UNIVERSITA' DEGLI STUDI DI VERONA

DIPARTIMENTO DI

Scienze Neurologiche, Neuropsicologiche, Morfologiche e del Movimento

SCUOLA DI DOTTORATO DI

Scienze Biomediche e Translazionali

DOTTORATO DI RICERCA IN

Scienze dell'Esercizio Fisico e del Movimento Umano

CICLO/ ANNO: XXIV/2008

TITOLO DELLA TESI DI DOTTORATO

Physiological and Physical Analysis in Anorexia Nervosa (AN) in-patients

S.S.D.: M-EDF/02

Coordinatore: prof. Federico Schena

Tutor: prof. Massimo Lanza

Dottoranda: dott.ssa MARTA ALBERTI

INDEX

PRESENTATION AND AIMS:

The research, in the field of Adapted Physical Activity (APA) in Anorexia Nervosa (AN), have investigated the effects of cognitive, behavioral and nutritional therapy (CBT) on: (i) *Body Composition*, (ii) *Energy Expenditure* and (iii) *Physical Capacities (PC)* in AN in-patients.

The research involved subjects with Anorexia Nervosa, admitted in Villa Garda Hospital – Department of Eating Disorder and Obesity – Garda, Verona, between 2010 and 2012.
The patients were sent to the Unit of Villa Garda Hospital from all over Italy by general practitioners or by eating disorder specialists. Patients were included if they met the following criteria: (i) age, 12-65 years; (ii) diagnosis of AN assessed by Eating Disorders Examination interview (EDE) 12.0D); (iii) failure of less intensive outpatient treatment or an eating disorder of such clinical severity as to be unmanageable in an outpatient setting. Subjects with active substance abuse and acute psychotic disorders were not considered for hospital admission.

The research study was divided into *three sections*.
The first section contains definitions and scientific background of eating disorders and anorexia nervosa in particular, together with its related psychopathologies, and treatment.
The second section describes the physiology of Eating Disorder, Anorexia Nervosa in particular, and providing, at the conclusion of the section, the three published studies dealing with basal metabolism and body composition in the experimental group of patients at Villa Garda Hospital.
The third section is devoted to physical activity related to Eating Disorders, especially Anorexia Nervosa. In the conclusion of this section, study 4 and 5 propose an innovative measurement of health related physical capacities and approach to new methodology for objective measurement of the quantity and quality of physical activity, in clinical context.

The following paragraphs describe briefly the key words mentioned in the definition of objectives.

The term *Anorexia Nervosa* was coined by William Gull in 1873, but this phenomenon was noticed much earlier by Richard Morton – London 1694. Morton in his "Treatise of Consumption" described a body edematous and bloated, a face pale and squalid, a stomach loathes every thing but liquid; he told that the strength of the patients declines at the rate. He

thought that the cause of this distemper is in the system of the nerves and speaks about a "...violent passions of the mind...". (S. Giordano, Exercise and Eating Disorders, 2010. p.10)

The *body composition* in patients with anorexia nervosa has been evaluated in numerous studies and using different approaches, but the few available studies comparing DXA with the ST method in the measurement of percentage body fat in patients with AN produced inconsistent findings. Some studies found that DXA gives a mean lower %BF than ST measurement in underweight patients with AN (Prior BM et al., 1997; Kohrt WM, 1998), while another study found an opposite result (Haas VK et al., 2009). These data underline the fact that body composition evaluation is a crucial issue for an accurate assessment of AN patients.

Total *energy expenditure* (TEE) in humans is determined by resting energy expenditure (REE), dietary-induced thermo- genesis, and energy cost of physical activity. (Donahoo w t et al., 2004; Ravussin E et al., 1992). Several studies showed that REE is low in underweight patients with AN compared with normal-weight controls (Melchior J C et al., 1989; Crueda C et al., 2007) and long-term recovered AN patients (Dellava J E et al., 2009). The low REE seems mainly due to the loss of lean body mass, a major determinant of REE (Miller Jr. A T et al., 1953), and to a lesser extent, to the effect of several neuroendocrine changes (e.g., thyroid hormones, adrenal hormones, and leptin) observed in underweight AN patients (deZwaan M et al., 2002).

It is a widely held clinical opinion that patients with anorexia nervosa (AN) are more physically active than the general population (Bratland-Sanda S. et al., 2010 -a) up to 80% of patients with eating disorders are affected by excessive and compulsive exercising that is recognized as a maladaptive behavior associated with the eating disorder psychopathology, poorer treatment outcome and higher risk of relapse (Bratland-Sanda S et al., 2010 –b; 43:266-73; Dalle Grave R et al., 2008). The main function of exercising in patients with AN is to control body shape and weight (Zunker C et al., 2011) but in a subgroup of patients it is also used to modulate mood (Dalle Grave R., 2009). Research suggests that patients with AN engage in longer periods of moderate-intense physical exercise than the nonclinical population (Kron L et al., 1978). However, no systematic data have been collected so far to classify the functional level of cardiovascular, muscular and resistance performances in AN

patients before and after weight restoration, in order to understand if the type and amount of physical activity performed by these patients could enhance or deteriorate health-related physical fitness components.

Cognitive and Behavioral Therapy (CBT) is the theory which develops the transdiagnostic treatment of eating disorders. It argues that food restriction stems from two main behavioral processes that characterizes the onset of an eating disorder: 1) control various aspects of their lives, 2) assessment of excessive weight and body shape and their control. (Dalle Grave, 2009)

Adapted Physical Activity (APA) is a professional branch of kinesiology / physical education / sport & human movement sciences, which is directed toward persons who require adaptation for participation in the context of physical activity (IFAPA, 2010).
Some researchers (Richarson, 2005) suggest that regular physical activity has the potential to improve the quality of life and well-being of people with serious mental illness thought two routes – by improving physical health and by alleviating psychiatric and social disability.

Physical Capacities (PC) are stable and enduring traits determined, for major part, genetically and which underpin the performance of individual skills. They include endurance, flexibility (or joint mobility) , strength, balance that are considered health related capacities, and speed. (President's Council on Physical Fitness and Sports, 2000)

SECTION 1

SCIENTIFIC DEFINITION AND BACKGROUND

Eating Disorders (ED) definition

The ED are characterized by gross disturbances in eating behavior. They include two specific categories: Anorexia Nervosa (refusal to maintain body weight at or above a minimally normal weight) and BN (recurrent binge eating followed by inappropriate means of compensation (self-induced vomiting, using laxatives, diuretics or other medications, fasting combined with activities physical compulsion) common to both disorders is a distorted perception of body image and body weight. Disorders that not meet any diagnostic criteria contained in DSM-IV (Diagnostic and Statistic Manual of Mental Disorders) are classified as Eating Disorders Not Otherwise Specified (NOS). (DSM-IV, 1994). Most recently two new eating disorders have been demarcated – *binge eating disorders* and *night eating syndrome*: their diagnostic status remains the subject of debate. (Fairburn et al, 2002)

Anorexia Nervosa definition

Anorexia Nervosa (AN) is a word of Greek origins: literally means lack of appetite. Contrary to what the name originally denoted, AN is not primarily characterized by lack of appetite. The suffer fights against hunger. The anorexia suffer engages much of their energies in the constant fight against food, hunger and absorption of calories. Anorexia is not a condition that just happens to the person. The subject willingly and deliberately defends his eating and exercise habits. The thus plays an important part in the initiation and perpetration of eating disorders. (S. Giordano, 2010)

AN is an ED characterized by severe food restriction, maintenance of abnormal low body weight, intense fear of weight gain and body image disturbance (DSM-IV, 1994)

It has been recognized in medicine for more than 150 years, but for much of the time was largely confined to affluent societies that espouse Western cultural ideals. It now occurs at all socioeconomic levels, and there are increasing reports for anorexia - like illnesses from non-Western societies. This disorder tends to run a chronic course and is associated with significant psychiatric comorbidity, serious medical complication, and considerable impairment in psychosocial functioning (C.V. Bewell et al, 2010)

History of Anorexia Nervosa

The following section is an extensive summary of the text of W.Vandereycken (2002), published in the text of Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

Throughout history we can recognize the heterogeneous manifestation of disturbed eating behavior. Traditionally, in medicine, both food avoidance and overeating were almost invariably looked upon as symptoms of a diversity of illnesses, predominantly gastrointestinal disorders. Preoccupations with body weight and shape, and the application of weight-control strategies such as dieting and purging have acquired popular and medical attention only in the last part of the 20th century (and only in Western or westernized countries). Hence, the specific syndromes anorexia nervosa and bulimia nervosa appear to be relatively "modern" clinical entities.

Until the 19th century, "anorexia" - the medical term for loss of appetite - was considered a symptom of several physical and emotional disorders. However for centuries, voluntary abstention from food was not primarily a pathological phenomenon; extreme fasting was part of the penitential or ascetic practice of many pious Christians. Later on, form of long-lasting food refusal, not accompanied by symptoms of well-known diseases such as tuberculosis, were more likely to stir up speculations about supernatural powers or demonic influences. Ultimately, extreme or unusual forms of food abstinence were looked upon as a sings of a mental disorders. Food avoidance and emaciation were common symptoms of well-known diseases such as hysteria, mania, melancholy, chlorosis, and all kinds of psychotic disorders. At the end of the 17th century, the English physician Richard Morton described the occurrence of "nervous consumption" - a wasting different from tuberculosis and due to emotional turmoil. This is often quoted as the first medical report of Anorexia Nervosa, but Morton's interesting case studies (of both a girl and a boy) did not attract any attention and feel into oblivion, until rediscovered three centuries later.

Morbid self-starvation only became recognize as a distinct clinical entity in the second half of the 19th century. The Parisian clinician Ernest-Vharles Lasègue and the London physician Sir William Withey Gull must be awarded "joint parenthood" for the first explicit description of AN. In April 1873, Lasègue published his article on "anorexie hystérique", which appeared in English translation shortly before Gull presented his paper on "anorexia hysterica" in October of the same year. In 1874 we can find the term "anorexia nervosa" in his lecture. According to

both clinicians, it was a psychogenic affliction that occurred predominantly in girls and young women.

The characteristics described by Gull and Lasègue are still valid today: severe weight loss, amenorrhea, constipation, restlessness, and no evidence of underlying organic pathology.

Although the French and British medical press showed some interest in the new syndrome, in many other countries (e.g., the United States, Germany and Italy) , Anorexia Nervosa remained largely a marginal phenomenon until well into the 20th century.

Initially AN was generally looked upon as a mental disorder. However, when in 1914 the German pathologist Morris Simmonds found lesion of the pituitary gland in some emaciated patients, AN became inextricably associated with "Simmonds' disease" or "pituitary cachexia". It took more than two decades for this erroneous idea to be clearly refuted. After Warld War II, the endocrinological view of AN made a rapid and smooth demise. Physicians' minimization of the psychological component then made room for psychiatric dramatization. In the period 1945-1960, psychiatry was strongly dominated by psychoanalytic views, and traces thereof can be found in contemporary theories on AN; for example, fear of food intake was linked to unconscious fears of oral impregnation. But interest in AN was not particularly great.

After 1960, this changed drastically due to the pioneering work of (German-born) American psychiatrist Hilde Brunch, who focused attention on the lack of self-esteem and the distorted body image of these patients. This led to the addition of two features to the original clinical picture, as described by Lasègue and Gull: the relentless pursuit of thinness and the characteristic disturbance of the body image. As such, AN evolved in the late 20th century from rare and little known clinical entity to a "fashionable" disorder of great interest to the general public.

NEW DISORDERS? Does the history of ED reflect the history of a changed ideal of beauty? Are these disorders a sing of a deranged obsession for thinness, the product of a new body culture, a morbid epiphenomenon of a consumer society? From the 15th century onward, Western society has idealized three types of female figures. Until the 17th century the tummy-centered and -by present standards-rather plump woman was admired. This "reproductive" type was then replaced by the "hour glass" model, with a narrow waist, full bosom, and round bottom. Since the late 19th century, the idealized shape for women has been the lean, almost "tubular" body type, deprived of any symbolism of fertility and motherhood. The thinness of the "new woman" expressed sexual liberation and rejection of the traditional female role. Parallel to this has been increasing aversion to overweight or corpulency. In the late of 19th

century, in the upper classes in particular, a new ideal of slenderness gradually arose: here, health concerns played only a minor role. Although certain plumpness still continued to be desirable, by the turn of the 20th century, the modern ideal of slenderness had come into being. The “battle against fatness” had started: Obesity was the “enemy” and physicians provided the “weapons”. Modern diet-culture emerged, and it is going to be with us for many years to come, probably together with eating disorders, “old or new”.

Classification and Diagnosis criteria of Anorexia Nervosa

The following section is an extensive summary of the text of Paul E. Garfinkel (2002), published in the text of Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

Since 1969, a variety of operational criteria for AN that emphasize sings and symptoms have been developed. The first such criteria were proposed by Gerald Russell in 1970. He emphasized (1) a behavioral disturbance - leads to a marked loss of body weight, (2) a characteristic psychopathology - characterized by a morbid fear of getting fat, and (3) an endocrine disorder - manifests itself clinically by amenorrhea in females and loss of sexual potency and sexual interest in males.

These criteria have evolved into the current DSM-IV (American Psychiatric Association 1994, 4th edition) and ICD-10 (from World Health Organization, 1993) criteria.

DSM-IV diagnostic criteria for AN:

1. "Refusal to maintain body weight at or above a minimally normal weight for age and height (e.g., weight loss leading to maintenance for body weight less than 85% of that expected; or failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected).
2. Intense fear of gaining weight or becoming fat, even though they are underweight.
3. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the current low body weight.
4. In postmenarcheal females, amenorrhea, i.e., the absence of at least three consecutive menstrual cycles. (A woman is considered to have amenorrhea if her periods occur only following hormone, e.g., estrogen, administration).

Specify type:

I. ***Restricting type***: during the current episode of AN, the person has not regularly engaged in binge-eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas).

II. ***Binge/Purging type***: during the current episode of AN, the person has regularly engaged in binge-eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas)."

(American Psychiatric Association -1994. *Diagnostic and statistical manual of mental disorders* - 4th ed. F50.0 (307.1), p. 597)

ICD-10 Diagnostic Criteria for AN:

1. "There is weight loss or, in children, a lack of weight gain, leading the body weight at least 15% below the normal or expected weight for age and height.
2. The weight loss is self-perception of avoidance of "fattening foods".
3. There is self-perception of being too fat, with an intrusive dread of fatness, which leads to a self-imposed low weight threshold.
4. A widespread endocrine disorder involving the hypothalamic-pituitary-gonadal axis is manifested in women as amenorrhea and in men as a loss of sexual interest and potency. (An apparent exception is the persistence of vaginal bleeds in anorexic women who are on replacement hormonal therapy, most commonly taken as a contraceptive pill).
5. The disorder does not meet criteria 1 and 2 for Bulimia Nervosa."

(World Health Organization -1993. IDC-10 *Classification of mental and behavioral disorders: Diagnostic criteria for research*, from "Eating disorders and Obesity", 2002, p.157)

Problems that remain in the diagnosis

Problems due to current levels of understanding

With regard to AN, the optimal weight threshold is not known and the need for amenorrhea as a criterion is questionable.

Problems due to the nature of the Eating Disorders

The character of Eating Disorder (ED) is heterogeneous. It's also sensitive to cultural influences that affect their expression and change over time. Eating Disorders also exist on a continuum that ranges from innocuous but persistent dieting, through subthreshold states of uncertain clinical significance, to full cases of AN of BN. While this continuum is beginning to the better defined, problems with categorization remain and probably always will. Yet another problem is that the presence of comorbid states can affect the clinical picture.

Problems due to overemphasis on diagnosis

Diagnosis, imperative for clinical practice, represents a form of communication that permits detailed examination, investigation of approaches to treatment, and delineation of prognosis. Used in a concrete or thoughtless manner, however, it may detract from, rather than enhance, care. One may make a diagnosis while knowing little about the patient as a person. Awareness

of psychological theories of development, unconscious conflict, or the therapeutic process is not needed to make a diagnosis. This absence of meaning must be addressed if we are to retain a humanistic orientation, whereas, it is impossible to treat suffering individuals if we are devoid of an awareness of history, symbolic meaning, conflict, ambivalence, social context, and the primacy of existential concerns. *(Paul E. Garfinkel, 2002)*

Clinical presentation of Anorexia Nervosa: *psychiatric presentation*

The following section is an extensive summary of the text of Pierre J.V. Beumont (2002), published in Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

The objective psychopathology is difficult to label. It has been termed hysterical, a phobia of weight gain, an obsession, or even a delusion, but perhaps an overvalued idea is best. Patients are overwhelmed by concerns about their bodies and deny that they feel themselves to be fat even when they are actually emaciated. They are preoccupied with ways to reduce their weight further or, at the least, to prevent any gain. Patients appear genuinely terrified at the prospect of being overweight, and some state openly that they would rather be dead than fat. Onto this core concern, other psychological symptoms are imposed, which are known to be semistarvation irrespective of cause. These include depressed mood, irritability, social withdrawal, loss of sexual libido, preoccupation with food, obsessional ruminations and rituals, and, eventually reduced alertness and concentration.

Dysphoria, an integral feature of the illness, is particularly important: many clinicians make the mistake of a second inappropriate diagnosis of mood disorder. Similarly, severe obsessional symptoms, usually relating to eating and food but sometimes of amore general nature, are common in AN's patients.

The illness is associated with premorbid perfectionism, introversion, poor peer relations, and low self-esteem. The patient is described as having been a biddable and helpful child, whose current obstinate refusal to eat is all the more extraordinary because of her previous compliance. However, these features are not found in all patients, some of whom are more extroverted and interactive, with outgoing personality profiles and a history of behavioral disturbance.

Patients react to efforts to alter their behavior with anger, deception, and manipulation, often inconsistent with their previous behavioral standards. With chronicity, they become absorbed by their illness, dependent on family or therapists, and restricted in their interests. The serious long-term effects of regression, invalidism, and social isolation come to dominate the clinical picture.

Many patients' emotional problems arise from separation anxiety and difficulties with identity. There is sometimes a "pathogenic secret", such as sexual abuse, which results in intense feelings of shame . Starving is a means of assuaging the pain and gaining control over

the course of sexual development. The patient holds on her emaciation as a form as self-realization and identifies with her wasted body.

Although this pattern of disturbance imparts conformity to the psychiatric presentation, the underlying phenomenology and psychodynamic psychopathology are varied. Each patient needs to be understood as an individual.

Dieting (restricting) and purging forms of AN

Anorexic behaviors, although all directed at either decreasing energy intake or increasing energy expenditure, are not uniform. Some patients employ only the restrictive behaviors commonly associated with "normal" dieting, such as undereating, refusal of high-energy foods, and *strenuous exercise.* This is defined the "dieting" or "restricting" form of the illness. These patients differ from healthy population mainly in the extent of these behaviors and their inability to desist.

Others also use vomiting and laxative or diuretic abuse: purging form of AN.

The distinction of these two forms of illness is important particularly in respect to prognosis.

Restricting behaviors

Food choice is determinate by misconceptions acquired from dubious sources such as popular magazines. In the 1960s, patients selectively avoided simple sugars and other carbohydrates (sweet and potatoes). In the 1980s and 1990s, fatty foods and red meat were considered "unhealthy", and vegetarianism has become the most common dietary perversion. Energy-reduced dietary products, foods with high fiber content, and supplementary vitamins are preferred. Further changes in the next decade may include an avoidance of genetically modified foods.

At the table patients cut their food into minute portions, choose inappropriate utensils (a teaspoon for dessert), eat painfully slowly, add excessive condiments, adopt a bizarre sequence of dishes, drink too much (or too little) fluid, dispose of food secretly, and count calories. This form of behavior result in conflict with the family: together with the patient, the family increases state of anxiety related to food, leading the patient to assume food in the company of others. A person affected by AN takes different foods and eats at different times, often late in the night, after hours of procrastination. Patients become overinvolved in reading recipe books, cooking, and may take over the responsibility of preparing the family meal, although they will eat hardly anything themselves. Other family members put on weight while the patient becomes thinner.

Purging behaviors: in addition to food restriction many patients use vomiting, laxatives and

diuretic abuse to induce future weight loss. This purging form of illness is particularly malignant, since their behaviors are injurious to health. Serious physical complications arise in patients who maintain a persistently low weight and in whom purging is prominent.

Strong cathartics or herbal laxatives are also taken, ostensibly to combat constipation, but really to induce diarrhea. Although patients believe the diarrhea will prevent them from absorbing calories, the weight loss produced is simply the result of dehydration. Oral diuretics have a similar effect.

Compared with *restricting-only* patients, purging anorexics are more likely to have problems with impulse control and substance abuse.

Physical Consequences

The undernutrition of anorexia nervosa differs from that of protein calorie malnutrition in a Third World setting in that patients are unlikely to have their illness compounded by parasitical infestation, but, like the victims of starvation, they are malnourished as well as undernourished - lacking in vitamins and other essential nutrients, and deficient in proteins. On nutritional restoration, they regain protein as well as fat tissue, unlike patients with diseases such as cystic fibrosis, in whom protein depletion is difficult to correct. The change in the typical anorexic diet result in a microcytic and iron deficient diet rather than microcytic anemia as in the past. Patients are also likely to be dehydrated.

There is no ideal way of determining the extent of malnutrition, measurement of body composition does not give a complete picture. The proportion of body fat in total body composition is reduced to under 10%, but this does not indicate the severity of protein loss. In contrast, a patient who has exercised strenuously may have replaced fat with muscle, and her low body fat may exaggerate the extent of undernutrition. Measuring body weight is similarly inaccurate because it makes no allowance for changes in body composition. Weight is only meaningful if related to the range of peers, that is, expressed as a percentage of ideal weight, a body mass index (BMI), or a BMI percentile.

Because current diagnostic criteria include subjects with BMI of 17.5 or even higher, some patients are thin rather than emaciated. Others, however, have lost 50% or more of normal body weight (BMI of 10 or less). Fortunately, the degree of malnutrition is usually less severe than that of undernutrition in patients with anorexia nervosa. Malnutrition in the earlier phases of the disease may be relatively mild and manifest only on signs such as the overgrowth of lanugo hair, alopecia and dry skin. However some patients do show more serious evidence of vitamin deficiency and significant protein depletion.

In the early phase of illness, the patient with Anorexia Nervosa chooses a diet low in energy-

dense foods. This kind of diet, together with the characteristically high level of activity, exerts a nitrogen-sparing effect, so that the initial weight reduction is due mainly to loss of fat. With severe weight loss, the glucose stored in glycogen deposits in the liver is soon exhausted and fat reserves are mobilized, leading to the formation of ketone bodies. These ketone bodies account for a sweet smell of acetone on patients' breath. As the body accommodates to semistarvation, gluconeogenesis is stimulated and protein tissue is broken down, leading to protein depletion, water loss from the intracellular compartment, electrolyte imbalance, and metabolic complications.

Staging

Diagnostic criteria of anorexia nervosa inadequately denote the patient's clinical condition. The psychiatric presentation also changes, so that anorexic cognitions are replaced by more profound mental disturbances. The course is typically one of remission and relapse until recovery or chronicity intervene. For these reasons, anorexia nervosa requires staging, like neoplasia; this will be the task for the future.

Overactivity

Most anorexia nervosa patients are overactive. It is almost as characteristic as the dietary restriction and just as difficult to modify. There are two kinds of presentation.

First: many patients exercise deliberate to burn calories and induce weight loss. Activity may be surreptitious, such as going up and down stairs frequently on various pretexts, or getting off public transport several stops before the destination and walking the rest of the way. Some quote this phrase: "never sit if you can stand, never stand if you can walk, never walk if you can run". The activity is strenuous physical exercise, usually in the form of aerobic classes or running and usually prefer to do it alone. It has a strongly obsessive character and is performed in a regular and rigid sequence. Patients feel guilty if they do not do the exercise.

Exercise and eating are linked by "debiting": the patient "earns" the right to eat by undertaking prescribed activities or, conversely, she "pays" for self-indulgence with an extra exercise session.

The second presentation is a persistent restlessness that occurs late in the illness. Beyond voluntary control, it is associated with sleep disturbance and is similar to the ceaseless overactivity seen in laboratory animals when they are deprived of food. Restlessness persists until the patient's physical condition has deterred to weakness and lassitude.

The overactivity may be related to the fall in core body temperature , which has been seen in severely ill patients.

The need to raise core body temperature, may also account for the paradoxical increase in

diet-induced thermogenesis noted during refeeding.

Medical and physical aspects of eating disorders

The following section is an extensive summary of the text Katherine A. Halmi (2002), published in Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

Physiology of Anorexia Nervosa

Physiological abnormalities are secondary to dieting, underweight state, vomiting, laxative misuse, excessive exercise or to other behavior directed toward losing weight. With nutritional rehabilitation and cessation of these bad behaviors, the physiological changes are reversed.

Cardiac and cardiovascular disturbances

Bradycardia and orthostatic hypotension (60 BMP in resting heart rate and diastolic blood pressure 60) are common findings in AN patients. Electrocardiographic (EKG) changes are common and reflect electrolyte disturbance; dizziness and frank syncope are not unusual.

Patients who use syrup of ipecac to induce vomiting, may develop an irreversible cardiomyopathy that usually result in death.

Gastrointestinal complications

Delayed gastric emptying is common in AN patients and is associated with feelings of fullness and bloating**.** Persistent laxative abuse may decrease the motility of the colon and result in true constipation.

Endocrine abnormalities

A lot of endocrine changes are present in AN, involving hypothalamic-pituitary-ovarian, adrenal, and thyroid axes, as well as growth hormone, insulin, neuropeptides, endogenous opioids leptin and neurotransmitters.

Amenorrhea one main diagnostic criteria of AN but with weight restoration normal luteinizing hormone (LH) secretion improve the normal menstrual cycles. Regular injections of gonadripin-relasing hormone (GnRH) in underweight patients, produce ovulation.

Mild hypercortisolism, with a blunting of diurnal rhythm, is common in AN. Elevated levels of corticotropin-relasing hormone (CRH), a potent anorectic hormone, return to normal levels with weight restoration. The secretion of both GnRH e CRH is highly influenced by neurotransmitters, norepinephrine and serotonin, with help to regulate eating behavior and influence mood.

Clinical evidence of hypothyroidism includes hypothermia, dry skin, bradycardia,

constipation, and delayed relaxation of the tendon reflexes. With weight gain reverse these dysfunctions.

Dopamine, serotonin, norepinephrine, growth-hormone and peripheral feedback mechanisms all influence the secretion of growth hormone from the pituitary gland. Anorexia Nervosa patients have a dysregulation of the growth hormone and this is a response to the starvation state, indicated a disturbance at the hypothalamic level.

Insulin and fasting blood sugar levels are decreased or in the low-normal range in AN. Glucose tolerance is commonly impaired and likely reflects the starvation state.

Neuropeptides have a role in regulating appetite, satiety, mood and neuroendocrine functions: they may contribute to the pathology of eating disorders. Satiety may be produced by several gastrointestinal hormones (cholecystokinin CCK, glucagon, somatostatin and bombesin): studies indicate that these hormones don't contribute to the initiation or maintenance of the eating disorders.

Dopamine and opioids have a role in modulating pleasure-reward responses to food and eating behavior. Abnormalities of opioid activity seem to state-related in that they reflect purging, severe food restriction or active bingeing.

Initially, leptin was regarded as a signal to reduce feeding and hence reduce body weight. However, numerous researches show leptin level in AN correlate positively with Body Mass Index (BMI) and amount of adipose tissue; that is, emaciated patients have extremely low levels of leptin that increase as the patients gain weight. It's a correct hypothesis that leptin is a signal of energy deficiency: when leptin levels in the blood fall, energy intake is reduced. In starvation falling leptin levels should promote increased food or energy intake, decreased energy expenditure and the metabolism of calories into fat.

Other abnormalities

Some studies using computerized tomography and magnetic resonance imaging have revealed cerebral atrophy and ventricular dilatation. In most cases, this appears to be reversible, but functioning imaging methods have not revealed consistent findings , so more studies are needed.

Elevation of serum enzymes may reflect fatty degeneration of the liver and is present in emaciated patients with AN and during their refeeding. Impaired temperature regulation is present in emaciated patients, with an abnormal automatic response to cold. They also have a sudden abnormal increase in core temperature in response to liquid feeding. Thus, the stability of their temperature regulation is impaired.

Dermatological manifestations of starvation in AN include loss of scalp hair, dry skin and

brittle nails. This kind of patients may develop an orange discoloration of their skin due to hypercarotenemia; they also will develop fine, downy facial hair termed *lanugo hair*. Self-induced excoriations or hair loss due to trichotillomania may be noted as manifestations of concomitant psychiatric conditions.

A great problem in patients with an ED is the dental damage, because of vomiting induced.

Anorexia and osteoporosis

Severe undernutrition is associated with low bone mineral density (BMD) in adult women (Hay P., et al., 1992; Grinspoon S., et al., 1999), in adolescent girls (Bachrach L., et al 1990; Turner J., et al., 2001) and in boys (Castro J., et al., 2002). Osteopenia and fractures are common in AN cronic patients. The pathogenesis underlying low BMD includes an uncoupling of bone turnover in adults with AN, with a decrease in bone formation and an increase in bone resorption markers, whereas in adolescents with AN, there is an overall decrease in bone turnover, in contrast to the state of increased bone turnover in healthy adolescents. Contributors to low BMD in AN include hypogonadism, undernutrition, an associate state of GH resistance, hypercortisolemia and possibly high ghrelin and peptide YY levels. Treatment of osteoporosis in AN patients remains controversial (Fairburn, 2002). Oral estrogen is not effective in improving BMD, however, rhIGF-I (a bone trophic factor) with estrogen has been shown that cause an increase in BMD in adults with AN. Currently, there are no therapeutic options for improving BMD in adolescents with AN with the exception of sustained weight recovery, that should be encouraged in all patients with AN, also associated with an adequate calcium and vitamin D intake. (Misra M, 2006)

Epidemiology and etiology of ED: *Distribution of Eating Disorders*

The following section is an extensive summary of the text of Hans Wijbrand Hoek (2002), published in Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

Epidemiological studies show that eating disorders are not distributed randomly among the population. Young females constitute the most vulnerable group. In clinical samples, only 5-10% of patients with an eating disorder are males. Eating disorders seem to be "Western" illnesses: They occur predominantly in industrialized, developed countries. Most reports of eating disorders outside the Western World tend to be of an anecdotal nature and show that eating disorders are uncommon in non-Western countries. Immigrants are more likely to develop an eating disorder than their peers in their country of origin. This type of evidence demonstrates that sociocultural factors play an important role in the distribution of ED.

People in some professions seem to be particularly at risk; fashion models and ballet dancers, for instance, seem to be at greater risk for the development of an eating disorder than many other professional group. However, what is not known is whether "preanorectic" persons are more readily attracted to the ballet world, or whether being a ballet dancer is the source of increased risk. In some countries, eating disorders are overrepresented among the middle and upper socioeconomic classes, but this social class bias might be connected with the structures, norms, and thresholds of the local health care system. In European countries such as the Netherlands, which has a rather generous state heath insurance system, class differences seem to have less impact on the presentation and recognition of eating disorders.

AN is also widely regarded as relatively "modern" disorder. In recent years, there has been such an increase in the number of patients receiving treatment for an eating disorder that some people are suggesting there is an "epidemic". Epidemiological data are not confirming that there has indeed been an equivalent increase in the number of cases in the general population.

Prevalence of Anorexia Nervosa

Researchers in epidemiology study the occurrence of disorders and try to determine the factors associated with vulnerability to their development. Incidence and prevalence are the two principal measures of the distribution of a disorder. The prevalence rate is the actual number of cases in a population at a certain point in time. The incidence rate is defined as the number of new cases in the population per year. Prevalence and incidence rates for eating disorders are commonly expressed as the rate per 100,000 population.

In the epidemiological research on eating disorders, prevalence studies vastly outnumber incidence studies. Prevalence studies of eating disorders are often conducted in high-risk populations such as schoolgirls or female college students.

The average figure for the point prevalence of AN thus determined is 280 per 100,000 young females (i.e., 0.28%).

Incidence of Anorexia Nervosa

Because the incidence of eating disorders is relatively low, no studies have been conducted on their incidence in the general population. It is impossible to screen a sufficiently large population, for instance, 100,000 people, for several years.

Although different strategies have been used in different studies, the result suggest an increase in the incidence of AN between 1930 and 1970. Since the 1970s, the incidence of anorexia nervosa in mental health care facilities in the Netherlands has been stable at around 5 per 100,000 population per year.

Researchers in Rochester, Minnesota, have screened not only the records of patients with a diagnosis of anorexia nervosa but also those of patients with amenorrhea, oligomenorrhea, starvation, weight loss, and other related diagnostic features. Between 1935 and 1989, the overall incidence of AN in the community of Rochester did not significantly increase. However, for 15- through 24-year-old females, a significant increase was found.

It is unclear whether the increase in cases reported in health care facilities reflects a true increase in the incidence in the community, since it might also be due to changes in diagnostic criteria, improved methods of case detection, or wider availability of services.

The incidence of AN obtained per 100,000 population per year were 4.2 in the United Kingdom and 8.1 in the Netherlands.

Future Directions

To date, most of the epidemiological research on eating disorders has been descriptive in character. Hence, there is a need for analytic epidemiological studies focused on their determinants. Such research is beginning, as shown by the recent publication of genetic-epidemiological studies and risk factor research.

Anxiety, Depression and Eating Disorders

The following section is an extensive summary of the text of Chynthia M. Bulik (2002), published in Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

The earliest clinical description of anorexia nervosa and bulimia nervosa noted the frequent presence of both depression and anxiety.

Subsequent investigations using structured diagnostic methodology in clinical and epidemiological samples and family studies have verified those early observations.

Of the many possible models of comorbidity, ***five*** are particularly plausible to explain the relation between eating, affective , and anxiety disorders. Each of these models yields a unique set of predictions.

1. Model one posits that depression and anxiety are sequel of eating disorders. It predicts the alleviation of anxiety or depressive symptoms with recovery from the eating disorders.
2. Model two posits that eating disorders are sequel of affective or anxiety disorders. It predicts a pattern of onset in which depression or anxiety manifest prior to the onset of eating disorders.
3. Model three posits that eating disorders are expressions of an underlying depressive or anxiety disorder eating disorders may be age-and gender-specific manifestations of depression or anxiety, with etiological factors completely shared among the classes of disorders.
4. Model four posits that eating, anxiety and affective disorders are different expression of the same underlying casual factor (e.g., neuroticism, neuroendocrine disturbance).
5. Model five posits that whereas eating, affective and anxiety disorders are unique sets of conditions, they may share some etiological factors. It make no predictions about whether the eating, depressive, or anxiety disorders manifest first but predicts the existence of both shared and independent etiological factors across the disorders.

Anorexia Nervosa and anxiety disorders

Clinical Manifestation

Anxiety in AN manifests in several forms. During the acute phase of the illness, women with anorexia nervosa are pervasively anxious about issues related to shape, weight and food. Slight increases in weight or transgressions of rigidly prescribed dietary rules result in severe anxiety. Parallels have also been drawn with obsessive-compulsive disorder, because individuals with AN display preoccupation with food, eating, weight and exercise.

Nature of the Comorbid Relationship

Both clinical and epidemiological data support substantial comorbidity between AN and anxiety disorders. Clinical studies have consistently noted elevated rates of anxiety disorders in women with AN. The most methodologically sophisticated studies suggest that well over half of women with anorexia nervosa report the lifetime presence of an anxiety disorder – most commonly generalized anxiety disorder, obsessive-compulsive disorder, and social phobia. Moreover, most of the studies indicate that the onset of anxiety disorders usually precedes the natural course of the two disorders, it may also indicate that childhood anxiety represents one significant pathway toward the development of anorexia nervosa. Thus the presence of AN significantly increases patient's risk of also suffering from a comorbid anxiety disorder.

Anorexia Nervosa and major depression

Clinical Manifestation

Clinical observation of women with anorexia nervosa commonly reveals depressed of flat affect, feeling of hopelessness and guilt, a sense of worthlessness, paralyzingly low self-esteem, irritability, insomnia and suicidal ideation and attempts.

Retrospective reports indicate that both patterns of onset occur – depression before anorexia nervosa and vice versa. Although depressed mood can occasionally improve with refeeding, several medium – and long-term outcome studies suggest that depression may persist even after recovery.

In addiction to the frequent comorbid pattern, family history studies have shown that relatives of individuals with AN are at significantly greater risk for major depression, than relatives of healthy controls.

Nature of the Comorbid Relationship

Studies on clinical samples of women with AN that have used structured psychiatric diagnostic instruments, have suggested a wide range of estimates (20-80%) for percentage of women who report at least one episode of lifetime major depression.

Epidemiological data are somewhat scarce due to the relative rarity of the condition; however extant studies suggest that major depression is the most commonly observed comorbid psychiatric disorder in women with AN.

The nature of this comorbid relation has been explored directly using twin studies. The result suggest not only the presence of unique sets of genes that contribute independently to anorexia nervosa and to depression, but also a shared genetic component indicating the existence of some genes that contribute to both anorexia nervosa and depression.

Course and outcome of anorexia nervosa

The following section is an extensive summary of the text of Patrik F. Sullivan (2002), published in Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

Accurate definition of the course and outcome of Anorexia Nervosa is fundamental to its characterization. "Course" refers to the temporal pattern of an illness from onset to subsequent recovery, partial recovery, non-recovery, or death. "Outcome" describes the state of affected individuals at some specified time after the development of a disorder. Both can be assessed in multiply ways.

Imbedded within these basic definitions, however, are a number of vexing complexities. First, there are fundamental uncertainties about whether the International Classification of Diseases (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) nosologies accurately characterize anorexia nervosa. Second, the potential diagnostic overlap between anorexia nervosa and bulimia nervosa remains incompletely understood. Third, "outcome" for anorexia nervosa has to be defined across a number of relevant domains. Fourth, the extant literature complicates the task of characterizing course and outcome by often neglecting the temporal dimension and by relying on clinical samples.

Mortality

The risk of mortality in follow-up samples of individuals with anorexia nervosa is substantial (approximately 6% per decade) and grossly elevated in comparison to individuals without anorexia nervosa. Mortality results from complications of chronic eating disorder or suicide. Over the past 25 years, risk of mortality has probably declined in association with improved recognition and treatment of anorexia nervosa.

Recovery

Over intermediate periods of follow-up, the majority of individuals with AN recover from the index illness. Approximately one-fourth continue to be symptomatic, and a sizable minority develops chronic anorexia nervosa. A potent risk factor for the development of bulimia nervosa is apparent "recovery" from anorexia nervosa. This process typically occurs within 2 years of onset of AN and in unusual more than 5 years after onset. In some respects, this can be viewed as moving from a visible (AN) to an invisible disorder (BN) whose the cardinal behaviors are easier to shield from relatives, friends, and health care professionals.

Presence of associated psychopathology

In comparison to control groups, individuals with a history of AN have higher prevalence of major depression and several anxiety disorders (particularly obsessive-compulsive and generalized anxiety disorder).

The main problem of interpretation is the nature of the relationship with the eating disorder. Is the increased prevalence of mood, anxiety, and substance use disorders a direct result of the eating disorder? Or, rather, are these features directly or indirectly involved in the etiology of AN? Whereas the former is relevant to the concept of outcome, the latter is more a confounding feature.

In conclusion we can say that the course of anorexia nervosa is not completely understood. In particular, the existence of a single pathway is very unlikely. Knowledge of the manner in which genes, environment, and individual choices interact to influence course and outcome is not known.

Risk factors for Eating Disorders

The following section is an extensive summary of the text of Ulrike Schmidt (2002), published in Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

The causation of ED is widely thought to be "multifactorial", myriad individual risk factors have been studied. As in other areas of research, there are definite fashions here. For example, during the 1960s and 1970s, an "anorexogenic family environment" was considered fundamental, and during 1980s and 1990s, childhood trauma, in particular, sexual abuse, was promoted as causally important. With the advent of new biotechnologies, we are seeing a revival of the interest in biological factors.

Methodological Issues

In order to appreciate the methodological difficulties in studying risk factors, it is useful to remember the definition of a "risk factor"; a factor that is associated with a disorder and may support a casual connection. Evidence supporting a causal link between a risk factor and a disorder is provided by (1) the factor preceding the disorder being studied; (2) the repeated appearance of the same risk factor in multiple risk factor studies; (3) the risk factor being associated with one disorder only; (4) the finding that an experimental intervention that eliminates the risk factor also eliminates the disorder.

Two main types of study are used to investigate risk factors, the case-control study and the cohort study, both of which have important advantages and disadvantages. The main advantage of case-control studies is that they are valuable when the condition of interest is relatively rare, as in the case of AN. The disadvantage relate to the many potential biases in the comparison of cases and controls.

Prospective cohort studies allow careful control of the nature and quality of the data recorded. However, these kinds of studies have problems of their own. Given the relative rarity of ED, they require extremely large numbers and may also need to be very long-term to detect associations between certain risk factors and onsets that may occur many years later.

Risk Factors for Anorexia Nervosa

There is general consensus that a genetic vulnerability increases the risk for developing AN; however, it is not yet known what it is that might be inherited and how this interacts with environmental risk factors. A predisposition for leanness may be important. Another possibility, for which there is converging evidence, is that genetic risk is conveyed via

personality traits of perfectionism, obsessionality, negative self-evaluation, and extreme compliance. Additionally, women with anorexia nervosa have high levels of exposure to a broad range of risk factors shared with other psychiatric disorders, including premorbid behavioral problems and psychiatric disorders, parental psychiatric disorders, and childhood adversity, including abuse and death among close relatives. Dieting seems to be relatively unimportant once the influence of other groups of risk factors has been taken into account.

A class of risk factors that so far has received relatively little attention is perinatal factors. A recent Swedish study found that girls born with a cephalhematoma and those born prematurely have an increased risk of developing AN. The authors suggest the possibility of a secondary interactional dysfunction between mother and child, for which there is support from work focused on the attachment patterns and early parenting of patients with AN.

Eating Disorders in males

The following section is an extensive summary of the text of Arnold E. Anderson (2002), published in Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

Despite being mentioned among the first case presentation in the England language 300 years ago, males with eating disorders have at times been ignored, neglected, dismissed because of statistical infrequence, or legislated out of existence by theoretical dogma.

Diagnosis and Clinical Features

The diagnostic criteria for males with anorexia nervosa are similar to those for females, but the symptomatic marker of reproductive hormone abnormality (loss of sexual appetite secondary to lowered testosterone) develops in a gradual manner unlike the more abrupt cessation of menses among females.

Males are affected by similar comorbid psychiatric conditions to those affecting females, especially mood and personality disorders. Contrary to previous assumptions, males are more severely afflicted by osteopenia and osteoporosis, with lower bone mineral density than equivalent female patients.

The notion of "reverse anorexia nervosa", sometimes called "muscle dysmorphia", has become well-established. It occurs almost exclusively in males and is characterized by the subjective thinness even when they are highly muscular. It is often associated with the abuse of anabolic steroids.

Epidemiology and Etiology

Males with eating disorders have reported since 1689.

In clinic samples, the ratio is somewhat lower with 10 to 20% of cases of anorexia nervosa being male.

In western societies, men are clearly exposed to less general sociocultural pressure to be slim and to diet, with only 10% as many articles and advertisements promoting dieting in magazines read by young males compared to young females.

Beginning in elementary school, boys are less likely to consider themselves in need of dieting but are equally dissatisfied with their body image. As many boys want to become bigger as want weight loss, and all want to be more muscular. Dieting in males is more likely to be related to participation in sports, past obesity, gender identity conflicts, and fear of future medical illness, than sociocultural endorsement of dieting. Adult males describe themselves as

overweight at weight 15% higher than females (with reference to ideal body weight).

Women feel thin, generally, only when below 90% of ideal body weight, whereas men rate themselves as thin when as high as 105% of ideal weight.

The idealized body image for males is usually V-shaped upper body (muscular, moderate in weight, with virtually no fat) as evidenced by changes in action toys and media ideals. More and more skin exposure is apparent in advertisements directed toward males, with particular emphasis on well-defined abdominal and chest muscles.

While the frequency of homosexual orientation among males with eating disorders is high at approximately 20%, it should be noted that this still applies to only a minority of cases. Nevertheless, homosexual orientation is an established risk factor. Another established risk factor is premorbid obesity, which is present in about 50% of cases.

Treatment

The basic principles of treatment in males and females are similar:

- Restoring normal weight;
- Interrupting abnormal behaviors;
- Treating comorbid conditions;
- Helping patients think differently about the value of weight loss or shape change;
- Preparing them for reintegration into their sociocultural, gender-specific roles.

Restoration of a healthy weight in males leads to increased testosterone, but 10-20% are left with some testicular abnormality.

Indications for hospitalization are independent of gender.

Males with eating disorders appreciate working with clinicians who are sensitive to male concerns. Women with eating disorders may stigmatize males with eating disorders, who often feel isolated in therapeutic groups of women.

Outcome

Being male is not an adverse prognostic factor. Men respond well to component treatment, with short- and long- term outcome being equal to that of females. Pre-illness sexual fantasy or behavior improves prognosis.

Probable facts

<u>Diagnosis and Clinical Features</u>

Males with eating disorders score lower on the Eating Attitudes Test (EAT) and in the drive for thinness score on the Eating Disorder Inventory (EDI), but are equally distressed on the Back Depression Inventory (BDI) and the Minnesota Multiphasic Personality Inventory

(MMPI), suggesting that screening questionnaires may not be asking the pertinent questions of males.

Compared to females, males with eating disorders are more likely to have substance abuse as comorbid condition. Recent pilot studies have reported that males with anorexia nervosa also suffer from decreased brain size secondary to self-semistarvation.

Epidemiology and Etiology

There appears to be a rough correlation between the prevalence of anorexia nervosa and the degree of social reinforcement for slimming, suggesting a dose-response curve independent of gender. The two genders probably experienced parallel increases in the incidence of eating disorders until the mild 1980s. At that time time, however, the distressed, cachetic appearance of the first male with AIDS decreased the value of slimness in men and returned the idealized image in males to one of more muscularity. Testosterone may have some protective effect on the development of eating disorders by crating a mesomorphic, athletic appearance that is incompatible with severe starvation.

Changes in secondary sexual characteristics and social functioning during puberty cause less distress in males, who therefore less likely to use eating disorders as a defense against maturation. The decreasing age of puberty may have affected boys less than girls.

Treatment

More than one male patient in a treatment program yields benefits such as the possibility of male-only patient groups, thereby allowing greater openness and confidence. It also helps patients to explore gender-specific aspects of etiology. Gender has less influence on treatment in severe cases.

With increasing weight , male manifestations of increased testosterone includes flirting, masturbation, and sexual comments. Males are more likely to benefit from weight training during treatment, since many develop prominent abdominal fatness on weight restoration and, as a result, quickly return to dieting.

Outcome

As with females, males have a worse prognosis when they have a very low weight or a long-established low weight, marked comorbidity, or an unsupportive family. Negative prognostic features also include failure to achieve a truly normal weight and lack of follow-up treatment.

Conclusion

There are many similarities in the clinical features, epidemiology, etiology, etiology, treatment, and outcome for males and females with eating disorders. These similarities are

sufficient to allow the clinician to identify cases and undertake the essentials of treatment. It is clear, however, that experience of being male in our society, from conception on, differs from that of being female. These differences include the effect of a steady state of gonadotropin, the percent of body fat needed for pubertal onset, the psychosocial experience of puberty, the genomic influence on body shape, as well as possible differences in how precursor amino acids for neurotransmitter synthesis are metabolized in the brain. In addition, the sociocultural environment differs from birth on in its reinforcement for dieting and weight loss, and these differences are evident even in elementary school.

Clinicians may be confident in diagnosing males with eating disorders, certain that early comprehensive treatment and good follow-up not only reduce mortality and morbidity but also increase quality of life.

In both genders, the goal of complete cure, defined by return to gender-specific cultural normality (not perfection), is achievable.

Gender, ethnicity, and eating disorders

The pronounced gender differences in the distribution of AN and Bulimia Nervosa (BN) have suggested the question of why ED are so disproportionately more common among female than among male. Evidence concerning genetic influences in inconclusive, and pharmacological treatments have limited efficacy, underlining the possibility that biological factors are not at the core of ED. Little prospective research establishes that hormonal or neurotransmitter dysfunction predate ED; one of the most promising findings, that dieting may trigger lowered 5-HT serotonin in women but not in men, underscores the interaction of a culturally induced behavior (dieting) and biological vulnerability. (*Striegel-Moore,2002)*

Research on gender differences has focused largely on cultural factors. In this line of research, risk for the development of an ED has been hypothesized to derive from women's subordinate position in society, female gender role socialization, and the contemporary female beauty ideal of extreme thinness.

The emphasis on the role of cultural factors in the etiology of eating disorders derived by the observation that eating disorders are less common among females from non-industrialized nations, certain ethnic minority groups within United States, and some experts described eating disorders as culture-bound syndrome (a problem of white females in Western industrialized societies). (*Striegel-Moore,2002)*

It's important to define terms such as Race, Ethnicity and Culture to clarify the general confusion regarding this terminology. Race is defined by cultural practices, due to its history as a biological category. Ethnicity defines the population by its ancestry, language and customs: it not necessarily implies specific physical characteristics such as skin color. Culture encompasses a multidimensional, complex construct that includes shared institutions, values, norms and language.

In defining the precise influence of gender and ethnicity, researchers need to move beyond current conceptualizations of risk factor. These ethnicity literature, for example, has focused mainly on body ideal as a risk factors. It's possible to conclude suggesting that gender and ethnicity are important in understanding the etiology and maintenance of eating disorders. In the future research the investigators will need to define and operationalize terms appropriately, select measures that have psychometric validity with all participants, and recruit representative epidemiological samples. (*Striegel-Moore,2002),*

It is important to mention the concept of body image because: although my research does not explore this section, the body image is a most fundamental concept in the development and maintenance of an Eating Disorder. In Anorexia Nervosa, the perception of body image is highly distorted and affect the course of the disease.

Body image

The term of Body Image (BI) refers to a multidimensional concept, which involves neurophysiological aspect refers to perceptual experiences such as visual, spatial, sensory judgments, physical sensations, body awareness, body recognition, physical appearance, body size, and shape. (Probst et al., 2008).

BI encompasses an individual's body-related self-perceptions and self-attitudes, and is linked to self-esteem, interpersonal confidence, eating and exercise behaviors, sexual experiences, and emotional stability. There are four dimensions of BI:

Perceptual: how we imagine ourselves to look.

Cognitive: how we think about or evaluate our body in terms of its appearance and function.

Affective (Emotional): feelings (i.e., comfortable, proud, anxious, disgusted) experienced in relation to our body's appearance and function.

Behavioral: what we do to reflect our positive or negative perceptions, thoughts, and feelings.

It's possible to speak about body reality and ideal body . The first refers to the actual physical characteristics: height, weight, body fat, lean body mass, bone structure, fitness, strength, disease, etc. the second means how we think our body should look and function.

Body image reflects an interplay between body reality and ideal body.

The recognition that human bodies naturally come in a wide range of shapes/sizes and that genetic factors are instrumental in determining one's weight and shape, can determinate an healthy Body Ideal.

A poor body image is associated with greater anxiety and depression symptoms; depressed and anxious persons view their appearance more negatively than do non depressed individuals, even if there are no differences in actual body shape and size; body image disturbance is an antecedent, not a consequence, of increased depression and anxiety.

Among adults, body satisfaction has been associated with fulfillment with personal interactions and overall life happiness, healthy dietary choices and physical activity performance, and increased sexual pleasure and activity frequency. Conversely, among adolescent youth, body shape and body weight dissatisfaction have been associated with plethora of psychological ill from eating disorders to major depression. (Huang et al., 2007)

Body Image and Body Dysmorphic Disorder

Body Dismorphic Disorder (BDD), also known as dysmorphophobia, is an intriguing disorder that has been described around the world for more than a century. BDD appears be relatively common in the general population and in psychiatric, dermatologic and cosmetic surgery

settings. Little is known about body image disturbance in BDD. (*Katherine A. Phillips, 2002)*
BDD consists of a preoccupation with an imagined defect in appearance; if a slight physical anomaly is present, the person's concern is markedly excessive. The preoccupation causes clinically significant distress or impairment, and it cannot be better accounted for by another mental disorder – such as anorexia nervosa.
In DSM-IV, BBD is classified as a somatoform disorder, whereas its delusional variant is classified as a psychotic disorder. (*Katherine A. Phillips, 2002)*

The relationship between BDD and Eating Disorders
The literature on BDD contains little investigation, discussion, or theorizing about its relationship to the eating disorders.
Much research has focused on obsessive-compulsive disorder, depression, schizophrenia, and social phobia. BDD and ED have some obvious similarities: a preoccupation with perceived appearance flaws, a disturbance in body image, and a sense that one's body in unacceptable, performance of repetitive behaviors, such as mirror checking and body measuring, and a similar age of onset and course of illness. (*Katherine A. Phillips, 2002)*
However there are some differences including a focus on body shape and weight versus more specific parts: patients with BDD have a general ugliness with overall appearance or overall body build, and patients with ED may focus on specific body parts, such as their stomach or hips.
BDD and eating disorders also differ in terms of gender distribution and are not as highly comorbid with each other as with many other disorders. Family history and treatment data, while limited, also do not strongly support the hypothesis that these disorders are closely related.
Another unanswered question is whether the DSM-IV diagnostic hierarchy is correct:

- Should BDD be diagnosed only if body image concerns are not better accounted for by an eating disorder?
- Might the eating disorders actually be a form of BDD given their important feature of disturbed body image?

While this seems unlikely given the disorders' apparent differences, the hierarchy needs to be empirically examined. (*Katherine A. Phillips, 2002)*

Body Image in Eating Disorders

A negative Body Image (BI) is a relevant characteristic of the various forms of eating disorders. In addition to an overestimation of the own body dimension and body avoidance and checking behavior, the main characteristic of body image problems are negative attitudes towards the own body. (Vock et al., 2008)

The psychological aspect refers to both cognitive (thought process and thinking style) and subjective (feelings, emotions, and mood) experiences. (Latner et al., 2008).

A literature review classifying the different methods used to assess the estimation of body size, and considers factors that have been shown to influence it. (Farrel et al., 2005)

In patients with A.N. a disturbed B.I. is main diagnostic criterion. Research in this area focuses primarily on two concepts: perceptual body size distortion and body dissatisfaction. An erroneous estimate of size of one's own body is defined as perceptual body size distortion and can be differentiated from a discrepancy between the perceived body and the desired ideal body, often described as self-ideal discrepancy. (European Vocks et al., 2008)

Many patients are preoccupied with their own body weight and at the same time seem to overestimate the actual size of their body considerably. Although it is widely accepted that there is size overestimation among eating disorder patients, some studies have challenged this claim.

Furthermore, few studies have empirically examined whether the degree of overestimation is more pronounced among patients with A.N. than among patients with B.N. (Vocks et al., 2008)

An excessive dissatisfaction with one's own body is considered a main risk factor for the development of a manifest eating disorder. Body dissatisfaction has been described as self-ideal discrepancy with a big difference between perceived body image and ideal body image indicating a high level of body dissatisfaction. Although similar to the concept of size estimation accuracy the role of self-ideal discrepancy in the etiology and maintenance of E.D. has been studied extensively, little research has examined the relative degree of self-ideal discrepancy among patients with anorexia versus bulimia nervosa. (Benninghoven et al., 2008)

It could therefore be argued that such overestimation is a symptom of the eating disorder that would improve as the core eating disorder psychopathology improved. (Farrel et al., 2005)

Body image disturbances are of high clinical relevance since they are not only a symptom of A.N. and B.N., but also play significant role in the maintenance and relapse process of these disorders. In spite of these findings, interventions aiming at improvement of attitudes towards

the own body and establishment of functional coping strategies for negative body-related thoughts and feelings are still often being neglected in the treatment of E.D. (Benninghoven et al., 2008)

In cognitive behavioral body image therapy (BIT), such interventions include body exposure as a main treatment component in order to reduce negative body-related emotions by means of habituation processes (Vocks et al., 2007), to sensitize for positive aspects of the own body (Jansen et al. 2005), and to correct the distorted view of oneself. These tasks should be extended to everyday life situations in order to overcome body checking and body avoidance behavior. Furthermore, cognitive techniques are applied in order to identify and modify negative body-related thoughts. (Benninghoven et al., 2008)

The earliest measures of BI were one-dimensional (cathexis scale - 1953 ◊ measures satisfaction with 40 body sites and function). Today we have the possibility to evaluate some multidimensional rating scales, commonly designed to asses the wide range of feelings and attitudes that patients with eating disorder display toward their own bodies: EDI (Eating Disorder Inventory), BAT (Body Attitudes Test), BSQ (body Shape Questionnaire), BAQ (Body Attitude Questionnaire), BUT (Body Uneasiness Test), SLC-90-R (Self-report symptom inventory-Revised).

Compulsive exercise in ED

Compulsive exercising is a common feature of patients with eating disorders. It has been reported more frequently in patients with restricting-type anorexia nervosa than with other eating disorders. It is associated with higher eating disorder psychopathology, dietary restraint, general psychopathology, and specific personality features (ie, higher levels of perfectionism, persistence, and lower novelty seeking). It is a potent maintaining mechanism of eating disorder psychopathology, and it increases the risk of overuse injuries, bone fractures, and cardiac complications. It also appears to be a predictor of poor treatment outcome. *(Dalle Grave, 2009)*

Clinic treatment of Anorexia Nervosa

The following section is an extensive summary of the text of Allan S. Kaplan (2002), published in Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

Eating Disorders Services

It's important for health care administrators and providers to attend to the organization of services, so that available resources are utilized in the most expedient and cost-effective manner. In particular the attention needs to be paid to the philosophical and conceptual characteristics such programs, their clinical and educational components, their role in advocacy, and their administrative structure.

The ideal comprehensive treatment program for eating disorders should have these four conceptual following characteristics:

1. *Should be multidisciplinary*. Because of the complex nature of ED The team should include a psychiatrist, including the medical management. The nonmedical clinicians should include psychologists trained in those evidence-based psychotherapies; a nutritionist experienced in the nutritional care of these patients; a social worker experienced in working the families of patients with ED; an occupational therapist skilled in the psychosocial rehabilitation of patients with anorexia nervosa and bulimia nervosa; the nursing staff familiar and confortable in dealing with medical and psychiatric needs of these patients.
2. *Should follow up-to-date published treatment guidelines*. The American Psychiatric Association's Practice Guidelines for the treatment of patients with eating disorders, published in January 2000. In addition the program should provide care in a wide range of modalities: individual, group and family psychotherapy, nutritional rehabilitation, pharmacotherapy, medical stabilization.
3. *Should provide evidence-based care*. This requires a database that evaluates the pre and post treatment status of patients, as part of a comprehensive and ongoing system of program evaluation.
4. *Should provide care that is cost-effective*. This can be accomplished by proving a range of treatment intensities in a "stepped care" fashion, so that the least intensive, least costly interventions are given to the largest number of patients initially, with the more intensive, more costly treatments (inpatient and day treatment) being reserved for the

sickest, most treatment-resistant patients who have not benefited from less intensive, less expensive outpatient treatment.

The ideal comprehensive treatment program for eating disorders should have these eight clinical following elements:

1. *Systematic and comprehensive initial evaluation*. The initial assessment should be conducted by a psychiatrist specialized in the medical care of eating disorders. This should include a complete psychiatric history and medical status, as well as a medical evaluation, including appropriate laboratory investigations and recommendations for appropriate pharmacotherapy. Following, the patient should be referred to one of the clinical components of the program for treatment.
2. *A brief psychoeducational program*. This should provide patients with detailed information relevant to their understanding of the psychobiology of eating disorders.
3. *Outpatient psychotherapy*. This should include cognitive-behavioral therapy (CBT) provided on an individual or group basis, following the published guidelines of Fairburn and others for effective CBT in the treatment of AN. Additional outpatient psychotherapy should include motivational enhancement therapy focused on increasing motivation to accept the changes necessary for recovery, as well as family or marital therapy.
4. Nutritional counseling. This provides individualized meal planning focused on increasing caloric intake and expanding macronutrient selection. This nutritional rehabilitation should include reducing starvation-related symptoms, medically safe weight gain, correcting nutritional deficiencies, achieving adequate, and encouraging healthy exercising.
5. An intensive day hospital treatment program. Ideally, this should run for 8 hours per day, 5 day per week. It should provide structured, supervised meals, ongoing medical monitoring, pharmacological therapy, and intensive group and individual therapy for seriously ill but medically stable patients with AN.
6. *An inpatient program*. This should provide 24 hour in-hospital care for seriously ill, medically unstable patients with AN. The goal of this program should be to stabilize patients medically and begin the process of nutritional and psychosocial rehabilitation, which can then continue in a partial hospitalization program.
7. *An aftercare and chronic care program*. This should focus on relapse prevention as well as vocational retraining and the provision of psychosocial support. Such support is also important for those treatment-resistant patients who continue to have

significant symptoms despite having been involved in intensive treatment programs.

8. *Specialized interventions for subgroups of patients*. Certain patients with an ED have a comorbid physical illness that require special clinical needs.

The ideal comprehensive treatment program for eating disorders should finally have some *educational* components:

1. *Public education*. A comprehensive eating disorder program should be responsive to its community, and provide educational material as well as regular forums for public education to its consumers.
2. *Professional education*. In addition to educating students of all disciplines who train within the clinical services, a professional education outreach program that focuses on educating and training local clinicians about eating disorders is an important component of a comprehensive eating disorder service.
3. Advocacy. An increasingly important role for a program in eating disorders is to act as an advocate in lobbying government and third-party payers for adequate insurance coverage and the financial resources needed in order to be able to adequately treat patients with severe ED.

Cognitive-Behavioral Therapy (CBT) for Anorexia Nervosa

A CBT model for understanding and treating this disorder was first described by Garner and Bemis in 1982, and further elaborated in a series of papers that specified some components of the complex treatment package. Until the past few years, the treatment was virtually untested (a state of affairs that contrasts sharply with the extensive study of Fairburn's CBT for Bulimia Nervosa, but matches the general status of treatment research in AN). Recently, this area has been invigorated by proposals for shifts in emphasis in the basic CBT model, offered both by its originators and other CBT experts in the ED field. Like the initial approach, however, these suggested revisions are based on clinical experience rather than accumulated evidence about the strengths or weaknesses of existing models. (*Kelly Bemis Vitousek, 2002)*

Cognitive-behavioral theory

Cognitive models focus on the variables that initiate and maintain anorexic symptoms rather than on remote etiological factors. According to cognitive theories, the core disturbance is a characteristic set of believes associated with the desire to control eating and weight. A fundamental premise is that the worth of the self is represented in the size and shape of the body. This dominant idea influences individuals to engage in stereotypical eating and

elimination behaviors, to be responsive to eccentric reinforcement contingencies, to process information in accordance with predictable cognitive biases, and, eventually, to be affected by the physiological and psychological sequelae of starvation – all of which strengthen the underlying premise. Although some of the consequences that maintain AN are automatic and unmotivated, dietary restraint and weight loss also serve valued functions for these individuals. (*Kelly Bemis Vitousek, 2002)*

Cognitive-behavioral intervention

CBT for AN is based on the approach delineated by Beck for the treatment of depression and anxiety, with adaptations to address specific features of this disorder. These include 1) the ego-syntonic nature of symptoms; 2) the interaction between physical and psychological elements; 3) specific belief related to food and weight; 4) pervasive deficits in self-concept.

Future directions

At present CBT is the better established than alternative forms of individual therapy for AN; however, it has yet to be demonstrated that CBT works better. In order to evaluate its relative efficacy, direct comparison between CBT and other psychotherapies designed for this population, are obvious next step. (*Kelly Bemis Vitousek, 2002)*

Prevention of Eating Disorders

Prevention is a relatively new domain of research and discussion in the field of ED: most of the systematic study has been conducted since 1990. Despite limited allocation of resources, the field has considerable growth in output, leading to the emergence of a cumulative body of knowledge that can help guide further developments. (*Niva Piran, 2002)*

While the field of prevention has seen considerable progress, many challenges remain.

Conceptual challengers relate to the need for 1) enhanced reliance on risk and protective factor and prevention research in constructing prevention programs, and possibly the integration of risk factor and prevention research; 2) further expansion in the cross-sectional and prospective study of social etiological factors; 3) integration of knowledge derived from the broader field of primary and secondary prevention, particularly the emphasis on generic risk and protective factors (self-esteem, life skills, competence and parental warmth), and on comprehensive programs; 4) incorporation of multilevel strategies and the assessment of consequent systemic changes at the policy, institutional, familial, and individual levels; 5) examination of participatory context-specific models of health promotion strategies in schools, such as those developed by the World Health Organization. (*Niva Piran, 2002)*

Methodological challenges relate to the need to 1) specify the goal, theoretical basis, rationale, and target population of each intervention strategy; 2) employ experimental designs with adequate sample size and follow-up periods that include more than one comparison group in more than one setting, and that allow for the examination of trends over time prior to the interventions being studied; 3) select outcome measures to match specific program goals, including the use of measures of systemic change and potential negative intervention effects; 4) specify implementation processes and requirements; 5) explore the pros and cons of alternative participatory approaches to health promotion interventions.

The field continues to gain momentum and work toward the development of best-practice models. (*Niva Piran, 2002)*

SECTION 2

METABOLISM AND REGULATION OF EATING AND BODY WEIGHT

Basic regulation of eating and body weight

Central Physiological Determinants of Eating Behavior and Body Weight

Disturbed eating patterns are a primary symptom of numerous psychiatric disorders. Increased understanding of the systems of the body and brain related to energy and nutrient balance may help to treat and prevent these common problems. (*Sarah F. Leibowitz , 2002)*

Researchers in neurobiology have used an integrative, interdisciplinary approach to study the multiple determinants of eating behavior, energy balance and body weight. These include diverse signals:

1. Simple nutrients in the blood (glucose, fatty acids, triglycerides, amino acids);
2. Classical neurotransmitter molecules for rapid, short-term communication;
3. Large neuropeptides for slower, more long-term action
4. Circulating hormones for both neuromodulatory and metabolic processes.

These signals derive from different peripheral organs, in particular, liver, pancreas, gastrointestinal tract, and also from different areas of the central nervous system, from the hindbrain to the forebrain. (*Sarah F. Leibowitz , 2002)*

Systems in the Body and in the Brain.

In the periphery, in both animals and humans, a variety of substances are believed to be involved, in the complex process of integrating physiological and behavioral systems geared toward energy and nutrient homeostasis. In addition to these hormones, the process of integrating metabolic information from the periphery with neurochemical signals in the central nervous system requires specialized functions of multiple brain areas:

1. the lower brainstem;
2. the pons-midbrain and thalamus;
3. the hypothalamus;
4. forebrain structures.

The role of the hypothalamus in this process, relating hormones and metabolism to behavior,

has received considerable attention. In fact a number of neurochemical and neuroendocrine systems has been identify in this structure and are believed to be involved in controlling appetite for the macronutrients, carbohydrate, fat and protein. They also modulate metabolism and contribute to the body's nutrient stores and ultimately, weight gain and adiposity. These systems, which are closely linked to and controlled by circulating hormones and metabolites, give a contribution to normal physiological functions. They are then evaluated in terms of their role in the development or maintenance of clinical eating and body weight disorders. (*Sarah F. Leibowitz , 2002)*

Regulation of food intake

The following section is an extensive summary of the text of W.F. Boron and E.L. Boulpaep (2002), published in the text of Fairburn "Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London", wide and still today a complete revision of the scientific literature on the history of AN.

It is the balance between food intake and energy expenditure that determines overall body weight. Food intake is primarily under the control of he hypothalamus, although higher CNS centers and other areas also play roles. Hypothalamic centers respond to two major kinds of afferent input: short-term factors that reflect daily meal activity and long-term factors that reflect whole-body energy stores.

Classic studies – in which investigators made lesion in, or electrically stimulated, specific brain regions – identified two areas in the hypothalamus that are important for controlling eating. The satiety center is located in the ventromedial nucleus (VMN).

The hunger (or feeding) center is located in the lateral hypothalamic area (LHA).

Short-term factors that regulate feeding

Investigators have proposed various theories to explain the short-term regulation of food intake, including models focusing on the regulation of levels of blood glucose (glucostatic), amino acids (aminostatic), or lipid (lipostatic). For example, hypoglycemia produces hunger and also increases the firing rate of glucose-sensitive neurons in the hunger center, but decrease the firing rate of glucose-sensitive neurons in the satiety center. Hypoclicemia also activates orexin-containing neurons in the LHA.

Long-term factor that suppresses appetite

A long-term factor that suppresses appetite is leptin (Greek "leptos" = thin), a protein secreted by adipocytes that binds to hypothalamic receptors; the plasma levels of leptin seem to reflect whole-body fat stores. The normal gene encodes a 167 amino-acid polypeptide hormone called leptin, which adipocytes produce. Because leptin is particularly effective when injected directly into the brain, leptin secreted into the blood by adipocytes may feed back on the brain to produce satiety (fig.57.10). In the brain, leptine binds to tyrosine-kinase-associated receptors, and inhibits expression of NPY (orexigenic), but stimulates expression of CART (anorexigenic). Plasma leptin levels reflect total-body fat stores (i.e., a long-term signal). Over

a wide range of body-fat mass, more fat is associated with higher plasma leptin levels. In addiction, leptin levels reflect the fed/fasting state (i.e., short-term signal).

Starvation and the role of carbohydrate, fat and protein stores

Starvation depletes body carbohydrates stores immediately, fat stores thereafter, and protein stores last. The average 70-kg adult uses approximately 2100kcal/day to support resting metabolic needs. During starvation, all of this energy must come from body stores. The total energy stores as glycogen in liver and skeletal muscle is at most approximately 3000 kcal. The body uses this glycogen preferentially during starvation, depleting it within 1.5 days. The average a70-kg adult also has fat stores of approximately 131,000 kcal. Mobilization and subsequent oxidation of this entire fat depot could theoretically sustain the body's resting metabolic requirement for approximately 20,000 kcal, sufficient for an additional 10 days. In reality, people seldom survive for 2 months without nutrition (even assuming unlimited water availability), because vitamin deficiencies and their associated effects begin to appear after a week or two and compromise body function. During starvation, fat becomes the fuel of choice once carbohydrate stores are expended. Fatty-acid oxidation continues at a constant rate throughout starvation. Ketone bodies from as a byproduct of fatty-acid oxidation during starvation and in diabetes mellitus (when luck of insulin inhibits glucose utilization). The liver releases the major keto-acids (acetoacetic and β-hydroxybutyric acid) into the circulation, thus lowering blood pH and creating a condition known as ketoacidosis. Acetone, another ketone produced by the liver, is eliminated in the expired air, accompanied by the fruity smell characteristic of ketosis. Ketone bodies can cross the blood-brain barrier and serve as primary fuel for the CNS when glycogen stores are depleted and the only means for generating glucose is by transamination of amino acids (gluconeogenesis) in the liver. Protein oxidation is rapid during the initial stage of starvation due to its use as a precursor for glucose in transamination reactions in the liver. Once easily mobilized protein has been consumed, the rate of gluconeogenesis falls markedly, and the body's protein stores are relatively conserved during starvation. Finally, during the latter stage of starvation, when the body has used most of its fat stores, protein becomes the only source of energy left, forcing the body to draw on these stores as a last gasp for survival.

Energy Intake and Body Weight

Energy intake is an especially critical element in the regulation of body weight because the flexibility in energy intake is very much greater then that in energy expenditure.

It's relatively easy to double energy intake on a single day, but extremely difficult to make a similar increase in energy expenditure. (*Susan A. Jebb, 2002)*

It is possible for an individual to starve or consume little energy on some days, yet the energy expenditure of a sedentary individual cannot be reduced by more than about 30%. Day-to-day variability in energy expenditure is estimated to be about 8%, compared to 25% for energy intake.

Changes in energy intake thus have considerable potential to influence body weight.

Control of energy intake

The relative maintenance of body weight over prolonged periods of time has been cited as evidence that energy intake is regulated to match energy needs. Advances in basic science have revealed some components of this metabolic control system. The picture is complex, involving a network of gastrointestinal, metabolic, and hormonal signals that are integrated in the brain and trigger a coordinated cascade of neuropeptides that either stimulate or inhibit consumption. (*Susan A. Jebb, 2002)*

Although most research on the control of energy intake has been conducted in small animals, there is good evidence that many of the pathways act in a similar manner in humans. The complexity of the system in humans is enhanced by a variety of additional cognitive factors that can in many circumstances override the innate physiological control of food intake. The nature of these cognitive factors is a product of various environmental factors, social and emotional influences, and learned experiences. Humans have the capacity to eat when they are not actually hungry or in need of food, perhaps prompted by a social occasion, or to reject some foods even at time of hunger, if they consider them to be unpalatable or are attempting to restrain their intake. (*Susan A. Jebb, 2002)*

The Resting Metabolic Rate –RMR

Is the amount of energy expended when an adult organism is awake but resting, not actively digesting, and thermal neutrality. Because work is not performed on the environment, all energy expended is releases as heat. Metabolic rate decreases below RMR by approximately 10% during sleep but can decrease by as much as 30% with starvation and increase 10-to 20-fold for short periods of vigorous exercise. (*Eric Ravussin, 2002)*

In most sedentary adults, RMR accounts for approximately 60-70% of daily energy expenditure (DEE). The DEE can be divided into three major components:

1. Basal metabolic rate (BMR) that represents 50-70% of daily expenditure;
2. Thermic effect of food, which represents approximately 10% of energy expenditure;
3. Energy cost of physical activity [spontaneous physical activity (SPA) unrestricted/voluntary physical activity], which represents 20-40% of daily energy expenditure. SPA has also been called non exercise activity thermogenesis (NEAT).

The strong relationship between RMR and body size has been known for many years and led to the development of equations still widely used to predict RMR in each sex based on height and weight. Although RMR correlates best with fat-free body mass, it is also, to a lesser extent, independently influenced by fat mass, age and sex. Together fat-free body mass, fat mass, age and sex, explain approximately 80-85% of the variance in RMR. The most variable component of daily energy expenditure is that expended during physical activity, which accounts for a large calories in very active people. However, sedentary adults exhibit a range of physical activity that represents only about 20-30% of the total expenditure. The level of physical activity can vary widely between people; one of the potential mechanisms underlying the variability in spontaneous physical activity is the activity of the sympathetic nervous system. (*Eric Ravussin, 2002)*

Peripheral Physiological Determinants of Eating and Body Weight

The relative importance of the peripheral controls of eating and body weight has increased significantly in the past 5 years. (*Gerard P. Smith, 2002)* This has been due to the realization that peripheral controls function at every meal, that so-called long –term controls of food intake act by modulating the potency of the peripheral controls, and the discovery of a new genetic obesity in rats that is due to spontaneous mutation of a mechanism of a peripheral control. All of this is the result of using meals as the functional unit of analysis for investigating the control of eating. *Meal size* is determinate by the integration of the *positive and negative feedback* produced by ingesting food stimuli. Positive feedback stimulates the central network that controls eating, and negative feedback inhibits it. The mouth and the nose are the principal sites of positive feedback; food stimuli in the mouth, stomach and small intestine produce negative feedback on eating. Eating continues as long as the potency of the positive feedback to the central network exceeds the potency of the negative one. Eating stops when the potency of negative feedback equals or exceeds the potency of the positive one. Both feedbacks are initiated by the *direct* contact of the mechanical and chemical stimuli of ingested food on preabsorptive receptors in the mouth, stomach, and small intestine. The relative potency of these feedbacks is determined not only by the potency of the peripheral feedbacks on neurons in the hindbrain but also by a number of the other categories of central stimuli that affect the central processing of the afferent feedback. These categories are diverse and important. They include stimuli related to metabolic sate, diurnal and ovarian rhythms, prior experience, social factors and, in humans, cultural factors. Because none of these diverse stimuli contact the preabsorptive receptors directly, they are classified as indirect controls of meal size. Note that all indirect controls affect meal size by modulating the central potency of the direct controls. So, we can conclude that recent research has demonstrated the importance of peripheral positive and negative feedbacks for the control of meal in humans. The mechanisms of these feedbacks provide the direct controls of meal size, and all other controls act by modulating the central potency of the direct controls. Because the sensory control of these feedbacks is possible in humans and in rodents, the feedbacks can be exploited for the experimental investigation of any molecular, neural, physiological or psychological control of eating. (*Gerard P. Smith, 2002)*

Constitutional Thinness and Resistance to Obesity

Throughout human evolution, selection pressures may have favored efficient energy storage and moderate adiposity. Such traits would increase the chances of survival during periods of famine or exposure to the elements. Conversely, traits producing inefficient energy storage or high metabolism, which would resist weight gain and fat storage, may have been selected against, and via natural selection, may be relatively rare. A comprehensive understanding of individuals who remain thin in the presence of strong environmental factors may assist with preventing individuals who are genetically predisposed form becoming obese and, ultimately, with the development of effective treatments for obesity. (*Cynthia M. Bulik, 2002)*

What is Thinness?

It is unclear whether thinness represents a distinct phenotype or merely the lower tail of the Body Mass Index (BMI) distribution. Several factors must be considered: it's possible to define thinness as having an age-, sex-, and ethnicity-adjusted BMI below the 10^{th} percentile. This is a suboptimal definition because the 10^{th} percentile will differ across populations and over time. The optimal definition of thinness should consider:

1. Stability over time, such that an individual has always been in the lower percentiles for age, sex and ethnicity;
2. Age;
3. Parity in women, given that pregnancy has been recognized as a life event related to the onset of obesity in some women
4. Regular dieting or weight loss efforts in order to maintain low BMI (because, constitutionally, thin individuals should be protected against the need to diet);
5. Behaviors and constitutions that could give rise to thinness phenocopies such as medical conditions, metabolic disorders or disorders of the digestive system, that could lead to or mimic thinness, and psychiatric disorders or their subclinical forms associated with loss appetite or weight (e.g., major depression, anorexia nervosa bulimia nervosa)
6. The use of substances that can lead to weight loss (e.g., crack, cocaine, heroin), or be used to prevent weight gain (e.g., nicotine). (*Cynthia M. Bulik, 2002)*

It's possible to summarize that evidence from animal studies strongly suggests that leanness and thinness are genetically influenced traits that can be bred. Sophisticated animal studies have reveled that certain genes confer resistance to the development of obesity even in the presence of an experimentally manipulated obesogenic diet. Studies of humans have shown

that thinness appears to be stable over time, is familiar, and may be substantially influenced by additive genetic effects. Intensive efforts directed toward understanding individuals who remain thin in an obesogenic environment may lead to important clues to the causes of and treatment for obesity. (*Cynthia M. Bulik, 2002)*

Leptin and Body Weight Regulation

Leptin –also known as OB protein- is a protein hormone, encoded by the OB gene, produced primarily by adipocytes, and secreted into the circulation, where it binds to a family of binding proteins. Leptin enters the brain though a specific receptor-mediated transport system in brain microvessels and acts on specific brain areas involved in the control of food intake and the regulation of energy balance. (*L. Arthur Campfield, 2002)*

The primary role of leptin is to coordinate the responses of brain neuropeptide and neurotransmitter pathways to provide a situationally appropriate regulation of food intake, metabolic rate, energy balance and fat storage.

Clinical studies of circulating leptin concentration have revealed the basic facts: Obese subjects have *higher* serum leptin concentration than lean individuals, and concentrations *increase* with increasing percentage of body fat.

Serum leptin concentrations in patients with eating disorders are appropriate for their percent body fat; that is, patients with Anorexia Nervosa have very low leptin levels, while overweight patients with bulimia nervosa have elevated leptin levels. Thus, the decreased food intake or failure to eat characteristic of AN is *not* a result of suppression of food intake by high leptin levels. (*L. Arthur Campfield, 2002)*

Leptin is produced and secreted from:

1. White fat;
2. Bone marrow,
3. Placenta;
4. Probably from fat within muscles and the other peripheral organs, including the stomach.

With the exception of the placenta and the stomach, the general rule appears to be that as fat content increases in fat cell within a tissue, the production and secretion of leptin also increase. When fat cells are devoid of lipid, the expression of the *ob* gene is severely reduced.

So, it's possible to summarize by saying that Leptin acts as *chef d'ÜÜ* to coordinate a variety of neuropeptide and neurotransmitter responses to generate an appropriate whole-body response with respect to body energy balance given the current physiological and environmental conditions in nonobese individuals. In this way, coordinated whole-body response to undernutrition, overnutrition, increased energy demand, and decreased energy demand is generated. Additional advanced in our knowledge of the leptin pathway, and its marked alterations in obesity, will surely lead to new pharmacological treatments for obesity, to be used as adjuncts to healthy eating and physical activity. (*L. Arthur Campfield, 2002)*

Loose coupling between appetite and physical activity

Understanding the interaction between physical activity and appetite control has both theoretical and practical implications. (*John E. Blundell, 2002)*

More than 40 years ago, the commonsense view implied that regulation of food intake functions with such flexibility that increased energy output due to exercise is automatically followed by an equivalent increase in caloric intake. This view supports the commonly held belief that *exercise is futile as form of weight control*, since the energy expended simple increases hunger and drives up food intake to compensate for the energy lost. However, there is now much evidence to demonstrate that physical activity does not automatically increase eating. Indeed, after exercise, food intake most often remains unchanged and, in certain circumstances, declines. Moreover, when physical activity is reduced (for example when an individual becomes more sedentary), food intake is not down-regulated; this leads a positive energy balance and weight gain. (*John E. Blundell, 2002)*

All of these finding suggest a rather loose coupling between physical activity and appetite control – at least in the short term.

The degree of this coupling may be different in men and women.

Just as certain metabolic variables (such as low basal metabolic rate, low energy cost of physical activity, low capacity for fat oxidation) can lead to a positive energy balance, we can envisage behaviorally mediated processes leading to hyperphagia or overconsumption. These processes may be patterns of behavior, the sensory or hedonic events that guide behavior, or sensations that accompany or follow eating. This cluster of events can be referred to as *behavioral risk factors*. (*John E. Blundell, 2002)*

Studies presentation

The studies that follow, all three have already been published (*Journal of Nutrition and Metabolism – study 1, Int Journal of Food and Sciences and Nutrition – study 2, Clinical Nutrition - study 3*) have been a necessary and important starting point to define the measurement of the basal metabolism and body composition - but in particular the percentage of fat mass - in a clinical setting.

We were able to shed light on the use of certain tools (Cosmed's FitMate, Armband and DXA) that were then necessary in Study 5 for measurement of anthropometric and physiological parameters, being able to calibrate the Actiheart (v.study5).

STUDY 1

Hindawi Publishing Corporation
Journal of Nutrition and Metabolism
Volume 2012, Article ID 652932, 6 pages
doi:10.1155/2012/652932

Clinical Study

Resting Energy Expenditure in Anorexia Nervosa: Measured versus Estimated

Marwan El Ghoch,[1] Marta Alberti,[2] Carlo Capelli,[2] Simona Calugi,[1] and Riccardo Dalle Grave[1]

[1] *Department of Eating Disorder and Obesity, Villa Garda Hospital, Via Montebaldo, 89, 37016 Garda (VR), Italy*
[2] *Department of Neurological, Neuropsychological, Morphological, and Exercise Sciences, University of Verona, 37131 Verona, Italy*

Abstract

Introduction: Aim of this study was to compare the resting energy expenditure (REE) measured by means of the Douglas bag method with the REE estimated with the FitMate™ method, the Harris Benedict equation, and the Müller et al. equation for individuals with BMI < 18.5 kg/m^2 in a severe group of underweight patients with anorexia nervosa (AN).

Methods: 15 subjects (14 females and 1 male, age range from 15 to 45 years; BMI range from 12.1 kg/m^2 to 16.8 kg/m^2) with AN consecutively admitted in an inpatient eating disorder unit participated in the study. The Douglas Bag method and the FitMate™ method – a small device designed for measurement of oxygen consumption – were used to measure REE, and the Dual-emission X-ray absorptiometry (DXA) to assess body composition.

Results: The Bland–Altman method showed that FitMate™method and the Müller et al. equation gave a reliableREE estimation, while the Harris-Benedict equation overestimated the REE, when compared with the Douglas bag method. No significant differences were also found between the Douglas bag method RRE and the FitMate™method and the Müller et al. equation REE, while a significant differences was found between the Douglas bag method RRE and the Harris-Benedict equation REE.

Conclusion: The data support the use of the FitMate™method and the Müller et al. equation, but not the Harris-Benedict equation, to estimate REE in severe underweight AN patients.

Key words: anorexia nervosa, eating disorder, calorimetry, oxygen consumption, metabolism, energy expenditure.

1. Introduction

Total energy expenditure (TEE) in humans is determined by resting energy expenditure (REE), dietary-induced thermogenesis, and energy cost of physical activity (Donahoo et al.

2004; Ravussin and Bogardus 1992). REE is the major fraction of TEE in sedentary people, accounting for approximately 70% of TEE (Ravussin and Bogardus 1992). Several studies showed that REE is low in underweight patients with AN compared with normal-weight controls (Bossu et al. 2007; Casper et al. 1991; Cuerda et al. 2007; Krahn et al. 1993; Ljunggren et al. 1961; Melchior et al. 1989; Platte et al. 1994; Polito et al. 1998; Russell et al. 2001; Scalfi et al. 1993; Schebendach 2003; Vaisman et al. 1988a; Vaisman et al. 1988b; van Marken Lichtenbelt et al. 1997), and long-term recovered AN patients (Dellava et al. 2009). The low REE seems mainly due to the loss of lean body mass, a major determinant of REE (Miller and Blyth 1953), and to a lesser extent, to the several abnormal neuroendocrine parameters (e.g., thyroid hormones, adrenal hormones, and leptin) prevailing in underweight AN patients (de Zwaan et al. 2002).

The accurate measurement of the REE in underweight AN patients is clinically useful because it may help us: i) predict the energy level necessary to promote weight restoration and; ii) optimize nutritional rehabilitation preventing severe medical complication such as the refeeding syndrome (Mehler et al. 2010). Indirect calorimetry, performed with the subject in supine position after an overnight fast, is most reliable method used to measure REE (Matarese 1997). Unfortunately, this technology is not available in the majority of the hospitals because it requires skilled technicians and sophisticated methodologies that are costly and difficult to apply in standard clinical settings (Cuerda et al. 2007).

Predictive formulas of REE may be used as an alternative to indirect calorimetry that may be utilized by clinicians. The most cited and used predictive formula is the Harris-Benedict equation which includes age, stature, and body weight to estimate REE (Harris and Benedict 1919). Unfortunately, data available on AN patients indicate that Harris-Benedict equation overestimates REE (Cuerda et al. 2007; Krahn et al. 1993; Marra et al. 2002). To overcome this problem, a correction of this equation was derived specifically for individuals

with AN (Schebendach et al., 1995) and validated in 37 hospitalized female AN patients (Schebendach et al. 1995). However, subsequent studies found that also the Schebendach formula is not clinical useful because underestimates the REE in patients with AN (Cuerda et al. 2007; Scalfi et al. 2001).

A method that might overcome the limits of predictive formulas requires the use of fat-free mass (FFM, kg), and fat mass (FM, kg) to estimate REE. By using this procedure Müller et al. developed different formulas for different range of Body Mass Index (BMI), including one for a BMI < 18.5 kg/m^2 (Müller et al. 2004). However, this procedure has never been implemented in AN patients by FFM and FM values assessed by means of gold standard body composition methods, such as Dual-emission X-ray absorptiometry (DXA).

Recently, advancements in technology have led to the development of small and not expensive devices, such as BodyGem™ (Melanson et al. 2004) and the FitMate™(Nieman et al. 2006), designed for estimating REE by measuring only oxygen consumption that might make the use of the indirect calorimetry more popular in clinical settings. Although, these devices have been shown to be accurate when compared with the Douglas bag system (Melanson et al. 2004; Nieman et al. 2006), no data are available on their use in severe underweight AN patients.

Aim of this study was to compare the results obtained by Douglas bag system in assessing REE with the FitMate™ method, the Harris Benedict equation, and the Müller et al. equation for individuals with BMI < 18.5 kg/m^2 in severe underweight AN patients.

2. Methods

2.1. Subjects

15 patients (14 females and 1 male) with AN participated in the study. All patients were voluntarily and consecutively admitted to the eating disorder inpatient unit of Villa

Garda Hospital during 2010. The patients were referred from all over Italy by general practitioners or by outpatients' eating disorder specialists. Indications for admission were the failure of less intensive treatments (e.g., outpatient treatment) or the presence of an eating disorder of clinical severity not manageable in an outpatient setting. Patients with active substance abuse, schizophrenia and other psychotic disorders were not included. The indications and contraindications for the inpatient treatment were evaluated during an eligibility interview completed by a senior specialist in the field (RDG). The Eating Disorder Examination interview (EDE) 12.0D (Fairburn and Cooper 1993) was used to generate operational definitions of the DSM-IV diagnoses of AN (American Psychiatric Association 1994).

Before participation, written informed consent was obtained from all subjects (or by the legal guardian for those less than 18 years old, in accordance with our institution's requirements). The protocol was approved by the Institutional Review Board of Villa Garda Hospital, Verona.

2.2. Measurements

Data collection included weight and height measurement, DXA body composition measurement, indirect calorimetry with the Douglas bag and the FitMate™ methods, Harris Benedict and the Müller et al. equations.

2.2.1. Body weight and height

Body weight was measured on a medical balance and height with a stadiometer by a medical doctor involved in the study. Patients were weighed wearing only underwear and without shoes before breakfast. The BMI was determined according to the usual formula of body weight divided the squared of height in meters.

2.2.2. Indirect calorimetry

Indirect calorimetry was performed the second day of admission using the Douglas Bag and the FitMate™ methods in a single session early in the morning before breakfast. The order of the two measurements was randomized. Participants were informed to fast overnight, to avoid drinking caffeinated beverages for at least 12 hours, and to abstain from physical activity prior the tests. Upon the arrival in the laboratory, participants rested on a medical bed with the upper part of the body partially raised (+ ¾°) and assumed a comfortable position while the instruments were prepared and calibrated and environmental data were recorded. Then, after 10 minutes at rest, the measurements were performed for 11 minutes, during which time the participants were instructed to lay quietly, to remain awake avoid fidgeting and hyperventilating.

The Douglas Bag method (Douglas, 1911) involves collection of the expired air in a large impermeable rubber bag, and subsequent volume and analysis of the exspired gases (Douglas 1911; Douglas and Priestly 1948). It has been served as the 'gold standard' method for many studies in the last decades (Brehm et al. 2004; Carter and Jeukendrup 2002; Nieman et al. 2006; Rietjens et al. 2001).

Expired gases were collected by using a mask connected to a two-way, low resistance respiratory valve whose expiratory outlet was fed to a 100 liter Douglas bag. After gas collection, expired gas composition and volume were assessed using a paramagnetic O_2 analyzer (Oxynos 100, Rosemount Analytical, USA), an infrared CO_2 meter (Binos 1, Lybold-Heraeus, D) and a dry gas meter (MCS, S.I.M. Brunt, Italy). Gas analyzers were calibrated before each experimental trial using gas mixtures of known and certified composition. $V'O_2$ and $V'CO_2$ in STPD conditions were calculated by applying standard equations implying the Haldane correction for inspired ventilatory volume. Respiratory quotient (RQ) was calculated as VCO_2/VO_2 and on the basis of the measured values of RQ the corresponding value of the energy equivalent of VO_2 in kJ was calculated. Then REE was

obtained calculated on the basis that 1 kcal equals 4,186 kJ. Finally, the daily REE was calculated by applying a simple proportion.

The FitMate™ is a small device designed for measurement of oxygen consumption and energy expenditure during rest and exercise (Cosmed, Rome, Italy). It uses a turbine flowmeter for measuring ventilation and a galvanic fuel cell O_2 sensor for analyzing only the fraction of oxygen in expired gases. It is considered to retain the performance of a metabolic cart with a standard mixing chamber or canopy. Sensors measured humidity, temperature, and barometric pressure for use in internal calculations. The FitMate™ uses standard metabolic formulas to calculate oxygen uptake, and energy expenditure is calculated using a fixed respiratory RQ of 0.85.

2.2.3. Body composition

Body composition was assessed by using DXA (iDXA Luner General Electric) in the third day of the admission. No special preparation was required, with exception that participants wore lightweight clothing for these measures and do not have any metal accessories.

2.2.4. Predictive formulas of REE

The Harris-Benedict equations (Harris and Benedict 1919) for women [655 + (9.6 x weight in kg) + (1.8 x height in cm) - (4.7 x age in years)] and men [(66,47 + (13,75 x weight in kg) + (5,0033 x height in cm) - (6,755 x age in years)], and the Müller et al. et al. equation for individuals with BMI < 18.5 kg/m^2 (Müller et al. 2004) [0.08961x FFM (kg) + 0.05662 x FM (kg) + 0.667] x 238.84 were used to estimate REE.

2.3 Statistical Analysis

The Bland-Altman method (Bland and Altman 1986) was used to study the concordance between the Douglas Bag method with the FitMate™ method, and the Harris-Benedict and Müller et al. equations. The z-test was used to evaluate whether the mean of the

differences between the values obtained by the three methods, with respect to Douglas Bag, was or was not significantly different from zero (Daniel 1991). Furthermore, the Wilcoxon Signed-Ranks Test was performed to compare the mean REE values of the Douglas Bag method with those of the , FitMate™method, the Harris-Benedict and the Müller et al. equations.

3. Results

Table 1 shows the 15 participants' data, with data summarized for age, height, weight, BMI and REE values. Age ranged from 15 to 45 years, and BMI ranged from 11.96 kg/m^2 and 16.9 kg/m^2, with 60% of participants having a BMI < 15 kg/m^2.

Figure 1 shows the Bland-Altman plots reporting the differences between REE values measured with Douglas bag and those obtained by using the other methods (FitMate™method, Harris-Benedict and Müller et al. equations from top to bottom). The mean of the differences between the RRE values estimated with Harris-Benedict equation and those measured with Douglas bag (bias = 284 kcal/day) was significantly different from zero 6.990; $p < 0.005$). Precision amounted to 158 kcal/day and the 95% limits of agreement ranged from 600 to -30 kcal/day. For the other two comparisons, the means of differences were not significantly different from zero (FitMate™ method - Douglas bag method =-1.85; Müller et al. equation - Douglas bag method =-0.125). Bias for the FitMate™ vs, Douglas bags was -43 kcal/day, precision (SD) turned out to be 90 kcal/day. In turn, the 95% limits of agreement ranged from 600 to -30 kcal/day. As far as the Müller and Douglas Bag comparison is concerned, the values were -5 kcal/day, 155 kcal/day, 305/-310 kcal/day, for bias, precision and limits of agreement, respectively.

The Wilcoxon Signed-Ranks Test showed no significant differences between the mean REE values estimated with the Douglas bag method and the mean values estimated with the FitMate™method (Z=-1.70, p=0.088) and the Müller et al. equation (Z=-0.23, p=0.820), but significant differences were found comparing mean REE values estimated with the Douglas bag method and with the Harris-Benedict equation (mean REE values: 920.5±124.0 vs 1205.0±99.2, respectively, Z=-3.35, p=0.001).

4. Discussion

The principal finding of this study on severe underweight AN patients is that the FitMate™method and the Müller et al. equation gave an acceptable REE estimation, while the Harris-Benedict equation overestimated the REE, when compared with the Douglas bag method.

The principal strengths of the study are the use of the Douglas bag method, the DXA, and the EDE interview, three instruments considered the gold standard to assess REE, body composition, and eating disorder diagnosis, respectively. Limitations of the study include the small number of participant, a common problem when studying rare disorder as AN, the absence of a control group and of longitudinal evaluation.

Participants in the study had severe underweight (mean BMI 14.50 kg/m^2), marked reduction of FM (mean FM% 9.70), and low REE (mean REE 920.00 kcal/day estimated with Douglas bag method). These data confirm that patients with AN admitted in specialist inpatient units have a condition of severe underweight (Vandereycken 1985) and, as previously reported (Kerruish et al. 2002), a marked loss of FM. They also show that the underweight and the alteration of body composition are associated with an hypo-metabolic status as consequence of the adaptation to under-eating and underweight (de Zwaan et al. 2002).

Our data confirm that Harris-Benedict equation overestimates the REE in underweight patients with AN (Cuerda et al. 2007; Krahn et al. 1993; Marra et al. 2002), and that it should not be used with this population. Using the Harris-Benedict equation to assess the energy need for refeeding underweight AN patients may led to prescribe an excessive energy intake that increase the risk to produce severe negative consequences, such as the refeeding syndrome (Mehler et al. 2010). This syndrome may include minor complications (e.g., transient pedal edema) or serious complications requiring immediate care (e.g., a prolonged QT interval or hypophosphatemia with associated weakness, confusion, progressive neuromuscular dysfunction, and cardiovascular collapse) (Yager and Andersen 2005).

The good new of our data, if confirmed by other studies, is that REE expenditure in underweight AN patients may be estimate with discrete accuracy by the FitMate™method, and by the Müller et al. equation. The FitMate™ method, in comparison with the expensive Douglas bag method that is it expensive and requires skilled technicians not usually available in standard clinical settings, is inexpensive, easy to operate, and can be used by a wide variety of health professionals to determine the energy need of underweight AN patients. The results reported in the present study confirm and extend those obtained on 60 not underweight healthy adults (N = 30 males, N = 30 females) where no significant differences between Douglas bag method and FitMate™ method for oxygen consumption and REE were found. Test-to-test reliability correlation coefficients for oxygen consumption for the FitMate™ and Douglas bag methods were $r = 0.94$ and $r = 0.95$, respectively (Nieman et al. 2006)

The Müller et al. equation is another alternative that may be widely used in eating disorder units to estimate REE. This because the DXA, measuring the FM and the FFM required by the Müller et al. equation, is a routine exam used by eating disorder unit to measure bone mineral density in all patients who have been amenorrheic for six months or more (American Psychiatric Association 2006).

In conclusion, our data support the use of the FitMate™method and the Müller et al. equation, but not the Harris-Benedict equation, to estimate REE in severe underweight AN patients.

Table 1 Clinical characteristics of the 15 participants (14 females and one male) with anorexia nervosa. Data are reported as means (SD).

Clinical Data	
Height (cm)	162.40 (8.75)
Weight (kg)	38.43 (5.42)
BMI(kg/m2)	14.53 (1.48)
Age(yr)	24.80 (9.04)
Body composition (DXA)	
Fat Mass (kg)	3.63 (2.68)
Percent Fat Mass (%)	9.70 (6.27)
Fat Free Mass (kg)	33.06 (5.08)
Percent Free Fat Mass (%)	85.63 (5.57)
Resting Energy Expenditure	
Douglas bag method (kcal/day)	920.53 (124.02)
FitMate™ method (kcal/day)	1007.13 (140.47)
Harris-Benedict equation (kcal/day)	1205.00 (99.16)
Müller et al. equations (kcal/day)	915.53 (113.39)

Abbreviations: BMI, body mass index; DXA, Dual-emission X-ray absorptiometry.

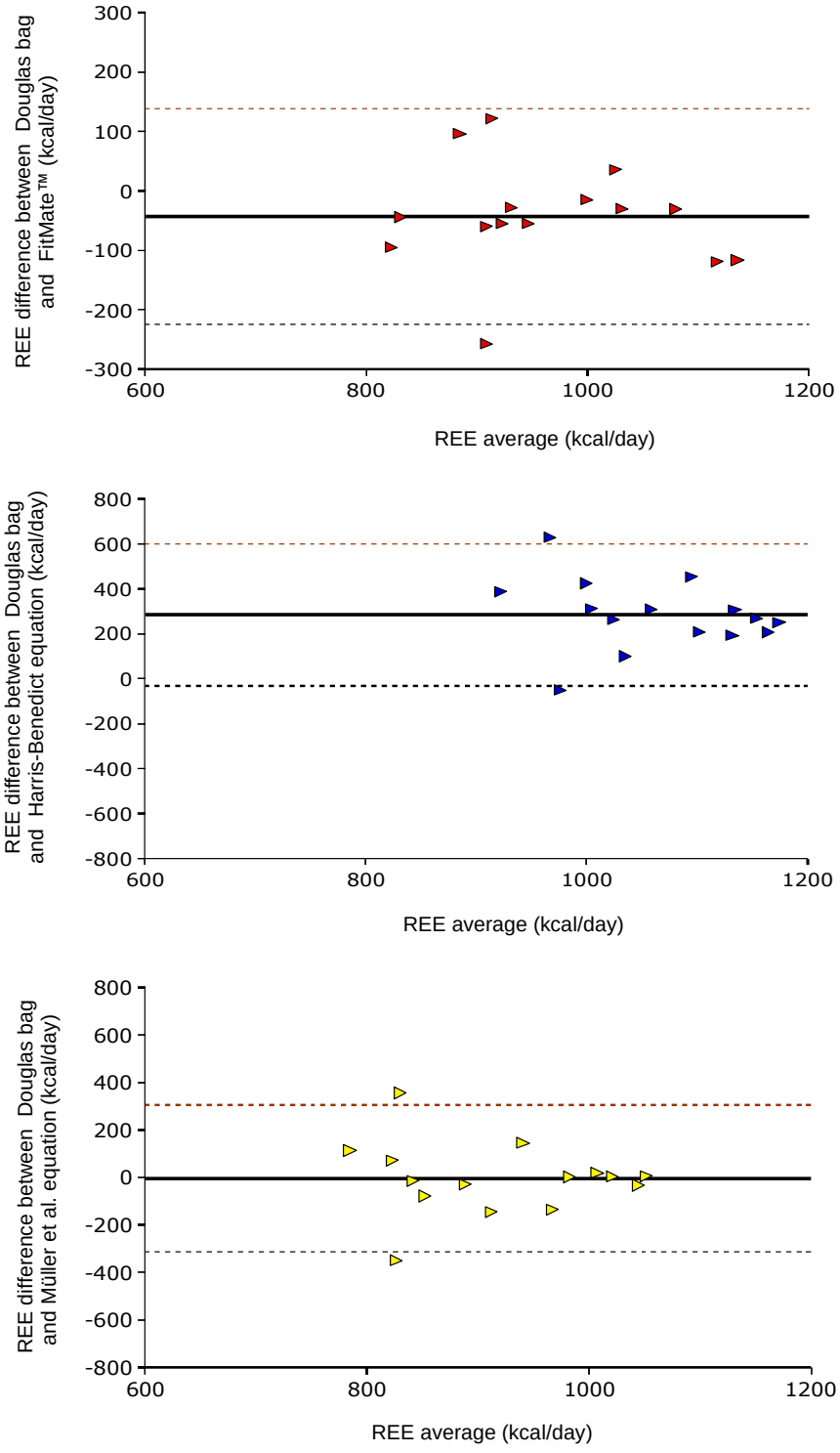


Figure 1. Bland Altman Plots.

References

American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders (4th ed.). American Psychiatric Association, Washington, D.C

American Psychiatric Association (2006) Treatment of patients with eating disorders,third edition. . Am J Psychiatry 163: 4-54

Bland JM, Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1: 307-310

Bossu C, Galusca B, Normand S, Germain N, Collet P, Frere D, Lang F, Laville M, Estour B (2007) Energy expenditure adjusted for body composition differentiates constitutional thinness from both normal subjects and anorexia nervosa. Am J Physiol Endocrinol Metab 292: E132-137

Brehm MA, Harlaar J, Groepenhof H (2004) Validation of the portable VmaxST system for oxygen-uptake measurement. Gait Posture 20: 67-73

Carter J, Jeukendrup AE (2002) Validity and reliability of three commercially available breath-by-breath respiratory systems. Eur J Appl Physiol 86: 435-441

Casper RC, Schoeller DA, Kushner R, Hnilicka J, Gold ST (1991) Total daily energy expenditure and activity level in anorexia nervosa. Am J Clin Nutr 53: 1143-1150

Cuerda C, Ruiz A, Velasco C, Breton I, Camblor M, Garcia-Peris P (2007) How accurate are predictive formulas calculating energy expenditure in adolescent patients with anorexia nervosa? Clin Nutr 26: 100-106

Daniel WW (1991) Biostatistics: A Foundation for Analysis in the Health Sciences, New York

de Zwaan M, Aslam Z, Mitchell JE (2002) Research on energy expenditure in individuals with eating disorders: a review. Int J Eat Disord 32: 127-134

Dellava JE, Policastro P, Hoffman DJ (2009) Energy metabolism and body composition in long-term recovery from anorexia nervosa. Int J Eat Disord 42: 415-421

Donahoo WT, Levine JA, Melanson EL (2004) Variability in energy expenditure and its components. Curr Opin Clin Nutr Metab Care 7: 599-605

Douglas CG (1911) A method for determining the total respiratory exchange in man. J Physiol 42: 1–2

Douglas CG, Priestly JG (1948) Human physiology: a practical course. Clarendon Press, Oxford

Fairburn CG, Cooper Z (1993) The eating disorder examination (12th ed). In: Fairburn CG, Wilson GT (eds) Binge eating: nature, assessment, and treatment. The Guilford Press, New York, pp. 317-360

Harris JA, Benedict FG (1919) A biometric study of basal metabolism in man publication no 279. Carnegie Institution of Washington, Washington, DC

Kerruish KP, O'Connor J, Humphries IR, Kohn MR, Clarke SD, Briody JN, Thomson EJ, Wright KA, Gaskin KJ, Baur LA (2002) Body composition in adolescents with anorexia nervosa. Am J Clin Nutr 75: 31-37

Krahn DD, Rock C, Dechert RE, Nairn KK, Hasse SA (1993) Changes in resting energy expenditure and body composition in anorexia nervosa patients during refeeding. J Am Diet Assoc 93: 434-438

Ljunggren H, Ikkos D, Luft R (1961) Basal metabolism in women with obesity and anorexia nervosa. Br J Nutr 15: 21-34

Marra M, Polito A, De Filippo E, Cuzzolaro M, Ciarapica D, Contaldo F, Scalfi L (2002) Are the general equations to predict BMR applicable to patients with anorexia nervosa? Eat Weight Disord 7: 53-59

Matarese LE (1997) Indirect calorimetry: technical aspects. J Am Diet Assoc 97: S154-160

Mehler PS, Winkelman AB, Andersen DM, Gaudiani JL (2010) Nutritional rehabilitation: practical guidelines for refeeding the anorectic patient. J Nutr Metab 2010

Melanson EL, Coelho LB, Tran ZV, Haugen HA, Kearney JT, Hill JO (2004) Validation of the BodyGem hand-held calorimeter. Int J Obes Relat Metab Disord 28: 1479-1484

Melchior JC, Rigaud D, Rozen R, Malon D, Apfelbaum M (1989) Energy expenditure economy induced by decrease in lean body mass in anorexia nervosa. Eur J Clin Nutr 43: 793-799

Miller AT, Jr., Blyth CS (1953) Lean body mass as a metabolic reference standard. J Appl Physiol 5: 311-316

Müller MJ, Bosy-Westphal A, Klaus S, Kreymann G, Luhrmann PM, Neuhauser-Berthold M, Noack R, Pirke KM, Platte P, Selberg O, Steiniger J (2004) World Health Organization equations have shortcomings for predicting resting energy expenditure in persons from a modern, affluent population: generation of a new reference standard from a retrospective analysis of a German database of resting energy expenditure. Am J Clin Nutr 80: 1379-1390

Nieman DC, Austin MD, Benezra L, Pearce S, McInnis T, Unick J, Gross SJ (2006) Validation of Cosmed's FitMate in measuring oxygen consumption and estimating resting metabolic rate. Res Sports Med 14: 89-96

Platte P, Pirke KM, Trimborn P, Pietsch K, Krieg JC, Fichter MM (1994) Resting metabolic rate and total energy expenditure in acute and weight recovered patients with anorexia nervosa and in healthy young women. Int J Eat Disord 16: 45-52

Polito A, Cuzzolaro M, Raguzzini A, Censi L, Ferro-Luzzi A (1998) Body composition changes in anorexia nervosa. Eur J Clin Nutr 52: 655-662

Ravussin E, Bogardus C (1992) A brief overview of human energy metabolism and its relationship to essential obesity. Am J Clin Nutr 55: 242S-245S

Rietjens GJWM, Kuipers H, Kester ADM, Keizer HA (2001) Validation of a computerised metabolic measurement system (Oxycon-Pro®) during low and high intensity exercise. Int J Sports Med 22: 291–294

Russell J, Baur LA, Beumont PJ, Byrnes S, Gross G, Touyz S, Abraham S, Zipfel S (2001) Altered energy metabolism in anorexia nervosa. Psychoneuroendocrinology 26: 51-63

Scalfi L, Di Biase G, Coltorti A, Contaldo F (1993) Bioimpedance analysis and resting energy expenditure in undernourished and refed anorectic patients. Eur J Clin Nutr 47: 61-67

Scalfi L, Marra M, De Filippo E, Caso G, Pasanisi F, Contaldo F (2001) The prediction of basal metabolic rate in female patients with anorexia nervosa. Int J Obes Relat Metab Disord 25: 359-364

Schebendach J (2003) The use of indirect calorimetry in the clinical management of adolescents with nutritional disorders. Adolesc Med 14: 77-85

Schebendach J, Golden NH, Jacobson MS, Arden M, Pettei M, Hardoff D, Bauman N, Reichert P, Copperman N, Hertz S, et al. (1995) Indirect calorimetry in the nutritional management of eating disorders. Int J Eat Disord 17: 59-66

Vaisman N, Corey M, Rossi MF, Goldberg E, Pencharz P (1988a) Changes in body composition during refeeding of patients with anorexia nervosa. J Pediatr 113: 925-929

Vaisman N, Rossi MF, Goldberg E, Dibden LJ, Wykes LJ, Pencharz PB (1988b) Energy expenditure and body composition in patients with anorexia nervosa. J Pediatr 113: 919-924

van Marken Lichtenbelt WD, Heidendal GA, Westerterp KR (1997) Energy expenditure and physical activity in relation to bone mineral density in women with anorexia nervosa. Eur J Clin Nutr 51: 826-830

Vandereycken W (1985) Inpatient treatment of anorexia nervosa: some research-guided changes. J Psychiatr Res 19: 413-422

Yager J, Andersen AE (2005) Anorexia Nervosa. N Engl J Med 353: 1481-1488

STUDY 2

We extended the analysis of the method utilized assessing REE in the clinical environmental on anorexia nervosa in-patients comparing the estimations provided by three different means of measuring: 1) a portable multisensor body monitor [SenseWear Pro2 Armband (SWA)], 2) FitMatee method, 3) the Müller equation for individuals with body mass index 18.5, and the latter being based on dual-energy X-ray absorptiometry assessment of body composition.

International Journal of Food Sciences and Nutrition,
2012; Early Online: 1–6

informa
healthcare

Resting energy expenditure assessment in anorexia nervosa: comparison of indirect calorimetry, a multisensor monitor and the Müller equation

MARWAN EL GHOCH[1], MARTA ALBERTI[2], CARLO CAPELLI[2], SIMONA CALUGI[1], NINO CARLO BATTISTINI[3], MASSIMO PELLEGRINI[3], SANDRA ŠUBAŠIĆ[1], MASSIMO LANZA[2], & RICCARDO DALLE GRAVE[1]

[1]*Department of Eating and Weight Disorders, Villa Garda Hospital, Via Montebaldo 89, I-37016 Garda (VR), Verona, Italy,* [2]*Department of Neurological, Neuropsychological, Morphological and Movement Sciences, University of Verona, Verona, Italy, and* [3]*Department of Applied Dietary Science, University of Modena, Modena, Italy*

Abstract

The aim of this study was to compare the estimations provided by three different means of measuring the resting energy expenditure (REE) in anorexia nervosa (AN) patients. REE was measured, after 24 hours of refeeding, using a portable multisensor body monitor (SenseWear Pro2 Armband - SWA), FitMate™ method and the Müller equation for individuals with BMI < 18.5, the latter being based on Dual Energy X-ray absorptiometry assessment of body composition. The mean differences between REE values estimated by SWA and those

provided by the Müller equation and the FitMate™ method were significantly different from zero in both cases. In contrast, the mean differences between FitMate™ method and Müller equation were weakly significantly different from zero, and a significant correlation was noted between these two methods. Conclusion: The SWA does not appear to be alternative to FitMate™ and Müller equation methods for assessing REE in AN patients.

Introduction

Anorexia nervosa (AN) is a common health problem afflicting mainly female adolescents and young women. It is associated with important physical health and psychosocial morbidity, and carries increased risk of death (Dalle Grave, 2011).

Assessment of resting energy expenditure (REE) plays an important role in the management of severely underweight AN patients. It consents quantification of the energy necessary to optimize nutritional rehabilitation, with the aim of restoring weight while preventing serious medical complications such as refeeding syndrome (Tresley and Sheean, 2008). The most widely accepted method of measuring REE (Matarese, 1997) is indirect calorimetry (IC), which is generally performed with the subject in a supine position after an overnight fast. Common IC techniques used for measuring REE are room open-circuit, hood/canopy open-circuit, open-circuit expiratory collection, and Douglas bag (Levine, 2005). The accuracy of the measurements obtained by these techniques varies enormously as complexity and cost. The most important limitation of these methods is their scarce availability in standard clinical setting since they require skilled technicians and sophisticated instrumentation, making it costly and difficult to apply (Cuerda et al., 2007).

Predictive formulae of REE, based on age, stature and body weight (Harris and Benedict, 1919), are therefore widely used by clinicians as an alternative to IC, but these unfortunately tend to overestimate REE in AN (Cuerda et al., 2007, Krahn et al., 1993, Marra

et al., 2002, Schebendach et al., 1995). To overcome this problem, Müller et al. developed formulas for different ranges of body mass index (BMI), one being BMI < 18.5 (Müller et al., 2004), based on fat free mass (FFM) and fat mass (FM) values assessed by means of Dual Energy X-ray absorptiometry (DXA). When compared to the Douglas bag method, the Müller et al. equation was found to yield an acceptable REE estimation in AN patients (El Ghoch et al., 2012).

Technological advances have recently provided relatively inexpensive means of estimating REE, such as the FitMate™ device (Nieman et al., 2006), based on measurement of oxygen consumption alone. These devices can facilitate the use of IC in clinical settings and FitMate™ in particular was found to be accurate when compared with the Douglas bag system in normal, overweight and obese subjects (Nieman et al., 2006), and in 15 AN patients after one day of refeeding (El Ghoch et al., 2012).

Technological tools designed to monitor exercise can also be used to indirectly estimated REE through specific algorithms, for instance, the Sense Wear Pro 2 Armband (SWA), a portable device that monitors various physiological parameters (heat flux, skin temperature, galvanic skin response and near-body temperature) and movement (accelerometer) (Papazoglou et al., 2006). This is potentially useful in patients with AN because, as well as providing a measure of REE, it can signal the presence of excessive exercising, a behaviour commonly observed in these patients (Dalle Grave et al., 2008b). However, to date, no study has validated SWA as a means of measuring REE in AN patients.

Thus, the aim of this exploratory study was to compare the REE measurements obtained using SWA with those yielded by both the FitMate™ and the Müller et al. equation in assessing REE in a sample of AN patients admitted to a specialist inpatient unit for eating disorders.

Subjects

Thirty-nine female subjects with AN voluntarily and consecutively admitted to the eating disorder inpatient unit of Villa Garda Hospital during the years 2010 and 2011 were recruited for the study. The patients were referred to the unit from all over Italy by general practitioners or outpatient eating disorder specialists. Diagnosis of AN was made, according to operational DSM-IV definitions (American Psychiatric Association, 2000), by means of the Eating Disorder Examination interview (EDE 12.0D, Fairburn and Cooper, 1993).

Informed written consent was obtained from all subjects (or their legal guardians in the case of patients less than 18 years old, in accordance with our institutional requirements). The protocol employed was approved by the Institutional Review Board of Villa Garda Hospital, Verona.

Measurements

Data were collected on the third day of admission after 24 hours of refeeding, with a diet of 1.500 kcal (carbohydrate 50%, protein 20%, fat 30%) composed of conventional foods and divided into four standard meals. Feeding was supervised by a dietician specialized in the treatment of eating disorders (Dalle Grave et al., 2008a).

Body height and weight. Before breakfast, body weight was measured with a monthly calibrated digital scale (SECA) to the nearest 0.05 kg in underwear. The subjects in light clothes, shoes off, were standing still in the middle of the scale's platform. Height was measured with a wall mounted stadiometer to the nearest 0.1 cm, calibrated on wall installation and recalibrated yearly. The subjects were standing with heels together, arms to the side, legs straight, shoulder relaxed and head in the horizontal plane ("look straight ahead"). Measurements were done by the same physician involved in the study. The BMI was determined according to the usual formula of body weight divided by the square of the height in meters.

Body composition. Body composition was assessed on the third day before breakfast using DXA (iDXA Luner General Electric). No special preparation was involved, except for ascertaining that participants wore lightweight clothing and removed any metal jewellery or accessories. Subjects were lying on the DXA scanner bed and were positioned within the scanning area in a supine position with the arms positioned and pronated to the side of the body, fingers and toes pointed and ankles fastened together with a Velcro belt to ensure standard positioning. Once positioned, subjects were instructed to remain as still as possible for the duration of the scan.

Indirect calorimetry. Indirect calorimetry was performed on room temperature in a single session before breakfast on the third day using the FitMate™ method. FitMate™ is a device designed to measure oxygen consumption and energy expenditure during rest and exercise (Cosmed, Rome, Italy), making use of a turbine flowmeter to measure ventilation and a galvanic fuel cell O_2 sensor to analyse the fraction of oxygen in expired gases. It is said to perform in a comparable fashion to a metabolic cart with a standard mixing chamber or canopy. Its sensors measure humidity, temperature and barometric pressure, parameters that are employed in its internal calculations; these generate the oxygen uptake and the energy expenditure using a fixed respiratory quotient (RQ) of 0.85 and the Weir's equation; REE = [3.9 (VO2) + 1.1 (VCO2)] 1.44 (Weir, 1949). The device has been shown to provide REE estimates comparable to those yielded by the Douglas bag method in a sample of 15 AN patients after one day of refeeding. The Bland and Altman plots showed no difference between the two procedures. Also the means of differences were not significantly different from zero. (FitMate method−Douglas bag method = 1.85. Bias for the FitMate versus Douglas bags was −87 kcal/day, and precision (SD) turned out to be 181. The Wilcoxon signed-ranks test showed no significant differences between the mean REE values estimated

with the Douglas bag method and the mean values estimated with the FitMate method (Z = −1.70, P = 0.088, effect size = 0.65) (El Ghoch et al., 2012).

In the present study, participants were asked to fast overnight, to abstain from smoking and drinking caffeinated and alcoholic beverages for at least 12 hours before the session and not to perform physical exertion prior to the tests. Patients were not in treatment with drugs medication influencing REE. Upon arrival in the laboratory, participants were placed in a comfortable position on a medical bed, with the upper part of the body partially raised (+ ¾°), while the instrument was prepared and calibrated (immediately before the measurements) and environmental data recorded. After 10 minutes at rest, measurements were performed over a fixed period of 11 minutes, during which the participants were instructed to lie quietly, to remain awake and avoid fidgeting and hyperventilating.

SWA. SWA (BodyMedia Inc, Pittsburgh, PA, USA) assesses both REE and physical activity. It was positioned over the triceps muscle on the upper right arm from the evening of the second day, and kept in place overnight (Papazoglou et al., 2006, Malavolti et al., 2007) until the FitMate™ measurement was performed to ensure that the patient abstained from any physical exertion before REE measurements. Then REE was obtained before breakfast on the third morning using Chronolife® (SensorMedics Inc.), a compatible software that incorporates demographic characteristics (gender, age, height, weight) and SWA measurements as acceleration, heat flux, galvanic skin response, skin temperature and near body temperature.

Previous studies examining the validity of SWA in assessing REE in normal, overweight and obese have produced contrasting results, for this reason its validity is still a matter of debate and needs to be clarified, especially in AN patients where no study testing the performance for this scope has been yet conducted (Frankenfield et al., 1998, Jakicic et al., 2004, Bertoli et al., 2008, Fruin and Rankin, 2004, Malavolti et al., 2007).

Predictive formula of REE. The following Müller et al. equation for individuals with a BMI <18.5 (Müller et al., 2004), was used to give another estimation of REE: ([0.08961 x FFM (kg) + 0.05662 x FM (kg) + 0.667] x 238.84.

The formula was chosen because it was validated in a group of underweight occidental females (n= 50; BMI <18.0) with an age ranging between 12 and 49 years old, which is similar to the age of our AN sample. The FFM and the FM were assessed using DXA.

Statistical Analysis

The Bland-Altman method was employed to study the agreement between the REE estimations provided by the SenseWear Armband (SWA), FitMate™, and Müller equation (Bland and Altman, 1986) methods. The z-test was used to evaluate whether the mean of the differences between the values obtained by the three methods was significantly different from zero or not (Daniel, 1991). Pearson product-moment correlation analyses were performed to evaluate the relationship between body weight, fat free mass (FFM), Müller et al. equation, SWA and FitMate™ methods. Partial correlation coefficients were calculated in order to evaluate the effect of age as a confounding variable. Statistical significance was set at $p < 0.05$. Data are presented as means and standard deviations (SD). All statistical analyses were carried out using SPSS Version 15.0 (SPSS Inc., Chicago).

Results

Table 1 shows a summary of the data pertaining to the 39 participants, for age, height, weight, BMI and REE values. The age of the patients ranged from 13 to 45 years, and their BMI fell between 9.63 and 17.33, with 64.1% of participants having a\ BMI < 15.0. The mean REE estimated with FitMate™ method, Müller et al. equation, and SWA were 962.56 kcal/day (200.74), 916.76 kcal/day (111.35), and 1073.77 kcal/day (132.27), respectively.

Table 1. Data representative of the 39 participants with anorexia nervosa, reported as means (SD) and ranges.

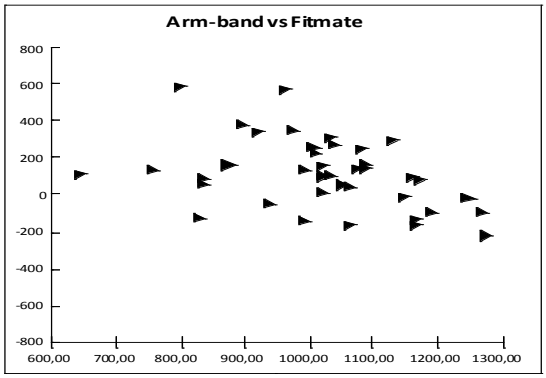
Clinical Data	***Mean (SD)***	***Range***
Height (m)	1.61 (0.07)	1.46 – 1.78
Weight (kg)	37.29 (5.40)	25.50 – 49.50
BMI (kg/m^2)	14.39 (1.75)	9.63 – 17.33
Age (years)	24.56 (8.62)	13 – 45
Body composition (DXA)		
Fat Mass (kg)	3.72 (2.27)	1.17 – 9.92
Percent Fat Mass (%)	9.97 (5.5)	4.10 – 23.30
Fat Free Mass (kg)	33.93 (4.96)	21.25 – 47.13
Percent Free Fat Mass (%)	85.52 (4.99)	73.50 – 92.30
Resting Energy Expenditure		
FitMate™ method (kcal/day)	962.56 (200.74)	501.0 – 1382.0
SenseWear system armband (kcal/day)	1073.77 (132.27)	697.0 – 1247.0
Müller et al. equations (kcal/day)	916.76 (111.35)	654.0 – 1210.0

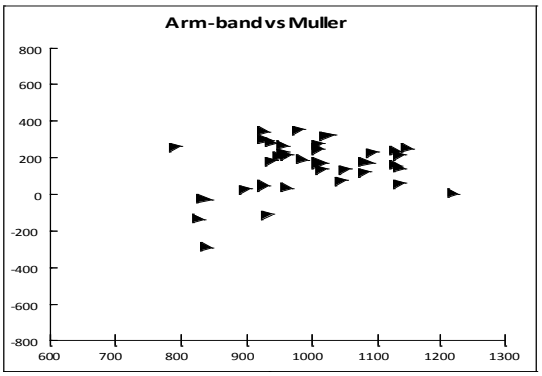
Abbreviations: BMI, body mass index; DXA, Dual Energy X-ray absorptiometry.

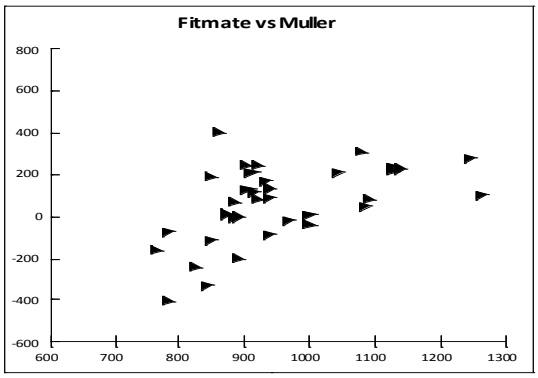
Figure 1, shows the Bland-Altman plots reporting the differences between REE values estimated by the three methods (FitMate™, SWA, and Müller). The mean of the differences between the REE values measured by SWA and those yielded by the Müller equation (bias=158.4 Kcal/day) and the FitMate™ method (bias=115.9 kcal/day) was significantly different from zero in both cases ($z=6.34$; $p<0.001$ and $z=3.68$, $p=0.001$, respectively). Comparison of the FitMate™ method and Müller et al. equation findings, on the other hand, showed a mean difference weakly significantly different from zero (bias=65.29 kcal/day, $z=2.06$, $p=0.047$) and a significant correlation ($r=0.35$, $p=0.040$) between the two.

A significant correlation was also found between weight and REE estimated by both SWA (r=0.39, p=0.013) and the FitMate™ method (r=0.35; p = 0.028), and between FFM and REE measured by the FitMate™ method alone (r=0.35; p = 0.041). No significant association was found between FFM and the REE yielded by SWA (r=0.31, p=0.075). No significant differences were found when all the analyses were controlled for age.

Figure 1. Bland-Altman plots comparing the three methods of measuring REE considered







Discussion

The principal finding of this study is that SWA is not interchangeable with either the FitMate™ method or the Müller equation in assessing REE in patients with AN. Although previous studies into SWA readings have been inconclusive, this is the first time that this device has been trialled in AN patients. Indeed, participants in the study were severely underweight (mean BMI = 14.39) featured markedly reduced FM (mean FM 9.97%), which confirms the clinical picture seen in AN patients treated in specialist inpatient units reported in the literature (Vandereycken, 1985, Kerruish et al., 2002). Their low REE (mean REE 962.56 kcal/day, as measured by IC) was also evident that the weight loss and alteration of body composition due to under-eating were associated with a hypometabolic state arising as an adaptive mechanism (de Zwaan et al., 2002).

Although similar studies are required to confirm these results, this assessment did benefit from the use of two gold-standard techniques to measure body composition and diagnose the eating disorder, i.e. DXA and the EDE interview, respectively. Furthermore, it is worth noting that the REE was evaluated after 24 hours of refeeding.

It should be noted, however, that the study has small sample size and did not feature longitudinal evaluation. Another limiting factor is the use of FitMate™ method as an IC that utilizes a fixed value of RQ, i.e. 0.85, to calculate REE. Indeed, in previous studies, poor agreement has been shown between REE calculated assuming constant and fixed values of RQ (0.85) in conjunction with a reliable criterion reference system (e.g. Deltatrac) in AN patients (Hlynsky et al., 2005). In fact, not considering VCO_2 tends to produce an underestimation of REE when the RQ is between 0.85 and 1.00 and an overestimation of REE at RQs between 0.70 and 0.85 (Holdy, 2004). This might explains the systematic underestimation of REE reported with instruments not measuring VCO_2 in starved AN

patients, who tend to be characterized by elevated RQ values greater than 0.85 (Hlynsky et al., 2005). However, it should be noted that a previous study testing, as in this case, AN participants after 24 hours of refeeding found that their RQ was not significantly larger than 0.85, and that FitMate™ method furnished good REE estimates with respect to the Douglas bag method (El Ghoch et al., 2012).

As previously reported (El Ghoch et al., 2012), the Müller et al. equation for individuals with BMI <18.5 is another feasible alternative of estimating REE in eating disorder units, using DXA to measure FM and FFM, two components of the Müller equation. Based on the current results, the Müller equation appears to be a more accurate method than the SWA, whose REE measurements may have been affected by the profound changes in temperature regulation, and the common occurrence of temperatures lower than 35.5 degree seen in AN patients (Palla and Litt, 1988).

Conclusions

The most important finding of this study is that SWA does not appear to be alternative to the FitMate™ and Müller equation methods for the assessment of REE in patients with AN. At the moment SWA should be used by clinicians treating AN patients only to assess the presence of excess exercise, a behaviour commonly observed in these patients (Dalle Grave et al., 2008b), but not REE. Future studies using gold standard methods to assess REE with samples followed longitudinally before and after weight restoration are needed to confirm this conclusion.

Conflict of interest

Authors declare that they know of no competing financial and personal conflicts of interests in relation to the work described.

References

American Psychiatric Association (2000). Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (text revision), Washington, DC: American Psychiatric Association.

Bertoli S, Posata A, Battezzati A, Spadafranca A, Testolin G & Bedogni G. (2008). Poor agreement between a portable armband and indirect calorimetry in the assessment of resting energy expenditure. Clin Nutr 27**:**307-10.

Bland JM & Altman DG. (1986). Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1**:**307-10.

Cuerda C, Ruiz A, Velasco C, Breton I, Camblor M & Garcia-Peris P. (2007). How accurate are predictive formulas calculating energy expenditure in adolescent patients with anorexia nervosa? Clin Nutr 26**:**100-6.

Dalle Grave R, Bohn K, Hawker D & Fairburn CG. (2008a). Inpatient, day patient, and two forms of outpatient CBT-E. In: Fairburn CG, ed. Cognitive Behavior Therapy and Eating Disorders. New York: Guilford Press, pages.

Dalle Grave R, Calugi S & Marchesini G. (2008b). Compulsive exercise to control shape or weight in eating disorders: Prevalence, associated features and treatment outcome. Compr Psychiatry 49**:**346–352.

Dalle Grave, (2011). Eating disorders: progresses and challenges. Eur J Int Med 22(2): 153-60.

Daniel WW. (1991). Biostatistics: A Foundation for Analysis in the Health Sciences, New York: John Wiley & Sons.

De Zwaan M, Aslam Z & Mitchell JE (2002). Research on energy expenditure in individuals with eating disorders: a review. Int J Eat Disord 32**:**127-34.

El Ghoch M, Alberti M, Capelli C, Calugi S & Dalle Grave R (2012). Resting energy expenditure in anorexia nervosa: measured vs. estimated. J Nutr Met. doi:10.1155/2012/652932.

Fairburn CG & Cooper Z. (1993). The eating disorder examination (12th ed). In: Fairburn CG & Wilson GT, eds. Binge eating: nature, assessment, and treatment. New York: The Guilford Press, 317-360.

Frankenfield DC, Muth ER & Rowe WA. (1998). The Harris-Benedict studies of human basal metabolism: history and limitations. J Am Diet Assoc 98**:**439-45.

Fruin ML & Rankin JW. (2004). Validity of a multi-sensor armband in estimating rest and exercise energy expenditure. Med Sci Sports Exerc 36**:**1063-9.

Harris JA & Benedict FG. (1919). A biometric study of basal metabolism in man publication no 279, Washington, DC: Carnegie Institution of Washington.

Hlynsky J, Birmingham C L, Johnston M & Gritzner S (2005). The agreement between the MedGem indirect calorimeter and a standard indirect calorimeter in anorexia nervosa. Eat Weight Disord 10**:**e83-7.

Holdy KE. (2004). Monitoring energy metabolism with indirect calorimetry: instruments, interpretation, and clinical application. Nutr Clin Pract 19**:**447-54.

Jakicic JM, Marcus M, Gallagher KI, Randall C, Thomas E, Goss FL & Robertson RJ. (2004). Evaluation of the SenseWear Pro Armband to assess energy expenditure during exercise. Med Sci Sports Exerc 36**:**897-904.

Kerruish KP, O'Connor J, Humphries IR, Kohn MR, Clarke SD, Briody JN, Thomson EJ, Wright K A, Gaskin KJ & Baur LA. (2002). Body composition in adolescents with anorexia nervosa. Am J Clin Nutr 75**:**31-7.

Krahn DD, Rock C, Dechert RE, Nairn KK & Hasse SA (1993). Changes in resting energy expenditure and body composition in anorexia nervosa patients during refeeding. J Am Diet Assoc 93**:**434-8.
Levine JA. (2005). Measurement of energy expenditure. Public Health Nutr 8(7A):1123-32.
Malavolti M, Pietrobelli A, Dugoni M, Poli M, Romagnoli E, De Cristofaro P & Battistini NC (2007). A new device for measuring resting energy expenditure (REE) in healthy subjects. Nutr Metab Cardiovasc Dis 17**:**338-43.
Marra M, Polito A, De Filippo E, Cuzzolaro M, Ciarapica D, Contaldo F & Scalfi L (2002). Are the general equations to predict BMR applicable to patients with anorexia nervosa? Eat Weight Disord 7**:**53-9.
Matarese LE. (1997). Indirect calorimetry: technical aspects. J Am Diet Assoc 97**:**S154-60.
Mehler PS & Andersen AE. (2010). Eating Disorders: A Guide to Medical Care and Complications Baltimore: Johns Hopkins University .
Müller MJ, Bosy-Westphal A, Klaus S, Kreymann G, Luhrmann PM, Neuhauser-Berthold M, Noack R, Pirke KM, Platte P, Selberg O & Steiniger J. (2004). World Health Organization equations have shortcomings for predicting resting energy expenditure in persons from a modern, affluent population: generation of a new reference standard from a retrospective analysis of a German database of resting energy expenditure. Am J Clin Nutr 80**:**1379-90.
Nieman DC, Austin M D, Benezra L, Pearce S, Mcinnis T, Unick J & Gross SJ. (2006). Validation of Cosmed's FitMate in measuring oxygen consumption and estimating resting metabolic rate. Res Sports Med 14**:**89-96.
Palla B & Litt IF. (1988). Medical complications of eating disorders in adolescents. Pediatrics 81**:**613-23.
Papazoglou D, Augello G, Tagliaferri M, Savia G, Marzullo P, Maltezos E & Liuzzi A. (2006). Evaluation of a multisensor armband in estimating energy expenditure in obese individuals. Obesity (Silver Spring) 14**:**2217-23.
Schebendach J, Golden N H, Jacobson M S, Arden M, Pettei M, Hardoff D, Bauman N, Reichert P, Copperman N, Hertz S & el al. (1995). Indirect calorimetry in the nutritional management of eating disorders. Int J Eat Disord 17**:**59-66.
Tresley J & Sheean PM. (2008). Refeeding syndrome: recognition is the key to prevention and management. J Am Diet Assoc 108**:**2105-8.
Vandereycken W. (1985). Inpatient treatment of anorexia nervosa: some research-guided changes. J. Psychiatric Res 19**:**413-22.
Weir JB (1949). New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol (Lond) 109:1–9.

STUDY 3

On the same line of the previous studies we tried to test the reliability of the skinfold measurement method for assessing body composition in AN. We evaluated the correspondence between body fat mass composition (percentage) measured with dual-energy X-ray absorptiometry (DXA) and estimated by means of skinfold thicknesses (ST) measurement, before and after weight gain in clinic contest.

Contents lists available at SciVerse ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Comparison between dual-energy X-ray absorptiometry and skinfolds thickness in assessing body fat in anorexia nervosa before and after weight restoration

Marwan El Ghoch [a,*], Marta Alberti [b], Chiara Milanese [b], Nino Carlo Battistini [c], Massimo Pellegrini [c], Carlo Capelli [b], Simona Calugi [a], Riccardo Dalle Grave [a]

[a] Department of Eating Disorder and Obesity, Villa Garda Hospital, Via Montebaldo, 89, 37016 Garda (Vr), Italy
[b] Department of Neurological, Neuropsychological, Morphological and Movement Sciences, Graduate School in Translation Biomedicine, PhD Course in Science of Physical Exercise and Human Movements, University of Verona, Italy
[c] Department of Public Health Sciences, University of Modena and Reggio Emilia, Italy

Abstract

Background & Aims: The aim of the study was to evaluate the correspondence between body fat mass composition (percentage) measured with dual-energy X-ray absorptiometry (DXA) and estimated by means of skinfold thicknesses (ST) measurement in patients with anorexia nervosa (AN), before and after weight gain.

Methods: Percentage body fat (%BF) was measured with DXA and estimated by ST measurements using Siri, Brozek, and Heyward equations in 27 adult patients with AN before and after weight gain (pre- and post-treatment) achieved with inpatient treatment and in 42 healthy age-matched controls.

Results: Due to Lohman criteria and Bland Altman plot there is no correspondence between the %BF measured with DXA and the %BF estimated by predictive equations based on ST measurements in patients with AN before and after weight gain, with the exception of Brozek equation which showed a mild agreement in pre-treatment AN. However, a correspondence was observed between the two procedures in healthy controls.

Conclusions: Our data supporting the use of ST measurements do not appear to be an alternative to DXA in estimating body fat percentage, before and after weight gain in patients with AN.

Key words: body composition; anorexia nervosa; eating disorders; fat mass; skinfold thicknesses; DXA.

Introduction

Anorexia nervosa (AN) is a disorder characterized by significantly low body weight associated with intense fear of gaining weight or becoming fat, undue influence of body weight or shape on self-evaluation, and amenorrhea (1). The restoration of an adequate amount of body fat is necessary for recovery from the disorder and the resumption of a regular menstrual cycle (2). It has also been reported that in weight-restored AN patients, lower percentage body fat (%BF) at the time of hospital discharge is associated with poorer outcome (3). These data underline the fact that body composition evaluation is a crucial issue for an accurate assessment of AN patients.

In body composition literature, body mass is classically divided into two components: fat mass and fat-free mass. The %BF can be investigated using models and methods of varying complexity and accuracy. Nowadays, in the absence of cadaver analysis as the 'gold standard', no single technique can be accepted as the most appropriate reference method. Some studies (4, 5) have provided evidence that DXA shows high accuracy in estimating body composition with respect to four component model in young adults. On the other hand, one study showed that in lean adults, DXA significantly underestimated BF (6). However, a recent study on adult AN individuals found a strong correlation between DXA and Computed Tomography (CT) independently of the level of hydration, and concluded that DXA can be used to assess body composition in AN patients (7).

Unfortunately, DXA is not usually available in standard clinical settings and, as a consequence, simpler and cheaper anthropometric measurements, such as skinfold thicknesses (ST) methods have been used to predict body composition in relation to body density (8). The most widely used method, that of Durnin and Womersley (9), uses the log sum of four ST to develop regression equations for males and females of different age groups. Other authors use the sum of three or five or seven ST in combination with circumferences and age (10,11) for

generalized regression equation. These approaches have not been subjected to systematic validation in separate samples or population as there are many factors that can affect their accuracy and precision. In clinical and field settings, several studies have compared the validity of several ST equations against DXA in different populations showing contrasting results (12-16). It seems that not only intra-individual changes in %BF, but also differences between populations could be over or underestimated.

The body composition in patients with AN has been evaluated in numerous studies and using different approaches, but the few available studies comparing DXA with the ST method in the measurement of %BF in patients with AN produced inconsistent findings. Some studies found that DXA gives a mean lower %BF than ST measurement in underweight patients with AN (4, 5), while another study found an opposite result (16). After weight restoration, one study found no significant differences between the two procedures in estimating the %BF (5), while another study found a fat mass overestimation with the ST measurement method (17).

The reasons for these discrepancies have not yet been clarified, but one possible explanation is the use of inappropriate predictive formulae for patients with AN. In addition, studies comparing DXA and ST measurements in patients with AN are subject to major limitations such as the very small number of participants (4, 5) or the absence of a longitudinal evaluation of %BF changes before and after weight restoration (16).

The purpose of the present study was to compare the most commonly used equations for predictions of percentage body fat from ST in patients with anorexia nervosa, assessing their degree of correspondence with %BF measured using DXA as the reference method.

Method

Participants

27 female patients with AN and 42 age-matched healthy normal weight female subjects participated in the study. All 27 patients were voluntarily and consecutively admitted to the eating disorder inpatient unit of Villa Garda Hospital during the years 2010 - 2011. Inclusion criteria were the following: (a) age, 18-45 years; (b) body mass index (BMI) ≤ 17.5 kg/m^2; (c) diagnosis of AN assessed by the Eating Disorder Examination interview (EDE 12.0D) (18,19); (d) failure of less intensive outpatient treatment or an eating disorder of clinical severity not manageable in an outpatient setting. Patients with active substance abuse, schizophrenia and other psychotic disorders were not included. Patients were carefully matched with 42 individuals of the same age (± 2 years) recruited randomly amongst the community. Exclusion criteria for the control group were the following: (a) BMI < 18.5 kg/m^2; (b) BMI ≥ 25 kg/m^2 (c) lifetime diagnosis of AN. Inclusion and exclusion criteria both for patients and participants and controls were evaluated during an eligibility interview completed by a specialist in the field (RD). The research was reviewed and approved by the Institutional Review Board of Villa Garda Hospital, Verona, and all participants gave written informed consent for the anonymous use of their personal data.

Inpatient Treatment Protocol

The treatment has been described in detail elsewhere (20). The treatment is manual-based, lasts 20 weeks and comprises 13 weeks of inpatient therapy followed by 7 weeks of day-hospital admission.

Measurements

All data from the AN group were collected on the third day of admission, after 48 hours of refeeding, and on the last day of day-hospital treatment by the same investigator. The data obtained from the control group were collected after the eligibility interview.

Body weight and height. Body weight and height were measured respectively using medical weighing scales and a stadiometer by a medical doctor involved in the study. Participants were weighed before breakfast wearing only underwear and without shoes. The BMI was determined according to the standard formula of body weight measured in kilograms divided by height in meters squared.

Body composition. Body composition was assessed in the morning by DXA (Prodigy Primo Lunar, A223040501, General Electric Company, Madison. WI 53707-7550, USA-EnCORE TM 2009 (v13.31) software). No special preparation was required, with the exception that participants had to wear underwear and not wear any metal accessories. DXA uses a source that generates X-rays, a detector, and an interface with a computer system for imaging the scanned areas of interest. The effective radiation doses involved are small (5-7 μSv), making the technique widely applicable. The concept of DXA technology is that photon attenuation in vivo is a function of tissue composition. Rectilinear scanning of the supine body divides the body into a series of pixels and within each, the photon attenuation is measured at two different energies. The DXA body composition approach assumes that the body consists of three components that are distinguishable by their X-ray attenuation properties: fat mass, fat free mass and bone mineral. It should be noted that DXA poses a problem if repeated frequently in young females, due to an accumulation of radiation exposure.

ST were measured in triplicate to the nearest 0.2 mm with GIMA Mechanical Plicometer (GMP) at the biceps, triceps, subscapular, and supra-iliac sites. The same trained investigator made all the ST measurements. All equations analyzed in this study are the most commonly used to predict body fat from ST in AN.

Body density (BD) was estimated using the age and sex specific predictive equations of Durnin and Womersley (21). The %BF was then calculated in patients with anorexia

nervosa by using the following equations: (a) Siri equation = (495/BD)-450 (22); (b) Brozek equation = (457/BD)-414 (23); and (c) Heyward equation = (526/BD) – 483 (24). The Heyward formula was retained because it is specifically adapted for use in AN. The following formula have been used to calculate BD in the different age ranges (21):

16-19 years BD = 1.1549 - 0.0678 x log (Biceps+Triceps+Subscapular+Supra-iliac).

20-29 years BD = 1.1599 - 0.0717 x log (Biceps+Triceps+Subscapular+Supra-iliac).

30-39 years BD = 1.1423 - 0.0632 x log (Biceps+Triceps+Subscapular+Supra-iliac).

40-49 years BD = 1.1333 - 0.0612 x log (Biceps+Triceps+Subscapular+Supra-iliac).

Statistical analysis

Means and standard deviations (SD) were computed for the quantitative and continuum variables. All baseline variables were tested for univariant normality using the Kolmogorov-Smirnov test and parametric or non-parametric tests were used, as appropriate.

The basal clinical characteristics of patients with AN before and after weight gain and the control group were tested for differences using t-test or Mann–Whitney U-test for independent samples and using paired t-test or Wilcoxon test for paired samples, as necessary. The validity of the equations was tested on the basis of analysis of the differences and by performing correlations between estimated and densitometry determined values.

Product moment correlation (and standard errors of estimate; SEEs) between the percentage body fat measured with DXA and those estimated with Siri, Brozek, and Heyward equations were computed. In addition, total error (E) was computed as suggested by Lohman (25).

In his extensive review, Lohman (25) formulated different principles for cross validation analysis. Among them we have considered the following: (1) comparable mean values should be produced; (2) SEEs are preferred over correlation coefficients because

correlations are affected by inter-sample variability, while SEEs are not; (3) the calculation of the total error (E) because it reflects the actual difference between true and estimated values; (4) the similarity of standard deviation (SD) of measured and estimated values.

The visual agreement between percentage body fat measured with DXA and those estimated and with Siri, Brozek, and Heyward equations was evaluated assessing the Bland and Altman plots (26). Limits of correspondence were calculated as mean of the difference - 2SD and mean of the difference + 2SD. The *z*-test was used to evaluate whether the mean of the differences between the values obtained by the three methods, with respect to DXA, was or was not significantly different from zero (27).

Results were considered significant when $p<0.05$.

Results

The clinical characteristics and body composition of patients with AN before and after weight regain, and controls are shown in Table 1. At admission, patients with AN had a mean BMI of 15.1±1.6 kg/m^2, indicating a severe state of underweight. At the end of treatment patients achieved a mean BMI of 19.1±1.2 kg/m^2, a value that is within the normal weight range as set out by the World Health Organization's classification (28). The %BF-DXA in the AN group after weight regain was not significantly different from those measured in controls ($z=-0.39$; $p=0.699$).

A significant similar correlation was found between the sum of the four ST and BMI in AN patients both before ($r=0.57$, $p=0.002$) and after ($r=0.59$, $p=0.001$) weight gain and in the control group ($r=0.52$, $p<0.001$).

The mean of differences between DXA and ST predictive equations was significantly different from zero for all the equations in the AN group before and after weight gain except Brozek equation in the pre-treatment AN group. In the control group, the mean of differences

between DXA and ST equations (Siri and Brozek) was not significantly different from zero (Table 2 bias and z tests). The Bland-Altman plots confirm the correspondence between %BF measured with DXA and ST measurement formulae in control group, and between %BF measured with DXA and Brozek formula in AN pre-treatment group (Figure 1).

The correlation's coefficients between the percentage body fat measured with DXA and those estimated with Siri, Brozek, and Heyward formulae are shown in Table 3. Significant correlations ranged from 0.40 for DXA vs Heyward equation in the pre-treatment AN group, to 0.47 for DXA vs Brozek and Heyward equations in the AN post-treatment group. For the predictive equations in which the means of differences were not significantly different from zero, correlations were r=0.75 (DXA vs Siri equation-control group), r=0.77 (DXA vs Brozek equation-control group) and r=0.40 (DXA vs Brozek equation pre-treatment AN group). While SEEs were 2.77%, 2.69% and 5.83% respectively (Table 3).

The total error (E) values ranged from 0.38% for Siri equation in control group to 1.59% for Heyward formula in the post-treatment AN group. For the three equations in which the mean of differences was not significantly different from zero, E values were 0.38 % and 0.36 % for Siri and Brozek equations respectively in the control group, and 0.93 % for Brozek equation in the pre-treatment AN group (Table 2).

Finally, the standard deviations of BF% measured using DXA were similar to those measured using ST predictive equations in all three groups (Table 1).

Discussion

The estimation of %BF is a difficult task to accomplish in patients with AN. This may explain the paucity of studies that have evaluated BF measurement in AN before and after weight gain.

This study evaluated the measurement of percentage change in BF longitudinally in patients with AN before and after weight gain and in a control age-matched normal weight group. We used DXA, albeit still debated as a gold standard technique for body fat measurement, but which exhibits a high level of precision in adults with AN (7). Moreover, DXA measurements are highly reproducible and the validity of DXA for measurement of body fat in different samples has been previously proved (29-31). The equations that have been chosen for the comparison with DXA are those most commonly used in clinical setting studies to predict body fat via ST in AN.

The primary finding of our study is that there is no correspondence between the %BF measured with DXA and the %BF estimated with predictive equations both before and after weight gain, with the unique exception of Brozek equation in the pre-treatment AN group which showed a mild correspondence with DXA. On the other hand, there is a strong correspondence between the two procedures in healthy controls (%BF-Siri equation vs %BF-DXA; %BF-Brozek equation vs %BF-DXA).

In fact, Siri and Brozek equations in the control group and Brozek equation in the pre-treatment AN group met the Lohman criteria (25): the means for the DXA and predictive equations values were similar and not significantly different. The estimates of body fat with SEE < 3% are considered excellent (2.77 %, 2.69 % of Siri and Brozek eqauations respectively) in the control group, but a SEE = 5.83 % in Brozek equation in the pre-treatment group can be considered very weak.

Although our data showed a significant correlation between percentage body fat measured with DXA and those estimated with ST measurement in patients with AN after weight regain, the Bland and Altman plots - a statistical procedure for assessing correspondence between two methods that is more sensitive to differences than to the

statistical correlations - showed no correspondence between the two procedures both before and after weight regain.

The non-reliability of predictive equations in which ST measurements are used as predictors of body density in anorexia nervosa is particularly evident when looking at individual patients. For example, in our sample, percentage body fat estimated with Siri equation can be 20% lower than that measured with DXA, which is an undesirable difference in the clinical setting. These paradoxical differences between DXA and the predictive equations used in our study in individual patients with anorexia nervosa were also reported by a previous study (16). We have also noticed negative values of percentage body fat derived from the three equations in some patients with AN before weight gain, which is a meaningless estimation that calls into question the usefulness of these predictive equations based on four ST measurements in these patients.

The reasons behind the failure of the predictive ST equations are rather obscure and would need further investigation. However, we speculate that before weight gain, the small amount of BF present in the body of these underweight patients alters the reliability of the available equations in assessing %BF. After weight gain, the significantly greater accumulation of body fat in the central regions (i.e., chest and abdomen) than in the extremities (i.e., arm, forearm, thigh and calf) observed in weight restored patients with anorexia nervosa (32), may greatly influence the reliability of percentage body fat estimation with ST measurement, which commonly measures central upper body ST, but not those measured by DXA, which measures total body fat distribution. In other words, the four skinfolds used in our study were probably not able to estimate all the body fat gained by patients with AN after weight gain. The measurement of the thigh and calf skinfolds, either independently or in combination with upper body ST, as suggested by some authors might be a useful strategy to improve the %BF estimation with ST measurements (33).

In conclusion, the ST method underestimated %BF when compared with DXA. Our findings are consistent with previous studies reporting that ST equations do not accurately predict %BF when compared with the reference method of DXA (16, 34-36). Therefore, comparison of the methods revealed that these techniques could not be used interchangeably in this population. Our hypothesis is that the regression equations developed from previous studies using ST measurement are not appropriate for this study group. These results show that the sum of the conventional ST equation was not specifically designed to estimate all the body fat in AN patients. For this reason, new regression equations should be developed, or existing equations should be revised for different populations. Our study is currently a pilot study and for this reason further comparative studies are still required to confirm and refine the accuracy of practical, non-invasive methods for monitoring body composition.

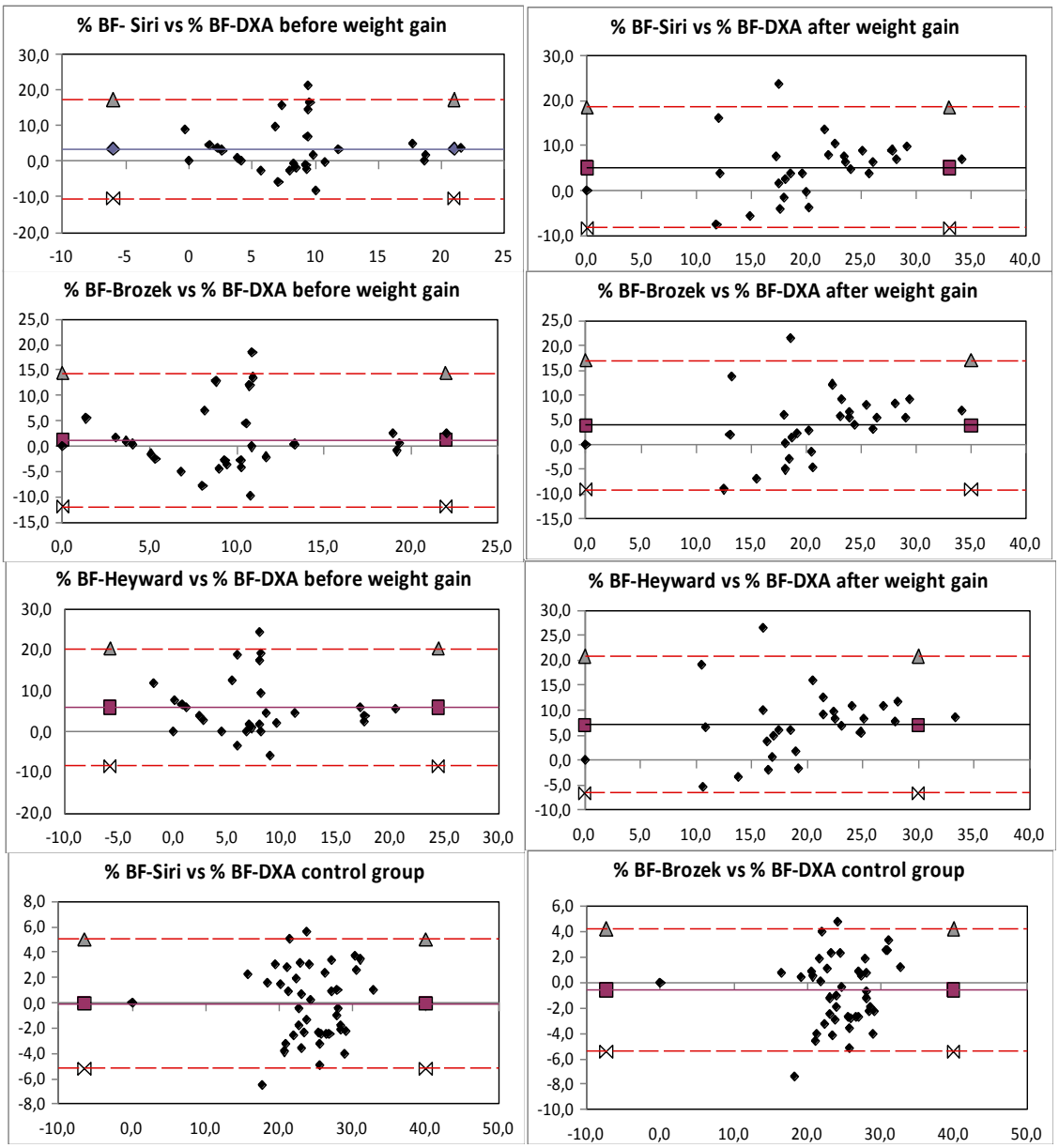


Figure 1. Bland Altman Plots
BF = Body Fat; DXA = dual-energy x-ray absorptiometry

Table 1
Clinical characteristics and body composition in 27 patients with anorexia nervosa (AN) before and after weight gain, and in 42 controls. Data are presented as mean (SD).

Clinical characteristics and body composition	Patients with AN before weight gain		Patients with AN after weight gain		Controls		Comparison between AN pre-treatment and control group		Comparison between AN post-treatment and control group		Comparison between AN pre- and post-treatment	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Test[a]	*p*	Test[a]	*p*	Test[b]	*p*
Age	26.6 (7.1)	19.0–45.0	–	–	25.1 (7.0)	18.0–45.0	$z = -0.77$	0.441	–	–	–	–
Height (m)	1.61 (0.08)	1.46–1.78	–	–	1.66 (0.04)	1.58–1.75	$t = -2.32$	0.026	–	–	–	–
Weight (kg)	39.3 (6.0)	25.5–52.3	49.7 (5.6)	36.3–58.6	59.1 (5.9)	51.4–71.2	$z = -6.93$	<0.001	$z = -5.23$	<0.001	$z = -4.54$	<0.001
BMI (kg/m^2)	15.1 (1.6)	12.0–17.4	19.1 (1.2)	16.3–22.1	21.7 (1.8)	18.6–24.9	$z = -6.97$	<0.001	$z = -5.51$	<0.001	$z = -4.54$	<0.001
DXA												
Body Fat (kg)	4.1 (2.5)	1.2–9.9	11.3 (3.6)	3.9–19.6	14.5 (3.3)	9.1–23.5	$t = -13.89$	<0.001	$t = 3.76$	<0.001	$t = -13.33$	<0.001
Body Fat (%)	10.7 (6.2)	3.9–23.3	23.7 (7.1)	8.0–37.6	24.6 (4.1)	14.5–33.3	$z = -6.51$	<0.001	$z = -0.39$	0.699	$z = -4.54$	<0.001
ST measurements												
Siri Body Fat (%)	7.2 (6.5)	−4.7 to 19.5	18.4 (5.7)	3.9–30.7	24.7 (4.1)	14.7–32.3	$z = -6.82$	<0.001	$z = -4.62$	<0.001	$z = -4.54$	<0.001
Brozek Body Fat (%)	9.4 (6.0)	−1.4 to 20.8	19.6 (5.2)	6.3–30.7	25.4 (3.7)	16.2–32.2	$z = -6.84$	<0.001	$z = -4.63$	<0.001	$z = -4.54$	<0.001
Heyward Body Fat (%)	4.6 (6.9)	−7.9 to 17.6	16.3 (6.0)	1.0–29.1	–	–	–	–	–	–	$z = -4.54$	<0.001

DXA = dual-energy x-ray absorptiometry; ST = skinfold thicknesses.
[a] *T*-test or Mann–Whitney test, as appropriate.
[b] Paired *t*-test or Wilcoxon test, as appropriate.

Table 2
Mean (SD) of differences (bias) between percent body fat measured with DXA and those estimated with Siri, Brozek, and Heyward formulae in AN patients before and after weight gain and in the control group.

		%BF with Siri formula						%BF with Brozek formula						%BF with Heyward formula					
		M	SD	95%CI	*z*	*p*	*E*	*M*	SD	95%CI	*z*	*p*	*E*	*M*	SD	95%CI	*z*	*p*	*E*
AN before weight gain	%BF with DXA	3.52	7.03	0.74–6.30	2.6	0.015	1.04	1.28	6.70	−1.37 to 3.93	1.0	0.331	0.93	6.12	7.21	3.26–8.97	4.4	<0.001	1.31
AN after weight gain	%BF with DXA	5.29	6.77	2.61–7.96	4.1	<0.001	1.34	4.07	6.58	1.47 to 6.68	3.2	0.003	1.20	7.37	6.84	4.67–10.08	5.6	<0.001	1.59
Controls	%BF with DXA	−0.11	2.90	−1.02 to 0.79	−0.3	0.793	0.38	−0.80	2.71	−1.64 to 0.04	−1.9	0.063	0.36						

DXA = dual-energy x-ray absorptiometry; %BF = percentage body fat; *z* = *z*-test; *E* = total error.

Table 3
Clinical correlations between the percent body fat measured with DXA and those estimated with Siri, Brozek, and Heyward formulae in AN patients before and after weight gain and in the control group. Pearson's correlation coefficients (*r*).

		%BF with Siri formula		%BF with Brozek formula		%BF with Heyward formula	
		r	SEE	*r*	SEE	*r*	SEE
AN before weight gain	%BF with DXA	0.39	5.85	0.40*	5.83	0.40*	5.83
AN after weight gain	%BF with DXA	0.46**	6.47	0.47**	6.44	0.47**	6.44
Controls	%BF with DXA	0.75**	2.77	0.77**	2.69		

DXA = dual-energy x-ray absorptiometry; %BF = percentage body fat; SEE = standard errors of estimate.
*$p < 0.05$; **$p < 0.001$.

References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (text revision). Washington, DC: American Psychiatric Association; 2000.
2. Frisch RE. Fatness and fertility. Sci Am. 1988; 258(3): 88-95.
3. Mayer LE, Roberto CA, Glasofer DR, Etu SF, Gallagher D, Wang J, et al. Does percent body fat predict outcome in anorexia nervosa? Am J Psychiatry. 2007; 164(6): 970-2.
4. Prior BM, Cureton KJ, Modlesky CM, Evans EM, Sloniger MA, Saunders M, et al. In vivo validation of whole body composition estimates from dual-energy X-ray absorptiometry. J Appl Physiol. 1997; 83(2): 623-30.
5. Kohrt WM. Preliminary evidence that DEXA provides an accurate assessment of body composition. J Appl Physiol. 1998; 84(1): 372-7.
6. Van der Ploeg GE, Withers RT, Laforgia J. Percent body fat via DEXA: comparison with a four-compartment model. J Appl Physiol 2003; 94: 499-506.
7. Bredella MA, Ghomi RH, Thomas BJ, Torriani M, Brick DJ, Gerweck AV, Misra M, Klibanski A, Miller KK. Comparison of DXA and CT in the assessment of body composition in premenopausal women with obesity and anorexia nervosa. Obesity (Silver Spring). 2010; 18(11): 2227-33.
8. Moreno LA, Joyanes M, Mesana MI, Gonzalez-Gross M, Gil CM, Sarria A, et al. Harmonization of anthropometric measurements for a multicenter nutrition survey in Spanish adolescents. Nutrition. 2003; 19(6): 481-6.
9. Lean ME, Han TS, Deurenberg P. Predicting body composition by densitometry from simple anthropometric measurements. Am J Clin Nutr. 1996; 63(1): 4-14.
10. Jackson AS, Pollock ML. Generalized equations for predicting body density of men. Br J Nutr. 1978; 40(3): 497-504.

11. Jackson AS, Pollock ML, Ward A. Generalized equations for predicting body density of women. Med Sci Sports Exerc. 1980; 12(3): 175-81.
12. De Lorenzo A, Bertini I, Candeloro N, Iacopino L, Andreoli A, Van Loan MD. Comparison of different techniques to measure body composition in moderately active adolescents. Br J Sports Med. 1998; 32(3): 215-9.
13. Rodriguez G, Moreno LA, Blay MG, Blay VA, Fleta J, Sarria A, et al. Body fat measurement in adolescents: comparison of skinfold thickness equations with dual-energy X-ray absorptiometry. Eur J Clin Nutr. 2005; 59(10): 1158-66.
14. Facchini M, Malfatto G, Sala L, Silvestri G, Fontana P, Lafortuna C, et al. Changes of autonomic cardiac profile after a 3-week integrated body weight reduction program in severely obese patients. J Endocrinol Invest. 2003; 26(2): 138-42.
15. Sartorio A, Narici M, Conti A, Giambona S, Ortolani S, Faglia G. Body composition analysis by dual energy x-ray absorptiometry and anthropometry in adults with childhood-onset growth hormone (GH) deficiency before and after six months of recombinant GH therapy. J Endocrinol Invest. 1997; 20(7): 417-23.
16. Haas VK, Kohn MR, Clarke SD, Allen JR, Madden S, Muller MJ, et al. Body composition changes in female adolescents with anorexia nervosa. Am J Clin Nutr. 2009; 89(4): 1005-10.
17. Scalfi L, Polito A, Bianchi L, Marra M, Caldara A, Nicolai E, et al. Body composition changes in patients with anorexia nervosa after complete weight recovery. Eur J Clin Nutr. 2002; 56(1): 15-20.
18. Mannucci E, Ricca V, Di Bernardo M, Rotella CM. Studio del comportamento alimentare con una intervista strutturata: la Eating Disorder Examination. Il Diabete. 1996; 8: 127-31.

19. Fairburn CG, Cooper Z. The eating disorder examination (12th ed). In: Fairburn CG, Wilson GT, editors. Binge eating: nature, assessment, and treatment. New York: The Guilford Press; 1993. p. 317-60.

20. Dalle Grave R, Bohn K, Hawker D, Fairburn CG. Inpatient, day patient, and two forms of outpatient CBT-E. In: Fairburn CG, editor. Cognitive Behavior Therapy and Eating Disorders. New York: Guilford Press; 2008. p. 231–44.

21. Durnin JV, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr. 1974; 32(1): 77-97.

III. Siri WE. Body composition from fluid spaces and density: Anal sis of methods. In: Brozek J, Henschel A, editors. Techniques for Measuring Body Composition. Washington DC: National Academy of Sciences; 1961. p. 223–44.

IV. Brozek J, Grande F, Anderson JT, Keys A. Densitometric Analysis of Body Composition: Revision of Some Quantitative Assumptions. Ann N Y Acad Sci. 1963; 110: 113-40.

V. Heyward SB, Stolarczyk LM. Applied Body Composition Assesment. Champaign; IL: Human Kinetics. 1996.

VI. Lohman TG. Skinfolds and body density and their relation to body fatness: A review . Human Biol. 1981; 53: 181-225.

VII. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986; 1: 307-310.

VIII. Daniel WW (1991) Biostatistics: A Foundation for Analysis in the Health Sciences, New York.

28. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i-xii, 1-253.

29. Wang ZM, Deurenberg P, Guo SS, Pietrobelli A, Wang J, Pierson RN, Jr., et al. Six-compartment body composition model: inter-method comparisons of total body fat measurement. Int J Obes Relat Metab Disord. 1998; 22(4): 329-37.
30. Wells JC, Fuller NJ, Dewit O, Fewtrell MS, Elia M, Cole TJ. Four-component model of body composition in children: density and hydration of fat-free mass and comparison with simpler models. Am J Clin Nutr. 1999; 69(5): 904-12.
6. Barbosa AR, Santarem JM, Jacob Filho W, Meirelles ES, Marucci JM. [Comparison of body fat using anthropometry bioelectrical impedance and DEXA in elderly women]. Arch Latinoam Nutr. 2001; 51(1): 49-56.
7. Orphanidou CI, McCargar LJ, Birmingham CL, Belzberg AS. Changes in body composition and fat distribution after short-term weight gain in patients with anorexia nervosa. Am J Clin Nutr. 1997; 65(4): 1034-41.
8. Eston RG, Rowlands AV, Charlesworth S, Davies A, Hoppitt T. Prediction of DXA-determined whole body fat from skinfolds: importance of including skinfolds from the thigh and calf in young, healthy men and women. Eur J Clin Nutr. 2005 ; 59(5): 695-702.
34. Deurenberg P, Deurenberg-Yap M. Validation of skinfold thickness and hand-held impedance measurements for estimation of body fat percentage among Singaporean Chinese, Malay and Indian subjects. Asia Pac J Clin Nutr. 2002;11(1): 1-7.
35. Kitano T, Kitano N, Inomoto T, Futatsuka M. Evaluation of body composition using dual-energy X-ray absorptiometry, skinfold thickness and bioelectrical impedance analysis in Japanese female college students. J Nutr Sci Vitaminol (Tokyo). 2001; 47(2): 122-5.

36. Watts K, Naylor LH, Davis EA, Jones TW, Beeson B, Bettenay F, et al. Do skinfolds accurately assess changes in body fat in obese children and adolescents? Med Sci Sports Exerc. 2006; 38(3): 439-44.

SECTION 3

PHYSICAL ACTIVITY AND EATING DISORDERS

Physical activity and Adapted Physical Activity in Mental Health

Physical Activity (PA) is defined as any bodily movement produced by skeletal muscle that results in energy expenditure. (PHR, 1985)

Adapted physical activity (APA) is a professional branch of kinesiology / physical education / sport & human movement sciences, which is directed toward persons who require adaptation for participation in the context of physical activity (IFAPA, 2010).

Some researchers (Richarson, 2005) suggest that regular physical activity has the potential to improve the quality of life and well-being of people with serious mental illness thought two routes – by improving physical health and by alleviating psychiatric and social disability. Physical activity interventions are a critical component of a biopsychosocial approach in recovery-oriented mental health services.

"Regular physical activity is associated with significant health benefits. It reduced the risk of cardiovascular disease, ischemic stroke, colon cancer, type 2 diabetes, osteoporosis, depression, fall-related injuries, and mortality. Regular fitness exercise is also highly beneficial for weight reduction and weight maintenance." (Dalle Grave, 2009, pag.1)

The energy cost of physical activity is a direct outcome of the frequency, duration, and the intensity of human movement performed in a variety of setting. Often expressed as kilocalories (or calories), energy expended in physical activity is related to the prevention of various chronic diseases, improved mental health, and reduced risks for obesity and related disabilities. All physical activities are of light, moderate, heavy intensity; they can be willful or compulsory; weekday or weekend activities. (President's Council on Physical Fitness and Sports, 2000)

Exercise is not synonymous with P.A.: exercise is a subcategory of P.A., that is planned, structured, repetitive and purposive in the sense that improvement or maintenance of the one of more components of physical fitness is an objective. Exercise, then is a subset of PA and may constitute all or part of each category of daily activity except sleep. (President's Council on Physical Fitness and Sports, 2000)

The most convincing evidence for the psychological benefits of exercise for clinical populations comes from research examining clinical depression. More modest but positive

effects of physical activity have been noted for generalized anxiety disorder, phobias, panic attacks, and stress disorders. Some authors concluded that exercise could alleviate secondary symptoms of schizophrenia, such as depression, low self-esteem, and social withdrawal. For some people, exercise also can be a useful coping strategy for the positive symptoms of schizophrenia, such as auditory hallucinations; physical activity may also play a role in reducing social isolation, can promote a sense of normalization, and offer safe opportunities for social interaction (Psychiatric services, 2005)

The American College of Sport and Medicine (ACSM, 1998, 2007), a national organization interested in promoting the health of all Americans, published a position statement that recommends appropriate amounts of exercise needed to attain minimal levels of physical fitness. Although not specific to various disabilities, these guidelines describe the frequency, duration, and intensity of exercise needed to develop and maintain cardiovascular fitness and reduce body fat. (ACSM, 1998)

The National Institute for Clinical Excellence (NICE 2004, 2009) revisited the version's guidelines for the use of physical activity for people with mild-moderate depression, in programs for people with minor and mild to moderate depression:

- ♣ Be delivered individually or in structured groups (according to patient preference) with the support of a competent practitioner;
- ♣ Provide an average of 3 sessions per week of moderate duration (45 min-1h) over 10-14 weeks (average 12 weeks) tailored to the individual to maximize adherence.

Implicit in this revised statement is that there is an optimal dose, considered substantial and may present a significant barrier to some individuals. (Mental Health and Physical Activity, 2009)

In mental health, but in particular in ED, we can find terms like compulsive or excessive that refers to a typical feature of exercise.

1. *Excessive exercising* refers to an unhealthy behavior adopted by a large subgroup of patients with eating disorders. This term is used by the DSM IV to characterize exercising as a symptom of bulimia nervosa and emphasizes the quantitative dimension of exercise.

Some authors have taken into account the compulsive feature of exercising, because this dimension seems to be the most important predictor of disordered eating attitudes and behaviors. AN patients who exercise excessively have poorer recovery rates, higher rates of relapse, and longer periods of hospitalization (Casper and Jabine, 1996; Carter et al., 2004; Strober et al.,1997).

Other studies have also found that excessively exercising AN patients display higher levels of

OCD (obsessive-compulsive disorder) symptoms and more pronounced obsessive-compulsive personality traits (Davis et al., 1998; Penas-Lledo et al., 2002). Excessive exercise interferes with important activities, occurs at inappropriate times or in inappropriate setting, or continues despite injury or other medical complications. "Unfortunately, no agreement exists on the threshold of classifying excessive exercising."(Dalle Grave, 2009, pag.1)

2. *Compulsive exercising* is a common feature of patients with an ED, in particular who are underweight, like anorectics, than in bulimics. It's a potent maintaining mechanism of ED psychopathology, increase the risk of injures and bone fractures, and also cardiac complications. "It's conflicts weight restoration, and it seems to be a negative predictor of treatment outcome." (Dalle Grave 2009, pag.1)

We can't forget the importance of the quality of life: this term connotes an overall sense of well being (USDHHS, 2000). Health related quality of life is limited to those aspects that can clearly be shown to affect mental or physical health (functional status and well-being); non-health related quality of life includes such factors as happiness and life satisfaction. Individual quality of life is identified as related to specific people or individuals. (President's Council on Physical Fitness and Sports, 2000) . In mental health diseases to achieve a sense of well being is part of the therapeutic goals. Compulsive exercising can be classified on the basis of its form and function. (R. Dalle Grave, 2009)

Physical Capacities

For Physical Capacities (PC) we mean a group of abilities that includes: endurance, strength, speed, joint mobility, and coordination.

Endurance: it's very important mainly for his action of prevention in cardiocirculatory pathologies.

Strength: a well-developed muscle is the best form of protection and strengthening support, for the musculoskeletal system; strength training has an important role in maintaining proper posture.

Speed: is important for the action-decision making in a movement, it is achieved at the cognitive level and his training improves the functions of the neuromuscular system.

Joint mobility: is important for improving the quantity and quality of movements; increased joint mobility makes fluid, gives harmony and expressivity to a movements, gives elasticity to a joints and prevents injuries to the joint and bone fractures.

Coordination: are based on processes of control and regulation of movements. There are different typologies of coordination, one very important is the balance control: it's the capacity to keep the body in a state of balance, of maintaining or recover after a shift.

(Weineck J., 2001)

Studies presentation

In the following studies, that conclude my research work, I have investigated extensively the area of physical health related.

In the *study 4* I utilized a battery of tests that measures the health related physical capacities, not yet used in the clinical field of eating disorders. We developed a new approach in the measurement of Physical Fitness in Anorexia Nervosa in-patients, before and after weight restoration. This article is accepted for publication from the *The Journal of Sports Medicine and Physical Fitness*.

In the *study 5* I measured the real amount of physical activity during the first period of hospitalization, highlighting the clinical characteristics, compared with the subjective, patient-reported same. This study is a work in progress; we are still analyzing the data for a more deep discussion, relating to a clinical context.

STUDY 4

Physical Fitness Before and After Weight Restoration in Anorexia Nervosa

Marta Alberti, PhD,[1] Christel Galvani, PhD,[2] Carlo Capelli, MD,[1] Massimo Lanza,[1] Marwan El Ghoch, MD,[3] Simona Calugi, PhD,[3] Riccardo Dalle Grave, MD[3]

[1]Department of Neurological, Neuropsychological, Morphological and Movement Sciences. University of Verona, Italy.

[2]Applied Exercise Physiology Laboratory, Department of Psychology, Exercise Science Degree Course, Catholic University of the Sacred Heart, Milano, Italy.

[3]Department of Eating Disorder and Obesity, Villa Garda, Garda, Verona.

Abstract

Aims: (i) To evaluate the feasibility of test for evaluating physical fitness (PF) in patients with anorexia nervosa (AN); (ii) to investigate the effects of nutritional rehabilitation in this population of patients and (iii) to compare their level of fitness scores (at baseline and after weight restoration) with an age-matched healthy control group.

Methods: PF was assessed with an adapted version of the Eurofit Physical Fitness Test Battery (EPFTB) administered to 37 consecutive female AN patients, at baseline and after weight restoration, and to 57 healthy age-matched females.

Results: The inpatient treatment, based on cognitive behavior therapy, was associated with a significant improvement in BMI (from 14.5±1.5 to 18.8±1.1, $p<0.001$) and in 5 out of 6 EPFTB tests ($p<0.05$) in the AN group. However, both in pre and post, AN patients showed significant lower EPFTB than the control group (all $p < 0.001$) with the exception of the Sit up score.

Conclusion: Results indicated that PF is lower in AN patients than in controls both at baseline and after weight restoration. Future studies should evaluate if the inclusion of an individualized health-enhancing physical activity program might improve the restoration of physical fitness.

Keywords:

Anorexia nervosa; inpatient treatment; weight restoration; physical fitness.

Introduction

Excessive and compulsive physical activity is commonly observed in patients with anorexia nervosa (AN).[1] The available data shows that the prevalence of excessive and compulsive exercising among eating disorder patients range from 39%[2] to 45.5%,[3] and reaches the 80% in inpatients with restricting type AN.[3] Excessive and compulsive exercising is recognized as a maladaptive behavior associated with the eating disorder psychopathology, poorer treatment outcome and higher risk of relapse.[3, 4] The main functions of exercising in patients with AN are to control body shape and weight[5] and to to modulate mood,[6] but in a subgroup of patients it might be an involuntary activity associated with stravation, as reported by animal studies showing that rats increase running as a consequence of food deprivation.[7, 8]

Research suggests that patients with AN engage in longer periods of moderate-intense physical exercise than the nonclinical population,[9] but it is not yet clear the effect of this type of exercising on physical fitness.

Physical fitness is defined as a set of attributes that people have or achieve relating to their ability to perform physical activity.[10] Physical fitness is also defined as a state of well-being with a low risk of premature health problems and the energy to participate in a variety of physical activities or capacities.[11] While both are good definitions, most experts agree that physical fitness is both multidimensional and hierarchical. Bouchard et al., for instance, presented a comprehensive model for physical fitness that includes morphological fitness, bone strength, muscular fitness, flexibility, motor fitness, cardiovascular fitness, and metabolic fitness.[12]

Few data are available on the physical fitness qualities of patients with AN. Some studies found lower muscular strength[13, 14] and lower aerobic fitness,[13, 15-18] but not significant differences in postural control[19] in respect with healthy controls. A recent study compared aerobic fitness – $\dot{V}O_{2max}$ on treadmill - and muscular strength – 1RM in leg and chest press -

in female inpatients (age ≥ 18 years; Body Mass Index or BMI ≥ 14.5 kg/m^2) with long-standing eating disorder and non-clinical controls.[1] The results showed lower level of muscular strength in AN patients compared with controls and no differences in aerobic fitness between patients and controls.

To our knowledge, only one study evaluated the effect of weight restoration on physical fitness in AN.[20] That study found that in AN patients muscle performance was restored by refeeding long before patients achieved normal nutritional status. However, no study has assessed the change of all health-related physical fitness qualities in patients with AN after weight restoration.

In this context, we aimed (i) to evaluate the feasibility of a selected series of tests for evaluating physical fitness in this population; (ii) to investigate the effects of inpatient cognitive behavioral therapy (CBT) on physical fitness in patients with AN; and (iii) to compare the level of fitness scores (at baseline and after weight restoration) with an age-matched healthy control group.

Materials and Methods

Participants. The sample consisted of 37 consecutive female patients (mean BMI 14.5 ± 1.5 kg/m^2; mean age 22.8 ± 8.6 years, mean age at onset 15.1 ± 2.8 years, median duration of illness 5 IQR [2-10] years), admitted to the eating disorder in-patient unit of Villa Garda Hospital (Northern Italy) between 2010 and 2011. The patients were referred to our institution from all over Italy by general practitioners or by eating disorder specialists. Patients were included if they met the following criteria: (i) age, 12 – 45 years; (ii) diagnosis of AN assessed by Eating Disorder Examination interview (EDE) 12.0D) [21] (iii) failure of less intensive out-patient treatment or an eating disorder of such clinical severity as to be unmanageable in an out-patient setting. In line with our protocol, subjects with active

substance abuse and acute psychotic disorders are not considered for hospital admission and the last-listed author (RDG) evaluated the presence of these two comorbid conditions during an eligibility interview before admission.

The AN patients were matched with a homogeneous group of individuals of the same age recruited randomly among young female students in the first year of the 'School of Exercise and Sport Sciences', University of Verona, Italy or by the community. Exclusion criteria were: a BMI < 18.5 kg/m^2; an inability to understand the correct application of the test; and being engaged in competitive sports or trained in a specific training program.

The research was reviewed and approved by the Institutional Review Board of Villa Garda Hospital, Verona, and all participants (or their legal guardians for the 12 (16.2%) patients and controls under 18) gave written informed consent to the anonymous use of personal data.

Treatment protocol. The treatment has been described in detail elsewhere.[22] The program is derived from the cognitive behavior treatment of eating disorders (CBT-E),[23] but has been adapted for an in-patient setting. The treatment is manual-based, lasts 20 weeks and comprises 13 weeks of in-patient therapy followed by 7 weeks of day-hospital admission, with the patient living close to the hospital and spending weekends at home. For the purpose of this study, AN patients did not participate in any therapeutic individualized physical activity sessions.

Assessments and measurements. All data were collected on the second day of admission and on the last day of day-hospital treatment in the patient group.

Weight and height. Weight (to the nearest 0.1 kg) was measured by calibrated scales and height (to the nearest 0.5 cm) by a stadiometer. Patients and controls were measured with

underwear and without shoes. The BMI was determined according to the formula of body weight divided by height in meters squared.

Fat mass. Skinfold thickness were measured in duplicate on the right side of the body with the subject standing in a relaxed condition at four sites (biceps, triceps, subscapular, suprailiac) with a Harpenden skinfold caliper. Skinfold thickness was measured to the nearest mm, except for low values (usually 5 mm or less) when it was taken to the nearest 0.5 mm. The percentage body fat was estimated from the logarithm of the sum of the skinfolds and by using the age-specific prediction equations of Durnin & Womersley (1974). For girls < 16 y of age the same formula as for girls < 20 y of age was used, as already done by other authors.[24]

Physical fitness and physical capacities. The physical fitness and capacities of the patients were evaluated by using a modified version of the Eurofit Physical Fitness Test Battery (EPFTB).[25] The standardized test battery was originally designed for children of school age and further modified for an adult population. The EPFTB is a set of physical fitness tests covering (i) aerobic fitness, (ii) musculoskeletal fitness, (iii) flexibility, and (iv) motor fitness. The present study assessed the different qualities using the following tests:

(i) Functional exercise capacity

- *Six-Minutes Walk Test*. This test is designed to evaluate functional exercise capacity. The aim of this test is to walk as far as possible for six minutes. Subjects are allowed to walk at their self-selected speed and a stop for a rest is permitted. At the end of the test the distance covered in six minutes is measured to the nearest meter. The test was performed according to the American Thoracic Society.[26]

(ii) Musculoskeletal fitness

- *Standing Broad Jump Test*. This test measures explosive legs power. The subject stands behind a line marked on the ground with feet slightly apart. A two-foot take -

off and landing is used, with swinging of the arms and bending of the knees to provide forward drive. The subject attempts to jump as far as possible, landing on both feet without falling backwards. The distance covered during the forward jump is then measured. Two attempts are allowed, and the best trial is taken into consideration for further analysis.

- *Handgrip Test*. This test measures grip or forearm muscle isometric strength. The subject holds the dynamometer (Hydraulic Hand Dynamometer, SH5001, Saehan Corporation) in the right hand to be tested, with the arm at right angles and the elbow by the side of the body. When ready, the subject squeezes the dynamometer with maximum isometric effort, which is maintained for about 5 seconds. The subject should be strongly encouraged to exert maximum effort. Two attempts are performed, and the best trial is taken into consideration for further analysis. The test was performed according to the testing position and protocol guidelines described by Ev.[27]
- *Sit-Up Test*. This test measures the endurance of the trunk muscles. It is performed with the hands placed at the side of the head, knees bent at 90°, and the feet secured by the therapist. A full sit up is defined as touching the knees with the elbows and returning the shoulders to the ground. The higher number of sit-ups performed in 30sec has been computed.

(iii) Flexibility

- *Sit-and-Reach Flexibility Test*. This test measures the flexibility of the lower back and the hamstring muscles. The subject sits on the floor with legs stretched out and knees locked and pressed flat to the floor and places the soles of the bare feet against a box, shoulder-width apart. With the palms facing downwards, and the hands side-by-side, the subject reaches forward along the measuring line as far as possible. After some practice trials, the subject reaches out twice and holds the positions for at least one-

two seconds while the distance is recorded. The best score is recorded to the nearest centimeter as the distance reached by the hand.

(iv) Motor fitness

- *Flamingo Balance Test*. The single leg balance test evaluates the ability to balance successfully on a single leg on a wood beam 50 cm long, 1,5 cm high and 3 cm wide. While balancing on the preferred leg, the subject, with bare feet and holding the instructor's hand, flexes the free leg at the knee and extends the foot of this leg so that it is held close to the buttocks. After the start, the number of falls in a 60-second period of balancing is counted. If there are more than 15 falls in the first 30 seconds, the test fails and a null score of is given.

The sequence in which the tests are performed may affect the results;[28] this specific sequence has been followed: flexibility, balance, muscular strength and endurance. The final test, after a suitable rest interval was the aerobic fitness test.

Statistical analysis .Continuous variables were categorized as mean (SD) and categorical variables as frequency (percentage). The clinical characteristics of AN patients and control group were tested for differences using t-test. T-test for paired sample test was used to analyze the differences between pre- and post-treatment values in AN patients. Univariate General Linear Models (GLM) were performed in order to compare AN post-treatment patients and the control group on each EPFTB item, controlling for BMI. Finally, the relationship between the change in BMI and the change in each EPFTB test scores in AN patients was assessed using Spearman’s correlation.

The test-retest reliability has been tested with the Intraclass correlation coefficients (ICCs).

Results

All measurements gave evidence of a substantial reliability, with ICC values always > 0.7 or 0.8. The only variables that had a moderate reliability were the ones related to body weight (BMI and % FM).

No significant differences were present between AN patients and controls in age (22.8±8.6 vs 25.9 ± 9.1 years, respectively, $t = 1.66$, $p = 0.101$). At baseline patients with AN had significant lower BMI and lower scores on all the EPFTB tests than controls (Table 1).

The treatment was associated with a significant increase in BMI and 63.9% of AN patients gained an amount of weight to fall within the World Health Organization's healthy BMI range (18.5 to 25.0). A significant increase of body fat also occurred (% FM). Moreover AN patients significantly improved their performance on the Sit-and-Reach Flexibility Test, Standing Broad Jump Test, Handgrip Test, Sit-Up Test, and Six-Minutes Walk Test. The performance on Flamingo Balance Test did not change significantly with the treatment (Table 1). Despite these improvements, at the end of treatment, AN patients maintained significant lower performance on all EPFTB Test scores than the control group, with the exception of the Sit-Up Test score, which was not significantly different between the two groups (Table 1).

Results were not significantly different, in a GLM controlled for BMI.

Table 1. Clinical variables in AN patients pre-, post-treatment and in the control group. Data are presented as mean (SD).

				Comparison between AN pre-treatment and control group			Comparison between AN post-treatment and control group			Comparison between AN pre- and post- treatment		
	AN pre-treatment (N=37)	AN post-treatment (N=37)	Control group (N=57)	Mean Change	t-test	p	Mean Change	t-test	p	Mean Change	t-test for paired samples	p
Age (years)	22.8 (8.6)	--	26.0 (9.1)	3.2	1.66	N.S.	--	--	--	--	--	--
BMI (kg/m^2)	14.5 (1.5)	18.8 (1.1)	21.1 (2.5)	6.6	14.61	<0.001	2.3	6.03	<0.001	4.4	19.07	<0.001
FM (%)	8.1 (5.9)	17.5 (7.3)	27.1 (4)	19	16.55	<0.0001	9.58	6.65	<0.0001	9.4	-8.9	<0.0001
6' walking test	540.7 (83.6)	578.9 (64.3)	685.1 (75.4)	144.5	8.49	<0.001	106.2	6.86	<0.001	38.2	3.64	0.001
Hand grip	23.5 (5.7)	25.6 (7.0)	32.8 (4.8)	9.3	8.23	<0.001	7.2	5.86	<0.001	2.6	3.22	0.003
Sit up	8.6 (6.8)	13.9 (4.6)	14.4 (3.5)	5.8	4.66	<0.001	1.4	1.72	N.S.	3.5	4.24	<0.001
Standing broad jump	112.9 (35.2)	120.1 (29.8)	162.3 (30.1)	49.3	6.92	<0.001	42.1	6.36	<0.001	8.1	2.73	0.011
Flamingo balance	13.0 (6.6)	13.4 (5.6)	8.4 (4.6)	4.6	3.80	<0.001	5.0	4.09	<0.001	0.05	0.05	N.S.
Sit and reach	5.6 (10.5)	8.8 (9.9)	12.6 (7.5)	7.0	3.52	<0.01	3.8	-2.13	<0.05	3.2	3.68	0.001

The analysis of the relationship among duration of illness, the change on BMI and the change on EPFTB test scores in AN pre and post-treatment found that only the delta Sit-Up Test score and delta Sit-and-Reach Flexibility Test score was significantly correlated with delta BMI. No significant correlations were found between duration of illness and change on EPFTB test scores (Table 2).

Table 2. Spearman's correlation coefficients among duration of illness, change on BMI and change on EPFTB Test scores

	6' walking test	Hand grip	Sit up	Standing broad jump	Flamingo balance	Sit and reach
Duration of illness	0.26	-0.02	-0.04	0.25	0.16	0.18
BMI	0.23	0.20	0.36*	0.15	-0.01	0.37*

* $p<0.05$

Discussion

This study presents three main findings: (i) the EPFTB is a feasible field battery of tests for assessing physical fitness in AN patients; (ii) weight restoration improves physical fitness in patients with AN; (iii) after weight restoration, AN patients, however, show lower physical fitness than age-matched non-trained controls.

The study has some points of strengths. First, it used a complete battery of field tests for the evaluation of fitness assessment, which is easy to perform in a clinical setting. Second, it longitudinally evaluated the changes in physical fitness in the AN group and compared the data with an age-matched control group. Moreover, the AN patients included in this study have a BMI lower that 14.5. Nevertheless, no injuries occurred while performing the EPFTB tests broth in pre -and in post – treatment conditions.

The study has also some limitations. First, the reliability and validity of Six-Minutes Walk Test, and Eurofit has not yet been assessed in AN. Second, the size of the patient group was small, however, it is difficult to recruit a large number of patients with a relative rare disorder as AN. Third, the data cannot be generalized to other eating disorder groups. Fourth, the control group was matched for age with the patient group, but not for other potential confounding variables that might have influenced physical fitness, like smoking, and medical comorbidity.

Our data confirm that AN patients had lower muscular strength (assessed with the Handgrip Test, Sit-Up Test, Standing Broad Jumping Test) than controls, and a deterioration in cardiorespiratory resistance (assessed with the Six-Minute Walk Test), flexibility (assessed with the Sit-and-Reach Flexibility Test), and balance (assessed with the Flamingo Balance Test) is present. All these fitness measures improved significantly with weight restoration, with the exception of motor fitness (assessed with the Flamingo Balance Test), even if all

fitness components remained significantly lower than those assessed in controls, with the exception of muscular endurance (assessed with the Sit-Up Test).

The lack of improvement of balance in AN patients after refeeding might be partially explained by the significant predominant increase of body fat that usually occurs in patients with AN during weight restoration.[29] We hypothesize that the time elapsed between pre and post test did not allow a sufficient muscular mass and force development necessary to obtain the adequate postural adaptations to the increase of body fat.[30]

The lack of difference in muscular endurance in the patients after refeeding compared with controls can be possibly explained by the fact that AN patients suffer of a severe type 2 atrophy[14] that influence maximal strength or explosive power but on the contrary does not affect endurance strength allowing AN patients reaching comparable endurance results with controls.

These data have clinical implications. First, assessment of physical fitness can be safely implemented in patients with AN admitted to in-patient eating disorder units. Second, discussion of the deterioration in physical fitness associated with underweight and undereating, and its significant improvement associated with weight regain, might help to engage patients in the treatment and in the difficult task of regaining weight. Finally, the incomplete improvement in physical fitness at the end of treatment, and the absence of correlations between changes in BMI and changes in EPFTB, with the exception of the Sit-Up Test score and the Sit and reach Test score, indicate that nutritional rehabilitation and weight regain are not sufficient *per se* to produce a complete restoration of physical fitness in AN patients.

Accounts from participants at the Human Starvation Study,[31] indicate that rehabilitation period was considered the most difficult part of the experiment, and that feelings of tiredness, and weakness were very slow to improve.[32] They reported not being

back to normal by the end of the 3-month recovery period and estimated that the time to achieve a full recovery ranged from 2 months to 2 years. [32] It is possible, also for patients with anorexia nervosa, that a normal fitness restoration requires a long period of weight maintenance after the weight restoration phase.

Conclusions

Future studies should investigate if an individualized health-enhancing physical activity program might contribute in enhancing health-related physical fitness qualities of patients with AN during the weight restoration phase. An healthy program of physical activity has the potential to improve the quality of life and well-being of people with serious mental illness by improving physical health and by alleviating psychiatric and social disability.[33] In addition, the inclusion of healthy exercising, if implemented in the form of social exercising, as suggested by some clinical guidelines,[6, 34] might help patients to escape from isolation, practice body exposure, facilitate the acceptance of the changes in their shape and weight, and to discharge the urge to exercise, a common problem observed in inpatient eating disorder units.[3]

References

1. Bratland-Sanda S, Sundgot-Borgen J, Ro O, Rosenvinge JH, Hoffart A, Martinsen EW. "I'm not physically active - I only go for walks": physical activity in patients with longstanding eating disorders. Int J Ear Disord 2010;43:88-92.
2. Shroff H, Reba L, Thornton LM, et al. Features associated with excessive exercise in women with eating disorders. Int J Eat Disord 2006;39:454-461.
3. Dalle Grave R, Calugi S, Marchesini G. Compulsive exercise to control shape or weight in eating disorders: Prevalence, associated features and treatment outcome. Compr Psychiatry 2008;49:346–352.
4. Bratland-Sanda S, Sundgot-Borgen J, Ro O, Rosenvinge JH, Hoffart A, Martinsen EW. Physical activity and exercise dependence during inpatient treatment of longstanding eating disorders: an exploratory study of excessive and non-excessive exercisers. Int J Eat Disord 2010;43:266-273.
5. Zunker C, Mitchell JE, Wonderlich SA. Exercise interventions for women with anorexia nervosa: a review of the literature. Int J Eat Disord 2011;44:579-584.
6. Dalle Grave R. Features and management of compulsive exercising in eating disorders. Phys Sportsmed 2009;37:20-28.
7. Pirke KM, Broocks A, Wilckens T, Marquard R, Schweiger U. Starvation-induced hyperactivity in the rat: the role of endocrine and neurotransmitter changes. Neurosci Biobehav Rev 1993;17:287-294.
8. Exner C, Hebebrand J, Remschmidt H, et al. Leptin suppresses semi-starvation induced hyperactivity in rats: implications for anorexia nervosa. Mol Psychiatry 2000;5:476-481.
9. Kron L, Katz JL, Gorzynski G, Weiner H. Hyperactivity in anorexia nervosa: a fundamental clinical feature. Compr Psychiatry 1978;19:433-440.
10. U.S. Department of Health and Human Services CfDCaP. National Center for Chronic Disease Prevention and Health Promotion. Physical activity and health: a report of the Surgeon General. Atlanta, GA; 1996.
11. President's Council on Physical Fitness and Sports. Definitions: Health, Fitness, and Physical Activity 2000. Series 3, No.9.
12. Bouchard C, Shepherd R, Stephens T. Physical activity, fitness and health. Leeds: Human Kinetics; 1994.
13. Einerson J, Ward A, Hanson P. Exercise responses in females with anorexia nervosa. Int J Eat Disord 1988;7:253-260.
14. McLoughlin DM, Spargo E, Wassif WS, et al. Structural and functional changes in skeletal muscle in anorexia nervosa. Acta Neuropathol 1998;95:632-640.
15. Fohlin L. Exercise performance and body dimensions in anorexia nervosa before and after rehabilitation. Acta Med Scand 1978;204:61-65.
16. Nudel DB, Gootman N, Nussbaum MP, Shenker IR. Altered exercise performance and abnormal sympathetic responses to exercise in patients with anorexia nervosa. J Pediatr 1984;105:34-37.
17. Biadi O, Rossini R, Musumeci G, et al. Cardiopulmonary exercise test in young women affected by anorexia nervosa. Ital Heart J 2001;2:462-467.
18. Rowland T, Koenigs L, Miller N. Myocardial performance during maximal exercise in adolescents with anorexia nervosa. J Sports Med Phys Fitness 2003;43:202-208.
19. Fontana MP, Menegoni F, Vismara L, et al. Balance in patients with anorexia and bulimia nervosa. Eur J Phys Rehabil Med 2009;45:335-340.

20. Rigaud D, Moukaddem M, Cohen B, Malon D, Reveillard V, Mignon M. Refeeding improves muscle performance without normalization of muscle mass and oxygen consumption in anorexia nervosa patients. Am J Clin Nutr 1997;65:1845-1851.
21. Fairburn CG, Cooper Z. The eating disorder examination (12th ed). In: Fairburn CG, Wilson GT, eds. Binge eating: nature, assessment, and treatment. New York: The Guilford Press; 1993:317-360.
22. Dalle Grave R, Bohn K, Hawker D, Fairburn CG. Inpatient, day patient, and two forms of outpatient CBT-E. In: Fairburn CG, ed. Cognitive Behavior Therapy and Eating Disorders. New York: Guilford Press; 2008:231–244.
23. Fairburn CG, Cooper Z, Shafran R. Cognitive behaviour therapy for eating disorders: a "transdiagnostic" theory and treatment. Behav Res Ther. May 2003;41(5):509-528.
24. Probst M, Goris M, Vandereycken W, Van Coppenolle H. Body composition of anorexia nervosa patients assessed by underwater weighing and skinfold-thickness measurements before and after weight gain. Am J Clin Nutr 2001;73:190-197.
25. EUROFIT: Handbook for the EUROFIT tests on physical fitness . Second edition. Strasbourg: Council of Europe; 1993.
26. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-117.
27. Ev J. Handgrip strength testing: A review of the literature. Aust Occup Ther 1999;46:120-140.
28. Oja P, Tuxworth B. Eurofit for Adults: Assessment of Health-Related FitnessFinland: Council of Europe Publishing; 1995:1-13.
29. Orphanidou CI, McCargar LJ, Birmingham CL, Belzberg AS. Changes in body composition and fat distribution after short-term weight gain in patients with anorexia nervosa. Am J Clin Nutr1997;65:1034-1041.
30. Ledin T, Fransson PA, Magnusson M. Effects of postural disturbances with fatigued triceps surae muscles or with 20% additional body weight. Gait Posture 2004;19:184-193.
31. Keys A, Brozek J, Henschel A, Mickelsen O, Taylor HL. The Biology of Human Starvation. Vol 2 Minneapolis: University of Minnesota Press; 1950.
32. Kalm LM, Semba RD. They starved so that others be better fed: remembering Ancel Keys and the Minnesota experiment. J Nutr 2005;135:1347-1352.
33. Richardson CR, Avripas SA, Neal DL, Marcus SM. Increasing lifestyle physical activity in patients with depression or other serious mental illness. J Psychiatr Pract 2005;11:379-388.
34. Murphy R, Straebler S, Cooper Z, Fairburn CG. Cognitive behavioral therapy for eating disorders. Psychiatr Clin North Am 2010;33:611-627.

STUDY 5

Objective and Subjective Assessment of Physical Activity in Anorexia Nervosa and Treatment Outcome

Alberti Marta, PhD[1], Marwan El Ghoch, MD[2], Riccardo Dalle Grave, MD[2], Carlo Capelli, MD[1], Massimo Lanza[1], Simona Calugi, PhD[2], Christel Galvani, PhD[3]

[1]Department of Neurological, Neuropsychological, Morphological and Movement Sciences. University of Verona, Italy.

[2]Department of Eating Disorder and Obesity, Villa Garda, Garda, Verona.

[3]Applied Exercise Physiology Laboratory, Department of Psychology, Exercise Science Degree Course, Catholic University of the Sacred Heart, Milano, Italy.

Abstract

Introduction: Excessive physical activity (PA) seems to be is a common and harmful behavior among patients with Anorexia Nervosa (AN), and it is considered as one of the specific maintenance mechanisms of Eating Disorder (ED), it has been also associated with poorer outcome following AN in-patient treatment. The aim of this paper is: (i) to compare objective and subjective assessment of PA; (ii) to examine the relationship between PA and the change of ED psychopathology during in-patient treatment.

Methods: PA was measured and estimated respectively by means of Actiheart (AH) and International Physical Activity Questionnaire (IPAQ) in 52 AN female during 20 weeks in-patient treatment.

Results: Due to Bland Altman plot there is no correspondence between PA estimated by IPAQ and that measured by means of AH. A significant correlation between the change of EDE global score and light physical activity (LPA) measured by AH, but not with that estimated by IPAQ.

Conclusion: Our data supporting the use of IPAQ do not appear to be an alternative to AH in estimating PA. An objective assessment of LPA may lead to an improvement in ED psychopathology during in-patient treatment.

Introduction

Excessive Physical Activity (PA) seems to be commonly observed among patients with Anorexia Nervosa (AN) (Casper, 1998; Kron, 1978), considering it to be a harmful behavior (osteoporosis, bone fracture) (LaBan,1995). In addition there is a negative relationship

between PA and percentage body fat in AN patients (Hechler, 2008). PA is also considered one of the specific maintenance mechanisms of Eating Disorder (ED), it has been associated with poorer outcome following AN inpatient treatment (Dalle Grave, 2008; Carter, 2004; Strober, 1997; Davice, 1994).

Excessive PA may take different forms, not only an increase of structured exercise, such as running and gym activities, but also during routine daily activities. This make its assessment a difficult task. Obviously an improvement in understanding of PA in AN may lead to the improvement of AN treatments.

In previous studies, different approaches have been used to evaluate PA, where most of them relied on self-report or subjective instruments (Hebebrand, 2003). Few studies have assessed PA objectively, and in this case unfortunately the majority of these employed devices with limited sensibility such as pedometers (Klein, 2007) compared with available devices such as accelerometers (Bouten, 1996; Westerterp, 1997; Birmingham, 2005; Holtkamp, 2006; Klein, 2007; Hechler, 2008; Bratland-Sanda, 2010b and c; Dellava, 2011), multi-sensor device (Klein, 2007) or measurements based on daily metabolic rate, such as doubly labeled water (Casper, 1991; Bouten, 1996; van Marken Lichtenbelt, 1997; Westerterp, 1997; Bossu, 2007).

Dellava has underline the importance of a precise methodology for assessment of PA (i.e., multiaxial and water-proof activity monitors) (Dellava, 2011), and a particular attention has to be placed on correctly monitoring of vigorous PA that may be considered a self injurious behaviour (Skarderud, 2009).

Excessive PA is one of the specific maintenance mechanisms of eating disorder. Strober et al showed that excessive exercisers have a shorter time to relapse, that implies that these patients seems to have poorer outcome following inpatient treatment, this conclusion has been underlined in other studies (Dalle Grave, 2008; Carter, 2004). Unfortunately the limitation of these studies is the assessment of PA, that was based on direct interview and on self-reported questionnaires. Because denial is a common process in AN (Vandereyche W, 1983; Couturier, 2006), it is possible that a subgroup of patients denied their symptoms or gave unreliable answer. In the other hand in one study, Klein et al (Klein, 2007) found no significant association between measured PA by means of Sensewear Armband and ED psychopathology.

Therefore, considering the controversial data concerning about the features of PA in AN patients, and its hypothetical role in affecting the ED treatment's outcome, we undertook this investigation with the aim: (i) to compare objective and subjective assessment of PA; (ii) to

examine the relationship between PA and the change of eating disorder (ED) psychopathology during in-patient and treatment.

Methods

Participants

Fifty two female patients with AN (age 24.4 ± 8.5 yr; BMI 14.3 ± 1.7 kg/m2; ; mean age at onset 15.1± 2.8 years, median duration of illness 5 IQR [2-10] years), were voluntarily and consecutively admitted to the ED in-patient unit of Villa Garda Hospital during the years 2010 - 2012. Inclusion criteria were the following: (a) age, 13-65 years; (b) body mass index (BMI) ≤ 17.5 kg/m2; (c) diagnosis of AN assessed by the Eating Disorder Examination interview (EDE 12.0D) (18,19); (d) failure of less intensive outpatient treatment or an eating disorder of clinical severity not manageable in an outpatient setting. Patients with active substance abuse, schizophrenia and other psychotic disorders were not included. Inclusion and exclusion criteria both for patients and participants and controls were evaluated during an eligibility interview completed by a specialist in the field (RD). The research was reviewed and approved by the Institutional Review Board of Villa Garda Hospital, Verona, and all participants (or their legal guardians for patients under 18) gave written informed consent for the anonymous use of their personal data.

Inpatient Treatment Protocol

The treatment has been described in detail elsewhere (Dalle Grave, 2008). The treatment is manual-based, lasts 20 weeks and comprises 13 weeks of inpatient therapy followed by 7 weeks of day-hospital admission.

Assessment and measurements

Body weight and height. Body weight and height were measured respectively using medical weighing scales and a stadiometer by a medical doctor involved in the study. Participants were weighed before breakfast wearing only underwear and without shoes. The BMI was determined according to the standard formula of body weight measured in kilograms divided by height in meters squared.

The Actiheart (AH)(Branched model, Actiheart Software, version 4.0)(Brage, 2004). Is a validated instrument in different populations (Brage, 2005; Crouter, 2008; Barreira, 2009) that combine heart rate monitor (HR) and movement sensor acceleration. Acceleration is measured by a piezoelectric element with a frequency range of 1–7 Hz (3 dB). AH is able to assess activity energy expenditure (AEE), duration and different intensities of PA. The AH was placed on the left side of the patients' chest, attached on the skin by two standard ECG

electrodes on the second day of hospitalization and was maintained for three 24-hours consecutive days.

International Physical Activity Questionnaire (IPAQ) - short form – is an instrument designed primarily for population surveillance of PA among adults (age range of 15-69 years) (Craig, 2003). It covers three domains of PA: walking, moderate-intensity activities and vigorous-intensity activities. The questionnaire also includes questions about time spent sitting as an indicator of sedentary behaviour. In each of the four domains the number of days per week and time per day spent in both moderate and vigorous activity or sedentary behaviour in the last seven days are recorded. The IPAQ was administered in all patients at the eighth day of hospitalization.

Data collected by AH were compared with the estimated self-reported PA by IPAQ. Outcome measures used were: activity energy expenditure (AEE), minutes of light PA (LPA); minutes of moderate PA (MPA); minutes of vigorous PA (VPA); sum of the minutes spent during moderate and vigorous PA (MVPA).

The Eating Disorder Examination (EDE) 12.0D (Fairburn, 1993) is an investigator-based interview that assesses the frequency of key behavioral and attitudinal aspects of ED during the preceding 4 weeks (28 days). It evaluates the major areas of eating disorder psychopathology in 4 subscales (restraint, eating concern, shape concern, and weight concern). It is carried out for diagnostic purposes and to evaluate the specific ED psychopathology by a senior specialist in the field (RD).

The Brief Symptom Inventory (BSI). is a Self- or interviewer-administered (Derogatis, 1983), consists of 53 items covering nine symptom dimensions: somatization, obsession-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism; and three global indices of distress: Global Severity Index, Positive Symptom Distress Index, and Positive Symptom Total. The global indices (T-Score – normal value < 63) measure current or past level of symptomatology, intensity of symptoms, and number of reported symptoms, respectively.

Statistics

Data analysis was performed using Stat View (version 5.0). Means and standard deviations are presented for all continuous measures. Pearson's correlation was used to explore the association between objective and subjective PA levels. Fisher's r to z transformation was carried out to locate significant differences. Student's t-test was used to determine differences between objective and subjective PA. Cohen's d effect size was also determined. A one-way ANOVA was used to evaluate disparities between time spent in

different intensity thresholds with the post hoc test of Scheffé. Univariate regression analysis was also performed to establish links between the change in EDE global score at the end of treatment and PA objectively measured.

The visual agreement between self reported (IPAQ) and objectively measured (Actiheart) PA. The Bland and Altman plots (Bland, 1986) show mean difference with 95% limits of agreement of AEE, MPA, VPA and MVPA. Limits of correspondence were calculated as mean of the difference - 2SD and mean of the difference + 2SD.

Results were considered significant when $p<0.05$.

Results

Statistical analysis showed a significant correlation between AH and IPAQ, for AEE and VPA respectively ($r = 0.321$; $p<0.05$ - $r = 0.660$; $p<0.0001$) (Table 1). The mean of differences between AH and IPAQ was significantly different from zero for AEE, MPA , VPA and MVPA. IPAQ significantly underestimates PA (Table 2). The Bland-Altman plots confirm the non correspondence between PA measured with AH and estimated by IPAQ for AEE, MPA , VPA and MVPA (Figure 1 and 2).

Physical activity patterns according to objective measurement

Figure 3 shows the hourly pattern of overall PA between 07:00 and 23:00 h. Periods before 7:00 and after 23:00 are not reported, as the majority of participants recorded no activity at these times. The activity pattern was characterized by several peaks throughout the day, in the morning, in the late afternoon and after dinner (Figure 3).

AN patients spent significantly longer periods in activity classified as sedentary and light, compared to activities classified as moderate or vigorous: SED 495 ± 189 mins day-1; LPA 343 ± 152 mins day-1; MPA 94 ± 112 mins day-1; VPA 6 ± 12 mins day-1; MVPA 100 ± 120 mins day-1. In details, time in SED was significantly larger than in LPA, MPA, VPA and MVPA ($p<0.0001$); time in LPA was significantly larger than in MPA, VPA and MVPA ($p<0.0001$); time in MPA was significantly higher than VPA ($p<0.0001$) (Table 3). If the minutes spent in PA are individually analysed, a great within-subject variability appears (Figure 4).

Associations between physical activity level and illness severity

To analyse the association between MVPA and all demographic and clinical parameters we carried out univariate regression models. The amount of exercise (MVPA) was negatively associated with the duration of illness ($\beta = -0.33$, $t = -2.45$, $p<0.05$) but positively associated with the minutes of exercise over the last 4 weeks diagnosed by the EDE interview ($\beta = 0.29$,

t = 2.16, p<0.05). Univariate regression model revealed that AEE (β = 0.69, t = 6.81, p<0.0001). There was no significant association between MVPA and BMI nor the other clinical parameters.

Associations between physical activity level and treatment outcome

Forty one patients (78.9%) completed treatment, whereas 11 (21.1%) were classified as drop-outs because of voluntary treatment discontinuation before the planned 20 weeks. Univariate regression analysis was performed to establish links between the change in EDE global score at the end of treatment and measured PA by AH. A significant correlation between the change of EDE global score and LPA measured by AH (beta=-0.36, t=-2.44, p=0.019).

Discussion

The strengths of the study are the use of an objective method for PA assessement. AH is a multi-sensor instrument that offers the best option for the assessment of PA, achieving higher accuracies than single sensor systems (Andre, 2007). The AH is waterproof device (Warren, 2010) and does not interfere with the performance of daily activities, and with the impossibility for the patients to remove it, in order to exercise without causing a loss of heart rate signal, becoming easy to determine non-wearing times. Moreover our sample, represents relatively a large study for a disorder that is not highly prevalent, and the use of EDE interview considered a gold-standard for the diagnosis of eating disorders. In the other hand the limitations are the absence of a longitudinal evaluation and the control group.

The main findings of the study are: (i) measured LPA seems to be a good predictor of the out-come of the treatment; (ii) AN patients spent significantly longer periods in activity classified as sedentary and light, compared to activities classified as moderate or vigorous; (iii) IPAQ significantly underestimated PA with respect to AH.

Therefore the use of objective assessment of PA is a more appropriate method to quantify PA with respect to those self-reported. Indeed, AN patients tend to under report the amount of daily PA and these results are consistent with an another study (Bratland-Sanda, 2010a).

It is difficult to compare our data with those arising from the literature because of the different types of PA assessments, difference in sample sizes (from 6 to 36 subjects), number of days during which PA has been monitored (from 2 to 7) and settings (in-patient, out-patient, free-living).

Minutes per day of MVPA are close to the ones observed by Bratland-Sanda (Bratler-Sanda, 2010b) in a population of 7 AN in-patients (MVPA 100 vs 93 min day-1). Conversely,

Hechler (Hechler, 2008) found a higher amount of PA (232 min day-1 from low to very high PA). Time observed in sedentary activities is consistent with Bouten (Bouten, 1996) classification when expressed in percentage of monitoring time (53 vs 60%) and is higher than the percentage of time spent in light or moderate to vigorous activities.

Our data are in accordance with Klein (Klein, 2007) indicating that some patients with AN are consistently more active than others, MVPA showing inter-person variation by up to 500 min per day. Despite a great range in MVPA across individuals, it has been possible to outline the trait of activity pattern among AN in-patients. The illustration of PA patterns of AN patients with several peaks of PA throughout the day is of relevance to clinicians in their assessment and treatment of increased activity, highlighting particularly three moments during the day, in the morning, in the late afternoon and after dinner. These data complete the findings of Bouten (Bouten, 1996) who underlined that subjects with AN showed nocturnal and early morning awakening.

The practical implications of this study are (i) the necessity of an accurate objective assessment of PA in clinical settings, especially for LPA, that seems to be correlated to the change of ED psychopathology (ii) the description of PA patterns of AN in-patients to improve the treatment and management of diseases.

Our study is currently a pilot study, but it is one of the first to introduce the importance of the objective assessment of PA, as a predictor of AN treatment out-come. For this reason further studies are still required to confirm our data.

Statement of authorship

All authors have authorship and have made substantial contributions and final approval of the conceptions, drafting, and final version.

Conflict of interest

All authors declare no competing financial interests in relation to the work described.

References

Andre D, Wolf DL. Recent advances in free-living physical activity monitoring: a review. J Diabetes Sci Technol. 2007 Sep;1(5):760-7.

Barreira TV, Kang M, Caputo JL, Farly RS, Renfrow MS. Validation of the Actiheart Monitor for the Measurement of Physical Activity. Int J Exerc Sci. 2009;2(1):60-71.

Birmingham CL, Hlynsky J, Whiteside L, Geller J. Caloric requirement for refeeding inpatients with anorexia nervosa: the contribution of anxiety exercise, and cigarette smoking. Eat Weight Disord. 2005 Mar;0(1):e6-9.

Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986 Feb;1 (8476):307-10.

Bouten CV, van Marken Lichtenbelt WD, Westerterp KR. Body mass index and daily physical activity in anorexia nervosa. Med Sci Sports Exerc. 1996 Aug;28(8):967-73.

Brage S, Brage N, Franks PW, Ekelund U, Wong MY, Andersen LB, Froberg K, Wareham NJ Branched equation modeling of simultaneous accelerometry and heart rate monitoring improves estimate of directly measured physical activity energy expenditure. J Appl Physiol. 2004 Jan;96(1):343–51.

Brage S, Brage N, Franks PW, Ekelund U, Wareham NJ. Reliability and validity of the combined heart rate and movement sensor Actiheart. Eur J Clin Nutr. 2005 Apr;59(4):561-70.

Bratland-Sanda, S., Sundgot-Borgen, J., Ro, O., Rosenvinge, J. H., Hoffart, A., & Martinsen, E. W. "I'm not physically active - I only go for walks": physical activity in patients with longstanding eating disorders. Int J Eat Disord. 2010 Jan;43(1):88-92.

Bratland-Sanda, S., Sundgot-Borgen, J., Ro, O., Rosenvinge, J. H., Hoffart, A., & Martinsen, E. W. Physical activity and exercise dependence during inpatient treatment of longstanding eating disorders: an exploratory study of excessive and non excessive exercisers. Int J Eat Disord. 2010 Apr 43(3):266-73.

Bossu C, Galusca B, Normand S, Germain N, Collet P, Frere D, Lang F, Laville M, Estour B. Energy expenditure adjusted for body composition differentiates constitutional thinness from both normal subjects and anorexia nervosa. Am J Physiol Endocrinol Metab. 2007 Jan;292(1):e132-7.

Carter JC, Blackmore E, Sutander-Pinnock K, Woodside DB. Relapse in anorexia nervosa: a survival analysis. Psychol Med. 2004 May;34(4):671-9.

Casper RC, Schoeller DA, Kushner R, Hnilicka J, Gold ST. Total daily energy expenditure and activity level in anorexia nervosa. Am J Clin Nutr. 1991 May;53(5):1143-50.

Casper RC. Recognizing eating disorders in women. Psychopharmacol Bull. 1998;34(3):267-9.

Couturier JL, Lock J. Denial and minimization in adoloscents with anorexia nervosa. Int J Eat Disord. 2006 Apr;39(3):212-6.

Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003 Aug;35(8):1381-95.

Crouter SE, Churilla JR, Bassett DR Jr. Accuracy of the Actiheart for the assessment of energy expenditure in adults. Eur J Clin Nutr. 2008 Jun;62(6):704-11.

Dalle Grave R, Bohn K, Hawker D, Fairburn CG. Inpatient, day patient, and two forms of outpatient CBT-E. In: Fairburn CG, ed. Cognitive Behavior Therapy and Eating Disorders. New York: Guilford Press, 2008:231–44.

Dalle Grave R, Calugi S, Marchesini G. Compulsive exercise to control shape or weight in eating disorders: prevalence, associated features, and treatment out come. Compr Psychiartry. 2008 Jul-Aug; 49(4):346-52.

Davis C., Kennedy SH, Ravelelski E., Dionne M. The role of physical activity in the development and maintenance of eating disordes. Psychol Med. 1994 Nov;24(4):957-67.

Derogatis LR, Melisaratos N. The Breif symptom Inventory: an intorductory report. Psycol Med. 1983 Aug;13(3):595-605.

Dellava JE, Hamer RM, Kanodia A, Reyes-Rodríguez ML, Bulik CM. Diet and physical activity in women recovered from anorexia nervosa: a pilot study. Int J Eat Disord. 2011 May;44(4):376-82.

Fairburn CG, Cooper Z. The eating disorder examination (12th ed). In: Fairburn CG, Wilson GT, eds. Binge eating: nature, assessment, and treatment. New York: The Guilford Press, 1993:317-60.

Fairburn CG, Cooper Z, Shafran R. Cognitive behaviour therapy for eating disorders: a "transdiagnostic" theory and treatment. Behav Res Ther. 2003 May; 41(5):509-28.

Hebebrand, J., Exner, C., Hebebrand, K., Holtkamp, C., Casper, R.C., Remschmidt, H., Herpertz-Dahlmann, B., Klingenspor, M. Hyperactivity in patients with anorexia nervosa and in semistarved rats: evidence for a pivotal role of hypoleptinemia. Physiol. Behav. 2003 Jun; 79(1), 25–37.

Hechler T, Rieger E, Touyz S, Beumont P, Plasqui G, Westerterp K. Physical activity and body composition in outpatients recovering from anorexia nervosa and healthy

controls. Adapt Phys Activ Q. 2008 Apr;25(2):159-73.

Holtkamp, K., Herpertz-Dahlmann, B., Hebebrand, K., Mika, C., Kratzsch, J., Hebebrand, J. Physical activity and restlessness correlate with leptin levels in patients with adolescent anorexia nervosa. Biol. Psychiatry. 2006 Aug;60(3):311–13.

Klein DA, Mayer LE, Schebendach JE, Walsh BT. Physical activity and cortisol in anorexia nervosa. Psychoneuroendocrinology. 2007 Jun;32(5):539-47.

Kron L., Kats J.L., Gorzynsky G., & Weiner H. Hyperactivity in anorexia nervosa: a fundamental clinical feature. Compr Psychiatry. 1978 Sep-Oct;19(5):433-40.

LaBan MM, Wilkins JC, Sackeyfio AH, Taylor RS. Osteoporotic stress fracture in anorexia nervosa: etiology, diagnosis, and review of for cases. Arch Phys Med Rehabil. 1995 Sep;76(9):884-7.

Skarderud F. Self-harm and sports—case reports. Tidsskr Nor Laegeforen. 2009 Apr;129(9):888–90.

Strober M, Freeman R, Morrell W. The long course of severe anorexia nervosa in adolescents: survival analysis of recovery, relapse, and outcome predictors over 10-15 years in prospective study. Int J Eat Disord. 1997 Dec;22(4): 339-60.

Vandereycken W, Venderlinden J. Denial of illness and the use of self-reporting measures in anorexia nervosa patients. Int J Eat Disord. 1983; 2:101-7

Van Marken Lichtenbelt WD, Heidendal GA, Westerterp KR. Energy expenditure and physical activity in relation to bone mineral density in women with anorexia nervosa. Eur J Clin Nutr. 1997 Dec;51(12):826-30.

Warren JM, Ekelund U, Besson H, Mezzani A, Geladas N, Vanhees L; Experts Panel. Assessment of physical activity - a review of methodologies with reference to epidemiological research: a report of the exercise physiology section of the European Association of Cardiovascular Prevention and Rehabilitation. Eur J Cardiovasc Prev Rehabil. 2010 Apr;17(2):127-39.

Westerterp KR, Bouten CV. Physical activity assessment: comparison between movement registration and doubly labeled water method. Z Ernahrungswiss. 1997 Dec;36(4):263-7.

Tables

Table 1. Correlations analysis between Actiheart and IPAQ data.

	Correlation r	**p value**
AEE (kcal day^{-1})	0.321	<0.05
MPA (min day^{-1})	0.183	ns
VPA (min day^{-1})	0.660	<0.0001
MVPA (min day^{-1})	0.219	Ns

AEE: activity energy expenditure; MPA: minutes of moderate physical activity; VPA: minutes of vigorous physical activity; MVPA: sum of the minutes spent during moderate and vigorous physical activity
r, Pearson correlation coefficient
p, Fisher's r to z

Table 2. Comparison of physical activity between Actiheart and IPAQ.

	AH	IPAQ	*F*	p	power
AEE (kcal day^{-1})	471 ± 241	90 ± 157	91.875	<0.0001	1.000
MPA (min day^{-1})	94 ± 112	51 ± 85	4.786	<0.05	0.574
VPA (min day^{-1})	6 ± 12	4 ± 18	.554	ns	
MVPA (min day^{-1})	100 ± 120	55 ± 89	4.668	<0.05	0.563

AEE: activity energy expenditure; MPA: minutes of moderate physical activity; VPA: minutes of vigorous physical activit.y; MVPA: sum of the minutes spent during moderate and vigorous physical activity
F, p, power: repeated measures ANOVA

Table 3. Percentage of awake time of minutes of sedentary, light or moderate, vigorous physical activity per day.

SED % of AT	LPA % of AT	MPA % of AT	VPA % of AT	MVPA % of AT
53 ± 19	37 ± 15	10 ± 12	1 ± 1	11 ± 13

SED: minutes of sedentary; LPA: minutes of light physical activity; MPA: minutes of moderate physical activity; VPA: minutes of vigorous physical activity; MVPA: sum of the minutes spent during moderate and vigorous physical activity; AT: awake time

Figure Legends

Figure Legends

Figure 1. Bland-Altman plot showing difference versus average values of self reported (IPAQ) and objectively measured (Actiheart) activity energy expenditure (AEE). The plots show mean difference with 95% limits of agreement of AEE.

Figure 2. Bland-Altman plot showing difference versus average values of self reported (IPAQ) and objectively measured (Actiheart) physical activity. The plots show mean difference with 95% limits of agreement of MPA (A), VPA (B) and MVPA (C).

Figure 3. AN patients physical activity patterns

Figure 4. Within-subject variability of MVPA a day

Figure 1

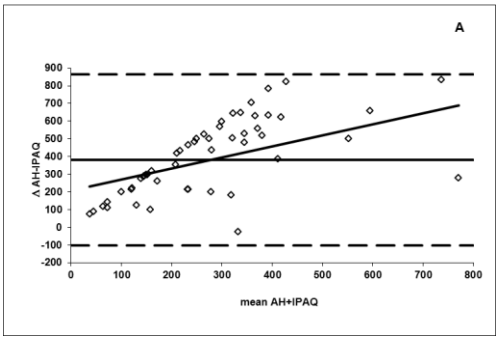


Figure 2

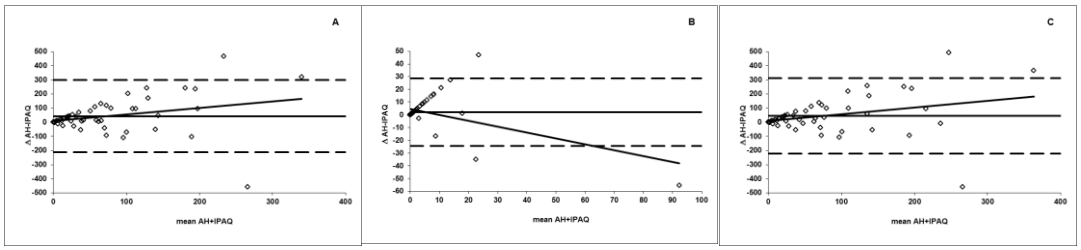


Figure 3

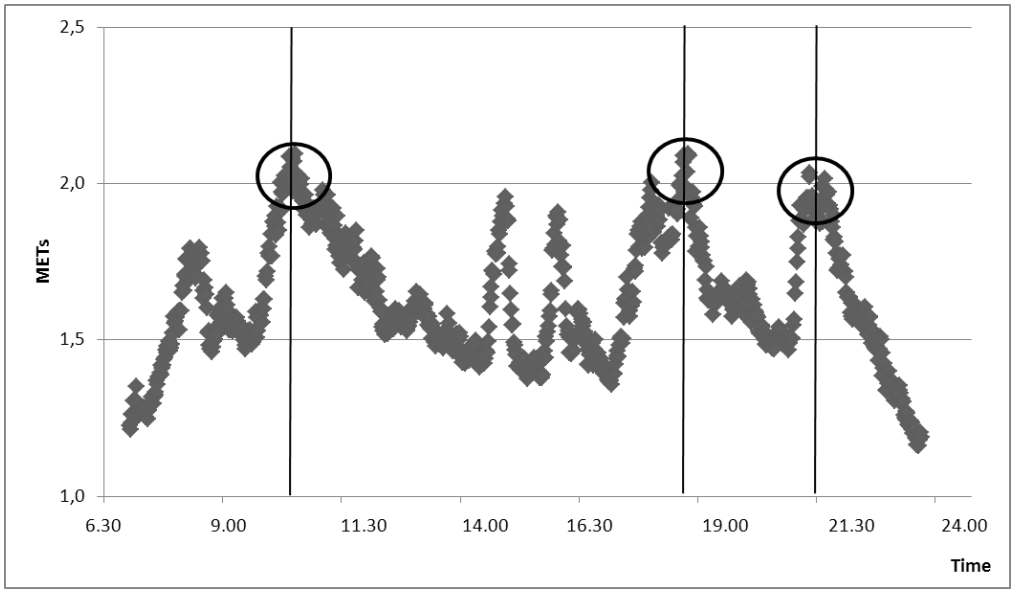
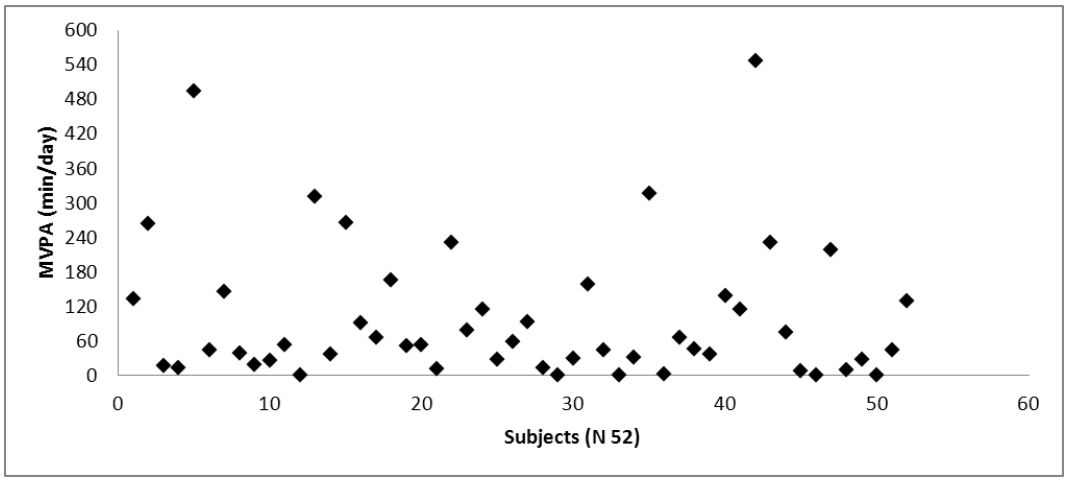


Figure 4



CONCLUSIONS

The disease presents a number of elements of contact with the moving body such as the altered perception of the body, misuse by the subjects of physical exercise as "control instrument" of body shape and weight. This is why he addressed my interest in this research.
The study of energy consumption and body composition have become ours first point of observation and analysis. In fact the diagnosis of excessive and compulsive exercise has also prompted our interest because the psychiatric diagnosis is not accompanied by an objective measurement of physical activity.
A second specific object of reflection and analysis concerning the physical health related condition of patients in hospital. We studied the correlation between current treatment and the course of treatment, until the discharge from the clinic.
In the first section of this thesis we show the state of the specific disease, comorbidities, and treatment approaches.
In the second section, we speak about the control and regulation of body weight and shape through an extensive bibliography, including three studies relating the aspects of the basal metabolism and body composition of patients.
The third section deals with the issue of physical health related, in-patient treatment, to study how they could be related with the development of specific clinical pathology and treatment.
The fifth study relates the amount of physical activity measured and estimated, using various tools, highlighting specific correlations with psychopathology.
From ours articles emerge what follow:

I. REE expenditure in underweight AN patients may be estimate with discrete accuracy, after just one day of refeeding, by the FitMate method, and by the Müller et al. equation. The FitMate method, in comparison with the Douglas bag method, is inexpensive, does not requires skilled technicians, and can be used by a wide variety of health professionals to determine the energy need of underweight AN patients.
II. SenseWear Pro2 Armband (SWA) does not appear to be an alternative to the FitMate and Müller equation methods for the assessment of REE in patients with AN. At the moment SWA should be used by clinicians treating AN patients only to assess the presence of excess exercise, behavior commonly observed in these patients (Dalle Grave et al. 2008b), but not REE.

III. The skinfold thicknesses (ST) method underestimated %BF when compared with DXA. Our findings are consistent with previous studies reporting that ST equations do not accurately predict %BF. There is no correspondence between the %BF measured with DXA and the %BF estimated with predictive equations both before and after weight gain, with the unique exception of Brozek equation in the pre- treatment AN group which showed a mild correspondence with DXA.

IV. The Eurofit Physical Fitness Test Battery (EPFTB) is a feasible field battery of tests for assessing physical fitness in AN patients; the weight restoration improves physical fitness in patients with AN; after weight restoration, AN patients, however, show lower physical fitness than age-matched non-trained controls.

V. Measured LPA seems to be a good predictor of the out-come of the treatment; AN patients spent significantly longer periods in activity classified as sedentary and light, compared to activities classified as moderate or vigorous; IPAQ significantly underestimated PA with respect to AH.

Overall it seems reasonable to draw the attention of researchers and clinicians with the following information:

a) The need to use advanced diagnostic tools for proper analysis and documentation of the clinical status of patients in relation to the measurement of basal metabolism (REE) and body composition (%FFM-%FM).

b) The opportunity to measure the physical abilities during hospitalization offers a more specific diagnosis about health status of patients.

c) Objective measurement of the amount and intensity of physical activity (LPA) during hospitalization was shown to be predictive of outcome of specific disease (EDE).

These data support, on the whole, my personal desire to grow, in the future, competence and collaboration between the Motor Sciences and the clinical treatment of Eating Disorders.

Future research in this area should, in my opinion, develop the survey further relationship between physical activity / Eating Disorders.

References

Bratland-Sanda S., Sungot-Borgen J., Ro O., Rosenvinge J.H., Hoffart A., Martinsen E.W., 2010 (a). "I'm not physically active – I only go for walks": Physical Activity in patients with Longstanding Eating Disorders. Int J Eat Disord; 43:88-92

Bratland-Sanda S, Sundgot-Borgen J, Ro O, Rosenvinge JH, Hoffart A, Martinsen EW., 2010 (b). Physical activity and exercise dependence during inpatient treatment of longstanding eating disorders: an exploratory study of excessive and non-excessive exercisers. Int J Eat Disord; 43:266-73

Adkin A.L., Frank J.S., Carpenter M.G., Peyser G.W., 2000. Postural control is scaled to level of postural threat, Gait Posture 12 : 87–93.

Ainsworth B. E., 2003. The Compendium of Physical Activities - President's Council on Physical Fitness and Sports. Series 4, No.2 June.

Allan S. Kaplan, 2002. Eating Disorders Services – Chapter 52. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

American Psychiatric Association, 2000 Eating disorders measures. American Psychiatric Association: Handbook of Psychiatric Measures. Washington, DC. 647-673.

American Psychiatric Association. Work Group on Eating Disorders. Practice guideline for the treatment of patients with eating disorders. Am J Psychiatry. 157; 1-39.

Andre D., Pelletier R., Farringdon J., Safier S., Talbott W., Stone R., Vyas N., Trimble J., Wolf D., Vishnubhatla S., Boehmke S., Stivoric J., Teller A. 2006.

Arnold E. Anderson, 2002. Eating disorders in males - Chapter 33. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

B. Bolmont, P. Gangloff, A. Vouriot, P.P. Perrin, 2002. Mood states and anxiety influence abilities to maintain balance control in healthy human subjects, Neurosci. Lett. 329 : 96–100.

Bachrach l, Guido D, Katzman D, Litt I, Marcus R. Decreased bone density in adolescent girls with anorexia nervosa. Pediatrics 1990;86:440-7.

Bailer U., de Zwaan M., Leisch F., Strned A., lennkh-Wolfsberg C., El-Giamal N., Hornik K, Kasper S., 2004. Guided self-help versus cognitive-behavioral group therapy in the treatment of bulimia nervosa. Int J Eating Disorders. 35:522-537.

Benninghoven D., Tetsch N., Jantschek G., 2008. Patients with eating disorders and

their siblings. An investigation of body image perceptions – Eur Child Adolesc Psychiatry 17:118-126 DOI 10.1007/s00787-007-0645-9.

Bewell-Weiss C.V., Carter J.C. Predictors of excessive exercise in anorexia nervosa. Comprehensive Psychiatry 51 (2010) 566-571.

Cash T.F., Grant J.R., 1995. The cognitive-behavioural treatment of body image disturbances, in: V. Van Hassel, M. Hersen (Eds.), Sourcebook of Psychological Treatment Manuals for Adults, Plenum Press, New York, pp.567–614.

Caspersen C. J., Powell K. E., Christenson G. M., 1985. Physical Activity, Exercise, and Physical Fitness: definition and distinctions for health-related research - Public Health Report, March-April, Vol.100, No.2 127.

Castro J, ToroJ, Lazaro L, Pons F, Halperin I. Bone mineral density in male adolescents with anorexia nervosa. J Am Acad Child Adolesc Psychiatry 2002;41:613-8.

CDMM, 2002. McGraw-Hill Concise Dictionary of Modern Medicine. © 2002 McGrawHillCompanies,Inc.http://medicaldictionary.thefreedictionary.com/physical+activity; download may 2009.

Chynthia M. Bulik, 2002. Anxiety, Depression and Eating Disorders - Chapter 34. . In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Claudino AM., Hay P., Lima MS., Bacaltchuk J., Schmidt U., Treasure J., 2006. Antidepressants for anorexia nervosa. Cochrane Database Syst Rev.

Corbin C. B., Pangrazi R. P., 2001. Toward a Uniform definition of Wellness: a commentary - President's Council on Physical Fitness and Sports. Series 3, No.15 December.

Cuerda C., Ruiz A., Velasco C., Breton I., Camblor M., and Garcıa-Peris P., "How accurate are predictive formulas calculating energy expenditure in adolescent patients with anorexia nervosa?" Clinical Nutrition, vol. 26, no. 1, pp. 100– 106, 2007.

Cuzzolaro M., Vetrone G., Garfinker PE., 2006. The body uneasiness test (BUT): development and validation of a new body image assessment scale – Eat Weight Disord. March; 11(1): 1-13

Cynthia M. Bulik, David B. Allison, 2002. Constitutional Thinness and Resistance to Obesity - Chapter 4. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Dalle Grave R. 2009. Features and management of compulsive exercising in Eating

Disorders. The physician and Sportmedicine – 0091-3847. October, No. 3, Volume 37.

Dalle Grave R., Calugi S., Marchesini G., 2008. Compulsive exercise to control shape or weight in eating disorders: prevalence, associated features, and treatment outcome – Comprehensive Psychiatry 49 346-352

Davis C., Kaptein S., 2006. Anorexia nervosa with excessive exercise: a phenotype with close links to obsessive-compulsive disorder – Psychiatry Research 142 209-217.

Deep A.L., Nagy L.M., Weltzin T.E., Rao R., Kaye W.H. 1995. Premorbid onset of psychopathology in long term recovered anorexia nervosa. Int J Eat Disord; 17: 291-7.

Dellava J. E., Policastro P., and Hoffman D. J., "Energy metabolism and body composition in long-term recovery from anorexia nervosa," International Journal of Eating Disor- ders, vol. 42, no. 5, pp. 415–421, 2009.

deZwaan M., Aslam Z., and Mitchell J.E., "Researchonenergy expenditure in individuals with eating disorders: a review," International Journal of Eating Disorders, vol. 32, no. 2, pp. 127–134, 2002.

Diener H.C., Dichgans J., Guschlauber B., Man H.. 1984. The significance of proprioception on postural stabilization as assessed by ischemia, Brain Res. 296 : 103–109.

Donahoo W. T., Levine J. A., and Melanson E. L., "Variability in energy expenditure and its components," Current Opinion in Clinical Nutrition & Metabolic Care, vol. 7, no. 6, pp. 599– 605, 2004

Donahoo W. T., Levine J. A., and Melanson E. L., "Variability in energy expenditure and its components," Current Opinion in Clinical Nutrition & Metabolic Care, vol. 7, no. 6, pp. 599–605, 2004

DSM-IV, American Psychiatric Association, 4th ed 1994;. Diagnostic and Statistical Manual of Mental Disorders.; Washington, DC.

Durand M. A. and King, M. 2003. Specialist treatment versus self-help for bulimia nervosa: A randomized, controlled trial in general practice. Br J Gen Prac. 53:; 371-377.

Ellison Z., Foong J., Howard R., Bullmore E., Williams S., Treasure J., 1998. Functional anatomy of caloric fear in anorexia nervosa (Letter), Lancet 352 : 1192.

Eric Ravussin, 2002. The Resting Metabolic Rate –RMR- . Chapter 10. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook

– second edition. The Guilford Press New York/ London.

F.O. Black, C.L. Shupert, F.B. Horak, L.M. Nashner. 1988. Abnormal postural control associated with peripheral vestibular disorders, in: O. Pompeiano, J.H.J. Allum (Eds.), Vestibulospinal Control of Posture and Locomotion, Elsevier, Amsterdam, pp. 263–275.

Falulkner G., Taylor A., 2009. Promoting physical activity for mental health: a complex intervention? – Mental Health and Physical Activity 2 1-2

Farrel C., Lee M. and Shafran R., 2005. Assessment of Body Size Estimation. Eur. Eat. Disorders Rew. 13, 75-88

Fontana M. P., Menegoni F., Vismara L., Galli M., Romei M., Bergamini E. , Petroni M. L., Capodaglio P. 2009. Balance in patients with anorexia and bulimia nervosa. Eur J Phys Rehabil Med; 45: 335-40.

Franchignoni F, Tesio L, Martino MT, Ricupero C., 1998. Reliability of four simple, quantitative tests of balance and mobility in healthy elderly females. Aging (Milano);10:26-31.

Galeazzi G.M., Monzani D., Gherpelli C., Covezzi R., Guaraldi G.P. 2006. Posturographic stabilisation of heralthy subjects exposed to lenght mirror image is inversely related to body.image preoccupations. Neurosc Lett; 410: 71-5.

Gerard P. Smith, James Gibbs, 2002. Peripheral Physiological Determinants of Eating and Body Weight - Chapter 2. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Gerdhem P, Ringsberg KA, Magnusson H, Obrant KJ, Akesson K. 2003. Bone mass cannot be predicted by estimations of frailty in elderly ambulatory women. Gerontology; 49:168-72.

Grinspoon S, Miller K, Coyle C, Krempin J, Amstrong C, Pitts S, et al. Severity of osteopenia in estrogen-deficient women with anorexia nervosa and hypothalamic amenorrhea. J Clin Endocrinol Metab 1999; 84:2049-55.

Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ) 2005– Short and Long Forms, revised November.

Guralnik JM, Simonsick EM, Ferrucci L, et al., 1994. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol Med Sci.;49:M85–M94.

Haas VK, Kohn MR, Clarke SD, Allen JR, Madden S, Muller MJ, et al. Body composition changes in female adolescents with anorexia nervosa. Am J Clin Nutr. 2009; 89(4): 1005-10.

Hans Wijbrand Hoek, 2002. Epidemiology and etiology of ED - Chapter 41. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Haskell W. L., Lee I.M., Pate R., Powell K. E., Blair S. N., Franklin B. A., Macera C. A., Heath G. W., Thompson P. D., Bauman A. 2007. Physical Activity and Public Health: Updated Recommendation for Adults from the American College of Sports Medicine and the American Heart Association.

Hay P, Delahunt J, Hall A, Mitchell A, Harper G, Salmond C. Predictors of ospteopenia in premenopausal women with anorexia nervosa. Calcif Tissue INt 1992; 50:498-501.

Hood J.D., Unsteadiness of cerebellar origin: an investigation into the cause, J. Laryngol. Otol. 94 (1980) 865–876.

Huang J. S., Norman G. J., Zabinski M. F., Calfas K., Patrick K., 2007. Body image and self-esteem among adolescents undergoing an intervention targeting dietary and physical activity behaviours – A.J of Adolescent Health 40 : 245-251.

Jackson, A. S., & Pollock, M. L. 1978. Generalized equations for predicting body density of men. British Journal of Nutrition, 40, 497-504.

Jackson, A. S., Pollock, M. L., & Ward, A. 1980. Generalized equations for predicting body density of women. Medicine and Science in Sports and Exercise, 12, 175-182

Jeffray R. Stowell, Dawson W. Hedges, Anna Ghambaryan, Colin Key & George J. Bloch, 2009. Validation of the symptoms of illness checklist (SIC) as a tool for health psychology research – Journal of Health Psychology

John E. Blundell, 2002. Loose coupling between appetite and physical activity - Chapter 8. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Karnath H.O., Ferber S., Dichgans J., 2000. The neural representation of postural control in humans, Proc. Natl. Acad. Sci. 97 : 13931–13936.

Katherine A. Halmi, 2002. Medical and physical aspects of eating disorders - Chapter 48. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Katherine A. Phillips, 2002. Body Image and Body Dysmorphic Disorder - Chapter 21. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a

comprehensive Handbook – second edition. The Guilford Press New York/ London.

Kathlee N. Franco, 2005. Eating disorders.Levenson J. Textbook of Psychosomatic Medicine.; Washington, DC. 311-334.

Kaye W.H., Bulik C.M., Thornton L., Barbarich N., Master K. 2004. Comorbidity of anxiety disorders with anorexia and bulimia nervosa. Am J Psychiatry; 161: 2215-21.

Kelly Bemis Vitousek, 2002. Cognitive-Behavioral Therapy for Anorexia Nervosa – Chapter 55. . In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Kohrt WM. Preliminary evidence that DEXA provides an accurate assessment of body composition. J Appl Physiol. 1998; 84(1): 372-7.

Kron L, Katz JL, Gorzynski G, Weiner H. Hyperactivity in anorexia nervosa: a fundamental clinical feature. Comprehensive Psychiatry 1978; 19:433-40

L. Arthur Campfield, 2002. Leptin and Body Weight Regulation - Chapter 6. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Lafond D., Duarte M., Prince F. 2004. Comparison of three methods to estimate the centre of mass during balance assessment. Journal of Biomechanics 37 1421-1426.

Latner J. D., Clyne C., 2008. Review article: The diagnostic validity of the criteria for Binge Eating Disorder – Int J Eat Disord; 41:1-14

McKenzie J.R., LaBan M.M., Sackeyfio A.H. 1989. The prevalence of peripheral neuropathy in patients with anorexia nervosa. Arch Phys Med Rehabil; 70: 2215-21.

McLoughlin D.M., Spargo E., Wassif W.S., Newham D.J., Peters T.J., Lantos P.L. et al. 1998. Structural and functional changes in scheletal muscle in anorexia nevorvosa. Acta Neuropathol; 95: 632-40.

Melchior J. C., Rigaud D., Rozen R., Malon D., and Apfel- baum M., "Energy expenditure economy induced by decrease in lean body mass in anorexia nervosa," European Journal of Clinical Nutrition, vol. 43, no. 11, pp. 793–799, 1989

Miller Jr A. T.. and Blyth C. S., "Lean body mass as a metabolic reference standard," Journal of Applied Physiology, vol. 5, no. 7, pp. 311–316, 1953.

Ministero della Sanità. Disturbi del comportamento alimentare. Maggio 2001. GIOFIL Banca Dati Sanitaria Farmaceutica., Roma.

Misra M., Klibanski A. Anorexia nervosa and osteoporosis. Rev Endocr Metalb Disord, 2006. 7:91-99.

Newton R., 1989, Review of tests of standing balance abilities; Brain Injury, Vol. 3, No. 4, Pages 335-343

Niva Piran, 2002. Prevention of eating disorders – Chapter 67. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Nora D. Volkow & Roy A. Wise, 2005. How can drug addiction help us understand obesity? Nature Neurosci. 8:; 555-560.

Patchell R.A., Fellows H.A., Humpries L.L. 1994. Neurologic complications of anorexia nervosa. Acta Neurol Scan; 89:111-6.

Patrick F.Sullivan, 2002. Course and outcome of anorexia nervosa - Chapter 40. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Paul E. Garfinkel, 2002. Classification and Diagnosis criteria of Anorexia Nervosa - Chapter 28. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Perna G., Alpini D., Caldirola D., Barozzi S., Cesarani A., Bellodi L., 2001. Panic disorders: the role of the balance system, J. Psych. Res. 35 : 279–286.

Pierre J.V. Beumont, 2002. Clinical presentation of Anorexia Nervosa (Pierre J.V. Beumont - Chapter 29. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

President's Council on Physical Fitness and Sports, March 2000. Definitions: Health, Fitness, and Physical Activity -. Series 3, No.9

Prior BM, Cureton KJ, Modlesky CM, Evans EM, Sloniger MA, Saunders M, et al. In vivo validation of whole body composition estimates from dual-energy X-ray absorptiometry. J Appl Physiol. 1997; 83(2): 623-30

Probst M., Pieters G., Vanderlinden J., 2008. Evaluation of Body Experience Questionnaires in Eating Disorders in Female Patients (AN/BN) and Nonclinical Partecipants – Int J Eat Disord; 41:657-665

Ravussin E. and Bogardus C., "A brief overview of human energy metabolism and its relationship to essential obesity," American Journal of Clinical Nutrition, vol. 55, supplement 1, pp. 242S–245S, 1992.

Richardson C. R., Faulkner G., McDevitt J., Skrinar G. S., Hutchinson D. S., Piette J. D., 2005. Integrating physical activity into mental health services for persons with serious

mental illness – Psychiatric services . Vol.56 No.3 March

Rondot P., Odier F., Valade D., Postural disturbances due to homonymous hemianopic visual ataxia, Brain 115 (1992) 179–188.

Ruth H. Striegel-Moore Linda Smolak, 2002. Gender, ethnicity and eating disorders - Chapter 45. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Sarah F. Leibowitz, 2002. Central Physiological Determinants of Eating Behavior and Body Weight - Chapter 1. . In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Seeger G., Braus D.F., Ruf M., Goldberger U., Schmidt M.H., 2002. Body image distortion reveals amygdala activation in patients with anorexia nervosa–a functional magnetic resonance imaging study, Neurosci. Lett. 326 : 25–28.

Susan A. Jebb, 2002. Energy Intake and Body Weight - Chapter 7 . In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Terence W. G., Shafran R, 2003. Eating disorders. Lancet. 361: 407-416.

Thaisetthawaktul P., Collazzo-Clavell M.L., Sarr M.G., Norell J.E., Dyck P.J. 2004. A controlled study of peripheral neuropathy after bariatric surgery. Neurology; 63: 1462-70.

The Development of the SenseWear® armband, a Revolutionary Energy Assessment Device to Assess Physical Activity and Lifestyle. Copyright © BodyMedia, Inc. All rights reserved.

Thiago V. Barreira, Minsoo Kang, Jennifer L. Caputo, Richard S. Farley and Matthew S. Renfrow. 2009. Validation of the Actiheart Monitor for the measurement of Physical Activity. Int J. Exerc. Sci. 2(1): 60-71.

Turner J, Bulsara M, McDermott B, Byrne G, Prince R, Forbes D. Predictors of low bone density in young adolescent females with anorexia nervosa. Int J Eat DIsord 2001;30:245-51.

Ulrike Schmidt, 2002. Risk factors for eating disorders - Chapter 44. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook – second edition. The Guilford Press New York/ London.

Vandereycken W., 2002. History of Anorexia Nervosa - Chapter 27. In Fairburn G.C. and Brownell K.D. 2002. Eating Disorders and Obesity , a comprehensive Handbook –

second edition. The Guilford Press New York/ London.

Vocks S., Wachter A., Wucherer M. and Kosfelder J., 2008. Look at yourself: can body image therapy affect the cognitive and emotional response to seeing oneself in the mirror in eating disorders? – Eur. Eat. Disorders Rev. 16, 147-154.

Wada M., Sunaga N., Nagai M. 2001. Anxiety affects the postural sway of the anterior axis in college students. Neurosci Lett; 302: 157-9.

Wada M., Sunaga N., Nagai M., 2001. Anxiety affects the postural sway of the antero-posterior axis in college students, Neurosci. Lett. 302 :157–159.

Walter F. Boron , Emile L. Boulpaep " Medical physiology" 2003. Elsevier Sauders

Weineck J, 2001. L'allenamento ottimale. Calzetti-Mariucci editori.

Wiston A.P., Jamieson C.P., Madira W., Gatward N.M., Palmer R.L. 2000. Prevalence of thiamine deficiency in anorexia nervosa. Int.J Eat Disord; 28: 451-4.

Yardley L., Luxon L., Bird J., Lear S., Britton J., 1994. Vestibular and posturographic test results in people with symptoms of panic and agoraphobia, J. Audiol. Med. 3: 48–65.

Zabjek K.F., Leroux M.A., Coullard C., Rivard C.H., Prince F. 2005. Evaluation of segmental postural characteristics during quiet standing in control and Idiopatic Scoliosis patients. Clin Biomech; 20: 483-90.

Zunker C, Mitchell JE, Wonderlich SA. Exercise interventions for women with anorexia nervosa: a review of the literature. Int J Eat Disord 2011

Web Sites

- International Standards for Anthropometric Assessment (2001) published by The International Society for the Advancement of Kinanthropometry (ISAK).
- w.topendsports.com/testing/tests/skinfolds.htm). October, 2009
- http://www.bio-lynx.com/actiheart.html. October, 2009.
- http://www.mult-sclerosis.org/RombergTest.html. October, 2009.
- http://www.topendsports.com/testing/tests/sit-and-reach.htm. October, 2009.
- http://www.topendsports.com/testing/tests/back-scratch.htm. October, 2009.
- http://en.wikipedia.org/wiki/Wii_Balance_Board. October, 2009
- http://www.hbm.com/en/menu/products/transducers-sensors/force-transducers/.October, 2009
- http://www.topendsports.com/testing/tests/walk-6min.htm. October, 2009
- http://www.ifapa.biz/?q=node/7 . January 2010