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Review of the association between obesity and ADHD

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Excess weight and obesity are defined by the WHO (World Health Organization) as abnormal or excessive fat accumulation that is unhealthy.¹ On the other hand, attention deficit hyperactivity disorder (ADHD) is defined by the presence of attention difficulties, poor motor regulation activity, and low impulse control.² The association between obesity and ADHD has been systematically investigated for twelve years. In this review article, previous studies that were relevant in establishing this relation are examined. Neurobiological hypotheses about the relation between obesity and ADHD are reviewed, and an association with addictions is considered.

Keywords: Obesity, Excess weight, ADHD, Impulsivity, Binge eating, Addiction

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Revisión de la asociación entre obesidad y TDAH

El sobrepeso y la obesidad son definidas por la OMS (Organización Mundial de la Salud) como una acumulación anormal o excesiva de grasa que es perjudicial para la salud¹. Por otro lado el TDAH (Trastorno por Déficit de Atención e Hiperactividad) se define por la presencia de dificultades atencionales, pobre regulación de la actividad motora y un bajo control de los impulsos². La asociación entre Obesidad y TDAH se investiga sistemáticamente desde hace doce años. En este artículo de revisión se expondrán estudios previos que son relevantes a la hora de establecer esta relación, se revisarán las distintas hipótesis neurobiológicas que asocian Obesidad con TDAH y se planteará su asociación con las adicciones.

Palabras clave: Obesidad, Sobrepeso, TDAH, Impulsividad, Atracones, Adicción.

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INTRODUCTION

The idea of viewing obesity as an eating disorder (ED) has gained acceptance in the last twelve years because it involves variable dysfunction in eating habits and affects the regulatory mechanisms of appetite, emotions, and body image perception. The state of being overweight can be defined as having a body mass index (BMI) of 25 to 29.9 kg/m², and obesity is defined as BMI greater than 30 kg/m². In Spain, up until 2012 the prevalence of excess weight and obesity among people aged 8 to 17 years reached 26% and 12.6%, respectively.³ The figures for excess weight and obesity among adults were, respectively: 25% and 16% (women), and 45% and 18% (men).³ The prevalence of obesity increased from 7.4% to 17.0% between 1986 and 2011.³ Although the major increase occurred during the 1980s, the prevalence today is the highest in our history because the slight increase in background figures has been sustained as people aged, especially in males and in relation to fewer years of schooling and lower income.³ ADHD begins to manifest itself before the age of 12 years. In psychiatric practice with children and adolescents, this diagnosis has become customary, whereas it tends to be underdiagnosed among adults. The worldwide prevalence of ADHD is 5% to 10% among schoolchildren with persistence into adulthood in more than 60% of cases.⁴

REVIEW OF STUDIES OF THE ADHD AND OBESITY ASSOCIATION

The first study that investigated this association directly was published in 2002.⁵ Our literature search started with that year. The studies included measured: (1) the prevalence of ADHD in minors and adults seen for problems of body weight, and (2) BMI and the prevalence of obesity (cross-sectional or longitudinal) in children and adolescents with a well-established diagnosis of ADHD. Review articles and studies that did not systematically measure this relation but added important information were also included. Isolated case reports, descriptive

studies without statistical analysis of the data, and doctoral dissertations were excluded.

We found seven studies that measured the prevalence of ADHD in obese subjects: five in clinical samples and two in the general population. The studies in clinical samples involved: 215 obese adults treated at a clinic specializing in obesity⁵; 90 adolescents (12-16 years), of whom 30 were obese and in treatment, 30 were obese and untreated, and 30 had the proper weight⁶; 26 obese children and adolescents (8-17 years) hospitalized in an eating disorder care unit⁷; 75 obese women referred to a specialized clinic for obesity treatment,⁸ and 56 obese children and 56 children of proper weight (10-18 years).⁹ Four of these five studies⁵⁻⁸ revealed a significantly higher prevalence of ADHD in obese patients compared to a control group or the age-specific reference body weight.¹⁰ In the study in which the prevalence of ADHD was not higher in patients with obesity,⁹ more symptoms of impulsivity, hyperactivity, and attention deficit were reported in the study group than in controls for several tests. The absence of an association between obesity and ADHD could be due to the fact that the study focused on the association between obesity and impulsivity; it did not use instruments specifically designed to detect ADHD nor did it examine this diagnosis as a primary or categorical variable.

One study in the general population was conducted on a sample of 991 children (aged 9-16 years) and found no association between ADHD and obesity.¹¹ Another study used specific screening instruments and structured psychiatric interviews in an initial sample of 34,653 adults from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).¹² The aim was to measure the association between being overweight and a diagnosis of ADHD (in adulthood and retrospectively), controlling variables such as socioeconomic status, mood, anxiety, and substance use disorder. After controlling confounding factors, it was concluded that ADHD detected in adults was not associated with obesity, but a history of ADHD symptoms in childhood was associated with obesity in adult women. This provides a basis for future longitudinal studies to evaluate the effect of treating ADHD in childhood on the weight of adult women.¹²

As in other reviews,¹⁰ we found studies with measurements of the weight of children with ADHD in clinical samples,¹³⁻²⁰ who had higher BMI^{13-16,18-20} or lipid concentration, and larger waist circumference¹⁷ than expected for their respective age groups.

A study in adults with a retrospective diagnosis of childhood ADHD showed a statistically significant association between ADHD, excess weight (OR 1.57; 95% CI=0.99, 2.70), and obesity (OR 1.69; 95% CI=1.01, 2.82) after controlling for the factor major depressive disorder. The association with binge eating disorder (in the previous 12 months) was not significant (OR 1.41, 95% CI=0.76, 2.53).²¹ Among the

methodological problems identified was the lack of a formal diagnosis of ADHD in adulthood, disregarding whether the patient was treated for ADHD, and underestimating the prevalence of binge eating disorder by not controlling for the tendency to hide this embarrassing symptom and limiting the search for it to 12 months.¹⁰

Among the patients who are candidates for bariatric surgery, 10.2% have ADHD; the prevalence of ADHD in the general population is 3% to 4% whereas in the obese population it might be as high as 27.4%.⁵ Among 187 candidates for bariatric surgery, a high prevalence of anxiety, depression, ADHD, and ED was found, and a strong correlation with all of them except ED.²² Although 8.2% of the sample had binge eating disorder, no association was found between binge eating and ADHD.²² Candidates with high scores on the ADHD scales expressed more difficulty in meeting the preparatory medical goals for surgery and more irregularity in adhering to treatment and attending follow-up appointments, all of which predicted more long-term health risks and the recurrence of obesity after surgery.²² The fundamental limitation was the use of self-administered scales and questionnaires without controlling for the sincerity of the answers (given patients' known fear of being disqualified for the surgical option if the mental profile is judged inadequate).

NEUROBIOLOGICAL MECHANISM UNDERLYING THE ASSOCIATION BETWEEN ADHD AND OBESITY

Executive dysfunction

The revised Barkley model attributes the inhibitory deficit of ADHD to poor executive function, from which the three cardinal syndromes (attention deficit, hyperactivity, impulsivity) and other common problems in ADHD derive: difficulty in translating thought into action, procrastination, poor sense of timing, and other.

Individuals with ADHD have dysfunction in five areas: self-restraint, nonverbal working memory, verbal working memory, self-regulation of emotions and motivation, and internalization of response.¹⁵ Of these five, poor inhibitory control contributes to the clinical expression of ADHD,²³ for example, the impaired ability to delay response followed by hasty and excessive behavior, and excessive response to stimuli, which has been linked with hypofunction of the orbitofrontal cortex that could affect limbic system connections.^{23,24} Studies in people with obesity increasingly find signs of executive dysfunction (distractibility, disorganization, etc.) together with the failure to comply with healthy habits.²⁴⁻²⁶ This makes sense when considering the frequent concurrence of ADHD.

Attention deficit

Among obese people, attention deficit is associated with diminished organizational capacity for schedules and eating and social habits.¹⁰ Inattention is associated with an amotivational state of sedentary routines that interfere with controlling weight gain and favor high-calorie food intake. They pay less attention to internal hunger and satiety cues.²⁷ When they are focusing their attention on something they are interested in, they may forget to eat, but when they are no longer distracted there is *rebound* appetite overstimulation.²⁷ The frustration caused by self-perception of an attention deficit can cause high-calorie overeating to relieve affective malaise and to compensate for feelings of failure.^{10,28} In addition, children with ADHD distract themselves more with electronic games and television, to the detriment of exercise time that could offset the calorie intake.²⁸

Impulsivity

Impulsivity is the tendency to respond without premeditation and act without considering the consequences, coupled with a relative inability to delay gratifying behavior. Impulse control disorders are characterized by the difficulty to resist an impulse, motivation, or temptation to consummate an act that is harmful to the person or to others.² Impulsivity defines the impulse control disorders (pyromania, kleptomania, pathological gambling, intermittent explosive disorder, and others)² and other related categories: addictive disorders, binge eating disorder with or without bulimia, and ADHD. This tendency to respond impetuously could lead to excessive calorie intake when not hungry, associated with a relative lack of concern about daily intake.²⁹ Aversion to delaying reinforcement favors the intake of high-calorie fast foods at the expense of balanced meals prepared at home and eaten more slowly.²⁹ Consequently, impulsivity as a permanent trait could perpetuate chronic high-calorie intake that might cause obesity.¹⁰

Bulimia nervosa (BN) is the eating behavior disorder that has been most studied in relation to ADHD. This comorbidity is easily explained given the impulsive profile of this ED, as opposed to others like restrictive type anorexia nervosa (AN).²⁹ The prevalence of ADHD among people with ED (3%–30%) has not been rigorously studied and the few available data are contradictory.^{29,30} The prevalence of BN in patients with ADHD ranges from 1% to 12%,¹⁷ being higher in adult women with ADHD.³¹ Binge eating occurs in compulsive purging type AN, BN, and in binge eating disorder or "compulsive eating" (CE) and in other forms of compulsive eating. When we only consider prominent behaviors, such as binge eating, the traditional eating disorders form a *continuum* with other psychiatric disorders and obesity. For that reason, it is difficult to obtain clear records of *comorbidity* with ADHD. It is confirmed that the

prevalence of over-eating (which exhibits variable analogy with the binge eating of BN, depending on the study) is high in adults with ADHD and it is suspected that it increases with the degree of obesity. When ADHD and obesity coexist, the odds ratio of binge eating is 3.97 times greater than in people who are obese but do not have ADHD.³⁰ However, we still do not know the extent and intrinsic quality of the relation between ADHD and classical EDs.²⁹⁻³³

Binge eating in ADHD might be attributed to impulsivity because the intensity of binge eating in EDs correlates with impulsivity scale measurements. However, the findings of investigation of cases of ADHD with concurrent ED refutes this,^{29,30,34} as binge eating correlates with attention deficit and even hyperactivity, but not with impulsivity. Three hypotheses exist: (1) Impulsivity is not a homogeneous or singular phenomenon, so the scales that measure impulsivity in ADHD do not measure the same in EDs, and vice versa. (2) Binge eating is a substitute source of satisfaction or relief from the anxiety derived from the attention and organizational problems of ADHD (cognitive overexertion, overcoming social rejection, frustration, and other). (3) Binge eating is a direct consequence that is marginal to emotional reactions, and executive and attention failures, because scheduling or the hunger signal is neglected due to not switching off absorbing tasks (paradoxical "over-focusing" derived from "alternating" and "divided" attention failures) and social rhythms are overlooked; when the hunger signal is again noticed, food intake is improvised without dedicating time to preparing healthier foods.^{29,30,33,35}

ADHD, obesity, anxiety, and depression

There are psychiatric disorders that are singularly frequent among people with ADHD, which may be due to dysexecutive syndrome, to the cardinal symptoms of ADHD, or to functional deficits and affective reactions secondary to the difficulty of adjusting to academic, occupational, and social settings. These disorders include mainly unipolar depression, dysthymia, and anxiety-phobic states, as well as many impulse control disorders and addictions.^{36,37} On the other hand, regardless of ADHD, obesity, mood disorders, and anxiety correlate strongly and there is evidence of bidirectional causality: an anxiety disorder can be either the origin or the consequence of obesity. What is new is the suggestion that ADHD might operate in this old association as a causal factor, or at least as an aggravant.³⁸⁻⁴⁰

Sleep disorders

Obesity causes respiratory abnormalities during sleep, such as apnea pauses. It is known that sleep apnea syndrome (SAS) produces symptoms similar to those of ADHD.^{10,38} Daytime drowsiness and diminished alertness

have been associated with three characteristic symptoms: irritability (which may be confused with motor restlessness), mental restlessness, and inattention.^{38,41} A study in adults with SAS proved that ADHD was not more frequent in those with SAS than in controls, but did not address the obesity factor, which is the most common cause of SAS in adults. When ADHD and SAS coexisted, the mental complaints were more severe than when only SAS was present.⁴² After a systematic review of publications up until 2011, it was concluded that 95% of patients with SAS have a symptomatic attention deficit, that there is a higher incidence of SAS in adults with ADHD (20%-30%), that SAS aggravates the symptoms of ADHD in that subgroup, and that the treatment of SAS improves ADHD symptoms at the pathophysiological level while the treatment of ADHD only sometimes improves SAS symptoms.⁴³ As the triple association of ADHD with SAS and obesity has not been well studied, the question remains open. In 2007, Samuele Cortese recommended that genuine ADHD should be suspected in adolescents with obesity and daytime drowsiness because it has not been rigorously shown that this inattention is due only to the effects of breathing disorders during sleep.^{44,45} There is also evidence that poor sleep (in quantity or quality) causes obesity.⁴⁶ As untreated ADHD correlates closely with dyssomnia and parasomnia, we could explain the association between ADHD and obesity using a chronobiological hypothesis.⁴⁷

Neurobiological link between obesity and ADHD

MC4-R is a 332-amino-acid protein encoded by a gene located on the single 18q exon of chromosome 22. A family study and two case reports suggest an association between mutations of this gene and ADHD.⁴⁸⁻⁵⁰ The MC4-R deficit has been linked to an alteration in the neuronal pathways that regulate hunger and satiety, and occurs in some abnormal eating behaviors.⁴⁸ Obese people homozygous for the MCR-4 gene mutation have a higher prevalence of ADHD, but not those who are heterozygous.⁴⁸

Brain-derived neurotrophic factor (BDNF) has been linked to the presence of ADHD and obesity.¹⁰ Studies in mice in which BDNF expression has been reduced or abolished reveal a phenotype of obesity, hyperphagia, and hyperactivity.⁵¹⁻⁵³ The case of a child with severe obesity, hyperactivity, and inversion *de novo* in the gene encoding BDNF has been reported.⁵⁴ Three children with obesity, ADHD, and low intellectual performance had microdeletions of the 11p14.1 chromosome that affected the gene expression of BDNF,⁵⁵ but it is unlikely that isolated alleles in such small case series explain the connection between BDNF and ADHD.⁵⁶

We would like to point out a study of genes associated simultaneously with ADHD and increased BMI in which 32 obesity alleles were compared with ADHD alleles isolated in

another study.⁵⁷ Two common alleles (suggesting polygenism) were identified, one corresponding to the NUDT3 region, which is linked to the family of proteins that protect against nucleotide damage; the other allele was located in the GPRC5B region and is expressed in 25% of the protein sequence of the metabotropic glutamate receptors.⁵⁷ Rare copy number variations (CNV) present in various subtypes of metabotropic receptors have also been associated with ADHD.⁵⁸ These findings open a promising field of research into the connections between glutamatergic transmission, obesity, and ADHD, as glutamate is the main excitatory neurotransmitter in the central nervous system and influences synaptic plasticity, neurodevelopment, learning, memory, motor activity, and the functional connection of cortical and subcortical dopaminergic circuits.

FOOD ADDICTION

People with ADHD and people with obesity share the neurobiological substrate that predisposes to addictions.⁵⁹ "Reward deficiency syndrome" is a model that explains the association observed between hypofunctional dopaminergic transmission and disorders involving intolerance of delayed gratification (or the search for immediate gratification).^{23,24,60} It is seen in people with severe obesity, particularly those who exhibit binge eating or extreme cravings for tasty foods.^{25,26}

Variations in the dopamine levels of the basal ganglia of obese subjects submitted to delays in food rewards and re-exposure have been found that are equivalent to those found in substance abusers.²⁷ The inverse correlation between the number of striatal dopamine D2 receptors and the BMI of obese people has been described, this pattern being analogous to that of those addicted to substances.²⁷ It is suspected that genes are shared by the three conditions: obesity, ADHD, and addiction.²⁸

Tasty foods (fatty, sugary, and salty) provide quick reinforcement and in the course of a scant two centuries have become inexpensive and easy to obtain and prepare. This has occurred in the context of a food culture of excess for which *Homo sapiens* is not genetically equipped due to its phylogeny as a foraging and hunting primate in environments of scarcity and cyclical famine (farming and livestock raising are acquired skills that are too recent to have left much of a genetic fingerprint, having appeared about 7000 years ago, and the addictive short-chain sugars only became abundant in the last five centuries).⁶¹ From this vantage point, ADHD seems to be an evolutionary remnant of remote times when it was advantageous to the carriers of its genes, by favoring more efficient foraging of disperse and scarce foodstuffs.⁶² Given feeding patterns in the present, which are based on rapidly satisfying appetite and abundant foods, this phenotype favors food addiction by

seeking immediate gratification and results in excess weight and obesity.⁶³ *Snacks, fast food or junk food*, and portable drinks (with high density sugar or caffeine content) activate cortico-subcortical reinforcement and pleasure circuits independently of the perception of hunger, without activating social attachment and the daily relational exercise of sharing meals. In support of this perspective, it has been demonstrated at the molecular and neuroanatomical level using neurochemical techniques, functional neuroimaging, and animal studies that these foodstuffs function as classic addictive substances like cocaine and heroin, with which neurobehavioral cross-sensitization occurs.⁶³⁻⁶⁶

People with ADHD are more predisposed to addictions. People with morbid obesity also sometimes develop severe *de novo* "cross addiction" to illegal substances after successful bariatric surgery. It is suspected that neuronal cross-sensitization exists between intermittent intake of sugars and other addictive substances, which is comparable to what has already been described during the alternating use of conventional drugs, such as alcohol, and opiates.^{63,64}

THERAPEUTIC IMPLICATIONS

There is evidence that treating ADHD in childhood prevents the development of excess weight, obesity and substance addiction in adulthood.^{12,13,67} When ADHD is detected in obese individuals, it is possible that treatments that improve ADHD optimize the results of treatment of obesity.^{68,69} The first recommendation is to prevent the occurrence of excess weight and EDs in the population of young people diagnosed with ADHD, and also to methodically search for psychopathology in children and adolescents with obesity. In adults with severe obesity and obesity resistant to conventional treatments, it is recommended that ADHD be sought using age-appropriate methods after a differential diagnosis of other causes of inattention and impulsivity: bipolar spectrum disorders, eating disorders, addictions, SAS, endocrine pathology, etc.^{22,68-70}

The first therapeutic step in idiopathic obesity is dietary and psychoeducational. Drug therapy is the second step and has yet to demonstrate its long-term effectiveness, although studies of the topic have been expanded and several drugs are about to be marketed.⁷¹ In 2009, a Canadian team measured the BMI change in 78 adults who had been diagnosed with ADHD during the routine screening of 242 consecutive cases of severe refractory obesity.⁷⁰ SAS was present in 56.4% of the sample, compulsive eating in 65%, and mood disorder in 88.4%. Once the comorbid conditions were resolved, treatment of ADHD with methylphenidate was proposed: 65 candidates accepted and the 13 who did not accept acted as controls. At the end, the mean variation from the initial weight was a loss of -10.35% in the treated group and a gain of +7.03% in the controls ($P < 0.001$). Two

conclusions of the study were, firstly, that ADHD should be considered the main cause of treatment failure in adults with severe obesity, as studies in candidates for bariatric surgery had already indicated; secondly, long-term improvement in weight cannot be attributed solely, or mainly, to the anorectic effect of methylphenidate because this side effect fades in a few months, while patients continue to lose weight or maintain the loss achieved without rebound 16 months later. Healthy habits improve as the cardinal symptoms of ADHD remit, resulting in improved self-direction, persistence, and resistance to distraction due to the new, improved management of the order and timing of meals, more ability to resist impulses (less bingeing); more efficient executive function makes it possible to comply with diet and initiate lasting changes.^{10,69}

Other authors suggest that methylphenidate prevents obesity and EDs because it reduces stress and fatigue due to executive overexertion, which otherwise tend to be relieved by overeating. Methylphenidate, by potentiating the mesocortical dopaminergic pathways that prioritize the activation of optimal brain networks for specific goals, prevents the inefficient dispersion of activations and the accelerated use of glucose reserves, which makes sugar craving and binge eating less likely (two experiences that, if repeated too often, can "condition" behaviors that could become set in an addictive pattern).⁷²

CONCLUSIONS

There is evidence that in a subset of cases obesity is directly favored and aggravated by untreated ADHD. The association between ADHD and obesity appears to be demonstrated, being stronger at higher BMI. Upon investigating the common causes of ADHD and obesity, we delve into the study of something that is at the core of the human condition: the *management of eating* and the *management of knowing how to act*, two complementary skills that ensure our survival as primates endowed with a powerful "social brain."

ADHD is a disorder with three cardinal symptoms (inattention, impulsivity, and hyperactivity), comorbid symptoms (depression, anxiety, addictions, sleep disorders, eating behavior disorders...), and typical psychosocial complications (conflictive relations, demoralization, poor academic performance...). Alone or together, these symptom clusters have been shown to be risk factors for obesity and converge into a final common pathway with other biological, psychological, and social factors. This condition can lead to obesity or contribute in large measure to its occurrence, either because, as a disorder of executive function, it causes a disorganized life style prone to uncontrolled eating, or because the anxiety and depression secondary to ADHD lead the patient to use food as a substitute and as an anxiety-relieving satisfaction, as in other EDs. Although compulsive

eating is common in people with ADHD who have obesity, binge eating is not a necessary or sufficient condition for the concurrence of ADHD and obesity.

ADHD involves an inherent neurobiological predisposition to addictions. If it is accepted that ADHD has a substrate of dopaminergic dysregulation, it is plausible that the reinforcement, gratification, and pleasure circuits are also affected. Thus, "tasty" meals (with more fats and sugars) could act as authentic addictive substances. This view allowed the repurposing of pharmacological (opioid antagonists, dopamine modulators, etc.) and psychosocial (self-help groups, "motivational interviewing" techniques, family therapy, etc.) therapies that were invented for the treatment of alcoholism and other addictions.

The concurrent presentation of ADHD and obesity requires specific therapeutic programs, especially in the case of obese adults who have been too long exposed to the frustrating experience of an undiagnosed ADHD and need to improve their self-esteem in order to successfully tackle obesity therapy.

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