Influence of Hormonal Profile on Resting Metabolic Rate in Normal, Overweight and Obese Individuals

Thomas G. Wright, Brian Dawson, Geoffrey Jalleh, Kym J. Guelfi

Aims: To investigate whether blood thyroid stimulating hormone (TSH), cortisol, insulin and glucose concentrations (plus glucose:insulin ratio; GIR) could improve the accuracy of resting metabolic rate (RMR) prediction in normal, overweight and obese persons. Methods: Predictive equations were developed and compared against indirect calorimetry measures for RMR in 217 weight-control clinic participants (n = 128 males and n = 89 females: ~24% normal weight, ~39% overweight and ~37% obese). Results: Using the common accuracy criteria of the proportion of predicted RMR within ±10% of measured RMR, our equations (using age, height, weight and gender, plus the blood factors, both independently and in combination) were accurate ~36–44% of the time, for the whole sample, and when separated by gender and weight class. Specifically, the addition of the blood hormone and glucose concentrations improved the accuracy of predicted RMR by only 1–8% (NS). Conclusions: Including blood TSH, cortisol, insulin, glucose and GIR into RMR prediction equations did not significantly improve estimation accuracy, which in any case only met a criterion of ±10% of the measured RMR ~40% of the time. Further work to refine the prediction of RMR is still needed, and at present, direct measurements should be made wherever possible.

Introduction

The resting metabolic rate (RMR) accounts for ~60–70% of daily energy expenditure [1, 2]. Accordingly, accurate RMR estimations are important in clinical settings for implementing effective weight control programs. However, RMR predictive equations often display large variability in accuracy [3–6]. While it is well accepted that individual fat free mass (FFM) is a prime factor in determining RMR [1, 3, 7], less is known about the potential impact of basal blood hormones such as thyroid stimulating hormone (TSH), cortisol and insulin on RMR. While some reports of the impact of these hormones on RMR and weight management are located in the literature in isolation [1, 8, 9], the combined impact of these variables on RMR has not been widely reported. If chronic abnormal concentrations of these hormones exist, and RMR is negatively affected, weight gain may be promoted or, perhaps more importantly, losing weight may be made
Levels of TSH are commonly higher in obese persons, but are decreased with large weight losses [10, 11]. Further, TSH does not exclusively target the thyroid gland, but is now known to act on various other tissues, including adipose tissue [12]. Knudsen et al. [13] reported that elevated serum TSH levels were associated with obesity: with serum TSH levels >3.6 mU/l, a significantly increased odds ratio for obesity of 2.1 existed, as compared with a comparison group with TSH levels of 1.00–1.99 mU/l. However, the effect of TSH on RMR remains unclear. Resting energy expenditure (REE) was found to correlate with TSH in patients receiving chronic thyroxine treatment when their thyroxine doses were altered [8], but no relationship was reported between REE and TSH in mostly overweight and obese euthyroid persons [9]. Therefore, the relationship between TSH and RMR requires further investigation, although it has been suggested that RMR is only 20–25% thyroid-dependent in humans [8].

Cortisol plays an important role in regulating blood glucose, energy production, inflammation, the immune system and wound healing [2], but if excessive cortisol is produced, as in stressful times, conditions such as weight gain (from overeating: especially around the abdomen) and insulin resistance may develop [14, 15]. Farag et al. [14] reported that the body mass index (BMI) of obese women was the major predictor of diurnal cortisol variation, and Márin et al. [15] found greater urinary cortisol output in obese women with large visceral fat accumulation. However, the potential impact of cortisol on RMR has not been widely researched. Christiansen and colleagues [16] found some evidence for the existence of a relationship between cortisol and RMR, with cortisol withdrawal associated with a 10% decrease in basal energy expenditure, together with a corresponding increase in TSH and insulin sensitivity. Furthermore, Brillon and coworkers [17] showed an increase in resting metabolism with hydrocortisone infusion to increase plasma cortisol concentrations. Accordingly, it has been suggested that glucocorticoids may induce obesity more so by influencing appetite and food intake, rather than via an effect on RMR [18]. Nonetheless, the relationship between cortisol and RMR requires further investigation.

With respect to plasma insulin, there is now strong evidence that greater than normal insulin (and blood glucose) concentrations, as well as the development of insulin resistance, represent primary challenges for weight loss [19]. Commonly, obese persons have higher blood insulin levels and more insulin resistance compared to normal weight individuals [1, 19], but again, whether these factors have any relationship to RMR has not been well investigated. Astrup and colleagues [1] have previously reported a moderate association between REE and insulin in a female (only) sample. Further indirect support for a relationship between insulin and RMR comes from studies reporting greater RMR in individuals with type 2 diabetes compared with non-diabetics, which has been suggested to be contributed to, at least in part, by insulin resistance [20]. Of note, the accuracy of prediction of RMR in obese individuals with type 2 diabetes has been shown to be improved when fasting plasma glucose was included as a variable [21]. Whether the addition of other variables such as fasting insulin concentrations, cortisol and TSH can further improve the accuracy of predicting RMR remains to be determined.

Given the common wide variability in predicted RMR values [3–6], and the changes in basal hormone concentrations that usually occur with weight loss [10, 11, 19], this study aimed at investigating the potential effects of TSH, cortisol, insulin and blood glucose concentrations, both independently and in combination, on RMR in normal, overweight and obese persons. This specific panel of hormones (and metabolite) was studied given they are commonly measured in a clinical setting. Based on the limitations of predicting RMR from current equations incorporating age, height, weight and gender, we sought to examine whether this hormonal profile is useful in improving RMR prediction.

**Methods**

Data on 217 participants (males: n = 128, females: n = 89) aged between 18 and 69 from a Perth (Western Australia) weight-control clinic database were retrospectively accessed for the study. For background information, at clinic entry (by self-referral or from a friend or doctor), participants were first evaluated (medical history, resting ECG, urinalysis and fasting blood profile) by a physician. Height (±10 mm) and body mass (±100 g) were measured and participants subsequently categorised for gender, age, body mass, BMI and WHO weight classes (normal weight, overweight and obese). Participants were excluded from clinic entry if they reported a recent myocardial infarction or major surgery, current steroid use, eating disorders, type 1 diabetes mellitus, were pregnant or on thyroid medications. At entry, all participants gave informed consent for their data to be used for research purposes and the University of Western Australia research ethics committee granted approval for the study.

The RMR was assessed via indirect calorimetry at the clinic after an overnight fast. Prior to assessment, all participants adhered to the following routine and guidelines: no exercise activity, food and fluids (other than water) or caffeine, alcohol or other drug...
consumption in the preceding 12 h. Compliance with these require-ments was confirmed verbally upon arrival to the clinic prior
to test commencement. Upon arrival, participants entered a quiet,
darkened room, and became supine on a padded bench, with head
and shoulders slightly elevated. They then commenced breathing
through a Hans Rudolph respiratory valve (with nose clip), main-
taining this set up through a continuous 30-min period. Ex-
pired air was collected into a Douglas bag during this period and
then analysed for FeO₂ and FeCO₂ concentrations (Applied Elec-
 trometry, SOV S-3A/1 and COV CD-3A, Pittsburgh, Pa.,
USA). The gas analysers were calibrated pre-test and verified
post-test with certified gravimetric gas mixtures (BOC Gases,
USA). A 120 l Tissot Tank (Collins, Braintree,
Chatswood, Australia). A 120 l Tissot Tank (Collins, Braintree,
Mass., USA) measured expired air volumes, with correction for the
volume used to analyse FeO₂ and FeCO₂ concentrations. Resting
VO₂, VCO₂, RER and RMR were then calculated via the Haldane
transformation using non-protein RER values [2].

On a separate occasion, and within 48 h of completing the RMR
assessment, participants attended the clinic (before 09:00 h) and
provided a fasting venous blood sample; these were then trans-
ported under controlled conditions to a commercial pathology
laboratory (Clinipath Pathology, Perth, Western Australia). This
centre is approved by the Therapeutic Goods Administration and
accredited by the National Australian Testing Authority (#2619).
To measure cortisol levels, insulin and TSH, blood was collected
into BD vacutainers containing fluoride oxa-
cide. The total sample was also separated into BMI categories
(mixed gender): 20–24.9 kg/m² (normal weight), 25–29.9 kg/m²
(overweight), >30 kg/m² (obese). Significance was accepted at p <
0.05.

Results

Participant characteristics are shown in table 1. Males
and females comprised 59 and 41% of the sample, respect-
ively. The total sample comprised ~24% normal weight,
~39% overweight and ~37% obese. Males were older,
taller and heavier, and had a greater RMR and resting
VO₂ than females (all p < 0.05). Normal weight partici-
pants were younger (p < 0.05) than overweight and obese,
and stepwise increments in weight, BMI, RMR and rest-
ing VO₂ were seen across all weight categories (all
p < 0.05). Blood hormone and glucose data is presented in
table 2. No differences were seen in TSH between
weight classes, but cortisol levels were higher in normal
weight (p < 0.05/0.01) and insulin and glucose signifi-
cantly higher in obese (p < 0.05/0.01), such that the GIR
was significantly lower in obese (p < 0.001). The mean
TSH, cortisol, insulin and glucose concentrations were
within normal ranges for all weight groups.

The RMR prediction equations for males and females
(based on age, weight, height and gender) were:

Males: 6.30 × weight (kg) + 9.16 × height (cm) – 4.87 × age
(years) – 216.96; and
Females: 9.55 × WT – 1.62 × HTCM – 0.54 × age + 980.92

<table>
<thead>
<tr>
<th>Participant characteristics</th>
<th>n</th>
<th>Age, years</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>BMI, kg/m²</th>
<th>Measured RMR, Kcal/day</th>
<th>Resting VO₂, l/min</th>
<th>Resting RER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>128</td>
<td>46.3±9.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>180.1±6.8&lt;sup&gt;b&lt;/sup&gt;</td>
<td>94.2±15.2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>30.0±4.1</td>
<td>1,802±426&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.26±0.06&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.82±0.11</td>
</tr>
<tr>
<td>Female</td>
<td>89</td>
<td>42.0±12.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>166.1±6.8&lt;sup&gt;b&lt;/sup&gt;</td>
<td>78.3±16.9&lt;sup&gt;c&lt;/sup&gt;</td>
<td>28.4±6.2</td>
<td>1,437±343&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.21±0.05&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.80±0.08</td>
</tr>
<tr>
<td>BMI class</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NW</td>
<td>53</td>
<td>39.6±12.0&lt;sup&gt;f&lt;/sup&gt;</td>
<td>172.6±9.4</td>
<td>69.2±10.0&lt;sup&gt;g&lt;/sup&gt;</td>
<td>23.1±1.4</td>
<td>1,458±447&lt;sup&gt;h&lt;/sup&gt;</td>
<td>0.21±0.06&lt;sup&gt;i&lt;/sup&gt;</td>
<td>0.80±0.08</td>
</tr>
<tr>
<td>OW</td>
<td>85</td>
<td>46.8±10.5&lt;sup&gt;e&lt;/sup&gt;</td>
<td>175.8±9.3</td>
<td>84.3±10.2&lt;sup&gt;f&lt;/sup&gt;</td>
<td>27.2±1.3</td>
<td>1,648±394&lt;sup&gt;j&lt;/sup&gt;</td>
<td>0.24±0.05&lt;sup&gt;k&lt;/sup&gt;</td>
<td>0.82±0.12</td>
</tr>
<tr>
<td>OB</td>
<td>79</td>
<td>45.3±10.0&lt;sup&gt;d&lt;/sup&gt;</td>
<td>174.1±10.2</td>
<td>103.8±13.7&lt;sup&gt;e&lt;/sup&gt;</td>
<td>34.2±3.6</td>
<td>1,786±417&lt;sup&gt;i&lt;/sup&gt;</td>
<td>0.26±0.06&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.81±0.09</td>
</tr>
</tbody>
</table>

Values are mean ± SD. BMI = Body mass index; NW = normal weight (BMI <25 kg/m²); OW = overweight (BMI 25–29.9 kg/m²); OB = obese (BMI >30 kg/m²). <sup>a–k</sup> Like symbols are significantly different within each sample (p < 0.05).
With all blood measures included, the equations were:

Males: 6.50 × WT + 10.16 × HTCM – 5.96 × age + 59.10 × TSH + 0.37 × cortisol – 3.52 × insulin – 5.34 × GIR + 32.68 × glucose – 670.52; and

Females: 8.81 × WT + 1.38 × HTCM – 2.02 × age + 10.05 × TSH + 0.28 × cortisol + 12.33 × insulin + 8.70 × GIR + 92.85 × glucose – 231.60

Table 3 shows that for the whole sample, plus when separated by gender and with the addition of the blood measures to the predictive equations, the developed equations only met the accuracy criterion of ±10% of the measured RMR ~36–44% of the time. Specifically, the addition of all the blood measures improved the accuracy of the predicted RMR by only ~1–8% (NS). Separating the sample by BMI category (normal, overweight and obese) did not change the level of accuracy of RMR prediction, both with and without the inclusion of blood measures. These predictive RMR equations are presented in online supplementary table 4 (for all online suppl. material, see www.karger.com/doi/10.1159/000382080).

Pearson correlations showed only small-to-moderate associations (r = 0.20 to 0.35) between RMR and insulin and glucose levels in the total sample and females (online suppl. table 5, which provides a full record of all correlational results). For body mass, in the total sample, males, overweight and obese groups, small-to-moderate negative relationships were recorded with cortisol (r = –0.32 to –0.24), while insulin and glucose recorded small to large correlations (r = 0.25 to 0.52) in the total sample, males and females. Similarly, for BMI, in the total sample and males, small negative relationships with cortisol were recorded (r = –0.27 to –0.19), while insulin recorded small to large associations in the total sample, both genders and all weight classes (r = 0.26 to 0.64). Glucose recorded small-to-moderate associations with BMI in the total sample, males, females and overweight (r = 0.22 to 0.37). For TSH, the only relationship found was with age in males (r = 0.24).

Table 2. Blood hormone and glucose values for normal weight, overweight and obese participants

<table>
<thead>
<tr>
<th></th>
<th>Normal weight (n = 53)</th>
<th>Overweight (n = 85)</th>
<th>Obese (n = 79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>2.2±2.1</td>
<td>1.9±0.9</td>
<td>1.9±0.9</td>
</tr>
<tr>
<td>Cortisol</td>
<td>479.3±185.6***, b</td>
<td>391.8±117.7***</td>
<td>382.2±180.6***</td>
</tr>
<tr>
<td>Insulin</td>
<td>5.7±2.4***</td>
<td>6.5±3.2***</td>
<td>13.6±7.9***</td>
</tr>
<tr>
<td>GIR</td>
<td>17.8±7.6***</td>
<td>16.6±7.4***</td>
<td>9.4±5.3***</td>
</tr>
<tr>
<td>BGL</td>
<td>4.7±0.5***, h***</td>
<td>5.3±0.5***, i</td>
<td>5.3±1.1***</td>
</tr>
</tbody>
</table>

Values are mean ± SD. TSH = Thyroid stimulating hormone; GIR = glucose:insulin ratio; BGL = blood glucose concentration. *–i Like symbols are significantly different within each group. * p < 0.05; ** p < 0.01; *** p < 0.001.

Table 3. Comparisons of the predictive equations with and without blood measures for the proportion of predicted RMR within ±10% of measured RMR

<table>
<thead>
<tr>
<th></th>
<th>Without blood measures, %</th>
<th>With blood measures, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>217</td>
<td>41.5</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>128</td>
<td>39.1</td>
</tr>
<tr>
<td>Female</td>
<td>89</td>
<td>43.8</td>
</tr>
<tr>
<td>BMI class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NW</td>
<td>53</td>
<td>41.5</td>
</tr>
<tr>
<td>OW</td>
<td>85</td>
<td>42.4</td>
</tr>
<tr>
<td>OB</td>
<td>79</td>
<td>35.5</td>
</tr>
</tbody>
</table>

RMR = Resting metabolic rate; BMI = body mass index; NW = normal weight; OW = overweight; OB = obese.
No significant differences in the proportions were found by total sample, gender or weight category.

Discussion

To examine the potential influence of blood hormones and metabolites, which commonly vary between normal and overweight/obese persons, on the prediction of RMR, we created predictive equations incorporating these factors, in addition to the standard variables of age, height, weight and gender. Our results showed that the addition of resting blood TSH, cortisol, insulin, glucose and GIR, both independently and in combination, did not improve the predictive accuracy of our developed RMR equations. Therefore, the hormonal measures used here appear unnecessary for RMR prediction; however, it is acknowledged that the hormone levels found here were all within a normal range, and higher/lower concentrations (and other hormones) may have different effects on RMR.

As RMR represents the single largest component of the daily energy expenditure in most people (especially the obese), much research attention has been directed towards predicting this value, as direct assessment requires the measurement of oxygen consumption and fuel substrate oxidation. However, using predictive equations for RMR estimation is often limited by large variations in
their accuracy [3–6] when assessed against a common criterion of ±10% of the measured RMR, so investigation of other variables to use in such prediction equations, in addition to the simple variables of age, height, weight and gender, is important. For instance, Gougeon and colleagues [21] found that the accuracy of RMR estimation was improved in obese individuals with type 2 diabetes when fasting plasma glucose was included as a variable. Accordingly, we investigated whether blood TSH, cortisol, insulin and glucose concentrations, which are commonly altered in obese compared with normal weight persons, might have some influence on RMR prediction in a mostly overweight/obese sample of Australians who had attended a weight control clinic. We found that when predicting RMR from the standard variables of age, height, weight and gender, the accuracy criterion of ±10% of the measured RMR was only met ~40% of the time, and that the blood measures, either independently or in combination, did not significantly improve the prediction accuracy. Although they did not develop prediction equations from their data, both Astrup et al. [1] and Johnstone et al. [7] found that FFM, and to a lesser degree, fat mass, to be strong contributors to RMR, and that triiodothyronine (T3) and leptin concentrations did not help explain the remaining variance.

Measuring TSH concentrations, as an indicator of thyroid function, is becoming more common in weight control settings, given the potential impact on metabolic rate and energy balance [8], and as TSH concentrations are often greater in obese persons [10, 11], although not necessarily above normal ranges. Previously, al-Adsani et al. [8] have reported a large negative association (r = –0.80) between REE and TSH levels, when varied thyroxine doses were used to induce changes in REE. These dose manipulations caused a wide range of peak TSH values within their sample, ranging from 0.42–18.00 mU/l, and with a mean of 5.21 mU/l. This value is well above the mean values recorded in our samples (~2.0 mU/l), which are in the lower part of the normal range (0.5–5.0 mU/l). Knudsen et al. [13] reported that in a large (n = 4,082) Danish population sample, for TSH values of 2.0–3.6 mU/l the odds ratio for a BMI of >30 kg/m² was slightly raised at 1.20, but for TSH values >3.6 mU/l, the odds ratio increased to 2.13; this suggests that TSH levels in the upper part of the normal range or greater may be more likely to influence bodily factors such as RMR. Despite ~75% of our total sample being overweight or obese, their mean TSH values were well within the normal range, and therefore, perhaps unlikely to have had any significant effect on RMR. This contention is supported by our lack of association recorded between TSH and BMI, in contrast with the significant positive relationship recorded between these two variables by Knudsen et al. [13]. Recently, Spadafranca et al. [9] have also reported no association between REE and TSH in mostly overweight or obese euthyroid subjects.

There is very little research on cortisol, insulin, glucose and GIR with respect to RMR, despite obese persons commonly having lower blood cortisol levels (but greater cortisol excretion) and higher blood insulin and glucose levels (and a lower GIR) compared with normal or overweight individuals [1, 15, 19]. However, whether these changes are causative factors, or only a consequence of obesity, remains unclear. Blood cortisol concentrations were highest in the normal weight cohort, but all values were in the normal range, and no associations were found with RMR across all weight and gender categories, and the addition of cortisol levels did not improve the prediction accuracy of RMR. Previously, Astrup et al. [1] reported a correlation of r = –0.37 between REE and plasma cortisol in 50 women (27 of whom were obese), but when included in a stepwise multiple regression analysis, no impact was seen. In our study, along with BMI, weak negative relationships (r = –0.19 to –0.27) were recorded with cortisol for the total sample and males only in our study.

With regard to insulin, reducing the glycaemic load may be an important element of weight loss programs for persons with high circulating insulin levels [19]. Our obese cohort had significantly higher blood insulin and glucose concentrations (albeit, still within the normal ranges) compared with the normal weight group, with moderate-to-large positive correlations (r = 0.25 to 0.64) recorded for both blood measures with body mass and BMI in the total sample, males and females, but smaller and inconsistent relationships were seen when the sample was separated into weight categories. The obese also had a significantly lower GIR (bordering on being insulin resistant) compared with the normal weight group, and similar (negative) relationships (r = –0.35 to –0.50) with body mass and BMI were found for the total sample, males and females, but these were lost when the sample was separated by weight category. With RMR, only small to moderate associations (r = 0.20 to 0.35) were found with insulin, glucose and GIR in the total and female samples, consistent with our main finding that the addition of these blood measures did not improve the prediction accuracy of RMR. Astrup et al. [1] also found a moderate (r = 0.47) relationship between REE and plasma insulin in their wholly female sample. However, our results contrast with those found by Gougeon and colleagues [21] who observed improved RMR estimation with the inclu-
sion of fasting plasma glucose in their sample of patients with type 2 diabetes. This difference may be explained on the basis of their participant group having much higher (and greater variation) fasting glucose concentrations compared with the present sample with mean fasting glucose concentrations within a euglycaemic range.

Although this is the first study to examine the effects of TSH, cortisol, insulin and blood glucose concentrations, both independently and in combination, on RMR in normal, overweight and obese persons, it is not without limitations. First, it is important to acknowledge that the participants in this study were a self-selected sample from one weight management clinic in Perth, Western Australia. It is possible that this group is not representative of the wider population, although it may be argued that the need for accurate RMR prediction is greatest in this sample, given a desire to take action regarding their health and weight status and the need for accurate advice about their specific dietary and physical activity needs. Furthermore, it should be acknowledged that our results are limited to the impact of cortisol, TSH, blood glucose and insulin on RMR. Whether other hormones such as, but not limited, to ghrelin and leptin may have an impact on RMR and can enhance the accuracy of predicting RMR remains to be determined. Future research should explore these issues.

In conclusion, in a sample comprising ~75% of overweight and obese persons, we found that the inclusion of blood TSH, cortisol, insulin, glucose and GIR into an RMR prediction equation (using also age, height, weight and gender), did not significantly improve the accuracy of estimation, which in any case only met a criterion of ±10% of the measured RMR only ~40% of the time. Further work to refine the prediction of RMR is needed, perhaps incorporating measures of FFM and ratings of habitual physical activity levels to determine whether RMR prediction accuracy can be improved to more acceptable levels. Until the accuracy of RMR prediction equations is further improved, direct measurements should be made wherever possible.

References


6 Johnstone AM, Murison SD, Duncan JS, Rance KA, Speaman JR: Factors influencing variation in basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex, circulating leptin, or triiodothyronine. Am J Clin Nutr 2005;82:941–948.


