and may also be important perioperatively in the form of reduced operative time, complications, and rate of recovery. Postoperatively, increased physical activity is associated with increased weight loss and better glucose control. However, a challenge to improving physical activity is that bariatric surgery patients tend to be both inactive and highly sedentary preoperatively and make only modest changes in these behaviors postoperatively. [Bond DS et al. *Surg Obes Rel Dis.* 2010; Bond DS et al. *Obes Surg.* 2011]. Although patients report substantial increases in activity (as high as 500%) following surgery based upon questionnaires, objective measures do not support these increases (Figure 1) [Bond DS et al. *Obesity (Silver Spring).* 2010].

Research indicating that many patients either do not change or make only modest changes in their physical activity postoperatively supports the American Association of Clinical Endocrinologists/The Obesity Society/American Society for Metabolic and Bariatric Surgery (AACE/TOS/ASMBS) guideline statement that negative beliefs and cognitions with respect to physical activity must also be addressed to improve activity levels. However, this statement does not provide specific, evidence-based guidelines to address the issue with patients.

The American College of Sports Medicine and ASMBS have developed guidelines to collaborate on a systematic review to publish a position paper to address this issue. As a first step, 7 critical questions have been developed. For example, the collaborators intend to examine whether patients increase physical activity following surgery, whether activity before surgery predicts activity following surgery, and whether activity prior to surgery predicts weight loss following surgery. The collaborators will examine the literature for answers to these questions and use National Institutes of Health Heart, Lung, and Blood Institute criteria to grade the quality of the evidence before publishing their position paper.

Lynn Bolduc, MS, RD, Eastern Maine Medical Center, Bangor, Maine, USA, addressed the 2013 AACE/TOS/ASMBS guidelines for the use of vitamins and minerals. Nutrient deficiencies are common following bariatric surgery, but deficiencies are also common in these patients prior to surgery. The requirements for postoperative assessment of nutritional state vary depending on the procedure but should include such tests as protein/albumin, iron, B_{12}, and 24-hour urinary calcium with additional analyses for some procedures. Supplementation recommendations vary based on the procedure, but may be empiric as screening can be costly. Calcium (as calcium citrate or in the diet), vitamin D, and a multivitamin with folic acid and thymine (and iron if not supplemented separately) are recommended. Vitamin D levels vary by season and ideally should be measured at different times of the year. There is insufficient evidence to recommend screening for essential fatty acids, vitamin E, and vitamin K at this time, although vitamin K levels should be checked if there are deficiencies in other fat-soluble vitamins. However, screening for vitamin A is recommended for biliopancreatic diversion and biliopancreatic diversion with duodenal switch. All patients should be monitored for anemia, and patients with anemia should be tested for other deficiencies as well.

After presenting detailed recommendations for screening and monitoring, Prof Bolduc concluded by emphasizing that the clinical practice guidelines are designed to help in decision making based upon the current state of evidence-based knowledge and that the release of the 2014 ASMBS Nutrition Guidelines may result in updated clinical practice guidelines as well.

Data on Neuroimaging and DBS in Obesity Are Limited

Written by Lynne Lederman

The neural control of food intake is a challenging area of research; it is not known how obesity and weight loss alter brain function. Christopher N. Ochner, PhD, Mount Sinai Hospital, New York, New York, USA, discussed what has been learned from neuroimaging in patients who have undergone bariatric surgery. Originally, studies focused on the hypothalamus to investigate the hypothesis that obese individuals have dysregulation of their homeostatic mechanisms. Subsequent hypotheses suggested that food intake was a balance between the desire to eat (involving activity of the ventral tegmental area, ventral striatum, dorsal striatum, amygdala, hippocampus, prefrontal cortex [PFC], and orbitofrontal cortex) and inhibition of eating (involving the dorsolateral PFC, inferior frontal gyrus, and cingulate cortex). Some studies appear to support the hypothesis that obese individuals receive more reward from food than normal-weight individuals; by contrast, other studies suggest that obese individuals receive less reward from food, causing them to overeat to make up for the reward deficit. The initial studies of neuroimaging in bariatric patients attempted to shed light on this seeming paradox.

Studies looking at alterations of central dopamine type 2 (D2) receptors before and after gastric bypass surgery using positron emission tomography in small numbers of patients have shown conflicting results. More

recently, a study using functional magnetic resonance imaging (fMRI) showed partial reversibility of hypothalamic dysfunction in 13 obese patients after massive weight loss compared with lean control patients (n = 8) [van de Sande-Lee S et al. *Diabetes*. 2011]. Another study of 17 obese women showed increased cerebral metabolism, particularly in the posterior cingulate gyrus, which decreased to levels similar to those in lean women (n = 16) after weight loss after bariatric surgery [Marques EL et al. *J Clin Endocrinol Metab*. 2014]. Both of these studies were unusual for the size of the patient population and the inclusion of control patients. Gastric bypass surgery has also been shown to reduce neural responses to high-calorie foods in 10 obese women but not low-calorie foods measured by fMRI [Ochner CN et al. *Ann Surg*. 2011]. Reductions in activation in key areas in the mesolimbic reward pathway mirrored a postsurgical reduction in the desire to eat high-calorie vs low-calorie foods.

What is driving these postoperative changes in neural responsivity is not known. A comparison of functional brain changes in patients associated with surgical (n = 15) vs behavioral (n = 16) weight loss showed increased responses to food cues in the bilateral temporal cortex in surgical patients and in the medial PFC in dieters [Bruce AS et al. *Obesity (Silver Spring)*. 2014]. This suggests that the method of weight loss affects changes in brain function.

Although more research is needed regarding the mechanisms behind pre- and postsurgical changes in neural responsivity to food cues, D2 receptor availability, and the role of the type of weight loss intervention, studies are being done to alter brain function to promote weight loss.

Donald M. Whiting, MD, Allegheny Health Network, Pittsburgh, Pennsylvania, USA, discussed the off-label use of deep brain stimulation (DBS) in refractory obesity.

The use of DBS assumes that there is abnormally functioning circuitry in the brain that can be regulated. DBS has an established role in the treatment of movement disorders and obsessive-compulsive disorders. Target areas in the brain for obesity include the lateral and ventromedian hypothalamus (VMH) or "satiety center," and more recently, the nucleus accumbens (NAc) or "reward center."

Early animal studies in rats showed that lesions in the VMH were associated with increased levels of body fat and insulin, hyperphagia, and obesity [Penicaud L et al. *Am J Physiol*. 1983; Cox JE, Powley TL. *Endocrinology*. 1981]. Bilateral low-frequency stimulation (LFS) stopped feeding behavior in hungry rats [Krasne FB. *Science*. 1962], whereas high-frequency stimulation (HFS) increased food consumption with no significant changes in weight [Laćan G et al. *J Neurosurg*. 2008]. However, stimulation of this region in humans was associated with a panic/anxiety reaction.

The lateral hypothalamic area (LHA) is a larger and therefore more desirable target with fewer physiologic effects, and has been implicated in feeding and energy expenditure. Early studies suggested that lesions in the LHA were associated with leanness and increased energy expenditure. In this region, LFS causes food seeking in animals in spite of satiety, whereas HFS resulted in weight loss in stimulated animals through food intake that was similar to that in the LFS group; HFS may raise the resting metabolic rate (RMR), leading to weight loss [Sani S et al. *J Neurosurg*. 2007].

A pilot study of DBS was conducted in 3 individuals with refractory obesity for whom bariatric surgery had failed [Whiting DM et al. *J Neurosurg*. 2013]. The primary objective of this study was safety; body weight change and energy metabolism were also assessed. The LHA was stimulated bilaterally using settings established for mood disorders.

At 35 months of follow-up (range, 30 to 39 months), there were only mild adverse effects and no serious adverse events. There was 1 electrode fracture requiring revision. DBS may have reduced binge-eating episodes in 1 patient, with improvement in body shape and self-image feelings in 2 patients. DBS did not have a negative effect on quality of life. However, LFS at the setting used for mood disorders caused weight gain. Therefore, settings were altered to determine the effect on RMR. When settings were used that appeared to increase RMR in metabolic chamber experiments, DBS was associated with weight loss in 2 patients and stable weight in 1 patient.

Only a small area of the LHA is involved in RMR augmentation via DBS, and there may be a diminished effect over time. Other areas of the brain may provide additional targets, such as the NAc, which provides a larger target area.

Many questions about the effect of bariatric surgery on neural responsivity remain to be answered, including whether weight loss is mediated by changes in receptor binding or in neural responsivity, and how long these changes last. Likewise, the role, if any, of DBS in refractory obesity needs to be determined by further definition of the appropriate target site and evaluation of efficacy and safety in a larger group of patients. The complex interaction between homeostatic and nonhomeostatic circuits suggests that a multitargeted approach to the treatment of obesity will be necessary.