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ORIGINAL ARTICLE

Treatment of refractory obesity in severely obese adults following management of newly diagnosed attention deficit hyperactivity disorder

LD Levy[1], JP Fleming[2] and D Klar[3]

[1]*Private clinical practice, Nutritional Disorders Clinic, Toronto, ON, Canada;* [2]*Private clinical practice, Toronto, ON, Canada and* [3]*Private clinical practice and Staff Dietitian, Diabetes Clinic, Toronto Western Hospital*

Objective: To determine whether attention deficit hyperactivity disorder (ADHD) pharmacological treatment of severely obese subjects with newly diagnosed ADHD would result in sustained weight loss.
Design: Longitudinal clinical intervention study of the effects of ADHD medication on weight change over 466 days.
Subjects: 78 subjects (6 male, 72 female, mean age 41.3 years, BMI 42.7 kg m^{-2}) out of 242 consecutively referred severely obese, weight loss refractory individuals were diagnosed as having ADHD. Sixty-five subjects received treatment and 13 remained as controls.
Methods: Standard screening tests identified subjects likely to have ADHD. A diagnosis was made in 78 subjects by semi-structured clinical interview. ADHD subjects were screened for comorbid conditions (binge eating disorder, mood disorder, sleep apnea, chronic pain, gastroesophageal reflux disease). Satisfactory resolution of symptoms of comorbid conditions was achieved prior to the introduction of pharmacotherapy for ADHD. Subjects not accepting, tolerating or remaining on ADHD medication served as controls. Weight was measured at sequential clinic visits after initiation of pharmacotherapy.
Results: Comorbid conditions were found to be highly prevalent (sleep apnea 56.4%, binge eating disorder 65.4%, mood disorder 88.4%). After an average of 466 days (s.d. = 260) of continuous ADHD pharmacotherapy, weight change in treated subjects was −12.36% of initial weight and in controls +2.78%, $P<0.001$. Weight loss in treated subjects was 15.05 kg (10.35%) and weight gain 3.26 kg (7.03%) in controls, $P<0.001$.
Conclusions: ADHD is a highly prevalent condition in the severely obese population. Treatment of ADHD is associated with significant long-term weight loss in individuals with a lengthy history of weight loss failure. This result is likely because of the positive effects of treatment on self-directedness, persistence and novelty-seeking behaviors. ADHD should be considered as a primary cause of weight loss failure in the obese. Individuals seeking medical or surgical weight loss should be evaluated for ADHD and treated appropriately before intervention. This may improve the outcome for medically managed patients and avoid complications in surgical subjects because of poor compliance with diet and supplement requirements.
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Keywords: attention deficit hyperactivity disorder; weight loss; refractory obesity; psychostimulants

Introduction

Recent literature suggests that attention deficit hyperactivity disorder (ADHD) is present to a far greater extent in obese individuals, both in the pediatric age range[1,2] and in adults,[1,3–5] than in other populations. In 2001, we presented a case study[6] suggesting that ADHD was a significant contributing factor, both in a male patient's development of obesity and in his longstanding weight loss failure. Its treatment resulted in very significant weight loss. Subsequently, we reported[7] on the prevalence of symptoms of ADHD in a group of 75 consecutively referred severely obese women, showing that 26.7% reported significant symptoms of ADHD in both childhood and adult life. A further study[8] of an additional 190 consecutively referred patients (mean BMI of 40.4 kg/m^2, 79.5% female) confirmed our earlier findings regarding the high prevalence rate of ADHD in the severely obese population. In that analysis, we showed that, depending on which testing measures were employed, between 33.7 and 38.2% of these patients were identified as having ADHD. These screening measures were shown by

Correspondence: Dr LD Levy, Nutritional Disorders Clinic, 34 Berwick Avenue, Toronto, ON, Canada M5P 1H1.
E-mail: drlancelevy@rogers.com
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semi-structured clinical interview to have a false-positive rate of less than 6.67%. Kessler *et al*.[9] has shown that false-negative results are obtained in 32% of those evaluated for ADHD using the same symptom inventory, suggesting that our estimates of the prevalence of ADHD in obese subjects may be conservative. As depression and sleep apnea are well known to occur more frequently in obese patients, we screened for these conditions using the World Health Organization-Centre for Epidemiological Studies-Depression[10] instrument and the Epworth Sleepiness Scale[11] to screen for moderate sleepiness. We observed that 52.1 and 29.4% of 190 subjects, respectively, had these coexisting clinical problems. However, our analysis of these findings showed that neither depression nor sleepiness could account for the observed symptoms of ADHD.[8]

The great majority of our subjects had weight loss histories showing that they were refractory to all interventions for at least 10 years. These subjects were similar, in this regard, to obese patients enrolled in published weight loss studies of the effectiveness of differing combinations of diet, weight loss drugs and exercise. In a review of Medline, Embase and Cochrane Clinical Trials Register's meta-analyses of such research studies, we were unable to find weight loss interventions yielding weight loss outcomes equal to, or greater than, a 5% reduction of initial body weight after 1 year.[12–16]

Owing to the high prevalence of ADHD in the severely obese population, as well as the implication that its effects result in refractory obesity, this study was carried out to determine whether the management of this syndrome would result in long-term weight loss.

Methods

Subjects

Study subjects were obtained from a consecutive sample of severely obese adult patients below the age of 66 years who had been referred to a medical specialist (LDL) for the treatment of refractory obesity. Seventy-eight subjects (32.2%) screened from a total group of 242 consecutive patients were ultimately diagnosed as having ADHD. Of these 78 subjects, 65 with ADHD were followed prospectively for a mean time of 466 days after the initiation of appropriate pharmacotherapy and formed the treatment group. Those subjects with ADHD who elected not to receive ADHD pharmacotherapy, or who had side effects and did not tolerate drug therapy, or who obtained no clear benefit from trials of several medications for ADHD were also followed as controls ($N = 13$, 16.6% of subjects). Although these subjects did not receive ongoing ADHD pharmacotherapy, they did take part in all other aspects of our weight loss management process.

Identification as probably having ADHD

An initial identification of patients who were likely to have ADHD was made in 112 individuals out of a group of 242 consecutively referred patients. The assessment was made by a comprehensive history obtained by a series of clinical interviews (LDL). This was complemented by a variety of paper and pencil screening inventories, including the Adult Self-Report Scale,[17] Wender Utah rating scale,[18] Epworth Sleepiness scale[11] and the Centre for Epidemiological Studies-Depression.[10]

Diagnosis of ADHD

Owing to the severe limitations inherent in considering a psychiatric diagnosis on the basis of responses to questionnaires, the majority of individuals who were identified as likely to have ADHD on any combination of tests, or by clinical interviews (LDL), were referred to a clinical psychologist (JPF) for a more comprehensive assessment. Owing to the cost involved, only 62 (79.4%) of the 78 subjects, who were ultimately diagnosed as having ADHD, agreed to attend a 2-hour semi-structured clinical interview.[19] These interviews included a review of a subject's history of weight problems, interpersonal relationships, school performance, career development, sleep problems, substance use, health status, family history of psychological distress and a review of current psychological distress. School report cards from childhood were reviewed when available. In addition, some of the subjects were assessed using the Reynolds Brief Intellectual Assessment Scale.[20] This was performed to assess general intellectual functioning and thus provide a baseline for judgment regarding a possible disparity between capacity and performance. For the 16 subjects who were not seen by JPF, their diagnosis was made by LDL on the basis of a lifelong history of neurodevelopmental problems consistent with those expected in individuals having ADHD. Test scores were also considered. However, the main diagnostic consideration was whether the subject had a convincing history of difficulties throughout life, in the areas where ADHD most exerts a negative influence. This history was obtained during the 5–8 clinic appointments between a subject's initial visit and the final diagnosis of ADHD.

Screening for Comorbid conditions

All subjects suffered from one or more of the following clinical problems: chronic daytime hypersomnolence, mood disorder, chronic pain, nocturnal eating syndrome, binge eating disorder, obstructive sleep apnea, and gastrointestinal symptoms compatible with the syndrome of gastroesophageal reflux disease.

Chart records specifically documented the presence of sleep apnea, confirmed by overnight sleep study. Symptoms establishing the diagnosis of binge eating disorder[21] were elicited by the examining physician, and mood disorder was similarly diagnosed by clinical assessment supported in some cases by Centre for Epidemiological Studies-Depression scores.

Chart review
Data were collected over a 27-month period. Charts were reviewed and final data for all subjects were completed by February 2008.

Anthropometric measurement
Information regarding weight and BMI change over time was collected for as long as the subject attended the clinic. Weights used in the data analysis were taken at three points in time. The first weight used for this analysis, weight no. 1, was obtained at the time of the second clinic visit. The second weight, weight no. 2, was obtained on average approximately 3 months later, when a diagnosis of ADHD was made. Weight no. 3 was recorded at the subject's most recent clinic visit. Weight no. 3 had to be obtained by telephone interview from 11 of 13 control subjects who had discontinued visits to the clinic prior to the study ending. Weight changes for both treated and control groups were computed from the date weight no. 2 was recorded to the date on which weight no. 3 was obtained.

Heights were measured in the clinic to the nearest 0.1 cm by a stadiometer, and weight was measured to the nearest 0.1 kg by a balance beam scale with the subject in indoor clothing.

Pharmacotherapy of ADHD
Clinical assessment of the baseline level of impairment owing to ADHD. During the evaluation process, subjects described in detail those situations where symptoms of inattention, distractibility, procrastination, impulsivity, internal sensation of restlessness, and poor working memory significantly affected their lives. This information was carefully recorded and later used by the clinician to quantify a subject's response to medication. Adequacy of treatment was determined by clinical judgment on the basis of a patient's reports of improvement in those symptoms most relevant to their functioning.

Timing of introduction of ADHD medication. Pharmacological treatment of ADHD was only initiated once subjects with comorbid medical conditions had experienced significant improvement. For example, daytime somnolence caused by proven apnea was treated with continuous positive airways pressure. Similarly, dysthymia, major depression, anxiety or seasonal affective disorder was treated with appropriate pharmacotherapy, light therapy and counseling. Gastroesophageal reflux disease symptoms were treated by standard methods. Wherever possible, significant pain generally attributed to osteoarthritis or fibromyalgia was adequately controlled using a multimodal pain management approach. The degree of improvement obtained was measured in some subjects using a sequentially administered Brief Pain Inventory.[22,23]

Medications. Psychostimulants were used almost exclusively in these subjects. The medications used included mixed salts amphetamine (Adderall XR), methylphenidate sustained-release capsule (Concerta), and sustained release dextroamphetamine sulfate (Dexedrine Spansules). Generally, Adderall was offered first, and the dose was titrated up over 4 weeks to a clinically effective level. If Adderall was not tolerated, a decision was made whether to try another amphetamine, Dexedrine Spansule, or to move to Concerta. In several cases, a nonstimulant, atomoxetine (Strattera), was used first because the subject had symptoms of residual anxiety refractory to earlier efforts at management. In several subjects, control of ADHD symptoms was achieved with a combination of atomoxetine and a psychostimulant.

Specific care was taken to ensure that evening coverage for ADHD symptoms was maintained by appropriate timing of administration of the chosen agent. In some cases, two doses of medication were required, the first on arising and the second, a smaller dose, in the midafternoon.

Dietary intervention
No subjects were on diet programs for the time between weight no. 1 and weight no. 2. Once comorbid conditions had been treated and the ADHD medication adequately adjusted, all participants, including control subjects, were offered individual assessment and diet instruction by the clinic's registered dietitian. As subjects had to pay ($100) for these consultations, only 39 patients (50%) elected to attend an initial dietary counseling session.

Generally, the calorie content of a reducing diet was individually considered by applying the Harris–Benedict formula[24] to calculate resting metabolic rate. In some cases, there was a large discrepancy between a subject's reported current dietary intake and what was calculated to be the calorie intake required to maintain weight in that weight stable subject. In such cases, resting energy expenditure was measured using Indirect Open Circuit Calorimetry[25,26] (Deltatrac metabolic monitor-Sensormedics Corporation, Anaheim, CA, USA). Activities of daily living[27] caloric expenditure estimates were added to resting metabolic rate to determine total daily calorie requirements. A calorie deficit diet was devised by subtracting 700 kcal from a calculated maintenance calorie intake.

The dietitian created three different choices for each meal and snack. Completed diet plans achieved a lower glycemic load[28,29] than the subject had been accustomed to before.

Activity counseling
All participants were counselled regarding the need to be physically more active. Activities were sought that would not risk injury or cause pain. We did not assess compliance in this area however anecdotally; many of the subjects receiving ADHD medication did report becoming more active.

Ongoing clinic visits
Subjects were seen by the clinic physician every 3 to 4 weeks after the initial period of medication adjustment. Weight and blood pressure were recorded. Adjustments were made as required to medications for ADHD. Occasionally, prescriptions were given for sleep disturbances and adjustments made to mood management agents as needed. Other medical problems were managed by the subject's personal physician as required.

Psychological counseling
A number of subjects were referred for additional psychological or psychiatric review during this study if their mood state required that, or if they wished to explore ways in which certain habits of a lifetime with ADHD could most effectively be improved upon.

Statistical analysis
Analysis of these data was accomplished using the Winks SDA, sixth edition, software program.[30]

Results

Diagnosis of ADHD
A diagnosis of ADHD was made by clinical evaluation after subjects were seen for diagnostic interviews by LDL ($N=16$), or for semi-structured interviews by JPF ($N=62$). In all, 69.6% of subjects screening positively for probable ADHD were confirmed in that diagnosis. Thus, 78 subjects, out of 242 referred patients (32.2%), were found to have ADHD. These patients were entered in the weight loss study as shown in Table 1.

Identification and management of comorbid conditions
Before starting ADHD medications, all subjects were assessed for the presence of certain comorbidities of obesity, and a large majority were found to require treatment for one or more comorbidities of sleep apnea, binge eating disorder or mood disorder. Adequate management of comorbid conditions required a median time of 81 days (inter-quartile range 121 days), after which subjects were offered medication for ADHD as shown in Table 2.

Characteristics of subjects prior to initiation of treatment for ADHD
Subject characteristics at the time of weight no. 2 were similar in both treated and control groups as shown in Table 3.

Medications used in the management of ADHD
Sixty-five subjects satisfactorily responded to one or more medications and continued clinic visits and pharmacotherapy until the study ended. A listing of medications employed in their treatment is shown in Table 4. Thirteen subjects (16.7%) were unmedicated as they were not willing to take medication, did not tolerate medication because of side effects, or did not find that medication afforded any benefit.

Table 1 Positive ADHD screening evaluation scores

Screening test	*Subjects positive* (%)
Positive wender/elevated restlessness/or elevated inattention score	85.7
Positive wender or inattention score $\geqslant$16	81.4
Inattention score $\geqslant$16	71.0
Restless score $\geqslant$16	65.2
Inattention and restless scores $\geqslant$16	58.0
Positive wender and inattention score $\geqslant$16	56.5
Positive ASRS (six item)	52.1
Positive wender	51.4

Abbreviations: ADHD, attention deficit hyperactivity disorder; ASRS, adult self-report scale.

Table 2 Identified co-morbid conditions

Medical conditions	*Number of subjects (%)*
Sleep apnea	44 (56.4)
Mood disorder	69 (88.4)
BED	51 (65.4)

Abbreviation: BED, binge eating disorder.

Table 3 Subject characteristics: $N=78$ (Male 6 and Female 72)

	Treated for ADHD	*Untreated ADHD (control)*	
Subjects	65	13	
Age	**41.3 (12.1)**	**38.8 (9.4)**	**$t(76)=0.71$, $P=0.48$**
BMI (Means, s.d.)	42.7 (9.33)	41.7(8.2)	$t(76)=0.37$, $P=0.71$

Abbreviations: ADHD, attention deficit hyperactivity disorder; BMI, body mass index.

Table 4 Pharmacotherapy profiles

Medication	*Subjects*
Adderall	37
Dexedrine	10
Adderall+Strattera	8
Strattera	6
Concerta	3
Dexedrine+Strattera	1

Weight changes observed in treated and control subjects
After a mean time of 466 days of observation, data collection was stopped and the results were analyzed. As seen in Table 5, there was no difference between the treated and untreated groups in weight change between the initial assessment weight and the weight at the time when treatment for ADHD was initiated. On average, treated subjects lost 12.36% of their weight during the course of treatment, whereas control subjects gained an average of 2.78%. The difference was highly significant ($t(76) = 7.02$, $P < 0.001$) both statistically and clinically. Effect size using Cohen's $d = 2.16$ Table 5 also reports the weight change in kilograms lost.

Role of dietary intervention
Subjects in both treated and control groups had an extensive history of dietary interventions and were judged by the clinic's dietitian to be very familiar with diet concepts. Only 50% of subjects had one meeting with the dietitian, and only five of these subjects, all from the treatment group, reported substantial adherence to the written menu plans after the first month. Records of dietary adherence were not kept after that time, as the data were too few to be significant.

Discussion

Low attrition rate among treated subjects
Our early observations had suggested that although obese subjects completely appreciated the importance of weight loss, their motivational energy (drive for thinness[31]) at the inception of a weight loss plan was low, at the 25th percentile (unpublished research, 1986). Attrition rates in published weight loss studies are generally very high.[32] Hence, we were concerned that our enrollment of 78 subjects would not yield enough completed cases to make possible a meaningful analysis of the effects of treating ADHD on weight loss. Despite this unpromising background, 65 of 78 subjects remained involved when this study was closed (83.3%). A possible reason for this low rate of attrition is that care was taken to engage patients deeply in the process of discovering what had caused their longstanding weight loss failure, and what could be done about it, before attempting to engage them in any weight loss program.[33] Another likely reason was that preliminary treatment of comorbid conditions, as well as the improvements in mood and energy that resulted, was strongly motivating to a group whose previous experiences at weight loss programs were wholly negative. Finally, we noted that, with the advent of the salutary effects of medication on ADHD symptoms, subjects spoke enthusiastically and in optimistic terms regarding their future plans in life. Presumably, this happy experience helped to promote both attendance at the clinic, and compliance with medication and other treatments.

Absence of weight change during the pre-medication phase of the study
No significant change in body weight occurred in either the treated or control groups during the time period from weight no. 1 to weight no. 2. Our clinical experience over the past 10 years has shown us that individuals with ADHD have an incredibly difficult time maintaining the life changes typically associated with weight loss.[8]

III. Why weight loss occurred synchronously with the relief of ADHD symptoms.
The subject's recollections of failed past efforts at weight loss highlighted how daily demands on their time and energy frustrated their weight loss plans. Typically new diet plans were launched with great intensity, and a lot of wishful thinking, about how they would fit everything in. To find time for new diet and activity requirements, most subjects put off some routine tasks and often went with less sleep. However, it was clear that within a few weeks they could not cope with competing demands and gave up, relapsing to old habits. Many individuals linked their failure to feelings of boredom and frustration with the mundane and repetitive demands of managing/deciding what to eat, shopping, cooking and paying attention to diet and activity plans. Every diet plan they tried ended in exactly the same way and for the same reasons. However, our analysis was that enduring problems with inattention, distractibility, impulsivity, restlessness, an inconsistent level of available energy, and poor working memory substantially interfered with time management and task completion. Subjects habitually suspended 'boring' weight loss

Table 5 Weight changes with ADHD management

N =	*ADHD-treated subjects* 65	*Untreated controls* 13	
Time between weight no. 1 and weight no. 2 (Median, days)	81 (IQR 121)	Untreated	
Weight changes (kg) between weight no. 1 and weight no. 2	0.03 (3.8)	0.59 (4.5)	$t(76) = 0.47$, $P = 0.64$
Duration of follow-up from weight no. 2 to weight no. 3 (Days)	466 (260)	472 (180)	$t(76) = 0.08$, $P = 0.93$
Weight change (%) Weight no. 2 to no. 3	−12.36 (7.24)	+2.78 (6.27)	$t(76) = 7.02$, $P < 0.001$
Weight change (Kg) Weight no. 2 to no. 3 (Means, s.d.)	−15.05 (10.35)	+3.26 (7.03)	$t(76) = 6.09$, $P < 0.001$
Difference in %weight change	15.14 (pooled 1.95)		

Abbreviations: ADHD, attention deficit hyperactivity disorder; IQR, inter-quartile range, Means, s.d.

related plans to gravitate toward tasks that were more urgent, more intrinsically stimulating or that had a greater likelihood of immediate success, as these were tasks that allowed them to function most effectively.

Once pharmacotherapy treatment was begun, we anticipated that improvements would occur in exactly those symptoms of ADHD that were most detrimental to successful weight loss. Careful inquiry was made as medication was titrated to determine the mechanism by which changes in symptoms of ADHD might have resulted in improved compliance with diet and physical activity plans over time. A distillation of our subject's comments showed that improvements in daytime energy, restlessness, distractibility, working memory, impulsivity and mood were instrumental in their successful execution of weight loss plans. Most often, improvements occurred in the order in which they had been listed.

Fundamentally, drug treatment led to improvements in self-directedness, a reduction in novelty seeking, and an increased capacity for persistence. An improved ability to be self-directed[34] was noted first, and this is a trait that is important for attaining any goal. As daytime energy improved, and restlessness and distractibility diminished, subjects could more consistently initiate behaviors congruent with their ultimate goal of weight loss. For example, they did not use food as before to restore energy or to focus attention. They could stay on task and finish their work expeditiously so that tasks related to meal preparation or physical activity could be done reliably. Subjects reported being more able to pay attention while eating, so that they were aware of the signals of hunger and fullness much sooner than before, allowing for better control over the amount consumed.

The second change was that subjects showed improvement in control over novelty seeking and had a much greater ability to be persistent in a task.[34] Control over both of these traits is highly important to success in a long-term project, such as weight loss.

As an example, subjects on medication reported that they felt calmer, less restless, and less impelled to seek intense, novel, and unplanned stimuli than ever before. Thus, feelings that earlier had led them to leave one task to begin a newer one, and generally one not congruent with a previously determined long-term goal, did not intrude and undermine their weight loss plans. Impulsive choices of food were curtailed, and exercise plans were not forgotten in favor of novel entertainment. With enhanced persistence, many felt they were able to continue with or elaborate new problem-solving strategies, as well as tolerate negative mood states, rather than using food or engaging in other impulsive actions to quickly relieve that distress.

Anorexiant and metabolic effects of stimulants and possible effects on weight loss

Weight loss occurs where energy balance becomes negative, either by virtue of a reduction in caloric intake or by increased calorie expenditure, or by both means.

Development of a reduced calorie intake. A significant early effect of ADHD medication was the reported loss of appetite in most, but not all, subjects. This was evident in the first 4–6 weeks. However, appetite suppression was noted to diminish and all but vanish within 2 months. This finding is consistent with reports on the failure of amphetamine agents in the treatment of obesity, beginning in the 1940s and ending in the late 1970s. The use of these agents to facilitate weight loss was discontinued, as the weight loss results were not longlasting,[35–37] side effects were common, and the rates of attrition very high.[37] There was also a growing appreciation of the medical and psychological risks associated with the use of these drugs.[38]

Our subjects reported that they experienced the greatest reduction in calorie intake because the medication reduced restlessness, fatigue and anxiety, and thus diminished the chronic use of food to assuage those feelings. Binge eating diminished very substantially or stopped altogether, and impulsivity in food selection was curtailed. They reported that they were much more aware of internal cues of hunger and fullness and could act on those feelings, often for the first time. Better time management allowed for meals to be planned, prepared and eaten in a more reliable and focused way, thereby reducing food consumption that was not hunger related.

Increased calorie expenditure. Although activity levels have been variously reported to rise, and to fall, when stimulants are used in children[39,40] or in adults,[41] our subjects uniformly reported feeling more alert and energized. A majority of the subjects treated reported greater daily physical movement than prior to treatment. It is reasonable to assume that this additional activity increased their total daily calorie expenditure. As the daily activity level was not objectively measured, it is not known how much this factor affected weight loss.

This study did not include the sequential measurement of resting metabolic rate. However, the existing literature was reviewed, and we found no adequate studies of metabolic rate while the subjects were taking stimulant medication. Studies carried out with the concomitant use of thyroid medication were discarded. Hence, it is unknown whether ADHD medications directly elevated the metabolic rate in the long term.

Weight gain in the control group

The control group of subjects gained weight at a rate that was four times the average annualized rate for Caucasian women aged 20–70 years.[42] One possible explanation for this is that by becoming involved in this study, a more positive energy balance had developed. To better understand this finding, we looked for examples of weight gain in control subjects in other studies. Numerous studies of surgical weight loss interventions showed that control group subjects did not gain weight nearly as rapidly as did our control group,

averaging in one large study only 0.1% of initial body weight gained after 2 years.[43] However, as this study's control subjects were a heterogeneous group, it is not possible to analyze further their high rate of weight gain. We have not found studies of weight changes in adults who failed a trial of psychostimulant medication for ADHD. Perhaps such failure results in a more negatively affected mood, a lower level of self-esteem, or reduced feelings of self-efficacy over time than would be seen in individuals with ADHD who were never treated. Presumably, these changes might contribute to an increased use of food to manage the altered mood state.

Implications of the high prevalence of ADHD in obese individuals considering weight loss surgery

Weight loss surgery, either by laparoscopic banding or gastric bypass, has become a very common treatment for refractory obesity. For individuals with high BMI and comorbid conditions, it is clear that the benefits outweigh the risks.[44] The outcomes measured are quantifiable ones, including weight lost, correction of metabolic derangement, reduced mortality, and reduced utilization of costly medical services over time.[45] However, there are less agreeable outcomes that include weight regain or failure to lose an adequate amount of weight,[46] leading to re-banding or conversion to gastric bypass.[47]

Given the problems that ADHD patients experience following routine and repetitive programs, it seems reasonable to believe that the unrecognized ADHD patient is significantly more likely to be at risk for those less agreeable surgical outcomes and for nutrient deficiency than an unaffected individual. Our unpublished observations on patients referred for assessment regarding failed gastric banding or gastric bypass show that such individuals are much less able to comply with postoperative dietary instructions in the long term than non-ADHD patients, and that ADHD was almost uniformly present as a factor contributing to weight loss failure. In addition, we noted that these patients were poorly compliant in taking crucial daily nutrient supplement requirements. To illustrate our concern about compliance failure in this group of patients, it is known that morbidly obese candidates for gastric bypass have a rate of vitamin D deficiency of 60%.[48] All patients are told that they must take daily vitamin and mineral supplements for life after surgery. Despite this warning, vitamin D deficiency is still present in 53% of gastric bypass patients 1 year postoperatively.[49] This deficiency, and likely many others, has to reflect problems with compliance. Hence, it would not be unlikely that, over the years, macro- and micronutrient deficiency may develop, or further worsen, to significantly affect health in the long term.[50,51] Therefore, it would seem to be important to ensure that patients undergoing these operations have been screened to identify and manage ADHD so that they are best able to benefit from the intervention.

Implications of the findings of this study for the management of the chronically obese

The overwhelming majority of weight loss programs stress dietary change and increased activity as essential to successful weight reduction. However, such strategies do not result in significant weight loss.[52–55] If more proof of the failure of this advice is needed, it is shown that, even in patients about to undergo weight loss surgery and those who are presumably highly motivated to comply, mandatory preoperative diet programs result in no significant weight loss.[56] Over the past 20 years, our observation is that chronically obese patients know what they need to do to successfully lose weight, but can neither sustain the effort nor make those changes permanent.

Adequate treatment of ADHD in previously diet-refractory patients resulted in improvement in so many aspects of mental and physical functioning that weight loss occurred. We suggest that it was sustained, without any recourse to further formal diet intervention, because the medication used provided sufficient durability of effect. This is in contrast to the short-term weight loss effect of amphetamines reported in studies carried out on obese subjects, the majority of whom would not have had ADHD.

Therefore, in the chronically and severely obese, a diligent search should be made for conditions that adversely affect daytime energy level, control over novelty seeking, persistence, and impulsivity, and those that impair self-directedness and short-term memory, before additional diet plans, or surgery is suggested. Where ADHD is found to be the underlying cause, it has to be pharmacologically treated to make long-term weight loss possible.

As the prevalence of ADHD in the seriously obese may be conservatively estimated at between 26.7[7] and 32.2 percent (78 of 242 subjects), many thousands of such individuals may benefit from screening for ADHD as a starting point in their efforts to lose weight.

Study limitations

The most significant limitation is that, for ethical reasons, subjects were not randomly assigned to treatment or control groups, and as a result they are therefore not directly comparable. Nevertheless, comparisons suggested that they were not significantly different on the demographic variables. The absence of a treatment reversal phase prevents us from asserting with certainty that the pharmacologic treatment of ADHD was the cause of the sustained weight loss. The results of the study cannot be generalized to the more general population of obese individuals, as our subjects consisted of a refractory group of medically referred patients. Last, the design does not allow us to determine whether weight loss might simply be attributable to the direct effects of stimulant medication on metabolism and appetite, rather than because of the impact of those agents on the symptoms of ADHD.

Conclusions

ADHD is a highly prevalent condition in the severely obese, weight loss refractory population. In these individuals, weight loss failure results from the deleterious primary effects of ADHD on cognition, energy, and on the expression of more goal-directed character and temperament traits. These cumulative effects inhibit the development and long-term maintenance of effective diet and lifestyle changes. Therefore, screening for ADHD should become part of the diagnostic assessment for the management of severe obesity. Individuals seeking medical or surgical weight loss should be evaluated for ADHD and treated appropriately before intervention. This may improve the outcome for medically managed patients and avoid complications or unsatisfactory weight loss outcome in surgical subjects, because of poor compliance with diet and supplement requirements. Treatment of ADHD may significantly enhance an individual's ability to sustain those interventions in diet and lifestyle required for the continuance of long-term weight loss.

Conflict of interest

The authors state no conflict of interest.

One author, LDL, conducted a hospital 'Grand Rounds' last year on the role of ADHD in the causation of weight loss failure in patients with ADHD. This presentation was funded by an unrestricted grant from Shire Pharmaceuticals. Reimbursement was paid for time out of the office, according to Honorarium Guidelines of the Royal College of Physicians and Surgeons of Canada.

References

1 Cortese S, Angriman M, Maffeis C, Isnard P, Konofal E, Lecendreux M *et al*. Attention-Deficit/Hyperactivity Disorder (ADHD) and Obesity: A Systematic Review of the Literature. *Crit Rev Food Sci Nutr* 2008; **48**: 1–14.
2 Waring ME, Lapane KL. Overweight in Children and Adolescents in Relation to Attention –Deficit/Hyperactivity Disorder: Results From a National Sample. *Pediatrics* 2008; **122** (1): e1–e6.
3 Liu LL, Li BM, Yang J, Wang YW. Does dopaminergic reward system contribute to explaining comorbidity obesity and ADHD. *Med Hypotheses* 2008; **70**: 1118–1120.
4 Davis C, Levitan RD, Smith M, Tweed S, Curtis C. Associations among over eating, overweight, and attention deficit hyper activity disorder: a structural equation modelling approach. *Eat Behav* 2006; **7** (3): 266–274.
5 Altfas JR. Prevalence of attention deficit hyperactivity disorder among adults in obesity treatment. *BMC Psychiatry* 2002; **2**: 9.
6 Fleming JP, Levy LD. *Disordered Eating and ADHD*. Presented at National Attention Deficit Disorder Association (ADDA) Conference Annual Meeting; Seattle 2001; May 3–6.
7 Fleming JP, Levy LD, Levitan RD. Symptoms of Attention Deficit Hyperactivity Disorder in severely obese women. *Eat Weight Disord* 2005; **10** (1): e10–e13.
8 Fleming JP, Levy LD. *Attention Deficit Hyperactivity Disorder, Depression and Sleepiness in Adults Referred for the Treatment of Obesity*. Presented at the North American Association for the Study of Obesity (NAASO) Conference Annual Meeting; New Orleans, 2007.
9 Kessler RC, Adler L, Ames M, Demler O, Faraone S, Hiripi E *et al*. The World Health organization adult ADHD self-report scale (ASRS): a short screening scale for use in the general population. *Psychol Med* 2005; **35**: 245–256.
10 Radloff LS. The CES-D scale. A self-report depression scale for research in the general population. *Applied Physiological Measurement* 1977; **1**: 385–401.
11 Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991; **14** (6): 540–545.
12 Heymsfield SB, van Mierlo CA, van den Knaap HC, Heo M, Frier HI. Weight management using a meal replacement strategy: meta and pooling analysis from six studies. *Int J Obes Relat Metab Disord* 2003; **27** (5): 537–549.
13 Rucker D, Padwal R, Li SK, Curioni C, Lau DCW. Long term pharmacotherapy for obesity and overweight: updated meta-analysis. *Brit Med J* 2007; **335** (7631): 1194–1199.
14 Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Pharmacotherapy for weight loss in adults with type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2005; **(1)**: CD004096. DOI:10.1002/14651858.CD004096.pub2.
15 Norris SL, Zhang X, Avenell A, Gregg E, Bowman B, Schmid CH *et al*. Long term effectiveness of weight loss interventions in adults with pre-diabetes: a review. *Am J Prev Med* 2005; **28** (1): 126–139.
16 Gardner CD, Kiazand A, Alhassan S, Kim S, Stafford RS, Balise RR *et al*. Comparisons of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A To Z Weight Loss Study: a randomized trial. *JAMA* 2007; **297** (9): 969–977.
17 Kessler RC, Adler L, Ames M, Demler O, Faraone S, Hiripi E *et al*. The World Health Organization Adult ADHD Self report Scales (ASRS): a short screening scale for use in the general population. *Psychol Med* 2005; **35** (2): 245–256.
18 Ward MF, Wender PH, Reimherr FW. The Wender Utah Rating Scale: an Aid in the Retrospective Diagnosis of Childhood Attention Deficit Hyperactivity Disorder. *Am J Psychiatry* 1993; **150**: 885–890.
19 Magnusson P, Smari J, Sigurdardottir D, Baldursson G, Sigmundsson J, Kristjansson K *et al*. Validity of self-report and informant rating scales of adult ADHD symptoms in comparison with a semi-structured diagnostic interview. *J Atten Disord* 2006; **9** (3): 494–503.
20 Reynolds CR, Kamphaus RW. *Reynolds Intellectual Assessment Scales and the Reynolds Intellectual Screening Test*; Professional manual, Psychological Assessment Resources Inc, 2003.
21 Spitzer RL, Yanovski S, Wadden T, Wing R, Marcus MD, Stunkad A *et al*. Binge Eating Disorder: its' further validation in a multi site study. *Int J Eat Disord* 1993; **13** (2): 137–153.
22 Lundorff L, Peuckmann V, Sjogren p. Pain management of opioid treated cancer patients in hospital settings in Denmark. *Acta Anaesthesiol Scand* 2008; **52** (1): 137–142.
23 Holen JC, Lydersen S, Klepstad P, Loge JH, Kaasa S. The Brief Pain Inventory. *Clin J Pain* 2008; **24** (3): 219–225.
24 Harris JA, Benedict FG. *A biometric Study of Basal Metabolism in Man*. Carnegie Institution of Washington: Washington, 1919.
25 Haugen HA, Chan LN, Li F. Indirect Calorimetry: a practical guide for clinicians. *Nutr Clin Pract* 2007; **22** (4): 377–388.
26 DaRocha EE, Alves VG, Da Fonseca RB. Indirect Calorimetry: methodology, instruments and clinical application. *Curr Prin Clin Nutr Metab Care* 2006; **9** (3): 247–256.
27 Shetty PS, Henry CJK, Black AE, Prentiss EM. Energy requirements in adults: an update of basal metabolic rate (BMR) and physical activity levels (PALs). *Eur J Clin Nutr* 1996; **50**: S11–S23.
28 Jenkins DJ, Kendall CW, Augustin LS, Franceschi S, Hamidi M, Marchie A *et al*. Glycemic Index: overview of implications in health and disease. *Am J Clin Nutr* 2002; **76** (1): 266s–273s.

29 Barclay AW, Petocz P, McMillan-Price J, Flood VM, Prvan T, Mitchell P *et al*. Glycemic Index, Glycemic Load, and chronic disease risk—a meta analysis of observational studies. *Am J Clin Nutr* 2008; **87** (3): 627–637.
30 Elliott AC. *Winks(™) SDA*, 6th edn. Texasoft: Cedar Hill, Texas, 2007.
31 Garner DM, Olmstead MP, Polivy J. Development and validation of a multidimensional eating disorder inventory for anorexia nervosa and bulimia. *Int J Eat Disord* 1983; **v.2** (2): 15–34.
32 Munro JF, MacCuish AC, Wilson EM, Duncan LJP. Comparison of Continuous Anorectic Therapy in Obesity. *Brit Med J* 1968; **1**: 352–354.
33 Levy LD. *Conquering Obesity: Your Guide to Healthy and Successful Weight Management*. Key Porter Books: Toronto, 2002.
34 Svrakic DM, Whitehead C, Przybeck TR, Cloninger CR. Differential diagnosis of personality disorders by the seven-factor method of temperament and character. *Arch Gen Psychiatry* 1993; **50** (12): 991–999.
35 Pearson JR. Drugs for obesity. *Br Med J* 1963; **2**: 853–855.
36 Hawirko L, Sprague PH. Treatment of Obesity by Appetite Depressing Drugs. *CMAJ* 1946; **v 54**: 26–29.
37 LeRiche WH, van Belle GE. A long term study on the use of appetite suppressants. *CMAJ* 1961; **85** (12): 673–675.
38 Resnick M, Joubert L. A Double Blind Evaluation of an Anorexiant, a Placebo, and Diet alone in Obese Subjects. *CMAJ* 1967; **97**: 1011–1015.
39 Hubel R, Jass J, Marcus A, Laessle RG. Over weight and basal metabolic rate in boys with attention deficit hyperactivity disorder. *Eat Weight Disord* 2006; **11** (3): 139–146.
40 Schertz M, Adesman AR, Alfieri NE, Bienkowski RS. Predictors of weight loss in children with attention deficit hyperactivity disorder treated with stimulant medication. *Pediatrics* 1996; **98** (4 Pt1): 763–769.
41 Boomstra AM, Kooij JJ, Oosterlaan J, Sergeant JA, Buitelaar JK, Van Someren EJ. Hyperactive night and day? Actigraphy studies in adult ADHD: a baseline comparison and the effects of methylphenidate. *Sleep* 2007; **30** (4): 433–442.
42 Baltrus PT, Lynch JW, Everson-Rose S, Raghunathan TE, Kaplan GA. Race/Ethnicity, Life Course Socioeconomic Position, and Body Weight Trajectories over 34 Years: The Alameda County Study. *Am J Public Health* 2005; **95**: 1595–1601.
43 Sjostrom L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B *et al*. Lifestyle, Diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med* 2004; **351** (26): 2683–2693.
44 Christou NV, Sampalis JS, Liberman M, Look D, Auger S, McLean AP *et al*. Surgery decreases long term mortality, morbidity, and health care use in morbidly obese patients. *Ann Surg* 2004; **240** (3): 416–423.
45 Sampalis JS, Liberman M, Auger S, Christou NV. The impact of weight reduction surgery on health care costs in morbidly obese patients. *Obes Surg* 2004; **14** (7): 939–947.
46 Angrisani L, Lorenzo M, Borrelli V. Laparoscopic adjustable gastric banding versus Roux en Y gastric bypass: 5-year results of a prospective randomized trial. *Surg Obes Relat Dis* 2007; **3** (2): 127–132.
47 Muller MK, Attigah N, Wildi S, Hahnloser D, Hauser R, Clavien PA *et al*. High secondary failure rate of rebanding after failed gastric banding. *Surg Endosc* 2008; **22** (2): 448–453.
48 Carlin AM, Rao DS, Meslemani AM, Genaw JA, Parikh NJ, Levy S *et al*. Prevalence of vitamin D depletion among morbidly obese patients seeking gastric bypass surgery. *Surg Obes Relat Dis* 2006; **2** (2): 98–103.
49 Carlin AM, Rao DS, Yager KM, Genaw JA, Parikh NJ, Szymanski W. Effect of gastric bypass surgery on vitamin D nutritional status. *Surg Obes Relat Dis* 2006; **2** (6): 638–642.
50 Ames BN. Low micro nutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage. *Proc Natl Acad Sci USA* 2006; **103** (47): 17589–17594.
51 Ames BN. A role for supplements in optimizing health: the metabolic tune up. *Arch Biochem Biophys* 2004; **423** (1): 227–234.
52 Linde JA, Erickson DJ, Jeffery RW, Pronk NP, Boyle RG. The relationship between prevalence and duration of weight loss strategies and weight loss among overweight managed care organization members enrolled in a weight loss trial. *Int J Behav Nutr Phys Act* 2006; **3**: 3.
53 Rucker D, Padwal R, Li SK, Curioni C, Lau DCW. Long term pharmacotherapy for obesity and overweight: updated meta analysis. *Brit Med J* 2007; **335**: 1194–1199.
54 Kopelman PG, Grace C. New thoughts on Managing Obesity. *Gut* 2004; **53**: 1044–1053.
55 Strychar I. Diet in the management of weight loss. *CMAJ* 2006; **174** (1): 56–63.
56 Jamal MK, DeMaria EJ, Johnson JM, Carmody BJ, Wolfe LG, Kellum JM *et al*. Insurance-mandated preoperative dietary counseling does not improve outcome and increases drop-out rates in patients considering gastric bypass surgery for morbid obesity. *Surg Obes Relat Dis* 2006; **2** (2): 122–127.