Question 1: A surgical approach to reducing excessive body fat is liposuction: the removal of adipose tissue. Over time, however, body adiposity typically returns to precisely the same value as before surgery. Why does liposuction not work? Contrast this with the effect of gastric surgery to treat obesity.

Answer: After undergoing liposuction, the person typically overeats until the original level of body fat is attained. This is because of the inherent need of the body to maintain energy homeostasis. The brain monitors the amount of body fat and acts to "defend" this energy store against perturbations. This theory is called the lipostatic hypothesis. Therefore, the body tries to rectify any alteration made to adipose tissue. Gastric surgery involves removal of ghrelin-secreting cells of the stomach. This causes a loss of appetite and is therefore a more effective treatment of obesity.

Question 2: Bilateral lesions of the lateral hypothalamus lead to reduced feeding behavior. Name three types of neuron, distinguished by their neurotransmitter molecules that contribute to this syndrome.

Answer: Bilateral lesions of the lateral hypothalamus cause anorexia (reduced feeding behavior). This is referred to as lateral hypothalamic syndrome. 1) A group of neurons in the lateral hypothalamus (LH) receiving direct input from the leptin-sensitive cells of the arcuate nucleus synthesize melanin-concentrating hormone (MCH). Injections of MCH into the brain stimulate feeding behavior. These lateral hypothalamic neurons have widespread connections with cortex, and are thus in a perfect position to inform the cortex of leptin levels in the blood and contribute to motivating the search for food. 2) A second group of LH neurons with widespread cortical connections contain another peptide called orexin; orexin injections

also stimulate feeding behavior. These cells also receive direct input from the arcuate nucleus and are thus informed of blood leptin levels. 3) Finally, LH neurons sensitive to NPY and AgPR inputs from the arcuate nucleus also stimulate feeding behavior.

Question 3: What neurotransmitter agonists and antagonists would you design to treat obesity? Consider drugs that could act on the neurons of the brain, as well as drugs that could act on the PNS.

Answer: There are four known orexigenic peptides. Two are made by neurons in the arcuate nucleus, neuropeptide Y and agouti-related peptide (AgRP), which projects to the lateral hypothalamus. Two other orexigenic peptides are made by neurons in the lateral hypothalamic area: melanin-concentrating hormone and orexin. These neurons project to widespread areas of cortex. Because these peptides stimulate feeding behavior, synthetic antagonists may decrease feeding behavior. In addition, two anorectic peptides made in the arcuate nucleus, alpha-melanocyte-stimulating hormone (alpha MSH) and cocaine-and-amphetamine-regulated transcript, inhibit feeding behavior. Synthetic agonists to these peptides may help decrease feeding behavior. A natural example of this type of treatment is provided by AgRP and alpha MSH, which are antagonistic peptides that compete for MC4 receptors on neurons in the lateral hypothalamus. Activating the MC4 receptors inhibits feeding, and blocking the receptor stimulates feeding. Alpha MSH is the receptor agonist and AgRP is a natural antagonist that blocks the stimulation of alpha MSH.

Question 4: Name one way the axons of the vagus nerve might stimulate feeding behavior and one way they inhibit it.

Answer: The vagus nerve carries most of the mechanosensory afferents from the stomach wall to the brain, which are stimulated when the stomach is full. The vagal sensory axons activate neurons in the nucleus of the solitary tract in the medulla. These signals inhibit feeding behavior. Cholecystokinin (CCK) is a peptide present in some of the cells that line the intestines that inhibits meal frequency. The major action of CCK as a satiety peptide is exerted on the vagal sensory axons. CCK acts synergistically with gastric distension to inhibit feeding behavior. The nucleus of the solitary tract receives visceral sensory input from the vagus nerve. This nucleus serves as an important integration center in the control of feeding. Because the gustatory nucleus is a division of this nucleus, satiety induced by a full stomach may be delayed while eating tasty food. Therefore, the vagus nerve may also participate in feeding behavior.

Question 5: What does it mean, in neural terms, to be addicted to chocolate? How could chocolate elevate mood?

Answer: Serotonin plays a crucial role in linking food and mood. Measurements of serotonin in the hypothalamus reveal that levels are low during the postabsorptive period, they rise in anticipation of food, and spike during a meal. Serotonin, derived from the dietary amino acid tryptophan, and tryptophan levels in the blood vary with the amount of carbohydrate in the diet. Chocolate may elevate mood by increasing in blood tryptophan and brain serotonin.

Question 6: Compare and contrast the functions of these three regions of the hypothalamus: the arcuate nucleus, the subfornical organ, and the vascular organ of the lamina terminalis.

Answer: The arcuate nucleus of the hypothalamus lies near the base of the third ventricle and is activated by a rise in blood leptin levels. Arcuate neurons are characterized by a

distinctive mix of peptide neurotransmitter molecules. 1) The arcuate nucleus comprises neurons that play an important role in inhibiting and stimulating feeding behavior. 2) The neurons of the subfornical organ are sensitive to circulating angiotensin II. Angiotension II levels rise in response to reduced blood flow to the kidneys, which occurs with low blood volume during dehydration. Neurons of the subfornical organ directly stimulate the magnocellular neurosecretory cells of the hypothalamus to release vasopressin and stimulate volumetric thirst. Circulating vasopressin causes the kidneys to conserve body water by reducing urine output. In this way, the subfornical organ helps regulate water balance in response to volumetric signals with both behavioral and humoral mechanisms. 3) The vascular organ of the lamina terminalis (OVLT) is a specialized region of the telencephalon lacking a blood-brain barrier. It is involved in osmometric thirst, the motivation to drink water when the blood is hypertonic. Neurons in this brain region sense blood hypertonicity associated with low blood volume. The OVLT neurons directly excite the magnocellular neurosecretory cells that secrete vasopressin and stimulate osmometric thirst. Lesions of the OVLT completely prevent the behavioral and humoral responses to dehydration but not the responses to loss of blood volume.