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Energy, substrate and protein metabolism in morbid obesity before, during and after massive weight loss

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OBJECTIVE: To investigate the effect of surgically induced weight loss on energy, substrate and protein metabolism of morbidly obese patients.
DESIGN: A prospective, clinical intervention study of morbidly obese patients before and after surgical treatment.
SUBJECTS: Eight morbidly obese patients (BMI 47.88 ± 7.03).
METHODS: Total energy expenditure (TEE; doubly labeled water method), sleeping metabolic rate (SMR; respiration chamber), body composition (deuterium oxide component of doubly labeled water), substrate metabolism (48 h dietary records, 48 h urine collection and gaseous exchange in the respiration chamber) and whole body protein turnover (primed-continuous infusion of L-[1-^{13}C]-leucine) were measured before, 3 and 12 months after vertical banded gastroplasty (VBG).
RESULTS: The TEE decreased as a result of a decreased SMR (64%) and non-SMR (36%; $P = 0.001$). SMR as a function of fat-free mass (FFM) decreased after weight loss ($P < 0.05$). The physical activity index (PAI), defined as TEE/SMR, was low and was not influenced by weight loss. Protein and carbohydrate oxidation decreased significantly after VBG ($P < 0.05$), although 3 months after VBG protein oxidation did not decrease enough to prevent loss of FFM. The energy used for protein turnover was approximately 24% of SMR and did not change after weight loss.
CONCLUSIONS: Compensatory processes that oppose weight loss of morbidly obese patients exist, as demonstrated by the disproportional reduction of SMR, and a low PAI. Protein turnover is not a major contributor to the disproportional reduction of SMR.
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Keywords: energy expenditure; substrate metabolism; protein turnover; morbid obesity; vertical banded gastroplasty

Introduction

Although the pathogenesis of obesity has not yet been elucidated, it becomes more and more clear that obesity is the result of genetic and metabolic disturbances, resulting in an energy imbalance. Several studies have shown that weight loss of obese subjects results in a reduction of resting energy expenditure (REE) larger than expected from changes in body composition.[1–7] Other studies underline the role of a decreased non-resting energy expenditure (NREE) in the reduction of total energy expenditure (TEE).[4,8,9] From the data of these studies it appears that weight loss of obese persons is not only associated with a reduced REE, but also with a reduced NREE, which may account for the poor long-term efficacy of conservative treatment for obesity. Under normal circumstances the contribution of NREE to TEE is approximately 30%, and is mainly determined by spontaneous physical activity.[10] A low physical activity, possibly accompanied by a low protein turnover, may lead to the development and maintenance of morbid obesity, because they favor a positive energy balance.

The contribution of protein turnover to REE is estimated to be 15%, and possibly higher in obese persons.[11–14] Protein turnover is closely controlled and represents a mechanism by which the energy expenditure might be regulated. Since protein is the largest solid component of lean body mass, the capacity of protein turnover to influence energy expenditure may be considerable. Therefore, a reduced whole body protein turnover could explain the disproportional reduction of REE in obese persons after weight loss.

Morbidly obese patients undergoing surgical treatment constitute a population with substantial and long-lasting weight loss.[15] Consequently, large metabolic changes are expected and long-term effects can be studied. To study the metabolic effects of weight loss it is, however, important to perform a restrictive procedure, such as a vertical banded gastroplasty (VBG), which induces weight loss via restricted intake. In the present study, the effect of massive weight loss after VBG on energy, substrate and protein metabolism of morbidly obese patients was investigated.

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Patients and methods

Patients

Eight morbidly obese patients, who fulfilled the criteria for surgical treatment, were included in the study[16] (Table 1). No obesity-related comorbidities, like diabetes or cardiovascular disease, were found in these patients, and no medication was used. A VBG was performed in all patients. The technique of the VBG is described in detail elsewhere.[17] Measurements were performed before VBG, and 3 months and 12 months after VBG. These particular time points were selected because rapid weight loss occurs 3 months after VBG, followed by a period of slow weight loss until 12 months after VBG, after which body weight is stable, as is demonstrated in previous studies.[17,18] All patients gave their written informed consent before participation in the study.

Energy expenditure

Sleeping metabolic rate (SMR) was measured during an overnight stay (20:00–07:30 h) in a respiration chamber. The subjects were not allowed to eat in the chamber and coffee or tea were allowed until 22:00 h. SMR was calculated over a period of three consecutive hours during minimal activity level as judged from Doppler radar observation. In the respiration chamber, the oxygen and carbon dioxide concentrations of the ingoing and outgoing air were measured with a paramagnetic analyzer (Magnos 6G, Hartman & Braun, Frankfurt, Germany) and an infrared analyzer (URAS 3G, Hartman & Braun, Frankfurt, Germany), respectively.[19] Energy expenditure was calculated using Weir's formula.[20] Total energy expenditure (TEE) was measured with the doubly labeled water method. Doubly labeled water was administered to the patients at 23:00 h after collection of a baseline urine sample. The dose was a mixture of 10% $H_2{}^{18}O$ in water and 99.8% ^2H_2O. Patients received a weighed amount, calculated to raise the baseline ^{18}O and ^2H levels by at least 250 ppm and 150 ppm, respectively. Initial urine samples were collected from the second voiding around 8:00 h the next morning. Final urine samples were collected after 7 and 14 days at 8.00 h in the morning and 18.00 h in the evening. Carbon dioxide production was calculated from isotope ratios in baseline, initial and final urine samples with the equation from Schoeller *et al*.[21] Carbon dioxide production was converted to energy expenditure using the mean respiratory quotient (RQ) measured in the respiration chamber. The non-sleeping metabolic rate (NSMR) was calculated as TEE minus SMR. Physical activity in daily life was expressed as the physical activity index (PAI): PAI = TEE/SMR.

Table 1 Patient characteristics

	Sex	*Age (y)*	*Heigh (m)*	*Body mass (kg)*	*BMI (kg/m²)*
1	Female	42	1.72	163.5	55.3
2	Female	32	1.64	116.9	43.5
3	Female	28	1.7	113.9	39.4
4	Female	24	1.7	113.2	39.2
5	Male	60	1.78	119.8	37.8
6	Female	54	1.59	135.2	53.5
7	Female	24	1.73	137.7	46
8	Female	40	1.64	140.6	52.3

Body composition

Body composition was assessed by means of the deuterium oxide component of doubly labeled water. The deuterium oxide dilution was measured in the urine sample of the second voiding in the morning, resulting in an equilibration time of 9–10 h. Total body water before administration was estimated from age- and gender-specific formulae.[22] Isotope abundance in the urine samples was measured with an isotope ratio mass spectrometer (VG Isogas, Aqua Sira, Cheshire, UK). Total body water was calculated as the deuterium dilution space divided by 1.04 for correction of a 4% over-estimation of total body water.[23] Fat-free mass (FFM) was calculated assuming 73.2% hydration.[24] Body mass (BM) was measured to the nearest 0.05 kg on a digital scale (Mettler, 240C, Greifensee, Switzerland). Fat mass (FM) was calculated as BM minus FFM.

Substrate metabolism

To measure substrate metabolism under free living conditions, the patients kept a dietary record and collected urine in an outpatient setting for 48 h just before entering the respiration chamber. Patients were instructed to keep their normal dietary habits for at least 3 days prior to the experiment. Dietary records were analyzed by the same dietitian at all time points. Energy intake before surgery was adjusted for TEE, assuming that all nutrients were equally underreported. At 3 and 12 months after surgery the dietary intake was not adjusted for TEE, because the patients were at an energy imbalance at that time. The carbohydrate, lipid and protein oxidation were obtained from measurements of oxygen consumption (VO_2) and carbon dioxide production (VCO_2) in the respiration chamber and total urinary nitrogen excretion as described by Frayn.[25] Nitrogen in urine was measured by standard automated techniques in the hospital clinical laboratory. Twenty-four hour protein oxidation was calculated from 24 h urinary nitrogen excretion, assuming a combustion of 6.25 g protein per gram nitrogen excreted. Carbohydrate and lipid oxidation were calculated from the gaseous exchange in the respiration chamber during 12 h. Carbohydrate and lipid oxidation values were extrapolated to 24 h values by adjusting for TEE minus protein oxidation.

Whole body protein turnover

Whole body protein turnover was determined by means of a primed-continuous infusion of L-

[1-^{13}C]-leucine (99 MPE, Cambridge Isotope Laboratories, Woburn, MA), 1 week before the energy expenditure measurements. After an overnight fast, a 4 h primed (0.5 mg/kg), continuous infusion of [1-^{13}C]-leucine dissolved in normal saline was administered at a rate of 0.5 mg/kg/h through an antecubital vein using a calibrated pump (model 561, IVAC). Just before the start of the [1-^{13}C]-leucine continuous infusion, the whole body bicarbonate pool was primed with $NaH^{13}CO_3$ (0.08 mg/kg). Blood samples were drawn from an intravenous venflon in the contralateral hand. Blood and breath samples were taken immediately before the start of the primed-continuous infusion and at 120, 150, 180, 210 and 240 min after starting the infusion. Blood samples were drawn in chilled-on-ice heparinized tubes and plasma was obtained by centrifugation (3500 rpm at 4°C for 5 min), frozen and stored at −80°C until analysis. Plasma [1-^{13}C]α-ketoisocaproic acid (KIC) enrichment (used as precursor pool for protein synthesis and leucine oxidation) was measured using a quinoxalinoltrimethylsilyl derative on a GC-MS system (Finnigan Incos XL, San Jose, CA) as previously described.[26] Expired air samples were obtained by having the subjects breathe normally for 3 min into a 6.75 l mixing chamber. After 3 min, a 15 ml Vacutainer® tube was filled with a sample of mixed air. $^{13}CO_2$ enrichment in the expired air was measured with a GC continuous flow isotope ratio mass spectrometer (Finnigan MAT-252). Recovery of $^{13}CO_2$ in breath was assumed to be 74%.[27,28] Steady state was achieved after 2 h of tracer infusion, as indicated by plasma KIC enrichment and $^{13}CO_2$ enrichment in breath samples. During the first and last hour of the infusion, the total CO_2 production rate of the subjects was measured by means of a computerized open-circuit ventilated hood system (oxycon-β, Mijnhard, The Netherlands).

Calculations of the rate of protein turnover were performed as described by Matthews *et al*.[29] In short, leucine turnover (Q) is measured from dilution of [1-^{13}C]-leucine infusion in plasma KIC at isotopic steady state: $Q = i[(E_i/E_p)\text{-}1]$, where i is the tracer infusion rate (μmol per kg per h), E_i is the enrichment of the [1-^{13}C]-leucine infused (MPE), and E_p is the plasma KIC enrichment at steady state (MPE). The rate of leucine oxidation is $O = F^{13}CO_2[(1/E_p)\ (1/E_i)] \times 100$, where $F^{13}CO_2$ is the rate of $^{13}CO_2$ released by leucine tracer oxidation (μmol ^{13}C per kg per h). From these calculations the rate of leucine incorporation into protein (protein synthesis, S) and leucine release from protein (protein breakdown, B) is obtained using the formula: $Q = S + O = I + B$, where I is protein intake, which was zero in this study. The leucine parameters were converted to corresponding estimates of whole body protein turnover by multiplying the leucine values by the constant (24 h per day/590 μmol leucine per gm protein) to give values in g protein per day.[29]

Statistics

Data are expressed as the mean value ± s.d. Differences between the values at the different time points were analyzed with the repeated measures analysis of variance (ANOVA) and the Bonferroni multi-comparison *post hoc* test. The relation between variables were tested by multiple regression analysis. Statistical significance was considered present at $P < 0.05$.

Results

Patients

Eight patients were included in the study and no patients were lost to follow-up. Patient characteristics are listed in Table 1. Body weight decreased significantly after VBG. The greatest weight loss occurred in the first 3 months, and between 3 and 12 months less weight was lost at a slower rate. After 12 months body weight was stable for at least 3 months. At 15 months after VBG the BM was 84.1 ± 14.8 kg.

Body composition

As a result of rapid weight loss during the first 3 months after VBG, FM and FFM decreased significantly (Table 2). The body weight loss in this period (26.3 kg), consisted of 66.5% FM and 33.5% FFM. During the next 9 months, in which weight loss was much slower, only the fat mass decreased significantly. During the latter period, body weight loss (20 kg) consisted of 97% FM and 3% FFM.

Energy expenditure

TEE, SMR and NSMR decreased significantly after VBG, however, when adjusted for FFM only TEE and SMR decreased significantly (Table 3). The latter does not necessarily mean that the SMR after weight loss is subnormal, because the intercept of the regression line between SMR and FFM is significantly different from zero. This is very nicely shown by Ravussin and Bogardus.[30] To investigate whether the energy

Table 2 Changes in body composition after vertical banded gastroplasty ($n = 8$)

	Before VBG	*After VBG*	
		3 months	*12 months*
BM (kg)	130.1 ± 17.5	103.8 ± 15.6*	83.8 ± 12.4**†
FFM (kg)	61.8 ± 9.2	53.0 ± 6.2*	52.4 ± 4.4*
FM (kg)	68.3 ± 11.7	50.8 ± 11.1*	31.4 ± 12.1**†

VBG = vertical banded gastroplasty; BM = body mass; FFM = fat-free mass; FM = fat mass. Data are expressed as mean ± s.d. *$P < 0.05$ and **$P < 0.001$ for differences with the values before VBG. † $P < 0.05$ for differences with the values 3 months after VBG (repeated measures ANOVA and Bonferroni multi-comparison *post hoc* test).

Table 3 Energy expenditure indices before and after vertical banded gastroplasty ($n=8$)

	Before VBG	*After VBG*	
		3 months	*12 months*
TEE (J/min)	9400 ± 1300	6700 ± 1000**	6900 ± 1200**
TEE/FFM (J/min kg)	154 ± 11	127 ± 18*	131 ± 18*
SMR (J/min)	5800 ± 800	4400 ± 400**	4200 ± 300**
SMR/FFM (J/(min kg))	95 ± 9	83 ± 6*	81 ± 4**
NSMR (J/min)	3600 ± 600	2300 ± 700*	2700 ± 1000*
NSMR (J/(mm kg))	59 ± 6	44 ± 13	50 ± 17
PAI	1.63 ± 0.08	1.52 ± 0.13	1.62 ± 0.19

VBG = vertical banded gastroplasty; TEE = total energy expenditure; SMR = sleeping metabolic rate; NSMR = non-sleeping metabolic rate; FFM = fat-free mass; PAI = physical activity index. Data are expressed as mean ± s.d. *$P<0.05$ and **$P<0.001$ for differences with the values before surgery. Differences between the values 3 and 12 months after VBG were not significant (repeated measures ANOVA and Bonferroni multi-comparison *post hoc* test).

expended by FFM during sleep is subnormal, the individual values of FFM and SMR at 3 and 12 months after VBG were compared to the regression line of FFM and SMR before VBG. The regression line of FFM and SMR before VBG was described as: SMR (MJ/day) = 1.89 + 0.105FFM (kg). The individual values of FFM and SMR 3 and 12 months after VBG are situated below the regression line, which suggests that the energy expended by FFM during sleep is subnormal after weight loss (Figure 1). The TEE decreased by 2500 J/min from before VBG to 12 months after VBG, while the SMR and NSMR decreased by 1600 and 900 J/min, respectively, in the same period. The reduction of TEE was mainly the result of a decreased SMR (64%), but also the result of a decreased NSMR (36%). The PAI was low and did not change significantly during or after weight loss (Table 3).

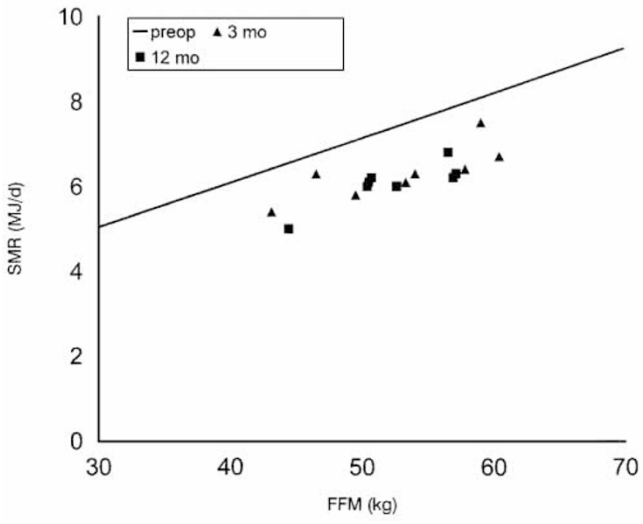

Figure 1 The individual values of sleeping metabolic rate (SMR) in relation to fat-free mass (FFM) at 3 months (triangles) and 12 months (squares) after vertical banded gastroplasty (VBG) are compared with the regression line of SMR and FFM before surgery (SMR = 1.89 + 0.105 FFM).

Substrate metabolism

Energy expenditure and energy intake decreased significantly at 3 and 12 months after VBG (Table 4), however, because the energy intake decreased more, an energy deficit occurred three months (ΔEE 5160 kJ/day) and 12 months after VBG (ΔEE 3830 kJ/day). Protein and carbohydrate oxidation decreased, while fat oxidation increased as a result of weight loss after VBG (Table 5). Carbohydrate intake and oxidation remained in balance during weight loss (Figure 2a). At 3 months after VBG protein intake decreased, however, protein oxidation did not decrease significantly, explaining the loss of protein mass (Figure 2b). Twelve months after VBG, the balance between protein intake and oxidation was almost regained, because protein intake recovered a little (ns), while protein oxidation decreased further and significantly different from preoperative values. Fat intake decreased 3 and 12 months after VBG, while fat oxidation increased significantly at 3 months after VBG, explaining the loss of fat mass (Figure 2c).

Whole body protein turnover

Twelve months after VBG a significant decrease of protein oxidation, breakdown, and synthesis occurred when expressed as gram protein per day (Table 6).

Table 4 Substrate intake before and after vertical banded gastroplasty ($n=8$)

	Before VBG	*After VBG*	
		3 months	*12 months*
Energy intake (kJ/day)	13540 ± 1970	4490 ± 1400**	6110 ± 3330**
Protein (kJ/day)	2290 ± 320	550 ± 310**	850 ± 520**
Protein (%)	16.9 ± 2.3	12.3 ± 4.5	13.9 ± 5.3
Fat (kJ/day)	4990 ± 1150	1690 ± 810**	2010 ± 750**
Fat (%)	36.9 ± 6.6	37.6 ± 9.5	32.9 ± 7.0
Carbohydrate (kJ/day)	6260 ± 1150	2250 ± 820**	3250 ± 150**
Carbohydrate (%)	46.2 ± 14.5	50.1 ± 15.8	53.2 ± 9.1

VBG = vertical banded gastroplasty. Data are expressed as mean ± s.d. **$P<0.001$ for differences with the values before surgery. Differences between the values 3 and 12 months after VBG were not significant (repeated measures ANOVA and Bonferroni multi-comparison *post hoc* test).

Table 5 Substrate oxidation before and after vertical banded gastroplasty ($n=8$)

	Before VBG	*After VBG*	
		3 months	*12 months*
EE (kJ/day)	13540 ± 1970	9650 ± 1460**	9940 ± 1400**
PTO (kJ/day)	2360 ± 1250	1370 ± 830	960 ± 400*
LPO (kJ/day)	5030 ± 1890	6330 ± 1320*	5540 ± 2010
CHO (kJ/day)	6150 ± 1420	1950 ± 1410**	3440 ± 2230*

VBG = vertical banded gastroplasty; EE = total energy expenditure; PTO = protein oxidation; LPO = lipid oxidation; CHO = carbohydrate oxidation. Data are expressed as mean ± s.d. *$P<0.05$ and **$P<0.001$ for differences with the values before VBG. Differences between the values 3 and 12 months after VBG were not significant (repeated measures ANOVA and Bonferroni multi-comparison *post hoc* test).

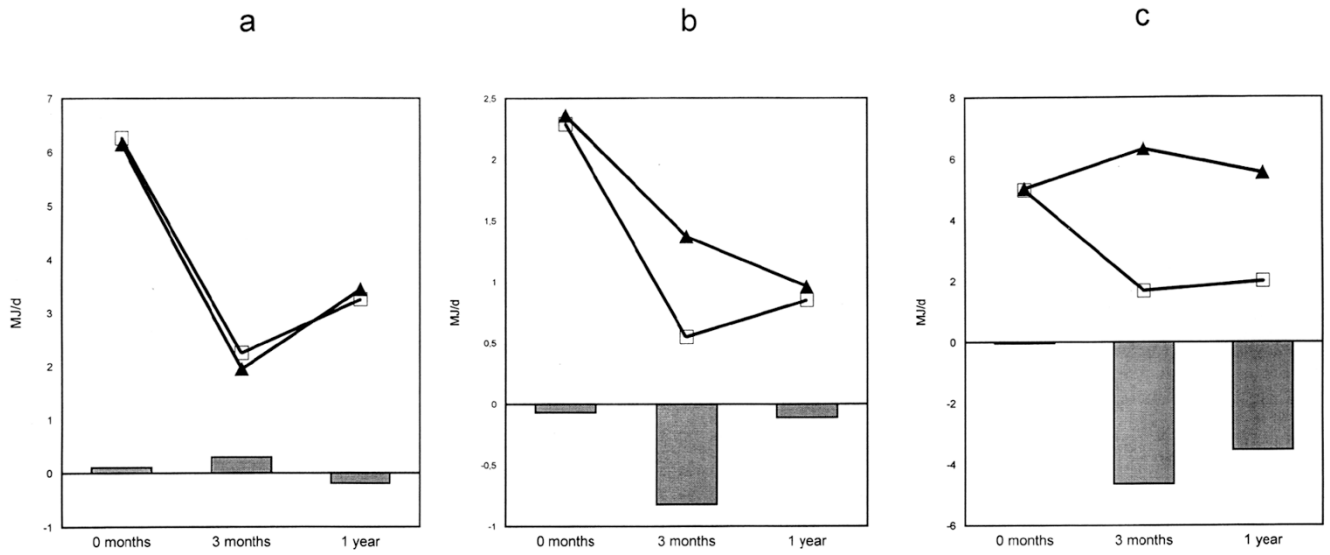

Figure 2 Carbohydrate, protein and fat intake and oxidation are shown in A, B and C, respectively. The intake is represented by squares and the oxidation by triangles. The bars represent the difference between intake and oxidation.

Three months after VBG this decrease was not significant with respect to protein synthesis. When expressed as gram protein per kg FFM per day, only protein oxidation decreased significantly during rapid weight loss at 3 months after VBG, but protein breakdown and synthesis did not change. Twelve months after VBG, protein metabolism expressed per kg FFM was not significantly different from preoperative values. Protein synthesis expressed as a percentage from PB was 82.4% before VBG, 90.9% at 3 months after VBG ($P < 0.01$), and 85.7% at 12 months after VBG (ns).

Assuming that each mole of oxygen consumed is linked to the synthesis of 6 moles of ATP, and that the energy expenditure associated with protein turnover is 1.04 kcal/g protein, the contribution of protein turnover to SMR was 23.2%±2.0% before VBG, 24.0%±1.0% at 3 months after VBG, and 24.3%±3.4% at 12 months after VBG.[11,13]

Table 6 Protein oxidation, breakdown and synthesis before and after vertical banded gastroplasty ($n = 8$)

	Before VBG	*After VBG*	
		3 months	*12 months*
PO (g/day)	77.1±20.7	31.9±7.4**	49.1±22.0*
PO/FFM (g/kg day)	1.25±0.29	0.60±0.13**	0.94±0.43
PB (g/day)	444.6±79.3	347.5±37.9*	339.9±69.9*
PB/FFM (g/(kg day))	7.21±0.81	6.58±0.50	6.45±0.98
PS (g/day)	367.5±78.1	315.6±32.7	290.8±59.8*
PS/FFM (g/(kg day))	5.96±0.90	6.00±0.39	5.51±0.77

VBG = vertical banded gastroplasty; FFM = fat-free mass. Protein oxidation (PO), breakdown (PB), and synthesis (PS) are expressed as gram protein per day (g/day) and as gram protein per kg FFM per day (g/(kg day)). Data are expressed as mean±s.d. *$P < 0.05$ and **$P < 0.001$ for differences with the preoperative values. Differences between the values 3 and 12 months after VBG were not significant (repeated measures ANOVA and Bonferroni multi-comparison *post hoc* test).

Discussion

In the present study, the reduction of SMR was larger than expected based on the reduction of FFM. The reduced SMR during the first 3 months after VBG is probably an adaptation to semi-starvation, however, 12 months after VBG, when weight loss was very mild, the disproportional reduction of SMR may reflect the persistent susceptibility of the formerly obese to weight regain. Several studies in which the subjects were used as their own controls, showed a reduction of resting metabolic rate larger than expected based on body composition.[1,2,4,6,7] Others showed that TEE, as determined by weight maintenance energy requirements, also reduced disproportionally following weight loss.[4,8] The present study revealed a significant decrease of NSMR, although the PAI remained unchanged. In this study, the PAI was defined as TEE/SMR as proposed by Westerterp *et al*.[31] However, when the BMR measured with the ventilated hood was used to determine the PAI, the same results were obtained. Westerterp *et al* also found a low PAI in morbidly obese patients before and after weight loss, and a negative relation between PAI and fat reduction.[31] A possible explanation for the latter is that patients are not able to maintain or increase activity levels as a result of a drastically decreased eating capacity after VBG. Ferro-Luzzi and Martino identified in an epidemiological survey, a critical level of PAI less than 1.80, below which the risk of obesity increases sharply.[32] From this point of view, the low PAI of the present study population may be a reflection of their propensity to become and remain obese.

Rapid weight loss during the first 3 months after VBG resulted in significant loss of FM and also FFM. On the other hand, slow weight loss after 3 months

resulted in loss of FM, while FFM was spared. Many underfeeding studies with overweight subjects showed that body weight lost is mainly composed of FM (71.7%–85.2%) and FFM is lost to a lesser degree (14.8%–28.3%).[1,2,4,7,33] Palombo *et al* studied the composition of weight loss in 82 morbidly obese patients after gastric bypass and found that FFM was mainly lost in the initial period of rapid weight loss.[34] The same phenomenon was demonstrated in our previous findings, and in the energy balance studies of Garrow.[18,35] The data of these studies indicate, that treatment modalities resulting in an extended slow weight loss are preferable, since slow weight loss results in loss of FM, while FFM is spared.

In the present study population of morbidly obese patients, in which the FM constitutes the largest body compartment, fat oxidation increased while fat intake decreased resulting in a massive loss of fat mass. On the other hand, carbohydrate and protein oxidation decreased and increased simultaneously with carbohydrate and protein intake. During semi-starvation protein oxidation decreased to a lesser extent than protein intake, resulting in a loss of FFM. One year after VBG, the energy deficit was much smaller, and protein balance was almost restored. From these data it appears that protein oxidation reaches a minimum limit during semi-starvation. Garrow identified an optimum rate of weight loss of 4.2 MJ/day at which FFM is spared and only FM is lost.[36] Because a lower limit for protein oxidation seems to exist, it is important to consider the possibility of the development of a protein deficiency syndrome during semi-starvation. After VBG, the susceptibility for protein malnutrition is very realistic not only as a result of massive weight loss, but also because these patients cannot consume some protein-rich nutrients, like meat. In a carefully designed study, MacLean *et al* found protein malnutrition in 47 out of 96 morbidly obese patients following gastroplasty.[37] These results emphasize the need of nutritional assessment and support of these patients after weight reducing surgery, especially during the phase of rapid weight loss.

The observed changes in body composition in this study can be explained by a normal physiological mechanism: a decreased carbohydrate intake results in lower insulin levels followed by an increased lipolysis and decreased carbohydrate and protein oxidation. The adaptive response to fasting seems to be mainly regulated by the carbohydrate restriction.[38,39] Sugerman *et al* performed a randomized prospective study comparing VBG with Roux-en-Y gastric bypass that included preoperative dietary separation of 'sweets eaters' *vs* 'non-sweets eaters'.[40] It appeared that the Roux-en-Y gastric bypass was superior to VBG with respect to sweets eaters, probably because of the development of dumping syndrome symptoms after carbohydrate ingestion. After VBG, sweets eaters lost significantly less weight than non-sweets eaters, which can be explained by the fact that the hyperinsulinemia does not resolve in patients in whom the carbohydrate intake is not adequately reduced. Brolin *et al* also found that the intake of milk, ice and solid sweets was significantly higher in the patients after VBG compared to Roux-en-Y gastric bypass.[41] These results indicate that a successful bariatric procedure must protect against excessive carbohydrate intake either by the surgical procedure itself or by intensive dietary support after surgery.

The results of the present study show that the energy expended per kg FFM decreased, while the protein turnover per kg FFM did not. Furthermore, protein turnover expressed as a percentage of SMR did not change during and after weight loss, which suggests that protein turnover is not a major contributor to the disproportional reduction of SMR. Other studies also found that obesity is not associated with an inherent abnormality of protein metabolism.[11,42] In the present study population, the protein synthesis expressed as a percentage of protein breakdown increased during semi-starvation, reflecting a protein-sparing process as the gap between protein synthesis and degradation narrows. Protein-sparing during semi-starvation was also demonstrated in other studies.[43–46] Jensen *et al* showed that obesity is associated with greater proteolysis and that the antiproteolytic actions of insulin are impaired due to insulin resistance.[47] This implies that obese patients are even more at risk for protein deficiency during weight loss compared to normal weight persons. Garlick *et al* investigated the influence of low-energy diets on protein turnover in obesity and concluded that the decrease in dietary energy did not influence protein turnover, but dietary protein was necessary to maintain protein turnover rates.[48] Although not significant, the protein intake as a percentage of diet following VBG decreased in the present study. Because the intake of some protein-rich nutrients is hampered in patients after VBG, the observed changes of protein turnover in this study may be the result of protein malnutrition. It is concluded that compensatory processes seem to exist which oppose weight loss of morbidly obese patients. The disproportional reduction of SMR during and after weight loss demonstrate the propensity to weight regain, which is also reflected in a low PAI. Although semi-starvation results in a significant decrease of whole body protein turnover, it is not a major contributor to the reduction of SMR. Slow weight loss results in loss of FM only, while rapid weight loss results in loss of FM and FFM. A protein-sparing mechanism during semi-starvation is likely to exist, which does not completely prevent loss of FFM during rapid weight loss after VBG.

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