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Childhood Obesity and Depression: Connection between these Growing Problems in Growing Children

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Abstract

Depression and obesity have been recognized as major public health issues in youths. Although they have traditionally been compartmentalized as separate physical and emotional health conditions, evidence suggests interactions and common pathways between them, implying that successful treatment should ideally target shared underlying mechanisms. The purpose of the present article is to review the pediatric diagnostic criteria for depression and obesity, highlight similarities in their clinical presentation, identify common pathways and underlying mechanisms, describe their developmental trajectories, and suggest areas for future study to guide development of innovative prevention and treatment initiatives.

Keywords

pediatric depression; pediatric obesity; inflammation; serotonin

introduction

Obesity and depression, conditions which have until recently been considered “adult” health problems, are now recognized as common conditions among youths. Recent data from the National Health and Nutrition Examination Survey estimate 17% of youths ages 2-19 years old to be overweight (1) compared to just 5% a few decades ago. Depression also impacts a large population of youths. Prevalence of major depressive disorder has been estimated to be 2% of children and 4-8% of adolescents (2). Note that in the following, “children” generally means up to 12 years of age, while “adolescents” are 13 years and above. The word “youths” is used when referring collectively to both groups. The high prevalence of these individual conditions is alarming given the health and socioeconomic burdens associated with these problems, and the limited efficacy of current treatment interventions. The Surgeon General has highlighted both pediatric obesity and depression as major public health issues in recent reports. In the 2000 report on children and mental health, the Surgeon General emphasized that recurrence of childhood depression episodes is common and depression “may leave behind psychological scars that increase vulnerability throughout early life.” In 2003, the Surgeon General testified on “The Obesity Crisis in America” that the annual cost of obesity in the US in 2000 was 117 billion dollars, and that obesity epidemics have been followed by pediatric

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epidemics of type 2 diabetes and hypertension (http://www.surgeongeneral.gov/reportspublications.html#calls).

While psychosocial and medication interventions are increasingly used to target childhood depression, the limited effectiveness of standard interventions is concerning. The state-of-the-art Treatment of Adolescents with Depression Study (TADS) reported that only 37% of adolescents treated with intensive, combination medication and psychotherapy treatment achieved remission at 12 weeks (3). Similarly, lifestyle and medication interventions for childhood obesity have failed to curb the growing epidemic of pediatric overweight, leading to the increased use of invasive bariatric surgery for morbidly obese adolescents (4).

For the most part obesity and depression have been compartmentalized as separate health problems of a physical and emotional nature, respectively (5). However, the fact that depression and obesity have shared symptoms such as sleep problems, sedentary behavior and dysregulated food intake, is not a mere coincidence but appears to be related to shared pathophysiological mechanisms. If this conceptual framework is correct, it implies that successful treatment for the comorbid conditions of obesity and depression should ideally target shared underlying mechanisms.

The purpose of the present article is to review the pediatric diagnostic criteria for depression and obesity, highlight similarities in their clinical presentation, review common pathways or other connecting mechanisms, describe their developmental trajectories, and suggest areas for future study with the eventual goal of improved therapeutic and preventive modalities.

Diagnoses of Childhood Depression and Obesity

Obesity and depression are diagnosed differently in children compared to adults. Depression criteria include depressed mood, anhedonia, fatigue, feelings of guilt or worthlessness, thoughts of death, as well as changes in sleep, appetite, or psychomotor activity. Problems with sleep, appetite, and psychomotor activity can occur in either direction, i.e. individuals may experience insomnia or hypersomnia; anorexia or increased appetite; psychomotor retardation or agitation. The Diagnostic and Statistical Manual IV text revised (DSM IV TR) criteria for a major depressive episode stipulate that five of nine possible depression criteria must be present for most of the time over a two week period, must be present most of the time, one of the criteria must include either depressed mood or diminished interest or pleasure (anhedonia), and the symptoms must be a change from prior functioning. There are two differences in how depression is diagnosed in youths compared with adults. Mood may be irritable, instead of depressed or anhedonic, and youths may meet symptom criteria if they fail to make expected gains in growth rather than experience weight loss from decreased appetite. In younger children diagnosis is challenging because of difficulty eliciting internalizing symptoms (e.g. feelings of hopelessness or guilt)

Subtypes of major depressive disorder include atypical, melancholic, postpartum, catatonic, or chronic depression features. Atypical depression describes individuals who experience mood reactivity plus two of the following symptoms: weight gain/increased appetite, hypersomnia, heavy, leaden feelings in arms or legs (leaden paralysis), and long standing pattern of interpersonal rejection sensitivity; whereas melancholic depression describes individuals with prominent anhedonia and three or more of the following symptoms: anorexia/weight loss, worsening depression in morning, early morning awakening, excessive guilt, marked psychomotor retardation or agitation. Similar to adults, a mixed presentation of depression is more prevalent than any of the specifier types. In a clinical sample of over 1,000 youth aged six to 19 years old with major depressive disorder, 15% of youths met criteria for atypical depression, with 21% of youths with symptoms of hypersomnia (6). Melancholic depression is more prevalent in adolescents compared with prepubertal children (7). In the

TADS study, 14% of youths met criteria for melancholic depression, and melancholic features were associated with poorer response to depression intervention(8).

Strictly speaking, "obesity" means excess of body fat. However, for practical reasons, clinical recommendations are based on the body mass index (BMI), which is calculated as the weight divided by the height squared, in metric units, i.e., kg/m^2. Because the numerator of the BMI is body weight, which also includes non-fat, or lean mass, some have argued that BMI should only be used as a screening tool, not a diagnostic tool (9). In adults, cutoff points for BMI are 25 kg/m^2 and 30 kg/m^2 (labeled "overweight" and "obesity", respectively). In children, however, normal growth patterns dictate the use of age- and sex-specific cutoff points. The presently accepted BMI-for-age growth curves were published by the Centers for Disease Control and Prevention (CDC) in 2000 and are based on United States national surveys from 1963-1994, i.e., before the current rise in obesity gained momentum (10). As a function of age, BMI exhibits a downward trajectory from infancy through age 6 years, whereupon an upward trajectory takes over. According to the CDC, children at or above the 85^{th} but below the 95^{th} percentile are considered "at risk for overweight" and those at or above the age- and sex-specific 95^{th} percentile are considered "overweight". This terminology makes sense because BMI is a measure of weight and not fatness, making it is possible (although extremely rare) that some children, especially adolescent boys, may be miscategorized if a high BMI percentile is equated with obesity. However, an expert panel convened by the American Medical Association has proposed labeling the 85^{th} percentile "overweight" and 95^{th} percentile "obese", concerned that avoidance of the term "obese" would lead to under-treatment (http://www.ama-assn.org/amednews/site/free/hlsd0709.htm, accessed 11/19/2007). Methods exist to estimate body fat content from skinfold thickness and, more precisely, by radioimaging techniques, but there are no criteria to interpret their results in terms of what constitutes a pathological amount of body fat. Therefore, this paper will use the terms "obesity" and "overweight" interchangeably.

Similarities in Clinical Presentation of Childhood Obesity and Depression

Those meeting the diagnostic criteria for depression are a heterogeneous population with differences in individual symptoms (e.g. sleep change can be insomnia or hypersomnia) as well as differences in combinations of symptoms (i.e. irritable or depressed mood is the only required symptom in the combinations). In this section, we review specific depression symptoms (both type of symptom and direction of impairment, e.g. insomnia) that may serve as links between childhood obesity and depression and possible targets for intervention for both disorders.

Sleep

Sleep problems are a prominent and difficult to treat feature of adolescent depression. In the TADS study of over 400 adolescents with a primary diagnosis of major depressive disorder, change in sleep was the most prevalent residual depression symptom in both youths whose depressive episode remitted as well as those whose depression failed to remit at 12 weeks (11). Adolescents with depression have prolonged sleep latency compared with non-depressed adolescents (12). Prolonged sleep latency is important because it is associated with increased risk of depression recurrence among youths (13). In children ages 7-17 years old with major depressive disorder, insomnia was associated with active suicidality, measured by presence of suicidal thoughts and plan (14).

Obesity, too, has connections to sleep problems. Overweight children are at increased risk for sleep apnea and obesity hypoventilation syndrome, which are associated with daytime somnolence and decreased nighttime sleep (15). A cross section sample of 383 youths ages 11-16 years old studied using objective activity monitoring (wrist accelerometer) indicated that

overweight youths experienced less total sleep time than non-obese youths, although there were no significant differences between the groups in measures of sleep disturbance (16). Relationship between sleep and obesity may be mediated at least in part by insulin resistance. In a study of obese children, insulin resistance was associated with shorter sleep duration by polysomnography (17). In healthy, young adults, short term partial sleep deprivation (4 h per night) results in increased insulin resistance (18) As early as 1999, it was proposed that sleep loss could explain the increased prevalence of diabetes and other cardiovascular factors in individuals with low socioeconomic status, possibly mediated through sympathoadrenal dysregulation (19).

While decrease in sleep is not a consistent feature of either depression or obesity, and in fact sleep may be increased in atypical depression, sleep deprivation may contribute to a worsening of both obesity and depression. As sleep deprivation is associated with increased hunger (20) and decreased insulin sensitivity, this symptom is likely to exacerbate or at least sustain obesity. Insomnia is also associated with increased suicidality in depressed patients. In other words, undertreated sleep problems in obese depressed children decreases chances of sustained recovery from depression and increases suicidal risk. It is unclear if individuals with depression are more vulnerable to the psychological distress caused by insomnia or if insomnia and depression severity are linked to underlying dysfunction in neurotransmitter systems that regulate both mood and sleep, e.g. serotonin system. Another system that is disrupted in sleep deprivation and may be of importance for both obesity and depression is the hypothalamic-pituitary-adrenal axis (see below) (21). An area for future research is to determine the threshold for sleep deprivation to have an impact on either mood or obesity in children at different stages of growth, i.e. differences in developmental sleep needs, and in non-depressed versus depressed children. However, it must be emphasized that it has not been irrefutably demonstrated that sleep deprivation is an independent risk factor for depression. Sleep is an appealing target for both depression and obesity interventions. Sleep can be measured objectively, there are both pharmacologic and behavioral options (e.g. sleep hygiene, relaxation techniques) to target sleep problems, and insomnia is associated with less social stigma that either depression or obesity.

Sedentary Behavior

Human locomotion behavior can be summarized in various ways. One way is to look at total amount of activity over a specific period (e.g. 24 h) as quantified by movement detection or its associated energy expenditure, which can be calculated with the use of indirect calorimetry. Another way is to look at time spent at various levels of intensity, typically segmented as sedentary, light, moderate, and vigorous. Time spent in sedentary activity, sometimes reduced to time spent watching TV, is sometimes a stronger correlate of obesity than total amount of activity or time spent in moderate/vigorous activity. In a prospective study of three year old children, TV viewing and physical activity measures at age 3 were better predictors of BMI at age 6 than eating habits (22) despite the fact that eating habits were assessed with great accuracy using direct observation by trained observers in the child's community environment. TV viewing has been identified as the strongest connection between a specific behavior and childhood obesity (23). The relationship between sedentary behavior and obesity is not explained solely by reduced physical activity. In a population of adolescent females, correlation between percentage body fat and internet viewing time persisted even after controlling for physical activity (24).

A core feature of depression is decreased interest and motivation for activity. Lack of activity does not need to cause weight gain to have an adverse effect on metabolism. In a study of adolescents, we found that independently of each other, body composition and physical activity were determinants of insulin sensitivity (25). Reports of interpersonal problems and feelings of ineffectiveness on the Children's Depression Inventory correlated with sedentary behavior

in young adolescents, ages 11-13 years old (26). With recent technology advances, there are expanded options for sedentary activity including video games, internet activity, and 24 hours of daily TV programming. Among a community sample of approximately 1,500 youth aged 10-17 years old who used the internet, 30% of youth with major depressive symptomatology (five depression criteria plus functional impairment) used the internet for at least 3 hours a day, compared with 14 % of youths with minor depressive symptomatology (3 depression criteria) and 12% of youths with no depressive symptoms (27).

Increased sedentary behavior may also contribute to worsening depression and obesity, as well as directly link these two conditions. Depression may cause increased sedentary activity secondary to depressed mood, fatigue, and decreased motivation. The combination of decreased physical activity and/or increased appetite can lead to unhealthy weight gain. Thoughts, mood, and behavior are linked conceptually in the cognitive behavioral model of depression. Interventions targeting one of these components are expected to impact the other two. For example, increased play time with peers may improve mood as well as thoughts of self-esteem (“other kids like to play with me”). Many sedentary activities are considered pleasurable by children, i.e. playing a favorite video game. However, exclusive pursuit of sedentary activities promotes social isolation as well as decreased physical activity. Increased sedentary behavior is also likely to sustain or worsen obesity unless there is significant reduction in food intake. Thus, reduction in sedentary activity may help improve obesity by increased energy expenditure and improve mood by increased social interaction/support.

In summary, the relation between obesity, depression, and inactivity is multidirectional. Inactivity is a cause of obesity. Depression may be a cause of inactivity and therefore promote obesity. Those with a large body have greater difficulty exercising and derive less pleasure doing so; the resultant inactivity may promote depression. An environmentally induced decrement in physical activity may lead to both obesity and depression through discrete or convergent pathways. It is likely that a comprehensive approach addressing all three issues directly will be clinically superior to one that only addresses one. However, sometimes it may be necessary to address obesity first (a clinical parallel would be the common notion that one can not even start meaningful treatment of depression in severely anorexic patient without addressing malnutrition first).

Appetite and Food Intake

Food intake is of importance in a discussion of obesity because obesity arises as a result of imbalance between energy intake and expenditure. One of the vegetative symptoms associated with depression is changes in appetite. Appetite is defined as the desire to eat. These changes can go in either direction (i.e., anorexia or hyperphagia), however, in this context we will concentrate on hyperphagia. In a community sample of adolescents with major depressive disorder followed prospectively, both increased appetite and depressed mood were significantly associated with recurrence of depression in adulthood (28), suggesting that increased appetite is a central feature of depression. In addition to general changes in appetite, food cravings, i.e., a strong desire for certain categories of food, may also develop during depressive episodes. An example of depression with food cravings is winter seasonal depression, which is characterized by worsening of mood during late fall and winter and remission of mood symptoms in the spring and summer. Individuals with seasonal depression report increased carbohydrate craving during the depressive episode (29). The weight gain also associated with the depressive episodes is likely a consequences of the food cravings. Swedo et al (30) estimate that seasonal affective disorder affects 1.7 – 5.5% of youths ages 9-19 years old based on a community study of over 2,000 youth. Key symptoms that discriminated between 60 subjects from this sample with seasonal affective disorder and 60 comparison subjects were “feel worst,” “eat most,” “sleep most,” and being “most irritable” in the winter,

i.e., both increased appetite and sleep during winter months was reported in youths with seasonal mood changes compared to youths without seasonal changes (30).

Obese and non-obese children differ in terms of physiologic factors that regulate food intake and satiety. Leptin is a peptide secreted by adipocytes (fat cells) which acts upon receptors in the hypothalamus, a center for satiety/appetite regulation. Increased leptin secretion is associated with decreased appetite. Obese youths compared with non-obese youths have higher levels of leptin, suggesting central and peripheral leptin insensitivity (31). After weight loss in obese youths, leptin levels have been shown to decrease, i.e. normalize (31,32). Ghrelin is another peptide hormone that roughly speaking has the opposite effects of leptin. It stimulates appetite and is increased in experimental sleep deprivation, possibly contributing to explain the connection between sleep and obesity (20). Ghrelin is correlated to behavioral food intake traits in children, and may therefore explain some genetic predisposition to obesity (33). Both leptin and ghrelin are changed by sleep curtailment in laboratory studies of adults (20), reemphasizing the multidirectional relations between affect, body composition, and sleep.

Similar to sleep and other phenomena discussed here, appetite is related to obesity and depression in an inconsistent fashion, likely resulting from both obesity and depression being conditions with heterogeneous etiology. Notably, however, among psychiatric diagnoses, appetite change is an exclusive symptom criteria of depression, not included in the diagnosis of anxiety, trauma, or psychotic disorders. Not even eating disorder diagnostic criteria include change in appetite. Rather, these disorders are defined by extreme changes in actual food intake, including binging and deliberate avoidance of food intake, suggesting that the normal relationship between appetite and food intake is impaired. In depression, increased appetite does not always result in increased food intake, although presumably increased hunger may result in greater emotional distress if an individual feels deprived of food intake needed to achieve feeling of satiety. In summary, both obesity and depression have tie-ins with appetite and food intake that are incompletely understood.

Negative Self Image

Depressive episodes are characterized by feelings of guilt and shame. In a clinic-referred population of depressed youths ages 11-20 years old, feelings of guilt, self-blame, and failure were more prominent in females than males (34), consistent with cognitive theories holding that greater vulnerability to depression in females compared with males may be due in part to a negative self-attribution style. Symptoms of guilt were endorsed more frequently along with externalizing behavior problems in children compared with adolescents in a clinical sample of over 1,000 children (35).

Also obesity is associated with a negative self image, although the negative association between self esteem/self image and obesity first reported in clinical samples appears to be less robust in community samples (36). Demographic characteristics have been identified as important moderators of the relationship between obesity and self-esteem. Weight cycling (37), gender (36), and culture have been identified as possible moderators between the relationship of depression and obesity. In a community sample of 2,813 Australian youths, body dissatisfaction mediated most of the relation in females (38). Cultural factors also appear to influence this relationship. In a non-clinical referred sample of overweight and at risk children, depression was significantly associated with body size dissatisfaction in Caucasian but not African American children (39). Thus, self-esteem is moderated by demographic characteristics such as gender in both conditions: obesity and depression. White females may be particularly vulnerable to low self-esteem due to obesity; studies of body image and depression may focus on this group. Hindering research and clinical applications, excessive feelings of guilt and decreased self-esteem may be more difficult to assess than the above neurovegetative symptoms, since these are abstract concepts and identification of these

symptoms needs to take into account gender and cultural differences in how they may be expressed. From a clinical perspective we posit that it may be possible to obtain a synergistic therapeutic effect by addressing obesity and depression *as well as* feelings of insufficience. While the presumption is typically that interventions that alleviate obesity and depression can improve self-esteem and feelings of guilt, interventions that target these negative feelings initially may conversely improve adherence to weight loss and depression treatments by reducing incapacitating feelings that interfere with motivation and energy to change, as well as self-perception that one can benefit from change.

Obesity and Depression: Shared Underlying Pathway?

While the above discussion suggests possible links between obesity and depression with specific depressive symptoms, and thus possible targets for interventions, the following section reviews possible underlying pathways between depression and obesity to identify possible targets for both prevention and intervention.

Increased inflammation and altered stress system may be a common link between obesity and depression. Obesity is considered a pro-inflammatory state. Animal and human studies have shown that obesity increases adipose tissue expression and secretion of pro-inflammatory cytokines, and treatments that reduce obesity or insulin resistance have a moderating effect of reducing inflammation (40). Levels of pro-inflammatory cytokine IL-6 have been shown to be higher in a population of overweight children compared to normal weight controls (41), and levels of C-reactive protein, a biomarker for inflammation and cardiovascular disease risk, were significantly higher in a community sample of otherwise healthy overweight youths compared to non-overweight youths (42).

Similarly, there is growing evidence from adult studies that depressive episodes are associated with dysregulation of inflammatory system. Pro-inflammatory cytokines IL-6 and tumor necrosis factor alpha have been shown to be higher in psychiatric inpatients with major depressive disorder compared with normal controls (43), and in patients with treatment refractory depression compared with normal controls as well as euthymic individuals who were previously treatment refractory (44). While cerebrospinal fluid IL-6 levels did not differ between adults with major depressive disorder and age-and gender- matched controls (45), significant diurnal elevations in plasma IL-6 levels and shift in its circadian rhythm were found in depressed adults compared with controls who were tightly matched by gender, age, BMI, and menstrual cycle phase, all variables that affect IL-6 levels (46). Increases in IL-6 after interferon alpha treatment of hepatitis C has also been associated with significant depression side effects (47). In children, a negative association between IL-6 and depression scores has been found in youths post hematopoietic stem cell transplantation (48). Early morning IL-6 levels 24 hours post motor vehicle accident predicted diagnosis of post-traumatic stress disorder (PTSD) in pediatric patients (49), suggesting that IL-6 has profound cerebral effects.

Centering on the hypothalamic-pituitary-adrenal (HPA) axis, Gold and Chrousos (50) developed a comprehensive model that posits two subtypes of depression as either upregulation (melancholic) or downregulation (atypical) of the stress system by changes in the HPA axis and sympathetic arousal, which also relate to changes in immune response. In the atypical depression model, decreased sympathetic activity and HPA axis activity result in increased sleep and appetite as well as reduced concentration and energy level; a reverse of functioning triggered by arousal state (“fight or flight”), triggered by sympathetic stimulation and corticotrophin releasing hormone mediated glucocorticoid secretion. Metabolic effects of HPA downregulation would include decreased insulin sensitivity and dyslipidemia, as well as increased fat mass. As mentioned earlier, insulin resistance is also a consequence of physical inactivity, possibly illustrating one of the several converging pathways that may explain the frequent co-occurrence of obesity and depression. Immune effect from HPA down-regulation

would be relatively increased inflammation, whereas, HPA up-regulation in melancholic depression would be associated with decreased appetite and sleep, and relative immunosupression. Charmandari et al (51) identified developmental issues related to this model (51), and emphasized that early childhood stress or trauma may have more long lasting effects on dysregulation of the stress system, causing hyperreactivity of the stress system, and impaired glucocorticoid negative feedback. While this model identifies a clear link between depression states and obesity, mixed depression states are much more common in childhood than either extreme subtype. In addition, the relationship between the stress system and depressive symptoms is likely to be affected by psychiatric comorbidity, particularly the high comorbidity between depression and anxiety disorders in youths. A clinical implication of the findings regarding insulin resistance, an important risk factor for type 2 diabetes, could be that one needs to be mindful about using medications that increase insulin resistance (like atypical neuroleptics) in treatment of depressed youth with obesity.

Current treatment for pediatric depression also highlights the possible role of serotonin in the relationship between obesity and depression. The serotonin selective reuptake inhibitors (SSRI's) are the most commonly prescribed medications for pediatric depression treatment. Serotonin has been linked with mood states, appetite, and sleep regulation. The connection between serotonin and food intake is related to appetite, food intake and food preference. Carbohydrate intake, unlike protein consumption, increases serotonin levels. Preference for carbohydrates by individuals with winter seasonal depression may be driven by underlying decreases in serotonin during mood episodes (52). Seasonal changes in serotonin transporter gene expression have been shown in adults with seasonal depression (53). SSRI agents are also used in the treatment of binge eating behaviors. A possible relationship between serotonin and HPA axis stress response has been identified by studying differences in the promoter region of the serotonin transporter gene. Girls who were homozygous for the short allele in the promoter region of the serotonin transporter gene have higher cortisol response to a stressor than girls with one long allele (54).

Also, treatment with mediators of inflammation, for clinical (55,56) and experimental goals (57,58) results in symptoms of depression and anxiety. For example, nearly 45% of patients treated with a high dose of IFN-α became depressed (59). A relationship between depression/suicidal ideation and cytokine treatment is further suggested by the cessation of depressive symptoms when cytokine treatment was discontinued (60). It has been reported that certain cytokines, such as IL-1, IL-2, and IFN-γ, induce the expression of the enzyme indoleamine-2,3-dioxygenase which shifts tryptophan (TRP) metabolism from serotonin synthesis toward the kynurenin (KYN) pathway (and the production of neurotoxic compounds) resulting in TRP depletion (61,62). TRP availability is the rate-limiting step in the synthesis of serotonin, and its reduced availability is associated with the induction of a depressive relapse in vulnerable patients (63,64). It has been consistently shown in patients with cancer and hepatitis, that treatment with IFN-α or IL-2 is associated with significant decreases in TRP, increases in KYN, and decreases in the TRP/KYN ratios (65). Moreover, the decrease in TRP, the increase in KYN, and the decrease in TRP/KYN ratio have been correlated with the severity of depression (66). Antidepressant treatment attenuates Interferon-α induced depressive symptoms (59), suggesting that mediators of inflammation induce, trigger or exacerbate depression, rather than merely inducing nonspecific sickness behavior. In summary, obesity is a pro-inflammatory state. The fact that inflammation causes depression may make obesity a risk factor for depression.

Obesity and Depression: Developmental Trajectories

Emerging longitudinal studies have investigated the complex relationship of obesity and depression over development. In a prospective study of over 9,000 youth, depressed mood

significantly predicted obesity at one year follow up, even controlling for baseline BMI, age, race, gender, socioeconomic status, and parental obesity (67). Although a limitation of the study is that weight and height were determined by self report, this fact is unlikely to explain the finding. A longitudinal study of a large birth cohort from Northern Finland assessed measures of obesity at ages 14 and 31 years old, along with measures of depression at age 31 years (68). Adolescent obesity was associated with adulthood depression. Additional studies have investigated relationship between weight and mood changes over time to characterize the relationship between obesity and depression. Anderson et al (69) assessed weight, height, depression, and anxiety in a community sample of youths at four time points over a 20 year time period. To take into account developmental considerations, weight changes were expressed in terms of body mass index z score changes and mental health outcome was measured using different structured assessments appropriate for age; e.g. psychopathology in children was assessed using parent and child report, whereas depression and anxiety in young adults was assessed using self report only (the BMI z score is a continuous measure of relative weight which corresponds with growth chart percentiles). Gender differences were identified in association between weight and anxiety. In females, anxiety was associated with higher BMI z score, whereas there was no significant relationship between weight and anxiety in males. Relationship between depression and weight also appeared to be modified by gender. In males, depression was associated with lower BMI z scores in childhood, but no significant relationship between weight changes and depression over development. In females, early childhood depression was associated with higher BMI z scores and higher weight gain than non-depressed females over development. Self report data from a cohort of almost 4,000 female college students indicated that women who reported weight cycling over a ten year period were more likely to report physician diagnosed depression and substance abuse than women who either reported weight loss, weight gain, or no significant changes in weight (70).

These longitudinal studies illustrate the role of gender in moderating the relationship between obesity and depression, which is consistent with the notion that these are heterogeneous conditions. The studies also suggest that, for specific clinical populations, intervention for one condition may also contribute to prevention of the other condition over development.

Conclusions

Investigation of the complex relationship between obesity and depression is challenged by many factors. First, the heterogeneity of depression. Different types of depression (e.g. atypical depression, reactive depression) and differences in depression phenomenology over development (childhood, adolescence, adulthood) make it difficult to conclude clear overarching association and interaction between depression and obesity. Also, depression may change over development from a unipolar mood disorder (depression episodes only) to a bipolar mood disorder, with depressive, manic, or mixed mood episodes. As the developmental course of bipolar disorder typically presents with episodes of depression before occurrence of mixed or manic states, studies of prepubertal youths with major depression are likely to include youths who will go on to develop bipolar disorder later in adolescence or adulthood. It is unclear if acute weight changes have a different association with depressive disorders from that of chronic obesity, as suggested by increased psychopathology in patients with weight cycling and binge eating. Also, obesity in otherwise healthy individuals may have less impact on mood symptoms than obesity in individuals with co-occurring hypertension, diabetes, or other obesity related illnesses. Comparison of different, more homogeneous subtypes of depression or obesity will aid in future investigation of these complex relationships.

Gender differences appear to moderate differences between obesity and depression. It would be interesting to assess if gender differences are consistent in populations of pre-pubertal youth, where cultural pressures, hormonal changes, and differences in body fat distribution are less

pronounced. However, changes in weight status with depression interventions, particularly non-medication interventions, are often not reported. It is unclear, for example, if cognitive behavioral therapy focused on depression treatment results in weight loss, and if these reductions may occur independent of mood improvement. Another example would be light treatment in seasonal depression. Given the propensity toward carbohydrate craving and weight gain during winter months, the impact of light therapy on weight as well as whether or not weight changes are associated with mood changes would inform obesity treatment in this depressed population.

Anxiety disorders are the most common psychiatric comorbid illnesses across the lifespan. However, there are significant developmental differences in the type of anxiety comorbidity (e.g. separation anxiety versus panic disorder) experienced by children, adolescents, and adults. Therefore, new investigation may elucidate how different anxiety disorders modulate the relationship between depression and the stress response.

Finally, longitudinal studies can be used to further identify childhood predictors of adult onset obesity and depression as well as factors that influence persistence of childhood obesity and depression into early adulthood. Understanding of the developmental sequence of factors that influence risk of these conditions is critical for planning timing and targets for prevention.

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