Weight change, energy balance, and mood: Clinical effects and underlying mechanisms

Feeding behavior affects emotional well-being

The evolutionary pressure to maintain a balance between energy intake and energy expenditure is considered to be one of the most fundamental physiological mechanisms. So being, humans and other complex organisms have evolved complicated systems to control the balance of energy intake and expenditure. The complicated mechanism that helps regulate eating involves centers of motivation and emotion in the brain. The dysregulation of energy balance can cause significant metabolic disease. Individuals who are unable to maintain a healthy energy balance suffer both physiologically and psychologically.

Weight control is not a simple matter of balancing food intake with energy expenditure; complex physiological and sociocultural frameworks surround our eating habits. Americans spend approximately 33 billion dollars on weight control programs each year. In addition to the health risks of diabetes and cardiovascular disease, epidemiological surveys have confirmed that obesity correlates with increased odds of depression and other mental illnesses. People who are extremely obese (BMI >40) and have a history of depression have a much higher rate of attempted suicide than those in the general population. Although weight loss would be expected to reduce the odds of depression and improve health and overall quality of life, weight loss alone is often inadequate for many patients who require behavioral therapy to achieve their optimal outcomes.

Weight reduction, when it is too rapid, can lead to health risks and other negative side effects. In addition to serious risks of dehydration, malnutrition, gallstones and electrolyte imbalances that may result from rapid weight loss, dieters are likely to suffer headaches, fatigue, irritability and anxiety. The psychological side effects have not been taken lightly. Retrospective results from therapeutic treatment of obesity as well as surgical treatment of obesity raised concerns that these treatments might exacerbate underlying depression in some patients. It is likely that the process of losing weight could partially explain the negative impact on mood in a proportion of subjects.
Clinical and epidemiological observations on obesity and weight loss

The incidence of depression in overweight and obese subjects is ~5% to 10% higher than the average. Results from the National Epidemiological Survey on alcohol and related conditions, which included 40,000 civilian non-institutionalized adults during 2001 to 2002, found that obese subjects had increased odds of mood, anxiety, alcohol and personality disorders. For the overweight and obese, the odds of having major depression, dysthemia, and manic episodes were increased (OR 1.45 to 2.7). Furthermore, the odds of having major depression increased with each unit increase in weight. Lifetime episodes of major depression were reported by 20.4% of obese (BMI >30.0 and <40.0) and 28.4% of extremely obese (BMI ≥ 40.0) subjects. Furthermore, overweight women (BMI = 25 to 29.9) were found to have increased odds of mood and bipolar disorders (OR 1.16 – 1.44). A review of the literature found that, although most overweight and obese individuals did not have mood disorders, they were more likely to be depressed or develop bipolar disorders. Although obesity and mood disorders could both result from a common pathogenic mechanism, it is not disputed that mood disorders and weight disorders can affect one another. Five different studies found that subjects who are depressed are more likely to have unhealtful weight changes (generally, weight gain in those under 55 years old and weight loss in those 55 or older). A recent study of 144 obese women found that body weight, self-image and other psychological factors had a reciprocal effect on one another.

It is likely that treatment of obesity would have a positive effect on mood in individuals whose depression is an outcome of long-term obesity. Since the odds of depression correlate with increases in weight, it is reasonable to expect weight loss to reduce those odds. However, a retrospective analysis of 36 studies found that better results were obtained when studies included cognitive-behavior therapy. In a study comparing weight loss in subjects who had underwent a general health education program with those that underwent treatment that included behavior changes in physical activity and dietary intake, subjects who had obesity intervention treatment had significantly greater weight loss as well as greater improvements in quality of life (QOL) and self image (p <0.05 for both). A study of subjects undergoing bariatric surgery to...
treat obesity found that of the 25% to 30% of subjects who were depressed prior, those whose depression was the result of distress about obesity had better post-operative outcomes. Those subjects that were extremely obese (BMI >40) also had significant impairments in QOL prior to bariatric surgery, and these subjects reported better post-operative improvements in QOL scores. However, when subjects had significant psychiatric problems, the response was sub-optimal. A 7-year study of the outcomes of bariatric surgery for severe obesity found that multi-intervention treatment improved QOL and sustained weight loss. Generally during weight loss treatment, patients' psychological outcomes are best when the subject’s mental state is more directly impacted by the obesity.

Although overall health and well-being are improved by weight-loss in the overweight and obese, too rapid weight loss, without adequate psychological and nutritional support, can lead to significant psychological problems in some subjects. Rapid weight loss resulting from rimonabant treatment was found to be associated with increased risk of depression and anxiety, as well as an increased risk of suicide during treatment. Studies of small groups in sports settings indicate that rapid weight loss resulted in significantly negative changes in mood and performance. In a study of 16 boxers who lost an average of 5.16% body weight in one week, the rapid weight loss was associated with poor performance in the match, as well as increased anger fatigue, tension, and reduced vigor. A study of 29 college wrestlers, 14 of whom underwent rapid weight loss, statistical analysis established poorer performance for rapid weight loss group in memory (recall tests); and greater mood negativity. In a study of weight loss' effect on mood and performance in 41 jockeys, subjects were questioned at lightest, optimal and relaxed riding weights; rapid weight loss impacted negatively on mood responses (anger, depression, vigor, confusion, and tension). This phenomenon may explain why many subjects do not report improved quality of life during weight loss treatment.

Weight regulation by the brain

One reason that obesity has been particularly difficult to overcome is that body weight as well as the physiology of hunger and satiety is controlled by the same regions
of the brain as mood and motivation. Investigations of appetite regulation by leptin, neuropeptide Y (NPY), serotonin, melanocortin and other factors, has indicated that the hypothalamus plays a key role in regulating the experiences of hunger and satiety.\textsuperscript{17-21} For example, an energy deficiency causes the release of the hormone ghrelin that activates NPY to positively affect NPY neurones which in turn, stimulate food intake and increase motivation. Serotonin inhibits neuropeptide Y and down-regulates this cascade.\textsuperscript{22} In a contrasting system, high fat stores cause an increase in circulating leptin, a factor that activates a number of systems including melanocortin, which signal decreased energy intake and increased energy expenditure.\textsuperscript{17,20,23} The physiological and neurological regulation of body weight is an extensive topic that cannot be fully described here; however, many of the factors involved in the regulation of body weight have been found to affect emotional and psychological well-being.

The brain reward system is a key to linking the neural regulation of appetite with mood and motivation.\textsuperscript{17,20} Dopamine's effect on the nucleus accumbens (hypothalamus) is important in reward processes, and thus plays a big role in reinforcement of feeding.\textsuperscript{17} NPY neurons in the articulate nucleus are involved in the control of mood, psychomotor activity and mental function.\textsuperscript{19} Melanocortins interact with neurons in the hypothalamus–pituitary axis, which is associated with mood disorders including depression.\textsuperscript{20} Other parts of the hypothalamus regulate sleep and wakefulness.\textsuperscript{19} Glutamate and NPY have been shown to produce responses in the hypothalamus\textsuperscript{24} and the hippocampus, a part of the brain that coordinates emotional and behavioral responses to external stimuli and is involved in goal-oriented cognitive function.

Obesity, anorexia, and some psychological diseases have been linked to the dysregulation of feeding by the hypothalamus. Disruptions in the machinery of leptin signalling lead to obesity.\textsuperscript{23,25} Serotonin is used in the treatment of depression as well as bulimia.\textsuperscript{20} Serum levels of leptin and cholesterol were found to be low in major depressive disorder, but high in schizophrenia.\textsuperscript{26} Some of these neurological effectors can influence addictions; Melanocortins can antagonize addictive properties of opiates and NPY is involved in the motivation and reward of alcohol consumption.\textsuperscript{20} Brain scans during hunger show significantly more activation in obese than lean subjects, suggesting that obese subjects may have more acute responses to that stimulus than their lean

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counterparts. The connections between neurological factors involved in weight regulation and disease suggest that adhering to a diet not only requires a high motivation to correct the obesity and a change in attitude towards eating, but also may require re-education of the neurological circuitry that regulates hunger and satiety.

Conclusions and recommendations

The best results are achieved when treatment for obesity includes regular interaction, positive reinforcement, and lasting behavior changes. Since depression and mood changes should be an anticipated event in patients who would receive treatment for obesity, it is prudent to consider equipping medical professionals with measures for managing it. There is adequate literature for managing depression when it arises. Considering that a history of depression is anticipated in 20% to 30% of the overweight and obese patients, physicians may need training on how to monitor for depression, and might be advised to take the patient’s history into account. Patients with a history of depression might require some additional monitoring, especially during the titration phase of their treatment, to ensure that they do not develop major depression. Patients who seem to be having cognitive or mood-related intolerance could be titrated at a slower rate, or have their doses reduced. The final results as to whether XXXX treatment affects mood will depend on the results of the phase 3 clinical studies, which are pending.
References


