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**Methods establishment of physical activity assessment in
anorexia nervosa – Pilot study results and feasibility**

**(Methodenetablierung zur Aktivitätserfassung bei Anorexia
nervosa – Pilotergebnisse und Machbarkeit)**

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Abbreviations

AN	Anorexia nervosa
ANEX	Anorexia nervosa and exercise
BaDo	Basis Documentation
BMI	Body mass index
BIQ	Body Image Questionnaire
CES	Commitment to Exercise Scale
CPM	Counts per minute
DLW	Doubly labeled water
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, fourth edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, fifth edition
ECG	Electrocardiogram
ED	Eating disorder
EDE	Eating Disorder Examination
EDI	Eating Disorder Inventory
EE	Excessive exerciser
HLPA	High level physical activity
ICD	International Statistical Classification of Diseases and Related Health Problems
IG	Inpatient group
IG_FU	Inpatient group at follow-up assessment
IPAQ	International Physical Activity Questionnaire
LLPA	Low level physical activity
LPA	Light physical activity
MET	Metabolic equivalent of task
MPA	Moderate physical activity
MVPA	Moderate to vigorous physical activity
NEB	Negative evaluation of the body
NEE	Non excessive exerciser

OG	Outpatient group
PA	Physical activity
PBD	Perception of body dynamics
PHQ	Patient Health Questionnaire
PSQ	Perceived Stress Questionnaire
REI	Reasons for Exercise Inventory
TSH	Thyroid stimulating hormone
VPA	Vigorous physical activity
WHO	World Health Organization
WTV	Wear time validation

1 INTRODUCTION

“Whereas most of us assess ourselves on the basis of our perceived performance in various domains – eg, relationships, work, parenting, sporting prowess – patients with anorexia nervosa (...) judge their self-worth largely or even exclusively, in terms of their shape and weight and their ability to control them.” (Fairburn & Harrison, 2003).

There are two possibilities of losing weight: On the one hand the consumption of food can be decreased; on the other hand, the amount of activity can be increased. To be healthy, both features, eating and activity, have to be in balance. In anorexia nervosa (AN) this balance spirals out of control because of simultaneous strict food restriction and excessive exercise (Zipfel et al., 2013). Our task is to understand the complex interactions between eating behavior and activity behavior in AN. Therefore we have to apply our findings on treatment to help AN patients recover a healthy balance (Zunker, Mitchell, & Wonderlich, 2011) (Gummer et al., 2015).

1.1 Anorexia nervosa

Anorexia nervosa (AN) is a mental disease affecting mainly young women (Zipfel, Giel, Bulik, Hay, & Schmidt, 2015). Severe underweight conditions, massive fear of weight gain, and body image disturbance are the primary characteristics of AN. An additional variety of psychiatric and somatic complications make it a very dangerous disease (Lowe et al., 2001).

1.1.1 Epidemiology

The lifetime prevalence of AN is about 1% in women and less than 0.3% in men (Treasure, Claudino, & Zucker, 2010) (Smink, van Hoeken, & Hoek, 2012) (Herpertz-Dahlmann, 2009). The point prevalence is assumed to be about 0.3% to 0.5%. AN can occur at any age, but it most often begins during puberty at the age of 13 to 19 years (Favaro, Caregaro, Tenconi, Bosello, & Santonastaso, 2009). At this age the incidence is about 50 cases per 100,000 person-years

(Teufel et al., 2009). AN patients have little insight into the illness and reject seeing a doctor, which makes it difficult to register the AN population. Stability of AN incidence rates over the last decades can be assumed (Currin, Schmidt, Treasure, & Jick, 2005). The discussed increase of incidences in the last two to three decades (Smink et al., 2012) is probably due to a more careful process of making diagnoses in AN (Teufel et al., 2009). Due to significant changes in eating disorder diagnosis in the Diagnostic and Statistical Manual of Mental disorders, fifth edition (DSM-5) in comparison to the former DSM-IV criteria, an increase in AN diagnoses has been determined (Mustelin et al., 2016) (Mancuso et al., 2015).

1.1.2 Diagnosis and classification of anorexia nervosa

According to the DSM-5, three criteria must be recognized for the diagnosis of AN:

- 1.) Restriction of energy intake, leading to significantly low bodyweight (significantly low weight is defined as a weight that is less than minimally normal)
- 2.) Intense fear of gaining weight or becoming fat
- 3.) Disturbance in the way one's body weight or shape is experienced (American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, 2013).

In the DSM-IV a fourth criterion was indicated in the diagnosis of AN: amenorrhea. This criterion was dropped in the DSM-5 (Roehr, 2013). The actual ICD-10 criteria are similar to the DSM-IV, and it has also been proposed that the ICD-11 drop amenorrhea as a criterion (Zipfel et al., 2015).

Additionally, AN can be divided into two subtypes. The restrictive subtype is limited to restrictive eating without any other methods used to lose weight and without binge eating. The purging subtype describes a form of AN with symptoms of binge eating and purging behaviors such as self-induced vomiting, excessive exercise, or misuse of laxatives (Teufel et al., 2009).

1.1.3 Etiology

The etiology of AN is multifactorial. It includes heritable genetic factors, neurocognitive modifications like problems with the processing of emotions, structural changes in the brain, dysfunction in subcortical regions, malfunctioning of serotonergic and dopaminergic systems, stress and anxiety. It is also rooted in personality traits such as perfectionism or obsession as well as hormonal changes during puberty and environmental factors like “the sociocultural pressure to be thin” (Schmidt, 2003). All of these characteristics play a role in the development of AN (Zipfel et al., 2015).

1.1.4 Complications and comorbidities

AN can cause severe somatic and psychiatric complications. Every organ system can be involved (Teufel et al., 2009). The musculoskeletal system (osteoporosis and stress fractures), the cardiovascular system (bradycardia, hypovolemia, long QT time and arrhythmias), the gastrointestinal system (gastric acid irritations after periodical vomiting) and the electrolyte household (hypokalemia and hyponatremia) are often affected. Endocrinological disturbances can include, for example, amenorrhea, hypercortisolism with elevated stress levels or low-T3-syndrome (Casper, 2006). AN is also strongly associated with major depressive disorder, anxiety disorder (Holtkamp, Muller, Heussen, Remschmidt, & Herpertz-Dahlmann, 2005), obsessive-compulsive disorder (Davis, Kaptein, Kaplan, Olmsted, & Woodside, 1998) and alcohol dependency (Root et al., 2010). These psychiatric comorbidities lead to risk factors resulting in worse treatment outcomes and higher relapse rates (Steinhausen, 2002).

1.1.5 Treatment of anorexia nervosa

An important step in the process of treatment is the identification of patients with AN at all levels of care. AN patients tend to be ambivalent about treatment. Some are afraid of treatment (Mander, Teufel, Keifenheim, Zipfel, & Giel, 2013), and, therefore, a substantial number of AN patients do not access treatment voluntarily (Keski-Rahkonen et al., 2007). However, early identification of AN patients is specifically important in adolescents (Herpertz-Dahlmann, 2015) and

at early stages of the illness because then full recovery is likely possible (P. J. Hay, Touyz, & Sud, 2012). Family-based treatment is primarily evident among adolescents, while for adult patients there is a variety of different psychological treatment options including, for example, enhanced cognitive behavioral therapy, interpersonal psychotherapy, psychodynamic therapy, or focal psychodynamic therapy without any clear superiority of one method over another (Zipfel et al., 2015). Inpatient treatment is an option for severe disease episodes. During inpatient therapy the weight gain should range from 500 g to 1400 g per week (P. Hay et al., 2014). Not only psychotherapy but also group therapy or physiotherapy can be part of a multidisciplinary inpatient therapy. Moreover, electrolytes, electrocardiogram (ECG) and fluids can be properly monitored (Herpertz et al., 2011).

In the last decade new treatments, such as cognitive remediation therapy (Lindvall Dahlgren & Ro, 2014) and neurobiological methods, such as deep brain stimulation or transcranial direct current stimulation have been shown to be effective in severe AN (Lindvall Dahlgren & Ro, 2014) (Zipfel et al., 2015). Additionally, relapse prevention has started to play a larger role in AN treatment (Giel et al., 2015) as well as several different types of prevention programs (Bailey et al., 2014). Pharmacotherapy is still not a treatment option for AN (Fairburn & Harrison, 2003).

1.1.6 Prognosis

AN is known as a mental disease with high mortality rates (Sullivan, 1995) and a poor long-term prognosis. The standardized mortality rate has been stated to be 5.86 (Arcelus, Mitchell, Wales, & Nielsen, 2011). Death in AN is a result of the various complications of malnutrition; however cardiovascular complications seem to be most dangerous (Sachs, Harnke, Mehler, & Krantz, 2016). Moreover, there is a high risk of suicide in AN. Up to 20% of patients with AN attempt suicide (Franko & Keel, 2006). Only around half of the AN patients reach full recovery (Steinhausen, 2002) (Papadopoulos, Ekblom, Brandt, & Ekselius, 2009) even after treatment durations of more than five years (Zipfel et al., 2015). High levels of chronification have been observed, especially in adults. In addition, up to 30% of AN patients have a relapse after inpatient

treatment; others develop bulimia nervosa or atypical eating disorders (Teufel et al., 2009). However, the understanding of AN has improved in recent years, leading to more appropriate treatment. As a result, recovery rates have started to decline (Zipfel et al., 2015).

A high age of onset, psychiatric comorbidities, a low body mass index (BMI) after first inpatient treatment, and high levels of physical activity (PA) elevate the risk of a poor treatment outcome in AN (Rigaud, Pennacchio, Bizeul, Reveillard, & Verges, 2011) (Strober, Freeman, & Morrell, 1997).

1.2 Physical activity in Anorexia nervosa

“...high levels of physical activity (PA) occur in 31 – 80% of patients with AN (Hebebrand et al., 2003) and lead to severe complications. Despite this fact, an elevated PA level is only a second order symptom for AN according to diagnostic and statistical manual 5. Increased PA in AN has been described since 1868 (Gull, 1997), but until today there is a lack of common definition for elevated PA in AN (Bratland-Sanda, Sundgot-Borgen, et al., 2010b). A great variety of descriptions can be found in the literature addressing the same phenomenon. Besides the various descriptions of manifestations, contradictory explanations of the causes and consequences of PA in AN can be found. The heterogeneity of hypotheses and evidence makes it difficult to measure and interpret PA in AN and difficult to compare the results.” (Gummer et al., 2015).

1.2.1 Definitions and manifestations of physical activity in Anorexia nervosa

“Physical activity in AN has been described as hyperactivity, overactivity, paradoxical overactivity, motor restlessness, diffuse restlessness, compulsive exercise or excessive exercise.” (Gummer et al., 2015) Rizk et al (2015) found seven different definitions for problematic exercise in AN. “This might be partly due to the various manifestations of PA in AN (Hebebrand et al., 2003): long-distance running or cycling, excessive participation in fitness programs at the gym and any other type of high intensity PA or long-lasting sport are often practiced by affected patients. Besides sports, PA can be easily integrated into everyday activities such as uninterrupted fidgeting, standing instead of sitting

while studying or watching television, carrying heavy bags, taking the stairs instead of the elevator, walking instead of taking the bus or doing sit-ups in public restrooms. Whether the different terms describe the same phenomenon and whether psychological components such as inner restlessness are included remain unclear. We will use the term high level physical activity (HLP) for all kinds of elevated PA (...) as it can be utilized for all forms of PA including sports and everyday activities, as an understandable topic term. This term has been used similarly before (Kostrzewa et al., 2013). HLP includes PA but no psychological aspects such as inner restlessness.” (Gummer et al., 2015).

1.2.2 Etiology of high level physical activity in Anorexia nervosa

“The origin of HLP in AN has been controversially discussed. HLP can be seen as a conscious action with the aim to burn calories and control shape or weight, meaning the ‘relentless pursuit of thinness’ (Dalle Grave, Calugi, & Marchesini, 2008). But there is also evidence that HLP can be an unconscious, uncontrolled symptom: neurobiological explanations for HLP in AN have been reviewed by Matta Mello Portugal et al. (Matta Mello Portugal et al., 2013). This regulation by hormones would support the hypothesis that HLP is a phylogenetically old mechanism for survival in a famine state (Scheurink, Boersma, Nergardh, & Sodersten, 2010). Leptin, for example, is a frequently discussed hormone that triggers the adaptation of an organism to food restriction. Changes of body fat are reflected by plasma levels of leptin. Exner et al. (Exner et al., 2000) showed that administration of leptin reduced starvation-induced hyperactivity in rats. Starvation-induced hyperactivity can be seen as a model for AN: semi-starved rodents reduce food intake when given access to a running wheel (Pierce, Epling, & Boer, 1986). However, whether or not, hyperactivity through hypoleptinemia is specific to AN could not be determined. Bouten, van Marken Lichtenbelt and Westerterp (Bouten, van Marken Lichtenbelt, & Westerterp, 1996) simply state that HLP reduces the value of food reinforcement, which simplifies to an avoidance of food (Davis et al., 1997). Excessive exercising is supposed to reduce rumination and the amount of time spent thinking about food or eating. Furthermore, excessive PA can reduce appetite. Cognitive behavioural components that influence HLP have

to be addressed. According to Meyer, Taranis, Goodwin and Haycraft (Meyer, Taranis, Goodwin, & Haycraft, 2011), there are four main correlates of HLPAs in eating disorder (ED): ED psychopathology, affect regulation, perfectionism and obsessive-compulsiveness. HLPAs seem to serve as a similar function in the ED as purging or bulimia. The inability to cope with adverse mood states, anxiety or depression can be seen as explanation of the maintenance of HLPAs in AN (Holtkamp, Hebebrand, & Herpertz-Dahlmann, 2004). In patients with high levels of ED psychopathology, exercise is associated with negative effects and elevated ratings of anxiety. Exercise has also been shown to decrease depressive symptoms (Bratland-Sanda, Sundgot-Borgen, et al., 2010a). HLPAs might be similar to addictive behaviour (Scheurink et al., 2010). Positive reinforcement is reflected by an enjoyable state experienced during exercise. Our group showed that PA stimuli activate the reward system in patients with AN (K. E. Giel et al., 2013). Negative reinforcement is reflected by the avoidance of withdrawal symptoms such as guilt, anxiety or depression. The fear of negative consequences again results in compulsive operations such as HLPAs. Compulsivity in general is linked with both HLPAs and ED. Literature shows significant relationships between AN and obsessive-compulsive personality traits. Davis, Kaptein, Kaplan, Olmstedt and Woodside (Davis et al., 1998) described the three aspects of obsessive-compulsive disorder, starvation and HLPAs as a 'self-perpetuation loop'. Another explanation by Carrera et al. (Carrera et al., 2012) presents HLPAs as a strategy of thermoregulation. Patients with AN tend to often feel cold even while wearing warm clothes indoors (Hillebrand, de Rijke, Brakkee, Kas, & Adan, 2005)." (Gummer et al., 2015)

1.2.3 Consequences of high level physical activity in Anorexia nervosa

"Consequences of HLPAs in AN patients include not only increased weight loss and a more severe ED psychopathology (Cook & Hausenblas, 2008), but also lethal cardiovascular and endocrinologic symptoms and problems of the muscular system (Bratland-Sanda, Sundgot-Borgen, Rosenvinge, et al., 2010) like overuse injuries, fatigue fractures and osteoporosis (Haddad, Bann, Hill, & Jones, 1997). HLPAs are also associated with a higher rate of treatment dropouts, longer duration of illness (Kostrzewa et al., 2013) or treatment (Solenberger,

2001), a higher risk of relapse (Strober et al., 1997) and a poorer treatment outcome (Dalle Grave et al., 2008).” (Gummer et al., 2015)

1.3 Measurement of physical activity in anorexia nervosa

As the understanding of the relevance of HLEPA in AN has become clearer in the past years the quantification of PA in AN has become a new challenge, not only in research but also in clinical context.

1.3.1 Subjective measurement of physical activity in Anorexia nervosa

“In the clinical context , HLEPA has been assessed by various subjective methods like questionnaires (Higgins, Hagman, Pan, & MacLean, 2013), self-ratings (Mond & Calogero, 2009) e.g. using visual analogue scales (Holtkamp et al., 2006) or activity diaries (Pirke, Trimborn, Platte, & Fichter, 1991), semi-structured interviews (Davies, Parekh, Etelapaa, Wood, & Jaffa, 2008), observations by experts (Halmi, Goldberg, Casper, Eckert, & Davis, 1979) and analyses of medical records (Crisp, Hsu, Harding, & Hartshorn, 1980). Van Elburg et al. asked nurses to rate the levels of PA of their patients (van Elburg, Hoek, Kas, & van Engeland, 2007). These methods are prone to error and bias due to missing recall ability or compliance. Additionally, patients with AN seem to underreport PA because of their perception of what can be considered PA (Bratland-Sanda, Sundgot-Borgen, et al., 2010a).” (Gummer et al., 2015).

1.3.2 Objective measurement of physical activity in Anorexia nervosa

“Daily PA assessment requires an objective method that can be used under normal living conditions. In 1970, Blinder, Freeman and Stunkard (Blinder, Freeman, & Stunkard, 1970) first utilized objective experimental methods using a pedometer (a device that counts steps). Bouten, van Marken Lichtenbelt and Westerterp (Bouten et al., 1996) first used the doubly labelled water (DLW) method to assess PA in AN. This method is still used today (Zipfel et al., 2013). DLW measures the total daily energy expenditure over a period of up to 3 weeks. It determines the average daily metabolic rate with the help of stable isotopes and combines it with the resting metabolic rate (Coward, 1988). The advantage of this method is accuracy concerning measurements and the experimenter is not dependent on the compliance of the participant. However,

DLW is a complex, expensive technique, and the outcome does not provide activity patterns in time. This is why the current use of accelerometry seems to be the standard objective activity measurement method in AN.” (Gummer et al., 2015).

1.3.2.1 Technology of accelerometry

“An accelerometer processes acceleration signals of the person wearing the accelerometer device and calculates the sum of the rectified and integrated acceleration curves from all three directions measured (longitudinal, transversal, sagittal). The final output is counts per minute.” (Gummer et al., 2015) The value of counts depends on the frequency and the intensity of the acceleration. The transformation of the raw acceleration into counts can be explained by a band-pass filter that exhibits low gain at very low frequency and at very high (un-human) frequency (Cain, Conway, Adams, Husak, & Sallis, 2013) “The result can be transformed into other units such as steps per hour, kilocalories per hour or metabolic equivalents. Besides energy expenditure, it also measures duration and intensity of PA and provides activity patterns through time. Plasqui, Bonomi and Westerterp (Plasqui, Bonomi, & Westerterp, 2013) reviewed the usage of accelerometry and drew the conclusion that accelerometers are best placed on the hip or lower back, although they can also be worn on the wrist, ankle or upper arm. Moreover, 3-5 consecutive days of monitoring seem to reliably estimate habitual PA. Trost, Mclver, & Pate (Trost, Mclver, & Pate, 2005) also found that one device per person is enough...” (Gummer et al., 2015) However, using more than one device in one person, the differentiation between for example sitting and standing improves, but simultaneously the wearing comfort and the practicability decreases (Plasqui et al., 2013). The epoch length should be one minute. “The epoch length is defined as the sampling interval. Some accelerometers have additional applications such as assessment of heart frequency, light intensity or skin temperature.” (Gummer et al., 2015) It could not be shown that those applications significantly improve the PA assessment (Plasqui et al., 2013).

1.3.2.2 Development of accelerometry assessment in Anorexia nervosa

“Comparison between the oldest and the newest device technology shows great developments in accelerometers, particularly in memory capacity, data storage, data evaluating software and wearing comfort. The oldest devices have incomparable technology: Falk, Halmi and Tryon (Falk, Halmi, & Tryon, 1985) describe the actometer (Timex 108 motion recorder, Timex Group USA Inc., Middlebury, CT, USA) used in their study as a ‘man’s mechanical self-winding wristwatch that has been modified such that the self-winding rotor directly drives the minute hand, which drives the hour hand and the calendar date in a normal fashion rather than winding the mainspring, which has been removed’. This procedure could only be utilized for four measurement periods spread throughout the day (waking up, lunch time, 6pm and bedtime). Thus, this accelerometer (...) does not assess activity continuously.

Kaye et al. (Kaye et al., 1986) used a so-called acceleration-sensitive device that measures continuously. However, movement has to be cumulated because of the small memory storage; thus, one count always represents 16 movements. The advanced for its time Tracmor device used by Bouten, van Marken Lichtenbelt and Westerterp (Bouten et al., 1996) still weighs 250g, while the newest devices like Actiwatch weigh only 18g. The newer Tracmor device used by Hechler et al. (Hechler et al., 2008) weighs 22g. Tracmor has to be attached to the lower back and is composed of an accelerometer unit and a portable data unit, which are connected by a flexible cable. More recent devices are always composed of only one unit. The device used most frequently in trials that have the aim to assess PA in AN is called ‘Actiwatch’ (Cambridge Neurotechnology, UK, 18g), validated by Puyau, Adolph, Vohra and Butte (Puyau, Adolph, Vohra, & Butte, 2002). An Actiwatch has to be placed at the right ankle and cannot be worn while swimming or showering. ‘ActiGraph’ (MTI model, USA, 19 g), validated by Freedson, Melanson and Sirard (P. S. Freedson, Melanson, & Sirard, 1998), has also been utilized in several studies. It works similar to ‘Actiwatch’ but is worn on the hip. Another device often used is the ‘SenseWear armband’ (Pro 3 armband, Pittsburg, USA, 45 g), which additionally measures heat flux, galvanic skin response and skin temperature so

that the wear-time can be validated. This is also possible with ‘Actiheart’, which combines a heart rate monitor with triaxial accelerometry. Actiheart has to be placed on the left side of the chest with two electrocardiogram electrodes and only weighs 8 g.” (Gummer et al., 2015)

1.4 Research questions

1.4.1 Methods establishment

What is already known about accelerometry assessment in AN?

In order to establish accelerometry as a method to assess PA in AN, we reviewed previous, objectively measured results. This provides an overview of different devices, utilization, combination of methods, validation, and limitations.

1.4.2 Anorexia nervosa and exercise (ANEX) pilot study

With the knowledge of the reviewed studies we construed the ANEX pilot study. The following questions defined this study:

1.4.2.1 Comparison of inpatients and outpatients

What are the differences concerning physical activity, eating disorder pathology, and psychopathology?

In the ANEX pilot study we measured PA with accelerometry, both in inpatients and in outpatients with AN. Self-perceived PA was measured with questionnaires to compare the results of subjective and objective PA assessment in the groups. Additionally, we analyzed the attitudes toward activity through eating disorder questionnaires and psychometric questionnaires. We tried to determine the effect of inpatient treatment on PA behavior and how PA behavior is interrelated with eating disorder pathology and psychopathology.

1.4.2.2 Comparison of inpatients and inpatients at follow-up

How does physical activity behavior change after treatment?

We performed an accelerometry assessment one month after treatment to compare the objectively-measured levels of activity during inpatient treatment and at follow-up. Thus, we tried to determine how PA developed after

hospitalization. This was another method used to identify if inpatient treatment had an effect on PA behavior.

1.4.3 Feasibility

Is accelerometry an appropriate method to assess physical activity in AN?

The usage of accelerometry was discussed critically as well as an overview of what should be considered and what can be improved in accelerometry as a method of PA assessment in AN. Additionally, the differences between study refusals and the participants of the ANEX pilot study, which were based on clinical characteristics, psychometric questionnaires, and qualitative analysis were shown. Thereby we tried to obtain an understanding of why study refusals occur so frequently and determine why accelerometry assessment or PA assessment, in general, is a problem for patients with AN.

2 METHODS

2.1 Study design

In the ANEX (anorexia nervosa and exercise) pilot study the levels of PA of patients with AN relating to inpatient treatment and psychopathology were assessed. The measurement of PA was performed objectively with accelerometry and subjectively with questionnaires. Also the psychopathology was assessed with questionnaires. Additionally, we evaluated analyses of electrocardiogram (ECG) and physiologic parameters. The ANEX pilot study was construed to evaluate the feasibility of a larger ANEX study.

2.2 Ethical approval

The ANEX study was submitted by the ethical review committee of the Faculty of Medicine of the Eberhard – Karls – University Tuebingen in August 2013.

2.3 Inclusion and exclusion criteria

2.3.1 Inclusion criteria

- female gender
- inpatients or outpatients at University Hospital Tuebingen, Department for Psychosomatic Medicine and Psychotherapy
- age > 18 years
- diagnosis of Anorexia nervosa (ICD F50.0) or subsyndromal AN with BMI <18.5 kg/m²
- informed written consent

2.3.2 Exclusion criteria

- significant substance abuse
- acute psychotic disorder
- bipolar disorders
- acute suicidal tendency

2.4 Study procedure

Patients were recruited from the Department of Psychosomatic Medicine and Psychotherapy at the University of Tuebingen. They were introduced to the ANEX study during the first appointment with the study staff. The meeting also aimed to answer questions and to discuss possible fears concerning the study. After this first appointment, AN patients were given the option of directly starting the first measurement or taking some time to think about their participation based on the written information that they received. All patients who finally decided to participate had to first complete a written consent form. Next they had to fill out the questionnaires, which included basis documentation and information regarding their PA, psychometric data, and eating disorders. Afterward they began the accelerometry measurement. The patients were instructed to wear the ActiGraph throughout four whole days except for when showering, swimming and sleeping. The outpatient group fulfilled one period of measurement, while the inpatient group had to fulfill two periods of measurement. This included four days of measurement during inpatient treatment about one month after admission and one follow-up measurement approximately one month after discharge (Figure 1).

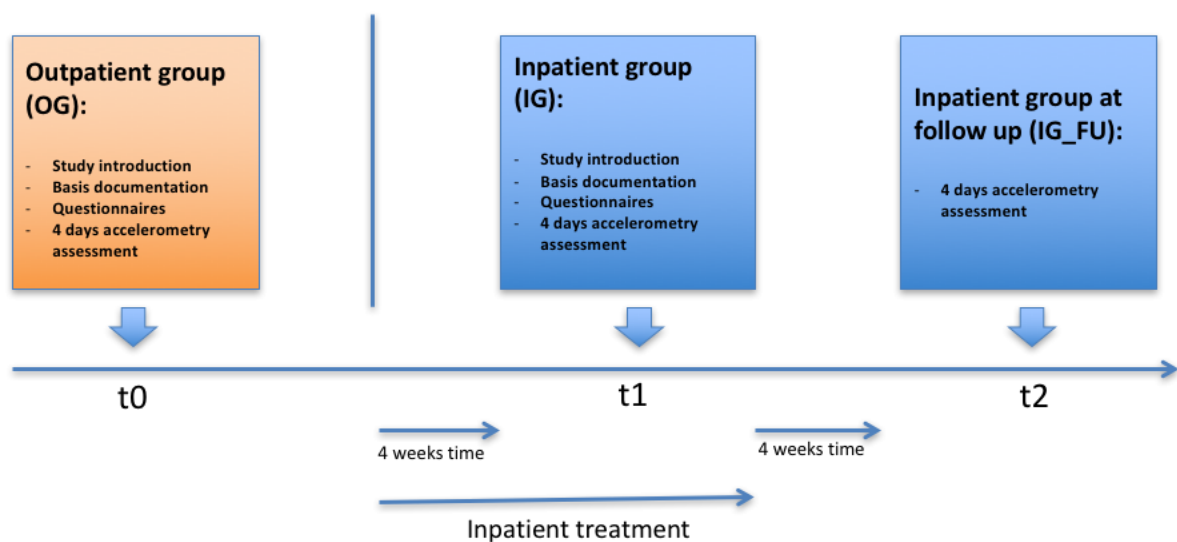


Figure 1: Study procedure

2.5 Physical activity assessment

PA was measured objectively with accelerometry and subjectively with questionnaires.

2.5.1 Objective PA assessment

2.5.1.1 Physical activity assessment with the GT3X+ ActiGraph

In the ANEX study we utilized ActiGraph devices (ActiGraph model GT3X+, Pensacola, USA) (Aadland & Ylvisaker, 2015). The device is attached to a belt and had to be worn around the waist for four consecutive days per measurement, except for when showering and during the night while sleeping. The ActiGraph is not only able to indicate whether a subject is standing, sitting or lying, but it also indicates when a device is not worn at all so that for example sedentary behavior and non-wear time can be distinguished. This is possible because in the absence of activity, when no counts are assessed, the total acceleration is measured in the down vector: When the device is worn around the waist and the subject is lying for example, the y-axis of the device reflects the down vector. If the ActiGraph is lying on a table, for example, the z-axis reflects the down vector (P.S. Freedson et al., 1998).

The ActiGraph accelerometer does not have any additional applications, such as heart rate or temperature sensors. To improve the compliance and the wear-time during the measurement periods, every participant had to make an activity diary with a focus on non-wear periods, meaning that the patient had to note when she showered, for example. Every participant received an information sheet with an explanation of how accelerometry works. Moreover, the study instructor always introduced the study to the patient and handed the device over personally. The patient could ask questions during this meeting and could contact the instructor whenever a problem arose during the measurement period. Additionally, the instructor contacted every patient during a measurement period on the second day via text message or email to ask if everything was going well with the ActiGraph. After the measurement the patient could get the results of the measurement for her own information.

2.5.1.2 Data analysis of the ActiGraph GTX3+

The analysis of the data of the ActiGraph devices was performed with the ActiLife software, which was provided by the ActiGraph company. After a measurement period the data had to be downloaded on a computer with ActiLife software. Activity data from day one to four was averaged to determine the mean daily physical activity for each patient.

Before data could be analyzed and compared, it was important to flag the information that was collected when the device was not worn. The wear time validation (WTV) function of ActiLife provided a summary of non-wear and wear times. Non-wear times were excluded from further analysis. For our WTV we used defaults developed by Troiano (2007). Troiano (2007) defined that a non-wear period has a minimum length of consecutive zeros of 60 minutes with a spike tolerance of 2 minutes, meaning that a detection of more than zero counts over a period of more than two minutes would end a non-wear-time period. The spike level to stop was defined as 100 counts per minute, meaning that a non-wear period would end if a count level exceeding this value was encountered. Additionally, wear-time periods shorter than six minutes were ignored, so that the minimum length of an acceptable wear period had to be greater than six minutes. After WTV all data was calculated relating to the total wear time during the four measurement days of each participant so results could be more easily compared.

Thereafter the data was summarized and could be transformed from counts per minute (CPM) into the following outcomes: percentage in light activity, percentage in moderate activity, percentage in vigorous activity and percentage in moderate to vigorous physical activity (MVPA), kcal/day, metabolic equivalents (METs) and steps/day. The cut point values (in counts per minute) for the activity intensities were 0 to 2689 for light, 2690 to 6166 for moderate, 6167 to 9642 for vigorous and >9643 for very vigorous activity. This means that the MVPA minimum count was 2690. These values have been validated by Freedson et al. (1998). It was possible to calculate the energy expenditure (kcal/min) value of above 1951 counts using the following formula (P. S. Freedson et al., 1998):

$$\text{If } CPM > 1951 \text{ then} \\ \text{kcal/min} = (0.00094 \times CPM + (0.1346 \times BM - 7.37418))$$

CPM = Counts per Minute

BM = Body Mass in kg

METs (metabolic equivalent of task) are multiples of the resting metabolic rate. One MET represents the amount of energy a person spends at rest, meaning also the amount of oxygen needed at rest or the power:

$$1 \text{ MET} = \frac{1 \text{ kcal}}{\text{kg} \cdot \text{h}} = \frac{3,5 \text{ ml } O_2}{\text{kg} \cdot \text{min}} = 58,2 \frac{\text{W}}{\text{m}^2}$$

The MET rate gives us multiples of the basal metabolic rate. 1.5 to 3 METs are defined as low PA; 3 to 6 METs are defined as moderate PA; and more than 6 METs are defined as exhausting PA (Ainsworth et al., 2011). A MET rate of 1.8 METs over a whole day represents a hard-working person. With the following formula the MET rate can be calculated with the number of average counts per minute (P. S. Freedson et al., 1998):

$$\text{MET Rate} = 1.439008 + (0.000795 * CPM)$$

CPM = Counts per Minute

2.5.2 Subjective PA assessment

In the ANEX study four different questionnaires were used to assess PA. Each questionnaire addressed different aspects of PA in AN, which explains the usage of more than one questionnaire.

2.5.2.1 IPAQ (International Physical Activity Questionnaire)

We used the German short version of the IPAQ, which was validated by Craig et al. (2003). This questionnaire assesses the time spent in specific types of activity (sitting, walking, moderate, and vigorous activity) during the previous seven days. It is also possible to calculate a total score of physical activity

during one week and to define a category of the activity level into low, moderate, or high exercise. Additionally, it is possible to calculate kilocalories spent per week. The results of the continuous values are presented in MET-minutes per week. One MET is the metabolic equivalent of task and is defined as resting metabolic rate ($4,184 \text{ kJ} \times \text{kg}^{-1} \times \text{h}^{-1}$). The specific types of activity are represented by multiples of the resting metabolic rate (vigorous = 8 METs, moderate = 4 METs, walking = 3.3 METs). For the total score, the particular MET score has to be multiplied by the minutes performed in the certain type of activity and the number of days performed during the week. The results are standardized for a person who weighs 60 kg. For transformation of METs into kilocalories the weight of the test person has to be taken into account.

2.5.2.2 CES (*Commitment to Exercise Scale*)

The CES assesses the individual's importance to exercising and the extent of exercising, reflecting both attitudinal and behavioral aspects. The German version of the test consists of eight items with continuous visual analogue scales (15.5cm) with bipolar adjectives at each end (for example: "never" and "always"). The score corresponds to the distance from the beginning of the scale to the cross of the test person on the scale. The total value is calculated by the mean of all eight items proportionally on a scale with ten points. The questions deal with the well-being influenced by exercising, the adherence to exercise despite adverse conditions, such as illness and the interfering of exercise with one's social life. Item 7 has a special value especially for patients with AN and was interpreted as a single score in this study. (Do you feel "guilty" that you have somehow "let yourself down" when you miss your exercise session?) (Mond & Calogero, 2009). The original English version of the CES was validated by Davis and Fox (1993).

2.5.2.3 REI (*Reasons for Exercise Inventory*)

We used the German version of the REI which is similar to the English original version: a 24-item scale that measures the motivation for exercise on a 7-point scale (from "not at all important" to "extremely important"). The aim is to find the specific reasons that people actually have for exercising. Reasons for exercise,

such as “to lose weight” or “to improve my mood” can be found as items, for example. The REI subscales, which result from the single items are weight control, fitness, health, body tone, physical attractiveness, mood improvement, and enjoyment (Cash, Novy, & Grant, 1994).

2.5.2.4 Questionnaire for registration of sports activities

The questionnaire for registration of sports activities assesses the kind of sports that the participant is involved in and the intensity of this engagement. The first question is: “Do you presently participate in sports?” This can be answered by “yes” or “no”. When the answer is “yes” the sports activity must be defined. Then the number of units per month in this particular sports activity has to be given. Moreover, the duration of each unit has to be defined. Choices include “less than 15 minutes,” “15 – 30 minutes,” “30 – 45 minutes,” “45 – 60 minutes,” and “more than 60 minutes”. Up to six different sports activities can be named. The result of this questionnaire shows the type of sports that are important in the sample. The questionnaire was construed by the Psychosomatic Department of the University of Tuebingen.

2.6 Psychometric instruments

2.6.1 Clinical diagnostics

2.6.1.1 BaDo (basis documentation)

To assess general biopsychosocial stress, social data, and medical history we utilized the basis documentation of the Department of Psychosomatic Medicine and Psychotherapy at the University of Tuebingen, which was introduced to the psychosomatic care units by the German Ministry of Health in 1994 with the aim to improving quality control. Basis documentation is used for every patient in this department (Heuft, Senf, Wagener, Pintelon, & Lorenzen, 1996).

2.6.1.2 PHQ (Patient Health Questionnaire)

The PHQ assesses the most common mental disorders on the basis of the DSM-IV. It was developed by Spitzer, Kroenke and Williams (1999). It determines major depressive syndrome, panic syndrome, alcohol syndrome, and eating disorders (binge eating and bulimia nervosa). Additionally, scales for

the “intensity of depression” are calculated from 9 items as well as a scale for “somatic symptoms” using 15 items and a scale for “stress” containing 10 items. This reflects the severity of the mental disorder. The PHQ also assesses the GAD-7-scale (generalized anxiety disorder), which is calculated based on seven questions. The German version of the PHQ (Gesundheitsfragebogen für Patienten, PHQ-D) was utilized in the ANEX study and was validated by Löwe et al. (2010).

2.6.1.3 PSQ (*Perceived Stress Questionnaire*)

The PSQ is used to assess a person’s level of stress. It consists of four scales (worries, tension, joy, and demand) with five items each. For each item there are four possible answers: “almost never,” “sometimes,” “often,” and “usually”. The patient determines how often activities occurred during the previous four weeks. One item says, for example: “You have too many things to do”. The PSQ was developed by Levenstein et al. (1993). The shorter German version of the PSQ, which was utilized in the ANEX study, was validated by Fliege et al. (2005). The original questionnaire consists of 30 rather than 20 items. The first three scores (worries, tension and joy) represent internal stress reaction, whereas the fourth one (demand) stands for the perception of external stressors. The polarity of the joy score has to be reversed so that a high mean value of the PSQ scales stands for a high level of stress.

2.6.2 Eating disorder diagnostic

2.6.2.1 EDE (*Eating Disorder Examination*) questionnaire

The EDE questionnaire is used to assess the specific pathology of eating disorders. The questionnaire consists of four subscales: restraint, eating concerns, shape concerns and weight concerns. Each scale has five to eight items, from which a mean value is calculated. The restraint scale and the eating scale show dysfunctions in eating behavior like feelings of guilt, while the shape scale and the weight scale indicate concerns about the body. Additionally, restrictive eating behaviors, such as “misuse of laxatives,” “misuse of diuretics,” “self-induced vomiting,” or “excessive exercising” can be identified by the EDE-

Q. The German version of the EDE that was utilized in the ANEX study was validated by Hilbert, de Zwaan and Braehler (2012).

2.6.2.2 EDI (*Eating Disorder Inventory*)

The EDI allows identification of the presence of an eating disorder. It can be used to distinguish between anorexia nervosa, both restrictive and purging types, bulimia nervosa, eating disorders not otherwise specified, and binge eating disorder. The questionnaire consists of 91 items. Each item is a statement that can be answered by “always,” “usually,” “often,” “sometimes,” “rarely,” or “never”. The possible answers are valued from 1 to 6. Eleven subscales are included: drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, maturity fears, asceticism, impulse regulation, and social unsureness. For the ANEX study, we particularly focused on “drive for thinness,” “perfectionism,” and “body dissatisfaction” because these aspects are most common in AN. We used the German version of the EDI, which was validated by Thiel et al. (1997). Zipfel et al. proposed the EDI item “What percentage of your exercise is aimed at controlling your weight” as a simple tool to divide study participants with AN into high-level exercisers and low-level exercisers (Zipfel et al., 2013). The separation was made using a cut-offset at less than 50%.

2.6.2.3 BIQ-20 (*Body Image Questionnaire*)

The BIQ-20 questionnaire is a test that consists of 20 items that aim at measuring the subjective body image and quantifying a body image disturbance. For each item there are five possible answers: “does not apply,” “hardly applies,” “partly applies,” “largely applies” and, “absolutely applies”. The answers were rated numerically from one (“does not apply”) to five (“absolutely applies”). The questionnaire covers two dimensions, each with ten items: the “negative evaluation of the body” (NEB) and the “perception of body dynamics” (PBD). The “negative evaluation of the body” represents the appraisal of one’s own body, meaning, on the one hand, the appearance, and on the other hand, the feeling of well-being with one’s own body. In this rating patients with body image disturbances like patients suffering from AN or transsexualism attain high

counts. The value for the first dimension can be seen as pathological in patients with AN when it exceeds 37. The second dimension, “perception of body dynamics” describes how much power, fitness, or health are felt by the patient, representing the movement and energetic aspects of the body. Low counts in this dimension represent depressive aspects of the body and seem to be more unspecific. This second dimension can be seen as pathological when the score goes under 19. The BIQ-20 was validated by Clement and Lowe (1996).

2.7 Physiologic parameters

2.7.1 Body – Mass – Index (BMI)

The BMI represents how height and weight of one person interact. The patients in the ANEX pilot study were weighed at the beginning of treatment. Inpatients with AN are weighed more often during the treatment, of course. The following formula represents the BMI:

$$BMI = \frac{\text{body weight (kg)}}{\text{body height (m)}^2}$$

2.7.2 Laboratory

All inpatients at the Department of Psychosomatic Medicine and Psychotherapy at the University of Tuebingen had blood taken as a routine at the beginning of treatment and the results were indicated as part of this study. The TSH (thyroid stimulating hormone), the number of leukocytes, the red blood count, and the hemoglobin were especially considered in the ANEX study.

2.7.3 ECG

As cardiovascular complications seem to be common in AN, all inpatients were routinely given an ECG at the beginning of treatment. For the ANEX study we utilized the QT interval in percent and the heart rate.

2.8 Statistics

The software SPSS was used to analyze all data. A descriptive analysis of the samples was done, comparing the outpatient control group and inpatient group

and in the end the inpatient group with its follow-ups and the outpatient group with the inpatient group at follow-up (IG_FU) (Figure 2).

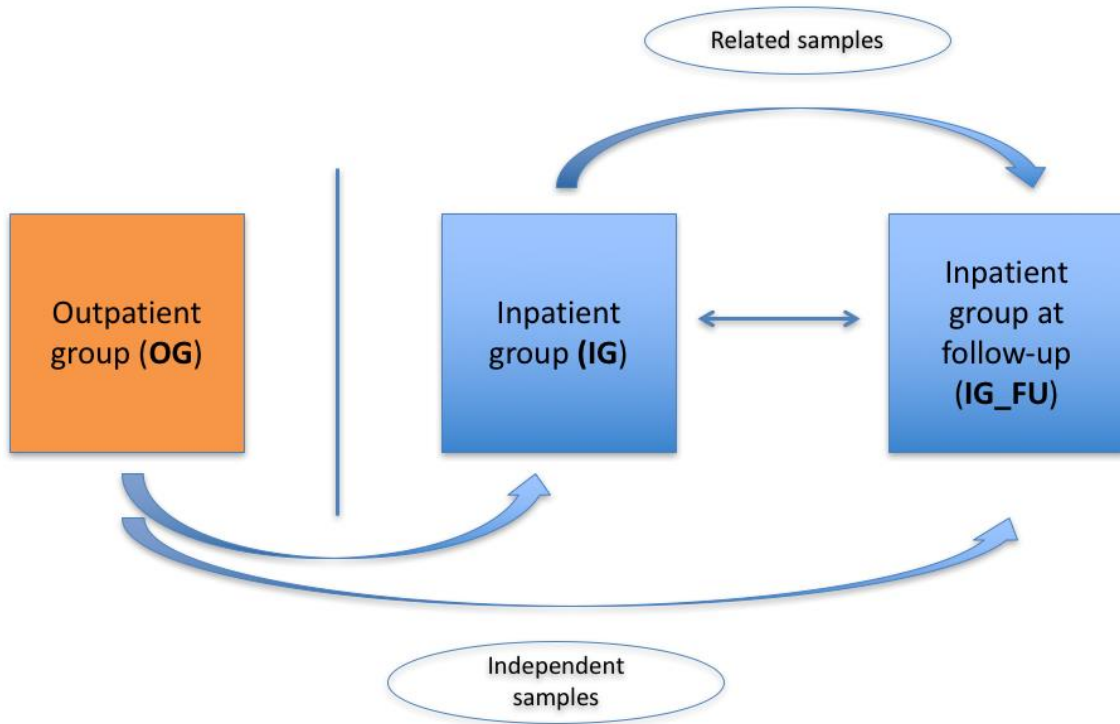


Figure 2: Relations of the different samples as basis of statistical analysis

Due to the explorative character of the ANEX study the level of significance was set at 0.05. Normal distribution of the study populations was assessed with the Kolmogorov-Smirnov test. Subsequently, we calculated with the help of the Wilcoxon and Mann-Whitney tests. We calculated effect sizes (Cohen's d) to evaluate practical relevance with the following formula:

$$d = \frac{(X_{EG} - X_{CG})}{s}$$

$$s = \frac{\sqrt{SD_{EG}^2 + SD_{CG}^2}}{2}$$

Cohen's $d > 0.8$ is defined as a large effect. Cohen's d between 0.5 and 0.8 is a medium effect, and a d between 0.2 and 0.5 is a small effect (Leonhart, 2004). We calculated correlations using the Spearman and Pearson correlation methods.

3 RESULTS

3.1 Systematic review of the literature

A systematic review of the literature, “High Levels of Physical Activity in Anorexia Nervosa: A Systematic Review” was published in the *European Eating Disorder Review* in 2015. Relevant results are given here. For further information, see Gummer et al. (2015). Twenty studies between 1985 and 2015 were identified as shown in Table 1. Since then one more trial using accelerometry as PA assessment method in AN was published (Gianini et al., 2016). A significant heterogeneity of study populations, measurements, device specifications, settings, and outcomes was found and resulted in a qualitative analysis.

3.1.1 Sample characteristics in included studies

“In the 20 reviewed trials, population size varied from 8 to 59 women (mean $n = 31,3$). Eleven studies dealt with inpatients with AN, while six trials had outpatients with AN as participants. Three studies had both outpatients and inpatients in their study population (Kostrzewa et al., 2013) (Carrera et al., 2012) (Keyes et al., 2015). Two of the trials explicitly focused on long-standing patients (Bratland-Sanda, Sundgot-Borgen, Rosenvinge, et al., 2010) (Bratland-Sanda, Sundgot-Borgen, et al., 2010b) and one focused on acute AN patients (Holtkamp et al., 2006). In two studies patients with ED in general were assessed, comparing AN, bulimia nervosa (BN), and eating disorders not otherwise specified (EDNOS) (Bratland-Sanda, Sundgot-Borgen, Rosenvinge, et al., 2010) (Bratland-Sanda, Sundgot-Borgen, et al., 2010b). Three studies included women recovered from AN (Dellava, Hamer, Kanodia, Reyes-Rodriguez, & Bulik, 2011) (Harris, McAlpine, Shirbhate, Manohar, & Levine, 2008) (Hechler et al., 2008). Eight of the 20 studies had a healthy normal weight control group; one compared AN patients with obese control patients (Westerterp & Bouten, 1997), while another compared AN inpatients and AN outpatients with either patients suffering moderate anxiety or healthy controls (Keyes et al., 2015).

In four studies, the study population was divided into a group of high exercisers/excessive exercisers (EE)/HLEPA and low exercisers/non excessive exercisers (NEE)/LLEPA. Two (Klein, Mayer, Schebendach, & Walsh, 2007) (Bratland-Sanda, Sundgot-Borgen, et al., 2010b) used the classification of EE/NEE suggested by Davis et al. (Davis et al., 1997) that defines patients as EE when they meet 3 criteria: (1) > 6h per week of accelerometry assessed MVPA (moderate to vigorous physical activity >1952 counts/min) upon admission; (2) reported persistence of this amount for > 1 month before admission; and (3) classification as exercise dependent symptomatic. Although Klein et al. (Klein et al., 2007) used the classification by Davis et al., they used the term 'high exerciser' instead of 'excessive exerciser'. Kostrzewa (Kostrzewa et al., 2013) simply classified by the amount of time spent in MVPA measured by accelerometry. Hofman et al. (Hofmann et al., 2014) divided the groups by the median of steps in one day. Due to the different classifications, the percentage of participants belonging to the HLEPA group varies in the different studies from 29% to 41.7%. The mean age varies from 12.8 to 33 years (mean = 24.4 years). Four studies included only adolescents, 6 studies included only adults (>17 years), and 10 studies included participants of every age.

Mean BMI in the particular studies varied from 14.3 to 18.0 kg/m² (mean BMI = 16.4 kg/m²) in the AN groups. Most studies had participants with a mean BMI of 14 to 16 kg/m². Only one study did not fit in with a mean BMI of 18 in the study population, which was explained by the high muscle mass of two participants (Birmingham, Hlynsky, Whiteside, & Geller, 2005)." (Gummer et al., 2015)

3.1.2 Problems with study dropouts

"Dropouts were mentioned in 11 studies. In other studies, up to one third of the participants had to be excluded from analyses. This was mostly because of missing data from the accelerometer (Kostrzewa et al., 2013) (Dellava et al., 2011) (Carrera et al., 2012) (Klein et al., 2007) (Birmingham et al., 2005) (Keyes et al., 2015) which was due to malfunctions, inactivity of the participant indicating misuse of the accelerometer, or when the accelerometer was not worn long enough per day. However, it is mostly impossible to discern whether data are incomplete due to technological limitations or non-compliance. In one

study (El Ghoch et al., 2013), ten patients dropped out of a 20-week treatment program, so the reason for dropping out was not associated with the accelerometer but probably with the long duration of the study. This was also the case for two studies where consecutive patients refused participation in the study (Bratland-Sanda, Sundgot-Borgen, Rosenvinge, et al., 2010) (Bratland-Sanda, Sundgot-Borgen, et al., 2010b). Bouten et al. (Bouten et al., 1996) excluded one participant from the study because of excessive sport activity. Fernandez-del-Valle et al. (Fernandez-del-Valle et al., 2014) described the process of inclusion very precisely in a flow diagram showing that most drop-outs quit the study not for intrinsic but external reasons such as concurrent hospitalization or care center relocation. None of the studies discussed problems and difficulties in recruitment and compliance of AN patients within the study context. Keyes et al. (Keyes et al., 2015) stated that the recruitment for a PA study might be biased since not all people with AN would participate.” (Gummer et al., 2015)

3.1.3 Assessment of physical activity in Anorexia nervosa

“In almost all trials one accelerometer per participant was used, but it was worn on different body positions. Only Falk et al. (Falk et al., 1985) utilized one device at the dominant wrist and another one on the ipsilateral ankle. In all studies the epoch length was set to 1 min, so that activity categories of counts/minute could be defined. The categorization was heterogeneous and only scarcely described. For example, Bouten et al. (Bouten et al., 1996) defined outputs of <1000 counts/minute as lying/standing/sitting activity, outputs of 1000 - 3000 as counts/minute as walking/cycling, and outputs of >3000 counts/minute as household/sports/exercise. In contrast, the classification in the trial of Bratland-Sanda, Sundgot-Borgen et al. (Bratland-Sanda, Sundgot-Borgen, et al., 2010b) defines activity with >1950 counts/minute as moderate to vigorous physical activity (Davis et al., 1997). Carrera et al. (Carrera et al., 2012) and Kostrzewa et al. (Kostrzewa et al., 2013) used a classification by Puyau et al. (Puyau et al., 2002) that defines <200 counts/minute as sedentary activity, 200-1800 counts/minute as light activity, and >1800 counts/minute as moderate to vigorous activity for a device worn on the lower leg.

Comparison between the oldest and the newest device technology shows great developments in accelerometry, particularly in memory capacity, data storage, data evaluating software, and wearing comfort. The two oldest devices have incomparable technology: Falk et al. (Falk et al., 1985) describe the actometer (Timex 108 motion recorder) used in their study as a 'man's mechanical self-winding wristwatch that has been modified such that the self-winding rotor directly drives the minute hand, which drives the hour hand and the calendar date in a normal fashion rather than winding the mainspring, which has been removed' (Falk et al., 1985). This procedure could only be utilized for four measurement periods spread throughout the day (waking up, lunch time, 6pm, and bedtime). Thus, this accelerometer is the only one of the review that does not assess activity continuously.

Kaye et al. (Kaye et al., 1986) used a so-called acceleration-sensitive device that measures continuously. However, movement has to be cumulated because of the small memory storage; thus, one count always represents 16 movements. The advanced for its time Tracmor device used by Bouten et al. (Bouten et al., 1996) still weighs 250g, while the newest devices like Actiwatch weigh only 18g. The newer Tracmor device used by Hechler et al. (2008) weighs 22g. Tracmor has to be attached to the lower back and is composed of an accelerometer unit and a portable data unit, which are connected by a flexible cable. More recent devices are always composed of only one unit. The device used most frequently in the trials of this review is called 'Actiwatch' (Cambridge Neurotechnology, UK, 18g), validated by Puyau et al. (Puyau et al., 2002). An Actiwatch has to be placed at the right ankle and cannot be worn while swimming or showering. 'ActiGraph' (MTI Model, USA, 19g), validated by Freedson et al. (P. S. Freedson et al., 1998), has also been utilized in several studies. It works similar to 'Actiwatch' but is worn on the hip. Another device often used is the „Sense Wear Armband“ (Pro 3 armband, Pittsburg USA, 45g), which additionally measures heat flux, galvanic skin response, and skin temperature so that the time it is worn can be validated. This is also possible with 'Actiheart', which combines a heart rate monitor with triaxial accelerometry. Actiheart has to be placed on the left side of the chest with two ECG electrodes

and only weighs 8g. One other device (RT3), utilized in the study of Birmingham et al. (Birmingham et al., 2005), has not been further described.

Assessment in most trials of this review included not only PA measurement with accelerometry, but also different types of questionnaires or diaries, etc., with the purpose of assessing all types and manifestations of PA and sports behaviour in AN. These methods can be seen in table 1.” (Gummer et al., 2015)

3.1.4 Time and duration of accelerometry assessment

“The duration of the assessment varied from 2 days to 7 days (mean = 4.5 days). Participants of all studies had to fulfil consecutive measurements.

PA measurement took place in an inpatient setting in most cases. In most studies, only one PA assessment was performed, which again was most often in the first weeks of inpatient treatment. Four studies performed three PA assessments. In one of those, PA was assessed 3 times during inpatient treatment (Bratland-Sanda, Sundgot-Borgen, et al., 2010b), and in another trial it was assessed at the beginning and at the end of inpatient treatment, as well as at the one-year follow-up. Hechler et al. (Hechler et al., 2008) measured in three different seasons of the year (winter, autumn, and summer). Fernandez-del-Valle et al. (Fernandez-del-Valle et al., 2014) measured PA before and after a high-intensity resistance training program and 4 weeks after detraining. Another trial included 2 measurements: at the beginning and at the end of treatment. Harris et al. (Harris et al., 2008) performed an experimental validation of PAMS. This study was excluded in the calculation of mean assessment duration.” (Gummer et al., 2015)

3.1.5 Clustered outcome topics

Clusters of studies with similar outcomes topics were made to get a better overview of the very different outcome parameters in the different studies.

3.1.5.1 Validation of accelerometry

“There are 5 studies that had the aim to validate a new method of PA assessment in AN. Westerterp & Bouten (Westerterp & Bouten, 1997) compared accelerometry with the DLW gold standard of PA assessment in 1997, and showed that the new method of accelerometry is as valid as DLW in

measuring daily activity in AN. Birmingham et al. (Birmingham et al., 2005) tried to develop a new equation to calculate the calorie requirement for refeeding in AN. They assumed that smoking cigarettes, anxiety, and PA have an influence on weight gain, which could not be confirmed by the results. Harris et al. (Harris et al., 2008) aimed to validate PAMS (Physical Activity Monitoring System). They could show that accelerometry is sensible and specific in distinguishing between lying, sitting, standing, and walking with different velocities, meaning that the acceleration of the device correlates with the energy expenditure and the walking velocity. Another discovery was made by van Elburg et al. (van Elburg et al., 2007), who found that evaluation of PA by nursing staff during inpatient treatment correlates with accelerometry results. They also found that self-ratings of PA in AN underestimate the real amount of PA. This was also affirmed by Alberti et al. (Alberti et al., 2013), who compared objective and subjective measurement of PA in AN.” (Gummer et al., 2015)

3.1.5.2 *Controlled trials assessing physically active behaviour in anorexia nervosa*

“In five studies, PA in AN patients and normal weight controls were compared. El Ghoch et al. (El Ghoch et al., 2013) and Bratland-Sanda, Sundgot-Borgen et al. (Bratland-Sanda, Sundgot-Borgen, et al., 2010b) measured higher PA levels in AN than in the controls, while Bouten et al. (Bouten et al., 1996), Hechler et al. (Hechler et al., 2008), Keyes et al. (Keyes et al., 2015) measured similar levels of mean daily PA in AN. However, Bouten et al. (1996) showed that AN patients had either very high or very low activity levels, while controls had moderate activity levels. Keyes et al. (2015) found that self-reported activity was higher than objectively measured PA in AN, as well as that participants with AN had a higher „drive to exercise“.

Hechler et al. (2008) found that time spent in low-moderate intensity activity was higher during summer in both groups, AN patients and healthy controls.

Some studies did not compare AN patients with healthy controls, but rather patients with high level physical activity (HLPAs) and low level physical activity (LLPAs). They found that AN patients with HLPAs were affected earlier by AN, the illness duration was longer, and the patients showed more fat tissue and higher

leptin levels after recovering (Kostrzewa et al., 2014). Also, for patients with HLPAs, PA was more important in regulating negative affects than for patients with LLPAs (Bratland-Sanda, Sundgot-Borgen, et al., 2010b). In comparison with LLPAs, HLPAs patients also had higher scores in the Commitment to Exercise Scale, which shows an association between activity behaviour before inpatient treatment and during inpatient treatment.” (Gummer et al., 2015)

3.1.5.3 Physical activity after recovery

“Beside this, there are two studies dealing with recovered AN patients. Dellava et al. (2011) aimed to find why recovered AN patients have a longstanding lower BMI. For this purpose, they measured diet and PA, as well as reasons for diet and PA in AN and healthy controls. They could not show any differences between diet and PA in quantity, but recovered AN patients instead chose food for health reasons. Kaye et al. (1986) found that short term recovered AN patients had significantly higher calorie intake and PA levels than long-term recovered AN patients and controls. Thus, HLPAs regressed after recovery. Hechler et al. (2008) included recovering AN patients in various stages of treatment. They found that the percentage of body fat was negatively correlated to PA, meaning that less PA could lead to a normalization of body fat.” (Gummer et al., 2015)

3.1.5.4 Investigated interrelations of physical activity and biological factors

“Six studies in this review had the purpose of finding a relation between PA level and certain factors. Falk et al. (1985) found that PA level in inpatients is suppressed by administration of cyproheptadine. Bouten et al. (1996) and Westerterp et al. (1997) found that high PA levels only occur in patients with a relatively high BMI (BMI of 17 kg·m⁻² or more). Holtkamp et al. (2006) showed a U-formed relation between PA levels and serum levels of the hormone leptin, while Klein et al. showed a positive correlation between cortisol levels and PA levels (Klein et al., 2007). Carrera et al. (2012) found an association between activity levels and ambient temperature, which displays PA in AN as a strategy

for warming up, besides burning calories (Dellava et al., 2011).” (Gummer et al., 2015)

3.1.5.5 Correlations of physical activity behaviour and treatment

“Four studies focus on the treatment of AN and how PA level and therapy interact. Kostrzewa et al. (2013) investigated how high activity levels are influenced by inpatient treatment and found that the PA level normalizes during treatment. They also found that AN patients who are classified as HLPAs before inpatient treatment did not have higher recovery rates than patients with low level PA. Despite this, HLPAs leads to longstanding consequences in recovery of leptin serum levels and body composition. In contrast, El Ghoch et al. (2013) found that treatment dropouts have almost twice as high PA levels than completers at the beginning of treatment. Falk et al. (1985) found that PA level increases in the first two weeks of inpatient treatment.

Alberti et al. (2013), however, showed that the more time spent in light PA at the beginning of the treatment, the less improvement can be seen in ED psychopathology at the end of therapy. In this context Bratland-Sanda et al. (2010) found that a reduction of PA in general correlates positively with ED psychopathology. Especially in HLPAs patients with ED, an improvement in ED psychopathology seems to result in a reduction in sport dependence and importance of PA to regulate negative effects. Additionally, Carrerra et al. (2012) showed that the more time spent in moderate to vigorous PA, the less anxiety occurs in AN. Holtkamp et al. (2006) showed that there is a relation between motor restlessness and inner restlessness. In contrast, El Ghoch et al. (2013) and Klein et al. (2007) could not find any significant association between ED psychopathology and PA. Falk et al. (1985) could not find a correlation between depression scales or personality measurements and PA. This shows that findings concerning psychopathology in general and other psychological measurements related to objectively measured PA in AN are highly contradictory.” (Gummer et al., 2015)

Table 1: Overview of literature about objectively measured physical activity in anorexia nervosa (Gummer et al., 2015)

Study	Sample	Mean age	Assessment	Time of assessment	Duration of assessment	Objective/ Purpose	Results
Keyes et al., 2015	Four groups: -18 AN inpatients -37 AN outpatients -34 anxiety patients -30 healthy controls	28,3	-accelerometry (Actiwatch) -questionnaires for ED pathology and anxiety -questionnaires for PA, reasons for exercise and drive for exercise -body composition (Inbody 3.0 Biospace machine)	not further defined	1 week	-find relationship between PA, drive for exercise, anxiety and ED pathology	-no significant differences in objectively measured PA between groups -self-perceived PA higher than objectively measured PA in AN groups -type of exercise: AN outpatients reported more walking and moderate exercise, AN inpatients reported more walking and less moderate or vigorous PA than other groups -higher drive for exercise in AN groups -reasons for exercise vary between groups: "improving tone" most important for AN groups
Fernandez-del-Valle et al., 2014	36 AN (restricting type) divided into two groups: - intervention group (n=18) - control group (n=18)	12,8	-accelerometry (ActiGraph) to ensure that patients were not excessive exercisers -muscular strength (weightlifting training machines) -BMI -agility (Timed Up and Go 3m/10m)	-before intervention -directly after intervention -4 weeks after intervention	Not further defined	-find out if 8 weeks of high-intensity resistance training (3 times a week) is able to rise muscle strength and agility without weight loss in AN restricting type -measure the persistence of the program	-PA was no outcome criterion, and there are no results reported -in the intervention group strength increased significantly after 8 weeks training program -agility improved in the intervention group -effects persisted after end of therapy
Kostrzewska et al., 2014	37 AN - 23 inpatients - 14 outpatients	15,2	- accelerometry - body fat assessment - leptin level - ghrelin level	- start of therapy - end of therapy - one year follow up	3 consecutive days	- influence of inpatients therapy on high levels of PA - consequences of high PA levels on physiological recovery	- High level PA (HLLPA) n=11, Low level PA (LLLPA) n=26 - HLLPA: age of onset earlier (duration of illness longer) - HLLPA does not have a negative effect on recovery - PA normalizes during therapy - HLLPA in the beginning of therapy has long-standing consequences for recovery of body composition
Hofmann et al., 2014	39 AN (divided in moderate and high activity group by median of steps)	27,3	- Sense Wear Armband (biaxial accelerometer, heat flux, galvanic skin responses, skin temperature) - irisin plasma levels - energy expenditure calculated	- inpatient treatment, not further defined	3 consecutive days	- investigation of the relationship of circulation, irisin levels, PA levels, and energy expenditure in AN	- no difference in irisin levels between the moderate and high activity groups - no association between irisin levels and various parameters of energy expenditure

El Ghoch et al., 2013	53 AN, 53 age-matched controls	24,5	- Sense Wear Armband (accelerometer)	- first week of inpatient admission (baseline); last week of day-hospital - end of treatment	4 consecutive days	- assess role of PA on treatment outcome - compare AN patients and controls	- Baseline: AN patients with higher moderate to vigorous PA (MVPA) than controls - Dropouts with higher MVPA (almost double) than completers - End of treatment: AN completers with higher number of steps, MVPA, and expenditure than controls - PA not correlated to ED psychopathology
Alberti et al., 2013	52 AN	24,4	- Actiheart (Accelerometer+heart frequency) - IPAQ	- second day of inpatient stay	3 consecutive days	- comparison of subjective (IPAQ) and objective (AH) measurement of PA in AN - consequences for treatment outcome	- IPAQ underestimates PA in comparison to AH - time spent in LPA > MVPA - higher levels of LPA at baseline associated in poorer improvement of ED pathology in the end
Carrera et al., 2012	37 adolescent <i>acute</i> AN, (32 outpatients, 5 inpatients)	15,3	- Actiwatch (PA), right ankle - daily values for temperature from local meteorological stations (AT) - standardized measures of anxiety, depression, and ED	- within first week of contacting ED center (outpatient)	3 consecutive days	- assess the effect of ambient temperature on physical activity in acute AN - find other factors contributing to hyperactivity	- cold group more active than warm group - AT has strongest correlation with PA (predictor of PA) - the more time spent in MVPA, the less anxiety
Dellava et al., 2012	15 AN (recovered), 18 healthy controls	32,5	- ActiGraph - reasons for exercise inventory - food journals - food choice questionnaire	- after 3 years without BMI under 17,5 nor engaging in binge eating or purging (outpatient)	3 weekdays and 1 weekend day	- quantify PA, analyze diet and reasons for PA, and diet in women recovered from AN - find reasons for maintained lower BMI in recovered AN patients	- BMI over two units lower in recovered women - macronutrient intake does not differ between both groups and is within normal ranges - reasons for food choices: recovered women select more for healthy benefits - no difference in PA between groups
Bratland-Sanda, 2010	- 59 inpatients with <i>long-standing</i> ED (AN,BN,EDNOS) - 53 age-matched controls	27,6	- ActiGraph (MTI Model) - VO2 max - muscular strength (Repetition maximum) - types of activity - Bone mineral density (BMD)	- within first 2 weeks of inpatient stay	7 consecutive days	- examine fitness, strength, BMD in inpatients with longstanding ED - associated and explanatory factors for BMD in inpatients	- no difference in aerobic fitness between patients and controls despite PA higher in the patients - muscular strength and BMD lower in AN - muscular strength and <i>high impact PA</i> associated with BMD - strength training is preferable for AN and specialized exercise professionals should be included in the treatment staff - BMD screening!
Bratland-Sanda et al., 2010	38 <i>longstanding</i> ED (AN, BN, EDNOS), separated in excessive exerciser (EE) and non-excessive exerciser (NEE)	30,9	- Accelerometer (MTI ActiGraph), right hip - exercise dependence scale - reasons for exercise inventory	- three times during the inpatient treatment period	7 consecutive days	- analyze changes in PA on ex dependence during treatment - find correlation between PA, ex motivation, ex dependence, and ED divide in EE and NEE - divide in EE (Excessive Exercisers) and NEE (Non EE)	- 29% were EE (classification of Davis et al.) - EE had higher EDI, Eating Disorder Examination (EDE), PA, ex dependence and importance of ex as affect regulation scores - reduction of PA positively correlated with EDI in whole sample - in EE reduced ED, psychopathology was correlated with reduction in ex dependence and perceived importance of ex to <i>regulate negative affects</i> (excessive PA as affect regulation strategy)

Harris et al., 2008	<ul style="list-style-type: none"> - eight AN, past weight restoration phase of illness - eight healthy controls 	36,0	<ul style="list-style-type: none"> - physical activity monitoring system (PAMS, 1,3kg), includes 4 inclinometers + 2 accelerometers + calorimeter 	- outpatient	30 min resting (resting metabolic rate), 15 min sitting, 15 min standing, 15 min walking	- laboratory validation of PAMS	<ul style="list-style-type: none"> - PAMS showed sensitivity and specificity in distinguishing lying, sitting, and standing - distinguished walking and standing still - correlation of acceleration with energy expenditure and walking velocity - PAMS seems to be a convincing technology of measuring PA in AN
Hechler et al., 2008	<ul style="list-style-type: none"> - 10 AN, recovering - 15 healthy controls 	23,0	<ul style="list-style-type: none"> - Tracmor triaxial accelerometer, waist-worn - percent body fat (dual-energy x-ray absorptiometry) 	- outpatient	6 consecutive days	<ul style="list-style-type: none"> - find differences in PA between outpatients with AN and healthy controls - relationship between body fat and PA - measure PA in three seasons 	<ul style="list-style-type: none"> - groups did not differ in PA - seasonal variation in PA could be found in both groups: more engagement in summer - body fat - negative correlation between time spent in lean mass index and body fat in AN
van Elburg et al., 2007	18 AN inpatients	17,9	<ul style="list-style-type: none"> - Actiwatch on right ankle - Nurse rating on visual analogue scale (0-10) - Same scale as self-rating + profile of mood states 	- during inpatient treatment, not further defined	3 consecutive days	- Compare self-report, Actometer, and nurse evaluation in PA evaluation of AN	<ul style="list-style-type: none"> - nurse ratings correlate significantly with actometer score - self-reported activity underestimates actometer scores - PA ratings by nurses higher than by self-rating on same score - Observation of hyperactivity made by nurses can be reliable and valid
Klein et al., 2007	36 AN	26,3	<ul style="list-style-type: none"> - Sense Wear Armband, wireless device (82g), worn on upper arm (biaxial accelerometer+ sensor for heat flow+skin temp+galvanic skin responses) - CES - 24h - urine for cortisol 	- Between days 2 and 14 of inpatient stay	48 consecutive hours	<ul style="list-style-type: none"> - quantify PA in AN - association between exercise history and PA - association between cortisol and PA/ „drive for activity“? 	<ul style="list-style-type: none"> - 41.7% categorized as „high exerciser“ (Davis' categorization) - „high exercisers“ higher PA counts and higher scores in CES -> association between inpatient PA and pre-hospitalization exercise behaviour (CES) - urinary cortisol positively associated with activity counts - no significant association between PA and affective psychopathology - categorization in „high exerciser“ makes sense
Birmingham, 2005	17 AN	25,0	<ul style="list-style-type: none"> - triaxial accelerometer (RT3) - Beck Anxiety Inventory 	- within first 72 hours of inpatient admission	48 hours	- find out if anxiety, cigarette smoking, or exercise contribute to caloric requirement for refeeding	<ul style="list-style-type: none"> - no significant correlation between energy requirements for weight gain and anxiety, exercise, or cigarette smoking - standard methods of estimating caloric requirements for refeeding remain indirect calorimetry (Harris-Benedict-Equation) and previous history
Holtkamp et al., 2005	26 acute AN	15,6	<ul style="list-style-type: none"> - Actiwatch, right ankle - Structured Interview for Anorexic and Bulimic Disorders (SIAB-EX) (3 months before) - 5-point Likert scale for motor restlessness - visual analogue scale for inner restlessness - serum leptin 	- first 4 days of inpatient treatment	4 consecutive days	<ul style="list-style-type: none"> - submit that leptin level and PA in AN have a negative correlation - relationship between leptin and various qualities of PA in acute AN 	<ul style="list-style-type: none"> - hypoleptinemia is a factor that leads to a variance of hyperactivity/restlessness in AN - relation between excessive ex over 3 months before treatment and PA in first 3 days of treatment - relation between motor and inner restlessness - U-shaped relation between mean daily activity and serum leptin (log10) - <i>Therapy: administration of leptin</i>

Westerterp et al., 1997	<ul style="list-style-type: none"> - 11 AN - 8 Obesity - 30 controls 	Not described	<ul style="list-style-type: none"> - Doubly labeled water (DLW, ADMR) combined with SMR (sleeping metabolic rate) triaxial accelerometry (Tracmor, 110x70x35mm, 250g) 	<ul style="list-style-type: none"> - 2 weeks of ADMR (inpatient stay) - first 7 consecutive days: Accelerometry 	7 consecutive days	<ul style="list-style-type: none"> - evaluate accelerometry with the DLW method (gold standard of PA assessment in 1997) 	<ul style="list-style-type: none"> - no significant difference between accelerometer PA levels and ADMR PA levels/64% of the variation in ADMR could be predicted in AN - overactivity in AN patients only occurs when BMI >17 - Tracmor is a good device for daily PA assessment under free living conditions
Bouten et al., 1996	<ul style="list-style-type: none"> - 11 AN - 13 controls 	33,0	<ul style="list-style-type: none"> - DLW: PAL (ADMR/SMR (respiration chamber)) - Accelerometry waist-worn (Tracmor, 16g device +250g data unit) 	<ul style="list-style-type: none"> - 7 consecutive days: Accelerometry (inpatient stay) - DLW on days 1 and 8 	7 consecutive days (only waking hours)	<ul style="list-style-type: none"> - comparison of level of daily PA in AN and normal weight controls - association PA and BMI 	<ul style="list-style-type: none"> - no difference in group average activity levels in AN and controls, but AN at either a low or a high level while controls at rather moderate level - metabolic rate lower in AN - high daily PA related to relatively high BMI in AN
Kaye et al., 1986	<ul style="list-style-type: none"> - 13 AN, recent weight rec - nine AN long-term weight rec - 11 controls 	25,0	<ul style="list-style-type: none"> - acceleration-sensitive device, waist worn - daily caloric intake (by kitchen) 	<ul style="list-style-type: none"> - 2-4 weeks after rec (first group) - 6 months after rec (second group) 	3 - 5 consecutive days (with stable weight)	<ul style="list-style-type: none"> - assessment of caloric consumption and activity levels in AN - comparison of recent weight recovered, long-term weight recovered AN and controls 	<ul style="list-style-type: none"> - Recent weight rec AN had significantly higher activity counts and caloric intake (kcal/kg/day) than long-term weight rec - treatment changes with graduated transition from hospital are important
Falk et al., 1985	- 20 AN (divided into 3 groups: cyproheptadine, amitriptyline, or placebo)	21,1	<ul style="list-style-type: none"> - actometer (Timex model 108 Motion Recorder, mechanical self-winding wristwatch) - Hamilton Rating score (depression) - Minnesota Multiphasic Personality Inventory 	- first 2 weeks of inpatient stay	Four measurements in 24 hours (wake up, noon, 6 PM, bedtime)	<ul style="list-style-type: none"> - measurement of energy expenditure of inpatient women - relationship between motor activity, weight, drug administration, and behavioural assessment 	<ul style="list-style-type: none"> - activity increases during first two weeks of hospitalization along with weight gain - PA level is initially strongly suppressed by cyproheptadine - no relationship between activity level and depression score or personality

AN: anorexia nervosa, ED: eating disorder, PA: physical activity, BMI: body mass index, HPLA: high level physical activity, MVPA: moderate to vigorous physical activity, BN: bulimia nervosa, EDNOS: eating disorder not otherwise specified, BMD: bone mineral density, IPAQ: International Physical Activity Questionnaire, LPA: low physical activity, AT: air temperature, EDI: Eating Disorder Inventory, CES, Commitment to Exercise Scale, ADMR: Average Daily Metabolic Rate, SMR: Sleep metabolic Rate, DLW: doubly labelled water, PAMS: physical activity monitoring system, AH: Actiheart

3.2 ANEX pilot study: Descriptive analysis of the samples

3.2.1 Diagnosis and comorbidities

Twenty-five women participated in the ANEX pilot study. Thirteen of them were classified as restrictive type AN, while 12 were classified as purging type AN as shown in Table 2. Using the inclusion criteria for the ANEX pilot study of subsyndromal AN ($BMI < 18.5 \text{ kg/m}^2$), 19 patients were diagnosed with AN (ICD10: F50.0), while four were diagnosed with subsyndromal anorexia nervosa and two patients were diagnosed with atypical anorexia nervosa (ICD10: F50.1). Twelve of the 25 participants were hospitalized at the inpatient unit of the Psychosomatic Department of the Tuebingen University Hospital, and they were defined as the inpatient group (IG). The same sample was assessed as the follow-up group (IG-FU) four weeks after inpatient treatment. Thirteen participants were outpatients at the Psychosomatic Department of the Tuebingen University Hospital (outpatient group - OG). Comparing the IG and OG, the mean BMI and the mean age were very similar (Table 2). The IG had a larger BMI range and a wider age range than the OG. The duration of illness was longer in the IG (9 years) than in the OG (6.7 years) indicating more complicated and more chronified cases of AN in the IG.

Table 2: Type of anorexia nervosa, age, BMI and duration of illness in groups

	OG (n=13)	IG (n=12)	Significance (p)
Restrictive AN n (%)	6 (46%)	7 (58%)	
Purging AN n (%)	7 (54%)	5 (42%)	
Age, mean \pm SD (range) years	23.77 \pm 3.70 (18-29)	24.83 \pm 5.86 (18-40)	0.59
BMI \pm SD kg/m^2	16.14 \pm 2.02 (14-19)	15.04 \pm 1.64 (13-19)	0.15
Duration of illness in years	6.69 \pm 3.73	9.00 \pm 7.28	0.34

AN: Anorexia nervosa, BMI: Body Mass Index, IG: inpatient group, OG: outpatient group, SD: standard deviation

Most of the participants had one or more psychiatric or psychosomatic comorbidities, which are detailed in Table 3. Three patients had somatic

comorbidities: one had epilepsy, one had Wolff-Parkinson-White syndrome, and one patient had hypothyroidism.

Table 3: Psychiatric comorbidities in the whole sample

Comorbidity	n (total)	%
depressive episode or recurrent depressive episode (F32/33)	16	72.7
Mental and behavioural disorders due to psychoactive substance use (F10-19)	9	40.9
Emotionally unstable personality disorder Borderline type (F60.31)	4	18.2
Obsessive - compulsive disorder (F42)	4	18.2
Persistent somatoform pain disorder (F45.4)	2	9.1
Panic disorder (F41.0)	1	4.5
Hyperkinetic disorder (F90.0)	1	4.5

3.2.2 Physiologic parameters

In the inpatient group laboratory parameters were measured as seen in Table 4. These values were measured at the beginning of inpatient treatment. This reduced selection of parameters was made because physiology was not the focus of this study.

Table 4: Laboratory results in the inpatient group

Laboratory	Inpatient group	normal value
TSH ± SD (range) in mU/l	1.52 ± 0.90 (0.53-3)	0.4 – 2.5
Red blood count ± SD (range) in Mio./µl	4.28 ± 0.64 (3.29 – 5.1)	4.0 – 5.4
Hemoglobin ± SD (range) in g/dl	12.86 ± 1.49 (11-14.7)	12 - 16
Leukocytes ± SD (range) per µl	5116.88 ± 1514 (2640-8220)	3800 - 10500

TSH: thyroid stimulating hormone, SD: standard deviation

Additionally, all inpatients had an ECG during treatment time. The results are demonstrated in Table 5.

Table 5: Electrocardiogram in the inpatient group

ECG	Inpatient group	normal value
QT interval \pm SD (range) in %	113.18 \pm 9.02 (100-130)	80 - 120
Heart rate \pm SD (range)	66.2 \pm 12.21 (48-87)	

ECG: electrocardiogram, SD: standard deviation

3.2.3 Physical activity

3.2.3.1 Accelerometry based physical activity assessment

The wear time of the OG was 2797.36 ± 863.54 minutes on an average, which is about 11.66 hours per day on an average. Two patients had been wearing the ActiGraph for fewer than five hours and they were excluded from the analysis. The wear time of the IG was the longest: 3398.64 ± 519.54 minutes on an average, which is a mean wear time of 14.16 hours per day. At the follow-up measurement the mean wear time was 3293.33 ± 398.66 minutes which is about 13.72 hours per day. For all measurements the longest wear time was 4180 minutes or 17.42 hours per day. The shortest wear time was 1093 minutes or 4.55 hours per day. The range of wear time was high, especially in the outpatients as seen in Figure 3.

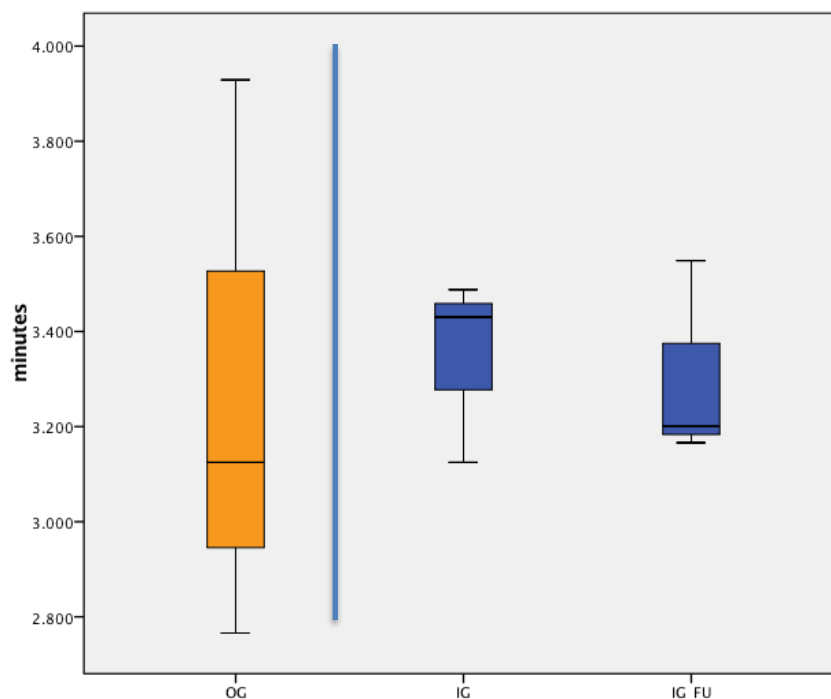


Figure 3: Mean daily wear time of the ActiGraph in groups

OG: outpatient group, IG: inpatient group, IG_FU: inpatient group at follow-up

Figure 4 shows three outputs of objective PA assessment at the different measurement points: kcal per day, steps per minute, and counts per minute.

Time and percentage in the activity levels are shown separately (Figures 5 and 6). Comparing the IG and the inpatient group at follow-up (IG_FU), kcal spent per day increased slightly after hospitalization. This was also the case for counts per minute. However, the number of steps per day decreased after hospitalization. The OG showed higher values than the IG in all three dimensions.

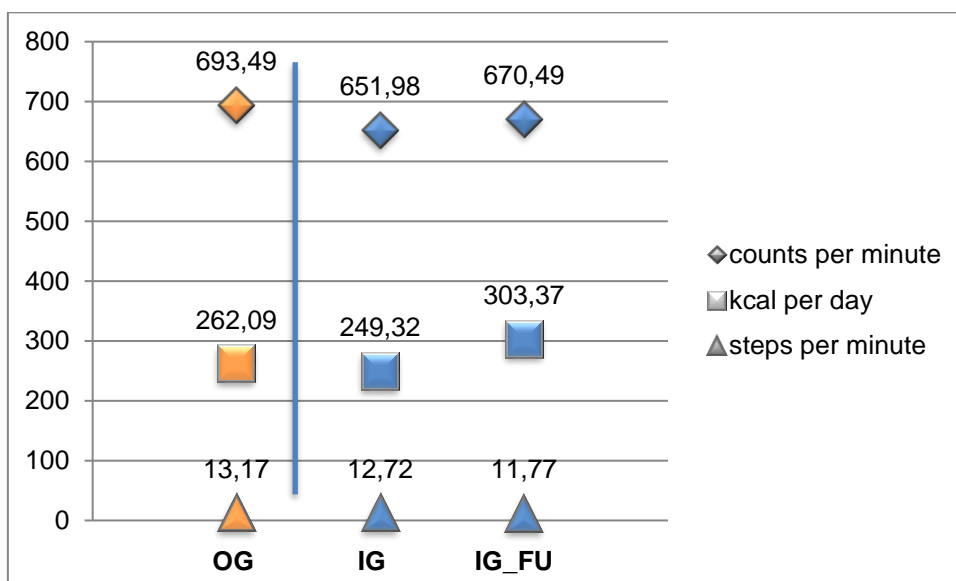


Figure 4: Objectively measured physical activity by groups

OG: outpatient group, IG: inpatient group, IG_FU: inpatient group at follow-up

As seen in Figure 5, the distribution of the PA into different levels only slightly differed between groups. The IG had the highest overall activity, which seems to be due to more time spent in LPA than the OG or the IG at follow-up. The IG also spent more hours in vigorous PA than OG and IG_FU (IG: 1.76 h/week; IG_FU: 0.88 h/week; OG: 1.10 h/week). The IG_FU spent the most hours of all three groups in moderate PA (IG_FU: 5.77; IG: 4.53; OG: 5.22).

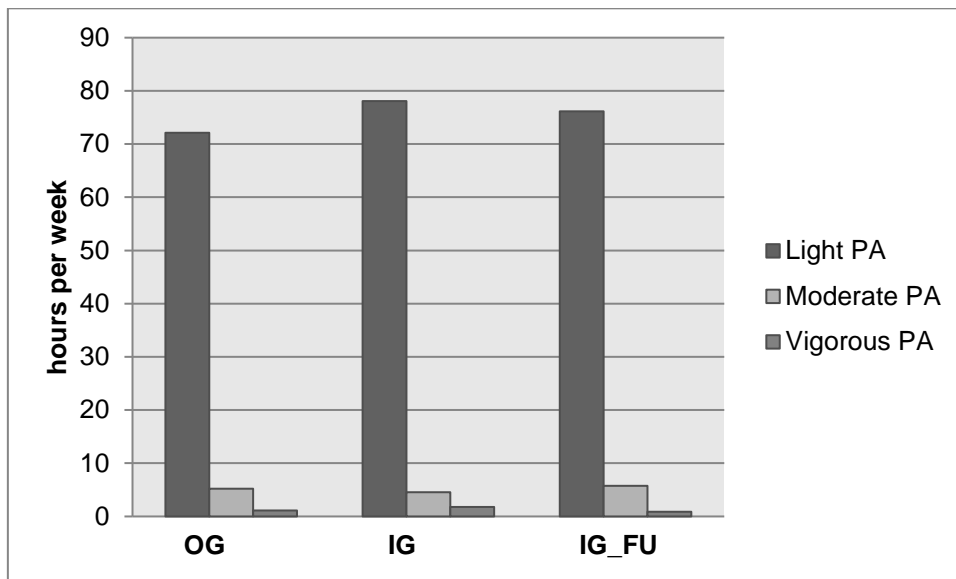


Figure 5: Distribution of wear time into different activity levels by groups

OG: outpatient group, IG: inpatient group, IG_FU: inpatient group at follow-up, PA: physical activity

The evaluation of the percentage of PA spent in moderate and vigorous and very vigorous PA (MVPA) showed a slight increase after treatment. The mean percentage of MVPA in IG was $7.35 \pm 6.15\%$ and the mean percentage of MVPA in IG_FU was $8.43 \pm 5.28\%$. However, the OG had a higher mean percentage of MVPA than the IG and the IG_FU. The OG spent $8.75 \pm 5.23\%$ of their activity in MVPA (Figure 6).

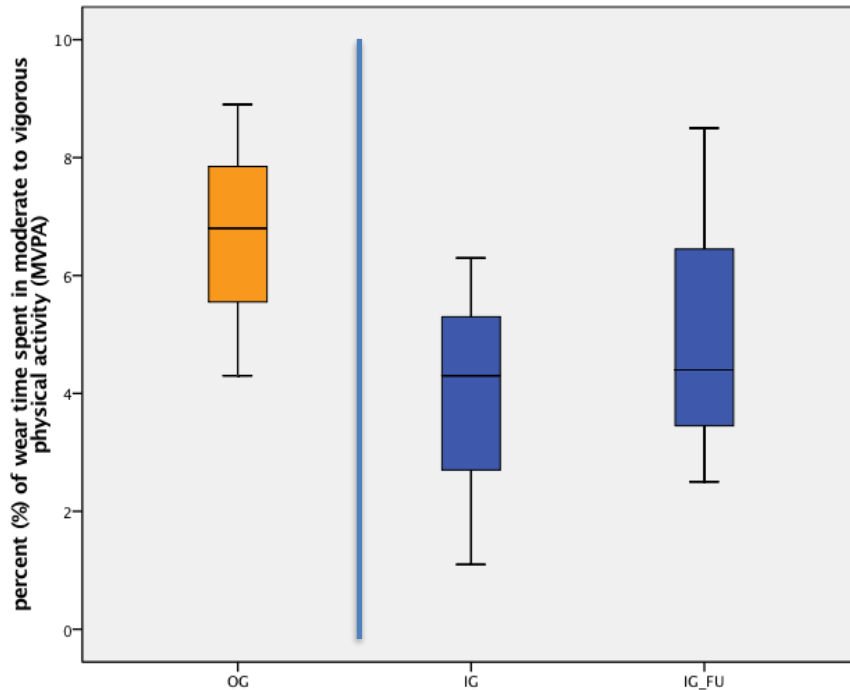


Figure 6: Portion of ActiGraph wear time spent in MVPA by groups

OG: outpatient group, IG: inpatient group, IG_FU: inpatient group at follow-up, MVPA: moderate to vigorous physical activity

Additionally, the ActiGraph measured the average MET rate of the entire wearing period of each participant. The MET rate was defined as multiple of the basal metabolic rate. The OG had a mean MET rate of 1.20 ± 0.19 METs, the IG had a MET rate of 1.15 ± 0.20 METs, and the IG at follow-up had a MET rate of 1.21 ± 0.22 METs. This shows that the energy expenditure was slightly lower in the inpatient setting.

3.2.3.2 Questionnaire based physical activity assessment

a) International Physical Activity Questionnaire

In the IPAQ the OG indicated more PA than the IG. The average number of reported hours per week in the IG was 12.23 ± 9.45 for walking hours, 1.70 ± 1.92 for moderate hours and 2 ± 5.26 for vigorous hours. The OG reported to spend 15.27 ± 12.54 hours per week walking, 8.73 ± 10.21 hours per week in moderate physical activity (MPA), and 6.98 ± 9.78 hours per week in vigorous physical activity (VPA). The reported amount of vigorous PA was significantly higher in the OG (OG>IG: $p<0.05$). This is demonstrated in Figure 7.

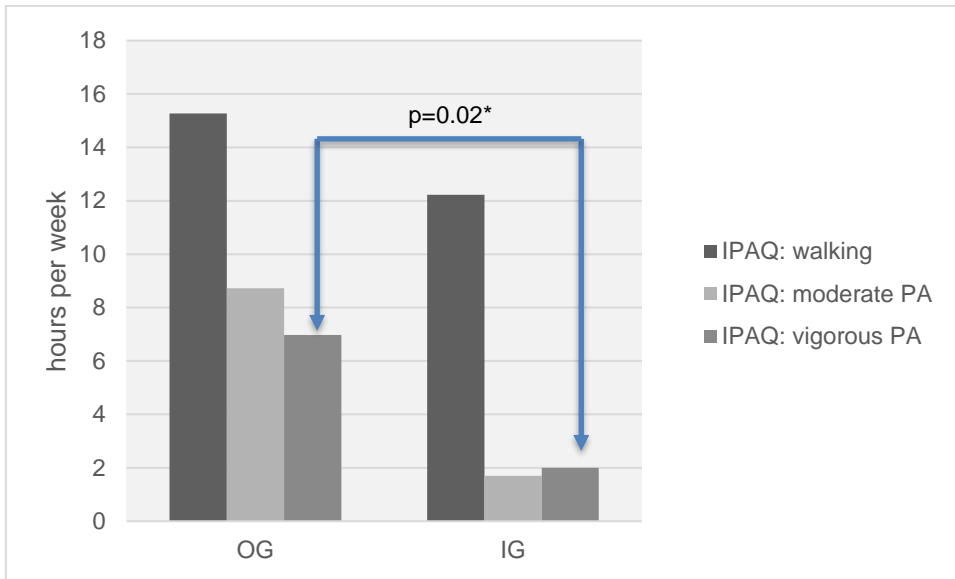


Figure 7: Self-perceived distribution of time into different activity levels by groups

Difference between OG and IG in walking hours: $p=0.65$, moderate physical activity: $p=0.15$ and vigorous physical activity: $p=0.02^*$

* = significance $p<0.05$

OG: outpatient group, IG: inpatient group, IPAQ: International Physical Activity Questionnaire, PA: physical activity

Figure 8 shows that the mean percentage in MVPA was significantly higher in outpatients than inpatients. The average reported percentage of time spent in MVPA was $16.22 \pm 19.60\%$ in the IG and $45.84 \pm 29.96\%$ in the OG (OG>IG: $p<0.05$).

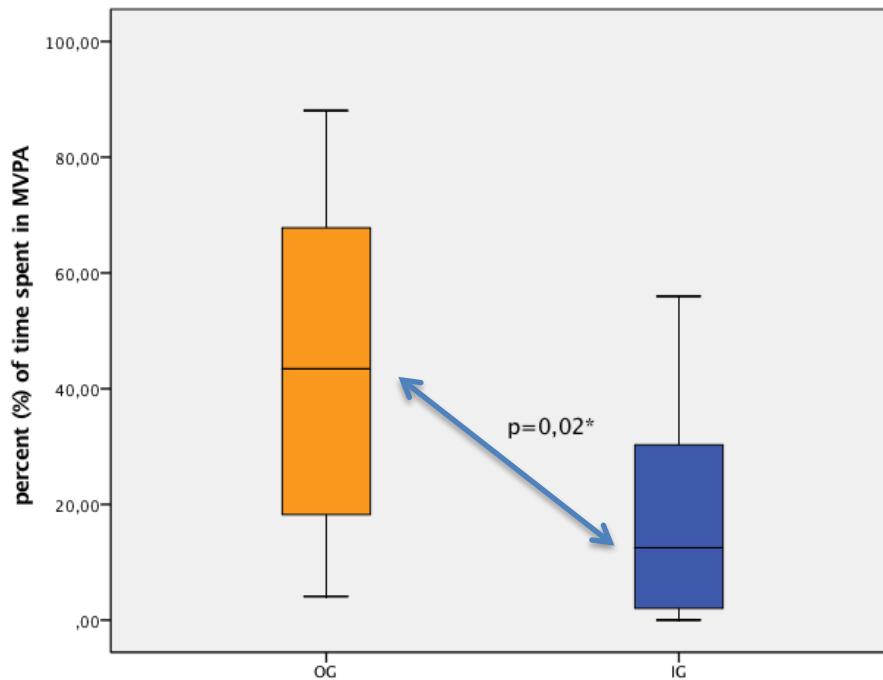


Figure 8: Self-perceived percentage of time spent in MVPA by groups (assessed with the IPAQ)

OG: outpatient group, IG: inpatient group, IPAQ: International Physical Activity Questionnaire, MVPA: moderate to vigorous physical activity

As the results of the IPAQ can be converted into kilocalories per day, we also analyzed these data. The OG spent significantly more kilocalories per day compared to the IG (IG=317.99 kcal/day, OG 892.64 kcal/day; OG>IG: $p<0.05$). Figure 9 shows that the range of kilocalories per day was very high in all participants, especially in the OG.

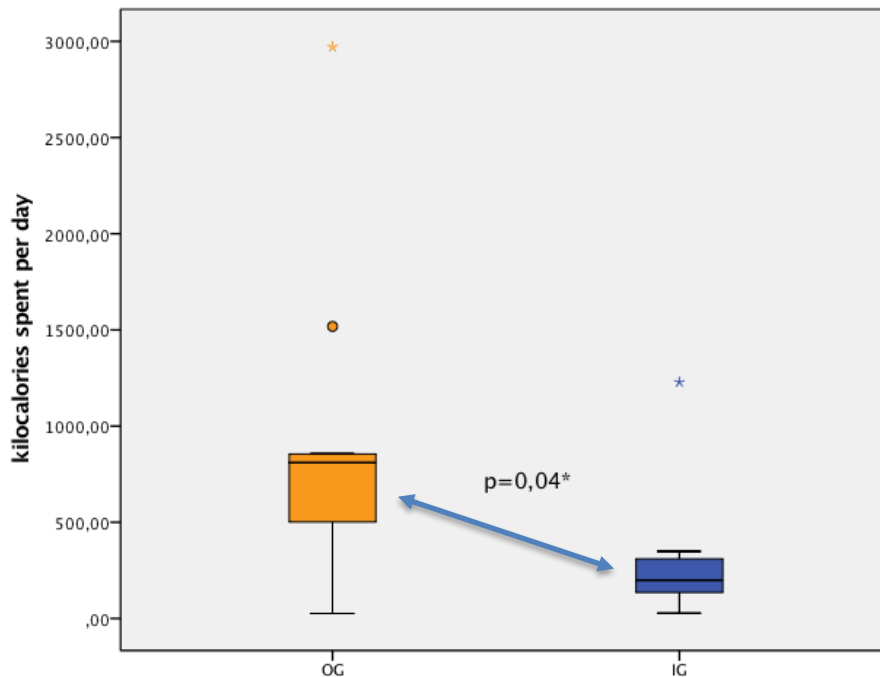


Figure 9: Kilocalories per day by groups (assessed with the IPAQ)

* = significance $p < 0.05$

OG: outpatient group, IG: inpatient group, IPAQ: International Physical Activity Questionnaire

b) Commitment to Exercise Scale

The OG showed higher commitment to exercise compared to the IG, while in the IG the range of the CES score was wider than in the OG (Table 6). CES was calculated on a 0 to 10 commitment score.

Table 6: Results of the commitment to exercise scale in groups

	OG	IG	significance
CES score	6.76 ± 1.29	4.34 ± 2.48	OG > IG*

* =significance $p < 0.05$

CES: Commitment to Exercise Scale, IG: inpatient group, OG: outpatient group

The seventh item of the CES can be evaluated separately. It indicates feelings of guilt when an activity is omitted. Both groups, the IG and the OG, showed

high scores in CES-7 (Figure 10). The OG showed higher scores than the IG (OG: 8.05, IG: 6.01).

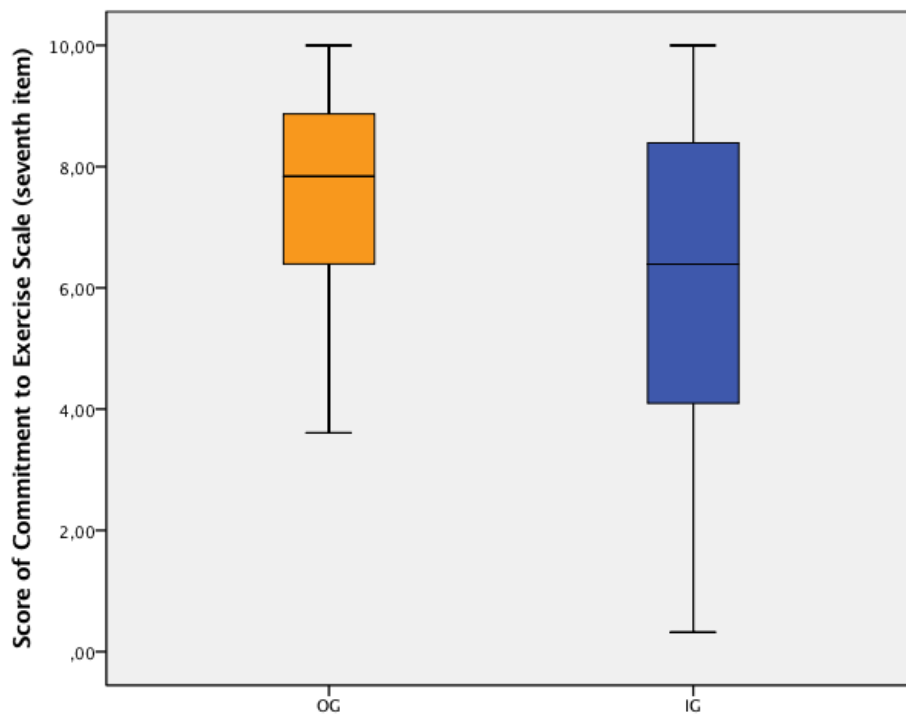


Figure 10: Seventh item of the CES by groups – feelings of guilt when leaving out PA

OG: outpatient group, IG: inpatient group, CES: Commitment to Exercise Scale, PA: physical activity

c) *Reasons for Exercise Inventory:*

The Reasons for Exercise Inventory (REI) aims to find individual reasons for PA. Looking at the whole sample the most important reason for the performance of PA seemed to be “weight control” and “fitness,” while least important was “enjoyment.” “Weight control” was represented with the three statements: “I am physically active because I want to be slim,” “I am physically active because I want to lose weight,” and “I am physically active because I want to hold my actual weight.” For the IG “physical attractiveness” seemed to be least important as shown in Figure 11, while “fitness” was a very important reason for them to be active. Interestingly for both groups “mood” also seemed to be quite important with a score of around 5 out of 6 for the IG and OG (IG=4.82; OG=4.98). There were no differences in the reasons for exercise between the IG and OG.

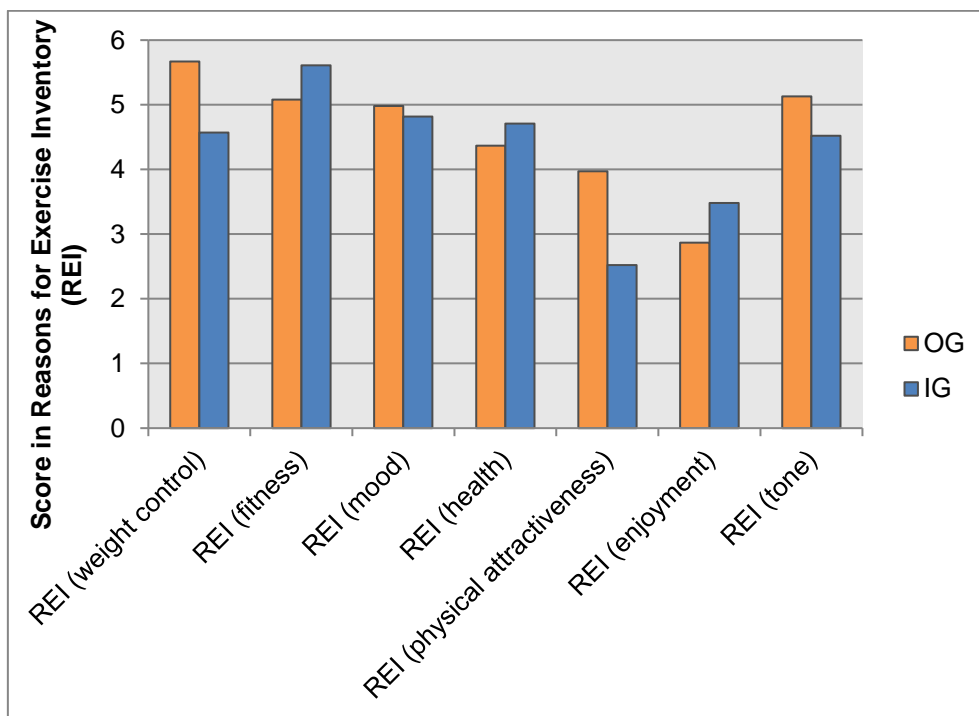


Figure 11: Reasons for Exercise Inventory results in groups

REI: Reasons for Exercise Inventory, OG: outpatient group, IG: inpatient group

Seventeen out of 25 patients stated in the sports questionnaire that they were doing one or more sports in their free time. Seven patients stated they did not

participate in any sports and one patient did not fill out the questionnaire. The different types of sports performed by the participants are shown in Table 7.

Table 7: Types of sports activities in the whole sample

sports	n	%
running	9	40.91
walking/hiking	6	27.27
dancing	6	27.27
cycling	4	18.18
fitness/aerobic	2	9.09
strength training	3	13.64
swimming	2	9.09
horse riding	2	9.09
yoga	1	4.55
playing the flute	1	4.55

3.2.4 ActiGraph and IPAQ in comparison

The total amount of reported activity in the IPAQ was lower than the measured activity with the ActiGraph. The IG reported an overall activity of 15.93 hours per week in the IPAQ. With the ActiGraph, 84.38 hours per week were measured. The OG reported a total amount of 30.98 hours per week in the IPAQ, while 78.45 hours per week were measured with the ActiGraph. In comparison to the results of the accelerometer, the IPAQ showed a very high percentage of MVPA in both the IG and OG (Figure 12). Comparing the IG and OG, the difference between the results of the IPAQ and the results of the accelerometer was larger in the OG (IPAQ>ActiGraph: p=0.01).

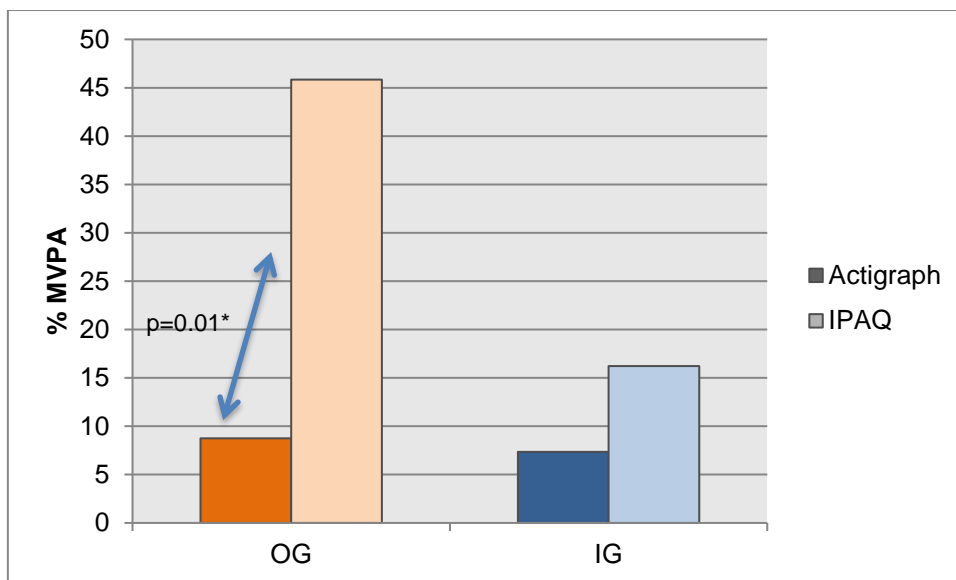


Figure 12: Comparison of objective (Actigraph) and subjective (IPAQ) assessment of MVPA between groups

*= significance p<0.05

OG: outpatient group, IG: inpatient group, IPAQ: International Physical Activity Questionnaire, %MVPA: percent of time in moderate to vigorous physical activity

Comparing the kcal per day measured with the ActiGraph and the kcal per day measured by the IPAQ, the subjectively measured values were also higher than the objectively measured values (Figure 13). This was especially true for the OG (IPAQ>ActiGraph: p=0.02). Also, the between group difference was larger in the results of the IPAQ by comparison to the results of the accelerometer.

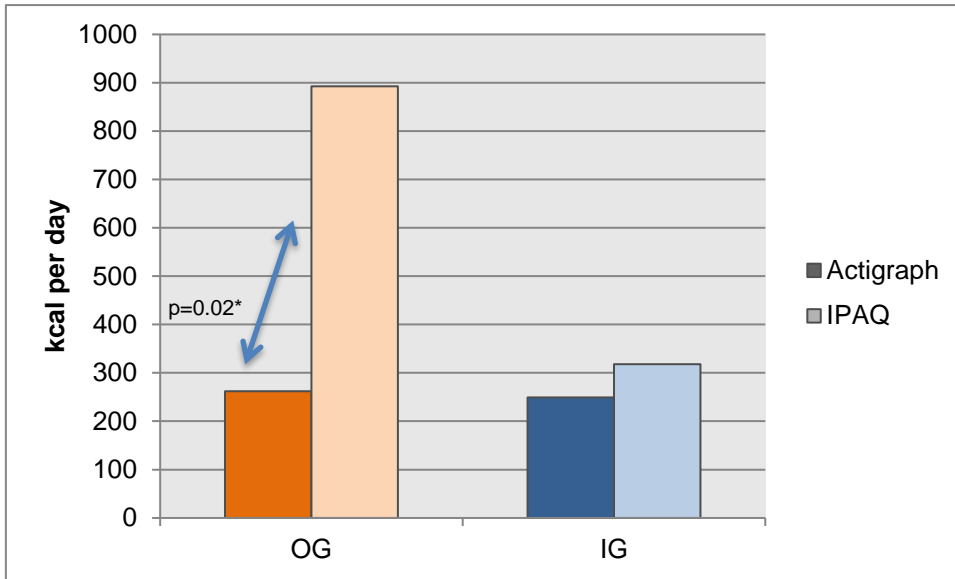


Figure 13: Comparison of subjective and objective measured energy consumption (kilocalories per day) between groups

*= significance $p < 0.05$

OG: outpatient group, IG: inpatient group, IPAQ: International Physical Activity Questionnaire, kcal: kilocalories

3.2.5 Psychometric questionnaires

3.2.5.1 Depression and perceived stress

There was a notifiable difference between the OG and IG in the depression score of the PHQ (Patient Health Questionnaire) with high ranges in both groups (Table 8). However, both values were high representing serious symptoms of depression. Also the results of the PSQ showed high levels of stress in both groups. Comparing the two groups of participants, the largest effect between the OG and IG was the dimension of “joy” of the PSQ. The IG reported to have less joy than the OG, but also less worries than the OG.

Table 8: PHQ and PSQ

	OG	IG	Significance (p)	Effect size (Cohen's d)
PHQ				
depression score ± SD	14.25 ± 5.19	16.42 ± 5.30	0.50	0.60
PSQ - subscales				
mean ± SD	0.58 ± 0.13	0.61 ± 0.16	0.43	0.29
worries ± SD	0.66 ± 0.24	0.55 ± 0.19	0.34	-0.72
tension ± SD	0.64 ± 0.19	0.72 ± 0.21	0.28	0.56
joy ± SD	0.35 ± 0.20	0.23 ± 0.18	0.30	-0.89
demand ± SD	0.34 ± 0.23	0.43 ± 0.17	0.24	0.63

Effect size: $d > 0.8$ = large effect, $0.5 < d < 0.8$ = medium effect, $0.2 < d < 0.5$ = small effect

PHQ: Patients Health Questionnaire, PSQ: Perceived Stress Questionnaire, SD: standard deviation

3.2.5.2 Eating disorder

Restraint, eating concerns, weight concerns, and shape concerns revealed similar results in IG and OG. Taken together, the EDE (Eating Disorder Examination) total score indicated that the OG and IG did not differ in their extent of eating disorder pathology. The subscales of the EDI showed noticeable differences between the OG and IG, especially in the subscale “social insecurity,” where the IG scored significantly higher than the OG (IG > OG: $p < 0.05$). Also, the mean scores of “body dissatisfaction,”

“ineffectiveness,” “interpersonal distrust,” and “interoceptive awareness,” were higher in the IG than in the OG. The subscales “perfectionism” and “maturity fears” were higher in the OG (Table 9). The two dimensions of the body image questionnaire (BIQ-20), the “Negative Evaluation of the Body” (NEB) and the “Perception of Body Dynamics” (PBD), were also shown in Table 9. There was an effect of the NEB when comparing the IG and OG (OG: 38.92; IG: 35.88). The PBD was 23.46 in the OG and 25.5 in the IG. Both, the results of the OG and the results of the IG indicate high rates of body image disturbances in the participants of this study.

Table 9: EDE, EDI and BIQ-20

	OG	IG	significance (p)	Cohen's d
EDE				
restraint	3.65 ± 1.77	3.55 ± 1.84	0.71	-0.08
eating concern	3.18 ± 1.61	3.20 ± 1.55	0.34	0.02
weight concern	3.65 ± 1.52	3.58 ± 1.95	0.66	-0.06
shape concern	4.41 ± 1.40	4.23 ± 1.46	0.55	-0.18
total	3.73 ± 1.47	3.64 ± 1.49	0.54	-0.09
EDI				
drive for thinness	30.09 ± 9.16	29.41 ± 11.14	0.8	-0.09
bulimia	16.36 ± 7.05	17.42 ± 8.54	0.71	0.19
body dissatisfaction	35.36 ± 11.20	41.75 ± 6.94	0.4	0.97
ineffectiveness	35.55 ± 8.71	40.83 ± 6.13	0.21	0.99
perfectionism	22.27 ± 3.82	20.58 ± 5.55	0.96	-0.5
interpersonal distrust	21.27 ± 7.58	26.41 ± 5.85	0.08	1.0
interoceptive awareness	35.18 ± 5.42	41.16 ± 8.72	0.1	1.16
maturity fears	26.82 ± 4.29	23.16 ± 6.55	0.23	-0.93
asceticism	26.09 ± 7.31	27.58 ± 5.65	0.98	0.32
impulse regulation	28.27 ± 4.94	27.33 ± 7.10	0.77	-0.22
social insecurity	26.27 ± 5.14	30.50 ± 5.70	0.02*	1.1
mean score	303.55 ± 28.20	326.17 ± 51.09	0.24	0.78
BIQ-20				
NEB (dimension 1)	38.92 ± 9.55	35.88 ± 6.71	0.327	-0.52
PBD (dimension 2)	23.46 ± 7.26	25.5 ± 6.46	0.562	0.42

* = significance p<0.05; effect size: d>0.8 = large effect, 0.5<d<0.8 = medium effect, 0.2<d<0.5 = small effect
 OG: outpatient group, IG: inpatient group, EDE: Eating Disorder Examination Questionnaire, EDI: Eating disorder Inventory, BIQ: Body Image Questionnaire, NEB: negative evaluation of the body, PBD: perception of body dynamics

3.3 ANEX pilot study: Correlates of physical activity

3.3.1 Commitment to exercise

The subjective importance of physical activity was measured with the Commitment to Exercise Scale (CES). The seventh item of the CES represents feelings of guilt when skipping a sports activity. CES_07 correlated significantly with accelerometry assessed PA parameters in all samples of the study (Table 10). Especially in the IG at follow-up, the CES_07 correlated significantly with the time spent in vigorous physical activity (VPA) ($p < 0.01$, $r = 0.791$). In the same sample there was a significant negative correlation between the CES_07 and the time spent in low physical activity (LPA) ($p < 0.01$, $r = -0.848$). Moreover, CES_07 correlated significantly with the time spent in moderate physical activity (MPA) in the OG ($p < 0.05$, $r = 0.721$) and with the time spent in VPA in the IG ($p < 0.05$, $r = 0.691$). A compilation of all correlations between commitment to exercise and objectively measured PA parameters is provided in the appendix.

Table 10: Correlation of the seventh item of the CES (feelings of guilt) with objectively measured physical activity parameters in groups

correlation		all	OG	IG	IG_FU
CES_07 with LPA	r	-0.319	-0.370	-0.134	-0.848**
	p	0.212	0.293	0.730	0.002
CES_07 with MPA	r	0.263	0.721*	0.227	0.049
	p	0.309	0.019	0.557	0.894
CES_07 with VPA	r	0.285	-0.122	0.691*	0.791**
	p	0.252	0.737	0.039	0.006
CES_07 with MVPA %	r	0.333	0.636*	0.391	0.494
	p	0.177	0.048	0.263	0.147

*= significance $p < 0.05$

**= significance $p < 0.01$

CES_07: seventh item of the Commitment to Exercise Scale – feelings of guilt when leaving out physical activity, OG: outpatient group, IG: inpatient group, IG_FU: inpatient group at follow-up, PA: physical activity LPA: light physical activity, MPA: moderate physical activity, VPA: vigorous physical activity, r: correlation coefficient

3.3.2 Reasons for exercise

Weight control as a reason for PA correlated significantly with objectively measured PA. Interestingly in the OG the correlation with percent of time in moderate to vigorous PA (MVPA) was positive, while in the IG, weight control as a reason for exercise correlated significantly negative with the percent of time in MVPA. In the IG there was a significantly positive correlation between health as a reason for exercise with steps/min ($p < 0.05$, $r = 0.821$), CPM ($p < 0.05$, $r = 0.815$) and especially percent in MVPA ($p < 0.01$, $r = 0.883$). In the OG no strong correlations were found; however, all of them were negative. Details of the correlations between reasons for exercise and objectively measured PA parameters can be found in the appendix.

Fitness, mood, physical attractiveness and tone as reasons for exercise did not correlate significantly with accelerometer assessed PA parameters. In the OG enjoyment as a reason for exercise correlated significantly negative with the time spent in low level PA (LPA). This is shown in Figure 14.

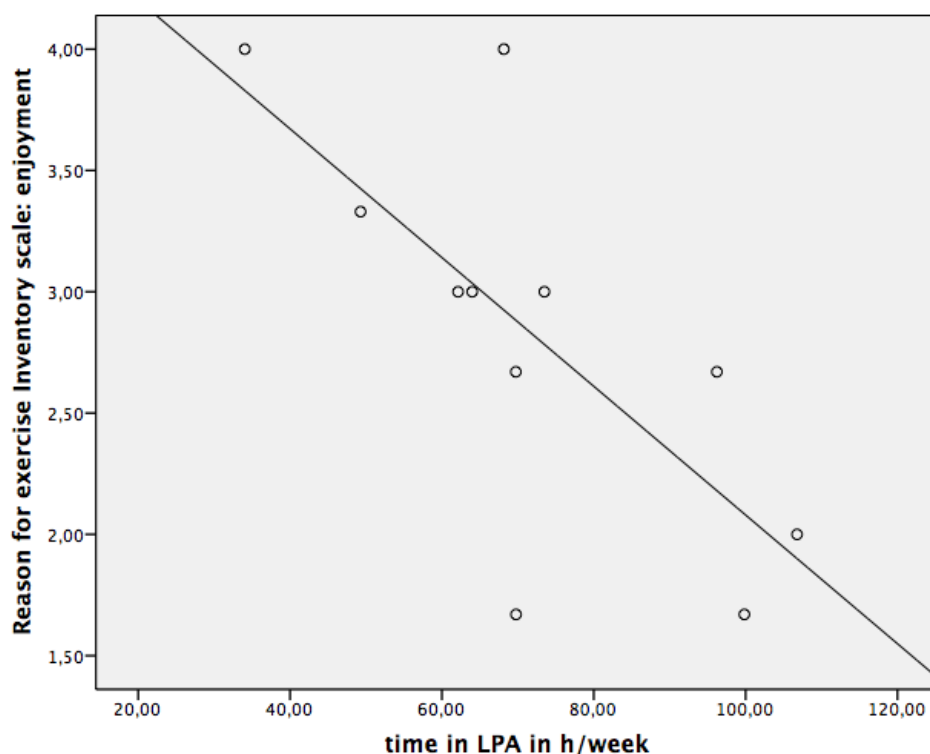


Figure 14: Correlation of enjoyment as reason for exercise and objectively measured time in LPA in the outpatient group

LPA: light physical activity, h/week: hours per week

3.3.3 Body image

There were only weak correlations between objectively measured PA and the first dimension of the Body Image Questionnaire (BIQ), “negative evaluation of the body” (NEB). The second dimension, “perception of body dynamics” (PBD) correlated significantly with counts per minute (CPM) in the OG ($p < 0.05$, $r = 0.647$). Additionally, PBD and the time spent in vigorous PA (VPA) correlated significantly in the OG ($p < 0.05$, $r = 0.689$). In the IG, PBD correlated significantly with the percent of time spent in moderate to vigorous PA (MVPA). In the whole sample there was a significant correlation between dimension 2 (PBD) of the BIQ and CPM ($p < 0.01$, $r = 0.584$). This is shown in Table 12. More correlations between body image and objectively measured PA parameters can be found in the appendix.

Table 11: Correlation of perception of body dynamics (PBD) with objectively measured physical activity parameters

correlation		all	OG	IG	IG_FU
BIQ-20 (PBD) with CPM	r	0.584**	0.647*	0.551	0.335
	p	0.009	0.031	0.157	0.417
BIQ-20 (PBD) with MVPA %	r	0.506*	0.287	0.753*	0.551
	p	0.027	0.392	0.031	0.157

* = significance < 0.05 ,

** = significance < 0.01

OG: outpatient group, IG: inpatient group, IG_FU: Inpatient group at follow-up, BIQ: Body Image Questionnaire, PBD: perception of body dynamics, CPM: counts per minute, VPA: vigorous physical activity, MVPA%: percent of time spent in moderate to vigorous physical activity, r: correlation coefficient

3.3.4 Depression

Figure 15 demonstrates a significant correlation between the depression score of the PHQ and the accelerometer assessed counts per minute (CPM) in the whole sample ($p < 0.5$, $r = -0.514$).

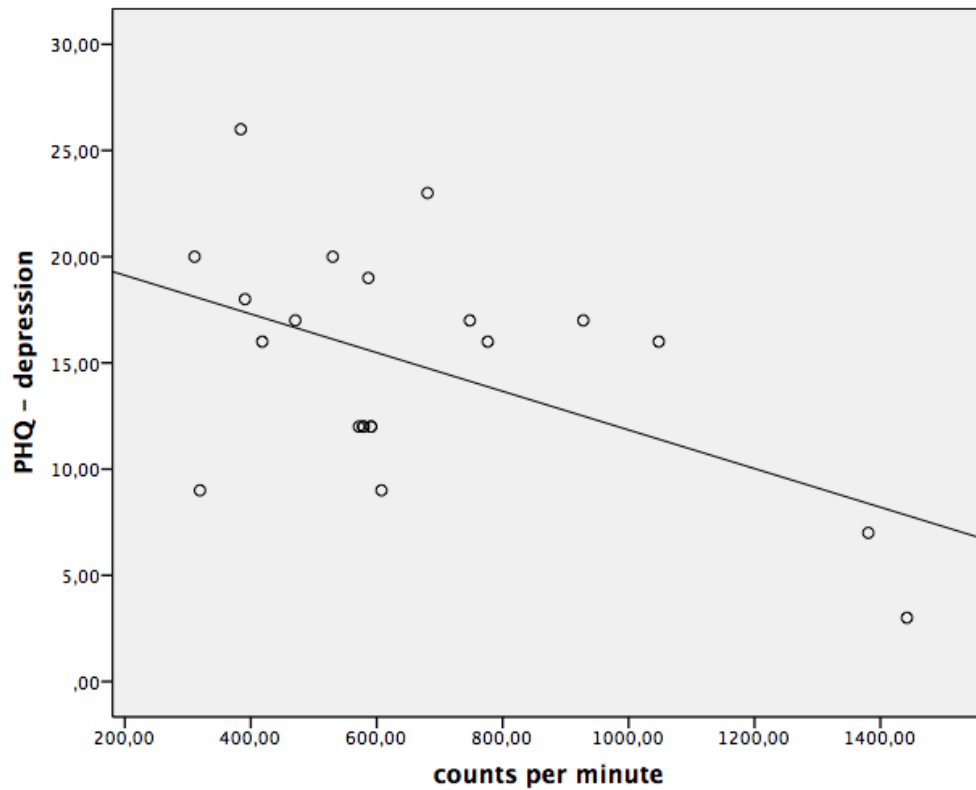


Figure 15: Correlation of depression (PHQ) and objectively measured counts per minute in all participants

PHQ: Patient Health Questionnaire

3.3.5 Stress

There was a significant correlation between the PSQ mean scale and the percent of time spent in MVPA ($p < 0.01$, $r = 0.568$) in the full sample. There was also a significantly negative correlation between worries as an item of the PSQ and time spent in VPA, especially in the OG ($p < 0.01$, $r = -0.788$) and in the whole sample ($p < 0.01$, $r = -0.606$), but also in the IG ($p < 0.05$, $r = -0.739$). Additionally, in the OG and in the full sample there was a significant correlation between worries and steps per minute (whole sample: $p < 0.05$, $r = -0.451$; OG: $p < 0.05$, $r = -0.635$) and between worries and percent of time in MVPA (whole sample: $p < 0.05$, $r = -0.527$; OG: $p < 0.05$, $r = -0.702$). A significant positive correlation was found between joy as an item of the PSQ and objectively measured PA: joy and steps per minute correlated significantly in the whole sample ($p < 0.05$, $r = 0.473$), in the IG ($p < 0.01$, $r = 0.852$) and in the IG_FU ($p < 0.01$, $r = 0.813$). Joy and time spent in MPA correlated significantly in the whole sample ($p < 0.05$, $r = 0.434$), in the IG ($p < 0.05$, $r = 0.787$), and especially in the IG_FU ($p < 0.01$, $r = 0.815$). An overview of all correlations of worries and joy with different PA parameters in the different samples can be found in Tables 13 and 14. A more detailed compilation of PSQ parameters and objectively measured PA parameters can be found in the appendix.

Table 12: Correlation of worries (PSQ) with objectively measured physical activity parameters

correlation		all	OG	IG	IG_FU
worries with steps/minute	r	-0.451*	-0.635*	-0.391	-0.447
	p	0.040	0.049	0.299	0.227
worries with MPA (h/week)	r	-0.178	-0.347	-0.209	-0.344
	p	0.441	0.326	0.620	0.365
worries with VPA (h/week)	r	-0.606**	-0.788**	-0.739*	-0.622
	p	0.004	0.007	0.036	0.074
worries with MVPA %	r	-0.527*	-0.702*	-0.547	-0.506
	p	0.014	0.024	0.128	0.165

* = significance <0.05,

** = significance <0.05,

OG: outpatient group, IG: inpatient group, IG_FU: Inpatient group at follow-up, PSQ: Perceived Stress Questionnaire, MPA: moderate physical activity, VPA: vigorous physical activity, MVPA%: percent of time spent in moderate to vigorous physical activity, r: correlation coefficient

Table 13: Correlation of joy (PSQ) with objectively measured physical activity parameters

correlation		all	OG	IG	IG_FU
joy with steps/minute	r	0.437*	0.090	0.852**	0.813**
	p	0.048	0.804	0.004	0.008
joy with MPA (h/week)	r	0.434*	-0.041	0.787*	0.815**
	p	0.050	0.910	0.020	0.007
joy with VPA (h/week)	r	0.338	0.360	0.817*	0.786*
	p	0.134	0.307	0.013	0.012
joy with MVPA %	r	0.456*	0.142	0.865**	0.790*
	p	0.038	0.696	0.003	0.011

* = significance <0.05,

** = significance <0.05,

OG: outpatient group, IG: inpatient group, IG_FU: Inpatient group at follow-up, PSQ: Perceived Stress Questionnaire, MPA: moderate physical activity, VPA: vigorous physical activity, MVPA%: percent of time spent in moderate to vigorous physical activity, r: correlation coefficient

3.3.6 Eating behavior

In the whole sample, taking all participants of all groups together, there was a positive correlation of weight concern as an item of the EDE with PA parameters (Table 15): Counts per minute (CPM) correlated significantly with weight concern ($p < 0.05$, $r = 0.045$) and time spent in vigorous PA (VPA) also correlated significantly with weight concern ($p < 0.01$, $r = -0.626$). In the IG a significant correlation between weight concern and VPA was found ($p < 0.05$, $r = -$

0.772). There were two significant correlations between shape concern and PA in the full sample: CPM correlated significantly with shape concern ($p < 0.05$, $r = -0.520$) and time spent in VPA correlated significantly with shape concern, too ($p < 0.01$, $r = -0.611$). Additionally, there was a significant correlation between shape concern and time spent in VPA in the IG ($p < 0.05$, $r = -0.730$). There was no correlation of any item of the EDE with any PA parameter in the IG at follow-up (Table 15).

Table 14: Correlation of weight concern and shape concern (EDE) with objectively measured physical activity parameters in groups

correlation		all	OG	IG	IG_FU
Weight concern with CPM	r	-0.441*	-0.308	-0.521	-0.595
	p	0.045	0.421	0.150	0.091
Weight concern with VPA (h/week)	r	-0.626**	-0.433	-0.772*	-0.534
	p	0.002	0.245	0.025	0.139
Shape concern with CPM	r	-0.520*	-0.619	-0.222	-0.067
	p	0.016	0.075	0.566	0.864
Shape concern with VPA (h/week)	r	-0.611**	-0.730*	-0.506	-0.328
	p	0.003	0.025	0.200	0.388

* = significance < 0.05 ,

** = significance < 0.01 ,

EDE: Eating disorder Examination, OG: outpatient group, IG: inpatient group, IG_FU: Inpatient group at follow-up, CPM: counts per minute, VPA: vigorous physical activity, r: correlation coefficient

Social insecurity as an item of the Eating Disorder Inventory (EDI) and objective PA parameters interrelated variously in the OG. CPM correlated significantly negative with social insecurity ($p < 0.05$, $r = -0.769$) and time spent in VPA correlated significantly with social insecurity ($p < 0.05$, $r = -0.702$). In the whole sample there was a significant negative correlation between ineffectiveness as an item of the EDI and CPM ($p < 0.05$, $r = -0.486$). This negative correlation between ineffectiveness and CPM also appeared in the OG ($p < 0.05$, $r = -0.687$). Moreover, there was a significant correlation between ineffectiveness and time spent in VPA in the OG ($p < 0.05$, $r = -0.680$). There could not be found any correlation between EDI items and accelerometry assessed PA parameters in the IG and in the IG at follow-up. A table with an overview of relevant

correlations between social insecurity and ineffectiveness (EDI) and objectively measured physical activity parameters can be found in the appendix.

3.4 Refusals, dropouts and missing data

During the ANEX pilot study 47 female patients with AN were introduced to the study. They were all patients at the Department of Psychosomatic Medicine and Psychotherapy at the University of Tuebingen. All of the 47 patients filled out PSQ, PHQ, EDI and the EDE and they all were registered with age, BMI and duration of illness. All patients that refused to participate were asked for their reasons. Reported reasons for refusal were mainly:

- Too much stress in general
- Fear of observation
- Feeling of pressure while wearing the accelerometer device
- That the instructor could think that the patient was lazy if there was not measured enough activity with the ActiGraph (this was the case even if the instructor explained that the amount of activity was not relevant)
- Fear that the ActiGraph would control them
- Patients did not want to talk about their reason for refusal
- patients were injured and stated that an activity measurement would not make sense

Twenty-five of the 47 females decided to take part in the ANEX pilot study. Two of the 25 participants dropped out during the process of the study, because they were stressed too much by wearing the ActiGraph. They reported that they had to think about the device all the time and that it was uncomfortable to wear. Two patients lost their accelerometer device and never found it again, so that measurement had to be repeated. One patient was extremely ambivalent. She decided not to participate on the first day and contacted the instructor on the next day because she wanted to participate. One day later she decided again not to participate. The instructor let her time to think. Finally, she participated. The process of inclusion including dropouts, refusals, and reasons for missing data is demonstrated in Figure 16.

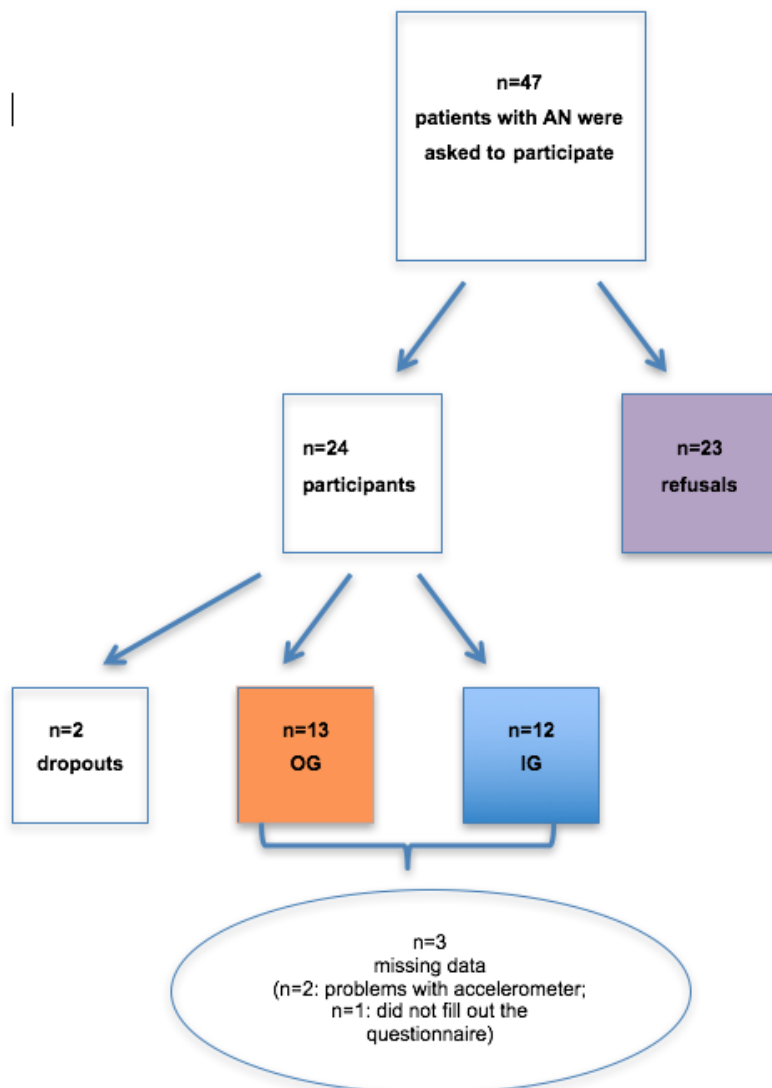


Figure 16: Process of study inclusion with study refusals, dropouts and missing data

AN: Anorexia nervosa, OG: outpatient group, IG: inpatient group

Comparing characteristics of study participants and study refusals, the mean BMI and the mean age were similar, while the duration of illness was slightly longer in the study participants (Table 16).

Table 15: BMI, age and duration of illness in study participants and study refusals

	study participants (whole sample)	study refusals	significance (p)
BMI ± SD	15.81 ± 1.93	15.35 ± 1.79	0.44
Age (years) ± SD	24.09 ± 4.98	24.57 ± 8.00	0.81
Duration of illness (years) ± SD	7.82 ± 5.93	5.91 ± 5.38	0.27

BMI: Body Mass Index, SD: standard deviation

The graduation level was higher in the study participants. Study participants had more university degrees and high school degrees (Figure 17).

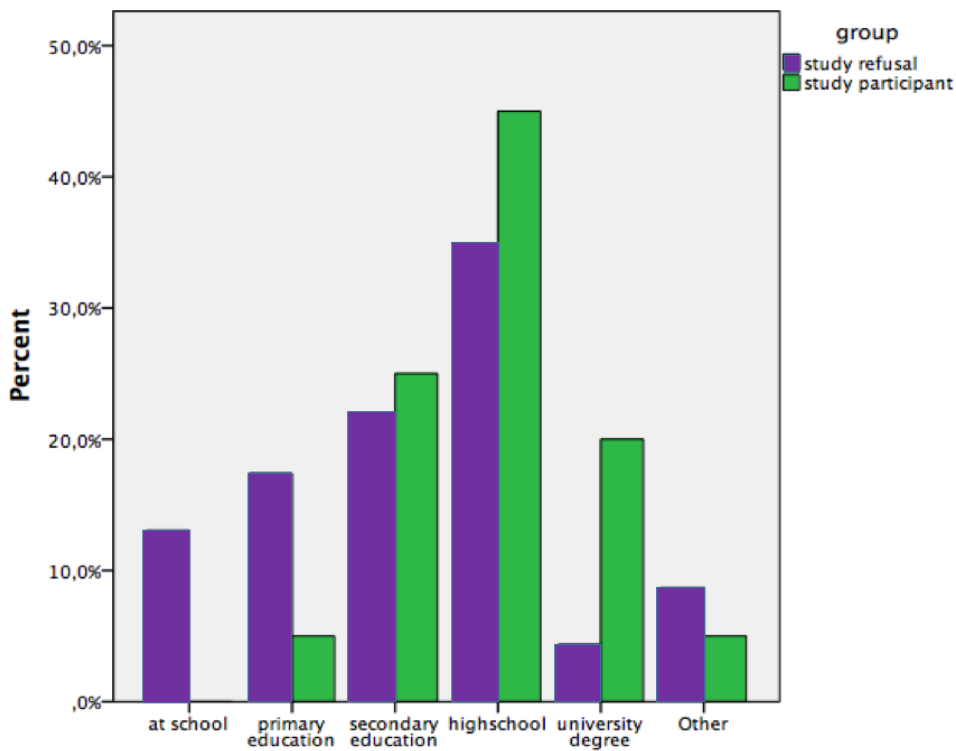


Figure 17: Percentage of the groups at different graduation levels

The depression score of the PHQ also indicated similar values in the study participants and the study refusals as to be seen in Table 17. The perceived stress was higher in the study refusals. The worries were stated to be especially

higher in study refusals and they reported less joy than the participants. The results of the PSQ with the four dimensions “worries,” “tension,” “joy,” and “demand” are shown in Table 17.

Table 16: PHQ and PSQ in study participants and study refusals

	study participants (whole sample)	study refusals	significance (p)	effect size (Cohen's d)
PHQ				
depression score	15.25 ± 5.68	15.74 ± 7.17	0.81	-0.11
PSQ				
Mean	0.59 ± 0.15	0.66 ± 0.19	0.17	-0.58
worries	0.60 ± 0.24	0.73 ± 0.28	0.10	-0.71
tension	0.67 ± 0.21	0.71 ± 0.28	0.61	-0.23
joy	0.31 ± 0.20	0.22 ± 0.18	0.14	0.67
demand	0.38 ± 0.22	0.39 ± 0.21	0.94	-0.07

effect size: $d > 0.8$ = large effect, $0.5 < d < 0.8$ = medium effect, $0.2 < d < 0.5$ = small effect
 PHQ: Patient Health Questionnaire, PSQ: Perceived Stress Questionnaire

Comparing the eating disorder questionnaires, study participants and study refusals had similar results. This is demonstrated in Table 18.

Table 17: EDE and EDI in study participants and study refusals

	study participants	study refusals	Signifi- cance (p)	effect size (Cohen's d)
EDE				
restraint	3.21 ± 1.89	3.79 ± 2.06	0.37	-0.41
eating concern	2.86 ± 1.69	3.54 ± 1.70	0.22	-0.57
weight concern	3.4 ± 1.67	4.26 ± 1.42	0.92	-0.78
shape concern	3.94 ± 1.62	4.54 ± 1.47	0.23	-0.55
total	3.37 ± 1.53	4.03 ± 1.54	0.19	-0.61
EDI				
drive for thinness	29.11 ± 10.66	28.28 ± 12.72	0.83	0.10
bulimia	15.95 ± 7.69	17.50 ± 10.87	0.62	-0.23
body dissatisfaction	37.37 ± 9.93	37.78 ± 11.59	0.91	-0.05
ineffectiveness	37.47 ± 8.20	38.78 ± 11.73	0.70	-0.18
perfectionism	22.26 ± 4.65	19.17 ± 6.01	0.09	0.81
interpersonal distrust	23.63 ± 7.51	23.89 ± 5.83	0.91	-0.05
interoceptive awareness	37.32 ± 8.23	36.89 ± 10.65	0.89	0.06
maturity fears	24.84 ± 6.18	27.78 ± 7.34	0.20	-0.61
asceticism	26.53 ± 6.74	24.72 ± 5.59	0.38	0.27
impulse regulation	27.53 ± 5.89	29.44 ± 7.64	0.40	-0.40
social insecurity	28.31 ± 6.24	29.22 ± 7.05	0.68	-0.19
mean score	310.32 ± 48.99	313.44 ± 67.98	0.87	-0.07

effect size: $d > 0.8$ = **large effect**, $0.5 < d < 0.8$ = medium effect, $0.2 < d < 0.5$ = small effect
 EDE: Eating Disorder Inventory, EDI: Eating Disorder Examination

4 DISCUSSION

The aim of this thesis was the establishment of accelerometry as a method to measure physical activity (PA) in anorexia nervosa (AN) and the assessment of its feasibility. In a systematic review all previous studies using accelerometry in AN were included. Subsequently, in the ANEX pilot study physical activity was measured objectively with the ActiGraph. This is the first study that uses several different output parameters of accelerometry to make statements not only about the quantity of activity, but also about the levels of activity. It also makes it possible to compare the results with diverse previous data of PA assessments in AN (Gummer et al., 2015) Given the fact that study refusals occurred frequently in this study and in similar previous studies (Bratland-Sanda et al., 2010) (Bratland Sanda et al., 2010b) (Keyes et al., 2015), this is a reflection of and provides insight into the background of PA in AN. So not only objective PA and self-perceived PA, but also commitment to exercise, reasons for exercise, eating disorder and general psychopathology were measured in outpatients and in inpatients. The inpatient group performed a second measurement one month after their discharge from the hospital. Thus, the development of PA after hospitalization could also be analyzed.

4.1 Establishment of accelerometry in anorexia nervosa

For the establishment of accelerometry as a standard method of PA assessment in AN an overview of the literature was made:

“In this first systematic review about PA measurement with accelerometry in AN, 20 studies were identified. The study populations consisted of females with an average mean BMI of 16.4 kg/m² and an average age of 24.4 years. Study population size varied from 8 to 59 women. PA assessment was fulfilled by different types of accelerometry devices, in most trials combined with questionnaires or further experimental measurements like ambient temperature, bone mineral density, or metabolic rate. Mean duration of PA assessment was 4.5 consecutive days. Most studies included one single PA measurement in the

first week of inpatient treatment, but the studies varied a lot with regard to the time of assessment. Purposes and results of the included studies appear heterogeneous, due to differing paradigms and outcomes within heterogeneous samples. Since some studies included only very few participants with consequential statistical limitations, statements have to be discussed conservatively. We therefore clustered the studies into five different groups. The first cluster of studies mainly concerned methodology, more precisely the validation of accelerometry in general or the comparison of accelerometry with other methods. These trials showed that accelerometry is a valid and reliable method of PA assessment in AN. The second cluster concentrated on the comparison of PA quantity in either AN and healthy controls, or in high and low exercising AN. They showed that AN had higher PA levels than healthy controls and that high exercising AN patients had more severe psychopathology, but the findings are contradictory. The third cluster discusses studies including women who have recovered from AN. These studies indicate that PA level stays abnormal for about half a year after recovery. The fourth cluster of studies aimed at finding reasons for HLEPA in AN and found that hormones like cortisol or leptin, BMI, or the ambient temperature may play a role. The fifth cluster of studies focused on the treatment to find how PA interacted with therapy. Studies from different groups additionally investigated psychopathology, where the results were conflictive about whether or not ED psychopathology and PA levels were associated.

Although it is not possible to draw a synthesis of all studies included in this review, we tried to find generally valid statements concerning PA in AN.” (Gummer et al., 2015)

4.1.1 Segmentation of the study population

“Concerning the sample characteristics, a segmentation of the study population into a high and a low exercise type, as presented in four studies of this review, should be discussed (Turner, Bryant-Waugh, & Peveler, 2009). It seems that high-exercisers need different key aspects in their treatment and longer support and supervision after inpatient therapy (K. Giel et al., 2013). With respect to this, it would make sense to define common criteria for a HLEPA subtype of AN

and a common terminology for that subtype. As this classification should be used in a daily clinical context, it would be reasonable to utilize a simple tool, such as that as proposed by Zipfel et al. (2013). The Eating Disorder Inventory (EDI-SC) item 'What percentage of your exercise is aimed at controlling your weight?' was used to distinguish between high-level and low-level exercisers by using a cut-off set at < 50%. Another classification suggested by Davis et al. (1997), taking into account the accelerometry output, implies that an objective PA assessment becomes standard therapy in AN, which is already implemented in some ED centers. With knowledge about HLPAs, this dysfunctional behavior can be addressed in cognitive-behavioral interventions, integrated in a background of eating behavior, and can affect regulation and personality (perfectionism, rigidity, or obsessive-compulsive traits, etc.). Additionally, physical therapy regarding HLPAs should be part of a special treatment for AN patients with HLPAs." (Gummer et al., 2015)

4.1.2 Evaluation of devices

"Concerning PA assessment, accelerometry is the most user-friendly method to objectively measure PA in AN. There are many slightly different types of validated accelerometers used in the studies. One type of accelerometer, for example, measures the heart frequency besides the triaxial accelerometry so that it can be seen when the study participant does not wear it. The disadvantage of this device is the usability and wearing comfort, because it has to be attached to the breast, which can again result in worse compliance of the participant. This is also true for a type of accelerometer armband, which additionally measures galvanic skin responses, heat flux, and skin temperature and gives clues when the participant does not wear the device. This can be important information, especially in inactive participants, because accelerometry is not able to distinguish between a person that does not move and a device that lies next to a person. The advantages of devices that only measure accelerometry are weight, price, and wearing comfort." (Gummer et al., 2015)

4.1.3 Categorization of activity levels

“The categorization of activity levels in AN is sparsely described in the studies and varies greatly. A generally accepted validated categorization of Sedentary PA, Low PA, and MVPA (moderate-vigorous physical activity) should get established with regard to the fact that devices can be worn as an armband, on the waist, or on the ankle. Proposals for classification have been made by Bouten et al. (1996), Bratland Sanda et al. (2010) and Kostrzewa et al. (2013).” (Gummer et al., 2015)

4.1.4 Combination of methods

“A combination of accelerometry and activity diaries, as well as activity questionnaires, like CES, is important. Subjective PA assessment underestimates PA in AN, shown by El Ghoch (2013) and van Elburg (2007). An additional item can be a nurse evaluation, as shown by van Elburg (2007). With such a combination of items, misuse of accelerometry or underestimating questionnaires can be detected.” One method that helps in this context is the DLW technique, because it cannot be influenced by the participant and offers exact values of basal metabolic rate and total daily energy expenditure. The disadvantage of not providing activity patterns in time can be eliminated by combining it with accelerometry. DLW in combination with accelerometry would be the most exact PA assessment method in AN; however, to our knowledge this combination has not been used.” (Gummer et al., 2015)

4.1.5 Treatment and recovery

“The time of assessment in the investigated studies was mostly in the first week of inpatient treatment, and in most trials only once. To get an idea of how treatment interferes with levels of PA in AN and to get to know how treatment has to be changed for adequate recovery rates (as well as in patients with HLPAs), data with more than one PA measurement is needed. Measurements before the start of a treatment are especially required, which, to our knowledge, have not been fulfilled at all. More studies comparing PA between outpatients and inpatients would also be important to find out how inpatient treatment contributes to HLPAs (Keyes et al., 2015). There is evidence (Kaye et al., 1986)

that weight gain in inpatient settings goes along with increased levels of PA, which could be assumed as a purging behavior to control weight during refeeding. However, there is considerable evidence to suggest that problematic exercise in the eating disorders is not just determined by weight control methods; aspects such as rigidity, compulsivity, and affect regulation are also important features that must be addressed (Meyer, Taranis, Goodwin & Haycraft, 2011).

Treatment of AN could often be modified in a way that patients with HLPAs are also treated adequately. The study of Kostrzewa et al. (2013) has to be taken into account. They found that there were greater changes in body composition in HLPAs patients with AN, meaning that fat tissue tends to grow faster in abdominal regions than at the extremities, which could be an understandable reason for treatment dropout or relapse, and should be a therapy issue (Giel et al., 2013).

Important for the modification of treatments would also be the physiological factors discussed in some studies of this review. Hypoleptinemia is associated with HLPAs. The administration of leptin has been successful in rats (Exner et al., 2000). As hypercortisolism and PA levels also seem to interfere, cortisol-antagonists are discussed, but, to our knowledge, have never been tried in humans.

In the two studies with recovered AN patients it can be seen that HLPAs are still an issue after recovery, which implies that it is important to supervise those patients and make follow-up examinations (Giel et al., 2013). As muscle strength interferes with physical fitness and BMD in AN, a training program with specialized exercise professionals could be a helpful supplement in the treatment and improve outcomes. A good example of a high-intensive resistance training program is presented by Fernandez-del-Valle et al. (2014)" (Gummer et al., 2015)

4.1.6 Psychopathology

"The relation between psychopathology and levels of PA is controversially discussed. Further research is needed to objectively compare measured PA levels in AN with features like ED psychopathology, anxiety scores, and

personality (Keyes et al., 2015). This can help in understanding the psychological background of PA in AN, if HLPAs are a method of regulating negative effects or anxiety or a result of a compulsive personality trait (Lloyd, Fleming, Schmidt, & Tchanturia, 2014).” (Gummer et al., 2015)

4.1.7 Dropouts

“What attracts attention regarding the study population is the number of dropouts. This arose mainly because of missing data from the accelerometer (also in more recent studies), showing that the accelerometer technique can still be improved and the choice of the accelerometer should be made carefully, even if differences between the devices are not crucial (Troost et al., 2005). Missing data from a device not only includes malfunction of the device itself, but also misuse of the device by the participant; how the missing data came about cannot always be detected afterwards. Five authors describe cases of not enough wear time or even no wear time at all. Bratland-Sanda et al. (2010) mention consecutive patients that even refused participation. Regarding those results and having problematic experiences with refusal and compliance around PA assessment, we propose that objective PA assessment in AN has not yet been discussed in a comprehensive way. It seems remarkable that not even half of the discussed trials of this review mention problems with refusal or compliance, while the rest does not mention this topic at all. We assume that wearing an accelerometer device represents a big problem for some patients with AN, especially in an inpatient setting, because it seems to constrain autonomy. Patients with AN show high needs for autonomy, which is already constrained in inpatient setting because eating behaviour is observed closely. So PA behaviour remains one behaviour that can hardly be controlled by anyone. This could make it more difficult to recruit participants for studies and also understandable as to why patients misuse the devices. Furthermore, it proves the high importance of PA for patients with AN.” (Gummer et al., 2015)

4.2 ANEX: Presentation and interpretation of the results

4.2.1 Alignment of the physical activity data

The World Health Organizations (WHO) global recommendation for health of adults indicates that everyone should perform 150 minutes of moderate PA per week or 75 minutes of vigorous PA per week or any equivalent combination of both activity levels. In our study the participants performed between 4.53 hours and 5.77 hours per week in moderate PA which is around 300 minutes per week in moderate PA and 0.88 to 1.76 hours in vigorous PA, which equates to around 60 minutes per week. Taken together the patients of our study seem to perform more than enough PA according to the WHO recommendations.

The Robert-Koch-Institute found in a survey that only 18.4% of healthy German females aged 18 to 29 years performed more than 2.5 hours of moderate to vigorous PA (MVPA) per week (Krug et al., 2013). Performing five or more hours of MVPA per week on an average, the participants of our study seem to be more active than the average age matched German healthy female. These data are based on subjective PA assessments. Unfortunately, there is not much objectively assessed data about PA in healthy individuals (Loyen et al., 2016). "Objective data of adults across Europe is currently limited." (Loyen et al., 2016) However, two studies assessed PA with the help of accelerometry: Cerin et al. (2014) performed a cross-sectional study in countries all over the world and found that people in Baltimore, USA, are the least physically active. They performed 25 minutes of MVPA per day, on an average. People in Christchurch, New Zealand were the most active with almost 50 minutes of MVPA per day. Similar results of accelerometry-based PA assessment in healthy individuals have been published by van Dyck et al. (2015) who measured an MVPA of 36 minutes/day as an average of measurements at ten different sites throughout the world. Also in that study, the amount of time in MVPA varied significantly from 29.2 minutes per day in the USA up to 51.0 minutes per day in Spain. Participants in the ANEX pilot study performed a mean of 50 minutes of MVPA per day. This shows again that, on an average, the participants of this study were more active than most healthy individuals.

Comparing objectively measured PA levels of this study with accelerometer assessed activity levels in patients with AN, a detailed compilation of the individual accelerometer outputs can be seen in Table 19. In comparison to all previous studies the participants of this study have a high, but not excessively high, level of PA. Comparison of PA has to be made very carefully because of different devices, different outputs, and different units. The output that has been used most frequently in the past was counts per minute (CPM). The percent or time in MVPA has also been used often, while steps, kcal and metabolic equivalents (METs) have been only used once or twice. Keyes et al. (2015) measured significantly lower counts per day in outpatients with AN than we did (Keyes: 249.73 CPM; ANEX: 693 CPM). It is not possible to compare those two values, because Keyes et al. (2015) measured day and night, and in our study we instructed the patients not to wear the ActiGraph while sleeping. However, this explains a lower average number of counts per minute. Kostrzewa et al. (2014) divided his sample into high level PA (HLPa) and low level PA (LLPA). Our results were somewhat comparable with the HLPa even if we did not divide the sample into high and low exercisers. (Kostrzewa: LLPA: 220,000 counts/day, HLPa: 400-550,000 counts/day; ANEX: 484,643 – 552,279 counts/day). Comparing our results with the results of Bratland-Sanda et al. (2010b) who divided the sample into excessive exerciser (EE) and non-excessive exerciser (NEE), our results rather resemble the results of the EE (Table 19). There have been more attempts to assess PA in AN than shown in Table 19, but the accelerometer devices were older and the outputs were not comparable with our results.

Table 18: Objectively measured physical activity in anorexia nervosa (2005 to 2016)

study	counts	steps	MVPA	kcal	METs
ANEX Pilot study	- OG: 693 CPM ≈ 484,643 counts/day - IG: 652 CPM ≈ 552,279 counts/day - IG_FU: 670 CPM ≈ 551,632 counts/day	- OG : 13.17 steps/min ≈ 9,210 steps/day - IG: 12.72 steps/min ≈ 10,807.68 steps/day - IG_FU: 11.77 steps/min ≈ 9,690.59 steps/day	- OG: 8.75% ≈ 61 min/day - IG: 7.35% ≈ 62 min/day - IG_FU: 8.43% ≈ 69 min/day	- OG: 262 kcal/day - IG: 249 kcal/day - IG_FU: 303 kcal/day	- OG: 1.20 METs - IG: 1.15 METs - IG_FU: 1.20 METs
Keyes et al. , 2015	- Outpatients: 249.73 CPM - Inpatients: 223.63 CPM				
Fernandez-del-Valle et al., 2014			- Control: 49.62 min/day in MVPA - Intervention 44.81 min/day in MVPA		
Kostrzewa et al., 2014	- LLPA: ≈ 220,000 counts/day - HLPA: ≈ 400-550,000 counts/day				
Hofmann et al., 2014		- Purging AN: 11,011 steps/day - Restricting AN: 9,804 steps/day - Atypical AN: 9,307 steps/day			- Purging AN: 1.85 METs - Restricting AN: 1.83 METs - Atypical AN: 1.80 METs
EIGHoch et al., 2013		8563.1 steps/day			
Alberti et al., 2013			99.5 min/day in MVPA		
Carrera et al., 2012	- Warm group: 230,068 counts/day - Cold group: 347,266 counts/day		- warm group: 3.78 % in MVPA - cold group: 6.47 % in MVPA		
Dellava et al., 2012	91,762 counts/day (weight recovered AN)				
Bratland-Sanda et al., 2010	- Admission: EE: 844 CPM, NEE: 526 CPM - Midway inpatient therapy: EE: 649 CPM, NEE: 550 CPM - Discharge: EE: 752 CPM, NEE: 403 CPM				
Hechler et al., 2008	842 CPM		103 min/day in MVPA		
Birmingham et al., 2005				251.1 kcal/day	

ANEX: anorexia nervosa and exercise, OG: outpatient group, IG: inpatient group, IG_FU: inpatient group at follow-up, AN: anorexia nervosa, PA: physical activity, kcal: kilocalories, MET: Metabolic Equivalent of Task, MVPA: moderate to vigorous physical activity, CPM: counts per minute, EE: excessive exerciser, NEE: non-excessive exerciser, HLPA: high level physical activity, LLPA: low level physical activity

Self-perceived PA assessment has been used much more often than accelerometry, and the IPAQ is one of the most often used methods. In the review of Loyen et al. (2016) 25 articles measuring physical activity in the general population in Europe were included. Sixteen of those studies used the IPAQ. The results of the included studies vary significantly. Forty-five minutes per week in moderate to vigorous PA (MVPA) were measured in Malta, while 960 minutes per week in MVPA have been assessed in the Netherlands (Loyen et al., 2016). In the ANEX pilot study the AN patients had a mean of 852 minutes per week in MVPA in the OG and 155 minutes per week in the IG. So the outpatients of the ANEX pilot study reported very high levels of PA compared with healthy individuals, while the inpatients reported rather low PA levels compared with healthy individuals. The reasons for the large differences of self-perceived PA levels between inpatients and outpatients are discussed below.

4.2.2 Comparison of outpatients and inpatients

4.2.2.1 Objective physical activity

There were no substantial effects in objectively measured PA between the IG and the OG. Taking weak effects into account, the IG had a longer duration of PA per day, meaning that the time spent active was higher in the IG than in the OG. The reason for this could be the longer wear time of the ActiGraph device in the IG. Longer wear time comes about as a result of time spent in bed or showering where the participants were instructed not to wear the ActiGraph (Troost, Mclver, & Pate, 2005) (P.S. Freedson, Melanson, & Sirard, 1998). Another reason for a longer wear time of the ActiGraph device could have been better compliance (Gummer et al, 2015). Comparing levels of activity, the percentage of time in MVPA was slightly lower among the IG. This is confirmed when comparing the number of steps per minute, the number of kilocalories per day and the counts per minute. Those parameters are not dependent on the wear time because their total values have been divided by the wear time before the final calculations. The IG was slightly less active than the OG, which supports our assumption. To conclude, the accelerometry data showed that the

inpatients were active for a longer period of time with less intensity, while the outpatients were active for a shorter period of time with higher intensities. This effect can be explained by the patients' setting: Inpatients do not have to go to work and they have a lot of time during the day, so they are able to spend more time being active. Additionally, inpatients tend to be more compliant because they are controlled by the inpatient staff if they wear the ActiGraph. The slightly lower intensities of PA in the IG can be explained because inpatients were sicker, more underweight and weaker than the outpatients, so their drive to exercise could be already satisfied by low PA (LPA) (Keyes et al., 2015). LPA includes, for example, walking which was indicated as a frequent activity by the participants of this study. The OG had slightly higher mean BMI, shorter duration of illness and fewer comorbidities. It can, therefore, be assumed that they were stronger than the IG which explains that they tolerated higher levels of PA, meaning a higher percentage of time was spent in moderate to vigorous PA (MVPA). One previous study also compared the objectively measured PA levels of outpatients and inpatients with AN (Keyes et al., 2015). With the help of accelerometry assessment they found no differences in accelerometer assessed PA, similar to this study. However, there was a tendency toward fewer counts per minutes (CPM) in inpatients than in outpatients. CPM were the only output of accelerometry documented by Keyes et al. (2015), so it was not possible to compare patterns of activity in a more detailed way. This shows that outpatients could be more active than inpatients, which is problematic because it is not controlled in any way. Additionally, it can be seen that a certain control, for example by inpatient staff could help to increase the wear time of the accelerometer.

4.2.2.2 Subjective physical activity

In contrast to the results of the accelerometer assessed data, the self-perceived measurement of PA showed significant differences between inpatients and outpatients. A detailed discussion of the reasons for the differences between accelerometry measured PA and self-perceived PA can be found below. Outpatients reported significantly higher performed vigorous PA (VPA) and significantly higher kilocalories spent per day than inpatients. The OG reported

to be active twice as long as the IG, meaning the total amount of activity during one week. The OG also reported spending three times as much time in moderate to vigorous PA (MVPA) than the IG with higher perceived intensities of PA in the OG. Moreover, all other parameters of subjectively measured PA are higher in the OG. The commitment to exercise has been shown to be significantly higher in the OG than in the IG. The OG seemed to estimate their activity much higher than the IG, but if objectively measured there is not a big difference between the activity levels of the two groups. One reason for this can be that the IG underestimated their PA while at the same time the OG overestimated their PA. Another reason could be a different sense of what can be defined as PA. Walking, for example, does not count as PA for some patients with AN. (Bratland-Sanda, Sundgot-Borgen, et al., 2010a). Findings like these have also been made by Keyes et al. (2015). They found that the AN outpatients reported more MVPA than AN inpatients and healthy controls, even though when objectively measured, there was no difference in PA. Alberti et al. measured subjective PA by using the IPAQ, and they found much higher values for MVPA compared to this study. Their sample consisted only of inpatients. Keyes et al. (2015) explains the overestimation of PA by AN patients in general by the fact that they are “physically compromised” (Keyes et al., 2015). But this does not explain why outpatients reported more PA than inpatients, because it can be assumed that the inpatients with AN were even more physically compromised than the outpatients with AN. Another assumption why the OG showed higher subjective PA than the IG can be the feeling of guilt when omitting an activity, which correlates with the amount of PA in both the IG and OG. The feeling of guilt is represented in the seventh item of the CES. The OG had higher scores in CES_07 than the IG. Mond et al. (Mond, Hay, Rodgers, & Owen, 2006) stated that the feeling of guilt when leaving out an activity is essential in the detection of eating disorders. The commitment to exercise has also been assessed by Keyes et al. (2015) and Bratland-Sanda, Sundgot-Borgen et al. (2010b). They both found high scores in the CES in patients with AN in general and significant correlations between high levels of measured PA and high scores in the CES. However, they did not separately evaluate the

CES_07 score. Keyes et al. (2015) did not find any differences between outpatients and inpatients in the CES.

Reasons for exercise were very similar among the OG and IG. In both groups weight control and fitness were most important, followed by mood and tone. The least important reason for exercise in both groups was physical attractiveness and enjoyment. However, there were big differences in the correlation of reasons for exercise with PA parameters between inpatients and outpatients. Weight control as a reason for PA correlated significantly positive with PA in the OG, while it was significantly negative in the IG. This shows that the cognitive impulsion behind being active is different between groups. This becomes confirmed when viewing health as a reason for exercise, which also had an opposite correlation in the IG and OG. Health correlated significantly negative with PA parameters in the OG and significantly positive in the IG. Being healthier motivated the IG to be more active. For the OG being healthy was rather connected with less PA. In the OG there was also a negative correlation between enjoyment and time spent in LPA. Activities in LPA include slow walking, slow cycling, or yoga, which are not the most fun sports activities, which makes it understandable that the OG did not perform LPA for enjoyment. In conclusion it can be said that the OG had higher levels of PA when they wanted to control their weight, while the IG had higher levels of PA when they exercised for health purposes. The version of the OG, being active to control weight, is often assumed to be the reason for exercise among AN patients, meaning they perform PA with the aim of losing weight (Thome & Espelage, 2007). Bratland-Sanda, Sundgot-Borgen et al. (2010b) showed that weight control was the most important reason for exercise in their samples. However, comparing excessive and non-excessive exercisers, they also demonstrated that negative affect regulation as a reason for exercise is more important for excessive exercisers. So excessive PA can be seen as an affect regulation strategy.

Keyes et al. (2015) found that improving tone was very important for AN patients as a reason for exercising while health and enjoyment were less important. Especially among outpatients, exercising for the reason of health was

not important (Keyes et al., 2015). Dellava et al. (2012) found that health was the most important reason for patients with AN to be active, followed by fitness and mood. All this showed that in AN the motivation for exercise is contradictory and cannot be reduced to the “cognitive desire to lose weight” (Keyes et al., 2015).

4.2.2.3 General and eating disorder psychopathology

There were no differences between the IG and OG in the results of any psychometric questionnaire beside social insecurity as an item of the EDI, which was shown to be higher among inpatients. This is consistent with the data of Keyes et al. (2015) who also did not find any differences in psychopathology between their inpatient and their outpatient group. However, there were some small and medium effects between the OG and IG. Perceived stress, depression, and eating disorder pathology were slightly higher in the IG. The correlations of psychometric data with objectively measured PA were also similar in IG and OG and show that high levels of PA went along with low depression, low stress, low worries, low shape and weight concerns, and a good body image. These results remain in contrast to previous findings. According to Meyer et al. (2011) eating disorder pathology and affect regulation belong to the main correlates of high physical activity. Also Bratland-Sanda et al. (2010a) stated that PA is a method for coping with negative affect. Similar results were found by Keyes et al. who identified the global EDE score as a predictor for the drive to exercise in patients with AN. They also found a positive correlation between EDE questionnaires and peak activity measured by accelerometry. These findings are contradictory, because Carrera et al. (2012) did not identify anxiety or depression as a relevant predictor for high PA levels in AN patients. Additionally, they did not find any correlations between eating disorder pathology and accelerometry assessed PA data. A negative correlation of psychopathology with PA as found in the results of this study showed that very active patients with AN had a better psychological constitution than patients with lower levels of PA. This is consistent with investigations made by Strohle et al. (2009), who found that depressive symptoms could be reduced in healthy people through regular PA. The significant and positive correlation

between the body image questionnaire concurred that good feelings of one's own body lead toward more PA in AN. All this showed that physical activity can be good for patients with AN. Kostrzewa et al. (2014) confirmed that high levels of PA do not necessarily result in poorer treatment outcomes. They further stated that high levels of PA could have a positive effect on the psychological status of patients with AN. The positive effects of PA should be fully utilized in the treatment of PA. Of course this should not exceed an intensity of PA that harms underweight patients. The type of activity has to be carefully chosen (Schlegel, Hartmann, Fuchs, & Zeeck, 2015). Muscle strengthening, for example, can be assumed to be better for patients with AN than fat-burning activities (Fernandez-del Valle et al, 2014). Schlegel, Hartmann, Fuchs and Zeeck (2015) developed a sports program for patients with AN that has the aim to "reduce unhealthy exercising." Fernandez-del-Valle et al. (2014) found that eight weeks of high-intensity resistance training increased strength and agility in patients with AN without weight loss. Additionally, current evidence of exercise intervention in AN is still weak (Zunker et al., 2011), especially in combination with the effects of exercise intervention on general psychopathology and on eating disorder psychopathology.

Interestingly there was a connection between social insecurity and physical activity, showing that participants with high scores in social insecurity tended to be less active, especially in the OG, but also in the IG. Kostrzewa et al. (2014) found that weight recovered patients had significantly lower scores in social insecurity than patients who were not weight recovered. This confirms again that there could be a connection between psychological well-being, specifically social interaction, and physical activity.

4.2.3 Changes of physical activity behavior after treatment

There is a distinct tendency that the overall activity and the intensity of PA increased slightly after hospitalization: the IG_FU had more counts per minute (CPM) and more kilocalories per day and they spent more percent of time in MVPA. This slight increase of activity after inpatient treatment can be explained variously: Patients were healthier after treatment, some of them were even weight recovered, so they had greater capacity for activity. They also had an

improved psychological condition, which was shown by better results in their eating disorder and general psychometric questionnaires. Additionally, the IG_FU were not controlled any longer by inpatient staff. Being out of the hospital offered more possibilities for being active, wherever and whenever the patients liked. Although the PA levels of both inpatients and inpatients at follow-up were evaluated as rather elevated compared with healthy individuals, it is important to supervise AN patients after treatment (K. Giel et al., 2013). In follow-up examinations PA should be mandatory issue to discuss with the patients.

Kostrezwa et al. (2014) who measured PA one year after treatment did not find a significant increase after treatment. They especially stated that high levels of PA did not have a negative effect on recovery rate. They even suggested that patients with high PA levels can achieve a better treatment outcome when their PA level is partly diminished and remains lower. The reason for this is that they found that high levels of PA lead to a higher percent of body fat after recovery, which leads to higher levels of leptin. Leptin has been shown to reduce stress (Malendowicz, Rucinski, Belloni, Ziolkowska, & Nussdorfer, 2007). Dellava et al. (2012) measured PA in recovered PA patients three years after weight restoration. They found that AN patients had only slightly higher PA levels than healthy controls. Even if those differences are very small, the authors point out that “very small differences in energy balance can result in drastic differences in BMI over time” (Dellava et al., 2012). Kaye et al. (1986) found that recent weight recovered AN patients who were assessed two to four weeks after recovery showed higher PA levels than long-term weight recovered AN patients, who were measured six month after recovery. This represents a normalization of elevated PA levels over time. All this shows that more evidence of the long-term development of PA in AN after inpatient treatment is needed.

However, in the results of this study correlations between the PA level at follow-up and the psychopathology showed very similar tendencies in the IG. Low depression, low stress and low ED pathology were connected with high PA levels after treatment and high scores in general and ED psychopathology were connected with low PA levels. This poses the question as to whether general

and eating disorder psychopathology would improve if PA levels were artificially raised in AN patients during treatment, for example with exercise interventions.

4.3 Feasibility

The question of whether accelerometry is a useful method to measure PA in AN can be answered when we try to understand the patients who do not want to participate in an accelerometry measurement. With this understanding the usage of accelerometry can be improved. Additionally, advantages and disadvantages of objective PA measurement, self-perceived PA, and the combination of both should be understood to make the correct decision when choosing the method of PA assessment in AN.

4.3.1 Study participation

Almost 50% of all AN patients who were asked to take part in the ANEX study refused to participate. Thus, the question what distinguishes those who refused participation in comparison to the participants is significant. We compared the age, the BMI, the duration of illness, the clinical basis documentation, the PSQ and the PHQ. Some moderate effects were seen. Perceived stress was higher among those who refused; perfectionism was higher in participants and maturity fears were lower in participants. Additionally, study participants achieved higher education levels than those who refused to participate.

When asked why they had declined to take part in the ANEX study, stress was the most frequently mentioned reason. Higher perceived stress as a result of psychometric data underlined that statement. The accelerometry assessment simply consisted out of wearing a belt around the body, which worked on its own and did not require additional operation by the study participant. The ActiGraph exclusively measured acceleration of the body. There was no integrated GPS that could track the patient's location. Literature indicates that dropouts and refusals are a problem in AN (Gummer et al., 2015). Given this circumstance, several methods to improve compliance and participation were performed in this pilot study:

- The study instructor had a lengthy individual conversation with each potential participant, precisely explaining the study and the device.
- The participant was able to think about her decision and was contacted again after a few days.
- When a patient decided to participate, email or phone contacts were exchanged so that she could contact the instructor with questions or problems.
- The instructor contacted the participant once during the accelerometry assessment to determine if everything was going well.

The fact that perfectionism was higher among study participants than refusals could be the manifestation of perfectionism itself. If a person strives for perfection, it is more difficult to refuse participation, especially if it is shown that there is a large interest in the department that AN patients participate in the study. However, this does not explain why accelerometry assessment is a problem for patients with AN. To the contrary, it could be that some participants were uncomfortable with participation, but they took part in the study because of their perfectionism, meaning that for them it was very hard to say “no.”

Those who agreed to participate had a more advanced educational level than their counterparts. It can be assumed that there was a higher understanding of the study and the accelerometry measurement among the participants. A clear understanding of the study information avoids misunderstandings, resulting in fewer doubts about control, observation, or side effects of wearing the accelerometer device. Another reason for increased participation among patients with higher education could be compassion with the study instructor, because they remembered a similar situation in which they too had to find study participants.

Taking all this this into consideration, there must have been a reason for AN patients that caused them to reject wearing the devices even though it was seen objectively as not stressful. One possible idea as to why accelerometry assessment was seen as stressful for AN patients could be the fact that they have a very high need for autonomy, which is restricted by inpatient treatment.

This has been previously discussed by Gummer et al. (2015). Inpatient therapy controls the eating behavior in a very extreme way, so that it seems far too much outside control for a patient with AN when the daily activity is also observed closely. El Ghoch et al. (2013) found differences between dropouts and completers in their study. They measured that the dropouts had higher (almost double) MVPA than completers at the onset of treatment (El Ghoch et al., 2013). This shows an interaction between the amount of PA and participant compliance. Ultimately, those patients with high levels of PA also had feelings of shame regarding this and simply did not want to divulge this in a study. To reduce stress and shame and to improve the compliance in further PA measurements in AN, an effective concept has to be developed for PA assessment in AN (a proposal for a concept can be found further below in this thesis). Moreover, PA assessment in AN has to be led by staff who are well informed of the doubts that AN participants have with accelerometry. This means that awareness that PA assessment is stressful for patients with AN is very important for further investigations.

4.3.2 Discussion of methods: ActiGraph and IPAQ

The results of the ANEX pilot study showed significant differences between objective PA assessment with the ActiGraph and subjective evaluation of PA with the International Physical Activity Questionnaire (IPAQ). At first sight those two very different methods appear advantageous to compare, because of the similar differentiation into hours in vigorous PA, moderate PA, and low or walking PA. Moreover, both results can be transformed into kilocalories per day, which is another useful parameter to analyze and compare activity. However, in our study AN patients underestimated the overall time of activity in the IPAQ compared to the ActiGraph: 16 hours of activity on an average was documented in the IPAQ compared to around 84 hours of activity per week measured by the ActiGraph. The walking hours reported in the IPAQ are especially lower than the LPA hours measured by the ActiGraph. This could be the case because the IPAQ specifies walking hours. Therefore, patients would try to recall the hours in the week where they went for a walk, but would neglect the walks to the toilet or to the meal rooms or general daily walking. Of course, those low level

activities were documented very exactly by the accelerometer. The accelerometer assesses every kind of activity, regardless of how low, which is very important in AN because low level activity, for example, fidgeting has been shown to contribute a lot of energy expenditure (Levine, Schleusner, & Jensen, 2000). Fidgeting has been observed quite often in patients with AN (Hebebrand et al., 2003). So the IPAQ might be a simple method for achieving an overview of self-perceived activity, but it does not give an exact image of activity levels. Alberti et al. (2013) and Bratland-Sanda et al. (2010a) also found that AN patients under-reported PA in comparison to accelerometry assessment. The title of the study of Bratland-Sanda et al. (2010a) concludes this very well: "I'm not physically active, I only go for walks." Another simple limitation of subjective PA measurement is the dependence on the recall ability of the patients.

Not only the IPAQ questionnaire but also the accelerometer can contribute to contradictory findings. Accelerometry assessment has been validated and it has been shown that it measures PA adequately (Westerterp & Bouten, 1997). It is not certain if some types of activity, for example, cycling or walking with heavy bags or walking stairs, can be recorded accurately by the accelerometer (Keyes et al., 2015). This can be demonstrated with one example of our results: accelerometer assessed PA increased in all different dimensions after treatment, comparing IG and IG_FU. Kilocalories, CPM, MET rates and percent of time in MVPA increased after treatment. The only parameter that did not increase, but rather decreased after treatment were steps per minute. However, in retrospect it is not possible to determine why this is the case. We can assume that patients were more active in other activities, such as climbing, muscle strengthening, cycling or volleyball, which lead to higher waste of kilocalories or higher CPM, but do not require a lot of steps.

Another problem with the accelerometers is compliance. As previously discussed, wearing an accelerometer is a very stressful task for patients with AN and it is difficult to control that fact that the accelerometer is worn throughout the whole assessment period (Bratland-Sanda, Sundgot-Borgen, et al., 2010b) (Gummer et al., 2015). In the case of missing data, it is not possible to determine if this is due to technological issues or due to a lack of compliance

(El Ghoch et al., 2013). A very simple reason for this, besides the psychological aspects, could be vanity. The ActiGraph is a red plastic cube, which is not very attractive. To improve compliance, perhaps a more attractive design would encourage young females to wear the device. It might also be easier to get AN patients to wear an accelerometry bracelet rather than a belt around the waist. However, the limitation in both objective and subjective PA assessment in patients with AN confirms that best practice for the quantification of PA in AN is the combination of both (Gummer et al., 2015). IPAQ questionnaires for the rough evaluation of PA and for alignment with the literature and accelerometer assessment for more detailed PA patterns could be controlled by the information of the questionnaires or by using an activity diary. Therefore, even if the comparison of the results of the two methods is difficult, a combination of both methods in future research is inevitable. However, results must be evaluated separately.

4.4 Strengths and limitations

This is the first study that concludes all literature about objective PA assessment in AN in which accelerometry as a method to measure PA in AN has been established. Also, it is the first study that attempts to relate the results to previous data and data of the general population so that the extent of hyperactivity can be ranked. Additionally, it is the first critical discussion of different methods to assess PA in AN.

The OG consisted of 13 participants and the IG consisted of 12 participants. These are very small sample sizes, even if ANEX was planned to be an explorative study. Higher sample sizes would increase the validity of the results.

4.5 Conclusion

The summary of previous studies in a systematic review of the literature showed that accelerometry seems to be a valid method to measure PA in AN. This justifies the establishment of accelerometry as a PA assessment method in AN. Many different kinds of measurements, devices, and samples have been previously used, which resulted in a variety of different outcomes. However, this represents the complexity of PA assessment in AN. A combination of

accelerometry with an activity diary, a nurse evaluation, standardized questionnaires, and interviews are important. Moreover, weak study participation and problems with dropouts occurred frequently and showed that PA is more relevant for patients with AN than evidence suggests.

The results of the ANEX pilot study showed that both outpatients and inpatients performed very high levels of PA. This has to be taken seriously because the balance of caloric consumptions shifts toward weight reduction over time even if the imbalance is only very small. This is especially important to know about outpatients where PA behavior cannot be controlled in any way. Inpatients demonstrated a tendency to be active at a low level, but for long periods of time. Low level activity can be unrecognized from the outside so that there is a danger of underestimation of the loss of calories through light PA (LPA) over time. There was no remarkable difference in objectively measured PA levels of outpatients and inpatients, but there is a difference between outpatients and inpatients regarding the reason for exercise. Outpatients exercised for weight control, while inpatients exercised to improve their health. Additionally, outpatients rated their PA to be much higher than the inpatients. This shows that inpatient treatment, even if it did not have an effect on the PA level itself, changed the attitudes and the understanding of PA. It also shows that PA is much more than a method to control weight for patients with AN. The fact that reasons for exercise can be very controversial and individual in patients is important to know for AN treatment. In inpatients and outpatients high levels of PA went along with low depression, low shape concerns, low weight concerns, a good body image, low worries, and low stress. High PA levels not only take the risk of losing weight but also indicate the subjective well-being of AN patients. Inpatient treatment should utilize healthy exercise as a supervised intervention so that positive effects of PA can be utilized and negative effects can be avoided.

Following treatment, the PA levels slightly increased. This has to be taken seriously, too, because even a small loss of calories through exercise and the new situation of food intake no longer being controlled can put the weight balance out of control.

The results of the review and the pilot study showed that accelerometry is an adequate method to assess PA in AN when it is combined with self-perceived or otherwise subjective PA assessment. Accelerometry itself is expedient in AN, because it perceives very small amounts of activity. However, the usage of accelerometry in AN is not trivial, and should be planned carefully as described below. Accelerometer assessment is a stress factor for patients with AN explaining the high rates of study refusals. Patients with AN are controlled in their all-day life, especially in their food intake and during inpatient treatment. PA is a means of maintaining autonomy and control, which is extremely important for patients with AN.

All this underlines the high psychological importance and the high complexity of PA in patients, which should be the topic for future investigations.

4.6 Implications for further investigations and treatment

To understand the importance and the complexity of PA for patients with AN, it is necessary to confirm and control the findings of this pilot study with larger samples of patients with PA and with a healthy control group. The studies should be designed as long-term measurements to assess the development of PA not only one month but also years after inpatient treatment. The assessment of psychological well-being, eating disorder pathology, social interaction, commitment to exercise, and the reasons for exercise is necessary and should be mandatory going hand-in-hand with the objective PA measurement. The combination of accelerometry and the IPAQ questionnaire as a subjective PA assessment method is important. In an inpatient setting the observation of nurses can be used to get an additional objective rating of PA (van Elburg et al., 2007) (Gummer et al, 2015).

PA assessment in AN is complex. It should always be planned very carefully with the knowledge that PA assessment represents a stressful situation for patients with AN. Recommendations for future studies assessing physical activity in anorexia nervosa to reduce stress in AN patients and improve study participation are subsequently listed:

- Study staff has to be aware of the doubts that AN patients have with PA assessment, especially with accelerometry.
- The functionality of accelerometry has to be explained carefully to the patients to avoid doubts of GPS tracking or control.
- Anonymity must be ensured.
- Effective time management is required to make use of as little time as possible.
- The study should not be made by the same department that makes the treatment to reduce the patients' doubts of control.
- A small financial compensation can serve as motivation.

There should be broader research about exercise interventions during treatment to determine if PA can improve mood and eating disorder pathology or even weight. In this context it is also important to establish exactly which types, frequencies, and levels of exercise or sports are helpful in patients with AN (Zunker et al., 2011) both from a short- and long-term point of view.

As PA seems to be a core factor of illness origin, duration, development, and outcome, PA assessment should become a standard measurement in AN treatment. PA levels should be tracked throughout the treatment process. Finally, broad data about PA levels in the healthy population is needed to be able to align pathological PA levels of unhealthy individuals, such as patients with AN.

5 Abstract

Anorexia nervosa (AN) is the mental illness with the highest standardized mortality rates. Not only restrictive eating behavior, low body weight, and fear of weight gain, but also early onset and chronic somatic and mental complications make it a very dangerous disease that has not yet been fully understood. Up to 80% of AN patients engage in high levels of physical activity (PA), which leads to an even larger imbalance of body weight.

PA in AN is complex and cannot be reduced to a conscious action with the aim of losing weight. There are several forms of manifestations, multiple definitions, and various explanations of the origin. Additionally, there are many severe complications as consequences of PA in AN. These complications include, for example, longer duration of the illness, longer treatment durations, higher relapse rates, and more psychiatric comorbidities. Thus, the quantification of PA in AN is important. In literature PA in AN is most often carried out through subjective methods such as questionnaires, self-ratings, or interviews. Unfortunately, the precision of these methods is not very high. However, accelerometry is an objective method, which measures PA exactly through the assessment of triaxial acceleration of the body.

The aim of this study was to establish accelerometry as a method of PA assessment in AN and to evaluate its feasibility in a pilot study. Therefore, the focus of this thesis lies on the methodology. To establish accelerometry in AN we concluded all literature that measured PA in AN with accelerometry in a systematic review. Subsequently, in the ANEX pilot study we measured PA in AN with the ActiGraph in 13 outpatients and 12 inpatients. The inpatients have been followed-up one month after treatment. Moreover, we assessed self-perceived PA with questionnaires as well as eating disorder pathology, stress, and depression. Many AN patients refused to participate, and in the ANEX pilot study we tried to determine the reasons for this.

Both AN outpatients and inpatients in our study had high levels of PA compared with standard activity levels of the general healthy population. Comparing outpatients and inpatients, there were no differences in objectively measured PA. However, the self-perceived PA and the commitment to exercise were significantly higher among outpatients. At follow-up, the objectively measured PA increased slightly. All in all, there was a positive correlation between psychological well-being and high levels of PA in all groups. Comparing study refusals and study participants, we found that those who refused perceived greater stress than those who participated.

Accelerometry seems to be a feasible method for measuring PA in AN especially because of its ability to measure activity patterns in time, activity levels and even tiny movements that are not self-perceived as activity but contribute to energy expenditure.

However, accelerometry can be a stressful task for patients with AN. Study staff should be aware of the high need for autonomy and self-control in AN. The ANEX pilot study was projected to be a pre-study for a larger ANEX study with much larger samples and more long-term results. Additionally, improved standard data about PA in healthy individuals is needed to compare results and to classify dangerous or pathological PA levels in AN. It is important to control PA levels after inpatient treatment in follow-up assessments. For outpatient therapy it is important to know that high levels of PA often play a significant role in the maintenance of the illness. In addition, it would be interesting to determine more about exercise interventions, its usability in AN treatment and its interaction with psychological well-being.

All this should contribute to a better understanding of PA in AN which again should be applied in further investigations and treatment to improve the prognosis in AN.

Abstract in German

Über alle psychischen Erkrankungen hinweg hat Anorexia nervosa (AN) die höchste standardisierte Mortalitätsrate. Ausschlaggebend dafür sind nicht nur das niedrige Gewicht, das restriktive Essverhalten und die massive Angst vor dem Zunehmen: Das niedrige Erkrankungsalter und chronische Verläufe mit sowohl somatischen als auch psychischen Komplikationen machen es zu einer gefährlichen Erkrankung, die bis heute nicht im Detail verstanden ist. Dazu kommt, dass bis zu 80% der AN Patientinnen sich überdurchschnittlich viel bewegen, was das Körpergewicht noch mehr aus dem Gleichgewicht bringt.

Körperliche Aktivität bei AN ist ein komplexes Thema und sollte nicht nur als eine Methode zur Gewichtsreduktion betrachtet werden: Aufgrund von unterschiedlichsten Manifestationen gibt es auch zahlreiche Definitionen und Versuche die Ursache der Hyperaktivität bei AN zu erklären. Außerdem gibt es ernstzunehmende Komplikationen als Konsequenz. Die Quantifizierung von Bewegung bei AN spielt deshalb eine immer größere Rolle in der Forschung und auch im klinischen Alltag. In bestehender Literatur wurde Bewegung meistens mit subjektiven Methoden wie z.B. Fragebögen oder Interviews gemessen. Diese spiegeln die körperliche Aktivität jedoch nicht sehr exakt wieder. Akzelerometrie hingegen ist ein objektives Verfahren, welches Bewegungen des Körpers durch triaxiale Beschleunigungsmessung sehr genau erfasst.

Das Ziel dieser Studie war die Etablierung von Akzelerometrie als objektive Messmethode für Bewegung in AN und die Prüfung ihrer Machbarkeit. Der Fokus dieser Arbeit lag also auf der Untersuchung der Methode. Zunächst wurde die bereits bestehende Literatur zur objektiven Bewegungsanalyse bei AN in einem systematischen Review zusammengefasst. Daraufhin wurden in der ANEX Pilot Studie bei 13 ambulanten und zwölf stationären Probandinnen objektiv die Aktivität gemessen. Die zwölf stationären Patientinnen hatten eine weitere Messung einen Monat nach Entlassung von Station. Außerdem wurden Fragebögen zur subjektiven Erfassung der Aktivität ausgefüllt, sowie psychometrische Fragebögen und Essstörungs-Fragebögen. Fast 50% der AN Patientinnen lehnten die Teilnahme an der Studie ab.

Sowohl die stationären als auch die ambulanten AN Patientinnen waren überdurchschnittlich aktiv. Beim Vergleich von den stationären und den ambulanten Patientinnen fiel auf, dass es kaum Unterschiede in der objektiv gemessenen Bewegung gab. Allerdings gab es große Unterschiede in der subjektiv gemessenen Bewegung durch Fragebögen, sowie in der Bewertung der körperlichen Aktivität. Einen Monat nach stationärer Therapie stieg die körperliche Aktivität leicht an. Insgesamt gab es eine positive Korrelation zwischen viel Bewegung und psychologischem Wohlbefinden in allen Gruppen. Studienverweigerer waren jedoch gestresster als die Teilnehmer.

Akzelerometrie scheint eine sinnvolle und valide Methode zur Aktivitätsmessung bei AN zu sein, vor allem durch die Fähigkeit auch Aktivitätslevel sowie Aktivitätsmuster bezogen auf die Zeit und kleinste Bewegungen zu erfassen, die subjektiv nicht wahrgenommen werden, aber dennoch zur Energiebilanz beitragen und bei AN relevant sind. Trotzdem sollte Akzelerometrie in AN immer vorausschauend und bedacht geplant werden, weil Bewegungsmessung für AN Patienten subjektiv belastend sein kann. Das große Bedürfnis von AN Patientinnen für Autonomie und Selbstkontrolle muss berücksichtigt werden.

Die ANEX Pilot Studie sollte in größerem Ausmaß wiederholt werden mit größeren Stichproben und einer längeren Erhebungsspanne. Außerdem sind standardisierte Aktivitätslevel der Normalbevölkerung notwendig, um die Ergebnisse als pathologisch einordnen zu können. Es ist wichtig, die körperliche Aktivität auch nach stationärer Therapie in Folgeuntersuchungen zu beobachten. Das gleiche gilt für die ambulante Therapie: Hier ist das Bewusstsein der Therapeuten ausschlaggebend, dass körperliche Aktivität eine große Rolle in der Aufrechterhaltung der Erkrankung spielt. Es wäre zudem interessant mehr über die Wirkung von Sport- oder Bewegungstherapie bei AN herauszufinden, insbesondere im Zusammenhang mit psychologischem Wohlbefinden.

All das sollte zu einem besseren Verständnis der AN beitragen, welches in weiteren Studien und in der Therapie angewandt werden kann, um dauerhaft die Prognose der AN zu verbessern.

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Appendix

REVIEW

High Levels of Physical Activity in Anorexia Nervosa: A Systematic Review

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Abstract

High level physical activity is a frequent symptom in patients with anorexia nervosa (AN), influencing the development, maintenance, complications, treatment success, relapse rate and severity of the disease. Accelerometry is assumed to be an objective method to assess physical activity (PA) in AN. We aimed to review objectively measured levels of PA in AN and to give an overview for clinical practice and future research. Data were searched in PubMed and PsychINFO until April 2015 following the preferred reporting items for systematic reviews and meta-analyses statement. Twenty studies fulfilled the inclusion criteria. A notable heterogeneity of measurements, outcomes, participants and settings was found. Overall, HPLA is not addressed enough by current evidence. A common valid terminology of HPLA is not available, and accurate criteria of different levels of PA must be defined to create comparability of future studies. Further objective PA assessments are needed to improve treatment outcome and relapse rate. Copyright © 2015 John Wiley & Sons, Ltd and Eating Disorders Association.

Keywords

Anorexia nervosa; Physical activity; Accelerometry

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Correlation of Commitment to Exercise Scale (CES) and CES_07 (seventh item) with objectively measured physical activity parameters

correlation		all	OG	IG	IG_FU
CES with LPA	r	-0,291	-0,212	0,143	-0,690
	p	0,258	0,556	0,760	0,058
CES_07 with LPA	r	-0,319	-0,370	-0,134	-0,848**
	p	0,212	0,293	0,730	0,002
CES with MPA	r	0,261	0,345	0,071	0,310
	p	0,311	0,328	0,879	0,456
CES_07 with MPA	r	0,263	0,721*	0,227	0,049
	p	0,309	0,019	0,557	0,894
CES with VPA	r	0,392	0,299	0,523	0,714*
	p	0,108	0,402	0,229	0,047
CES_07 with VPA	r	0,285	-0,122	0,691*	0,791**
	p	0,252	0,737	0,039	0,006
CES with MVPA %	r	0,223	0,103	0,323	0,476
	p	0,373	0,777	0,435	0,233
CES_07 with MVPA %	r	0,333	0,636*	0,391	0,494
	p	0,177	0,048	0,263	0,147

OG: outpatient group, IG: inpatient group, IG_FU: Inpatient group at follow-up, CES: Commitment to Exercise Scale, CES_07: seventh item of the CES, LPA: light physical activity, MPA: moderate physical activity, VPA: vigorous physical activity, MVPA%: percent of time spent in moderate to vigorous physical activity, r: correlation coefficient

* = significance <0,05, ** = significance<0,05

Correlation of reasons for exercise (weight control and health) with objectively measured physical activity parameters

correlation		all	OG	IG	IG_FU
REI (weight control) with steps/min	r	-0,032	0,662*	-0,775*	-0,018
	p	0,901	0,026	0,041	0,969
REI (weight control) with CPM	r	-0,052	0,385	-0,786*	-0,523
	p	0,807	0,242	0,043	0,229
REI (weight control) with MVPA %	r	-0,108	0,681*	-0,818*	-0,342
	p	0,669	0,021	0,024	0,452
REI (health) with steps/min	r	0,273	-0,516	0,821*	0,107
	p	0,274	0,104	0,023	0,819
REI (health) with CPM	r	0,250	-0,581	0,815*	0,643
	p	0,318	0,061	0,021	0,119
REI (health) with MVPA %	r	0,378	-0,465	0,883**	0,571
	p	0,121	0,149	0,008	0,18

*= significance $p < 0,05$

**= significance $p < 0,01$

OG: outpatient group, IG: inpatient group, IG_FU: inpatient group at follow-up, REI: Reasons for Exercise Inventory, CPM: counts per minute, MVPA%: percent of time spent in moderate to vigorous physical activity, r: correlation coefficient

Correlation of Body Image Questionnaire (BIQ) and objectively measured physical activity parameters

correlation		all	OG	IG	IG_FU
BIQ-20 (NEB) with CPM	r	-0,169	-0,269	-0,407	-0,323
	p	0,49	0,424	0,317	0,453
BIQ-20 (NEB) with VPA in h/week	r	-0,216	-0,252	-0,414	-0,347
	p	0,375	0,455	0,355	0,399
BIQ-20 (NEB) with MVPA %	r	-0,062	-0,314	-0,506	-0,371
	p	0,801	0,346	0,201	0,365
BIQ-20 (PBD) with CPM	r	0,584**	0,647*	0,551	0,335
	p	0,009	0,031	0,157	0,417
BIQ-20 (PBD) with VPA in h/week	r	0,645	0,689*	0,709	0,443
	p	0,003	0,019	0,074	0,272
BIQ-20 (PBD) with MVPA %	r	0,506*	0,287	0,753*	0,551
		0,027	0,392	0,031	0,157

OG: outpatient group, IG: inpatient group, IG_FU: Inpatient group at follow-up, BIQ: Body Image Questionnaire, NEB: negative evaluation of the body, PBD: perception of body dynamics, CPM: counts per minute, VPA: vigorous physical activity, MVPA%: percent of time spent in moderate to vigorous physical activity, r: correlation coefficient
 * = significance <0,05, ** = significance<0,05

Correlation of worries, joy and Perceived Stress Questionnaire (PSQ) mean count with objectively measured physical activity parameters

correlation		all	OG	IG	IG_FU
worries with steps/minute	r	-0,451*	-0,635*	-0,391	-0,447
	p	0,040	0,049	0,299	0,227
worries with MPA (h/week)	r	-0,178	-0,347	-0,209	-0,344
	p	0,441	0,326	0,620	0,365
worries with VPA (h/week)	r	-0,606**	-0,788**	-0,739*	-0,622
	p	0,004	0,007	0,036	0,074
worries with MVPA %	r	-0,527*	-0,702*	-0,547	-0,506
	p	0,014	0,024	0,128	0,165
joy with steps/minute	r	0,437*	0,090	0,852**	0,813**
	p	0,048	0,804	0,004	0,008
joy with MPA (h/week)	r	0,434*	-0,041	0,787*	0,815**
	p	0,050	0,910	0,020	0,007
joy with VPA (h/week)	r	0,338	0,360	0,817*	0,786*
	p	0,134	0,307	0,013	0,012
joy with MVPA %	r	0,456*	0,142	0,865**	0,790*
	p	0,038	0,696	0,003	0,011
PSQ mean with steps/minute	r	-0,493*	-0,242	-0,613	-0,461
	p	0,023	0,501	0,079	0,212
PSQ mean with MPA (h/week)	r	-0,332	-0,040	-0,502	-0,370
	p	0,154	0,912	0,205	0,327
PSQ mean with VPA (h/week)	r	-0,509*	-0,551	-0,845**	-0,658
	p	0,018	0,099	0,008	0,054
PSQ mean with MVPA %	r	-0,568**	-0,364	-0,734*	-0,573
	p	0,007	0,302	0,024	0,106

OG: outpatient group, IG: inpatient group, IG_FU: Inpatient group at follow-up, PSQ: Perceived Stress Questionnaire, MPA: moderate physical activity, VPA: vigorous physical activity, MVPA%: percent of time spent in moderate to vigorous physical activity, r: correlation coefficient

* = significance <0,05, ** = significance<0,05

Correlation of social insecurity and ineffectiveness (EDI) with objectively measured physical activity parameters

correlation		all	OG	IG	IG_FU
social insecurity with CPM	r	-0,410	-0,769*	-0,154	-0,156
	p	0,104	0,015	0,693	0,689
social insecurity with VPA (h/week)	r	-0,104	-0,702*	-0,593	-0,386
	p	0,664	0,035	0,121	0,305
ineffectiveness with CPM	r	-0,486*	-0,687*	-0,398	-0,453
	p	0,030	0,041	0,289	0,221
ineffectiveness with VPA (h/week)	r	-0,270	-0,680*	-0,671	-0,442
	p	0,250	0,044	0,069	0,258

EDI: Eating Disorder Inventory, OG: outpatient group, IG: inpatient group, IG_FU: Inpatient group at follow-up, CPM: counts per minute, VPA: vigorous physical activity, r: correlation coefficient

* = significance <0,05, ** = significance<0,05

7 Erklärung zum Eigenanteil

Die Arbeit wurde in der Abteilung Innere Medizin VI, Psychosomatische Medizin und Psychotherapie des Universitätsklinikum Tübingen unter Betreuung von Prof. Dr. Martin Teufel durchgeführt.

Die Konzeption der Studie erfolgte durch mich in Zusammenarbeit mit Prof. Dr. Martin Teufel. Die Auswahl und Bestellung der Messgeräte sowie die Einarbeitung in die Funktionalität und Anwendung der Messgeräte sowie der dazugehörigen Software erfolgte selbstständig von mir mit Unterstützung durch Prof. Dr. Martin Teufel.

Sämtliche Aufklärungsgespräche, Untersuchungen und Messungen wurden von Ricarda Gümmer durchgeführt. Zwei Messungen wurden unterstützt durch Linda Mühleisen.

Die statistische Auswertung erfolgte nach Anleitung von Prof. Dr. Martin Teufel durch mich.

Ich versichere, das Manuskript selbstständig verfasst zu haben und keine weiteren als die von mir angegebenen Quellen verwendet zu haben.

In diese Dissertation sind Teile eines von mir selbst geschriebenen bereits veröffentlichten Textes eingegangen:

Gummer, R., Giel, K. E., Schag, K., Resmark, G., Junne, F. P., Becker, S., Teufel, M., Zipfel, S., (2015). **High Levels of Physical Activity in Anorexia Nervosa: A Systematic Review**. Eur Eat Disord Rev, 23(5), 333-344. doi:10.1002/erv.2377

Diese Veröffentlichung wurde von mir selbst verfasst. Die Koautoren unterstützten mich beim Korrigieren des Manuskriptes und standen beratend zur Seite bei der Auswertung der Literaturrecherche. Die Koautoren sind mit der Verwendung der Daten im Rahmen dieser Dissertation einverstanden.

Ricarda Gümmer

8 Veröffentlichungen

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