




Psychological and nutritional correlates of objectively assessed physical activity in patients with anorexia nervosa

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Abstract

Background: Physical activity (PA) plays a role in the course of anorexia nervosa (AN).

Objective: To assess the association between PA, nutritional status and psychological parameters in patients with AN.

Method: Using a wearable activity monitor, PA was assessed in 60 female AN inpatients, by step count and time spent in 4 metabolic equivalent (MET)-intensity levels: sedentary behaviour, light, moderate and vigorous PA. In addition, BMI, psychological (patient-reported outcome questionnaires) and nutritional parameters (body fat, energy and macronutrient intake) were assessed.

Results: The study population spent little time in vigorous PA. BMI on admission and discharge was higher when more time was spent in sedentary behaviour, and lower with more time spent in light PA. Relationships between PA and patient-reported outcomes were weak and limited to an association between vigorous PA and compulsiveness. Low fat mass was associated with more time spent in light PA, while subjects with higher step counts showed less intake of energy, carbohydrates and fat.

Conclusion: The relationship between inadequate food intake and increased PA in patients with AN requires further investigation.

KEYWORDS

adolescents and adults, anorexia nervosa, body fat, food intake, physical activity

1 | INTRODUCTION

High levels of physical activity (PA), such as “over-exercising,” but also steady performance of low intensity activity are common in patients with anorexia nervosa (AN) (Campbell & Peebles, 2014). Drive for exercise has been described as a common symptom in subjects with AN, widely reported by health professionals and patients

alike (Casper, 2018; Sternheim, Danner, Adan, & van Elburg, 2015). Increased PA in AN was associated with increased treatment drop out (El Ghoch et al., 2013) and lack of remission, or relapse (Alberti et al., 2013; Dalle Grave, Calugi, & Marchesini, 2008; Rigaud, Pennacchio, Bizeul, Reveillard, & Verges, 2011), thus negatively impacting on the course of AN. The reported prevalence of high PA ranges between 31 and 80% (Dalle Grave

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et al., 2008; Gummer et al., 2015), likely depending on different definitions and measurement methods, since a commonly accepted terminology is currently lacking (Noetel, Dawson, Hay, & Touyz, 2017; Rizk, Lalanne, Berthoz, Kern, & Godart, 2015). Prevailing measurement tools include self-report of PA assessed with questionnaires or interviews, yet subjective assessment is prone to be inadequate, especially in patients with eating disorders (Alberti et al., 2013; Keyes et al., 2015). Objective techniques more accurately quantify PA. In a previous study, we determined PA patterns by using the SenseWear armband and identified higher levels of light intensity PA as a distinctive PA pattern in adult AN inpatients compared to healthy controls (Lehmann et al., 2018). Levels of PA vary widely, also in inpatient settings and when restrictions of movement have been part of the treatment programme, pointing towards the variance and complexity of different PA patterns in AN patients. Therefore, it seems to be fundamental to conduct sophisticated PA assessments, for example, to not only measure steps, but also the time spent in different intensity levels. While high PA has often been described in AN patients, the underlying mechanisms for altered PA are not fully understood. Several studies suggest associations between high PA and eating disorder-specific psychological factors, such as eating disorder severity (Shroff et al., 2006; Steinglass et al., 2011), obsessive-compulsiveness and symptoms of anxiety disorders (Keyes et al., 2015; Meyer et al., 2016; Solenberger, 2001; Steinglass et al., 2011). Additionally, previous research has also focused on the neurobiological regulation of increased PA during severe energy restriction in order to facilitate the search for food. A decrease in body weight sensed by leptin or other endocrine mediators could activate a phylogenetic pathway to counteract starvation (Carrera et al., 2012; Exner et al., 2000). Regulatory factors in a homeostatic body weight regulatory system are likely bi-directional, rather than uni-directional (Muller, Geisler, Heymsfield, & Bosty-Westphal, 2018; Ross, Mandelblat-Cerf, & Versteegen, 2016). Thus, low body fat in an underweight state might not only be the consequence, but also the origin of high PA (Exner et al., 2000). Concomitantly, in experimental studies involving the activity-based anorexia model, food restriction triggered excessive wheel-running in rodents (Exner et al., 2000; Scharner et al., 2016). In another rodent study, a high fat diet induced inactivity (Bunney, Zink, Holm, Billington, & Kotz, 2017). To our knowledge, no study has investigated the relationship between nutrient intake and objectively measured PA in patients with AN. This study aimed to analyse PA patterns in AN inpatients, and to assess their clinical, psychological and nutritional correlates. We expected a lower intake of energy and fat as well as a

Highlights

- Objective data on physical activity of inpatients with Anorexia Nervosa
- Comparison of different intensity levels of PA
- Assessment of both psychological and nutritional parameters in relation to PA

lower BMI and less body fat mass at admission in patients with higher PA. Furthermore, we hypothesised an association between high PA and higher scores in patient-reported AN pathology-related outcome measures.

2 | METHODS

2.1 | Study design and ethics

This study was approved by the ethics committee of the Charité-Universitätsmedizin Berlin (Protocol Number EA2/034/14) and conducted from November 2014 to July 2018. All assessments were conducted according to the Declaration of Helsinki. Written informed consent was provided by all patients and in the case of underage patients also by their caregivers.

2.2 | Study population and clinical data

We enrolled 60 females who were consecutively recruited after admission to inpatient treatment that took place in two different settings. Adolescent patients (13–18 years) were treated at the Department of Child and Adolescent Psychiatry and adults (aged ≥ 18 years) in the Department of Psychosomatic Medicine at the Charité, Universitätsmedizin Berlin. Management of physical activity differed in the two inpatient settings in this study, yet in both groups limitations of movement were in place to support the achievement of the expected target for weight gain of 500 g/week. Restrictions were present and managed by nursing staff in the adolescent group according to clinical stability measured by BMI percentile, ranging from certain resting times per day to participation in physical therapy. Yet, there was no mandatory bed rest or individual surveillance during free movement on the ward. In the adult treatment setting external limitation of physical activity was not generally present, but rather used within the psychotherapeutic regimen. Generally, free movement in and outside the ward was possible, but

participation in physical therapy was not promoted. Regarding dietary management, patients of both groups were given meal plans in the beginning of their treatment programme to enable the targeted weight gain of 500 g/week. Within the limits of these caloric requirements, the choice of meal composition and special food items was subject to the patients influence. For adolescent patients, dietary plans started with an individual but set amount of kcal/d and was increased in accordance with weight development until the targeted weight gain was reached. In the adult setting metabolic rates and caloric demand for weight gain were estimated and an additional intake of at least 500 kcal/d was prescribed. In both treatment settings, mealtimes were supervised by clinical staff. Study inclusion criteria were female sex, a diagnosis of AN according to ICD-10 (World Health Organization, 2008) and age between 13 and 40 years. We excluded patients over the age of 40 to participate in our study as we presume a higher probability of a rather complex course of disease in AN patients of older age, including possible comorbidities with influence on their activity. Our aim was to exclude patients which would probably show a different physical activity because of reasons of chronicity at an older age. Therefore, we chose the age of 40 as our cut-off age, as used in a previous study (Gianini et al., 2016). Exclusion criteria were any somatic comorbidities with a strong influence on physical activity (e.g., multiple sclerosis or severe anaemia). Reviewing the patients' medical records, we obtained clinically assessed age of onset of AN, duration of illness, number of preceding inpatient therapies, presence of amenorrhea, psychiatric comorbidities (depression, anxiety disorder, obsessive-compulsive disorder, Borderline), and current medications (sedating or stimulating antidepressants, antipsychotics, L-Thyroxine) upon admission and discharge.

2.3 | Anthropometric data

Anthropometric baseline data were measured upon admission to inpatient treatment, after consenting to the study (17 ± 14 days after admission) and at discharge with standardised equipment. Height and weight were measured by using a stadiometer (seca 216, Hamburg, Germany for the adolescent and the adult group) and a digital scale (KERN, MCB, Berlin, Germany for adolescents and Soehnle 2,790, Backnang, Germany for adults). For estimation of the nutritional status of the patients, we used the BMI calculated as kg/m^2 . Fat mass was assessed using Bioelectrical Impedance Analysis (BiaCorpus R, Medi-Cal Healthcare GmbH, Karlsruhe, Germany for adolescents, and Nutriguard-M, Data Input,

Darmstadt, Germany for adults) and calculated with sex-specific equations, subtracting fat-free mass from body weight (Sun et al., 2003).

2.4 | Assessment of physical activity

To measure PA, a portable accelerometric SenseWear-Armband (SenseWear PRO3 armband; BodyMedia, Inc., Pittsburgh, PA) was used over three standardised consecutive days and in combination with the manufacturer's software (SenseWear Professional, Version 8.1, SMT medical technology, Würzburg, Germany), as described previously (Lehmann et al., 2018). PA assessment took place 24 ± 13 days after admission to inpatient treatment for adolescents and 4 ± 3 days for adults (with the difference being related to the requirement of both legal guardians providing written informed consent to a minor's participation in research in Germany). PA levels were defined using the standardised indicator of metabolic equivalents (METs) to classify activity intensity independent of age, sex or weight. METs are a commonly used index for PA in the literature (SMT medical technology GmbH&Co. KG, 2006–08), representing the intensity of PA ranging from 1.1 during seated activities to 3–5 for most kinds of exercise, up to a maximum of 20 METs in the area of competitive sports. We divided PA into four different intensity levels, as reported previously (El Ghoch et al., 2013; Lehmann et al., 2018; Stengel et al., 2017):

- Sedentary behaviour, ranging from 1.1 to 1.8 MET points
e.g., light, seated activities
- Light PA, ranging from 1.9 to 3 MET points
e.g., slow-paced walking, housework
- Moderate PA, ranging from 3.1 to 5.9 MET points
e.g., bike riding, playing tennis
- Vigorous PA, >6 MET points
e.g., sprinting.

2.5 | Patient-reported outcome measures

To measure psychopathology related to AN, exercise dependence and obsessive-compulsive behaviours, the following patient-reported outcome measures were used in their respective German versions: Eating Disorder Examination Questionnaire (EDE-Q) (Battle, 2013; Mond, Hay, Rodgers, Owen, & Beumont, 2004), Compulsive Exercise Test (CET) (Goodwin, Haycraft, Taranis, & Meyer, 2011; Meyer et al., 2016), Exercise Dependence Scale – Deutsch (EDS-D) (Dalle Grave et al., 2008; Muller et al., 2015), Obsessive-Compulsive Inventory - Revised

(OCI-R) (Davies, Liao, Campbell, & Tchanturia, 2009; Roberts, Lavender, & Tchanturia, 2011), and the Symptom Checklist 27 (SCL-27) (Henn, Braks, Brian, Herke, & Hardt, 2013).

2.6 | Statistical analyses

A p -value of 0.05 was set as significance threshold. In figures, p -values were indicated with + ($p \leq .1$, trend), * ($p \leq .05$), ** ($p \leq .01$), *** ($p \leq .001$). All variables were tested two-sided. Measures were tested for Gaussian distribution by Kolmogorov–Smirnov-test. Descriptive statistics are mean \pm standard deviation [minimum - maximum], median (25th/75th percentile) [minimum - maximum], or absolute frequency (relative frequency %) as appropriate for distribution. Group differences were tested by either t -test, Wilcoxon rank sum test, or Fisher's exact test according to distribution. Correlations were computed as Spearman rank correlations. P -values for all our findings have been adjusted for multiple testing using the false discovery rate approach (Benjamini & Hochberg, 1995). All other tests relate to secondary hypotheses or exploratory analyses, and significance levels are reported with their nominal values. Analysis were conducted using R version 3.5.3.

3 | RESULTS

3.1 | Study population

The demographic and clinical characteristics of the study population are presented in Table 1 and in the Table S1. Comparison of the two age groups indicated a similar distribution of AN subtypes ($p = .521$), with most subjects being classified as restrictive type (65%). With a later age of onset (18 vs. 14 years, $p = .007$), the adults had a longer illness duration (72 vs. 4 months, $p = .007$). The adolescents had a significantly longer inpatient stay (98 vs. 31 days, $p = .007$) and higher BMI at discharge ($p = .007$), with a corresponding higher BMI change ($p = .007$) in the presence of comparable baseline BMI ($p = .206$). The following psychiatric comorbidities were present: depression ($n = 17$, 28.3%), anxiety disorder ($n = 4$, 6.7%), obsessive–compulsive disorder ($n = 3$, 5%), and borderline personality disorder ($n = 4$, 6.7%). At baseline, 25% of the whole study population were on medications, that is, sedating ($n = 5$, 8%) and stimulating antidepressants ($n = 9$; 15%), antipsychotics ($n = 3$; 5%) and L-Thyroxine ($n = 3$; 5%), with significantly more adults versus adolescents being prescribed medications (47.6% vs. 12.8%, $p = .010$).

TABLE 1 Demographic and clinical characteristics of the study population

Parameter	Total group $n = 60$	Adolescents $n = 39$	Adults $n = 21$	p adults vs. adolescents
Age [years]	16 (14/21) [13–38]	15 (14/16) [13–17]	23 (20/29) [18–38]	.007
Admission BMI [kg/m ²]	15.4 \pm 2.0 [10.8–20.4]	15.7 \pm 1.7 [13.3–20.4]	14.7 \pm 2.3 [10.8–20.1]	.206
Discharge BMI [kg/m ²]	16.9 \pm 2.0 [11.7–20.5]	17.8 \pm 1.3 [13.8–20.5]	15.3 \pm 2.2 [11.7–20.1]	.007
BMI change [%]	10.5 \pm 9.6 [–3.6–38.6]	13.7 \pm 10 [–3.6–38.6]	4.5 \pm 4.8 [–2.8–13.9]	.007
Fat mass [kg]	4.3 \pm 4.2 [–4.8–15.5]	4.8 \pm 3.3 [1.0–12.6]	3.4 \pm 5.5 [–4.8–15.5]	.578
Fat mass [%]	9.0 \pm 8.8 [–15.4–25.8]	10.6 \pm 6.2 [2.5–23.7]	6.2 \pm 12.0 [–15.4–25.8]	.381
Energy intake [kcal]	1700 \pm 731 [126–3,250]	1938 \pm 659 [700–3,250]	1,248 \pm 655 [126–2,160]	.007
Carbohydrate intake [%]	52.6 \pm 6.1 [42.7–68.7]	51.3 \pm 4.1 [44.5–61.4]	55.1 \pm 8.2 [42.7–68.7]	.206
Fat intake [%]	28.2 \pm 8.3 [6.7–44.1]	31.9 \pm 3.8 [24.6–47.8]	21.1 \pm 10.0 [6.7–44.1]	.007
Protein intake [%]	15.3 \pm 4.0 [8.2–28.2]	13.5 \pm 2.4 [8.2–22.3]	18.6 \pm 4.3 [11.5–28.2]	.007

Note: Mean \pm SD or median (25th/75th percentile; range); AN, Anorexia Nervosa; BMI, Body Mass Index; Intake of energy, carbohydrates, fat and protein indicated as median per day. p -values have been adjusted for multiple testing using the false discovery rate approach.

3.2 | Quantitative analysis of objectively assessed physical activity patterns

Physical activity measures are shown in Table 2, indicated as average time in minutes per day. In the entire study population, sedentary behaviour was inversely correlated with moderate PA ($\rho = -0.648$, $p = .007$, Table S2) and with light PA ($\rho = -0.732$, $p = .007$, Table S2). Most of the PA time was spent in sedentary behaviour (74.2%) and light PA (15.5%). On average the entire study population displayed very little vigorous PA. Compared with adolescents, adult AN patients showed comparable numbers of steps per day ($p = .154$), more time spent in moderate PA (76 min. vs. 143 min., $p = .007$), and less time spent in sedentary behaviour (712 min. vs. 608 min., $p = .007$). The total step count was significantly associated with the other activity parameters, with an inverse correlation to sedentary behaviour ($\rho = -0.438$, $p = .007$) and a direct correlation to moderate PA ($\rho = 0.85$, $p = .007$) and vigorous PA ($\rho = 0.337$, $p = .007$). Furthermore, an inverse association of step count was observed with recumbent time ($\rho = -0.403$, $p = .017$). There were no differences between the adolescent and adult group regarding the measured inactivity parameters, recumbency and sleep (Table 2).

3.3 | Relationship of physical activity to body mass index

PA showed significant associations to BMI upon both admission and discharge (Figure 1). Correcting for the length of the inpatient stay, the mean BMI% change per week ($p = .659$) and weight gain in g/week ($p = 1.000$) were comparable between age groups. On a trend level, BMI on admission was higher, when more time was spent in sedentary behaviour ($\rho = 0.328$, $p = .058$; Figure 1a), while it was significantly lower when more time was spent in light PA ($\rho = -0.581$, $p = .007$, Figure 1b). At discharge, subjects with a higher BMI ($\rho = 0.472$, $p = .007$, Figure 1c) spent more time in sedentary behaviour, and less time in light PA ($\rho = -0.452$, $p = .007$; Figure 1d). BMI change during inpatient treatment was significantly higher in adolescent versus adult patients (2.0 vs. 0.6 BMI units or 13.7 vs. 4.5% of baseline BMI, $p = .007$; Table 1). However, average weight gain was 297 g/week in the entire study population, being 299 g/week in the adolescent and 293 g/week in the adult group ($p = 1.000$). The other studied activity intensities were not significantly related to percentage BMI change during inpatient treatment. Step counts were not significantly related to BMI upon admission ($\rho = 0.178$, $p = .462$; Table S2) or discharge ($\rho = -0.023$, $p = 1.000$; Table S2) or to percentage BMI change throughout inpatient treatment ($\rho = -0.200$, $p = .359$; Table S2).

TABLE 2 Physical activity indicated as median per day

Parameter	Total group n = 60	Adolescents n = 39	Adults n = 21	p adults vs. adolescents
Steps	8,768 (6,669/13,295) [1883–31,876]	8,218 (6,522/10,214) [1883–24,536]	11,695 (7,946/16,616) [3665–31,876]	.154
SB [min] $\geq 1, 1-1.8$ MET-points	652 (595/733) [373–868]	712 (630/774) [373–868]	608 (555/651) [475–805]	.007
LPA [min] $\geq 1.9-3$ MET-points	136 (89/188) [41–510]	105 (73/173) [41–510]	166 (118/189) [81–353]	.162
MPA [min] $\geq 3.1-5.9$ MET-points	90 (53/141) [2–268]	76 (43/113) [2–268]	143 (91/197) [30–250]	.007
VPA [min] ≥ 6 MET-points	1 (0/6) [0–86]	2 (0/6) [0–69]	0 (0/4) [0–86]	.359
Recumbency [min]	504 \pm 59 [407–758]	508 \pm 63 [415–758]	497 \pm 49 [407–601]	.821
Sleep [min]	436 \pm 48 [336–537]	438 \pm 47 [337–537]	431 \pm 51 [336–525]	.857

Note: Mean \pm SD or median (25th/75th percentile; range). p -values have been adjusted for multiple testing using the false discovery rate approach. Abbreviations: LPA, light physical activity; MET, metabolic equivalent; MPA, moderate physical activity; SB, sedentary behaviour; VPA, vigorous physical activity.

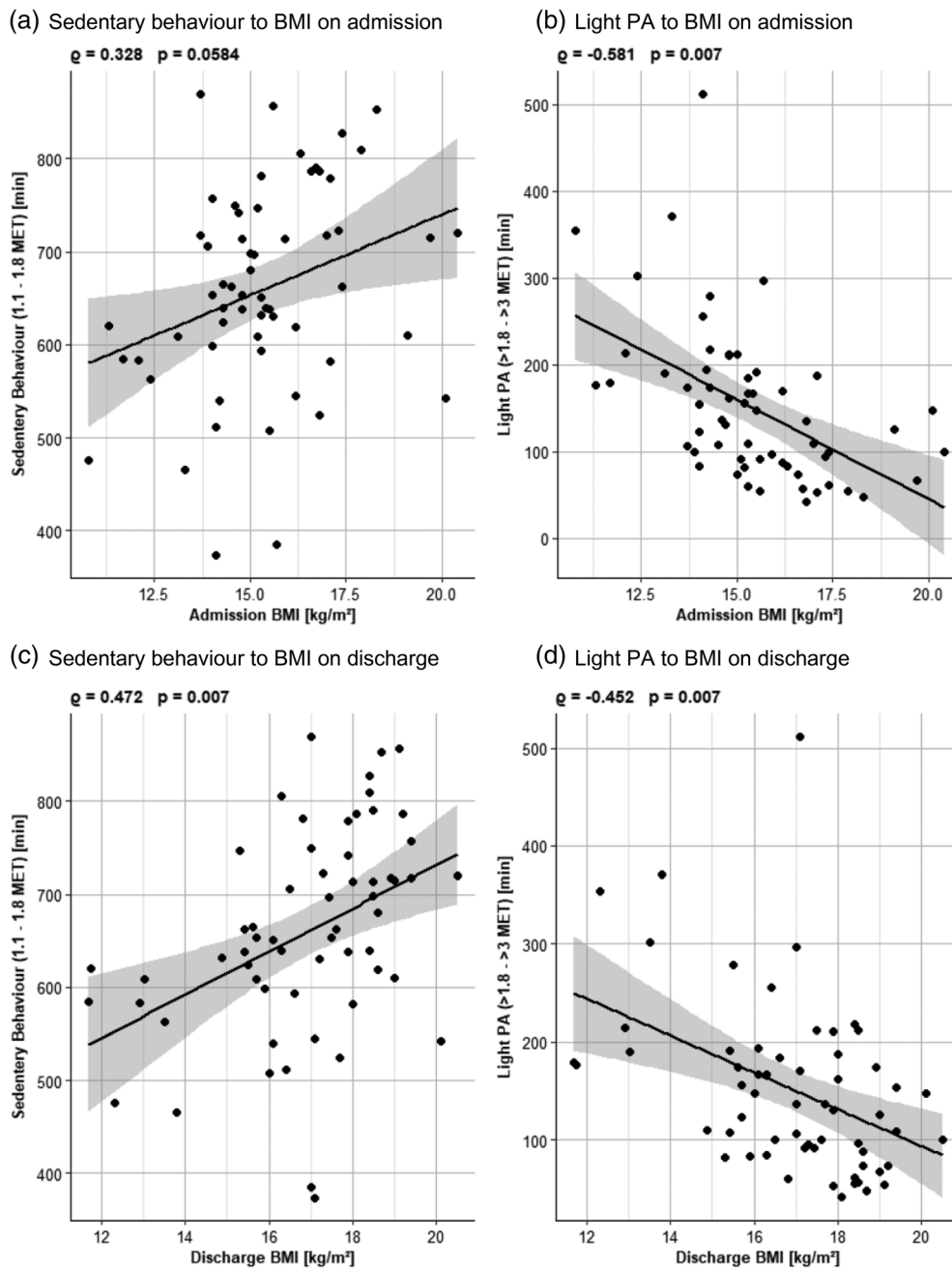


FIGURE 1 PA in relation to BMI on admission and discharge. (a) Sedentary behaviour to BMI on admission. (b) Light PA to BMI on admission. (c) Sedentary behaviour to BMI on discharge. (d) Light PA to BMI on discharge

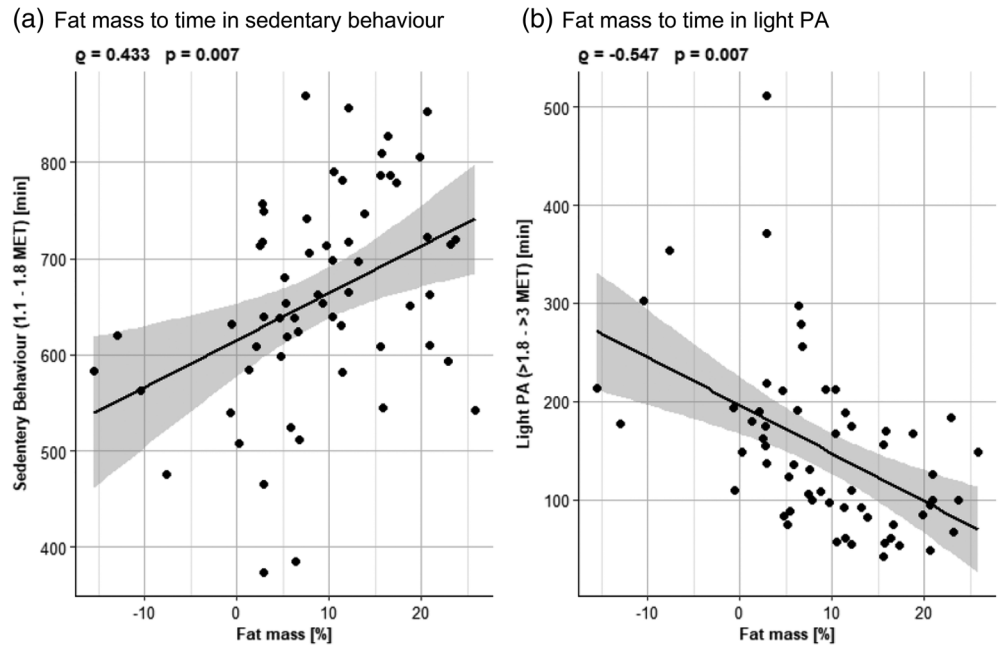
3.4 | Relationship between physical activity and fat mass

While percentage fat mass and step count were not significantly associated ($\rho = 0.011$, $p = 1.000$; Table S2), percentage fat mass was directly related to the time spent in sedentary behaviour ($\rho = 0.433$, $p = .007$; Figure 2a), and inversely associated to light PA ($\rho = -0.547$, $p = .007$; Figure 2b). A similar pattern as for the association between BMI and PA was observed, namely a shift in the direction of the associations between fat mass and PA, from a direct relationship with sedentary behaviour to an inverse relationship with light PA.

3.5 | Relationship between physical activity and psychological factors

With an average of 3.8 EDE-Q total points, the whole study population had severe AN psychopathology. None of the assessed PA parameters were significantly associated with the EDE-Q total score, nor with any of its subscales. Though a broad number of patients was diagnosed with depression (28.3%) no significant relationships with the activity parameters could be identified, neither with other present comorbidities or by scoring of the SCL-27, a screening report for possible psychiatric symptoms (Tables S2 and S3). Additionally, no associations could

FIGURE 2 Biological correlates to PA. (a) Fat mass to time in sedentary behaviour. (b) Fat mass to time in light PA



be detected between medication and PA parameters (Table S3). Although as many as 20.8% of the study population scored positively for exercise dependence on the *EDS*, no significant association between exercise dependence status and step count ($p = .335$) or other PA parameters was found. Time in vigorous PA was the only PA parameter with a significant association to patient-reported outcome measures at admission, especially items linked to compulsiveness. The more time spent in vigorous PA, the higher the patients scored on the CET subscales of avoidance and rule driven behaviour ($\rho = 0.392$, $p = .019$, Table S2) and, on a trend level, exercise rigidity ($\rho = 0.336$, $p = .067$, Table S2). Twenty-eight of 54 (51.9%) subjects who completed the CET questionnaire scored as compulsive exercisers.

3.6 | Relationship between physical activity and nutrition

The mean baseline energy intake in the entire study population was 1700 kcal/d (range: 126–3,250 kcal/d). Compared to adults, adolescents had a significantly higher energy intake (1938 kcal/d vs. 1,248 kcal/d, $p = .007$, Table 1) and fat intake (31.9% vs. 21.1%, $p = .007$, Table 1). The lower the daily energy intake ($\rho = -0.373$, $p = .025$, Figure 3a) and fat intake ($\rho = -0.38$, $p = .019$; Figure 3b) was, the higher was the step count. Conversely, the higher the consumption of fat, the more time was spent in sedentary behaviour ($\rho = 0.482$, $p = .007$, Figure 3c). Time in moderate PA was inversely associated with fat intake ($\rho = -0.408$, $p = .007$; Table S2).

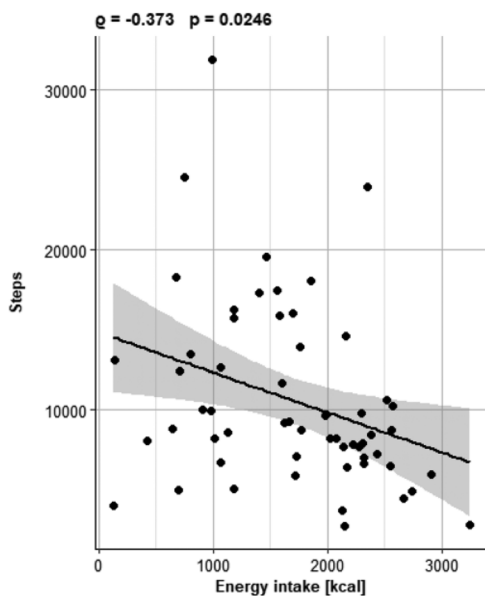
4 | DISCUSSION

The present study characterised objectively assessed PA of a mixed adolescent and adult sample of inpatients with AN at the start of inpatient treatment and sought to identify whether anthropometric, psychopathological and nutritional factors were significantly associated with PA patterns. The following main findings emerged: (a) AN inpatients presented very limited average time per day spent in vigorous PA, and adults displayed significantly more time in moderate PA than adolescents; (b) Admission and discharge BMI, as well during inpatient treatment were inversely related to light PA; (c) Associations between patient-reported outcomes at admission and objectively measured PA were weak; (d) In comparison, nutritional parameters showed considerably stronger associations than patient-reported outcomes. For example, the more body fat was present, the more time was spent in sedentary behaviour and the less time was spent in light PA; and the higher the intake of energy and dietary fat, the more time was spent in sedentary behaviour.

4.1.1. | PA patterns in patients with AN

Study participants spent, on average, 652 min (74.2%) in sedentary behaviour, 136 min (15.5%) in light PA, and only 90 min (10.2%) in moderate PA and 1 min (0.1%) in vigorous PA. In a comparable study, the ActiHeart accelerometer (Alberti et al., 2013) detected 495 (52.8%) min/d of sedentary behaviour, 343 (36.6%) of light PA, 94 min/d (10.0%) of moderate PA and 6 min/d (0.6%) of vigorous PA. While the

(a) Energy intake to step count



(b) Fat intake to step count

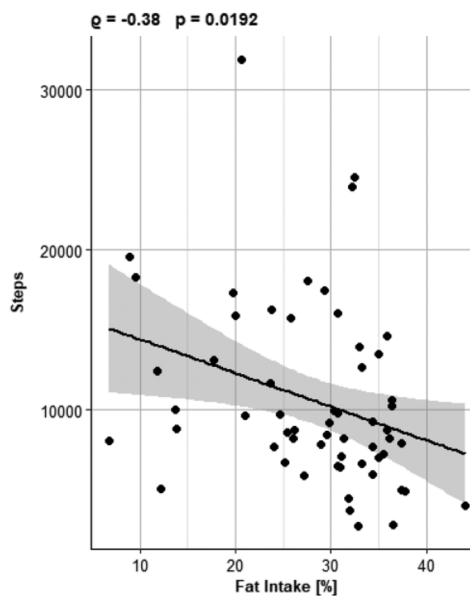
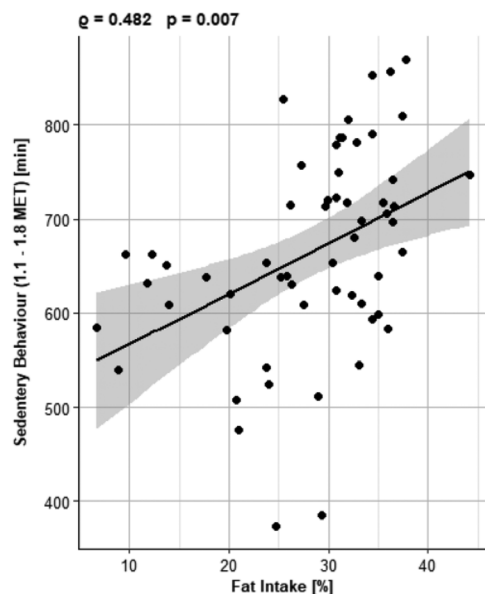


FIGURE 3 Intake of energy and fats. (a) Energy intake to step count. (b) Fat intake to step count. (c) Fat Intake to sedentary behaviour

(c) Fat intake to sedentary behaviour



percentage of vigorous PA and moderate PA were similar, patients in this study spent more time in sedentary behaviour and less time in light PA. Using the SenseWear Armband, El Ghoch et al. measured PA in 52 AN adolescent and adult inpatients (El Ghoch et al., 2013) with light PA (defined as <3 METs, comparable to sedentary behaviour plus light PA in this present study) being present for 304 min/d, moderate PA (3–6 METs) with 37 min/d (10.8%) and vigorous PA (>6 METs) with 0.9 min/d (0.3%). While the proportion of the activity levels of lower intensities varied in previous studies, vigorous PA was always only present in small amounts and might suggest the plain labelling of “excessive exercise” PA to be inadequate. PA intensity patterns differed between the present study and the

study of El Ghoch et al., but the overall step count results were comparable (8,563 in the present study and 8,768 in the study by El Ghoch). Thus, PA assessment based of different intensity levels provides more precise information than the use of simple step counts. Importantly, along these lines, evidence on increased light PA in AN, sometimes also described in literature as “fidgeting,” keeps accumulating (Belak et al., 2017; Haas et al., 2018; Lehmann et al., 2018). Comparing adolescent and adult patients in the present study, moderate PA was higher in the adult group, and adolescents spent more time in sedentary behaviour. However, the different PA patterns across the two age groups may not be explained solely by the factor of age but might also have resulted from the two different treatment settings, with

differences in the clinical management of PA in adolescents (more restrictive) as describes in the methods section. The majority of previous studies provided objectively measured data on PA in either adolescent (Carrera et al., 2012; Holtkamp et al., 2006) or adult AN samples (Dalle Grave et al., 2008; Sauchelli et al., 2015). Studies reporting on combines data from mixed adolescent and adult groups in comparable treatment setting did not find associations between PA and age (Alberti et al., 2013; El Ghoch et al., 2013). With respect to an effect of age or duration of illness on PA levels, previous studies have yielded conflicting results: while some studies found no significant association between age and PA and duration of illness (Bouten, Van Marken Lichtenbelt, & Westerterp, 1996; Dalle Grave et al., 2008; Sauchelli et al., 2015), others showed that the more physically active AN group showed an earlier onset and thus a longer duration of AN (Kostrzewa et al., 2013). In summary, other clinical features, especially illness duration and their interactions need to be further examined, as age per se does not seem to explain differences in PA.

4.1.2. | Relationship between physical activity and body mass index

Consistent with our hypothesis, high light PA was inversely associated with BMI upon admission and discharge. Reports on the association between PA and BMI in AN have varied. On the one hand, Gianini et al. (2016) found an inverse association between BMI change and light PA, assessed as “time on feet,” at discharge from inpatient treatment in 61 AN patients, and activity counts were positively related to BMI in AN patients, but not in healthy controls (Bouten et al., 1996). On the other hand, no strong direct association between BMI and steps or different PA intensities was found (El Ghoch et al., 2013), and BMI did not differ when comparing a high-level PA and a low-level PA group of 37 adolescent AN inpatients (mean BMI = 15.7 ± 1.4) (Kostrzewa et al., 2013). Interestingly, in a meta-analysis, no detrimental effect of supervised exercise training in AN could be detected (Vancampfort et al., 2014). These findings underline the importance of PA management to successfully treat AN, which might not necessarily entail simple restriction, but rather incorporation of healthful PA. Further studies applying objective PA assessments are needed to systematically evaluate the effect of an exercise intervention on PA patterns and BMI outcomes.

4.1.3. | Relationship between physical activity and psychological factors

Contrary to our hypotheses, psychological factors were only weakly associated with objectively measured PA. In the

present study, no correlations were found between PA parameters and the EDE-Q scores or the Global Severity Index of the SCL-27, which is consistent with results from two previous studies (Belak et al., 2017; El Ghoch et al., 2013). Depression or anxiety disorders did also not show a significant association with objectively measured PA (Carrera et al., 2012; Klein, Mayer, Schebendach, & Walsh, 2007). In contrast, associating activity counts per minute assessed by the ActiGraph accelerometer in 38 adult AN inpatients with patient-reported outcomes, the “excessive exercisers” subgroup defined by objective PA cut-offs presented with higher scores in the EDE-Q, the Eating Disorder Inventory and the EDS (Bratland-Sanda et al., 2010). Although this group scored higher in eating disorder related psychopathology outcomes both on admission and discharge, the decrease of scores throughout treatment did not differ between the more active and less active group. Regarding the SCL-27 and its depression subscale, an inverse correlation to time spent in moderate PA was presented in the study of Sauchelli et al. (2015). Here, higher PA showed a positive effect on general psychiatric symptoms. Although “excessive” PA has been discussed as being theoretically strongly connected to compulsiveness (Dalle Grave et al., 2008; Goodwin et al., 2011; Shroff et al., 2006), only few studies have provided objectively assessed data. In the present study, very high intensity PA presented associations with subscales of the Compulsive-Exercise Test. This finding might indicate that high level exercise is mainly present in AN patients showing compulsive traits. After adjusting for multiple testing, no significant association was found between PA and inpatient medication. Other studies have not reported any consistent findings regarding PA in patients with AN and prescription of certain medication (Gianini et al., 2016; Gummer et al., 2015).

4.1.4. | Relationship between physical activity and nutrition

In our study, higher body fat was associated with more sedentary time, and higher caloric as well as dietary fat intake were associated with a lower step count and less time in moderate PA. Despite the two treatment settings in the present study and subsequently different PA and refeeding management strategies, these associations were highly significant. While a causal relationship and directionality of the results cannot be derived from correlational analyses, it might be worthwhile to speculate that energy and fat intake and storage affect the endogenous regulation of PA in underweight subjects. Similarly, in a previous study, body fat mass was inversely related to light PA in 10 female outpatients, whereas this correlation was not found in the healthy female control group

(Hechler et al., 2008). Body fat and sedentary behaviour were positively associated in a study investigating PA in 71 adult healthy control subjects (81.7% females) with the Sensewear-Armband (Myers, Gibbons, Finlayson, & Blundell, 2017). While in normal weight subjects, lower PA would eventually lead to higher fat mass and explain the pathophysiology of obesity, the activity-based anorexia rodent model of starvation and neurobiological regulatory mechanisms of feeding and activity (Ross et al., 2016) provides another approach to understand PA in AN. The rodent model suggests that absence of food promotes PA to increase the probability to find food to prevent starvation (Exner et al., 2000). While dietary composition was not assessed in these early and ground-breaking rat experiments, Bunney et al. compared two cohorts of male mice fed with the same caloric content, but with different nutrient composition. The group receiving a high-fat diet presented more time in inactivity compared to mice fed with chow, possibly under regulatory control of the hormone orexin (Bunney et al., 2017). These results indicate that a high-fat diet induces inactivity and lowers spontaneous PA, and the findings from the present study in an AN population correspond to these results. To our knowledge, the relationship between dietary composition and objectively measured PA in acute AN has so far not been studied. In a pilot study, comparing the energy intake and objectively measured PA of 15 recovered adult AN patients with 20 healthy control subjects, no significant relationship between intake of energy or percent intake of any macronutrient and activity counts was shown (Dellava, Hamer, Kanodia, Reyes-Rodriguez, & Bulik, 2011). In the present study, however, patients were only recently admitted to hospital treatment and in an acute illness phase, a difference in design that could explain the divergent findings.

5 | CONCLUSION

Limitations of the present study include the lack of a healthy control group to enable comparison of PA with the AN population. Our present findings are not applicable to patients over the age of 40. For analysis of patient-reported outcomes our sample size was small, especially for the analysis of sub-scores. Moreover, the mixture of adolescents and adults managed in different inpatient settings might have influenced the results, and the age subgroups were relatively small. Additionally, we focused only on inpatients, baseline assessments occurred at variable times post-admission, and we did not have assessments of PA prior to admission. Thus, results cannot be extended to AN patients managed in the ambulatory setting. Conversely, strengths of this study include the

objectively assessed PA in patients with AN, both globally and at different levels of intensity, triangulation of PA, AN psychopathology, other psychopathology and dietary patterns, as well as comparative outcome analysis of the two age groups. PA regulation is a complex phenomenon and PA assessment requires sophisticated methods. High level PA was associated with compulsive features, yet the present data underline the importance of investigations to better understand biological correlates to alternations of PA in AN patients. Both body fat and nutritional intake might contribute to the endogenous regulation of PA in AN. Therefore, poor nutritional intake as well as abnormal PA patterns may present interrelated biological maintenance factors of AN, which provide treatment targets for improved outcomes. To assess this hypothesis, future studies should assess PA, dietary intake and AN psychopathology with sophisticated measures, in a sufficiently large sample and longitudinally, both during inpatient treatment as well as in post-discharge ambulatory setting.

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CONFLICTS OF INTEREST

Dr. Correll has been a consultant and/or advisor to or has received honoraria from: Alkermes, Allergan, Angelini, Boehringer-Ingelheim, Gedeon Richter, Gerson Lehrman Group, Indivior, IntraCellular Therapies, Janssen/J&J, LB Pharma, Lundbeck, MedAvante-ProPhase, Medscape, Merck, Neurocrine, Noven, Otsuka, Pfizer, Recordati, Rovi, Servier, Sumitomo Dainippon, Sunovion, Supernus, Takeda, and Teva. He has provided expert testimony for Bristol-Myers Squibb, Janssen, and Otsuka. He served on a Data Safety Monitoring Board for Boehringer-Ingelheim, Lundbeck, Rovi, Supernus, and Teva. He received royalties from UpToDate and grant support from Janssen and Takeda. He is also a shareholder of LB Pharma.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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