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## Physical activity, body weight, and resumption of menses in an orexia nervosa $^{\star}$

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#### ABSTRACT

Few data are available on long-term outcomes and increased physical activity at the end of inpatient treatment in patients with anorexia nervosa. Hence we assessed the association between physical activity, measured objectively by Sense Wear Armband (SWA), and body mass index (BMI; kg/m<sup>2</sup>) and menses resumption at oneyear follow-up in 32 females with anorexia nervosa who had restored normal body weight by the end of a specialist inpatient treatment. Combined logistic regression models used to evaluate the relationship between variables at discharge, BMI and resumption of menses at one-year follow-up revealed no significant association between BMI at one-year follow-up and physical activity patterns at inpatient discharge. However, total daily steps at inpatient discharge were significantly lower in patients who had resumed menstruation, as confirmed by logistic regression analysis. A small reduction in daily steps at inpatient discharge (~1000 steps) was found to increase the probability of menses resumption at one-year follow-up by ~3%. These data provide preliminary indications as to the potential usefulness of assessing daily steps to predict the resumption of menses at oneyear follow-up in patients with anorexia nervosa who restore body weight by the end of inpatient treatment, although confirmation on larger samples is urgently required.

#### 1. Introduction

A subgroup of patients with anorexia nervosa fails to maintain the normal weight achieved by the end of inpatient treatment (El Ghoch et al., 2016b; Kaplan et al., 2009), and some patients report the persistence of secondary amenorrhea, despite the maintenance of normal weight at follow-up (Brambilla et al., 2003; Jacoangeli et al., 2006). Since normal-weight maintenance is one of the most important goals of anorexia nervosa recovery (Kaplan et al., 2009), and resumption of menses is associated with complete weight normalization (Golden et al., 1997) and return of physical health (Popat et al., 2008), the identification of factors associated with these two major outcomes has important clinical implications.

In patients with anorexia nervosa, a high level of physical activity is a feature (Alberti et al., 2013; Casper et al., 1991; El Ghoch et al., 2013; Gianini et al., 2016) associated with longer inpatient treatment (Solenberger, 2001), poorer outcome (i.e. higher rates of inpatient dropout and lesser improvement in eating disorder psychopathology) (Alberti et al., 2013; Dalle Grave et al., 2008; El Ghoch et al., 2013), and more rapid relapse (Strober et al., 1997). However, although two studies have found that after inpatient weight restoration patients with anorexia nervosa display higher levels of physical activity than controls (El Ghoch et al., 2013; Gianini et al., 2016), few data are available on the role of increased physical activity at the end of the inpatient treatment and long-term outcomes (Gianini et al., 2016). Moreover, though there has been some speculation (El Ghoch et al., 2013; Jacoangeli et al., 2006), no study has thus far analysed the association between objectively measured physical activity patterns in weightrestored patients with anorexia nervosa, and body weight and menstrual resumption one-year after inpatient discharge.

The aim of this study was therefore to detect any correlation between physical activity measured objectively in a sample of shortterm weight-restored females with anorexia nervosa, and their BMI and menstrual status one year after inpatient discharge.

#### 2. Methods

#### 2.1. Participants and treatment

Participants were 32 consecutive short-term weight-restored fe-

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males with anorexia nervosa treated as inpatients in the Eating Disorder Unit of Villa Garda Hospital, a subgroup of whom (n=15) has been included in a previously published study (El Ghoch et al., 2016a). The treatment they received has been described in detail elsewhere (El Ghoch et al., 2014), and consists of 20 weeks adapted version of the enhanced cognitive behavioural therapy (CBT-E) for eating disorders (Fairburn, 2008). The programme involves two stages: 13 weeks in an inpatient clinic, followed by 7 weeks of day hospital. During the first stage, patients were given assistance with eating by a CBT-trained dietician. The inpatient unit provided patients with four meals a day (breakfast, lunch, snack and evening meal) in a communal dining room. When they reached a BMI≥18.5 kg/m<sup>2</sup> (or the corresponding BMI centile in adolescents), patients were encouraged to eat autonomously both inside and outside the unit. Weekly weigh-ins and real-time food monitoring were continued, and patients were helped to address residual dietary restraint and maintain or improve upon the weight they had restored.

Inclusion criteria for this study were the following: (i) age 13–45 years with menarche before anorexia nervosa onset; (ii) diagnosis of anorexia nervosa at inpatient admission as per the Diagnostic and Statistical Manual of Mental Disorders criteria (DSM-IV) (American Psychiatric Association, 1994) (iii) BMI≥18.5 kg/m<sup>2</sup> (or the corresponding BMI centile) for a period of at least four weeks before discharge during the day-hospital phase; (iv) absence of three or more consecutive menstrual cycles at inpatient admission and discharge. The return of menses or any menstrual activity prior to the target BMI of 18.5 kg/m<sup>2</sup> (or the corresponding BMI centile), and the use of medications known to affect body weight, body composition and/or menses resumption (e.g., oestrogen replacement therapy, olanzapine, mirtazapin, valproic acid and beta blockers) were the only two exclusion criteria. Both adolescent and adult patients were included, since they shared secondary amenorrhea as a clinical feature.

Upon completion of the programme, patients were referred to community-based outpatient care, and were regularly contacted by the research staff.

#### 2.2. Assessment

#### 2.2.1. Body weight and height

During the last week of day-hospital phase ( $T_1$ ) body height and weight were measured by a nurse affiliated with the study using a medical stadiometer and weighing scales, respectively. These measurements were taken before patients had breakfasted, ensuring that they wore only underwear and no shoes. Each patient's BMI was then calculated as per the standard formula of body weight (in kilograms) divided by height (in metres squared), and the BMI centile corresponding to an adult BMI≥18.5 kg/m<sup>2</sup> was calculated according to the procedure described by Cole et al. (Cole et al., 2007).

#### 2.2.2. PA Assessment

In the last week of the day-hospital phase (T<sub>1</sub>), patients were fitted with a Sense Wear Armband (SWA, Body Media Inc, Pittsburgh, PA) in order to assess their physical activity. The SWA is known to be a valid tool for assessing physical activity, as compared with gold-standard instruments (St-Onge et al., 2007), and is considered a useful device for monitoring physical activity in patients with anorexia nervosa (El Ghoch et al., 2013). This device relies on a two-axis accelerometer, and sensors to detect heat flux, galvanic skin response, skin temperature, and near-body ambient temperature minute-by-minute, and thereby automatically calculate the energy expended in physical activity based on body weight, and height. The patients' handedness and smoking status (smoker or non-smoker) were also taken into account, and patients were instructed to keep the SWA in place over the triceps muscle on the dominant arm (right arm in the right-handed and left arm in the left-handed) for four whole consecutive days, except for when they bathed or risked wetting it. At the end of the monitoring

period, proprietary SWA software was used to calculate the following four variables per day:

- Duration of light physical activity: expressed in seconds, this was taken as the duration of physical activity inferior to 3 Metabolic Equivalent Tasks (METs).
- Duration of moderate-vigorous physical activity: expressed in seconds, this was taken as the duration of physical activity equal to or greater than 3 METs.
- Expenditure during moderate-vigorous physical activity: expressed in kilocalories, this was taken as the physical activity expenditure equal to or greater than 3 METs.
- Daily steps: expressed in number of steps, this was the number of steps recorded during each 24-h period.

#### 2.2.3. Eating disorder psychopathology

At the end of treatment ( $T_1$ ), patients were interviewed according to the validated Italian version of the 12th edition of the EDE (Mannucci, 1996) in order to characterize their eating disorder pathology. Conducted by a trained interviewer, the EDE is an accepted method of assessing the frequency of key behavioural and attitudinal features of eating disorders in the period preceding the interview (28 days). Patient's responses are scored on a 7-point scale from 0 to 6, and higher scores reflect a greater severity or frequency of the feature in question. On the EDE, a global score is used to generate a comprehensive, detailed profile of the psychopathological features of each eating disorder patient, supported by 4 subscales used to assess dietary restraint, eating concern, weight concern, and shape concern, respectively (Cooper et al., 1989).

#### 2.2.4. General psychiatric features

The validated Italian version of the Brief Symptom Inventory (BSI) was administered at  $T_1$ , and the Global Severity Index (GSI) was used to generate a psychiatric profile of the patients based on their responses (De Leo et al., 1993; Derogatis and Melisaratos, 1983). The BSI is used to obtain scores for 53 items, grouped so as to measure 9 symptom dimensions and 3 global indices of psychological distress. Patients score their level of concern, from 0 (not at all) to 4 (extremely concerned), about the symptoms they have experienced over the course of the preceding week.

#### 2.2.5. Clinical outcomes

- *BMI*. Body weight and height were measured at one-year follow-up (T<sub>2</sub>) using the procedure described above, and the patients' BMI was calculated by the same standard formula.
- *Menstrual status*. Menstrual status at one-year follow-up (T<sub>2</sub>) was ascertained by direct interview. Patients who reported three or more menstrual periods over the preceding six months, including at least one menstrual period in the preceding three months, were assigned to the "menstruating group" (Misra et al., 2006). Patients who had experienced no spontaneous menstrual cycles at one-year follow-up comprised the "non-menstruating group".

Informed written consent for the use of their anonymous personal data was obtained from all patients, and the Institutional Review Board of Villa Garda Hospital, Verona, Italy, reviewed and approved the study design.

#### 2.3. Statistical analysis

Significant differences between menstruating and non-menstruating patients in terms of demographic and clinical parameters were tested by the Mann–Whitney test. Effect sizes were calculated in order to enable their magnitude to be assessed more readily (effect size classification: r=0.1 small, 0.3 medium, and 0.5 large) (Kazis et al.,

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