Measured resting metabolic rate, respiratory quotient, and body composition in patients with narcolepsy: a preliminary report of a case–control study

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This case–control study compared the body composition, resting metabolic rate (RMR), and respiratory quotient (RQ) of narcolepsy patients with those of body mass index (BMI)-gender and age-matched controls. This study included 14 male patients with narcolepsy and 14 matched controls. The narcolepsy patients were subdivided into two subgroups (n = 7/each): those with cataplexy (NT1) and those without cataplexy (NT2). Anthropometric measurements, bioelectric impedance analysis, and indirect calorimetry were used in addition to the calculation of common body-composition indices (conicity index, abdominal volume index, and body adiposity index). Our results showed no significant difference in fat percentage, fat mass, fat-free mass, and TBW among NT1, NT2, and controls (p > 0.05). Compared to matched controls, there was a reduction of muscle mass in both NT1 and NT2 subgroups. The RMR was similar in all groups, while patients in the NT1/NT2 subgroups had a lower RQ, used more fat and fewer carbohydrates during the fasting period. These findings give an insight into the distinctive state of altered metabolism in patients with narcolepsy, especially the resting metabolic rate, which was not altered in NT1 vs. NT2 compared to the controls when matched for BMI, age, and gender.

Westphal was the first to describe narcolepsy in 18771. Unlike healthy individuals, people with narcolepsy enter their first rapid eye movement (REM) phase immediately after the onset of sleep2. Narcolepsy type 1 (NT1) is accompanied by cataplexy (sudden loss of muscle tone triggered by mostly positive emotion), whereas narcolepsy type 2 (NT2) is an absence of cataplexy3. Narcolepsy, particularly NT1, is associated with hypocretin (orexin-A) deficiency due to the loss of hypothalamic orexinergic neurons and leads to irresistible attacks of sleep, cataplexy, hypnagogic hallucinations, and sleep paralysis, with symptoms beginning as early as ten years of age4,5. There is no known cure for narcolepsy at present, although the symptoms can be managed. Several factors, such as lifestyle and genetic factors6, and more recently, autoimmune/inflammatory processes7, have been linked to the etiology of narcolepsy. The prevalence of NT1 is 25–50/100,000 individuals worldwide, with an incidence of 0.74/100,000 person-years8; the prevalence of NT2 is higher at 56/100,000 individuals8,9. The few available studies in Saudi Arabia have reported a prevalence of approximately 40/100,000 individuals10,11.

Besides sleep symptoms, several studies have documented an increase in body mass index (BMI) around the onset of narcolepsy in children12 and adults13,14. This may be attributed to the loss of orexin-A-producing neurons, which modulate feeding behavior, resting metabolic rate (RMR), respiratory quotient (RQ), and some

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hormones, and thus potentially exert a major influence on energy expenditure\textsuperscript{15}. Furthermore, a study of adipose tissue distribution by MRI in patients with narcolepsy showed a distinctive pattern, including excessive subcutaneous adipose tissue rather than visceral adipose tissue and no effect on brown adipose tissue\textsuperscript{16}. The pose tissue distribution by MRI in patients with narcolepsy showed a distinctive pattern, including excessive narcolepsy (lacking hypocretin)\textsuperscript{20}. However, regarding patients with NT1, research on the metabolic rate is still BMI-matched controls. A previous study reported obesity with a lower metabolic rate in a mouse model of found no differences between the resting metabolic rates (RMRs) of narcolepsy patients and those of age- and BMI-matched controls. A previous study reported obesity with a lower metabolic rate in a mouse model of narcolepsy (lacking hypocretin)\textsuperscript{30,31}. However, regarding patients with NT1, research on the metabolic rate is still inconclusive\textsuperscript{35,37}. Although the BMI increase associated with narcolepsy is well-established, the relationship between narcolepsy and other metabolic measures such as body fat/muscle distribution and RQ independent of BMI are not well documented, and the available evidence is inconsistent\textsuperscript{15,19}. Understanding the body fat/muscle distribution of narcolepsy patients may shed a light on the mechanisms and type of weight gain that occurs in narcolepsy. Previous studies have mainly used measures such as BMI and the waist − hip ratio to measure body hormones levels and to study the metabolic rate. A recent study showed that narcolepsy patients have lower RMR than that of the BMI- matched controls. Thus, this study aimed to identify the differences in the body composition, RMR, and RQ of patients with narcolepsy (type 1 and 2), and those of healthy sex- age- and BMI-matched controls using a multi-frequency bioelectric impedance analyzer to measure body composition and an indirect calorimetry device to measure RMR and RQ.

### Results

Table 1 presents the polysomnographic and multiple sleep latency rest recordings of patients with narcolepsy.

Table 1. Polysomnographic and multiple sleep latency test recordings of patients with narcolepsy.

| Variables                        | Narcolepsy type 1 | Narcolepsy type 2 | p-value |
|----------------------------------|-------------------|-------------------|---------|
| Epworth Sleepiness scale         | 19.5 ± 3.5        | 16.9 ± 4.4        | 0.310   |
| **Polysomnographic findings**   |                   |                   |         |
| Sleep latency (min)              | 5.5 ± 1.4         | 7.1 ± 2.2         | 0.222   |
| Latency to rapid eye movement (min) | 54.8 ± 12.5      | 96.8 ± 20.1       | 0.008   |
| Sleep efficiency (%)             | 80.4 ± 5.7        | 84.5 ± 5.1        | 0.310   |
| Stage N1 (%)                     | 15.1 ± 3.3        | 6.9 ± 2.1         | 0.008   |
| Stage N2 (%)                     | 50.1 ± 4.2        | 64.8 ± 3.2        | 0.008   |
| Stage N3 (%)                     | 11.3 ± 2.2        | 11.5 ± 2.2        | 0.690   |
| Stage R (%) (Rapid eye movement sleep) | 23.5 ± 3.4       | 16.8 ± 2.8        | 0.008   |
| Arousal index                    | 26.2 ± 5.1        | 18.3 ± 4.2        | 0.016   |
| **Multiple sleep latency test**  |                   |                   |         |
| Sleep latency (min)              | 2.4 ± 0.4         | 3.1 ± 0.6         | 0.032   |
| Sleep onset rapid eye movement periods (average) | 3.6 ± 0.4        | 2.7 ± 0.3         | 0.008   |
| Rapid eye movement latency (min) | 2.7 ± 0.3         | 4.2 ± 0.9         | 0.008   |

As shown in Table 4, differences in body composition (BFP, FM, FMI, FFMI, and FMMA) among groups were not significant. However, the muscle masses of both the NT1 and NT2 subgroups were significantly lower than of the control group (34.26 ± 2.46 kg, and 31.41 ± 4.74 vs. 61.53 ± 8.60 kg, respectively; F = 63.9; df = 2; p = 0.000). While, in the NT1 subgroup, the only significant
correlation with RMR was Wt, PBF, and FM. The correlations of RMR in the matched-control group is very similar to the NT2 subgroup.

Discussion
This case–control study is one of the few studies on body composition, RMR, and RQ of narcolepsy patients. We found that the patients in the narcolepsy subgroups had a lower RQ, and lower muscle mass compared to the control group; they also utilized more fat and fewer carbohydrates, which is consistent with our hypothesis that narcolepsy patients have lower RMR compared to their BMI-matched controls. However, our findings showed that RMR and body composition measures (BFP, FM, FMI, FFMI, and TBW) were similar between the narcolepsy patients and controls.

Table 2. Demographic data among study groups.

| Variables          | Narcolepsy type 1 | Narcolepsy type 2 | Control         | χ²  | p-value |
|--------------------|-------------------|-------------------|-----------------|-----|---------|
| Smoking            |                   |                   |                 | 1.80| 0.49    |
| Non-smoker         | 57.1              | 57.1              | 85.7            |     |         |
| Smoker             | 42.9              | 42.9              | 14.3            |     |         |
| Physical activity  |                   |                   |                 | 15.26| 0.01    |
| No regular physical activity | 28.6          | 14.3              | 64.4            |     |         |
| Regular physical activity for 15 min | 57.1         | 85.7              | 7.1             |     |         |
| Regular physical for 30 min | 0.0            | 0.0               | 21.4            |     |         |
| Regular physical for 60 min | 14.3         | 0.0               | 7.1             |     |         |
| Marital status     |                   |                   |                 | 1.71| 0.42    |
| Married            | 28.6              | 57.1              | 57.1            |     |         |
| Not married        | 71.4              | 42.9              | 42.9            |     |         |
| Occupation         |                   |                   |                 | 0.49| 0.78    |
| Not employee (has no fixed job) | 42.9           | 71.4              | 28.6            |     |         |
| Employee (has a fixed job) | 57.1           | 28.6              | 71.4            |     |         |
| Residence          |                   |                   |                 | 2.10| 0.35    |
| Live outside the urban area | 42.9           | 28.6              | 14.5            |     |         |
| Live inside the urban area | 57.1           | 71.4              | 85.5            |     |         |

Table 3. Anthropometric and clinical characteristics of the study subgroups. Values with the different superscripts within a raw are statistically significant according to the Bonferroni posthoc test (p < 0.05).

| Variables                              | Narcolepsy type 1 (with cataplexy) mean ± sd (n = 7) | Narcolepsy type 2 (no cataplexy) mean ± sd (n = 7) | BMI-matched control mean ± sd (n = 14) | p-value |
|----------------------------------------|-------------------------------------------------------|---------------------------------------------------|----------------------------------------|---------|
| Age (year)                             | 25.29 ± 3.59a                                         | 30.14 ± 6.15a                                      | 27.86 ± 4.38a                         | 0.287   |
| Height (cm)                            | 174.86 ± 5.40a                                        | 172.81 ± 4.53a                                     | 167.82 ± 3.58b                        | 0.009   |
| Weight (kg)                            | 102.79 ± 13.25a                                       | 93.19 ± 21.51a                                     | 92.34 ± 21.90b                        | 0.212   |
| BMI (kg/m²)                            | 33.73 ± 5.18a                                         | 31.19 ± 7.05a                                      | 32.77 ± 7.54a                         | 0.655   |
| WC (cm)                                | 110.93 ± 9.35a                                        | 106.86 ± 16.19a                                    | 101.93 ± 16.62a                       | 0.221   |
| HC (cm)                                | 118.86 ± 8.82a                                        | 112.28 ± 13.55a                                    | 110.21 ± 15.68a                       | 0.277   |
| WHR                                    | 0.93 ± 0.07a                                          | 0.95 ± 0.05a                                       | 0.92 ± 0.04a                          | 0.610   |
| Systolic blood pressure (mmhg)         | 114.86 ± 11.42a                                       | 108.57 ± 15.12b                                    | 119.57 ± 9.98b                        | 0.122   |
| Diastolic blood pressure (mmhg)        | 75.86 ± 7.86a                                         | 74.14 ± 10.75a                                     | 85.14 ± 7.94b                         | 0.017   |
| Fasting glucose level (mg/dl)          | 97.43 ± 9.47a                                         | 100.43 ± 11.28a                                    | 93.43 ± 10.14a                        | 0.577   |
| Measured rmr (quark rmr)               | 2075.29 ± 112.57a                                     | 2035.14 ± 527.12a                                  | 2053.86 ± 434.49a                     | 0.983   |
| Respiratory quotient                   | 0.72 ± 0.04a                                          | 0.73 ± 0.06a                                       | 0.81 ± 0.07b                          | 0.006   |
| Volume of oxygen/min                   | 309.14 ± 17.55a                                       | 301.71 ± 74.52a                                    | 300.00 ± 64.26a                       | 0.946   |
| Volume of carbon dioxide/min           | 222.71 ± 15.32a                                       | 223.00 ± 68.67a                                    | 241.71 ± 52.72a                       | 0.629   |
| Percentage of utilized fat             | 80.11 ± 3.83a                                         | 73.17 ± 11.48a                                     | 54.71 ± 22.86b                        | 0.003   |
| Percentage of utilized carbohydrates   | 3.69 ± 3.38a                                          | 9.24 ± 13.99a                                      | 27.95 ± 22.05b                        | 0.006   |
whereas reduced lean body mass occurs mainly due to sarcopenia\(^{23}\). with a redistribution of fat and lean mass because of the intra-abdominal fat accumulates more than the total fat, whereas the mean age of the narcolepsy patients in the Poli et al. study was 38.2 years. Increasing age is associated both studies had different ages and BMIs. The average age of the narcolepsy patients in this study was 27.2 years, RMR of the narcolepsy patients was reduced but not significantly, compared to the controls\(^{24}\). However, although ence in RMR of the NT1 and NT2 subgroups. This result is in contrast to the study by Chabas et al., in which the we found no significant case–control difference in measured RMR. Furthermore, there was no significant differ-

The results of this study also revealed a similar body composition measures (except muscle mass) between the narcolepsy patients and controls, in contrast to the results of a previous case–control study on metabolic alterations in narcolepsy patients and idiopathic hypersomnia patients. The study by Poli et al., which involved the use of the BMI and waist-hip ratio to measure body fat, reported significant differences in the metabolic parameters, including WC, high-density lipoproteins, glucose/insulin ratio, and daily energy intake, between the narcolepsy patients and controls\(^{25}\). The difference in the results may be because the study populations of both studies had different ages and BMIs. The average age of the narcolepsy patients in this study was 27.2 years, whereas the mean age of the narcolepsy patients in the Poli et al. study was 38.2 years. Increasing age is associated with a redistribution of fat and lean mass because of the intra-abdominal fat accumulates more than the total fat, whereas reduced lean body mass occurs mainly due to sarcopenia\(^{23}\).

The results of this study, however, are compatible with those of a previous cross-sectional study that reported no significant group differences in the supraclavicular brown adipose tissue fat of adolescent narcolepsy patients compared to healthy participants, suggesting that the brown adipose tissue is not affected by orexin under ther-

| Variables                  | Narcolepsy type 1 (with cataplexy) mean ± SD (n = 7) | Narcolepsy type 2 (no cataplexy) mean ± SD (n = 7) | BMI-matched control mean ± SD (n = 14) | p-value |
|---------------------------|-----------------------------------------------------|---------------------------------------------------|---------------------------------------|---------|
| Body fat percent (%)      | 30.7 ± 5.36\(^*\)                                    | 30.2 ± 5.21\(^*\)                                 | 28.31 ± 8.08\(^*\)                    | 0.553   |
| Fat mass (kg)             | 31.75 ± 10.04\(^*\)                                  | 28.94 ± 12.21\(^*\)                               | 27.44 ± 14.18\(^*\)                  | 0.346   |
| Fat mass index            | 10.48 ± 3.62\(^*\)                                   | 9.70 ± 4.07\(^*\)                                 | 9.74 ± 4.97\(^*\)                    | 0.665   |
| Fat free mass (kg)        | 69.70 ± 5.22\(^*\)                                   | 64.00 ± 9.92\(^*\)                                | 64.53 ± 9.02\(^*\)                   | 0.367   |
| Fat free mass index       | 22.82 ± 1.83\(^*\)                                   | 21.42 ± 3.13\(^*\)                                | 22.90 ± 2.97\(^*\)                   | 0.500   |
| Muscle mass (kg)          | 34.26 ± 2.46\(^*\)                                   | 31.41 ± 4.74\(^*\)                                | 61.53 ± 8.60\(^*\)                   | 0.000   |
| Total body water (l)      | 51.03 ± 3.81\(^*\)                                   | 46.87 ± 7.28\(^*\)                                | 53.32 ± 5.40\(^*\)                   | 0.104   |
| Conicity index            | 1.33 ± 0.07\(^*\)                                    | 1.34 ± 0.06\(^*\)                                 | 1.26 ± 0.08\(^*\)                    | 0.095   |
| Abdominal volume index    | 24.84 ± 4.26\(^*\)                                   | 23.33 ± 7.40\(^*\)                                | 21.36 ± 7.04\(^*\)                   | 0.222   |
| Body adiposity index      | 33.53 ± 5.05\(^*\)                                   | 31.43 ± 5.81\(^*\)                                | 32.69 ± 7.02\(^*\)                   | 0.063   |

Table 4. Body composition parameters among study subgroups. Values with the different superscripts within a raw are statistically significant according to the Bonferroni posthoc test (p < 0.05).

The Stanford Sleepiness Scale and symptoms in narcolepsy type 1 vs type 2 subgroups. \(^*\)Significance based on Chi-Square test.

| Variables                  | Narcolepsy type 1 (with cataplexy) Mean ± SD (n = 7) | Narcolepsy type 2 (No cataplexy) Mean ± SD (n = 7) | p-value |
|---------------------------|-----------------------------------------------------|---------------------------------------------------|---------|
| Stanford sleepiness scale | 3.57 ± 1.81                                          | 3.57 ± 1.13                                        | 0.248   |
| Suffering from interrupted sleep; n(%) | 4 (57.1)                                              | 1 (14.3)                                          | 0.094\(^*\) |
| Suffering from sleep paralysis; n(%)        | 5 (71.4)                                              | 1 (14.3)                                          | 0.037\(^*\) |
| Suffering from hypnagogic hallucination; n(%) | 7 (100.0)                                             | 4 (57.1)                                          | 0.051\(^*\) |
| Suffering from cataplexy; n(%)             | 7 (100.0)                                             | 0 (0.0)                                           | < 0.001\(^*\) |

Table 5. The Stanford Sleepiness Scale and symptoms in narcolepsy type 1 vs type 2 subgroups. \(^*\)Significance based on Chi-Square test.
| Variables                  | Narcolepsy type 1 (with cataplexy) (n = 7) | Narcolepsy type 2 (No cataplexy) (n = 7) | BMI-matched Control group (n = 14) |
|---------------------------|---------------------------------------------|-------------------------------------------|----------------------------------|
| Age (years)               | r 0.180                                    | −0.334                                    | −0.122                           |
|                           | Sig. (2-tailed) 0.699                       | 0.465                                     | 0.679                            |
| Weight (kg)               | r 0.857*                                    | 0.964**                                   | 0.802**                          |
|                           | Sig. (2-tailed) 0.014                       | 0.000                                     | 0.001                            |
| Height (cm)               | r 0.243                                    | 0.396                                     | 0.304                            |
|                           | Sig. (2-tailed) 0.599                       | 0.379                                     | 0.290                            |
| BMI (kg/m²)               | r 0.536                                    | 0.786*                                    | 0.736**                          |
|                           | Sig. (2-tailed) 0.215                       | 0.036                                     | 0.003                            |
| Waist circumference (cm)  | r 0.536                                    | 0.786*                                    | 0.648*                           |
|                           | Sig. (2-tailed) 0.215                       | 0.036                                     | 0.012                            |
| Hip circumference (cm)    | r 0.739                                    | 0.607                                     | 0.863**                          |
|                           | Sig. (2-tailed) 0.058                       | 0.148                                     | 0.000                            |
| Waist hip ratio           | r 0.000                                    | 0.321                                     | 0.031                            |
|                           | Sig. (2-tailed) 1.000                       | 0.482                                     | 0.916                            |
| Conicity index            | r −0.111                                    | 0.655                                     | 0.481                            |
|                           | Sig. (2-tailed) 0.812                       | 0.111                                     | 0.081                            |
| Abdominal volume index    | r 0.536                                    | 0.786*                                    | 0.648*                           |
|                           | Sig. (2-tailed) 0.215                       | 0.036                                     | 0.012                            |
| Body adiposity index      | r 0.321                                    | 0.714                                     | 0.781**                          |
|                           | Sig. (2-tailed) 0.482                       | 0.071                                     | 0.001                            |
| Percent body fat          | r 0.775*                                    | 0.893**                                   | 0.398                            |
|                           | Sig. (2-tailed) 0.041                       | 0.007                                     | 0.159                            |
| Fat mass (kg)             | r 0.821*                                    | 0.893*                                    | 0.552*                           |
|                           | Sig. (2-tailed) 0.023                       | 0.007                                     | 0.041                            |
| Fat mass index            | r 0.714                                    | 0.847*                                    | 0.503                            |
|                           | Sig. (2-tailed) 0.071                       | 0.016                                     | 0.067                            |
| Fat free mass (kg)        | r 0.667                                    | 0.821*                                    | 0.793**                          |
|                           | Sig. (2-tailed) 0.102                       | 0.023                                     | 0.001                            |
| Fat free mass index       | r 0.321                                    | 0.750*                                    | 0.736**                          |
|                           | Sig. (2-tailed) 0.482                       | 0.050                                     | 0.003                            |
| Muscle mass (kg)          | r 0.536                                    | 0.679                                     | 0.793**                          |
|                           | Sig. (2-tailed) 0.215                       | 0.094                                     | 0.001                            |
| Total body water (l)      | r 0.667                                    | 0.821*                                    | −0.095                           |
|                           | Sig. (2-tailed) 0.102                       | 0.023                                     | 0.748                            |

Table 6. Correlation of the measured RMR with the main study parameters in narcolepsy type 1, type 2, and control subgroups. **Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed).
This higher percentage of fat oxidation and a lower percentage of carbohydrate utilization may suggest a state of insulin resistance, which is a characteristic of the metabolic system of narcolepsy patients, even at an early age\cite{25}. Animal models with hypocretin-deficiency may develop an inability to differentiate preadipocytes in the brown adipose tissue, resulting in a reduction of thermogenesis and energy expenditure\cite{30}. Moreover, hypocretin has been shown to regulate the metabolism of muscle glucose\cite{27}. Collectively, these mechanisms may explain narcolepsy-associated obesity despite reduced caloric intake\cite{14}. The insignificantly higher CI ($F = 3.0; df = 2; p = 0.068$), as a measure of abdominal obesity, in narcolepsy patients supports our conclusion and may explain the possible higher frequencies of medical comorbidities such as obesity, type 2 diabetes, cardiovascular diseases, etc., in the narcolepsy population\cite{14}. Previous studies on RQ variation in the narcolepsy patients showed that poor sleep efficiency is associated with a higher fasting RQ\cite{29}. However, the results of other studies do not support these findings\cite{30,31}. These inconsistencies may be due to differences in the study designs and methods of RQ measurement.

The significant correlation of RMR with anthropometric parameters such as the BMI was maintained in the control group and NT2 subgroup, while in NT1, it became insignificant. This was in line with the results of Dahmen et al.\cite{32}, in which narcoleptic patients with lower BMI had reduced RMR. However, Dahmen et al. did not compare the NT1 vs. NT2 subgroups of the disease. Loss of the association between RMR and BMI in the NT1 subgroups might support the autoimmune or neurodegenerative etiologies of the NT1.

The major strength of this study is that it is one of the few studies that compare the body composition, RMR, and RQ of narcolepsy patients with those of gender-age-and-BMI matched controls. Previous investigations have mainly focused on the differences in the BMI of narcolepsy patients and healthy individuals\cite{3,4,33}; few studies have investigated the metabolic characteristics of narcolepsy patients independent of BMI. The present study involved the use of standardized validated instruments and scales for the assessment of several parameters, which further strengthens the study. A limitation of this study is the relatively small sample size, although we calculated the needed sample size to detect the changes in RQ in the current data, the estimated sample size was 16 (see Supplementary file: Appendix 1). Nevertheless, we cannot exclude type I error, which may have decreased the power of the study. Moreover, this study did not include females or adjust for dietary intake and exercise activity. The current study assessed the RMR; therefore, future studies should determine metabolic rate during activity, because the alterations in narcolepsy might be in the active phase.

In conclusion, compared to sex-age-BMI matched control, this study showed that narcolepsy patients have a lower RQ, and muscle mass. We also found that RMR and body composition measures (BFP, FM, FMI, FFMI, and FFMI) were similar between the narcolepsy patients and controls. These characteristics observed in the NT1 and NT2 patients are important for understanding the pathophysiology of the disease. Narcolepsy patients could benefit from muscle-building exercises to improve muscle mass and to lower the conicity index. Further studies of narcolepsy patients of both sexes are needed to broaden the understanding of the pathophysiology of the disease, especially regarding the metabolism of substrates.

**Subjects and methods**

**Participants and recruitment.** This case–control study included 14 male patients diagnosed with narcolepsy and 14 BMI- and age-matched healthy male subjects. All patients were recruited from the University Sleep Disorders Center, College of Medicine, Riyadh, Saudi Arabia, and the healthy controls were recruited from the Therapeutic Nutrition Clinic of the College of Applied Medical Sciences, King Saud University Medical City (KSUMC), King Saud University. Inclusion criteria for the patients were as follows: adult patients (> 18 years) diagnosed with narcolepsy using the International Classification of Sleep Disorders, 3rd edition (ICSD-3)\cite{3} and absence of comorbidities such as obstructive sleep apnea (OSA) (via polysomnography), diabetes, endocrine disorders, debilitating diseases, and psychiatric problems. The narcolepsy patients were further divided into NT1 and NT2 subgroups (n = 7, each subgroup).

Narcolepsy was diagnosed according to the International Classification of Sleep Disorders, third edition (ICSD-3)\cite{3}. Overnight polysomnographic study (PSG) followed by a multiple sleep latency test (MSLT) was done\cite{6}. For NT1 diagnosis, the presence of irresistible attacks of sleep, in addition to a mean sleep latency of < 8 min on the MSLT with evidence of two sleep-onset rapid eye movement periods (SOREMPs) (or one SOREMP on PSG and one or more on MSLT) and clear cataplexy "more than one episode of generally brief (< 2 min), usually bilaterally symmetrical, sudden loss of muscle tone with retained consciousness"\cite{3}. On the other hand, NT-2 was diagnosed if the mean sleep latency was < 8 min on the MSLT and two SOREMPs (or one SOREMP on PSG and one or more on MSLT), but cataplexy was absent\cite{6}. Other causes of excessive daytime sleepiness were excluded. Moreover, all participants were asked to maintain a minimum of 8 h in bed for 3 consecutive days before commencing the study (verified via sleep diaries).

Regarding antinarcoleptic medications, all patients in the NT1 subgroup were on modafinil therapy, while in the NT2, only 5 out of 7 were taking Modafinil. The control group consisted of 14 healthy sex-age-and-BMI-matched adult volunteers. All volunteers were interviewed by a sleep medicine specialist to rule out coexisting sleep disorders. Additionally, a validated Arabic version of the STOP-Bang questionnaire was used to assess the risk of OSA\cite{4,2}. Those with high risk for OSA were excluded.

All participants were evaluated from December 2017 to June 2018. The Ethics Committee of the King Khalid University Hospitals, KSUMC, approved this work under the reference number IRB# E-15–1,484. Accordingly, all methods and protocols were carried out following relevant guidelines and regulations.

**Procedures.** All participants attended an information session about the study, signed a written informed consent form, and filled out a health history questionnaire. All anthropometric measurements were recorded,
body composition was identified using the bioelectrical impedance analysis (BIA) technique, and RMR measurement by indirect calorimetry was performed for all study participants.

**Measures.** Self-report measures. Patient characteristics, smoking history, and physical activity history were assessed via a self-report questionnaire that each study participant filled under the supervision of a research team member. In addition to completing the SSS, a 7- statement ranging from 1 (alert) to 7 (sleep onset soon)35, and presence or absence of sleep symptoms such as interrupted sleep, sleep paralysis, hypnagogic hallucination, and cataplexy.

Anthropometry. Height (Ht) was measured while each participant stood with their heels, buttocks, shoulders, and occiputs touching the vertical stadiometer (Seca Model 206 stadiometer; Seca Co, Germany), and eyes looking along the Frankfort plane. Weight (Wt) was determined to 0.1 kg accuracy on a Seca scale, participants stood barefoot and wore minimal clothes. BMI was calculated with the equation Wt(㎏)/Ht(m)2. Waist (WC) and hip (HC) circumferences were measured using inelastic tape placed at the upper edge of the iliac crest and the most prominent point of the gluteal region. The average of the two measurements was used in the analysis. The waist–hip ratio (WHR) was calculated as WC/HC36.

Body composition. A multi-frequency bioelectric impedance analyzer (TANITA BC-418 analyzer; Tanita Co, Japan) was used to measure the body fat percentage (BFP), fat mass (FM), fat-free mass (FFM), muscle mass, and total body water (TBW). The calculation of fat mass index (FMI) and fat-free mass index (FFMI), were found using the following formula: FMI = FM(kg) /Ht2(m2), and FFMI = FFM(kg) /Ht2(m2)37. Other clinically valid anthropometric body-compositional indices were calculated using these equations: (1) The conicity index (CI), where CI = WC(m) /0.109 × [weight (㎏)/height (m)]38; (2) The abdominal volume index (AVI), where AVI = [2 × (WC)3 + 0.7 × (waist – hip)]'[1,00039, and (3) The body adiposity index (HC/Ht1.5)40.

**RMR measurement.** An indirect calorimetry device (QUARK RMR; COSMED, Inc., Italy) was used to measure RMR and other indirect calorimetry-related parameters of all participants. Room temperature was maintained at a comfortable level (about 25 °C). All participants were instructed to come to the indirect calorimetry lab at between 8 and 11 am after fasting for at least 12 h and abstaining from strenuous physical activity and not smoking for 24 h. Every day, the device was warmed-up and calibrated before its first use. The participant was asked to lay comfortably and completely still on the bed for 16 min without sleeping or moving. Measurement sessions with at least 5 min of minor gas volume variations (VO2 and VCO2 of less than 10%) were considered indications that the participant had reached the steady-state and was used for analysis41. The parameters that were measured and used for analysis were RMR, O2 volume (VO2), CO2 volume (VCO2), the RQ, percentage of utilized fat (Fat%), and percentage of utilized carbohydrates (CHO%).

Other measures. Other clinical parameters, including systolic/diastolic blood pressure and fasting blood glucose level, were also recorded. Blood pressure was measured on the left arm of the patient using a digital sphygmomanometer (Omron Healthcare Co, Japan) while the patient sat with relaxed legs. Glucose level was checked with a digital glucometer (ACCU-CHEK, Hoffmann-La Roche Ltd, USA)42.

Statistical analysis. Statistical Package for the Social Sciences (SPSS, version 25; SPSS Inc., USA) was used to analyze all data. Continuous variables were expressed as means ± standard deviations, and dichotomous variables were expressed as percentages and categories. For continuous variables, normal distribution was tested using Shapiro–Wilks test and found that RMR, RQ, VO2, VCO2, FFM, FFMI, and TBW were normally distributed (p > 0.05), while the remaining were not normally distributed. For normally distributed data, the one-way ANOVA test was used, while for variables that failed the normality test, the Kruskal–Wallis test was used to compare the means of the NT1, NT2, and control groups. Furthermore, a general linear model with the Bonferroni correction for pairwise comparison was used. The Mann–Whitney U test was used to compare means of the NT1 and NT2 subgroups. Cross-tabulation and the chi-square test were used to analyze categorical variables. Spearman’s correlation coefficient was used to identify the correlation between RMR and the study variables in the study subgroups.

Data availability
The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Author contributions
M.M.A., study protocol, data analysis, IC supervision, and study measurements; A.S.B., recruitment, and measurements for narcolepsy patients; G.S.A., manuscript writing and data collection; A.M.A, IC measurements; M.S.A, anthropometric/BIA measurements and other study measurements.

Competing interests
The authors declare no competing interests.

Additional information
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