Substrate oxidation influences liking, wanting, macronutrient selection, and consumption of food in humans¹–³

Laurent Brondel, Laurine Landais, Michael A Romer, André Holley, and Luc Pénicaud

ABSTRACT
Background: Several carbohydrate-based models of feeding have been described. The influence of the substrate oxidation rate on liking, wanting, and macronutrient selection, however, is not known in humans.

Objective: The aim of this study was to investigate the influence of the substrate oxidation rate on the above variables.

Design: A randomized 4-condition study was conducted in 16 normal-weight men (mean ± SD age: 23 ± 3 y). The sessions differed in the composition of breakfast, which was either high in carbohydrates (HC) or low in carbohydrates (LC) or high in fat (HF) or low in fat (LF). Two hours and 20 minutes after breakfast, energy expenditure (EE) and respiratory exchange ratios (RERs) were measured. Next, olfactory liking for 4 foods (sweet and fatty) and ad libitum energy intake (carbohydrate- and fat-rich bread) were evaluated.

Results: EE was higher (P < 0.001) and subsequent intake was lower (P < 0.01) after the HC and HF breakfasts than after the LC and LF breakfasts. The HC and LC breakfasts induced a higher RER (P < 0.001), lower olfactory liking for sweet foods (P < 0.05), and the consumption of a lower proportion of carbohydrate-rich bread (P < 0.05) than did the HF and LF breakfasts. The HF breakfast induced the lowest RER (P < 0.001), the lowest olfactory liking for fatty foods (P < 0.05), and the lowest proportion of fat-rich bread consumed (P < 0.01). Above all, a negative correlation was found between the RER and olfactory liking for sweet foods (P < 0.001).

Conclusion: A high fat oxidation rate induces a strong liking for carbohydrates and a low liking for fats, which lends new support to the carbohydrate-based model of feeding. This trial is registered at clinicaltrials.gov as NCT01122082.

INTRODUCTION
As for many other animals, human beings must be able to adapt to cope with major discontinuities in the supply of and the demand for energy. Because food consumption is a discontinuous process, chemical food energy is stored mainly as glycogen and fat. It is well recognized that stores of carbohydrate are small, whereas those of fat are large (1). For this reason, it has been hypothesized that low carbohydrate stores may trigger adaptive changes in fuel oxidation and eventually in energy intake (2).

With regard to the control of energy intake by carbohydrates, 3 successive theories have been proposed. First, Mayer (3) suggested that glucose-sensitive neurons located in specific areas of the central nervous system exert positive or negative feedback on food intake (the glucostatic theory). Later, Russek (4) argued that glucose receptors are present in the liver (the hepatostatic hypothesis) and therefore that liver glycogen content influences food intake. More recently, Flatt (5) proposed that carbohydrate status could play an important role in the regulation of food intake (the glycogenostatic model) because of the priority given by the body to the carbohydrate balance over the fat balance.

Studies in mammals (5–10) have provided support for the above-mentioned carbohydrate-based models of feeding. In contrast, in humans, older short-term studies of dietary manipulation of glycogen stores found that such manipulations produced minor (11, 12) or no effects (13–15) on total energy intake. Recently, however, carbohydrate oxidation has been observed to predict subsequent ad libitum energy intake, but contradictory results have been reported. Some authors found that a 24-h carbohydrate balance evaluated in a respiratory chamber over 3 d correlated negatively with subsequent total energy intake (16), whereas others found that the carbohydrate balance measured in a respiratory chamber for 4 d correlated positively with post-chamber ad libitum energy intake (17). Whatever the cause of the discordance between these results, to our knowledge only Snitker et al (12) studied the influence of glycogen stores and carbohydrate utilization on both total energy intake and self-selected macronutrients. They reported that glycogen stores and glucose utilization had no effect on the selection and intake of carbohydrates. In their study, however, the subjects had extremely high intakes (~200 % of normal-weight-maintenance requirements), which makes the results difficult to interpret.

In accordance with the carbohydrate-based models of feeding, one may nonetheless expect that food choices, in addition to “liking” and “wanting” [the 2 components of the reward system (18, 19)], could be influenced by glucose utilization. More precisely, one may expect that a high fat oxidation rate could

¹ From the Centre des Sciences du Goût et de l’Alimentation, UMR 6265 CNRS, UMR 1324 INRA, Université de Bourgogne, Dijon, France (LB, LL, MAR, AH, and LP); the Service d’Hépato-Gastroentérologie du CHU de Dijon, Dijon, France (LB); and the UFR de Médecine de l’Université de Bourgogne, Dijon, France (LB).
² Supported by a grant from the Centre National de la Recherche Scientifique (CNRS) (France).
³ Address correspondence to L Brondel, Centre des Sciences du Goût et de l’Alimentation, 15 rue Hugues Picardet, 21000 Dijon, France. E-mail: laurent.brondel@u-bourgogne.fr.
increase olfactory liking and wanting for carbohydrates and that a high carbohydrate oxidation rate would have less of an influence on the reward system. The present study was designed to investigate this hypothesis in humans.

SUBJECTS AND METHODS

Subjects

The participants were 16 normal-weight men with a mean (±SD) BMI (in kg/m²) of 22.7 ± 2.5 and a mean (±SD) age of 23 ± 3 y. Women were not included because hormonal variations during the menstrual cycle may affect appetite (20) and because sociocultural influences on food intake may be higher in women (21).

The inclusion criteria were good health, the absence of medication, moderate physical activity (irregular and <5 h/wk), a low smoking habit (<5 cigarettes/d), and a normal BMI (20–25). The exclusion criteria were eating disorders, dieting or fasting, aversion for the foods offered, and an elevated “cognitive restriction of eating” score (≥7) according to the Three-Factor Eating Questionnaire (22). Mean (±SD) scores for “cognitive restriction of eating,” “eating disinhibition,” and “susceptibility to hunger” were 4.3 ± 2.1, 5.6 ± 1.7, and 4.9 ± 3, respectively.

All of the participants were students at the University of Dijon (Burgundy, France). They were not informed about the aim of the experiment and the food measurements performed. The participants were individually tested in a laboratory to limit the influence of habits, social eating, and cognitive factors on eating behavior (23, 24). All of the participants gave their written consent to participate in the experiment, which was approved by the Regional Ethics Committee of Burgundy (France).

Experimental sessions

The 4 experimental sessions were organized in a random order over 4 consecutive weeks (one session per week). The sessions differed in the composition of the breakfast. Each breakfast was composed of 300 g cottage cheese (627 kJ; 13.2 g carbohydrate, 0.3 g fat, 23.1 g protein) mixed with 90 g sucrose (HC4), 6 g aspartame (LC), 40 g vegetable oil (HF) or 40 g paraffin oil (LF). Therefore, the HC and HF breakfasts had the same high energy content (2115 ± 10 kJ), and the LC and LF breakfasts had the same low energy content (638 ± 11 kJ). The HC and LF breakfasts were sweetened to the same degree, and the HF and LF breakfasts had a similar fatty taste and consistency (according to preliminary tests). All of the HC, LC, HF, and LF breakfasts were of matching volumes and weights.

Study design

The day preceding each session, the subjects consumed a standard dinner composed of ravioli pasta (418 kJ/100 g, with an energy composition of 51% carbohydrate, 31% fat, and 18% protein), apple compote (339 kJ/100 g; 99% carbohydrate, 1% fat, and 0% protein) and sweetened natural yogurt (314 kJ/100 g; 69% carbohydrate, 11% fat, and 20% protein). The subjects were allowed to eat as much as they wanted, but they were encouraged to eat the same quantities before each of the 4 sessions (they were offered one 800-g can of ravioli pasta, one 100-g container of apple compote, and one 125-g container of yogurt; and the amounts eaten were evaluated in a semiquantitative way using a food questionnaire). After dinner, the subjects were not allowed to eat (only water was authorized) and were required to remain at home, performing only moderate physical activity.

On the morning of the experimental session (Figure 1), the subjects arrived at the laboratory by bus or car (ie, without excessive physical activity) in a fasting condition. They arrived at 15-min intervals (between 0700 and 0830), with each subject arriving at the same time for each session. The subjects then rated their hunger sensation and ate 1 of the 4 breakfasts in its entirety. The duration of the intake varied according to the subject and the breakfast and ranged from ~3 to 7 min. Immediately after eating their breakfast, the subjects rated their postprandial hunger and their hedonic sensations associated with eating the breakfast. Then, after voiding, the subjects were weighed (precision ±100 g) and instructed to lie down on a bed in a reclining position either alone or with another subject in the room. During this resting period, the subjects could read, listen to music, or nap. Absolute rest, without reading or music, was imposed during the last 10 min of this period. The temperature of the room was controlled at 21 ± 1°C.

Two hours and 20 min after the end of the breakfast (the mean start time of the measurements was 1010), indirect calorimetry measurements were performed for 15–20 min. The measurements were performed on subjects while in a reclining position. Expired gasses were collected through an oronasal mask (Hans Rudolph Inc) and analyzed in real time and for each respiratory cycle by using an open-circuit system (Vmax SPECTRA 29S; Sensormedics Corp). The first 5–10-min period was not analyzed (this served to make the subjects familiar with the apparatus and to achieve a steady relaxed state, as determined by the pulmonary ventilation rate). During the following 5 min, the subjects were left alone and were instructed to remain calm. During the final 5 min, steady state was measured by an experimenter who was blinded to the composition of the breakfast consumed by the subjects. As currently accepted (25) and as previously observed during a 10-h period after the intake of different breakfasts (26), protein oxidation was assumed to proceed at a constant rate; therefore, it was not evaluated via measurements of nitrogen excretion in urine.

Five minutes after the indirect calorimetry measurements, olfactory liking was evaluated for 4 separate food items (the mean start time of the evaluation of olfactory liking was 1030). The foods presented were honey, maple syrup, melted butter, and mayonnaise. The first 2 items were therefore rich in carbohydrates and the other 2 rich in fat. Each food item was presented in a random order in separate small cups and assessed orthonasally for ~5–10 s at a distance of 50–100 mm from the nose (the total duration of olfactory evaluation was 2–3 min). After hunger evaluation, a snack was offered (the mean snack time was 1035). The snack consisted of 4 different choices of bread slices served on a plate. The slices were made of sandwich bread (~2.3 g, 27 kJ; 72% carbohydrate, 15% fat, and 13% protein) spread with honey (~1.8 g, ~24 kJ; 99% carbohydrate, 0% fat, and 1%
protein), strawberry jam (≈2.2 g, ≈23 kJ; 99% carbohydrate, 0% fat, and 1% protein), butter (≈1 g, ≈31 kJ; 0% carbohydrate, 99% fat, and 0% protein), or full-fat soft cheese (≈1.4 g, ≈15 kJ; 5% carbohydrate, 87% fat, and 7% protein). The first 2 types of bread with spread were therefore rich in carbohydrate and the other 2 rich in fat. All of the bread choices were of a similarly pleasant palatability, according to preliminary tests. The bread (50 slices) was randomly distributed on a plate, and each type of spread was easily identifiable by the subjects (principally by its color and appearance). The subjects were informed that they could eat as much as they liked of whatever kind of bread with spread they wanted (the consumed bread was replaced at approximately the middle of the intake period). Hunger, the hedonic rating of each type of bread, and the global hedonic rating of the snack were evaluated immediately after intake.

**Subjective measurements**

All subjective ratings (hunger, olfactory liking, and hedonic ratings of the cottage cheese and the bread with spread) were evaluated by using 10-cm visual analog scales. The question asked to evaluate hunger was “How hungry do you feel at this moment?” The scale was anchored with “not at all” (0) and “extremely” (+10) at its extremities. The question asked to assess olfactory liking for the 4 food items was “When you smell this food now, how much pleasure do you feel?” The scales ranged from “very little” (−5) to “very much” (+5). The question asked to evaluate the hedonic sensations induced by each of the consumed foods was “At this moment, how pleasant does this cottage cheese/this bread seem?” The scales ranged from “very unpleasant” (−5) to “very pleasant” (+5).

**Statistical analysis**

EE and oxidation from carbohydrate and fat oxidation were calculated from the RER. Olfactory liking values for the sweet/fatty food items were obtained by calculating the means of the corresponding olfactory likings (honey and maple syrup, melted butter and mayonnaise). The number of pieces of carbohydrate-rich and fatty bread consumed was obtained by calculating the total of the consumed slices of bread with honey and strawberry jam as well as the slices of bread with butter and full-fat soft cheese.

Differences between the experimental sessions were analyzed by using 2-factor repeated-measures ANOVA, with consideration of the sweet/fatty taste and the caloric content of the breakfasts. Whenever statistical differences were detected, Tukey’s post hoc test was applied to isolate the group that differed from the others. Multiple linear regressions were performed with EE, the RER, olfactory liking and the number of consumed pieces of bread as dependent variables. Analyses were conducted by using SigmaStat software (version 3.1; Systat Software Inc). A linear random-effects model was also used to assess the relation between the variables (eg, the RER and the olfactory liking for the sweet and fatty food items) while considering the repetition of the measures. This analysis was performed by using Stata version 11.0 (StataCorp). Significance was set at $P < 0.05$.

**RESULTS**

**Breakfast**

Preprandial hunger was similar in the 4 situations (Table 1). Hunger decreased similarly from before to after intake [$F(1,45) = 68.23$, $P < 0.001$] in the 4 situations. Postprandial hunger was similar after the consumption of the 4 breakfasts.

After intake, the hedonic rating was lower for the fatty breakfasts than for the sweet breakfasts ($P < 0.05$; Table 1).

**EE, RER, and fuel oxidation**

The values for EE were higher after the HC breakfasts than after the LC breakfasts ($P < 0.001$; Table 1), with no influence of sweet/fat taste and no significant interaction of taste with calories. For the RER, the interaction of taste with calories was significant ($P < 0.001$), and Tukey’s post hoc test showed that the RER was higher after the HC breakfast than after the LC or HF breakfasts ($P < 0.001$; Table 1). Consequently, the interaction of taste with calories was significant for carbohydrate oxidation ($P < 0.001$) and...
a higher carbohydrate oxidation was seen after the HC breakfast than after the LC or HF breakfasts (P < 0.001; Table 1). Significant inverse differences were noted for fat oxidation.

In summary, EE was higher after ingestion of the HC breakfasts than after the LC breakfasts and the breakfasts richest in carbohydrate induced the highest RER.

**Olfactory liking**

The mean olfactory liking for the sweet food items was lower after the sweet breakfasts than after the fatty breakfasts (P < 0.05), with a trend toward an interaction of taste with calories (P = 0.06), which indicated a lower olfactory liking for the sweet food items after the HC breakfasts than after the HF or LF breakfasts (P < 0.01 and P < 0.05; Table 1). The mean olfactory liking for the fatty food items did not differ according to the taste or the caloric content of the breakfasts, but an interaction of taste with calories (P < 0.05) indicated a lower olfactory liking for the fatty food items after the HF breakfasts than after the LF breakfasts (P < 0.05; Table 1).

Above all, a negative correlation between the RER and olfactory liking for the sweet food items (P < 0.001) and a nonsignificant positive correlation (P = 0.24) between the RER and olfactory liking for the fatty food items were observed, as shown in Figure 2 (for a rise in RER value of 0.1, a mean decrease of 0.9 ± 0.3 in sweet olfactory liking was expected). Consequently, when the RER was <0.862 (the median value of the RER), olfactory liking for the sweet food items was higher than that for the fatty food items (0.4 ± 2.3 compared with −1.3 ± 1.4, P < 0.001). In contrast, when the RER was >0.862, olfactory liking for the sweet food items did not differ from olfactory liking for the fatty food items (−0.4 ± 2.0 compared with −1.0 ± 1.7). No significant correlation was noted between EE and olfactory liking.

In summary, the richest breakfast in carbohydrate induced the lowest olfactory liking for the sweet food items, whereas the richest breakfast in fat induced the lowest liking for the fatty food items; olfactory liking for the sweet food items correlated negatively with the RER measured previously; sweet food items were more liked than were fatty food items when subjects were in a state of preferential fat oxidation.

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**TABLE 1**

Breakfast intake, postprandial metabolism, olfactory liking, and snack intake in the 4 conditions

<table>
<thead>
<tr>
<th></th>
<th>HC</th>
<th>LC</th>
<th>HF</th>
<th>LF</th>
<th>P value (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast intake (VAS)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Preprandial hunger</td>
<td>4.8 ± 1.9</td>
<td>4.9 ± 2.5</td>
<td>4.4 ± 2.3</td>
<td>4.1 ± 1.9</td>
<td>T: &lt;0.05</td>
</tr>
<tr>
<td>Postprandial hunger</td>
<td>1.9 ± 1.6</td>
<td>2.5 ± 1.9</td>
<td>2.5 ± 2.3</td>
<td>1.9 ± 1.2</td>
<td></td>
</tr>
<tr>
<td>Hedonic rating</td>
<td>0.1 ± 2.5</td>
<td>0.5 ± 2.0</td>
<td>−1.2 ± 2.3</td>
<td>−1.2 ± 1.8</td>
<td>T: &lt;0.05</td>
</tr>
<tr>
<td>Postprandial metabolism</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>EE (J · min⁻¹ · kg⁻¹)</td>
<td>75.5 ± 7.1</td>
<td>66.8 ± 8.1</td>
<td>73.4 ± 5.9</td>
<td>67.4 ± 6.7</td>
<td>C: &lt;0.001</td>
</tr>
<tr>
<td>RER</td>
<td>0.94 ± 0.05</td>
<td>0.85 ± 0.04</td>
<td>0.83 ± 0.04</td>
<td>0.85 ± 0.06</td>
<td>T: &lt;0.001</td>
</tr>
<tr>
<td>CHO oxidation (%)</td>
<td>78 ± 14</td>
<td>49 ± 14</td>
<td>44 ± 16</td>
<td>50 ± 20</td>
<td>T: &lt;0.001</td>
</tr>
<tr>
<td>Olfactory liking (VAS)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Sweet food items</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preprandial hunger</td>
<td>4.0 ± 1.6</td>
<td>5.0 ± 2.2</td>
<td>4.6 ± 2.0</td>
<td>4.9 ± 1.9</td>
<td>C: &lt;0.05</td>
</tr>
<tr>
<td>Hedonic rating</td>
<td>3.2 ± 1.9</td>
<td>2.4 ± 1.3</td>
<td>2.9 ± 1.0</td>
<td>3.0 ± 2.0</td>
<td>C: &lt;0.01</td>
</tr>
<tr>
<td>Bread slices (slices)</td>
<td>31 ± 1</td>
<td>44 ± 2</td>
<td>32 ± 1</td>
<td>35 ± 16</td>
<td>C: &lt;0.01</td>
</tr>
<tr>
<td>CHO-rich bread (slices)</td>
<td>9 ± 7</td>
<td>15 ± 12</td>
<td>15 ± 9</td>
<td>14 ± 10</td>
<td>C: &lt;0.05</td>
</tr>
<tr>
<td>Fat-rich bread (slices)</td>
<td>22 ± 10</td>
<td>28 ± 16</td>
<td>17 ± 8</td>
<td>22 ± 10</td>
<td>T: &lt;0.05</td>
</tr>
<tr>
<td>Energy intake (kJ)</td>
<td>2617 ± 1005</td>
<td>3722 ± 1838</td>
<td>2537 ± 913</td>
<td>2931 ± 1256</td>
<td>C: &lt;0.01</td>
</tr>
<tr>
<td>Snack intake</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preprandial hunger</td>
<td>0.8 ± 1.8</td>
<td>0.1 ± 2.2</td>
<td>0.4 ± 2.2</td>
<td>0.3 ± 2.4</td>
<td>T: &lt;0.05</td>
</tr>
<tr>
<td>Hedonic rating</td>
<td>−0.9 ± 1.7</td>
<td>−1.1 ± 1.8</td>
<td>−1.9 ± 1.0</td>
<td>−0.7 ± 1.6</td>
<td>I: &lt;0.05</td>
</tr>
<tr>
<td>Postprandial hunger</td>
<td>1.4 ± 0.9</td>
<td>1.8 ± 1.2</td>
<td>0.9 ± 0.9</td>
<td>1.9 ± 1.3</td>
<td>C: &lt;0.01</td>
</tr>
<tr>
<td>Hedonic rating</td>
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</tr>
</tbody>
</table>

All values are means ± SDs; n = 16. Breakfasts composed of cottage cheese with sucrose [high-carbohydrate (HC)], aspartame [low-carbohydrate (LC)], vegetable oil [high-fat (HF)], or paraffin oil [low-fat (LF)] were consumed in 4 randomly assigned conditions. The HC and HF breakfasts had the same high energy content, whereas the LC and LF breakfasts had the same low energy content. The HC and the LC breakfasts were sweetened to the same degree, and the HF and the LF breakfasts had a similar fatty taste. Two hours and 20 minutes after consumption, postprandial metabolism [energy expenditure (EE), the respiratory exchange ratio (RER), and carbohydrate (CHO) oxidation] was evaluated for 20 min. Olfactory liking was then measured for sweet food items (honey and maple syrup) and for fatty food items (melted butter and mayonnaise) by using 10-cm visual analog scales (VAS). Next, 4 different bread slices spread with honey and strawberry jam (carbohydrate-rich bread) or butter and full-fat soft cheese (fat-rich bread) were consumed ad libitum. Two-factor repeated-measures ANOVA indicated the main effects of the caloric content of the breakfasts (C) or taste of the breakfasts (T) and the C × T interaction (I). Values sharing the same letter were significantly different. "p < 0.001, "p < 0.01, "p < 0.05 on the basis of Tukey’s post hoc test.
A value in the 4 situations. Postprandial hunger remained lower after the HC breakfasts than after the LC breakfasts ($P < 0.01$; Figure 3A). Consequently, the proportion of the fat-rich bread consumed was lower after the fatty breakfasts than after the sweet breakfasts ($P < 0.05$), with a significant interaction of taste with calories ($P < 0.01$), which indicated a lower proportion of the fat-rich bread consumed after the HF breakfasts than after the HC or LF breakfasts ($P < 0.01$; Figure 3B).

The EE measured before the snack correlated negatively both with the total number of bread slices with spread subsequently consumed ($P < 0.01$) and with the amount of carbohydrate-rich bread consumed ($P < 0.01$; Figure 4A). For a rise in EE value of $10 \, \text{J} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$, mean decreases of $6.8 \pm 2.2$ in the number of total bread slices consumed and $3.5 \pm 1.2$ in the number of carbohydrate-rich bread slices consumed were observed. No significant correlation was noted between EE and the amount of fat-rich bread consumed (Figure 4B).

Finally, the RER did not correlate with either the total number of bread slices consumed during the snack or with the amount of carbohydrate- or fat-rich bread consumed.

**Snack**

Preprandial hunger was lower after the HC breakfasts than after the LF breakfasts ($P < 0.05$; Table 1). Hunger decreased from before to after intake [$F(1,15) = 9.18$, $P < 0.01$] by a similar value in the 4 situations. Postprandial hunger remained lower after the HC breakfasts than after the LC breakfasts ($P < 0.05$).

The number of bread slices consumed during the snack was lower after the HC breakfasts than after the LC breakfasts ($P < 0.01$; Table 1). This lower intake was of the carbohydrate-rich bread with spread ($P < 0.05$), with an interaction of taste with calories ($P < 0.05$), indicating that less-carbohydrate-rich bread was consumed after the HC breakfast than after the HF or LC breakfasts ($P < 0.01$; Table 1). The lower intake after the HC breakfasts also included the fat-rich bread because less of this bread was consumed after the HC breakfasts ($P < 0.01$) and the fatty breakfasts ($P < 0.05$; Table 1). Because both the number of bread slices consumed and the nature of the bread consumed varied in the 4 situations, the proportions of the carbohydrate- and fat-rich bread consumed were calculated. The proportion of the carbohydrate-rich bread consumed was higher after the fatty breakfasts than after the sweet breakfasts ($P < 0.05$), with an interaction of taste with calories ($P < 0.01$), which indicated a higher proportion of carbohydrate-rich bread consumed after the HF breakfasts than after the HC or LF breakfasts ($P < 0.01$; Figure 3A). Consequently, the proportion of the fat-rich bread consumed was lower after the fatty breakfasts than after the sweet breakfasts ($P < 0.05$), with a significant interaction of taste with calories ($P < 0.01$), which indicated a lower proportion of the fat-rich bread consumed after the HF breakfasts than after the HC or LF breakfasts ($P < 0.01$; Figure 3B).

The EE measured before the snack correlated negatively both with the total number of bread slices with spread subsequently consumed ($P < 0.01$) and with the amount of carbohydrate-rich bread consumed ($P < 0.01$; Figure 4A). For a rise in EE value of $10 \, \text{J} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$, mean decreases of $6.8 \pm 2.2$ in the number of total bread slices consumed and $3.5 \pm 1.2$ in the number of carbohydrate-rich bread slices consumed were observed. No significant correlation was noted between EE and the amount of fat-rich bread consumed (Figure 4B).

Finally, the RER did not correlate with either the total number of bread slices consumed during the snack or with the amount of carbohydrate- or fat-rich bread consumed.
After intake, the hedonic ratings for the snack did not differ between the 4 sessions (Table 1). Hedonic ratings for each type of bread also did not differ between the 4 sessions, but an interaction of taste with calories (P < 0.05) indicated a lower hedonic rating for the carbohydrate-rich bread consumed after the HC breakfast than after the HF breakfast (data not shown, P < 0.01).

Taken together, these results indicate the following: 1) the subjects consumed fewer bread slices—in particular, less carbohydrate-rich bread—after the high-calorie breakfasts, with a significant influence of EE on consumption; 2) the subjects consumed less fat-rich bread after the fatty breakfasts, with no influence of EE on this consumption; and 3) the substrate oxidation rate (ie, the RER) had no significant influence on consumption.

**Correlations with olfactory liking or preprandial hunger**

Olfactory liking ratings for sweet food items did not correlate with the amount of carbohydrate-rich bread consumed during the snack. A significant correlation was noted between hunger ratings before the snack and the number of bread slices consumed during the snack (for a hunger rise of 1, an average increase of 3.2 ± 1.0 bread slices consumed was expected; P < 0.01). A significant correlation was also noted between hunger ratings before the snack and the amount of carbohydrate-rich bread consumed subsequently (for a hunger rise of 1, an average increase of 1.8 ± 0.7 carbohydrate-rich bread slices consumed was expected; P < 0.01).

**Multiple linear regressions**

The value of EE depended only on the number of calories consumed during breakfast (P < 0.001) in a model [F(4,59) = 3.40, P < 0.05, r² = 0.187] that considered the 4 independent variables imposed or measured before the EE measurements (ie, taste and caloric content of the breakfast, hunger, and hedonic ratings after the breakfast). The RER depended on the taste (P < 0.01) and caloric content (P < 0.01) of the breakfasts in this model [F(4,59) = 6.22, P < 0.001, r² = 0.297].

Olfactory liking for the sweet food items was related to postprandial hunger after breakfast (P < 0.05) and, to a lesser extent, to the RER (P = 0.084) in a model [F(6,57) = 2.38, P < 0.05, r² = 0.197] that considered the 6 independent variables imposed or measured before olfactory liking measurements (ie, the taste and caloric content of the breakfast, hunger and hedonic ratings after breakfast, EE, and the RER). In contrast, olfactory liking for the fatty food items was not related to any of these variables.

Both the number of bread slices consumed and the amount of carbohydrate-rich bread consumed during the snack depended on EE (P < 0.001) in a model [F(7,56) = 4.05, P < 0.001, r² = 0.336, and F(7,56) = 3.43, P < 0.01, r² = 0.300] that considered the 7 independent variables imposed or measured before the snack (ie, the sweet/fat taste and caloric content of the breakfast, the hunger and hedonic ratings after breakfast, EE, and the RER). In contrast, olfactory liking for the fatty food items was not related to any of these variables.

**DISCUSSION**

Our hypothesis was that a high fat oxidation rate would increase liking and wanting for carbohydrates and that a high carbohydrate oxidation rate would have less of an effect. These correlations were observed for olfactory liking: when the fat oxidation rate was high, the subjects liked sweet food items and did not like fatty food items; when the carbohydrate oxidation rate increased, liking for carbohydrate food items decreased and liking for fatty food items increased. In contrast, the carbohydrate/fat oxidation rate did not significantly influence wanting for the carbohydrate- or fat-rich bread (selection and consumption).

These results are summarized in Figure 5 and discussed below.

**Olfactory liking and the respiratory exchange ratio**

The liking component of the food reward system was studied through the perceived olfactory pleasantness of 4 food items,
which had a high “sweet image” (honey and maple syrup) or a high “fat image” (melted butter and mayonnaise). As suggested by others (19, 27), it is difficult to ascertain the acuity of food liking or food hedonic sensations by explicit ratings. In the present study, as in others [eg, (28)], liking was considered an affective reaction that reflected the acute hedonic effect of a stimulus. Furthermore, explicit olfactory liking but not explicit flavor liking was evaluated to minimize a potential cognitive influence of flavor liking on subsequent food consumption.

Olfactory liking for the sweet/fatty food items depended on the RER (ie, the carbohydrate-to-fat oxidation ratio). Analysis by ANOVA indicated that olfactory liking for sweet food items was lowest after the sweet breakfasts, which also induced the highest RER. Conversely, olfactory liking for fatty food items was lowest after the fatty breakfasts, which also induced the lowest RER. A significant correlation was observed between olfactory liking for sweet food items, and multiple linear regressions revealed that olfactory liking for sweet food items (but not for fatty ones) was related to the RER.

The correlation between the RER and olfactory liking for fatty food items was not significant. However, one subject systematically expressed low olfactory liking ratings for melted butter and another subject low olfactory liking ratings for mayonnaise (these ratings were the only ratings with a mean value of less than −4). When these ratings were excluded from the statistical analyses, the correlation between the RER and olfactory liking for fatty food items became significant (P < 0.05). Therefore, it can be hypothesized that an especially low liking for a given food could outweigh the influence of the substrate oxidation rate on olfactory liking for this food.

The hypothesis that the metabolic state influences the liking component of the reward system is supported by several previous observations. First, the nutritional state modulates opioid-mediated food liking in animals (29–31). Second, cellular glucopenia induced by the peripheral administration of 2-deoxy-D-glucose increases the perceived pleasantness of sucrose in humans (32). Of course, in these studies, numerous metabolic and postconsumption factors may have influenced food liking, but the influence of the carbohydrate-to-fat oxidation ratio cannot be excluded.

In summary (Figure 5), the consumption of different sweet/fatty breakfasts changed the RER values, which in turn influenced olfactory liking for sweet/fatty food items. Therefore, the substrate oxidation rate tended to support the carbohydrate-based models of feeding in humans (3–5). In contrast, the carbohydrate-to-fat oxidation ratio did not influence wanting because no significant correlation was observed between the RER and the amount or the nature of the bread subsequently consumed.

**Wanting and EE**

The wanting component of the food reward system was assessed by the number of slices and the nature of the bread selected during the snack. Indeed, the subjects were presented with a forced choice based on a realistic procedure, rather than a forced choice based on a photographic procedure, as in other studies [eg, (33)]. Consequently, implicit and objective drive processes, which can be seen as a directed impulse or a demand for a targeted food stimulus, effectively reflected the wanting component of the reward system, ie, incentive salience/motivation (34).

The wanting for the carbohydrate-rich bread depended on the caloric content of the breakfasts and on EE. Indeed, the least-carbohydrate-rich bread (number of slices and proportion) was consumed after the sweetest carbohydrate breakfast (HC), which induced the highest EE; the amount of carbohydrate-rich bread consumed during the snack correlated negatively with EE; and multiple linear regressions showed that the amount of carbohydrate-rich bread consumed was related only to EE. The influence of EE on food intake has also been observed in humans. Studies have shown that a high thermic effect of food correlated positively with satiety (38–42) and a high 24-h carbohydrate oxidation rate predicted subsequent lower ad libitum food intake (16). These results and those of the present study indicate that high carbohydrate ingestion leading to a high glucose oxidation rate may decrease, at least partly, the subsequent intake of carbohydrates, although some studies have not reached the same conclusion (14, 15).

The subjects’ wanting for the fat-rich bread depended on both the caloric content and the fatty taste of the breakfast consumed, with no influence of EE on consumption. Hepatic metabolism may be involved because the oxidation of hepatic fatty acids influences feeding behavior in rats and mice (43, 44) as well as in humans (45, 46). Other factors, such as the nature of the fat ingested, neural mechanisms and peripheral enterostatin, cholecystokinin, and apolipoprotein A-IV cannot be excluded (47, 48).
In summary (Figure 5), the ingestion of HC breakfasts induced a lower consumption of bread slices during the snack, with an influence of EE on the consumption of carbohydrate-rich bread.

Liking, wanting, and alliesthesia

Our results showed no relation between olfactory liking for sweet/fatty food items and wanting for carbohydrate- or fat-rich bread, as shown by the absence of a significant correlation between these 2 variables. This result is consistent with those of previous studies, which observed a dissociation between the 2 components of the reward system (18, 30, 34, 49).

In the present experiment, the relation between the reward system (principally the liking component) and homeostatic drives was consistent with the usefulness of hedonic sensations, as noted by Cabanac (50, 51). This author showed that a given stimulus could arouse different hedonic sensations (i.e., alliesthesia) according to the subjects’ internal state to restore the stability of the milieu intérieur (internal environment). The stronger liking for sweet food items associated with the weaker liking for fatty food items when subjects were oxidizing fat (i.e., in a relative deficiency of carbohydrate stores) and the indifferent liking for sweet and fatty food items when subjects were oxidizing carbohydrates (i.e., with relatively replete carbohydrate stores) support this hypothesis.

In conclusion, a high fat oxidation rate induces a strong liking for carbohydrates and a low liking for fats. These results provide new evidence to support the carbohydrate-based models of feeding to maintain carbohydrate stores in humans. In an independent fashion, food wanting is influenced mainly by energy status (the energy content of the food consumed previously and the subject’s EE). This study highlights the importance of considering the metabolic state of subjects when foods are tasted in food design fashion, food wanting is influenced mainly by energy status (the carbohydrate stores) and the indifferent liking for sweet and fatty food items when subjects were oxidizing carbohydrates (i.e., with relatively replete carbohydrate stores) support this hypothesis.

REFERENCES