachment style that could provide a better understanding regarding the role of the family in adolescent AN. Lastly, although we tried to obtain information on re-hospitalization from several sources, some of the information may remain confidential.

Despite these limitations, our study highlights the importance of achieving full target weight during inpa-

tient treatment of adolescent AN for prevention of relapse and re-hospitalization. Our results indicate that reaching even 98% of the target weight might not be sufficient. This missing 2% (which usually means a small difference of only 1kg or less) has a significant impact on the clinical outcome and can help in the prediction of re-hospitalization. Therefore, premature discharge, without reaching the target weight, may contribute to the probability of relapse and re-hospitalization. These results highlight how important it is for policy makers to aim for longer hospitalization, enabling patients to achieve target weight in full during hospitalization. Moreover, patients and their families should receive psycho-education about the importance of achieving full target weight.

Authors' contributions

- **IH,** conception and design, analysis and interpretation of data.
- **ABS,** conception and design, interpretation of data, critical revision, final approval.
- **GG,** conception and design, critical revision, final approval.
- AH, conception and design, and interpretation of data, critical revision, final approval.
- **MH,** conception and design, critical revision, final approval.
- **SF,** conception and design, interpretation of data, critical revision, final approval.

The authors declare that they have no competing interests.

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Search Activity in Anorexia Nervosa and Bulimia Nervosa in the Acute Stage of the Illness and Following Symptomatic Stabilization

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ABSTRACT

Background: We examined problem-solving strategies in anorexia nervosa-restricting (AN-R) type and in normal weight binge/purge (B/P) eating disorders (EDs).

Method: Twenty-four inpatients with AN-R and 22 with B/P EDs were assessed within two weeks of admission and two weeks from discharge for problem-solving, ineffectiveness, ED symptomatology, depression and anxiety; 32 controls were similarly assessed once.

Results: While we found less adaptive problem-solving strategies in patients with B/P EDs vs. controls at baseline, no such difference emerged for patients with AN-R. An improvement from admission to discharge in problem solving, depression and trait-anxiety was found for the B/P but not the AN-R group.

Conclusions: Patients with AN-R and B/P EDs show different profiles of problem-solving strategies both in the acute stage of their illness and following symptomatic stabilization.

INTRODUCTION

INEFFECTIVENESS

Eating disorders (EDs) are mental disorders with grave long-term consequences on one's physical and emotional health (1). An important focus of concern in patients with EDs relates to their often-pervasive sense of ineffectiveness (2, 3). Ineffectiveness is defined as an overall sense of inadequacy, incompetence, helplessness, negative self-perception, mistrust and low self-esteem (3-10). Several studies have found that in comparison to controls, women with both anorexia nervosa (AN) and bulimia nervosa (BN) report of a greater sense of ineffectiveness (5, 11-15). Ineffectiveness in patients with AN and BN has been shown not only with respect to ED-related issues, i.e., feeling unable to control eating-related urges despite exerting great efforts for control, but also in the individual's professional life and relations with others (11-15). Interestingly, Wagner et al. (11) have found no association between ED-related and a more general sense of ineffectiveness. By contrast, Espelage et al. (15) have found a significant correlation between the severity of ineffectiveness in the areas of eating/weight and in other domains. In addition, whereas one study has found no differences in ineffectiveness in AN vs. BN patients (15), another study has shown greater ineffectiveness in BN (16).

SEARCH ACTIVITY

Problems in search activity (SA) may be potentially akin to ineffectiveness. However, ineffectiveness relates mainly to a sense of inadequacy, based on personality-related propensities of reduced motivation (17), rigidity and avoidance (18), and an emotional basis of helplessness (12, 14), faulty self-perception and low self-esteem (5). By contrast, the search activity (SA) concept (19-21) proposes a neurocognitive conceptualization to the classification of adaptive and maladaptive problem-solving

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strategies. SA is designed to change the situation and/or the subject's attitude to it. It assumes that trying to obtain control (although not necessarily achieving it) provides immunity against helplessness. In contrast, a person making no effort to actively seek a solution is at greater risk for helplessness (19-21).

Rotenberg (19-21) conceptualizes that individuals may choose out of four problem-solving strategies in problematic situations: 1) *SA* – active search for a solution in an unclear situation, integrating ongoing feedback between the chosen behavior and its potential consequences; 2) *Stereotypic strategy* – active behavior chosen because it is grounded in habit and because its consequences can be predicted with certainty; 3) *Chaotic strategy* – active behavior chosen without the search of feedback between the behavior and its consequences, leading to lack of control over the stressful situation; 4) *Passivity* – passive renunciation of active search for a problem-solving strategy, with the expectation that the solution will come from sources outside of the individual.

Both SA and stereotypic behavior are conceptualized as active, goal-oriented, adaptive forms of behavior. The advantage of SA over stereotypical behavior is in its flexibility and creativity in terms of the choice of the solution, which allows for changing the strategy if necessary. Both chaotic behavior and passive renunciation are conceptualized as maladaptive problem-solving strategies (19-24).

According to the SA concept, people may use these four strategies in different combinations. Nevertheless, in every situation, they have one method which they prefer and another method which they reject.

AIMS AND HYPOTHESES

The aim of the present study was to assess ineffectiveness and SA in patients with EDs. Patients with restricting type anorexia nervosa (AN-R) are characterized with active goal-oriented behavior, persistence and over-control (18, 25), yet also with obsessionality, perfectionism, rigidity (18, 25-28) and a tendency to avoid changes (27-29). This constellation may lead to a heightened tendency to use stereotypic behavior in situations requiring problem-solving. Thus, we suggest that compared with healthy individuals, patients with AN-R will make less use of SA and more use of stereotypic behavior.

Unlike patients with AN-R, those with binge/purge (B/P) type EDs are characterized, in addition to the aforementioned characteristics, also with impulsivity and affective and behavioral dysregulation (25, 30-35), likely leading to fluctuations between behavioral (25) and emotional (30, 34, 35) extremes. Thus, we suggest that patients with B/P EDs may solve problems with increased use of chaotic behavior and passive solutions.

Accordingly, the following are our hypotheses:

Patients with EDs in the acute phase of their illness will use more pathological problem-solving strategies and will show greater ineffectiveness than control participants.

Patients with B/P EDs will use more pathological problem-solving strategies and will show greater ineffectiveness than patients with AN-R in the acute phase of the illness.

Problem-solving and ineffectiveness will be negatively correlated in all participants both on admission and discharge.

Patients with more severe ED and comorbid symptomatology will show more dysfunctional problem-solving strategies, both in the acute phase of their illness and following symptomatic stabilization.

Patients with both ED types will show an improvement in their problem-solving strategies and reduction of ineffectiveness upon the stabilization of weight and disordered eating. Nonetheless, because patients with AN-R are less disturbed than patients with B/P EDs at baseline, we expect them to show more adaptive and less maladaptive problem-solving also upon the improvement of their ED.

METHODS

We used a two-stage design. In the first stage we compared acutely-ill ED patients with normal controls. In the second stage, stabilized ED patients were compared to the acutely-ill condition.

POPULATION

The study group included 46 female adolescents with EDs, aged 13 to 18, hospitalized in the Pediatric Psychosomatic Department at the Safra Children's Hospital, Sheba Medical Center, Tel Hashomer, Israel. Twenty-four patients were diagnosed with DSM-V (36) AN-R, and 22 with normal weight B/P EDs (girls with AN-B/P were not included in the study either because they refused to participate or they were released before the end of treatment).

Inclusion criteria were: 1. female gender; 2. being over the age of 13; 3. good understanding of the Hebrew language; 4. parents and patients agreeing to participate in the study, including in the follow-up assessment; and 5. completing inpatient treatment. *Exclusion criteria* were lifetime or current schizophrenic spectrum disorder, bipolar disorder, substance use disorder, organic–brain

disorder, mental retardation, and lifetime or current medical illness potentially affecting appetite or weight (e.g., diabetes mellitus or thyroid disorders).

The control group included 32 female adolescents aged 13 to 18, recruited from families of the staff of the Sheba Medical Center. Inclusion criteria for control participants were: 1. absence of lifetime or current psychiatric disorders, medical disorders or chronic medication use; 2. no stigmata indicative of an ED; and 3. regular menses since menarche. The weight of adolescent controls had to be over 85% of ideal body weight according to the sex-specific growth charts from the CDC in 2000 (www.cdc.gov/growthcharts), found adequate also for Israeli youngsters (37). Controls were matched to the research patients by age, fathers' and mothers' country of birth, and economic status (defined by the participant on a four-point scale, where 1 represents the best and 4 the worst condition).

INSTRUMENTS

INTERVIEWS

The presence of EDs and other psychiatric disorders in the research patients, and their lack in the control participants, was established using the Structured Clinical Interview for Axis I DSM-IV Disorders–Version 2.0 (SCID-I I/P, Version 2.0) (38). The diagnoses were adapted for the DSM-V (36).

QUESTIONNAIRES

Problem-solving has been evaluated using the Behavioral Attitudes and Search Evaluation (BASE) questionnaire (39). Participants are presented with 16 situations requiring solutions. In each situation, the participant is offered four problem-solving solutions: search activity (SA), stereotypic behavior, chaotic behavior and passive renunciation. For each situation, participants are required to select their most preferred solution and their least preferred/most rejected solution. Each solution gets one point. The range of the BASE score is from +16 (one solution is preferred in all 16 points) to 16 (one solution is rejected in all 16 situations). The test situations are indefinite, so that no solution is more advantageous than others, i.e., all four solutions look equally acceptable (20, 39).

An example for the different solutions follows. A child is unable to answer a question in his homework. The family seeks advice. 1. It is a very hard question. Leave it for now and tomorrow ask the teacher to explain to you how to solve it (passive renunciation). 2. Repeat your solution once again, but this time be careful not to make any mistakes (stereotypic strategy). 3. Make a diagram of the question. Maybe it will help you to find a new solution (SA). 4. Try to do something with the data. Maybe you will be able to answer the question eventually (chaotic solution).

For the present study, we have constructed two additional measures: one measure reflects the combined use of SA and stereotypic behavior, both representing adaptive goal-oriented behavior. The other measure reflects the combined use of chaotic behavior and passive renunciation, both representing maladaptive strategies. The internal consistencies of the 6 scales of the BASE range between a=0.80 -a=0.92. Previous studies have verified the validity of the BASE in differentiating between men and women (19, 21), younger and older adolescents (23, 24), and normal controls from patients with somatic, psychosomatic, anxiety and depressive disorders (19-22, 24, 39). To the best of our knowledge, SA has not as yet been studied in EDs.

Ineffectiveness was evaluated using the ineffectiveness scale of the **Eating Disorder Inventory-2 (EDI-2)** (5) that has been shown to successfully differentiate Israeli people with and without EDs (40). The internal consistency of the EDI-2-Ineffectiveness scale (EDI-2-I) was a=0.91.

Severity of pathological eating behavior was assessed using the **26-items Eating Attitudes Test** (**EAT-26)** (41). This scale assesses pursuit of thinness, dieting, restricting and binge/purge behaviors, and was previously shown to successfully differentiate Israeli patients with and without EDs (42). The internal consistency of the EAT-26 in the present study was a=0.92.

Depression was assessed using the 21-item **Beck Depression Inventory-II (BDI-II)** (43). **Anxiety** was assessed using the 40-item **State-Trait Anxiety Inventory (STAI)** (44) that measures the severity of anxiety at the time of examination (STAI-State) and the general tendency to display anxiety (STAI-Trait). Both scales were previously used in patients with EDs (45), including in Israeli samples (40). The internal consistencies of the BDI, STAI-State and STAI-Trait in the present study were a=0.90, a=0.95 and a=0.96, respectively.

PROCEDURE

Participants and parents, in the case of minors under the age of 18, signed a written informed consent, after the aims of the study were explained. The study was approved by the Helsinki Committee of the Sheba Medical Center. Participation was voluntary and anonymous.

Patients were interviewed on admission with the SCID-I/P Version 2.0 (38) independently by two experienced child and adolescent psychiatrists (DS, AHL). The degree of inter-rater reliability (according to the correlation coefficient procedure) between the two psychiatrists for the diagnosis of an ED and comorbid psychiatric disorders was r=0.92, and r=0.89, respectively. Diagnoses were confirmed in clinical meetings of the department's team. The study's questionnaires were distributed in a random order by master's level clinical psychology students within two weeks of admission, when the patients' medical condition was stable. The height of the patients was assessed monthly, and their weight weekly during the morning hours until discharge, according to standardized procedures.

The second assessment occurred within two weeks from discharge. To be discharged from inpatient treatment, patients with AN-R were required to have reached their required weight and maintain it for two consecutive weeks. Patients diagnosed with normal weight B/P EDs were required to be abstinent from B/P behaviors for two consecutive weeks according to their recordings in daily food monitoring sheets. Body mass index (BMI) for patients with AN-R was at least 19 kg/m^2 at discharge.

Controls were similarly interviewed by a master's level clinical psychologist (YN) who was trained by the principal investigator (DS). This researcher also administered the study's questionnaires to the controls. The weight and height of the controls were taken last according to standardized procedures, to reduce their influence on the study's findings.

STATISTICAL ANALYSIS

Data was coded and analyzed using SPSS software, version 11.01. Differences among the control and the two research groups on admission were analyzed using multivariate analysis of variance (MANOVAs). Tukey's post-hoc comparison tests were used to examine the specific differences among the three groups.

At the second stage of the study, changes from admission to discharge for the AN-R and B/P type ED patients were analyzed using ANOVA with repeated measures (ED groupXtime). The correlations among problem-solving and other variables on admission and discharge, as well as the correlations between the changes in these variables from admission to discharge, were assessed using Pearson Coefficient Correlations for numerical data, Spearmen rho's for ordinal data and chi-square analyses for categorical data.

RESULTS

No differences were found in the various measures assessed among the 18 patients with BN and the four patients with purging disorders. We therefore related to this cohort as one group diagnosed with normal weight B/P EDs.

DEMOGRAPHIC AND CLINICAL PARAMETERS

Between-group differences were found for the demographic and clinical dimensions [$F(5,148)=4.5$, $p<0.01$]. Specifically, the BMI of females with AN-R (M=14.96, SD=1.6; range 13-16 kg/m^2) was significantly lower than that of B/P ED (M=21.76, SD=3.2, range 18-22 kg/m^2) and control participants (M=20.9, SD=2.7, range 19-22 kg/m^2). Second, patients with AN-R were younger (M=14.8, SD=1.35) than both B/P ED (M=16.18, SD=1.4) and control participants (M=16.28, SD=1.44). Third, AN-R (M=1.25, SD=0.44) and control participants (M=1.38, SD=0.57) reported of a higher socioeconomic status than females with B/P EDs (M=1.86, SD=0.71). Nonetheless, no significant correlations were found among the baseline BASE strategies and BMI, age or socioeconomic status (results not shown). No significant differences were found among participants with AN-R, B/P EDs and controls in paternal and maternal country of origin (results not shown).

BASELINE FINDINGS

SEARCH ACTIVITY (SA)

All three groups used all four problem-solving strategies, and chose, or rejected, each of these strategies at least once. Nonetheless, significant between-group differences were found for the BASE [$F(6,148)=3.0$; $p<0.01$]. Whereas no differences were found for SA, stereotypic behavior and chaotic behavior (results not shown), we found significant between-group differences in the use of passive renunciation. Specifically, patients with B/P EDs rejected the passive strategy less (M= -0.73, SD=2.7) than control participants (M= -3.81, SD=3.99). Patients with AN-R, although tending to reject the passive solution, were not different from the other two groups (M=-3.46, SD=3.07)

In addition, significant differences were found between patients with B/P EDs and controls when combining the adaptive (SA + stereotyped behavior) vs. the maladaptive strategies (chaotic behavior + passive behavior). Specifically, patients with B/P EDs rejected the adaptive forms of behavior (M= -0.27, SD=3.4), whereas the control participants adopted them (M= 2.74, SD=3.1). Patients with AN-R, although tending to adopt the adap-

tive solutions, were not different from the two other groups (M=1.08, SD-3.5). By contrast, females with B/P EDs used maladaptive problem-solving strategies (M= 0.27, SD=3.4), whereas the control group rejected them (M= -2.74, SD=3.1). Patients with AN-R, although tending to reject the maladaptive solutions, were not different from the other two groups (-1.08; SD=3.5).

ED-RELATED AND COMORBID PARAMETERS

Significant between-group differences were for EAT-26, EDI-2-I, BDI, STAT-State, and STAI-Trait [F(10,132)=6.6, p<0.001]. For all scales, patients with both AN-R and B/P EDs fared worse than controls (see Table 1).

A full negative correlation (r= -1, p< 0.001) was found on admission between the combined adaptive and maladaptive problem-solving strategies. In addition, in AN-R and control participants, SA correlated negatively with passive renunciation. Third, in patients with B/P EDs, chaotic behavior correlated negatively with passive renunciation (results not shown). Fourth, for all groups, elevated EDI-2-I on admission was associated with less use of adaptive strategies (r= -0.376, p<0.05), and with greater use of maladaptive strategies (r= 0.376, p<0.05). Last, among girls with B/P EDs, higher STAI-State was associated with less use of adaptive strategies (r= -0.47, p<0.05), and with greater use of maladaptive strategies (r= 0.47, p< 0.05).

Table 1. *Between-group differences in eating behavior and comorbid variables on admission*

Variable	Group	Mean	SD
EAT-26	Controls[a]	8.16	6.89
	AN-R[b]	36.17	19.35
	B/P[b]	38.24	19.84
BDI-II	Controls[a]	4.78	7.35
	AN-R[b]	21.60	12.12
	B/P[b]	26.95	14.99
STAI-State	Controls[a]	36.81	9.47
	AN-R[b]	55.39	12.93
	B/P[b]	53.80	16.71
STAI-Trait	Controls[a]	37.47	8.94
	AN-R[b]	51.09	10.93
	B/P[b]	57.71	14.99
EDI-2-I	Controls[a]	1.64	2.64
	AN-R[b]	9.43	7.96
	B/P[b]	12.62	9.01

Note: AN-R: anorexia nervosa restricting type; B/P: binge/purge eating disorders; EAT-26: Eating Attitudes Test-26: BDI-II: Beck Depression Inventory-II; STAI: State Trait Anxiety Inventory; EDI-2-I: Eating Disorders Inventory-2-Ineffectiveness; Means with different letters indicate significant between-group differences (p < 0.05). Means with similar letters indicate no significant between-group difference in the respective column

SECOND STAGE: DIFFERENCES BETWEEN ADMISSION AND DISCHARGE

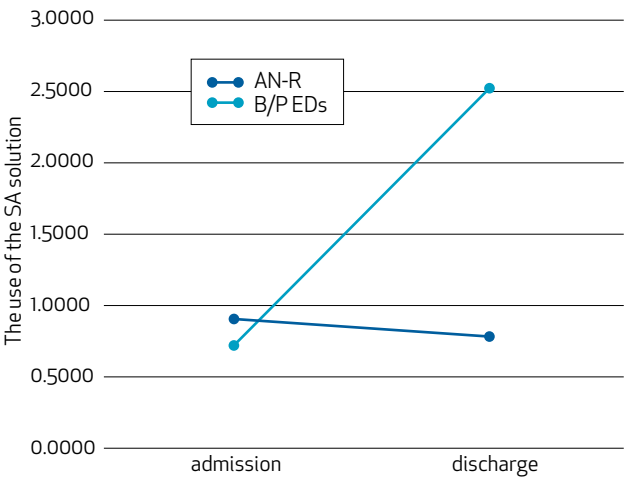
All ED participants evaluated at baseline were also assessed at discharge. A significant increase from baseline was found at discharge in the BMI of patients with AN-R (19.5±0.6 kg/m^2). No significant change was noted at discharge in the BMI of patients with B/P EDs [21.09±1.28 kg/m^2; F(groupXtime)(1)=7.8, p<.0001].

With respect to the problem-solving strategies, we found a groupXtime effect only for SA [F(groupXtime)(1)=6.3, p<0.001). Specifically, whereas no change was found for the AN-R group, patients with B/P EDs used the SA strategy to a significantly greater extent when being symptomatically stabilized, compared to the acutely-ill condition (see Figure 1).

No significant findings were reported for stereotypic behavior. For chaotic behavior, we found separate time [F(1)=4.5, p<0.05) and group [F(1)=13.44, p<0.01] effects but no interaction. Both groups improved from admission to discharge, although improvement was more robust for the B/P ED group. For passive renunciation, there was only a group effect [F(1)=5.9, p<0.02], with B/P patients showing a tendency to improve and AN-R a tendency to deteriorate from admission to discharge.

A groupXtime interaction was also found when combining the two adaptive [F(1)=4.7, p<0.05] and the two maladaptive [F(1)=4.7, p<0.05] problem-solving strategies. Specifically, patients with B/P EDs showed greater

Figure 1. *The use of the SA solution over time in inpatients with AN-R and B/P EDs*



Note: SA: Search Activity, AN-R: anorexia nervosa restricting type. B/P EDs: binge/purge eating disorders

use of adaptive, and lesser use of maladaptive strategies from admission to discharge, whereas no change was shown for patients with AN-R (see Figures 2, 3).

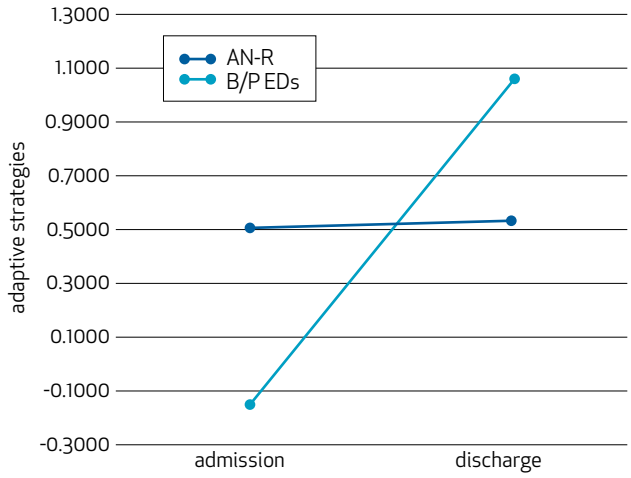
Insert Figures 2,3 about here

A groupXtime interaction was found also for BDI [F(1)=9.6, p<0.01] and STAI-Trait [F(1)=7.4, p<0.01]. For both parameters, an improvement was shown from the acute stage of the illness to symptomatic stabilization in B/P ED patients, whereas no change was found in the AN-R group (Figures 4, 5). These patients remained significantly depressed and anxious at discharge.

Insert Figures 4,5 about here

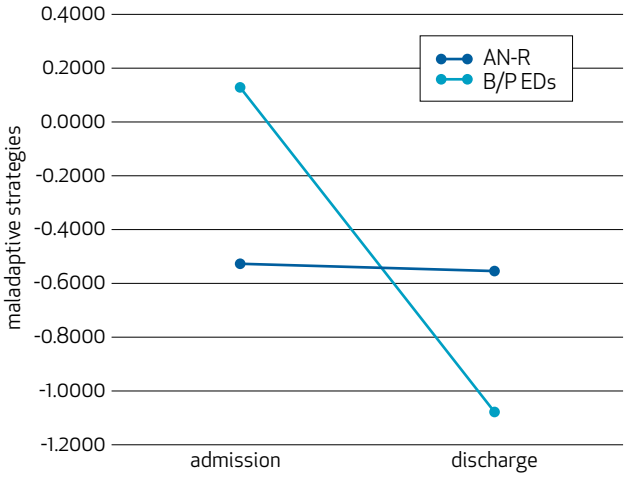
A time effect was shown for the EAT-26 [F(1)=5.6, p<0.5] and STAI-State [F(1)=8.5, p<0.01], with both

Figure 2. *The use of adaptive strategies over time in inpatients with AN-R and B/P EDs*



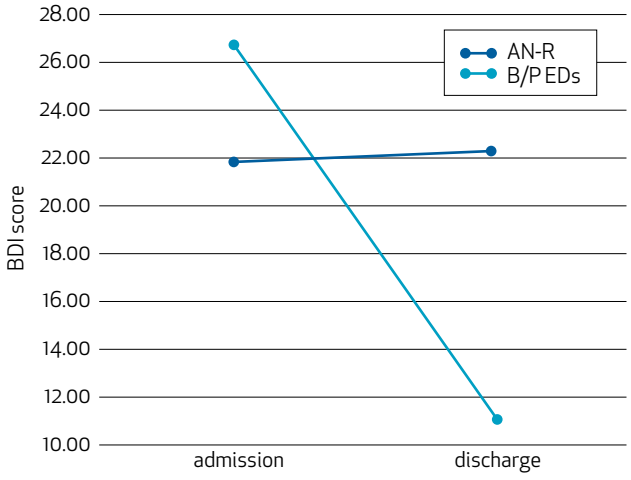
Note: AN-R: anorexia nervosa restricting type; B/P EDs: binge/purge eating disorders

Figure 3. *The use of maladaptive strategies over time in inpatients with AN-R and B/P EDs*



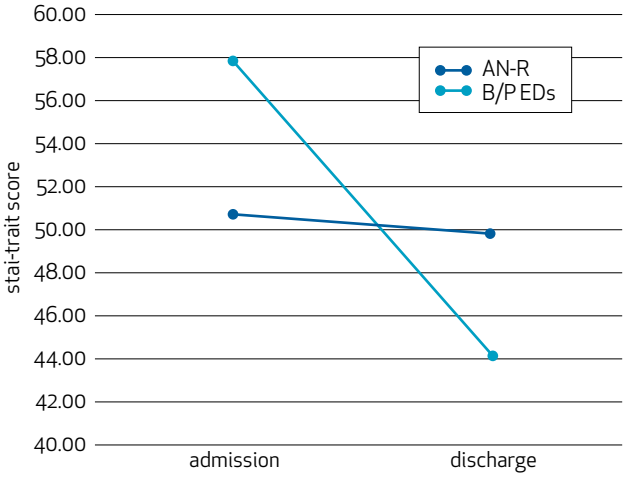
Note: AN-R: anorexia nervosa restricting type; B/P EDs: binge/purge eating disorders

Figure 4. *BDI-II score over time in inpatients with AN-R and B/P EDs*



Note: AN-R: anorexia nervosa restricting type. B/P EDs: binge/purge eating disorders; BDI=II: Beck Depression Inventory-II

Figure 5. *STAI-Trait score over time in inpatients with AN-R and B/P EDs*



Note: AN-R: anorexia nervosa restricting type. B/P EDs: binge/purge eating disorders; STAI: State Trait Anxiety Inventory

ED groups showing an improvement from admission to discharge. No significant findings were shown for EDI-2-I.

With respect to discharge correlations, we found a full negative correlation (r= -1, p< 0.001) between the combined adaptive and maladaptive problem-solving strategies. No correlations were shown between the combined BASE strategies and any of the other variables in patients with AN-R (results not shown). One correlation was found for patients with B/P EDs, in that BMI was negatively associated with the adaptive BASE combination (r= -0.595, p<0.01), and positively associated with the maladaptive BASE combination (r= 0.595, p<0.01).

Correlations were found for the AN-R group between all psychometric parameters assessed on admission and discharge except for chaotic behavior and EDI-2-I (results not shown). By contrast, only one correlation was found in patients with B/P EDs, in that EAT-26 scores on admission and discharge were significantly correlated (results not shown).

PREDICTION

In patients with AN-R, the use of adaptive strategies at discharge was associated with the use of these strategies at baseline (r= 0.668, p<0.01), and rejected by the use of maladaptive strategies at baseline (r=-0.668, p<0.01). The opposite pattern was found for the use of maladaptive strategies at discharge (results not shown). No associations were shown in patients with B/P EDs between the use of adaptive/non-adaptive strategies at discharge and any of the premorbid/baseline data assessed (results not shown).

Last, assessing the associations between the changes from admission to discharge in problem solving vs. the other variables, we found that decrease in passive renunciation was positively associated with a similar decrease in EAT-26 (r=0.37, p<0.05) and STAI-Trait (r=0.36. p<0.01).

DISCUSSION

The aim of this study was threefold: to assess whether problem-solving would differ among acutely-ill female adolescent inpatients diagnosed with AN-R and B/P EDs, and healthy controls; to assess whether maladaptive problem-solving strategies in patients with EDs would improve upon weight restoration and stabilization of ED symptoms; and to assess the factors putatively associated with these findings.

THE ACUTELY-ILL CONDITION

Our first hypothesis was partly confirmed. Thus, no between-group differences were found between baseline SA, stereotypic behavior and chaotic behavior. Only passive renunciation was rejected less by patients with B/P EDs than by control participants. In addition, patients with B/P EDs rejected the adaptive forms of behavior (goal-directed + stereotypic behavior) and adopted the maladaptive strategies (chaotic behavior + passive renunciation), whereas an opposite pattern was shown for the control group. In contrast to our second hypothesis, patients with AN-R were not different from the other two groups in any of the problem-solving measures. These findings suggest that except for renunciation of search, it is the different use of active vs. non-active strategies in general, rather than a specific strategy, that distinguishes patients with B/P EDs from controls.

Second, contrary to our third hypothesis, we have found a different baseline profile for ineffectiveness vs. problem-solving, in that EDI-2 ineffectiveness is more pathological in both patient groups compared with the controls. This suggests that in keeping with the only moderate correlations found between baseline EDI-2-Ineffectiveness and the BASE dimensions, the two constructs may represent different aspects of overall ineffective handling of problems. As noted earlier, ineffectiveness likely reflects a sense of inadequacy based on personality-related and emotionally-related propensities of reduced motivation, rigidity, avoidance, helplessness, faulty self-perception and low self-esteem (5,17,18, 27, 31). By contrast, SA is a neurocognitive construct, reflecting the person's problem-solving capacities in everyday functioning.

Some suggest that comorbid depression and anxiety may interfere with the ability of patients with EDs to problem-solve above and beyond the influence of the ED per se (46, 47). Our findings may support this contention, in that elevated anxiety in patients with B/P EDs has been associated with the use of less adaptive methods. Nonetheless, other studies show that women with EDs may reveal greater ineffectiveness in solving problems even when the effect of depression is controlled (12,13,15, 48).

While we have shown greater disturbance in problem-solving between females with B/P EDs and controls, no such difference has emerged for patients with AN-R. One explanation is that the B/P variant usually represents as a more severe form of an ED than AN-R, at least with respect to comorbid psychiatric and personality disorders (25, 30, 35). Alternatively, whereas acutely-ill girls with AN are actively and relentlessly attempting to control their weight (6-8), acutely-ill girls with B/P EDs usually

feel overwhelmed in losing control over their eating (34, 46). These differences may occur although both groups have shown similarly high baseline levels of ED-related pathology, depression, anxiety and ineffectiveness.

CHANGE FROM ADMISSION TO DISCHARGE

Contrary to our fifth hypothesis, we found a different profile of change from admission to discharge in patients with AN-R vs. B/P EDs. Thus, a groupXtime interaction was found for SA, adaptive and maladaptive problem-solving, depression and trait-anxiety. For all variables, patients with B/P EDs improved significantly, whereas no change was found in patients with AN-R. A significant improvement from the acute condition of the ED to weight and symptomatic restoration in both groups was found for chaotic behavior, eating-related pathology and state-anxiety.

The improvement in problem-solving in patients with B/P EDs and the reduction in depression and anxiety may be related to a decrease in their uncontrollable B/P behaviors. Other studies of our group have similarly shown that the decrease in disordered eating in stabilized B/P ED in comparison to the acutely-ill condition may lead to greater organization exemplified in reduction of disorganized thinking and greater emotional control (49). By contrast, patients with AN-R, who must gain weight against their will, may feel helpless in losing their sense of control over their eating during hospitalization. This condition, alongside the rigid personality constellation of patients with AN-R and their inclination to avoid changes (18, 25-27, 31) may be associated with a lack of improvement in their coping, depression and anxiety, as well as in disorganized thinking (49).

Lastly, the association found between reduction in passive renunciation and reduction in disordered eating and trait-anxiety may suggest that symptomatic improvement may intervene in reducing the use of maladaptive passive problem-solving strategies.

LIMITATIONS AND SUGGESTIONS FOR FUTURE RESEARCH

The main limitation of our study concerns the relatively small sample size that has not allowed for an examination of a possible association of comorbid psychiatric disorders with the BASE dimensions. Nonetheless, we have related to the association of problem-solving with self-rated depression and anxiety, the most common comorbid disturbances in patients with EDs (35). The small number of participants has also not allowed for the assessment of factors potentially predicting the change in problem-solving from admission to discharge.

Second, there seems to be an innate problem in the BASE questionnaire, at least for the current population, in that the maladaptive construct represents the exact opposite of the adaptive profile, rather than both representing different models (a full negative correlation [r= -1, p< 0.001] has been found between the combined adaptive and maladaptive search strategies both on admission and discharge). Third, as the control participants have been assessed only once, our findings do not control for potential practice effects. Lastly, as our population includes inpatients, our findings cannot be generalized to individuals with less severe EDs.

In conclusion, the current prospective longitudinal study assessed the ability of female adolescent inpatients with AN-R and B/P EDs to effectively solve their everyday problems. We found that whereas in the acute phase of the illness, patients with B/P EDs fared worse that controls, these patients used more adaptive and less maladaptive strategies than patients with AN-R when achieving symptomatic stabilization. Future studies should include larger numbers of ambulatory patients with EDs, assessed from the acute stages of the illness to recovery, to verify whether the use of active vs. non-active problem-solving strategies would influence the course and outcome of the ED.

Contribution of the authors

Nachum Y: conception and design, analysis and interpretation of data, drafting of critical revision, final approval.

Rotenberg V: conception and design, analysis and interpretation of data, final approval.

Enoch-Levy A: analysis and interpretation of data, drafting of critical revision, final approval.

Stein D: conception and design, analysis and interpretation of data, drafting of critical revision, final approval.

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The Impact of Δ⁹-THC on the Psychological Symptoms of Anorexia Nervosa: A Pilot Study

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ABSTRACT

Background: Δ⁹-Tetrahydrocannabinol (Δ⁹-THC) is the active compound of *Cannabis sativa* with appetite-stimulating properties. This study evaluated the effect of low doses of oral Δ⁹-THC on self-reported symptoms of patients suffering from chronic anorexia nervosa (AN).

Methods: Nine female subjects over 18 years of age participated in the study. Six were diagnosed according to DSM-IV criteria with AN restrictive type and three with active AN binge-purge type. Their mean age was 45.0±3.2 years and their BMI was 16.1±1.6 kg/M². They completed questionnaires before and after treatment with Δ⁹-THC (1 mg/day for one week and 2 mg/day for three weeks). The primary outcome was improvement in the way patients perceived their eating behavior.

Results: Significant improvements were found in self-reported body care, sense of ineffectiveness, asceticism and depression. There were no significant changes in BMI.

Conclusions: Δ⁹-THC may be an effective component in treating the psychological symptoms of AN.

INTRODUCTION

Anorexia nervosa (AN) is a psychiatric illness characterized by an abnormally low body weight, intense fear of gaining weight and a distorted perception of body weight. Diagnostic criteria also include refusal to maintain weight at or above a minimally normal weight for age and height, or failure to reach expected weight; fear of gaining weight despite being underweight; disturbances in body perception, or undue influence of weight and shape on self-evaluation, or denial of the seriousness of low weight, and amenorrhea (DSM-IV, 1994). AN usually starts as a restricting subtype, with 30-60% of restricting patients progressing to binge-purging AN or bulimia nervosa (BN) (1, 2). The prevalence of AN in young females is 0.3-0.5% (3).

AN is associated with high rate of DSM-IV Axis I comorbidities. Between 40-70% of these patients have lifetime affective (mainly depressive) and anxiety (mainly obsessive compulsive and social phobia) disorders, and similar rates of patients with bingeing/purging AN have lifetime substance use disorders (SUDs) (4). The lifetime mortality rate in AN is between 5-20% (5), higher than that reported for most psychiatric disturbances (5).

AN is a chronic disorder with recovery occurring usually after 4-10 years (1, 2). Recovery - defined in terms of achieving normal weight, regular menstrual cycles and normal eating patterns for a period of at least one year - occurs in 40-50% of AN patients (1, 2). Despite treatment, around 20% of patients with AN show a chronic non-remitting pattern over time. Such a disease course may be associated with a long duration of illness until receiving treatment, refusal to accept and maintain treatment, severe disturbances in body image, obsessional-ritualistic eating and physical exercise, presence of purging/bingeing and comorbid disorders, maladaptive relations with family members, dysfunctional social skills, and a history of childhood sexual abuse (1, 2).

The etiological underpinnings of AN are complex and multifactorial, including social, genetic, psychological and biological predispositions (6). Understanding how severe

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weight loss might affect brain function may assist in better understanding the etiology and lead to the development of new therapeutic strategies. In order to accomplish it we have developed three experimental animal models of AN which represent different aspects of the disorder: diet restriction, activity wheel and separation stress (7-9).

The plant Cannabis sativa and its active ingredient, Δ^9- tetrahydrocannabinol (Δ^9-THC) are known appetite stimulators (8, 9). Following the discovery of the endocannabinoids anandamide and 2-arachidonoylglycerol (2-AG) (amide and ester of the essential fatty acid arachidonic acid respectively that bind to the cannabinoid receptors), we tested their effects on appetite in these mice models (10, 11). A small dose of anandamide (0.001 mg/kg) improved food consumption and cognitive function and normalized neurochemical changes caused by diet restriction in both the hypothalamus and hippocampus, responsible for appetite regulation and learning, respectively. Diet-restricted mice treated with anandamide for one week consumed 44% more food than controls and performed better in the eight arm maze test testing spatial memory (11). This was accompanied by higher norepinephrine (NE) and dopamine levels in the hypothalamus and hippocampus, serotonin (5-HT) in the hypothalamus and lower 5-HT in the hippocampus. NE turnover in the brain increased following anandamide administration and corticosterone concentrations in the plasma were normalized (11). Administration to mice of SR 141716A, an antagonist of the CB1 cannabinoid receptor, led to significant weight loss (11). These results suggested the therapeutic potential of manipulating the endocannabinoid system. Furthermore, 0.001 mg/kg Δ^9-THC given to Sabra mice increased food consumption by 22%, with some improvement of cognitive function. A decrease in dopamine and 5-HT and increase in NE were observed without any addictive effects. SR 141716A reversed these effects (8). AN is also characterized by anhedonia whereby patients experience little pleasure or reward. Reward pathways and the endocannabinoid system have been implicated in mediating food intake. The effect of sub-chronic (6 days) Δ^9-THC (0.1, 0.5, or 2.0 mg/kg/day) has been assessed on normal and high-fat diet (HFD) intake, body weight, running wheel activity (RWA), thermogenesis in brown adipose tissue (BAT) and lipid metabolism in white adipose tissue (WAT). Limited time availability of food and continuous access to running wheels led to anorexia and significantly reduced body weight. Δ^9-THC (0.5 and 2.0 mg/kg/day) stimulated food intake with moderate effect on RWA. Δ^9-THC (2.0 mg/kg/day) combined with HFD produced increased food intake, reduction in RWA, attenuation of body weight loss and changes in markers of thermogenesis in BAT and lipolysis in the WAT. The results have shown the effectiveness of the endocannabinoid system in attenuating the weight loss associated with the development of ABA by both increased food intake and reduced energy expenditure (12).

The activity-based anorexia (ABA) paradigm was optimized so that food-restricted wheel-running mice displayed anorexia, reduced body weight and disrupted activity and circadian cycles (13). The effects of Δ^9-THC and the endocannabinoid uptake inhibitor OMDM-2 were investigated in C57BL/6 mice. Daily Δ^9-THC (0.5 mg/kg) decreased survival in the ABA animals but increased feeding in the survivors, OMDM-2 (3 mg/kg) increased food intake, but not sufficiently to reverse weight loss (13).

In human subjects, studies assessing the acute appetitive effects of Δ^9-THC showed an increased intake, elevated hunger ratings and enhanced food appreciation (14-17). Gross et al. (14) compared the effects of high doses of THC (from 7.5 mg/day to 30 mg/day) and diazepam in 11 patients with primary AN after a weight loss of 25%, even though benzodiazepines may also increase food intake. The medication was discontinued over the weekend to avoid addiction, and THC-induced weight gain was slightly higher (1 kg) than observed during diazepam treatment. Three patients (27%) withdrew after experiencing severe dysphoric reactions during active treatment, suggesting that high-dose THC was not tolerated in the treatment of primary AN. Hollister et al. (15) gave Δ^9-THC to a group of patients after fasting and to a group that ate normally. Each group received 32 mg/day of Δ^9-THC that was taken in a low caloric soft drink. The study showed that Δ^9-THC significantly increased food intake.

Nelson et al. (16) showed a median weight gain of 1.3 kg over 28 days on relatively small daily doses of THC (2.5 mg) in an interventional phase II study in patients with cancer-associated anorexia. Strasser et al. (17) compared the effects of cannabis extract, delta-9-tetrahydrocannabinol, and placebo on appetite and quality of life in Adult patients with advanced cancer with cancer-related anorexia-cachexia syndrome. Cannabis extract standardized for 2.5 mg THC and 1 mg cannabidiol) or THC (2.5 mg) or placebo orally, twice daily for 6 weeks. Cannabis extract at the oral dose administered was well tolerated by these patients with cancer-related anorexia-cachexia syndrome. No differences in patients' appetite or quality of life were found either between cannabis extract, THC, and placebo or between cannabis extract and THC at the dosages investigated. Beal et al. (18) had shown long-term, safe use of dronabinol for anorexia associated with weight loss in patients with AIDS (19). Haney et al. (19) showed in a multicenter, double-blind, placebo-controlled parallel-group

trial in participants with AIDS-induced anorexia a minor weight gain in the THC group of 0.5 kg above placebo after receiving 5 mg THC daily over 6 weeks.

Bedi et al. (20) showed in HIV-positive marijuana smokers, that high dronabinol(a synthetic cannabinoid) doses safely and effectively increased caloric intake. However, repeated high-dose dronabinol appeared to result in selective tolerance to these effects. These findings indicate that HIV-positive individuals who smoke marijuana may require higher dronabinol doses than are recommended by the FDA. Andries et al. (21) investigated the orexigenic and anabolic effects of dronabinol in 25 women over 18 years with AN of at least 5 years duration. A prospective, randomized, double-blind, controlled crossover study was conducted between 2008 and 2011 at a specialized care center for eating disorders. The patients were randomized to treatment with either dronabinol-placebo or placebo-dronabinol. In addition to the standardized baseline therapeutic regimen, the participants received dronabinol, 2.5 mg twice daily for 4 weeks and matching placebo for 4 weeks, separated by a 4-week wash-out period. Primary outcome was the mean change in body weight. Secondary outcome was score changes on the Eating Disorder Inventory-2 (EDI-2). Data were analyzed for the 24 patients who completed the trial. During dronabinol treatment, participants gained 0.73 kg ($p < 0.01$) above placebo without significant psychotropic adverse events. Dronabinol significantly predicted weight gain in a multiple linear regression including EDI-2 body dissatisfaction score and leptin. EDI-2 subscale scores showed no significant changes over time. The dronabinol therapy was well tolerated. The effect of dronabinol therapy on physical activity in AN was tested by Andries et al. (22) in a randomized, controlled double-blind study. The cannabinoid agonist treatment was associated with a modest increase in physical activity in adult women with severe and longstanding AN. Additionally, there was a strong relationship between the circulating levels of leptin and physical activity in these chronically undernourished patients. Low dose dronabinol did not affect the concentration or the activity of the circulating IGF-system in women with severe and chronic AN. However, the results suggest that such treatment may alleviate the increased hypothalamic-pituitary-adrenal axis activity seen in these patients (23). The majority of trials investigating the orexigenic effects of cannabinoids (8-23) have reported increased appetite and body weight, providing evidence of the effects of CB1 agonist treatment in humans and the safety of using it in underweight individuals.

In view of the above considerations, we decided to perform a small pilot study to treat AN patients for a 4-week period of time with low doses of THC, in order to determine effects on appetite and cognition and avoid any psychotropic effects of the drug. This study is one of only three that has tried to assess the effect of THC in the treatment of AN. Taking into account the limited treatment options for severe AN and the high morbidity and mortality rate for this psychiatric disorder, and their poor cooperation in treatment, we justify this preliminary trial with a small sample size since any progress is of clinical importance.

METHODS

This research is a preliminary open-label trial with no placebo control group due to the difficulties to recruit patients with AN to cooperate in research protocols in general, and in placebo trials in particular.

Participants. Ten female volunteers aged ≥18 y diagnosed with AN according to DSM-IV criteria (1, 2) were recruited from the outpatient eating disorder treatment facility at the Rambam Medical Center, Haifa, Israel. The patients, with a mean age was 45.0±3.2 years, were suffering from chronic AN (average duration seven years). Mean body mass index (BMI) (weight and height were measured at the clinic) was 16.1±1.6 kg/m^2. The participants were examined for comorbidities including personality disorders using a structured clinical interview for DSM-IV that was reached by experienced psychiatrists via standard clinical interview procedures (MINI-SCID)(24).

Exclusion criteria included: physical and mental illnesses which might cause weight loss not related to AN, drug treatment which might increase weight, affective or psychotic mental illnesses and a history of drug/alcohol abuse during the year preceding the treatment. Ten female volunteers aged ≥18 met the entry requirements and were enrolled, six had AN restrictive type and four had AN binge purge type. Nine of the participants completed the study, with one dropout (patient 2). This participant was withdrawn after one week due to deterioration in mental state and the need for psychotropic medication.

No adverse or side effects were observed and the remaining participants showed willingness and full compliance during the course of the study. Of interest to note that during recruitment, some AN patients refused to participate because of fear of gaining weight from the minute amounts of olive oil used as a solvent for the drug. It was very difficult to recruit 10 women to participate.

All the patients were at a severe chronic state of the illness, thus the changes in psychological symptoms may count as relatively significant.

All women were receiving weekly supportive psychotherapy, biweekly nutritional therapy, and medical and psychiatric follow-up about every three months. They were in moderate to severe medical and psychiatric condition, and they had nutrition and medical supervision about once in two weeks, and psychiatric treatment as needed. They had no other treatment.

INSTRUMENTS

Participants were requested to complete the following surveys:

Eating Disorder Inventory (EDI-2) (25). The EDI-2 is a widely used 91-item questionnaire designed to provide a broad assessment of the prevalence and intensity of psychological traits known to be associated with eating disorders. The EDI-2 is organized into 12 primary scales, three of which are specific to eating disorders and nine are general psychological scales that are highly relevant to eating disorders. It also provides six composites that measure eating disorder risk, ineffectiveness, interpersonal problems, affective problems, over-control, and general psychological maladjustment. The overall Summary Score was used as a primary outcome measure. The Hebrew translation of this inventory was found valid and reliable (26).

Eating Attitude Test (EAT-26) is a widely used standardized self-report measure of symptoms and concerns characteristic of eating disorders (27). The EAT-26 has been particularly useful as a *screening* tool to assess "eating disorder risk." The tests are rated on a six-point scale in response to how often the individual engages in specific behaviors. The EAT-26 includes three subscales, oral control, dieting and bulimia, and can be scored according to subscales and total score (27).

The Beck Depression Inventory (BDI–II) is one of the most useful tools for assessing depressive symptoms in both clinical and non-clinical settings (28). It is a 21-item scale that asks responders to choose one out of four statements that best describe their feelings over the last two weeks. Responses are scored from 0-3, and total scores range from 0-63, with higher scores indicating greater levels of depressive symptomology. A score of 0-9 indicates no depression, 10-18 indicates mild depression, 19-29 indicates moderate depression and 30+ indicates severe depression (28).

The Body Shape Questionnaire (BSQ) is a 34-item instrument designed to measure concerns about body shape among young women. The BSQ is based on the notion that disturbance of body image is a central feature of both anorexia nervosa and bulimia. Although a number of assessment procedures have been developed that deal with various aspects of body image, the BSQ is one of the few measures that focus on concerns about body shape. This is especially important because concern about body shape is one of the key dimensions distinguishing the disorder of anorexia. In particular, the BSQ focuses on the phenomenological experience of "feeling fat." The BSQ can be used for both assessment purposes and to evaluate response to treatment. Responses are scored in a 6-point Likert type scale with responses ranging from "always" = 6 to "never" = 1. Scores on the BSQ can range from 34-204, with a higher score indicating more body dissatisfaction. The BSQ has demonstrated high internal consistency (29).

Spilberger State and Trait Anxiety Inventory (STAI) is a commonly used measure of trait and state anxiety (30, 31). It is used in clinical settings to diagnose anxiety and to distinguish it from depressive syndromes. It also is often used in research as an indicator of caregiver distress. Participants were instructed to avoid driving, alcohol use, psychotropic drugs and drug abuse during the course of the experiment. They were requested to report any other drug used during the four weeks of experiment. A one-hour visit at the beginning of each week included score of weight gain, caloric consumption and psychiatric evaluation.

Diagnosis and symptoms: DSM-IV diagnosis was made using the Mini International Neuropsychiatric Interview for DSM-IV Axis I Disorders (MINI) (24)**.**

PROCEDURE

The participants were initially screened for eligibility upon signing a consent form. Study assessment took place at baseline (week 0) and at the end of week 4 and included survey filling. Δ^9-THC was prepared from crystalline cannabidiol, CBD (99% purity) according to Gaoni and Mechoulam (32).

Δ^9-THC was dissolved in olive oil. The THC container was slightly heated by touching prior to administration to the patients. Each push of the bottle released one drop. In the first week of the experiment, 3 drops were administered to the patients by placing them under the tongue, each day at 16:00pm, a total of 1 mg/day. In the following three weeks, three drops were taken in the morning and three at 16:00pm each day, a total of 2 mg/day. The patients were shown how to administer it by a staff member who provide the participants an explanation about the study, possible side effects, not to drive or to take more than the dosage suggested.

Diaries were provided along with the study medication to record daily administration of the drug and feelings

concerning appetite and anxiety. The medication was given for a 4-week period. Questionnaires were administered at baseline T1 as well as at the end of intervention period, T2. The experimental protocol was approved by the Helsinki Committee of the Ministry of Health no. 1960. The procedures followed were in accordance with the Helsinki Declaration of 1975 as revised in 1983. Written consent was provided by each patient at the beginning of the study.

STATISTICAL ANALYSIS

For each survey, sub-scales concerning certain parameters were analyzed: in EDI-2 – drive for thinness (DT), bulimia (B), body dissatisfaction (BD), ineffectiveness (I), impulse regulation (IR) and social insecurity (SI), in BDI – depression rank, in BSQ – feeling and positions regarding body image, feeling of comfort as a result of touch, body care, and body protection, in Spielberger test – anxiety rank, in EAT-26 – diet, bulimia and anorexia sub-scales. Each survey was scored at week 0 and at week 4 for the same participant, in order to reveal within-subject differences as a result of the treatment with Δ^9-THC. Results were analyzed by paired Student t-tests. P value<0.05 was considered significant. Data are presented as mean ± standard error of the mean (SEM).

RESULTS

BODY WEIGHT CHANGES

The average weight gain over four weeks was 0.95kg (p= 0.24). From Table 1, it seems that the weight of most of the participants (except no. 4 whose diagnosis was EDNOS-AN and patient no. 10) actually gained weight.

EDI-2 TEST

A significant decrease in the asceticism sub-scale was observed in this test (p=0.049). The decrease in ineffectiveness sub-scale nearly reached statistical significance (p=0.08). No significant differences were found in other sub-scales (Table 2). There were no other significant differences in the total EDI-2 test between baseline and post-treatment scores.

BDI TEST

There was a significant decrease in depression rank in the Beck depression inventory test (3.12 vs 2.50, p<0.049).

BSQ TEST

A significant increase was found in body care sub-scale (p=0.02). No significant differences were observed in other sub-scales (Table 3).

Table 2. *Baseline and post-treatment scores of the EDI-2 test, including sub-scales, presented as mean ± SEM*

	baseline (week 0)	end of experiment (week 4)	p-value (2-tailed)
Drive for thinness	13.22±1.95	13.44±2.06	0.86
Bulimia	2.44 ± 1.31	3.11 ± 1.36	0.19
Body dissatisfaction	11.11 ± 2.41	11.33 ± 2.86	0.89
Ineffectiveness	15.22 ± 3.82	11.22 ± 3.37	0.08
Perfectionism	7.89 ± 1.24	7.89 ± 1.94	1.00
Interpersonal distrust	5.78 ± 1.52	7 00 ± 2.01	0.36
Internal awareness	9.22 ± 2.27	11.44 ± 3.35	0.45
Maturation fear	10.22 ± 2.36	8.22 ± 2.40	0.21
Asceticism	10.00 ± 2.46	7.06 ± 1.61	0.049
Impulse regulation	10.33 ± 2.84	12.44 ± 4.03	0.57
Social insecurity	6.89 ± 1.56	6.67 ± 0.90	0.9

Table 3. *Baseline and post-treatment scores of the BSQ test, including sub-scales, presented as mean ± SEM.*

	baseline (week 0)	end of experiment (week 4)	p-value (2-tailed)
Body image	14.22±2.53	14.67±2.53	0.76
Touch	18.33±2.6	18±2.78	0.77
Body protection	17.56±2.1	18.44±2.79	0.44
Body care	19.22±1.87	20.22±1.79	0.02

Table 1. *Baseline and post-treatment characteristics of the participants in the study*

Subject	Age (yr)	AN subtype'	Weight (kg) at week 0 (baseline)	Weight at week 4	Weight change	Height (m)
1	42	restrictive AN	40.70	40.85	+1.50	1.55
3	21	restrictive AN	28.00	32.50	+ 4.50	1.77
4	25	binge purge AN-EDNOS	57.50	56.10	-1.40	1.69
5	38	restrictive AN	38.50	38.70	+ 0.20	1.50
6	19	restrictive AN	38.10	41.50	+ 3.40	1.57
7	24	binge purge AN	50.00	52.50	+ 2.50	1.64
8	34	restrictive AN	46.40	47.60	+1.20	1.55
9	48	binge purge AN-EDNOS	57.00	57.50	+ 0.50	1.71
10	25	binge purge AN	39.50	37.00	- 2.50	1.58

EAT-26

No significant differences were found in any of the sub-scales or in the total score of this test .

SPIELBERGER STATE AND TRAIT

There were no significant changes in the anxiety rank scored in this test.

DISCUSSION

Low dose Δ^9-THC significantly improved depression rank and asceticism and body care sub-scales, with a positive effect on ineffectiveness and body weight (1.9 kg /4 weeks, $p<0.098$), but might affect also the patient's psychological traits. From the information provided in Table 1, it seems that the body weight of most of the participant (except no. 4 whose diagnosis was EDNOS-AN and patient 10), gained weight in absolute terms. This supports the hypothesis that the intervention seems to have been helpful also in terms of weight gain, but that the strength of the study was not adequate to show this. The weight changes implied that participants adopted a less restricted attitude towards body feeling and self-esteem in general, which may have caused an improved mood. This hypothesis should be examined in future research.

No side effects for Δ^9-THC were observed in the low doses used in this study in contrast to the findings for higher dosages (14). Cannabinoids may stimulate appetite and increase body weight in AIDS and cancer patients (16-23) as well as food craving (33). Nelson et al. (16) reported that 2.5mg Δ^9-THC, given orally two or three times a day to cancer patients with anorexia, resulted in an increase in food intake, in the low dosage group (two times a day). In the high dosage group (three times a day), the patients experienced severe side effects, especially dizziness and nausea. In addition, a biphasic effect was noticed in animal models, following cannabinoids agonist treatment where low doses are anxiolytic but anxiogenic in higher ones together these results support the use of lower doses as in the current pilot study.

Plasse et al. (34) reported the effect of dronabinol as an appetite stimulant in cancer patients. Results were inconsistent although some patients did actually gain weight. However, there was a reduction in the rate of weight loss in all groups, which was significant at doses of 2.5 or 5mg administered four times a day. AIDS patients, who were losing 0.93kg/month, showed a weight gain of 0.54 kg/month after receiving 2.5 mg dronabinol three times a day.

Hollister (15) gave Δ^9-THC to a group of patients after fasting and to a group that ate normally. Each group received 32 mg/day of Δ^9-THC that was taken in a low caloric soft drink. The study showed that Δ^9-THC significantly increased food intake.

The effect of Δ^9-THC on patients with AN has been evaluated using Δ^9-THC in much higher doses. In Gross et al. (14) Δ^9-THC was given three times a day to subjects with AN, and the dosage was increased over a two-week period from 7.5 mg to 30 mg (about 0.22-0.88 mg/kg). No weight increase was found in the Δ^9-THC-receiving patients in comparison with the placebo treated patients. However, Gross et al. (14) pointed out that the placebo used – diazepam - was known to cause an increase in food intake when taken in certain doses. Furthermore, at higher doses there were no significant effects on food intake, and there was a possibility of developing tolerance to the drug with cannabinomimetic side effects (14).

Andries et al. (21) investigated the effects of treatment with a synthetic cannabinoid agonist on body weight and eating disorder-related psychopathological personality traits in women with severe, enduring AN. This add-on, prospective, randomized, double-blind, controlled cross-over study was conducted between 2008 and 2011 at a specialized care center for eating disorders. Twenty-five women over 18 years with AN of at least five years duration were randomized to treatment with either dronabinol-placebo or placebo-dronabinol. In addition to the standardized baseline therapeutic regime, the participants received dronabinol, 2.5 mg twice daily for four weeks and matching placebo for four weeks, separated by a four-week wash-out period. Primary outcome was the mean change in body weight. Secondary outcome was score changes on the Eating Disorder Inventory-2 (EDI-2). Data were analyzed for the 24 patients who completed the trial. It was shown that dronabinol therapy to severe enduring patients with AN during four weeks of exposure induced a small but significant weight gain in the absence of severe adverse events. The 25 participants received dronabinol 2.5mg twice daily for four weeks, the participants gained 0.73kg above placebo without side effects. Dronabinol significantly predicted weight gain in a multiple linear regression including EDI-2 body dissatisfaction score and leptin, EDI subscale scores showed no significant changes over time. Dronabinol therapy was well tolerated. During four weeks of exposure it induced a small but significant weight gain in the absence of severe adverse events (21).

The level of physical activity is inappropriately high in up to 80% of the patients suffering of anorexia nervosa

(AN), as a result of conscious efforts to lose weight, affect regulation and biological adaptive changes to starvation induced by hypothermia and neuroendocrine mechanisms. Andries et al. (22) detected the effect of dronabinol on physical activity in patients with chronic and stable AN, and the role of leptin and cortisol in this process.

This prospective, randomized, double-blind, crossover study was conducted at a specialized care center for eating disorders. Twenty-four adult women with AN of at least five years duration received either the dronabinol-placebo or placebo-dronabinol sequence. Physical activity was monitored during the fourth week of each intervention. Body weight, leptin and urinary free cortisol excretion were measured repeatedly during the trial. Changes in behavioral dimensions related to AN were assessed by Eating Disorder Inventory-2.

The total duration of physical activity did not change, while its average intensity increased by 20% (P = 0.01) during dronabinol therapy, resulting in an increased energy expenditure with 68.2 kcal/day (P = 0.01) above placebo.

This randomized, double-blind study revealed that cannabinoid agonist treatment was associated with a modest increase in physical activity in adult women with severe and longstanding AN. Additionally, they detected a strong relationship between the circulating levels of leptin and physical activity in these chronically undernourished patients.

Andries et al. (23) detected changes in IGF-I, urinary free cortisol and adipokines during dronabinol therapy in AN: results from a randomized, controlled trial.

Cannabinoid agonists are used to treat cachexia of various causes, but their interactions with the hormonal systems that are involved in energy metabolism have not been previously described in humans. Therefore they found it of interest to assess interactions between the synthetic cannabinoid agonist dronabinol and insulin-like growth factor I (IGF-I), urinary free cortisol (UFC) and adipokines in patients with chronic AN. This was a prospective, double-blind randomized crossover study, conducted at a specialized care center for eating disorders. The results are based on 24 adult women with chronic AN who completed the study. The participants received dronabinol (oral capsules, 5mg daily) and matching placebo over four weeks, separated by a four-week washout period. Bioactive IGF was determined by a cell-based bioassay, whereas total IGF-I, IGFBP-2 and -3 and the two adipocines leptin and adiponectin were measured by immunoassays. Dronabinol treatment caused a small, yet significant increase in BMI as compared to placebo (+0.23 kg/m(2); P = 0.04). This modest weight gain predicted a corresponding increase in bioactive IGF-I, while the amount of daily energy expenditure due to physical activity had a comparable but opposite effect. Nevertheless, neither IGF-I, bioactive IGF nor the IGFBPs levels changed significantly during dronabinol intervention as compared to placebo. Adiponectin also remained unaffected by the weight gain, whereas plasma leptin showed a transient increase at three weeks (P < 0.05). Their results showed that low-dosage therapy with dronabinol affected neither the concentration nor the activity of the circulating IGF-system in women with severe and chronic AN. However, their results suggest that such treatment may alleviate the increased hypothalamic-pituitary-adrenal axis activity seen in these patients.

Montelone et al. (35) suggested that endocannabinoids are involved in food-related reward and suggest a dysregulation of their physiology in AN. Low dose Δ9-THC might normalize these systems and improve psychological symptoms before weight gain.

Following the promising results of Andries et al. (21) with dronabinol 2.5mg twice daily for four weeks, the small impact on body weight might be due to the low dose of THC administered (2.0 mg/daily), another possibility is that the THC administered contained traces of cannabidiol. Morgan et al. (36) showed that cannabidiol attenuates the appetitive effects of Delta 9-tetrahydrocannabinol in humans smoking their chosen cannabis. The ratio of THC: Cannabidiol might affect appetite. Thus, if the extract contained relatively high dose of cannabidiol it might be less effective.

Therefore, higher sample size and THC dose might result in increased body weight.

STUDY LIMITATIONS AND STRENGTHS

This study is one of only three that have evaluated the effectiveness of THC in the treatment of AN and is therefore very timely and important taking into account the limited treatment options for AN and the high morbidity and mortality rate. However this study was an open-label pilot trial with no placebo control group and with a small sample size. An additional limitation was the lack of measure of compliance with the medication regimen.

All women were receiving weekly psychotherapy, biweekly nutritional therapy, and medical and psychiatric follow-up every three months. This treatment they were receiving at the time of the intervention. It is not possible to rule out that the improvement was due to their ongoing therapy although we think that this is unlikely.

However, the present study is the first to show improvement in the psychological symptoms of patient with AN when treated with Δ^9-THC , without side effects, such as: depression rank, asceticism, ineffectiveness and body care. All the patients were at a severe chronic state of the illness, thus the changes in psychological symptoms may count as clinically important. These encouraging results on a group of chronic AN patients suggest that low doses of Δ^9-THC should be further studied as an adjunct to the treatment of patients with AN.

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A Double Blind, Randomized Cross-Over Trial of Tyrosine Treatment on Cognitive Function and Psychological Parameters in Severe Hospitalized Anorexia Nervosa Patients

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ABSTRACT

Background: Anorexia nervosa (AN) is characterized by self-induced malnutrition, affecting body image, mood, cognition and survival. Tyrosine, an essential amino acid is the precursor of catecholamines. The use of tyrosine to treat AN is based on experiments on diet restricted mice, in which it increased food consumption, improved cognitive function and elevated brain catecholamines. We evaluated the effect of oral tyrosine administration on the cognition and emotional state of patients with AN. We hypothesized that tyrosine may improve cognitive function without changing body weight, thus "kick-start" nutritional rehabilitation.

Methods: 19 female hospitalized patients with chronic AN were supplemented with L-tyrosine (100 mg/kg/day)/ placebo capsules for a three-week period in a double blind, randomized, cross-over study. Participants were evaluated cognitively and psychologically.

Results: Tyrosine shortened reaction time and test duration in memory tasks and improved depressive mood. No side effects were noted with the use of tyrosine.

Conclusions: Tyrosine may improve cognitive function and psychological traits associated with AN.

INTRODUCTION

Anorexia nervosa (AN) is a bio-psycho-social disorder in which changes in nutritional habits and body image distortion occur, leading to marked weight loss and malnutrition (1). Anorexia nervosa (AN) patients are characterized by perfectionism and obsessional personality traits. This AN-related personality type is associated with an exaggerated cognitive control and impaired cognitive-behavioral flexibility (2).

Essential amino acids including tyrosine, a precursor of catecholamines (CAs), are depleted in AN (3). Since lack of tyrosine may cause impaired cognition and distortion in body image, the patient sees himself as fat and continues dieting. These deficiencies may contribute to the physiologic-somatic and behavioral-psychologic changes, leading to a vicious cycle of dieting and weight loss (1).

Major weight loss and dieting can cause impairment in cognitive function even in healthy people (4). Studies on patients with AN have found a connection between lower body mass index and higher level of cognitive impairment, loss of short-time memory, reduced concentration and motor-perception ability, space-visual perception and problem-solving ability (4). Tyrosine transfer through the blood brain barrier (BBB) depends on other competing plasma amino acid concentrations and the nutritional status (5). The ratio of tyrosine to the other large neutral amino acids in starved animals is significantly lower than in controls. Administration of tyrosine to animals increases CA synthesis (6). Furthermore, tyrosine (100

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mg/kg/day orally) caused a 25% increase in CAs secretion during 24 hours relative to the basic normal level in healthy subjects (7). Tyrosine hydroxylase, the enzyme that synthesizes CAs, is usually unsaturated, and CA synthesis depends upon tyrosine availability (8). Tyrosine hydroxylase content and activity have been measured in various brain regions of AN patients and were shown to be markedly reduced in all brain regions. That may be as a result of low tyrosine levels (8).

We have previously shown in an animal-model of AN that tyrosine availability during severe diet restriction (DR) was a limiting factor in the synthesis and metabolism of norepinephrine. Severe DR in mice reduced cognitive function and adreno-receptor status that were restored by 100 mg/kg/day tyrosine administration. Further, the combination of DR and physical activity led to enhanced levels of serotonin. Administration of tyrosine normalized serotonin levels, improved food consumption, cognitive function and physical activity (less fatigue) (9).

CAs play a role in the patho-physiology of anxiety and mental disorders (10)patients were classified as asymptomatic, improved or symptomatic. Affective and anxiety disorders were assessed by a structured psychiatric interview (Diagnostic Interview Schedule. In some cases of AN, when weight is restored, anxiety and depression disappear (10)patients were classified as asymptomatic, improved or symptomatic. Affective and anxiety disorders were assessed by a structured psychiatric interview (Diagnostic Interview Schedule. Consequently, anxiety, depressive disorders and elevated stress seen in AN may result, in part, from a disturbance in CAs homeostasis caused by starvation (11)catecholaminergic neurotransmitters. In animals, administration of tyrosine, a food constituent and precursor of the catecholamines, reduces these behavioral and neurochemical deficits. Using a double-blind, placebo-controlled crossover design we investigated whether tyrosine (100 mg/kg. Tyrosine supplementation to healthy persons (100 mg/kg/day) decreased environmental stress (11)catecholaminergic neurotransmitters. In animals, administration of tyrosine, a food constituent and precursor of the catecholamines, reduces these behavioral and neurochemical deficits. Using a double-blind, placebo-controlled crossover design we investigated whether tyrosine (100 mg/kg, improved task performance, mood and cognitive function, and decreased diastolic blood pressure. Similarly, improvements in memory and psychomotor ability were observed (11-catecholaminergic neurotransmitters. In animals, administration of tyrosine, a food constituent and precursor of the catecholamines, reduces these behavioral and neurochemical deficits. Using a double-blind, placebo-controlled crossover design we investigated whether tyrosine (100 mg/kg14). The major problem in initiating treatment of patients with AN is overcoming the fear of weight gain and resistance to eating. In the current study, we investigated whether tyrosine administration can improve cognitive function and psychological condition of AN patients. We hypothesize that tyrosine may improve mood and cognitive function without changing body weight and thus "kick-start" nutritional rehabilitation and cognitive function.

METHODS

ETHICAL CONSIDERATIONS

This study was approved by the Helsinki Committee of the Sheba Hospital, registered under ClinicalTrials.gov Identifier No. NCT2062/2000.

STUDY GROUP

The study group included nineteen women, aged 18 to 35 years, who fulfilled the DSM -IV criteria for AN, and who were admitted for hospitalization treatment in the Eating and Weight Disorders Center at the Sheba Hospital, Tel Hashomer. The details of the study were explained to each patient by a senior psychiatrist, and each patient signed an informed consent form. The study was conducted 3-7 days after the hospitalization day.

STUDY DESIGN

This study was conducted as a randomized, double blind, cross-over study. Each participant was given 100 mg/kg tyrosine or 100 mg/kg placebo (corn starch) per day, divided into five doses. Each course of tyrosine or placebo administration lasted three weeks. Between the two periods, there was a one-week "washout" in which no supplements were given. Ten subjects received tyrosine during the first course of the study and placebo during the second course, while the rest of the group received the opposite. The treatment order was determined randomly. Both tyrosine and placebo were administered in 500 mg capsules, identical in appearance. The three-week duration of the courses was determined based on studies of healthy subjects, showing beneficial effects of tyrosine on cognitive performance and emotional state within a few days or even 24 hours after administration (13). Another consideration was that hospitalization of the patients was limited generally to eight weeks.

The study parameters, including physical condition, were collected at three time points:

On admission (baseline), at the end of the first three-week period (first course) and at the end of the second three-week period (second course).

Participants were instructed to avoid driving, alcohol use, psychotropic drugs and drug abuse during the course of the experiment. They were requested to report any other drug used during the four weeks of experiment. A one-hour visit at the beginning of each week included score of weight gain, caloric consumption and psychiatric evaluation.

STUDY MEASUREMENTS

Neuropsychological indices: Neuropsychological parameters were collected using a computerized system, CTB-HPB (Computerized Test Battery for Assessment of Human Performance and Behavior, developed by the Israel Institute for Biological Research, Ness Ziona, Israel).

The following are five cognitive tests that were used and their theoretical constructs: Mark Numbers - Attention to Details and Quantitative Reasoning (14). Digit-symbol Substitution Test - Perceptual Speed and Associative Learning (a modified form of the Wechsler Test) (15). Successive Pattern Comparison - Spatial-visual Memory (16). Warrington Recognition Test - Verbal Memory (17). Four-Choice Serial Reaction Time - Psychomotor Ability (18).

In order to obtain reliable results, identical conditions were maintained in terms of test times, testing environment, presence and guidance of the same researcher, and random order of the tests.

Prior to testing, each patient was trained on the tests for seven sessions, thereafter performing the baseline test. Trainings were carried out before every test session throughout the study. This was done as training patients in neuropsychological tests can reduce anxiety and enhance cooperation.

EMOTIONAL STATE AND TRAITS

Psychiatric evaluation was performed at hospitalization as a semi-structured psychiatric interview in accordance with DSM-IV criteria and SCID-I questionnaire, Structural clinical interview for axis I (19) . A senior psychiatrist carried out the psychiatric evaluation.

Psychological and behavioral traits data were evaluated by self-report questionnaires filled in at three points in time points mentioned above.

We used five questionnaires:

Eating Disorders Inventory-2 (EDI-2) (19). The EDI-2 is a widely used 91-item questionnaire designed to provide a broad assessment of the prevalence and intensity of psychological traits known to be associated with eating disorders. The EDI-2 is organized into 11 primary scales, three of which are specific to eating disorders and eight are general psychological scales that are highly relevant to eating disorders. It also provides six composites that measure eating disorder risk, ineffectiveness, interpersonal problems, affective problems, over-control, and general psychological maladjustment. The overall Summary Score was used as a primary outcome measure. The Hebrew translation of this inventory was found valid and reliable.

Beck Depression Inventory (BDI) (19) is one of the most widely used tools for assessing depressive symptoms in both clinical and non-clinical settings. It is a 21-item scale that asks responders to choose one out of four statements that best describes their feelings over the last two weeks. Responses are scored from 0-3, and total scores range from 0-63, with higher scores indicating greater levels of depressive symptomology. A score of 0-9 indicates no depression, 10-18 indicates mild depression, 19-29 indicates moderate depression and 30+ indicates severe depression.

State-trait Anxiety Inventory (STAI) (20) is a commonly used measure of trait and state anxiety. It is used in clinical settings to diagnose anxiety and to distinguish it from depressive syndromes. It also is often used in research as an indicator of caregiver distress.

Multidimensional Perfectionism Scale (MPS) (21). Perfectionism can lead to a variety of emotional, physical, and interpersonal problems. The MPS scale measures three trait dimensions of perfectionism — self-oriented, other-oriented, and socially prescribed — to help patients understand their behavior. The MPS explores the motivational, interpersonal, and cognitive aspects of perfectionistic behavior and relates those characteristics to mental and physical health problems, relationship problems and achievement difficulties. *Leyton Obsessional Inventory.* The Leyton Obsessional Inventory (LOI) is a self-report questionnaire that assesses obsessional symptoms (22).

ADDITIONAL NUTRITION SUPPLEMENTS

Body weight was monitored weekly throughout the study. All patients received a well balanced diet with increased energy intake depending on weight gain, as well as vitamin D (200 IU) and calcium (400 mg) supplements. The patients received diet containing carbohydrates (55%), proteins (15-20%) and fatty acids (25-30%). Calorie intake elevated gradually. The increase in caloric intake

was about 500kcal per week from the initial intake of the patients (800kcal) in order to create 0.5kg increase in body weight until BMI reached the level of 19.

MEDICATIONS

Fifteen subjects of the study group (19) took psychiatric drugs during the study period. The most frequently used psychiatric drugs were from the SSRI group and risperidone (Risperdal). Some of these drugs can affect cognitive function. According to research evidence, this effect is not completely clear and it seems that if such an effect exists, it lasts a short time only (23).

STATISTICAL ANALYSIS

The effects of tyrosine /placebo on the dependent variables (neuropsychological and emotional parameters) compared to baseline were tested by MANOVA for repeated measures (SPSS version 17). If a significant difference was found in the F test, post hoc comparisons were carried out (using Bonferroni corrections, or simple main effects contrasts for interaction) to find out specific, significant differences. Data were tested for correlation (Pearson test) between BMI (with the same three points baseline, after tyrosine and after placebo) and the neuropsychological and emotional parameters.

RESULTS

PARTICIPANTS

The mean age of participants was 22.8 years (Table 1). Onset of disease was earlier, on average at the age of 16.5 years. The average duration of disease was 6.3 years. Many patients had suffered repeated episodes of the disease and were considered severe, chronic patients. Only two participants had not completed 12 years of schooling, whereas two participants had completed B.A. degrees.

Table 1. *Characteristics of the study subjects*[1]

Characteristic	Study group (n=19)
Age (yrs)	22.8 (5.4)
Onset of disease age (yrs)	16.5 (2.5)
Duration of disease (yrs)	6.3 (4.9)
Number of prior hospitalizations	1.4 (0.7)
Education (yrs)	12.6 (3.2)
Baseline BMI	15.5 (1.6)
BMI at the end of first course	17.4 (1.3)
BMI at the end of second course	18.9 (1.0)

[1]All values are mean+ SDs

THE EFFECT ON BODY WEIGHT

All the patients increased their body weight during the study although there was no significant change between the groups first treated with tyrosine or with placebo. It was a pre-exquisite that the patients had to gain weight or else they would have been withdrawn from the study.

EFFECT OF TYROSINE ADMINISTRATION ON COGNITIVE FUNCTION

There was no interaction between the order of treatment and changes in cognitive function. No correlation was observed between weight increase during the study and changes in cognitive function.

WARRINGTON RECOGNITION TEST

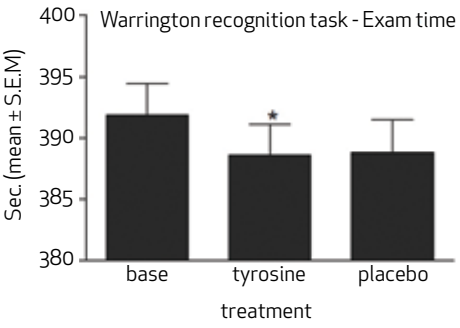
Exam time: Tyrosine administration resulted in a statistically significant shortening of the mean test time ($p<0.05$) as compared to baseline data, 383 sec. and 392 sec., respectively. Placebo administration also shortened mean exam time to 388 sec., but this result was not found to be of statistical significance (Figure 1).

Response time: The median response time for correct responses was shortened by both tyrosine (0.96 sec.) and placebo (0.91 sec.) administration, compared to baseline (1.04 sec.), in a statistically significant manner ($p<0.001$ for main effect) (Figure 2).

MARK NUMBERS

Exam time: The duration of this test was shortened compared to baseline for tyrosine administration, and this difference was close to statistical significance ($p<0.067$). A significant quadratic contrast ($p<0.048$) was found

Figure 1. *Effect of tyrosine treatment or placebo on time to complete the Warrington recognition exam in AN patients. Data are means ± SEM. There was a significant main effect of treatment ($F(2/36)= 3.19$, $p<0.05$). Post hoc, Bonferroni tests indicated that tyrosine treatment was significantly better than baseline ($p<0.05$). n=19*



for tyrosine effect, indicating shortened exam time after tyrosine administration, whereas after placebo administration, exam time increased back to a level similar to baseline (Figure 3).

Emotional state and traits: We did not find any interaction between the order of treatment and emotional parameters. No correlation was observed between weight increase during the study and the emotional parameters.

EFFECT OF TYROSINE ADMINISTRATION ON EMOTIONAL PARAMETERS

Tyrosine administration resulted in a statistically significant reduced depression score compared to baseline (p<0.03). From mean BDI score of 26.9 at baseline, it reduced to 21.7 after tyrosine administration. After placebo administration the score was reduced to 23.3 (not significant), n=19 (Figure 4).

EDI: There was a significant decline in Drive for Thinness subscale, throughout the study by both tyrosine (M=9.4, SEM=1.6, F [1,18]=4.76, p=0.043) and placebo (M=9.3, SEM=1.7, F [1,17]=9.28, p=0.007), compared to baseline (M=12.0, SEM=1.6), n=19. The number presenting the reduction in the EDI-2 Drive for Thinness scale represents the median finding for both evaluation points.

In summary, tyrosine administration caused a statistically significant improvement in the parameters of test duration and shortened response times in the Warrington recognition test (verbal memory) and exam time of the Mark numbers test (attention to details and quantitative reasoning). In the Warrington recognition test response time was shortened by both tyrosine and placebo administration in a statistically significant manner.

Depression score was reduced significantly with tyrosine administration but not with placebo. No exclusive effect of tyrosine on EDI-2 was found. Other cognitive tests and the self-rating emotional scales were not different between the groups. There were no side effects except for the inconvenience of taking several capsules a day that were delivered during meals.

Figure 2. *Effect of tyrosine treatment or placebo on reaction time for correct responses for the Warrington recognition exam in AN patients. Data are means ± SEM. There was a significant main effect of treatment (F(2/36)= 9.15, p<0.001). Post hoc, Bonferroni tests indicated that both tyrosine (p<0.044) and placebo (p<0.007) treatments were significantly better than baseline. n=19*

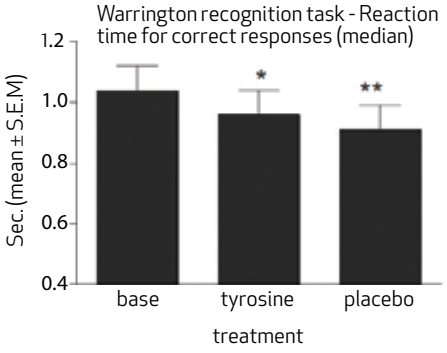
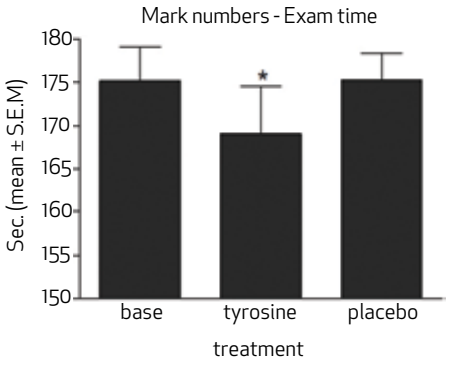


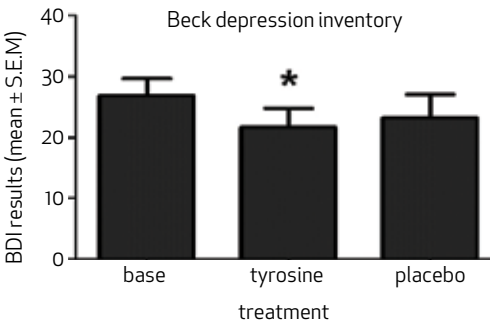
Figure 3. *Effect of tyrosine treatment or placebo on time to complete the Mark numbers exam in AN patients. Data are means ± SEM. There was close to significant main effect of treatment (F(2/36)= 2.97, p<0.064). Post hoc, Bonferroni tests indicated tyrosine effect better than baseline (p<0.067). Quadratic contrast was significant for tyrosine treatment (p<0.048). n=19*



DISCUSSION

Anorexia nervosa is a multifactorial disorder (24) with bio-psycho-social antecedents. It is a chronic relapsing psychiatric disorder with a largely unknown pathophysiology. Dopamine has been implicated in the pathophysiology of

Figure 4. *Effect of tyrosine treatment or placebo on Beck depression score in AN patients. Data are means ± SEM. There was a significant main effect of treatment (F(2/32)= 3.25, p<0.05). Post hoc, Bonferroni tests indicated that tyrosine treatment was significantly better than baseline (p<0.03). n=19*



the disorder by both preclinical and clinical studies (25).

We postulated that part of the complex psychologically and emotional disturbances occur as a result of a lack of essential dietary-derived neurotransmitter precursors. We have focused on tyrosine and the catecholamine pathways since studies in animals and in human subjects suggest that its administration may affect brain CA levels and improve cognition and mood (25-27).

The present study investigated the effect of a single amino acid supplement on cognitive function and on emotional state of 19 hospitalized chronic AN patients. Most of them had been ill for more than five years before the study. This was as a randomized, double blind, cross-over study. Each participant received a three-week course of 100 mg/kg tyrosine and a similar course of 100 mg/kg placebo per day.

Both the placebo and tyrosine groups were supplemented with similar amounts of proteins (1.5mg/kg) between 15-20% of the diet content as was indicated by the similar amount of blood albumin and globulin detected in their blood during the clinical trial.

In AN patients, when the body is under negative energy balance and elevated stress and characterized by decrease in proteins metabolism there is not enough tyrosine derived from the metabolism. Getting extra tyrosine by taking supplements may enhance its blood levels and availability, which increase its transfer through the BBB and might improve performance and memory as well as enhance body weight.

In order to obtain reliable results, we performed learning plots for all the patients in order to study the tests. Identical conditions were maintained regarding test times, testing environment, presence and guidance of the same researcher and random order of the tests.

Regarding cognitive function, the effect of tyrosine supplementation to AN patients was marked by increasing the rate and by hastening responses, as shown in the Warrington recognition test and Mark Numbers test. Apparently, memory-related performance is affected by tyrosine supplementation, as was found similarly in studies supplementing tyrosine to healthy subjects (12). Cerebral atrophy caused by AN is well described in the literature (28). We assumed that our participants may have had such changes as they suffered from chronic anorexia with many years of underweight and malnutrition. This may also be a reason that prevented them from achieving greater improvements. Weight, as an isolated factor, did not affect cognitive function or emotional parameters over the relatively short period of this study.

Emotional and behavioral assessments obtained from the self-administered questionnaires were of five types, examining the level of depression, the severity of the eating disorder, anxiety, perfectionism and the degree of obsessiveness. The reduction in depression score after tyrosine supplementation is compatible with evidence from previous studies (29). These studies showed favorable effect of tyrosine supplementation on depression both in patients and in healthy persons.

Tyrosine serves as a precursor of CAs, especially dopamine, which plays a central role in depression. In various studies, tyrosine supplementation was found to be associated with an improvement in depression levels, whereas in other studies, mood deterioration and dejection were observed in healthy persons supplemented with a tyrosine-free diet (29). Although we know from other studies that improvement in emotional parameters depends on weight and that there is a positive correlation between starvation and depression (30), with tyrosine supplementation we found an improvement in depression that was not connected to weight gain. Such an effect suggests that tyrosine might cause an improvement in mood before weight gain.

The Drive for Thinness sub-scale derived from EDI-1 improved significantly by both tyrosine and placebo. This is an encouraging finding since we know from prospective studies that changes in attitudes may take longer time, even a few years after maintaining normal weight and menses, as shown in the treatment of abnormal attitudes and traits (31).

Limitations of the study include the fact that it was undertaken in hospitalized patients with severe AN. This precludes the generalization of the findings to ambulatory populations with less severe illness.

As in other studies, we also encountered a few cases of placebo effect. One can explain this by the contribution of a more personalized relationship with the test subjects, by the increased attention paid to them deriving from the study.

We found large variance in cognitive results which reduced the statistical significance. We are aware of the fact that most of the test subjects (15 patients) were undergoing an intensive treatment process, and received in some phase of the study psychiatric drugs that were liable to influence cognitive function. Also, the limited number of participants included chronic patients in serious condition who may experience some irreversible brain changes and are not the most suitable candidates for such treatment. In addition diagnosis was achieved

only by one evaluator. We have not assessed the validity (Cronbach Alpha) of the self-rating scales for the present study.

Results might be more favorable in patients with AN at the onset of their disease, especially since the treatment is without side effects. There is a need for future studies that should be carried out on a large scale. The effect of tyrosine administration can be tested over a longer time period and, also, in a larger dosage of 150 mg/kg (as already documented in the literature), where it is possible that the effect might be greater. Tyrosine should also be tested in patients with early disease. Chronic patients should be tested separately from non-chronic patients, thus reducing the variance in the cognitive findings.

In summary, tyrosine supplementation has a beneficial effect on cognitive function and depression in patients with severe chronic anorexia nervosa. Tyrosine supplementation might prove to be a useful treatment in the management of patients with anorexia nervosa.

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Author Disclosure

No conflict of Interest

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כתב עת ישראלי לפסיכיאטריה

האם הרגלי אכילה חריגים הם הפרעות אכילה?

ש' קרייטלר, תל אביב

רקע: המחקר עוסק בסוג מסוים של הרגלי אכילה לא רגילים, שאינם ממוקדים במשקל, שונים מהפרעות אכילה, ולא פתולוגיים. הם מאופיינים על ידי דפוסים כגון: סוג, כמות, אופן וסגנון אכילה שסוטים מאלה שמקובלים במשפחתם או בתרבותם של בעלי ההרגלים הללו. כיום על פי הקטגוריות של ה־DSM–5 אנשים אלו היו מוגדרים כסובלים מהפרעת צריכת מזון הימנעותית (FID–AR) או הפרעת אכילה בלתי ספציפית (FED–US). השאלה הייתה אם זוהי צורה מתונה של הפרעות אכילה או מערכת התנהגויות עצמאית. מטרת המחקר הייתה לבדוק באיזו מידה אפשר לכלול התנהגויות אכילה בלתי טיפוסיות אלה באבחנה של הפרעות אכילה, זאת באמצעות בחינת הציונים של נבדקים בעלי התנהגויות אכילה אלו בשאלון של האוריינטציה הקוגניטיבית להפרעות אכילה (ED–CO), שהוא מדד לנטייה כללית להפרעות אכילה.

שיטה: המדגם כלל 250 תלמידים בבית ספר תיכון (120 בנים ו־130 בנות) בני 16–18 שנים. הועברו להם השאלון של עמדות כלפי אכילה (EAT–26), שאלון הרגלי אכילה חריגים (EEH) והשאלון של אוריינטציה קוגניטיבית להפרעות אכילה (ED–CO).

תוצאות: לא נמצאה התאמה בין הציונים בשאלוני EAT–26 ובשאלוני EEH. בעלי ציונים גבוהים בשאלון EAT–26 היו בעלי ציונים גבוהים יותר במשתנים אחדים של שאלון ED–CO מאשר בעלי ציונים גבוהים או נמוכים בשאלון EEH. בעלי ציונים גבוהים ונמוכים בשאלון EEH נבדלו זה מזה ברוב המשתנים של שאלון ED–CO.

מגבלות: ההתנהגויות החריגות לא הוגדרו במונחים של קריטריוני האבחנה החדשים של ה־DSM–5 שפורסמו לאחר סיום המחקר הנוכחי. נוסף על כך, המדגם הוגבל לטווח הגילים 16–18, בעוד טווח הגילים של רוב הפרעות האכילה הוא 12 עד 25, והרגלים חריגים יכולים להופיע גם בגילים מבוגרים יותר.

מסקנות: הרגלי אכילה חריגים (EEH) הם גילויים של נטייה כללית להפרעות אכילה אך הם נבדלים מהפרעות אכילה ואפשר לראות בהם גילויים עצמאיים להפרעות אכילה.

שאלון ה־EDE–Q בעברית: תוקף מבנה ותוקף מתכנס בקרב מדגם בקהילה

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רקע: השאלון EDE–Q, שנכתב במקור באנגלית, משמש לסינון ולעזרה באבחון הפרעות אכילה. מטרת המחקר הנוכחי הייתה לבחון את הנוסח העברי של השאלון מבחינת תוקף מבנה, תוקף מתכנס ומאפייני סינון במדגם בקהילה שאינו קליני בישראל.

שיטה: השאלון EDE–Q תורגם לעברית והועבר ל־292 מתנדבים מהקהילה (18% גברים) באופן מקוון יחד עם כלי דיווח עצמי נוספים מתוקפים.

תוצאות: ניתוח גורמים מגשש ומאשש אישרו במידה רבה את מבנה הגורמים המקורי, אם כי תתי־הסולמות של חששות ממשקל ומצורת הגוף התכנסו לגורם אחד. התוצאות מצביעות על תוקף מתכנס מוצלח ועל מאפייני סינון טובים.

מגבלות: כל המשתתפים היו מבוגרים, רובם נשים, ולא הייתה אבחנה חיצונית שניתן היה להיעזר בה כקריטריון.

מסקנות: המאפיינים הפסיכומטריים החיוביים של EDE–Q המופיעים במחקר זה מוסיפים את הנוסח העברי לרשימה הולכת ומתארכת של תרגומי EDE–Q התקפים בתרבויות מגוונות. מכשיר חשוב זה זמין כיום לקלינאים ולחוקרים ישראלים, ואפשר להיעזר בו. נוסף על כך אפשר לבדוק בעזרתו את התכונות הפסיכומטריות גם באוכלוסיות גדולות ומגוונות יותר.

דימוי גוף כוללני: מדד DKB–35 בעברית

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רקע: DKB–35 הוא מדד מקיף של קשר חיובי עם הגוף. לשאלון המקורי בגרמנית יש תכונות פסיכומטריות טובות. מטרת המחקר הנוכחי הייתה לתרגם את השאלון לעברית ולבדוק את תכונותיו הפסיכומטריות בעברית.

שיטה: 292 מתנדבים מהקהילה ענו על שאלון מקוון שכלל כמה שאלונים: DKB–35, שאלון שביעות רצון מהחיים ושאלון תסמיני אכילה מופרעת, EAT–26. הנתונים יוצאו ל־SPSS גרסה 21.0.

תוצאות: הודגמו תוקף מבנה, מהימנות ותוקף מתכנס ומבחין של השאלון בגרסתו העברית. חמשת תתי־הסולמות המקוריים במדד זה – קבלה של הגוף, חיות, נרקיסיזם של הגוף, מגע גופני והגשמה מינית – שוחזרו בניתוח הגורמים המאשר.

מסקנות: אפשר להשתמש ב־DKB–35 בעברית בהקשר של בריאות הנפש בכלל ובהקשר של תהליך ההחלמה מהפרעות אכילה בפרט.

הפער בין משקל בשחרור מאשפוז למשקל היעד כמנבא אשפוז חוזר בקרב מתבגרים חולי אנורקסיה נרבוזה

ע' הטמן, ע' ברונשטיין קלומק, ג' גולדצויג, א' הדס, מ' הורוביץ וס' פניג, מרכז שניידר לרפואת ילדים

רקע: מטרת המחקר הנוכחי הייתה לבדוק אם הפער בין המשקל בשחרור מאשפוז למשקל היעד מנבא אשפוז חוזר בקרב מתבגרים חולי אנורקסיה נרבוזה.

שיטה: 51 מתבגרים מאושפזים הסובלים מאנורקסיה נרבוזה נשקלו והשלימו שאלוני דיווח עצמי במהלך הקבלה לאשפוז והשחרור ממנו. נבחנו דיווחים בנוגע לאשפוז חוזר במשך השנה הראשונה לאחר השחרור.

תוצאות: 19 מאושפזים (37.25%) נזקקו לאשפוז חוזר. הפער בין המשקל בשחרור למשקל היעד באחוזים, אשפוזים קודמים והסטטוס המשפחתי במשפחת המוצא נמצאו כמנבאים אשפוז חוזר.

מגבלות: גודל מדגם קטן, תקופת מעקב קצרה באופן יחסי ושימוש בשאלוני דיווח עצמי. נוסף על כך לא נכללו מדדים הבוחנים את תפיסת הקשרים המשפחתיים ואת סגנון התקשרות, אף שנתונים כאלה היו מאפשרים הבנה טובה יותר של תפקיד המערכת המשפחתית באשפוז חוזר.

מסקנות: המחקר מדגיש את חשיבות המשקל בעת השחרור לפרוגנוזה ארוכת טווח. אי־הגעה למשקל היעד בשחרור היא מנבא לאשפוז חוזר בקרב מתבגרים חולי אנורקסיה נרבוזה.

פעילות חיפוש לצורך פתרון בעיות בקרב חולי אנורקסיה נרבוזה ובולימיה נרבוזה בשלב החריף של המחלה ולאחר התייצבות תסמינית

י' נחום, ו' רוטנברג, ע' חנוך־לוי וד' שטיין, תל השומר

רקע: מטרת המחקר הייתה לבדוק פעילות חיפוש לצורך פתרון בעיות בקרב הסובלות מאנורקסיה נרבוזה רסטריקטיבית (א"נ–ר) או מהפרעות אכילה שכוללות בולמוסים או התנהגויות מטהרות (הקאות או שימוש במשלשלים; ה"א–ב"מ).

שיטות: 24 מאושפזות הסובלות מא"נ–ר ו־22 מאושפזות הסובלות מה"א–ב"מ נבדקו בתוך שבועיים ממועד קבלתן לאשפוז ושוב שבועיים לפני שחרורן מהאשפוז באמצעות שאלונים לבחינת פעילות חיפוש לצורך פתרון בעיות, חומרת התסמינים הקשורים להפרעות אכילה, דיכאון וחרדה; 32 נבדקות בקבוצת ביקורת הוערכו באופן דומה פעם אחת.

תוצאות: בעת הקבלה לאשפוז נמצא שנבדקות הסובלות מה"א–ב"מ משתמשות באסטרטגיות פחות יעילות לפתרון בעיות לעומת נבדקות בקבוצת הביקורת. לא נמצא הבדל מעין זה בנבדקות הסובלות מא"נ–ר. בסוף האשפוז נמצא שיפור באסטרטגיות לפתרון בעיות ובמדדי דיכאון וחרדה תכונתית בקרב נבדקות הסובלות מה"א–ב"מ, אך לא בקרב נבדקות הסובלות מא"נ–ר.

מגבלות: מספר קטן של נבדקות, קיומה של הערכה אחת בקרב נבדקות קבוצת הביקורת

מסקנות: אצל נבדקות הסובלות מא"נ–ר או מה"א–ב"מ נראים פרופילים שונים של פעילויות חיפוש לצורך פתרון בעיות, גם בשלב החריף של מחלתן וגם עם הגעתן להתייצבות תסמינית.

ההשפעה הפסיכולוגית של Δ^9–THC על חולי אנורקסיה נרבוזה: מחקר קליני בקנה מידה קטן

י' אברהם, י' לצר, ד' חסיד, וא' בארי, ירושלים, חיפה

הקדמה: Δ^9–Tetrahydrocannabinol (Δ^9–THC) היא התרכובת הפעילה ב־Cannabis sativa והיא בעלת תכונות מעוררות תיאבון. המחקר בדק את ההשפעה של כמויות קטנות של Δ^9–THC הניתן דרך הפה על תסמינים מדווחים של חולי אנורקסיה נרבוזה.

שיטות: 9 נשים מעל גיל 18 השתתפו במחקר. 6 אובחנו לפי קריטריון DSM–IV כחולות אנורקסיה רסטרקטיבית ו־3 כחולות אנורקסיה binge–purge type. וגילם 45.0±3.2 שנים. BMI=16.1±1.6 kg/M2. הנבדקות טופלו ב־Δ^9–THC במינון של 1 מ"ג ליום לשבוע ו־2 מ"ג ליום לשלושה שבועות ומילאו שאלונים לפני הטיפול ואחריו. התוצאה הראשונית הייתה שיפור בדרך שבה הנבדקות התייחסו להפרעת האכילה שלהן.

תוצאות: חל שיפור ניכר בדרך שבה הנבדקות דיווחו על התייחסות לטיפול בגוף, הרגשת חוסר האונים, חומרת המחלה והרגשת הדיכאון. לא חלו שינויים ניכרים ב־BMI.

מגבלות: מספר המשתתפים היה קטן והנבדקות היו ביקורת של עצמן.

מסקנות: Δ^9–THC הוא מרכיב יעיל בטיפול בתסמינים הפסיכולוגיים של אנורקסיה נרבוזה.

ההשפעה של טירוזין על התפקוד הקוגניטיבי ועל פרמטרים פסיכולוגיים בקרב מאושפזים החולים באנורקסיה נרבוזה חמורה – מחקר אקראי כפול סמיות

מ' ישראלי, א' רם, ר' ברנדייס, צ' אלתר, י' אברהם וא' בארי, האוניברסיטה העברית בירושלים

רקע: אנורקסיה נרבוזה מאופיינת בתת־תזונה הנגרמת באופן ספונטני ומשפיעה על מצב הרוח, תדמית הגוף, היכולת השכלית וההישרדות. טירוזין, חומצת אמינו הכרחית, היא חומר הבסיס ביצירת קטכולאמינים במוח. השימוש בטירוזין לטיפול באנורקסיה נרבוזה מבוסס על ניסיונות שנעשו במודלים של חיות מעבדה. כאשר עכברים גודלו תוך הקפדה על הגבלת מזון, הזרקה של טירוזין העלתה את צריכת המזון ואת רמות הקטכולאמינים במוח וכן שיפרה את היכולת השכלית של העכברים. בעקבות ממצאים אלו נבדקה ההשפעה של מתן פומי של טירוזין על היכולת השכלית ועל המצב הפסיכולוגי של חולות באנורקסיה נרבוזה. השערת המחקר הייתה שטירוזין יכול לשפר את היכולת הקוגניטיבית בלי שיחול שינוי במשקל גוף, ועל ידי כך תיתכן האצה בשיקום התזונתי.

שיטות: 19 מאושפזות חולות באנורקסיה נרבוזה כרונית קיבלו טירוזין (100 מ"ג לק"ג ליום) או פלצבו בקפסולות לתקופה של שלושה שבועות במחקר כפול סמיות. במהלך המחקר נבדקו היכולת השכלית והמצב הפסיכולוגי של החולות.

תוצאות: טירוזין שיפר את זמן התגובה ואת משך המבחן במבחני זיכרון וכן את מצב רוחן של החולות (הפחתה של דיכאון). לא נראו תופעות לוואי כתוצאה מהשימוש בטירוזין.

מסקנות: טירוזין יכול לשפר את היכולת השכלית ובעיות פסיכולוגיות הקשורות לאנורקסיה נרבוזה ולסייע לשיקום תזונתי.

*הניסיון הקליני הוא תולדה של שיתוף פעולה בין המחלקה למטבוליזם ותזונת האדם בביה"ס לרפואה בירושלים והמחלקה להפרעות אכילה במרכז הרפואי שיבא, תל השומר