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Sleeve gastrectomy and Roux-en-Y gastric bypass exhibit differential effects on food preferences, nutrient absorption and energy expenditure in obese rats

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Abstract

OBJECTIVE—All available treatments directed towards obesity and obesity-related complications are associated with suboptimal effectiveness/invasiveness ratios. Pharmacological, behavioral and lifestyle modification treatments are the least invasive, but also the least effective options, leading to modest weight loss that is difficult to maintain long-term. Gastrointestinal weight loss surgery (GIWLS) is the most effective, leading to >60–70% of excess body weight loss, but also the most invasive treatment available. Sleeve gastrectomy (SGx) and Roux-en-Y gastric bypass (RYGB) are the two most commonly performed GIWLS procedures. The fundamental anatomic difference between SGx and RYGB is that in the former procedure, only the anatomy of the stomach is altered, without surgical reconfiguration of the intestine. Therefore, comparing these two operations provides a unique opportunity to study the ways that different parts of the gastrointestinal (GI) tract contribute to the regulation of physiological processes, such as the regulation of body weight, food intake and metabolism.

DESIGN—To explore the physiologic mechanisms of the two procedures, we used rodent models of SGx and RYGB to study the effects of these procedures on body weight, food intake and metabolic function.

RESULTS—Both SGx and RYGB induced a significant weight loss that was sustained over the entire study period. SGx-induced weight loss was slightly lower compared with that observed after RYGB. SGx-induced weight loss primarily resulted from a substantial decrease in food intake and a small increase in locomotor activity. In contrast, rats that underwent RYGB exhibited a substantial increase in non-activity-related (resting) energy expenditure and a modest decrease in nutrient absorption. Additionally, while SGx-treated animals retained their preoperative food preferences, RYGB-treated rats experienced a significant alteration in their food preferences.

CONCLUSIONS—These results indicate a fundamental difference in the mechanisms of weight loss between SGx and RYGB, suggesting that the manipulation of different parts of the GI tract may lead to different physiologic effects. Understanding the differences in the physiologic mechanisms of action of these effective treatment options could help us develop less invasive new treatments against obesity and obesity-related complications.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

Keywords

gastric bypass; metabolism; metabolic surgery; energy expenditure; animal models; sleeve gastrectomy

INTRODUCTION

Obesity is not a lifestyle choice or a flaw of character, but a serious disease with complex pathophysiology and devastating effects. The prevalence of this serious disease has increased dramatically throughout the world over the last 25 years. Unfortunately, its long-term control remains poor, and only gastrointestinal weight loss surgery (GIWLS) is associated with weight loss that is sustained over a long period of time.¹⁻⁴ However, similar to all of the other available treatment options, GIWLS is associated with suboptimal effectiveness to invasiveness ratio.¹⁻⁴ Pharmacological, behavioral and lifestyle modification treatments (for example, dieting and exercise) are the least invasive options, but are also the least effective options. These options generally lead to a modest 5–10% loss of total body weight (TBW) that is difficult to maintain long-term.⁴ More than 95% of individuals regain all of the weight and many people gain more weight than was lost initially, thus exacerbating their obesity.

In contrast, Roux-en-Y gastric bypass (RYGB), the most effective GIWLS treatment, induces substantial and sustained weight loss. Patients typically lose over 40% of their TBW and maintain >80% of the initial weight loss for a lifetime.² RYGB, however, is the most invasive option available. Although it has long been the reference standard for GIWLS, alternative procedures that induce significant weight loss with lower morbidity have been explored more recently. Sleeve gastrectomy (SGx) is one of the less invasive alternatives. In SGx, a narrow sleeve of gastric tissue is created by removing 90% of the greater curvature part of the stomach. The immediate results of this procedure are comparable to those of RYGB, and include similar short-term weight loss and improvement of obesity-associated co-morbidities.⁵⁻⁷ However, some reports have recently suggested that the long-term outcomes of SGx and RYGB may be different, and there are increased concerns that a significant number of SGx-treated patients may regain the weight and may require re-operation and conversion to RYGB.⁸⁻¹⁰

The fundamental anatomic difference between the two procedures is that in SGx only the anatomy of the stomach is changed and there is no reconfiguration of the intestine. Therefore, comparing these two operations provides a unique opportunity to study the ways that different parts of the gastrointestinal (GI) tract contribute to the regulation of physiological processes, such as the regulation of body weight, food intake and metabolism. In addition, understanding the mechanisms by which GIWLS induces its profound and sustainable effects could facilitate the design of more ideal weight loss treatments that should combine maximal effectiveness and minimal invasiveness.

To explore the physiologic mechanisms by which the different types of GIWLS induce their effects, we and others have recently developed rodent models of several weight loss procedures.¹¹⁻¹⁷ In addition, recent investigations have focused on the similarities between SGx and RYGB and their effects on glucose metabolism and insulin secretion.¹⁸ In this study, we used a rodent model of each of the two procedures to study the effects of the two procedures of body weight, food intake and metabolic function. Our results indicate a fundamental difference in the mechanisms of weight loss between RYGB and SGx, suggesting that the manipulation of different parts of the GI tract may lead to different physiologic effects. Understanding the differences in the physiologic mechanisms of action

of RYGB and SGx could identify targets for enhancing the effectiveness of each of these procedures and facilitate the development of new, less invasive and more effective, treatments for obesity and its metabolic complications.

MATERIALS AND METHODS

Animals

All experiments were approved by and performed in compliance with the Institutional Animal Care and Use Committee of Children's Hospital Boston and Massachusetts General Hospital. Animals were individually housed and were maintained on 12 h light–dark cycle (lights on at 0700 hours) in a facility with an ambient temperature of 19–22°C and 40–60% humidity. We utilized the Long Evans strain (Charles River Laboratories, Wilmington, MA, USA) that is highly susceptible to diet-induced obesity. Male rats were used in all experiments. Obesity was induced by placing the animals on a high-fat diet (HFD) for ~12–14 weeks (D12492 diet; Research Diets Inc., New Brunswick, NJ, USA). This diet provides 60% of total energy as fat, 20% as carbohydrate and 20% as protein.

Operations

For all surgical procedures, general anesthesia was used. Each rat was placed in a chamber and inhalation anesthesia (4% isoflurane, oxygen flow 2 l per minute) was delivered until the rat lost its righting reflex. The animal was maintained throughout the preparation and surgery period on inhalation anesthesia (on a scavenged mask circuit of isoflurane 1–4% to effect). Sterile procedures were followed in all operations. The animals were kept on a temperature-controlled surgical board (38°C) in dorsal recumbency. A sterile surgical drape was placed over the entire animal and surgical area.

Sleeve gastrectomy

As soon as the rat was anesthetized, a 7FR catheter was passed through the mouth to the stomach, and then the tube was advanced to the duodenum. This tube was used to standardize the size of the sleeve. A 4–5 cm midline abdominal incision was made extending about two-thirds the length of the abdomen to the xiphoid cartilage and a self-retaining retractor was placed. The liver was gently retracted cranially, using 3' cotton tip applicators. Blunt dissection was carried along the greater curvature of the stomach with the cotton tip applicators; and the greater curvature was freed from its attachments. The greater curvature was then removed with a laparoscopic stapler. A sleeve was created along the lesser curvature carefully preserving the gastroesophageal junction and the pylorus. The surgical incision was closed with 3.0 silk sutures in two layers (Figure 1a).

Roux-en-Y gastric bypass

The procedure has been described in detail before.¹¹ Briefly, the two parts of the stomach (rumen or forestomach and glandular stomach) that are separated by a visible white ridge were identified. Blunt dissection was carried out along the greater curvature of the stomach with cotton tip applicators; and the greater curvature was freed from its attachments. The forestomach was then restricted with a laparoscopic stapler. The pouch was drained via a Roux-en-Y gastroenterostomy. For the Roux-en-Y reconstruction, the ligament of Treitz was identified and the jejunum divided within a distance of 10 cm from the duodenum. A 5–10 mm incision was made to the gastric wall just above the stapling line. The gastrojejunostomy was created with a running suture (6.0 or 7.0 silk). An end-to-side jejunojejunostomy was created in the same way within 15 cm from the gastrojejunostomy. The wound was closed with 3.0 silk sutures in two layers (Figure 1b).

Sham operation

Rats undergoing a sham operation were used as controls. The sham operation consisted of laparotomy, jejunal transection and reanastomosis and was performed in rats that were carefully age- and weight-matched with rats undergoing RYGB or SGx procedure.

Energy expenditure and activity measurements

The Oxymax Lab Animal Monitoring System (CLAMS) was used (Columbus Instruments, Columbus, OH, USA). All animals were placed in the cages of the indirect calorimeter system for acclimation before experimental measurements. The CLAMS system is located in a temperature-controlled room, and the temperature inside the cages was documented at a constant 29 °C. This temperature is in the thermoneutrality zone for rats, so all measurements were performed under thermoneutral conditions. Measurements were performed for 72 h, during which animals had access to food (HFD) and water *ad libitum*. Oxygen consumption, carbon dioxide production and heat production were recorded for each animal. Resting energy expenditure was calculated by correlating oxygen consumption, food intake and activity based on the recordings of the metabolic system.

Food preference studies

To examine the food preferences (HFD vs low-fat diet) of RYGB- and SGx-treated animals, the rats were presented with the choice of the two diets for 1 week. The experiment was performed the eighth postoperative week. The two diets that we used were the HFD D12492 (Research Diets Inc.) and the normal chow diet Labdiet 5001 (Purina Mills LLC, St Louis, MO, USA). The chow diet provides 13.5% of the total energy as fat, 58% as carbohydrates and 28.5% as protein.

Foods were presented in separate containers simultaneously. For the assessment of food intake, rats were individually housed in cages with elevated racks without bedding. Food intake was determined each day by weighing the amount of food remaining from the previous day's allowance and any spillage. The position of the containers was different every day.

Postoperative care

Postoperatively, all animals were put back on the same diet that they were before the procedure (for example, diet-induced obese (DIO) animals were placed back to HFD). This diet was reintroduced, about 7 days after the operation. A postoperative feeding protocol was necessary for the immediate postoperative period and it was given for approximately a week after the procedure. Animals were given no food for 2 days following the operations. For the following 5 days (postoperative days 3–7), the rats were given Vital HN liquid diet (Abbott Nutrition, Columbus, OH, USA). Full details of the postoperative protocol and care have been described in detail previously.^{19,20} On average, rats ate 30 ml of the diet per day (~30 calorie per day). This feeding protocol had a minimal effect on the measured outcomes (for example, body weight, energy expenditure, etc), because all analyses were performed 8 weeks postoperatively. Furthermore, sham-operated animals received the exact same postoperative protocol (including the 2 days of fasting and 5 days of the maintenance diet) and therefore, any possible influence of the postoperative diet was accounted for.

RESULTS

Differential effects of SGx and RYGB on body weight

To determine whether SGx and RYGB induce weight loss in obese rats, we performed these procedures on DIO Long Evans rats at 3 months of age (SGx-DIO ($n = 15$), RYGB-DIO (n

= 15)), and compared them with age- and weight-matched rats that under-went a sham operation (sham-DIO ($n = 10$)). Eight weeks after surgery, SGx-treated rats weighed more compared with RYGB-treated rats (575 ± 18 vs 534 ± 11 g, respectively; $P < 0.05$), but 10% less than sham-DIO animals (575 ± 18 vs 638 ± 9 g; $P < 0.05$). As shown in Figure 2a, during the first 6 postoperative weeks, there was no statistically significant difference in the body weight loss between SGx- and RYGB-treated groups. So, the observed difference (4%) in the weight loss between the two groups was established in the last 2 weeks of the study. Both SGx- and RYGB-treated rats continued to exhibit normal grooming and behavior, indicating that the observed weight loss did not result from a toxic effect of the operation.

Differential effects of SGx and RYGB on food intake and food preference

To determine the mechanisms by which SGx induces weight loss, we first measured the food intake of animals that underwent SGx, RYGB or sham operation. As shown in Figure 2b, SGx-treated rats exhibited a larger decrease in food intake compared with either sham- or RYGB-treated animals. Both experimental groups increased their food intake gradually, but SGx-treated animals continued to exhibit the least food consumption over the entire period of this study.

We then determined whether RYGB and SGx have an effect on food preferences. We performed a food choice experiment at postoperative week 8, in which SGx-DIO, RYGB-DIO and sham-DIO rats were exposed, before and after surgery, to two different diets: an HFD and a regular low-fat diet (normal chow). As expected, before surgery, all groups showed an increased preference for the HFD. More specifically, 84% ($\pm 2.7\%$) of the calories were derived from the HFD and 16% ($\pm 2.6\%$) from normal chow. As shown in Figure 2c, after surgery, the food preference of SGx-treated animals did not change; the animals continued to consume a significantly higher amount of HFD than normal chow ($84 \pm 0.9\%$ vs $16 \pm 0.9\%$). In contrast, animals that underwent RYGB exhibited a dramatic change in their food preferences after surgery. While more than half of the total calories were still derived from HFD ($59 \pm 8\%$) in these animals, the normal chow-derived calories comprised 41% ($\pm 3\%$) of their daily intake. To determine the timing that the difference in the preference for HFD is exhibited between the SGx- and RYGB-treated animals, we performed a food choice experiment in a group of thin Long Evans rats that were placed on a low-fat diet since weaning. After SGx and RYGB operation, these rats remained on the low-fat diet for 8 weeks, and then they were presented with two food choices, the HFD and the normal chow. As shown in Figure 2d, in the first meal after the introduction of the two diets, in RYGB-treated rats, 70% of the calories were derived from the HFD and 30% from normal chow. In contrast, SGx-operated animals consumed only HFD. In the subsequent meals of the first day of the food choice experiment, RYGB-treated rats further decreased the amount of calories derived from HFD, while in the SGx group, 93% of the calories were derived from the HFD. Overall, these data suggest that SGx-treated animals continue to exhibit after surgery a preference for HFD, while the RYGB-treated animals exhibit a consistent acceptance and preference to low-fat diet. This difference in food preference is established very early after the introduction of HFD to SGx-treated animals.

Differential effects of SGx and RYGB on nutrient absorption

To examine the potential contribution of changes in nutrient absorption to the observed weight loss after SGx and RYGB, we measured the calories that were lost in the fecal output of the two groups (Figure 2e). There was a 58% increase in total fecal energy density in the RYGB group compared with sham-operated mice. Although the average fecal density was 8% higher in the SGx group in comparison to sham-operated animals, this difference did not reach statistical significance.

Differential effects of SGx and RYGB on energy expenditure

To examine the potential contribution of changes in energy expenditure (EE) to the observed weight loss after SGx and RYGB, we performed whole-animal indirect calorimetry (Figure 3). Energy expenditure data were presented as cumulative oxygen consumption and were normalized by TBW as well as allometric scaling ($TBW^{0.75}$).²⁰

As shown in Figures 3a and b, total oxygen consumption (VO_2) was 13% higher in the SGx group than in the sham-operated rats. This difference was due to an increase in activity-related VO_2 , since there was no difference in resting VO_2 between the two groups. More specifically, activity-related VO_2 increased by 40% in the SGx group (cumulative VO_2 : 77×10^3 vs 55×10^3 ml per hour per kg; $P < 0.05$). SGx-DIO rats exhibited more activity episodes (29 ± 3 vs 22 ± 4 episodes; $P < 0.05$) and spent more time behaving actively than the sham-DIO animals (613 ± 37 vs 460 ± 75 min; $P < 0.05$) (Figures 3c and d).

In comparison to RYGB, SGx showed a resting VO_2 decrease of 31% (90 ± 3 vs $131 \pm 6 \times 10^3$ ml per hour per kg) and total VO_2 decrease of 20% (175 ± 3 vs 219 ± 5 ml per hour per kg) (Figure 3a). Analyzing the data with allometric scaling also generated similar results (Figure 3b). There was no difference in the Respiratory Quotient between SGx- and RYGB-treated animals (0.79 ± 0.1 vs 0.8 ± 0.1 ; data not shown).

DISCUSSION

The aim of this study was to compare the effects of RYGB and SGx in rat models of the procedures. The fundamental observation is that SGx induces weight loss primarily by decreased calorie intake, while RYGB-induced weight loss is associated primarily with an increase in EE and a decrease in nutrient absorption.

Interestingly, SGx-treated rats exhibited an increase in locomotor activity, resulting in a slight increase in total EE in comparison to sham-treated animals. This finding may be explained by the decreased food intake observed after SGx, since many studies have shown that chronic food restriction stimulates spontaneous activity in rodents, zebrafish and non-human primates.²¹⁻²⁴ These studies have suggested that food restriction induces changes in brain neuropeptide levels that likely contribute to the increase of spontaneous activity, and often attribute this increase to foraging activity and behavior. The SGx-treated animals exhibited an increase in locomotor activity, despite *ad libitum* access to food. Thus, it is likely that the chronic reduction in food intake, per se, leads to neurohormonal changes that trigger the increase of the locomotor activity observed in SGx-treated rats and calorie-restricted animals.

Non-activity-related EE was decreased in SGx-treated animals in comparison to sham-operated animals, although this trend was not statistically significant. This finding may also be explained by the chronic decrease in food intake observed in these animals. This is in agreement with studies that have shown that starvation and chronic food restriction are associated with decreased resting EE, as an effort to conserve energy.²⁵⁻²⁷ In contrast, RYGB-treated animals exhibited an increase in their resting EE. The increase in non-activity-related EE may be a unique feature of procedures with rerouting of intestinal alimentary flow, since other procedures that involve only gastric (and not intestinal) manipulation, such as gastric banding do not increase EE. Others have also shown that EE is increased in procedures such as RYGB and biliopancreatic diversion.^{11,28-33} These data support the hypothesis that restricting the volume of the stomach is not necessary for the increase in non-activity-related EE observed in these weight loss procedures. It appears that the key components for this increase are the rearrangement of the anatomy of the GI tract, and the lack of duodenal exposure to nutrients and/or the accelerated jejunal exposure to

undigested nutrients. The cascade of events that ultimately leads to the augmentation of EE and the associated weight loss is likely initiated by a receptive mechanism that senses the changes in alimentary flow and alters GI–central nervous system communication so as to modify the central regulation of energy balance.

Another important observation in this study is the change in food preferences observed after RYGB, but not after SGx. SGx led to decreased total food intake without changing the percentage of calories derived from HFD, suggesting that SGx prevents HFD-induced hyperphagia without changing the preference for this diet. The decreased fat acceptance observed after RYGB is unlikely to represent avoidance behavior. The rats that underwent RYGB did not avoid consumption of HFD completely when other choices were also available. Thus, an aversion due to complications from ingestion of the HFD is unlikely (for example, dumping syndrome). In addition, the change in the dietary pattern occurred within 30 min of introduction of the different diets, suggesting a mechanism with rapid onset. This can be mediated by hormonal mechanisms that involve increased satiety for fatty foods. For example, the enhanced secretion of hormones such as CCK, PYY and GLP-1 observed after RYGB could induce fat-specific satiety. An alternative mechanism could involve changes in the neuronal circuits that are responsible for the hedonic value of food, which could lead to a decrease in the reward value of the HFD. These results confirm previous clinical observations in RYGB patients. In two studies, patients reported increased preference for HFD before surgery that was reversed after RYGB surgery.^{31,34} In contrast, patients that underwent vertical-banded gastroplasty did not exhibit this change in food preferences.³¹ Other studies have reported a shift to what is called ‘soft calorie eating’ (that is, consumption of high-calorie liquids and soft foods), in patients undergoing weight loss surgical procedures that restrict gastric volume (that is, banding procedures).^{31,35,36} This suggests a behavioral adaptation due to the perception that the GI canal has been narrowed. Changes in food preferences have also been reported in animal models of jejunoileal bypass.^{37,38} Thus, this effect may be another unique feature of procedures with rerouting of intestinal alimentary flow. Overall, these profound and sustainable effects of weight loss surgery in rats suggest that behavioral and psychosocial factors may not be the primary contributors to the effects of weight loss surgery in humans.

The effect of weight loss surgery on food intake is difficult to be assessed in animal models. One study presented no difference between SGx-treated and sham-operated animals.³⁹ Other investigators have reported a decrease in food intake after SGx compared with sham operation, but no difference compared with RYGB.⁴⁰ Several studies have shown a decrease in food intake after SGx ranging from 34.5 to 65%.^{18,41,42} In addition, one recent study reported that animals who underwent SGx exhibited a change in food preferences, similar to RYGB-treated animals.⁴³ In our experience, after any weight loss procedure, animals decrease their food intake in the immediate postoperative period, and then gradually increase their food consumption. Thus, when assessing food intake, it is important to take into account the timing of the measurements. This can explain the variability of the reported food intake data. One additional factor that may explain these variable results is the standardization of the size of the sleeve. In humans, sleeve size is standardized through the use of a ‘bougie.’ In our rodent studies, we use a 7FR tube as a bougie to standardize the size of the sleeve. In our experience, it is difficult to standardize the sleeve without the use of this bougie. Another potential confounding factor in animal studies is the choice of the sham operation. For the past several years, we have examined many different interventions for the sham surgery group (for example, intestinal transections, gastrotomy and repair, simple laparotomy, different intestinal anastomoses such as end-to-end or side-to-end). We have not found any differences in the outcomes of the sham procedures. The sham procedure reported in this study is our standard sham operation for all our recent studies and is well

established in the literature. It is, however, essential to perform experiments long after the surgical intervention, so any effects resolve by the time of the experiments.

The findings of this study may have clinical implications. The differential effects of RYGB and SGx suggest the potential for means of enhancing the effectiveness of SGx by combining it with pharmacological therapies targeted at increasing EE. For example, since SGx does not cause weight loss through an increase in resting EE, the outcome of the procedure could be augmented by the addition of agents and treatments that improve this component. Further examination of the differences in the physiological and molecular mechanisms by which SGx and RYGB exert their effects will extend our understanding of gastric and intestinal contributions to weight and metabolic regulation. These studies also underscore the utility of the surgical manipulation of the GI tract in animals as a novel model system to study the physiology of energy balance and the pathogenesis of obesity similar to the way that investigators use genetic or pharmacological manipulation of animals. By deconstructing and understanding the physiologic mechanisms by which weight loss surgery works, we may be able to develop novel, less invasive therapies for obesity and its metabolic complications.

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Figure 1.

SGx and RYGB in rats. The rodent procedures closely reproduce the operating steps of the human procedures. **(a)** In SGx, a narrow gastric tube (sleeve) is constructed by removing the greater curvature part of the stomach. Thus, the procedure is characterized by the significant reduction of gastric volume and the expedited delivery of nutrients to duodenum. These intraoperative photographs show the technique we have developed in rats. The size of the gastric sleeve is standardized using a 7FR catheter that is passed through the rat mouth into the stomach and then is advanced into the duodenum (upper panel). Using a stapler, 60–70% of the rat stomach is resected over this ‘bougie’ (middle panel), preserving the gastroesophageal junction and pylorus and creating a gastric tube along the lesser curvature (lower panel) that has the size of the bougie (dashed lines). The middle and lower panels show the operating field through the surgical microscope. ES, esophagus; S, stapler; GS, gastric sleeve; SL, staple line; P, pylorus. **(b)** In RYGB, two intestinal limbs are connected in a ‘Y’-shaped configuration. The proximal stomach is divided, creating a small gastric pouch (~30 ml), and the distal portion is brought up and joined to the gastric pouch, while the proximal portion of the cut jejunum, the biliopancreatic limb, that drains the secretions from the distal stomach, the liver and the pancreas, is attached to the side of the Roux limb. Thus, after the procedure, ingested food travels from the esophagus into the gastric pouch and then passes directly into the mid-jejunal segment comprising the Roux limb. The intraoperative photographs show the technique we have developed in rats. The stomach is placed between the two sides of a stapler, using a cotton tip applicator (upper panel) and the gastric pouch is created by firing the stapler. Middle and lower panels show the operating field through the surgical microscope during (left) and after (right) the construction of the gastrojejunostomy (middle panel) and the jejunojunction (lower panel). GP, gastric pouch; S, stapler; RL, Roux limb; GJ, gastrojejunostomy; BP, biliopancreatic limb; JJ, jejunojunction.

Figure 2.

Differential effects of RYGB and SGx on body weight, food intake, food preferences and nutrient absorption. **(a)** SGx-treated rats weighed more than RYGB-treated rats 8 weeks postoperatively. This statistically significant difference in weight was established during the last 2 weeks of this 8-week period, since in the first 6 weeks postoperatively, RYGB- and SGx-treated rats exhibited the same amount of weight. The weight change in body weight (ΔBW) is expressed as $[Average BW_{SHAM} - BW_{RYGB}]$ or $[Average BW_{SHAM} - BW_{SGx}]$; $*P < 0.05$. **(b)** SGx-treated animals exhibited the largest decrease in food intake in comparison to RYGB and sham-operated animals. **(c)** Eight weeks postoperatively, rats were exposed to two different food choices: normal chow and HFD. SGx-operated animals continued to prefer the HFD to low-fat diet after surgery. In contrast, animals that underwent RYGB exhibited a significant change in food preferences and $>40\%$ of their total daily calorie intake was derived from low-fat diet (normal chow); $*P < 0.05$. **(d)** In a separate group of RYGB- and SGx-treated animals, we evaluated the timing that the difference in the preference for HFD is exhibited between the two groups. At the end of the first day of the introduction of the HFD, only 51% of calories were derived from HFD in RYGB-treated group, despite the initial increase in HFD consumption observed in the first meal. In contrast, animals in the SGx surgery group preferred almost exclusively the HFD; $*P < 0.05$. **(e)** There was a statistically significant increase in total fecal energy density after RYGB in comparison to sham-treated rats and in comparison to SGx-treated animals. SGx-treated animals also exhibited increased average fecal density in comparison to sham-operated animals, but the difference was not statistically significant. Total fecal density was estimated as the product of the daily total fecal output (in grams) and the calories per gram of fecal output which were calculated using bomb calorimetry; $*P < 0.05$.

Figure 3.

Assessment of energy expenditure after SGx, RYGB and sham surgery in rats. **(a)** Energy expenditure data presented as cumulative oxygen consumption, normalized by TBW. Activity-related energy expenditure increased in the SGx group in comparison to sham-treated rats, causing an increase in total energy expenditure. In comparison to RYGB, SGx-treated animals exhibited decreased resting and total energy expenditure. **(b)** In this panel, energy expenditure is reported as cumulative oxygen consumption normalized by allometric scaling ($[\text{TBW}]^{0.75}$). This normalization did not change the pattern and the magnitude of the differences observed in energy expenditure among the study groups. **(c)** Activity episodes were higher in SGx-treated rats in comparison to sham-operated animals. Additionally, time spent in activity was higher in SGx-treated rats in comparison to sham-operated animals. **(d)** Oxygen consumption and activity tracings of SGx-treated (upper panel) and sham-treated rats (lower panel). SGx-treated rats exhibited higher activity during both dark and light period. * $P < 0.05$.