Sleep comprises non rapid eye movement (NREM) sleep which consists of stages 1 through 4 and rapid eye movement (REM) sleep. REM sleep is defined by eye movements and appearance of low voltage electroencephalographic activity similar to that seen during waking (1). Deep NREM sleep (stage 3/4) is called slow wave sleep (SWS). Although the physiological role of each sleep stage remains to be elucidated, short sleep duration has been suggested as a risk factor for weight gain, insulin resistance, type 2 diabetes, hypertension and depression (2–4). Other studies also revealed that alterations in endocrine function were caused by restriction of sleep time or SWS interruption without affecting total sleep time, which may increase the risk of developing insulin resistance and type 2 diabetes (5).

Dietary factors influence sleep architecture. For example, the availability of dietary tryptophan shortens sleep latency and increases NREM sleep, SWS and sleep time (6–11). Glycine ingestion before bedtime improves subjective quality of sleep and shortens latency of sleep and SWS without affecting sleep architecture (12). The macronutrients fat and/or carbohydrate also affect sleep quality. Phillips et al. reported a shorter SWS duration with a high-carbohydrate meal (PFC=10 : 10 : 80) compared to that of a high-fat meal (PFC=10 : 78 : 12), in which subjects were given experiment meals throughout the day and sleep was monitored for two consecutive nights (13). Afaghi et al. reported that a very low-carbohydrate meal (PFC=38 : 61 : 0) for the evening meal increased SWS and decreased rapid eye movement (REM) sleep compared to the control mixed meal (PFC=15.5 : 12.5 : 72) (14). In these previous studies, time course of sleep architecture was not reported, and it was not reported whether the changes in sleep architecture were transient or persisted throughout the sleep period.

Energy metabolism during sleep was not monitored in previous reports studying the effects of macronutrient intake on sleep (13, 14), but it is plausible that metabolism consumption of macronutrients is related to changes in sleep architecture. Our previous study revealed correlations of sleep stage with energy metabolism and nutrient oxidation (15). Energy expenditure during REM sleep was significantly higher than that.
during sleep stages 2 and SWS, and carbohydrate oxidation during REM sleep was significantly higher than that during SWS. Changes in whole body energy metabolism during sleep seem to reflect changes in activity of the central nervous system. However, it is also theoretically possible that whole body energy metabolism affects sleep architecture. Animal experiments of prolonged fasting observed an increase in SWS when most of the energy was derived from fat oxidation (16). Similarly in humans, SWS increased after 2–3 d of fasting (17). These reports may imply that changes in substrate oxidation cause a modulation of sleep.

In the present study, substrate oxidation during sleep was manipulated by changes in the dietary composition of dinner, and its effects on sleep architecture and metabolism during sleep were assessed using polysomnography and whole body indirect calorimetry with improved transient response (18).

**MATERIALS AND METHODS**

**Subjects.** Ten healthy young males were recruited in this study after giving their written informed consent. Physical characteristics of subjects were 24.6±0.7 y of age, 172.9±1.3 cm of height, 67.6±2.3 kg of body weight and 17.4±1.1% of body fat. Subjects had no complaints of sleep disorders. Subjects who were involved in night work, planned long-distance jet travel, involved in night work, planned long-distance jet travel, did the subjects during the interval between the trials were asked to abstain from exercise and to keep their regular sleep-wake schedule, which were verified using a wrist motion sensor Actigraph and self-reported diary. Subjects were also asked to abstain from consumption of alcohol and caffeine. On the trial day, subjects consumed a normal breakfast (0800 h) and lunch (1200 h). The experimental dinner (high-carbohydrate dinner: HCD or high-fat dinner: HFD) was consumed at 2000 h. After preparation for polysomnographic recording, subjects entered the metabolic chamber at 2300 h. From 2340 h, the subject quietly lay on the bed to measure the resting metabolic rate before sleep, and remained on the bed until lights off at 2400 h. The measurement of energy metabolism and polysomnographic recording continued until at 0800 h of the next morning.

**Normal and experiment meals.** The normal breakfast and lunch were individually standardized, based on estimated energy requirement for Japanese (19) assuming a physical activity factor of 1.5, which accounts for the lower physical activity during the last 5 and half hours before sleep. The energy content of breakfast and lunch were 841±36 and 838±43 kcal, respectively. Expressed as a percentage of total energy, the meals contained 13% protein, 19% fat and 63% carbohydrate (breakfast), and 15% protein, 24% fat and 60% carbohydrate (lunch). Energy content of HCD and HFD were 798 kcal and 770 kcal, respectively (Table 1). The experimental dinner had a macronutrient profile of 10% protein, 10% fat and 80% carbohydrate (HCD) or 10% protein, 78% fat and 12% carbohydrate (HFD) of total energy intake.

**Sleep stage.** Sleep was recorded using a polysomnograph (Alice 5, Philips Respironics, Tokyo, Japan). Four electroencephalograms (C3/A2, C4/A1, O1/A2, and O2/A1), two electrooculograms, one submental electromyogram, and one electrocardiogram were recorded. The records were coded, and 30-s epochs were used to score sleep stages according to standard criteria (20) by

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**Table 1. Experiment meals.**

<table>
<thead>
<tr>
<th>Menu</th>
<th>High-carbohydrate dinner (HCD)</th>
<th>High-fat dinner (HFD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Energy (kcal)</td>
<td>Protein (g)</td>
</tr>
<tr>
<td>Boiled rice</td>
<td>453</td>
<td>6.3</td>
</tr>
<tr>
<td>Bread</td>
<td>158</td>
<td>4.8</td>
</tr>
<tr>
<td>Bean-starch vermicelli</td>
<td>98</td>
<td>1.9</td>
</tr>
<tr>
<td>Cracker</td>
<td>88</td>
<td>6.2</td>
</tr>
<tr>
<td>Dairy products</td>
<td>88</td>
<td>6.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>798</strong></td>
<td><strong>19.2</strong></td>
</tr>
<tr>
<td><strong>PFC (%)</strong></td>
<td><strong>10</strong></td>
<td><strong>10</strong></td>
</tr>
</tbody>
</table>
an investigator without knowledge of the conditions. A sleep cycle was defined as the duration from the beginning of sleep (or end of previous sleep cycle) to the end of REM sleep (21).

**Indirect calorimetry.** The airtight metabolic chamber measures 2.00 × 3.45 × 2.10 m (FHC-15S, Fuji Medical Science Co., Ltd., Chiba, Japan). Air in the chamber is pumped out at a rate of 80 L/min. Temperature and relative humidity of incoming fresh air were controlled at 25.0 ± 0.5˚C and 55.0 ± 3.0%. The chamber is furnished with an adjustable hospital bed, desk, chair and toilet.

Concentrations of oxygen (O2) and carbon dioxide (CO2) in outgoing air were measured with high precision by online process mass spectrometry (VG Prima B; Thermo Electron Co., Winsford, UK). Precision of mass spectrometry, defined as the standard deviation for continuous measurement of calibration gas mixture (O2, 15%; CO2, 5%), is 0.0016% for O2 and 0.0011% for CO2, respectively. At every minute, O2 consumption (VO2) and CO2 production (VCO2) rates were calculated using an algorithm for improved transient response (18).

Macronutrient oxidation and energy expenditure were calculated from VO2, VCO2 and urinary nitrogen excretion (N) (22). Rates of N, an index of protein oxidation, were assumed to be constant during the calorimetry.

Glucose oxidation (g/min) = 4.55 VCO2 (L/min) – 3.21 VO2 (L/min) – 2.87 N (g/min)
Fat oxidation (g/min) = 1.67 VO2 (L/min) – 1.67 VCO2 (L/min) – 1.92 N (g/min)
Protein oxidation (g/min) = 6.25 N (g/min)

Once the rates of glucose, fat and protein oxidation have been computed, the total rate of energy production can be estimated by taking into account the caloric equivalent of the three substrates. Conversion factors for caloric equivalents were 4.10 kcal/g protein (25.625 kcal/g urinary nitrogen), 3.74 kcal/g carbohydrate and 9.50 kcal/g fat (22).

**Physical activity.** Physical activity was measured with a uniaxial accelerometer activity monitor (ActiGraph, Ambulatory Monitoring Inc., Ardsley, NY). All subjects wore the wristwatch accelerometer in zero-crossing mode (23). Gross motor activity of the accelerometer was estimated at 1-min intervals. Subjects wore an accelerometer from the beginning of sleep the day before the experiment to the end of the experiment (32 h).

**Autonomic nervous system activity.** The R-R intervals of the electrocardiogram were continuously monitored using a telemetric heart rate monitor (LX-3230, Fukuda Denshi Co., Ltd., Tokyo, Japan) and the power spectrum of the heart rate variability was estimated using the maximum entropy method. The spectra measured were computed as amplitudes (i.e., areas under the power spectrum) and were presented in square milliseconds (ms²). Parasympathetic and sympathetic nervous system activity were estimated as high frequency (HF; 0.15–0.4 Hz) and as a power ratio of low frequency (LF; 0.04–0.15 Hz) to high frequency (LF/HF), respectively (24).

**Statistical analysis.** Data in the text, tables and figures are given as means ± SE under the experimental conditions. Then, mean values in every sleep cycle (first, second, third and fourth sleep cycle) were calculated for each subject. A paired t-test was used for comparison of sleep parameters, energy metabolism and autonomic nervous system activity during a whole sleep period.

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**Fig. 1.** Changes in energy metabolism and sleep stages during one night for one subject. Results under HCD conditions are shown in the left panel and those under HFD conditions are shown in the right panel. Energy expenditure ( ), carbohydrate oxidation ( ) and fat oxidation ( ) are shown in the upper panel. Plots are means at every 5 min. Sleep stage (Awake, REM, sleep stage 1–2 and SWS) are shown in the lower panel. First, second, third, and fourth mean first sleep cycle, second sleep cycle, third sleep cycle, and fourth sleep cycle, respectively.
Nutrient Composition of Dinner, Sleep, and Energy Metabolism

For comparison of sleep parameters, energy metabolism and autonomic nervous system activity among sleep cycles, repeated measures two-way analysis of variance (ANOVA) followed by the Bonferroni post hoc test was used. Statistical analysis was performed using SPSS statistical software (version 19.0; SPSS Japan, Tokyo, Japan).

**RESULTS**

**Time course of energy metabolism during sleep and sleep stage**

An example of time course of energy metabolism during sleep and sleep stage during a night is shown in Fig. 1. Energy expenditure was similar between the two dietary conditions (463 kcal/480 min for HCD and 463 kcal/480 min for HFD), but substrate oxidation during the sleep was affected by the nutritional composition of dinner. Oxidation of carbohydrate was higher and that of fat was lower under HCD conditions compared with those under HFD conditions, especially during the first half of sleep in this case. A sleep cycle, punctuated by the end of REM sleep, was observed 4 times during the night; SWS was observed during the first 3 sleep cycles under HCD conditions and during the first 2 sleep cycles under HFD conditions. The total amount of SWS during the whole sleep period was similar for the two dietary conditions (HCD: 35.5 vs. HFD: 35.0 min/480 min).

**Sleep architecture**

Sleep parameters are summarized in Table 2. When all sleep parameters were averaged during the whole sleep period, there was no significant difference between the two dietary conditions. When analyzed in each sleep cycle, SWS during the first sleep cycle was significantly lower under HCD conditions compared with that under HFD conditions (p<0.05) (Fig. 2). In the fourth sleep cycle, SWS was not observed.

**Sleep energy metabolism**

The time course for mean energy metabolism during sleep is shown in Fig. 3. Compared to HFD conditions, carbohydrate oxidation during the whole sleep period was higher and fat oxidation during the whole

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**Table 2. Sleep parameter during the whole sleep period.**

<table>
<thead>
<tr>
<th></th>
<th>High-carbohydrate dinner (HCD)</th>
<th>High-fat dinner (HFD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time in bed (min)</td>
<td>480</td>
<td>480</td>
<td>ns</td>
</tr>
<tr>
<td>Total sleep time (min)</td>
<td>443.0±7.9</td>
<td>455.8±2.1</td>
<td>ns</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>92.3±1.7</td>
<td>95.0±0.4</td>
<td>ns</td>
</tr>
<tr>
<td>Awake (min)</td>
<td>28.1±8.2</td>
<td>20.2±1.8</td>
<td>ns</td>
</tr>
<tr>
<td>REM (min)</td>
<td>89.9±5.3</td>
<td>81.8±8.4</td>
<td>ns</td>
</tr>
<tr>
<td>Stage 1 (min)</td>
<td>69.8±23.4</td>
<td>61.2±5.5</td>
<td>ns</td>
</tr>
<tr>
<td>Stage 2 (min)</td>
<td>261.5±28.4</td>
<td>287.8±7.9</td>
<td>ns</td>
</tr>
<tr>
<td>SWS (min)</td>
<td>22.0±6.3</td>
<td>24.8±5.4</td>
<td>ns</td>
</tr>
<tr>
<td>Sleep latency (min)</td>
<td>10.8±5.2</td>
<td>4.7±1.0</td>
<td>ns</td>
</tr>
<tr>
<td>First sleep cycle time (min)</td>
<td>119.7±13.4</td>
<td>127.4±13.1</td>
<td>ns</td>
</tr>
<tr>
<td>Second sleep cycle time (min)</td>
<td>118.9±8.6</td>
<td>114.6±10.1</td>
<td>ns</td>
</tr>
<tr>
<td>Third sleep cycle time (min)</td>
<td>109.9±6.8</td>
<td>116.3±6.8</td>
<td>ns</td>
</tr>
<tr>
<td>Fourth sleep cycle time (min)</td>
<td>104.5±15.9</td>
<td>82.4±17.3</td>
<td>ns</td>
</tr>
</tbody>
</table>

* A fourth cycle is shown in only eight subjects, because a fourth cycle didn’t appear in two subjects.
ns: not significant.

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Fig. 2. REM sleep and SWS. Mean values±SE of REM sleep and SWS for HCD (◼) and HFD (□) condition are shown in the left and right panel, respectively. Statistical analyses were performed on data for every sleep cycle by repeated measures two-way ANOVA, followed by Bonferroni post hoc tests. *p<0.05.
sleep period was lower after consumption of HCD. Accumulated carbohydrate (HCD: 265 ± 20 vs. HFD: 167 ± 22 kcal/480 min, p < 0.001) and fat oxidation (HCD: 158 ± 22 vs. HFD: 269 ± 13 kcal/480 min, p < 0.01) were significantly different between the two dietary conditions, while energy expenditure was similar (HCD: 514 ± 18 vs. HFD: 522 ± 20 kcal/480 min, ns).

The average respiration quotient during the sleep was also different between the two dietary conditions (HCD: 0.87 ± 0.01 vs. HFD: 0.81 ± 0.01/480 min, p < 0.01).

When energy metabolism was separately compared in each sleep cycle between the two dietary conditions, significant differences in substrate oxidation were only observed during the first (p < 0.01) and second (p < 0.05) sleep cycle. Substrate oxidation during the third and fourth sleep cycle was similar under the two dietary conditions (Fig. 4).

Physical activity during daytime and previous night’s sleep time

There was no significant difference in sleep time for the previous night (HCD: 440.5 ± 16.0 vs. HFD: 428.5 ± 16.0 min, ns). Physical activity during the daytime (from 0600 h to 0000 h) in the trial day (HCD: 157.0 ± 12.2 vs. HFD: 155.2 ± 8.6 counts/min, ns) and during sleep (HCD: 12.3 ± 2.4 vs. HFD: 11.2 ± 1.5 counts/min, ns) were comparable between HCD and HFD conditions.
Autonomic nervous system activity during sleep

The index of autonomic nervous system activity during the whole sleep period was similar under the two dietary conditions (HCD: $2.92\pm0.34$ vs. HFD: $2.75\pm0.24/480$ min. $p>0.1$ for sympathetic and HCD: $850\pm159$ vs. HFD: $896\pm188/480$ min. $p>0.1$ for parasympathetic nervous system activity). When compared in each sleep cycle, there were no significant differences in autonomic nervous system activity between the two dietary conditions ($p>0.1$).

**DISCUSSION**

The main findings of the present study were that SWS was decreased during the first sleep cycle but was not changed during the second and third sleep cycle by ingestion of HCD compared with those of HFD conditions. Accumulated SWS during the whole sleep period was not affected by dietary conditions. During the first and second sleep cycle, carbohydrate oxidation was increased and fat oxidation was decreased under HCD conditions compared with HFD conditions.

The effect of the difference in the macronutrient composition of dinner on sleep was limited during the first sleep cycle in the present study. Phillips et al. reported changes in accumulated SWS during the sleep, in which macronutrient composition similar to our experimental meal was used but consumed for 2 consecutive days (13). The potential reason for difference between the two studies seems to be the period of nutritional intervention in the experimental protocols. Thus single ingestion of an experimental meal seems to be insufficient to induce dietary changes in the sleep architecture of the whole sleep period.

Our study design could not determine whether these outcomes were primarily determined by changes in dietary carbohydrate intake per se or those of fat. Carbohydrate oxidation during sleep differed in the following order: REM>stage $1/2$>SWS (15). Although correlation between carbohydrate oxidation and sleep stage does not necessarily mean a causal relationship between the two variables, it is possible that carbohydrate oxidation suppresses SWS. Consistent with this notion, single ingestion of a very low-carbohydrate meal (<1% carbohydrate) increased SWS and suppressed REM sleep compared with the normal control meal (14). Alternatively SWS was promoted by elevation of fat oxidation. Jenkins et al. examined the effects of high fat-induced obesity on sleep in mice, in which the increases of NREM sleep were positively correlated with the increases in the body weight (25). However, the high-fat feeding had an acute effect on NREM sleep before the development of obesity, suggesting that sleep responses to food intake were related to enhanced oxidation of fat rather than the increases in the body weight. In geese and humans, SWS significantly increased after fasting (16, 17), when most of the energy was derived from fat. Though the interplay between substrate oxidation and sleep architecture remains poorly defined, the elevation of fat oxidation may be one important factor in the control of sleep. The plausible mechanism by which fat oxidation increases NREM sleep is an increase in plasma concentration of ketone bodies. Another study in mice reported that increases of the plasma ketone ratio (acetoacetate/β-hydroxybutyrate) were associated with increased EEG delta power in NREM sleep (26), which has been used as physiological markers of deep sleep and homeostatic need for sleep (27). Plasma ketone bodies were not measured in the present study, but it is reasonable to expect their increase after HFD consumption (28). Alternatively, an increased level of ghrelin and cholecystokinin after the consumption of high-fat foods (29) may mediate the effect of the macronutrient on sleep architecture, since these hormones increase SWS or NREM sleep when administered in human or rodent studies (30–32). However, it is unclear whether physiological changes in hormone level from ingestion of a meal are enough to affect sleep.

Although substrate oxidation and sleep stage seem to be related, these two physiological events didn’t completely concur. Effects of dietary manipulation on sleep architecture were only observed during the first sleep cycle, while those on substrate oxidation remained significantly different until the second sleep cycle. Homeostatic regulation of sleep might have interfered with the effect of energy metabolism. According to the generally accepted view on sleep regulation, it results from an interaction between a homeostatic process and a circadian process (33). It has been shown that partial or total sleep deprivation gives rise to increased SWS in the recovery night; thus the sleep was adjusted to the amount required for personal conditions depending on homeostatic regulation (34). It is possible that increased SWS during the first sleep cycle after HFD suppressed SWS during the following sleep cycles.

Sleep stage and energy expenditure are strongly regulated by autonomic nervous system activity (35, 36). Because effects of the nutrient composition of the meal on parasympathetic and sympathetic nervous system activity had been reported (37, 38), indices of autonomic nervous system activity were also measured in the present study. However, activities of autonomic nervous systems during whole sleep and every sleep cycle were similar between the two dietary conditions. The present study suggested that changes in sleep architecture induced by HCD or HFD were not mediated by changes in autonomic nervous system activity.

SWS during the first sleep cycle is related to subjective sleep quality and daytime sleepiness (39), and it is tied to growth hormone release (14, 40). Decrease in growth hormone release is associated with a cluster of cardiovascular risk factors, including increased visceral fat and insulin resistance (41). Since about 20% of adults are dissatisfied with their sleep state in Japan (42), an increase in SWS during the first sleep cycle by dietary manipulation might improve subjective sleep quality and decrease cardiovascular risk, particularly among the subpopulation with a short sleep period observed in an epidemiological study (43).

There are several limitations of this study. Firstly, the whole room calorimeter enables us to measure whole
body energy metabolism, but it does not provide information about energy metabolism in individual organs, particularly in the brain, changes in the neuronal activity of which is manifested as sleep. Secondly, to induce a clear difference in substrate oxidation, subjects consumed meals with extreme nutrient compositions in the present study, which are rarely consumed in our habitual meals. Further studies with moderate nutrient composition of meals remain to be done. Furthermore, high fat meals with different fatty acid compositions are known to induce different physiological responses. A recent study substituting dietary monounsaturated fat for saturated fat for 3 wk increased resting energy expenditure and changed the mood of subjects (44). Depending on the composition of fatty acid, effects of HFD on sleep may be different. Thirdly, breakfast and lunch were individually standardized but all subjects consumed the same amount of the experimental meal for dinner. Therefore, relative size of the last meal before sleep was different among the subjects. However, there was no association between body weight and sleep architecture (total sleep time, sleep efficiency, sleep latency, each sleep stage or each sleep cycle time). We believe that comparison between high-carbohydrate and high-fat dinners is still valid. Finally, subjects ate the experiment dinner 4 h before their bedtime. Our laboratory previously reported that a late evening meal (2230 h) shifted the postprandial change in energy metabolisms toward late at night compared to that after a normal meal (1900 h) (45). It is plausible that the combination of a late evening dinner with changes in dietary composition, which is observed in many industrialized societies (46), might have profound effects on sleep architecture. It remains to be studied whether the effects of nutritional intervention on sleep architecture would last until the next morning if dinner was shifted to late at night.

CONCLUSION

Single ingestion of a high-carbohydrate meal at dinner increased carbohydrate oxidation and decreased fat oxidation during sleep, and decreased SWS compared with that of a high-fat meal. Changes in substrate oxidation during sleep affected sleep architecture, which may explain at least part of the correlation between energy metabolism and sleep stages.

Acknowledgments

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Nutrient Composition of Dinner, Sleep, and Energy Metabolism


