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## Original article

## Evaluation of a short protocol for indirect calorimetry in females with eating disorders and healthy controls

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## SUMMARY

**Background and aims:** To enable clinicians to identify the clinical picture and treatment progress and to adjust eating plans according to personal energy needs, it is important to know the patient's correct resting metabolic rate (RMR). Indirect calorimetry (IC) is the preferred method for assessment of RMR, but long duration of measurement increases the load on the patients, and reduces the effectiveness in clinical and scientific settings. Further; not all patients reach a valid RMR according to the suggested best practice protocol, with 5 min of steady state (SS) where respiratory gas volume exchange varies less than 10%. The aim of this study was to evaluate the possibility for an abbreviated RMR protocol and SS criterion.

**Methods:** Forty two women diagnosed with bulimia nervosa or binge eating disorder (eating disorder group, ED), originally recruited for an outpatient treatment study, and 26 age and gender matched healthy controls (HC) were studied during a single, prolonged IC measurement. Participants rested for 10 min in supine position wearing a two-way breathing facemask, before a continuous measurement period of 20 min. Results from a standard 5 min SS criterion was compared to an abbreviated 3 min SS criterion. Both SS-criteria were evaluated through three different SS protocols (<10% variation in respiratory gas exchange), being: 1) measurement during the first 3 or 5 min, 2) measurement after discarding the first 5 min, and 3) the lowest identified RMR during the 20 min of measurement.

**Results:** About 50% of the participants reached an early SS in both the defined SS minute criteria. Participants reaching a valid SS throughout the 20 min of measurement increased from ~90% to 100% with an abbreviated 3 min SS. With a 5 min SS criterion, the median (range) RMR for the 3 protocols were 1639.9 (1239.2), 1508.8 (1457.6) and 1500.6 (1328.8) respectively for the ED group, and 1702.2 (1239.4), 1608.4 (1076.4) and 1594.8 (1029.2) respectively for the HC group, ( $p > 0.05$  for all between-group analysis). With a 3 min SS criterion, the median (range) RMR were 1533.6 (1298.2), 1461.2 (1406.1), and 1395.8 (1447.3) respectively for the ED group and 1681.7 (1332.4), 1613.7 (1266.0) and 1523.1 (1050.3), respectively for the HC group, ( $p > 0.05$  for all between-group analysis). Lowest measured RMR was different compared to the other two SS protocols in both the ED- and the HC group, and for both the 5 min- and the 3 min SS criteria, respectively ( $p < 0.04$ ). Furthermore, a SS of 3 min resulted in lower RMR compared to 5 min SS ( $p < 0.00$ ) and an increased number of participants classified as hypometabolic ( $RMR_{measured}/RMR_{calculated} < 0.9$ ).

**Conclusions:** An abbreviated measurement protocol to identify the lowest RMR using IC was not successful. Abbreviating the SS criteria from 5 to 3 min, resulted in a lower RMR, hence encouraging further examination of the validity of shorter SS criterion than practiced today.

Registered in Clinical Trials by id-number NCT02079935, and approved by the Norwegian Regional Committee for Medical and Health Research Ethics with id-number 2013/1871. The trial in which control persons were recruited, is approved by the Norwegian Regional Committees for Medical and Health

**Abbreviations:** ED, eating disorder; RMR, resting metabolic rate; BN, bulimia nervosa; IC, indirect calorimetry; EE, energy expenditure; SS, steady state; BED, binge eating disorder; RCT, randomized controlled trial; CV, coefficient of variation;  $VO_2$ , volume of oxygen;  $VCO_2$ , volume of carbon dioxide; HC, healthy control; RMR5, RMR achieved during the first 5 min of measurement; RMR3, RMR achieved during the first 3 min of measurement; DC, direct calorimetry.

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## 1. Introduction

The different diagnosis of eating disorders (ED) are characterized by eating and dieting behaviors such as fasting, restrictive eating and low energy availability, normal and/or chaotic eating pattern, weight loss and/or frequent weight fluctuations [1]. Resting metabolic rate (RMR) has been reported low in persons with anorexia nervosa [1–3], reduced [2–6], normal [7] or increased [8] in persons with bulimia nervosa (BN), and normal [14] in persons with binge eating disorder (BED). RMR is important in treatment of ED, not only as a tool for identifying the patients' energy needs to design individual diets, meal plans and exercise programs, but also to identify the clinical picture and treatment progress [9–11].

Indirect calorimetry (IC) is the preferred method for the assessment of RMR in clinical and research settings [9,12–15]. It is assumed that the energy consumption measured for a short, defined period, gives a reliable estimate for the mean 24 h resting energy expenditure (EE) [16–18]. To reduce the vulnerability of IC to random bias from biological systems, technical- and methodological errors, achieving a steady state (SS) in the variability of gas exchange has been suggested [13,19–23]. A best practice protocol was suggested by Compther et al., in 2006, revised in 2015 [21,23], suggesting a rest of 10 min, then to discard the first 5 min of measurement and identify a SS of 5 min with a coefficient of variation (CV) for  $\text{VO}_2$  and  $\text{VCO}_2$ , less than 10% [18,20,21,23,24]. However, results and practice have differed; some do not consider rejecting the first 5 min [19,25], while others indicate that no more than 5 min of rest is needed to achieve a valid measure [22,24,26]. The choice of 5 min as a valid SS with <10% variation in respiratory gas exchange seems arbitrary, and mainly based on the fact that a longer period (10 min) is too strict for most participants to achieve a SS [18]. A shorter SS period will result in a shorter protocol, that decreases the load for the participants, and increases the efficiency in practical (clinical) and scientific work. The potential for a shorter SS period, has previously been investigated [18,19,22,24,26,27]. However, results have been evaluated towards a variety of references, often being the mean RMR from a longer period of measurement [18,20,22,24,28,29]. None of these protocols have examined the lowest RMR or reflected the true 24-h RMR.

The main aim of the present study was to compare three different IC-protocols for RMR measurement, to explore the potential for an abbreviated protocol. Secondly we aimed to explore the potential for an abbreviated SS period of 3 min in women with BN or BED, and in healthy female controls.

## 2. Materials and methods

### 2.1. Subjects

This study is part of a larger, randomized, controlled, outpatient treatment study for ED (The Physical Exercise and Dietary Therapy Study, the PED-t study), aiming to test the effect of a new treatment method. Recruitment procedure, and inclusion and exclusion criteria, have been described in details elsewhere [30]. The recruitment of participants for this original trial were semiannually, and participants recruited during autumn 2016 (42 out of totally

119 participants) were included in the present RMR study. To evaluate whether the outcomes in the present methodological study are population specific, and in order to keep a decent ratio of 2:1 between population of interest and control-population, a group of 26 age and gender matched healthy female controls (HC) were included. The women in this group were originally recruited as controls for another ongoing health- and exercise trial lead by our research group. The inclusion criteria for the HC group were being female between 18 and 40 years, a BMI between 18 and 30, being physically active (>2 training sessions per week), but not at a competitive level.

### 2.2. Ethical statement

All participants signed an informed consent.

The main study PED-t is approved by the Norwegian Regional Committees for Medical and Health Research Ethics the 16th of December 2013 (id: 2013/1871), and prospectively registered in Clinical Trials the 17th of February 2014 (id: NCT02079935). The trial in which control persons were recruited, is approved by the Norwegian Regional Committees for Medical and Health Research Ethics the 18th of January 2017 (id: 2016/1718), and prospectively registered in Clinical Trials the 24th of December 2016 (id: NCT03007459).

### 2.3. Protocol

Participants were asked to come to the laboratory after an overnight fast (12 h) between 07.30 AM and 10.00 AM. They were instructed to refrain from exercise the last 24 h, and to be passively transported to the laboratory. Participants were weighed in their underwear and height was measured with a fixed stadiometer (Seca scale, Mod: 8777021094, S/N: 5877248124885). Participants laid down in supine position on a mattress, covered by a blanket and with head resting on a pillow.

RMR was measured by IC using a respiratory gas analyzer (Oxycon Pro, Jaeger, Germany). Ambient conditions were registered and the analyzer was gas and volume calibrated each morning prior to the measurements, according to the recommendations stated in the user manual from the manufacturer (user manual for Oxygen Pro, Jaeger, Germany). A total of 6 participants were measured each day. Gas exchange and ventilatory variables were measured continuously using the breath-by-breath method. Participants were instructed to rest for 10 min, wearing a two-way breathing mask covering their nose and mouth (2700 series; Hans Rudolph, Inc). Thereafter, the measurement period started by connecting the mask to the gas analyzer, and data collection continued for a total of 20 min.

### 2.4. Analysis

All data output were given in 30 s intervals, and calculated as means per minute. To reduce errors caused by gas remaining in the tubes, the data from the first 30 s were erased from the analysis. A valid RMR was defined according to the current recommendation emphasizing the importance of a SS, being defined as 5 min periods with less than 10% CV for  $\text{VO}_2$  and  $\text{VCO}_2$  [17,18,21,23,27].

Additionally, abbreviated SS periods of 3 min were identified. Each single 5 and 3 min SS period was calculated from each subsequent minute throughout the 20 min with measurement.

RMR was calculated using the abbreviated Weir formula [31]:

$$3.94 (\text{VO}_2) + 1.1 (\text{VCO}_2) \times 1.44$$

To evaluate the necessary duration of a protocol for valid RMR-measurement and at the same time determining the lowest RMR, three different protocols were analyzed. Further, to evaluate the potential for a shorter SS period, each of these three protocols were evaluated separately with a 5 min SS period, and with a 3 min SS period, respectively (see Fig. 1). Our research questions were the following:

- 1) How many participants reach a SS of 5 min, and of 3 min respectively, with CV for  $\text{VO}_2$  and  $\text{VCO}_2 < 10\%$ ; a) during the first 5 min of measurement, and b) after discarding the first 5 min of measurement?
- 2) What is the lowest RMR achieved with the two defined SS criteria respectively, evaluated through the total assessment period (20 min)?
- 3) Do the lowest valid RMR from the 5-min SS and from the 3-min SS differ?

## 2.5. Statistics

Results were analyzed with IBM SPSS Statistics 24 for Windows. All results were tested for normality using Shapiro–Wilk test, and data are presented as mean and standard deviation (SD) when normally distributed, or as median and range when being skewed. Normal distributed data were compared using a two-tailed paired sample t-test when studying outcomes for each group separately, and a two-tailed independent sample t-test when comparing between-groups differences. For non-parametric data, Mann–Whitney test were used for between-group differences, while Wilcoxon rank test was used to evaluate within-group differences. Statistical significance was defined as  $p < 0.05$ . Bland Altman plots were created to evaluate the agreement between the lowest RMR from the 3 min SS and the lowest RMR from the 5 min SS for the ED group and HC group respectively.

Sample size was based on the available sample of participants recruited for the original treatment study during the 6th and very last recruitment period. The number of participants is within the recommended number for Bland Altman analysis, and in line with the number previously being reported in similar studies, ranging from 10 to 194 participants, with ~40 participants being the more typical [2,5–8,18–20,22,24–28,32,33].

All calculations and comparisons are between the ED group (participants with diagnosis of BN or BED combined) and the HC group. Due to the potential for different results between the two diagnostic groups, separate within- and between-analysis were performed.

## 3. Results

A total of 42 participants with an ED and 26 HC agreed to participate. Table 1 presents the details for age, body weight, height and BMI in the two groups.

### 3.1. RMR measurement for 5-min SS intervals

Less than 50% of the ED group and 60% of the HC group reached a SS during the first 5 min of measurement. The proportion of successful RMR measurements (valid SS) increased in both groups when evaluating the RMR-protocol with rejection of the first 5 min and the RMR-protocol searching for the lowest RMR during the total 20 min of measurement (>90% of the participants). Table 2 presents the results from the 5 min SS protocols.

Comparing the three different protocols with 5 min SS periods within the ED group, reveals differences between all measurements. The RMR value achieved during the first 5 min of measurement (RMR5) was higher than that attained when discarding the first 5 min,  $p = 0.019$ . Further, the lowest 5 min SS RMR value achieved during the whole measurement period, was lower than both RMR5 ( $p = 0.001$ ) and the RMR achieved after discarding the first 5 min ( $p = 0.00$ ). Separate between-analysis for the two diagnostic groups revealed no differences between the two sub-groups with ED on the different outcomes ( $p > 0.08$ ). Furthermore, separate within-analysis for the two diagnostic groups, revealed that only the lowest RMR5 differed significantly from the other two protocols, in both diagnostic groups ( $p < 0.00$ ).

Comparing the three different protocols with 5 min SS periods within the HC group reveals differences only with the lowest RMR variable. The lowest 5 min SS RMR value identified, was lower than both RMR5 ( $p = 0.002$ ) and RMR achieved after discarding the first 5 min ( $p = 0.00$ ).

### 3.2. RMR measurement for 3-min SS intervals

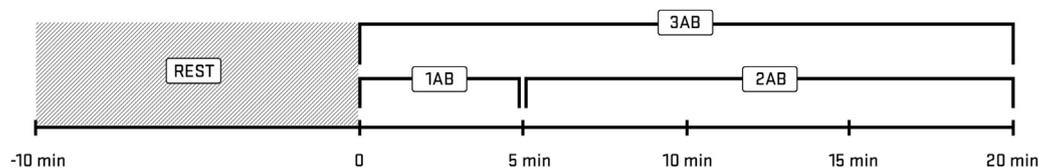
The use of an abbreviated SS-period of 3 min did not increase the number of participants achieving a valid RMR measurement during the very first minutes of measurement. However, the 4–10% in the two study groups that did not reach SS in the following periods with the use of 5 min SS, were now able to reach a valid SS

**Table 1**

Age, bodyweight, height and BMI for the ED and HC groups. Age is presented as median (range), others are presented as mean (standard deviation). p-values are reported for differences between groups.

	ED group (n = 42)	HC group (n = 26)	p-value
Age, years	30 (23)	27 (18)	0.52
Body weight, kg	73.8 (17.6)	66.1 (10.9)	0.03
Height, cm	168.3 (5.9)	168.4 (6.1)	0.97
BMI, kg/m <sup>2</sup>	26.0 (5.7)	23.3 (3.3)	0.02

ED, Eating disorder; HC, healthy control; BMI, Body Mass Index.



**Fig. 1.** Overview of the total protocol. We measure each participant once, during a continuous 20 min measurement, initiated by a 10 min rest. Post-evaluation of the measurement is performed studying the possibility of three different protocols and with a steady state (SS) where respiratory gas exchange varies <10%. Protocol 1: reaching a SS during the first 5 min of measurement, protocol 2: the first SS achieved after discarding the first 5 min of measurement, and protocol 3: the lowest RMR achieved during the complete 20 min of measurement. Each protocol is evaluated according to two different SS criteria; a traditional SS of 5 min (A) and an abbreviated SS of 3 min (B).

**Table 2**

RMR values from the three protocols with 5-min SS periods in the ED and HC groups. The number reaching a steady state is in absolute numbers with percent in parenthesis, for each measurement period. Results are given in median with range in parenthesis, and reported with 95% confidence intervals. p-values are reported for differences between groups.

	ED group (n = 42)	HC group (n = 26)	p-value
RMR first 5 min (kcal)	1639.9 (1239.2)	1702.2 (1239.4)	0.45
95% confidence interval	1392.8–1723.4	1475.7–1814.6	
N (%)	19 (45.2)	15 (57.7)	
RMR discarding first 5 min (kcal)	1508.8 (1457.6)	1608.4 (1076.4)	0.62
95% confidence interval	1428.5–1642.6	1458.6–1693.5	
N (%)	38 (90.5)	23 (88.5)	
RMR lowest, lasting 5 min, (kcal)	1500.6 (1328.8)	1594.8 (1029.2)	0.74
95% confidence interval	1384.2–1592.1	1386.6–1610.8	
N (%)	38 (90.5)	25 (96.2)	

RMR, Resting Metabolic Rate; ED, Eating Disorder; HC, Healthy Control; kcal, kilocalorie.

with the 3 min SS periods (100% achieved valid RMR measurement). The results from the three different protocols with 3-min SS periods are presented in Table 3.

Within the ED group, the three different protocols with 3-min SS periods were all significantly different. The RMR value achieved during the first 3 min of measurement (RMR3) was higher than that attained when discarding the first 5 min ( $p = 0.040$ ). Furthermore, the lowest 3 min SS RMR value achieved during the whole measurement period, was lower than both RMR3 ( $p = 0.00$ ) and RMR achieved after discarding the first 5 min ( $p = 0.00$ ). Separate between-analysis for the two diagnostic groups revealed a significant difference for the RMR achieved during the first 5 min, with mean (SD) RMR 1380.1 (335.1) and 1765.9 (266.9) for the BN-group and BED-group, respectively ( $p = 0.014$ ). No further between-group differences were found ( $p > 0.07$ ). Furthermore, separate within-analysis for the two diagnostic groups, revealed that only the lowest RMR3 differed from the other two protocols, in both diagnostic groups ( $p < 0.00$ ).

Within the HC group, the three different protocols with 3-min SS periods differed only when comparing to the lowest RMR variable. The lowest 3 min SS RMR value achieved during the whole measurement period, was lower than both RMR3 ( $p = 0.001$ ), and RMR achieved after discarding the first 5 min ( $p = 0.00$ ).

**Table 3**

RMR values from the three protocols with 3-min SS periods in the ED-and the HC group. The number reaching a SS is given in absolute number and in percent in parenthesis for each measurement period. Results are given as median with range in parenthesis, and reported with 95% confidence intervals. p-values are reported for differences between groups.

	ED group (n = 42)	HC group (n = 26)	p-value
RMR first 3 min, (kcal)	1533.6 (1298.2)	1681.7 (1332.4)	0.42
95% confidence interval	1366.4–1702.5	1467.6–1784.6	
N (%)	20 (47.6)	16 (61.5)	
RMR discarding first 5 min, (kcal)	1461.2 (1406.1)	1613.7 (1266.0)	0.51
95% confidence interval	1395.5–1606.3	1433.3–1674.6	
N (%)	42 (100)	26 (100)	
RMR lowest, lasting 3 min, (kcal)	1395.8 (1447.3)	1523.1 (1050.3)	0.42
95% confidence interval	1310.3–1520.0	1346.1–1559.1	
N (%)	42 (100)	26 (100)	

RMR, Resting Metabolic Rate; ED, Eating Disorder; HC, Healthy Control; SS, steady state.

### 3.3. Comparing RMR from 3 min SS and 5 min SS

RMR from 3 min SS was lower than the RMR from 5 min SS in both study groups, respectively (see Table 4). Separate within-analysis for the two diagnostic groups revealed that the difference between the lowest 5 min SS and lowest 3 min SS was only significant for the BED-group with mean difference (SD) 64.4 (81.4), ( $p = 0.00$ ), and with no difference for the BN-group with mean difference (SD) 13.8 (36.5), ( $p = 0.12$ ). The agreement between the lowest RMR from the two SS periods is illustrated with Bland Altman plot in Fig. 1 (ED group) and Fig. 2 (HC group).

The visual agreement of the Bland–Altman plot demonstrated a tendency of underestimation in mean, with the 3 min SS measures on average 39.1 (SD 67.3) kcal lower than 5 min SS in participants with ED, and 52.89 (SD 65.8) kcal lower in controls respectively (Figs. 2 and 3). The 95% confidence limits of agreement varied from +92.8 kcal to –171.1 kcal (total range of 264 kcal), and +83.6 kcal to –189.4 kcal/day (total range of 273 kcal), for participants with ED and controls, respectively. Three participants with ED and one HC-participant were outliers of the 95% limits of agreement.

The number of participants in the ED group achieving their lowest, valid SS was spread during the assessment period; during both the 5 min SS and 3 min SS (Figs. 4 and 5). Only ~50% of the ED-participants and ~45% of the HC-participants (results from the latter not presented) had achieved their lowest SS by measurement minute 10 in both SS conditions.

## 4. Discussion

The main finding in this study is that an abbreviated protocol was not successful in identifying the lowest RMR for the majority of the participants, neither with the original practice for SS criteria with 5 min, nor with an experimental abbreviated SS-period of only 3 min. Secondly, our results indicate that a shorter SS criterion (3 min) will increase the numbers of participants reaching a valid RMR.

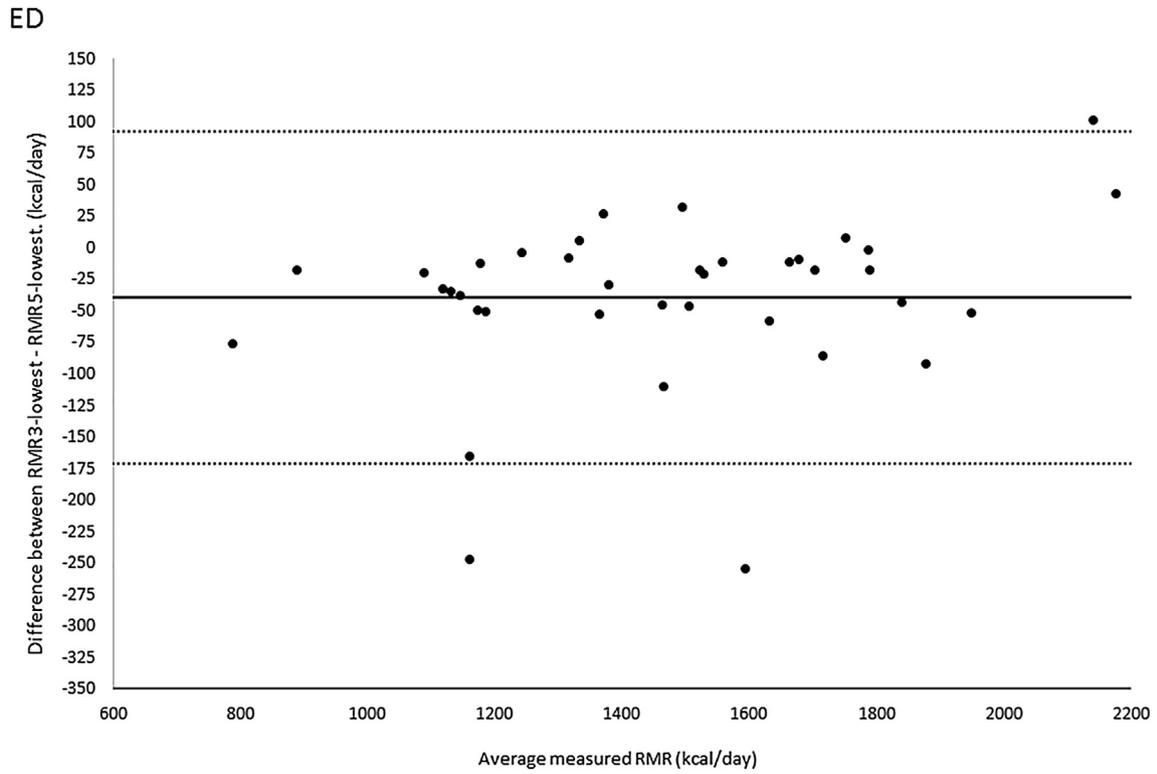
Only 45% of the ED group reached a valid SS of 5 min during the first 5 min of measurement, confirming findings from other studies of an unstable, fluctuating the first phase of measurement [18,21,23,24,26,28]. In addition, RMR differed significantly depending on the protocol used for a valid RMR measurement. The lowest RMR value was significantly different from both the RMR achieved during the very first 5 min of measurement, and the first, subsequent RMR achieved after discarding the first 5 min of measurement. Most participants achieved their lowest RMR during a later period of measurement, with more than 83% of the population reaching their lowest RMR after the first 5 min of measurement (Fig. 3). Reducing the time for a valid SS from 5 min to 3 min, did not improve these results noticeably.

**Table 4**

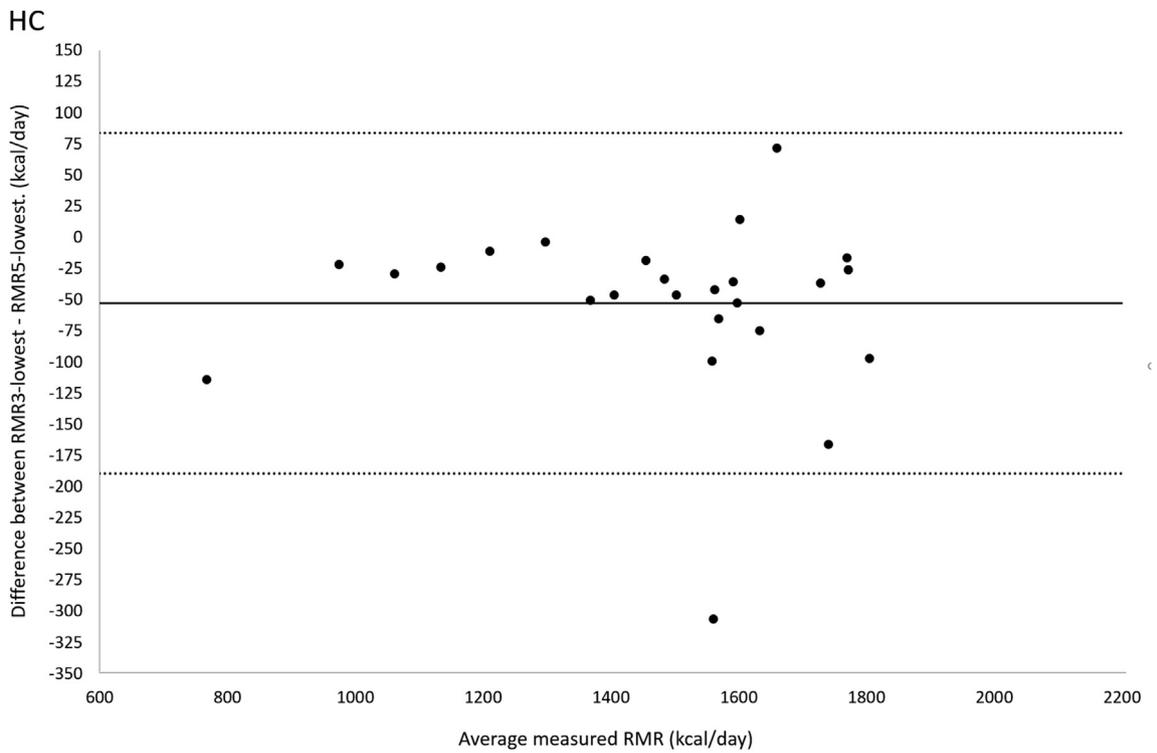
Comparing the lowest RMR attained with 5-min SS (RMR5-lowest), with the lowest RMR attained with 3-min SS (RMR3-lowest) in ED group and HC group, respectively. RMR values are given as median with range in parenthesis, and reported with 95% confidence intervals. p-values are for within-group comparison of the two different RMR SS criteria.

	ED group (n = 42)	HC group (n = 26)
RMR5-lowest, kcal	1500.6 (1328.8)	1594.8 (1029.2)
95% confidence interval	1384.2–1592.1	1386.6–1610.8
RMR3-lowest, kcal	1395.8 (1447.3)	1523.1 (1050.3)
95% confidence interval	1310.3–1520.0	1346.1–1559.1
Wilcoxon signed rank test	$p < 0.00$	$p < 0.00$
	$Z = -3.91$	$Z = -3.78$

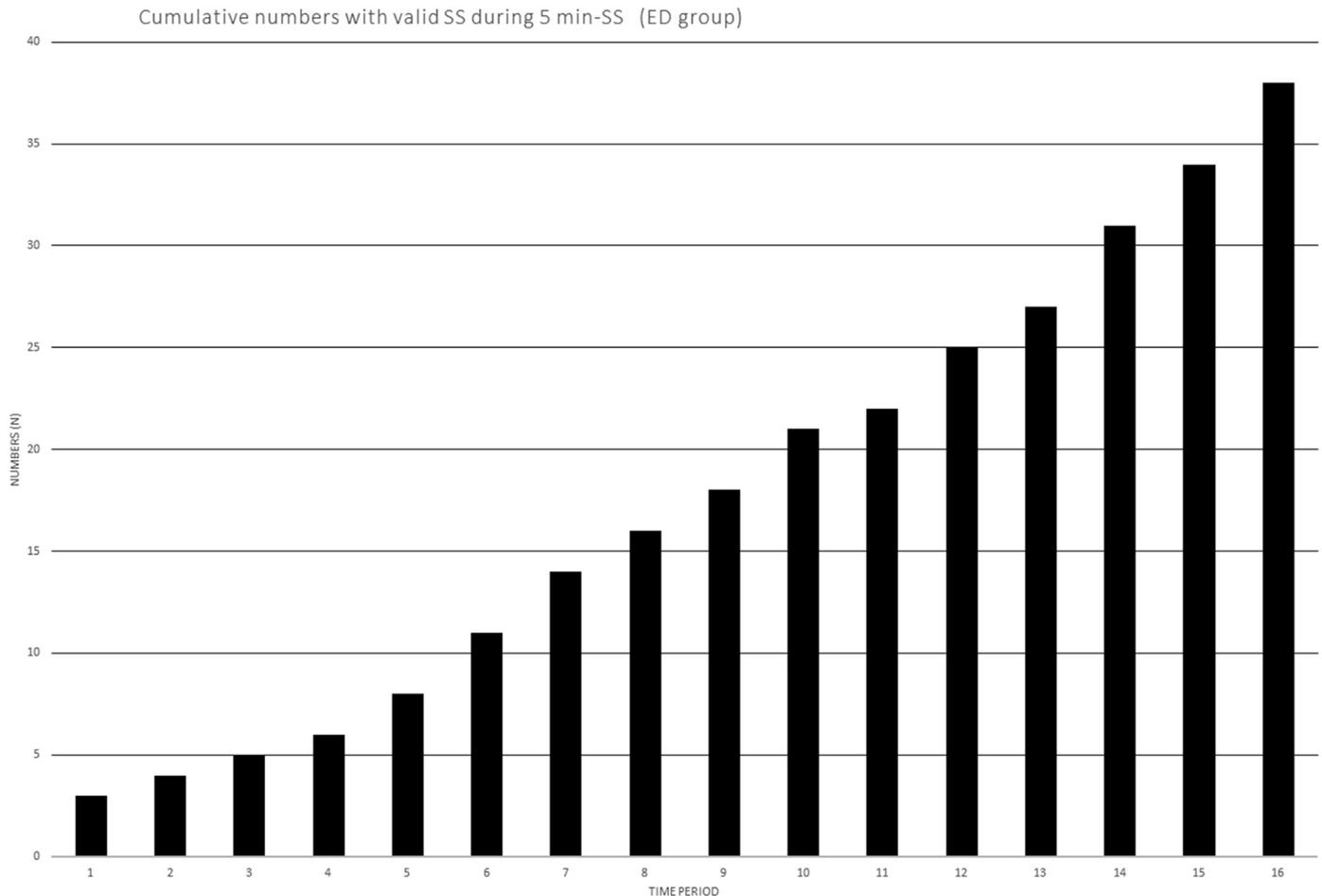
RMR, Resting Metabolic Rate; SS, Steady State; ED, Eating Disorder; HC, Healthy Control.



**Fig. 2.** Bland Altman plot of agreement between the lowest resting metabolic rate (RMR) with 3-min steady state (SS) (RMR3-lowest) and the lowest RMR with 5-min SS (RMR5-lowest) in the eating disorder group (ED). SS is defined as a 3 or 5 min period respectively, where respiratory gas exchange varies <10%.



**Fig. 3.** Bland Altman plot of agreement between the lowest resting metabolic rate (RMR) with 3-min steady state (SS) (RMR3-lowest) and the lowest RMR with 5-min SS (RMR5-lowest) in the healthy control group (HC). SS is defined as a 3 or 5 min period respectively, where respiratory gas exchange varies <10%.

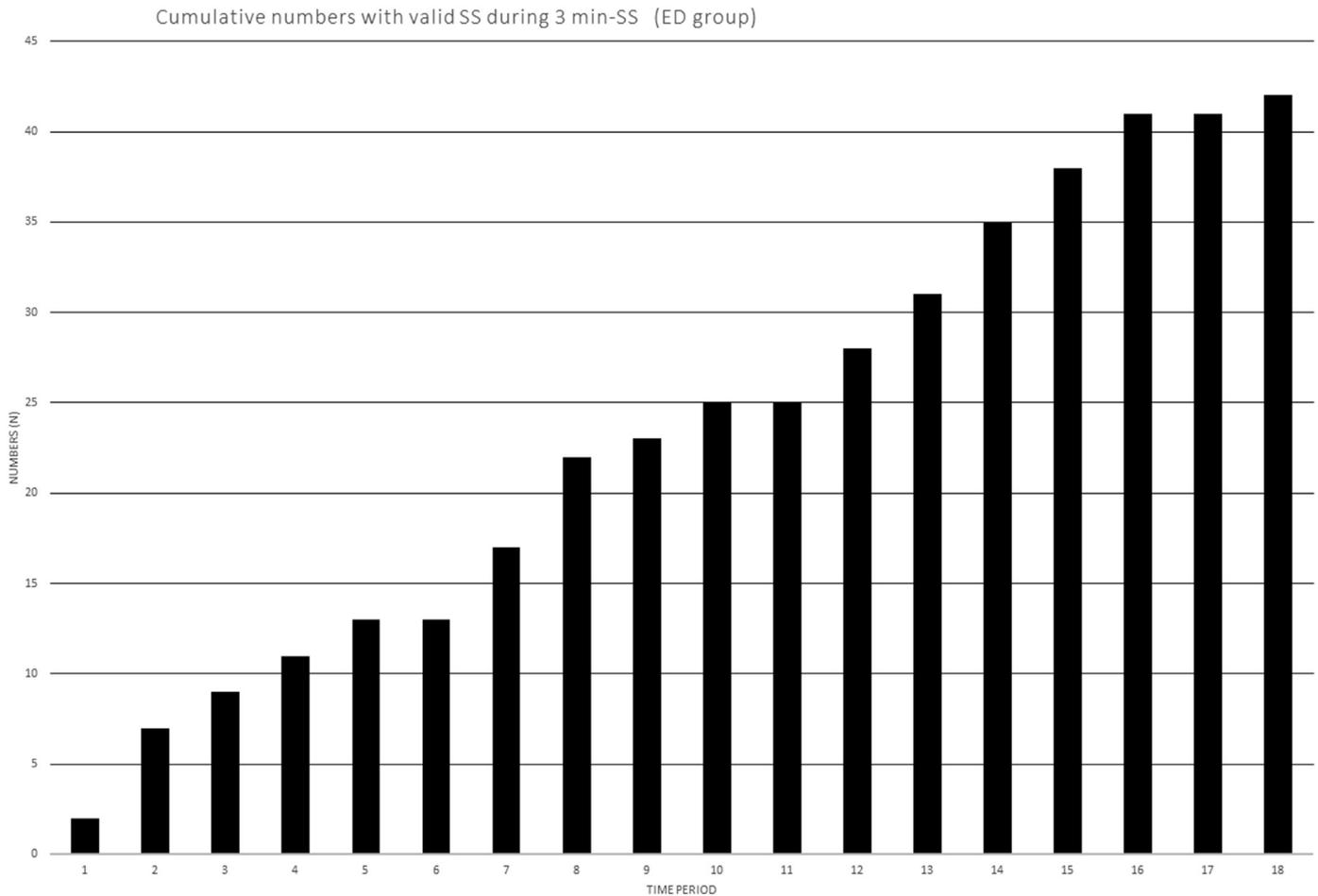


**Fig. 4.** The cumulative numbers from eating disorder group (ED group) achieving a valid SS during the 5 min steady state (SS) periods, based on their lowest resting metabolic rate (RMR) achieved. SS is defined as 5 min period, where respiratory gas exchange varies <10%. Each time period in the panel constitutes 5 min, with the first period counting from minute 1, and each subsequent period counts from the next, subsequent minutes (a total of 16 time periods).

Our results further suggest that the practice with discarding the first 5 min of measurement and then to identify the first upcoming 5 min of SS [18,20–22,27], is not adequate. If the purpose of measuring RMR is to find the lowest EE, results from our study indicate a need for an extended assessment period. We found the individuals' lowest RMR value dispersed over the 20 min measurement period, with ~50% achieving their lowest results during the last part of the period. Borges et al., 2016 and Horner et al., 2001 [18,24] reported no significant difference between RMR measured for subsequent SS periods, which is in contrast to our protocol, in which each subsequent 5-min period was defined from each consecutive minute. Thus, we suggest that with the wider defined period-interval, they might have ignored intermediate periods with SS resulting in even lower RMR.

We found the lowest RMR attained to be significantly lower with a 3-min SS period compared to a 5-min SS period. Unfortunately, our design does not enable us to decide which of these measures are the most valid. The choice of use will have clinical impact, and deserves further research. Reeves et al. (2004) found a 3-min SS vs 5-min SS to be just outside a predetermined clinical acceptance to limits of agreement [27]. However, this criterion was based on a restrictive evaluation of natural daily variance (<2%), and not on the clinical impact per se. Daily variations in non-clinical populations have been found to be 3–6% [25,34–37], and a cut off for acceptable differences of <2% might therefore be too strict.

McEvoy et al. (2009) compared intervals of 2–5 min of SS in patients with traumatic brain injury, allowing a level of agreement of 10% due to a higher variability in critically ill participants [19]. They found the 3-min SS to be at 96% of agreement with the 10% level, and suggested the use of an abbreviated period of 3- or 4 min, if a 5-min SS was not achievable. In line with both Reeves et al. (2004) and McEvoy et al. (2009) [19,27], we found an increasingly higher number of participants reaching a valid SS with shorter SS-definition (>76%). An evaluation of a reduced RMR is based on the ratio between the measured RMR and the calculated rate (most often Harris Benedict equation), and any ratio below 0.9 is regarded clinically low [9,38–40]. Hypo-metabolism has previously been found in persons with AN and in elite athletes where energy availability has been kept too low [33,38,39,41]. To our knowledge, no previous studies have evaluated the capability of an abbreviated protocol to identify those with a reduced RMR. Our results reveal poor agreement between the two different SS criteria, and with a total variation within the HC- and ED-population of 16 and 17% respectively, the agreement between the two different SS criteria is too low. With reference to the results attained from the lowest RMR during 5 min SS in our study, 33% of the ED group (4 individuals missing a valid SS) and 23% of the HC group (1 individual missing a valid SS) will be classified as hypo-metabolic (calculations not shown). By looking into the two different ED groups, the results are 25% in the BED-group and 41% in the



**Fig. 5.** The cumulative numbers from eating disorder group (ED group) achieving a valid SS during the 3 min steady state (SS) periods, based on their lowest resting metabolic rate (RMR) achieved. SS is defined as a 3 min period, where respiratory gas exchange varies <10%. Each time period constitutes 3 min, with the first period counting from minute 1, and each subsequent period counts from the next, subsequent minute (a total of 18 time periods).

BN-group. If the results from the lowest RMR during the 3 min SS are favored, the number with clinically low RMR, increases to 52% in the ED group (no missing values), with status quo in the HC group (no missing values). For the two different ED groups, the results are 45% in the BED-group and 59% in the BN-group, respectively. In contrast to the findings by Wadden et al., 1993, results in the present study showed that also women with BED diagnosis had reduced RMR [42]. The discrepancy might be explained by methodological differences such as differences in mean BMI (lower BMI in the present study), and/or the RMR protocols.

If a 3 min SS period turns out to be comparable to results from a 24-h RMR or direct calorimetry measurement (DC), more participants will get valid measures, and potentially, an increased number of participants with impaired metabolism can be identified. According to the results from our lab, also in line with those of McEvoy et al. (2009) and Reeves et al. (2004) [19,27], the total duration of an RMR-protocol should be of longer duration ( $\geq 20$  min), as only 50% of the participants was able to achieve a valid SS during the first 10 min of measurement.

Limitation of our results is the lack of any DC or a 24-h RMR measurement, enabling us to validate the protocols. While a 5 min SS previously has been validated [18–24], the 3 min SS has not been validated against any such optimal measure. Best practice summary from 2015 suggests a rest period of 20–30 min before measurement

is initiated [23], but was previously suggested to be of sufficient duration with 10–20 min if no intensive exercise was performed during the preliminary hours [21]. Our participants rested in a supine position for only 10 min, which might have caused the higher RMR values during the first 5 min of measurement. However, most participants were spending time at rest in seated position for 15–90 min in our lab before measurement due to waiting, and the chances of increased RMR due to movement, is therefore limited. The procedure in our measurements were close to the suggested best-practice [21,23], still challenging the question on whether an abbreviated protocol and 3-min SS criterion is feasible.

In summary, our findings suggest that an abbreviated measurement protocol for RMR by IC is neither sufficient to identify the lowest possible RMR, nor to result in valid RMR for most participants. This conclusion was not affected by whether the SS period was of 5- or 3 min. Furthermore, abbreviating the SS period from 5 min to 3 min, increases the number of participants reaching a SS throughout the protocol, and results in an even lower RMR. Our results confirm the need of at least 10 min of rest before measuring RMR, and further suggest at least 20 min of measurement if more participants are to reach a valid RMR, also enabling a lower RMR to be captured. Further studies are recommended to explore the potential for a shorter SS criterion, mainly by validating it to a more precise measure of 24 h RMR.

## Statement of authorship

TFM recruited the participants and kept logistics of testing, performed the RMR- and statistical calculations, and had the leading part in manuscript preparations. KMEE did most of the RMR measurements, statistical calculations and manuscript participation. JSB is the project leader, participated in recruitment and screening of participants, controlled the statistical calculations and participated in manuscript preparations. TS was the lab-leader responsible for lab procedures and staff-training, participated in the planning of- and controlled the analysis, and participated in manuscript preparation.

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## Conflict of interest statement

Nothing to declare.

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