

## Comorbidity of Attention Deficit and Hyperactivity Disorder and Obesity: A Systematic Review

*Dikkat Eksikliği Hiperaktivite Bozukluğu ve Obezite Birlikteliği: Bir Sistematik Gözden Geçirme*

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### Abstract

In this review, systematical evaluation of potential relationship between attention deficit hyperactivity disorder (ADHD) and obesity is aimed. Based on DSM-IV or DSM-5 criteria, written in English and/or Turkish except the case reports, systematic reviews and meta-analysis published in the Pubmed database between January 1990 and December 2017 are included in the study. Evidence based on empirical analysis suggests that subjects with ADHD are heavier than expected. Moreover, nearly all reviewed studies indicate that the prevalence of ADHD in obese patients, especially those treated in obesity clinics, may be higher than expected. Future studies will be useful in regulating the health policies and increasing the quality of life for ADHD and obesity, both of which are high-risk morbidity.

**Keywords:** ADHD, impulsivity, obesity.

### Öz

Bu çalışmada dikkat eksikliği hiperaktivite bozukluğu (DEHB) ve obezite arasındaki potansiyel ilişkinin, sistematik olarak incelenmesi amaçlanmıştır. Bu amaçla DSM-IV ya da DSM-5 ölçütleri esas alınarak İngilizce ve/veya Türkçe olarak yazılmış, Pubmed veri tabanında Ocak 1990-Aralık 2017 tarihleri arasında yayımlanan, olgu sunumları, sistematik derlemeler ile meta-analizler dışında kalan makalelerden tam metnine ulaşılabilenler çalışmaya dahil edilmiştir. Ampirik olarak elde edilen kanıtlar, DEHB tanımlı olguların beden ağırlıklarının beklenenden daha ağır olduğunu göstermektedir. Ayrıca, gözden geçirilmiş çalışmaların tamamına yakını özellikle obezite kliniklerinde tedavi gören obez hastaların DEHB prevalansının da beklenenden daha yüksek olabileceğini düşündürmektedir. İleride yapılacak çalışmalar, her ikisi de morbidite riski yüksek tanılar olan DEHB ve obezite için gerekli sağlık politikalarının düzenlenmesi ve bu olguların yaşam kalitelerinin artırılması açısından yararlı olacaktır.

**Anahtar sözcükler:** DEHB, dürtüsellik, obezite.

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**ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)** is one of the most common neuropsychiatric disorders of childhood, which is characterized by inattention, hyperactivity and impulsivity symptoms starting in childhood and not appropriate to the age and level of development of the children (Still 1902, Pliszka 2007). ADHD is seen in 3-7% of school-age children based on the American Psychiatric Association (APA) data (APA 1994, Pliszka 2007). In two highly comprehensive meta-analysis studies conducted in the recent years, the average prevalence of ADHD among the whole world was found to be between 5.9-7.1% and 2.6-4.5% (Willcutt 2012, Polanczyk et al. 2015). It has been demonstrated that the clinical symptoms of ADHD are in two dimensions as "Attention deficit" and "Hyperactivity-impulsivity". The attention deficit is often characterized by symptoms such as being unable to concentrate with short-span of attention, difficulty in attention to detail, many carelessness errors, difficulty in giving attention to any obligatory activity, difficulty in completing the task, difficulty in owning the belongings and being very forgetfulness whereas hyperactivity presents itself as restlessness, not be able to staying with calm, continuously playing with his hands or feet, not sitting in the same place for a long time, climbing everywhere especially in childhood and, having difficulties in silently playing or having fun, and talking too much. Impulsivity includes a group of signs of urgency, impatience, ignoring rules, acting or talking without thinking, intruding to conversations, seeking novelty and preferring risky behaviors (Mukaddes 2015).

Obesity has become a national health problem in our country like all over the world because of its increasing frequency and diseases accompanying with it. Overweight and obesity are defined by the World Health Organization (WHO) as abnormal or excessive fat accumulation that may impair health (WHO 2014). In order to clinically identify obesity, Body mass index (BMI) obtained by the ratio of weight to the height square ( $\text{kg}/\text{m}^2$ ) is used. According to the international classification based on BMI adopted by WHO and various European epidemiologists with minor changes, the BMI was defined for adult age group as the following; It is overweight when it is between 25.0-29.9; Stage I obesity as it between 30.0-34.9; Stage II obesity as 35.0-39.9; and stage III obesity when it is  $\geq 40$  as (WHO 1997). BMI for children and adolescents is age- and gender-specific and is usually referred to as BMI for age. According to the Centers for Disease Control and Prevention (CDC), in children and adolescents of the same age and gender, having a BMI of 95 percentile and over is defined as "childhood obesity" and being between 85-94 percent of childhood as "overweight" (Ogden and Flegal 2010). In addition, in a longitudinal study that lasted for eight years between 9-16 years of age, "childhood obesity" term was used for children who were obese in childhood but had normal weight when in their adolescence ages (12 years) and "adolescence obesity" was defined for adolescents whose weight was normal when they were children. "Chronic obesity" term was utilized for children those who had obese (weighted regularly in each year) throughout the study period (Mustillo et al. 2003). The National Health and Nutrition Examination Survey (NHANES), which investigated the prevalence of obesity in children and adolescents aged with 2-19 years between 2003 to 2006, was reported 16.3% of children and adolescents to be obese (Ogden et al. 2008). A preliminary study report conducted in our country titled with "Turkey Nutrition and Health Survey-2010" revealed that the proportion of overweight was 34.6%, the proportion of overweight and obese was 64.9%, and morbidly obese patients was found to be 2.9%. In

addition, the rate of children who are overweight in the 6-18 age group was 14.3%, and the rate of those who are overweight and obese was 22.5% (Ministry of Health 2010).

A number of studies have reported a significant association between obesity and ADHD, but others failed to confirm these findings (Cortese et al. 2015). The default relationship between ADHD and obesity might seem paradoxical because, rather than being hyperactive, individuals with obesity are often described as lazy. However, it is reported that ADHD, characterized by impulsivity and inattention, may lead to dysregulated eating patterns with consequent weight gain (Cortese et al. 2014). Obesity and ADHD are common pathologies, so if there is a relationship between the two disorders, understanding this will be of great importance for both academic and clinical studies as well as preventive medicine. In this review, it is aimed to review the researches conducted in order to evaluate the possible relationship between ADHD and obesity/overweight status and to systematically examine the data obtained from these studies.

## Method

To evaluate the relationship between ADHD and obesity, studies evaluating the weight status of individuals with ADHD and evaluating the prevalence of ADHD in obese patients were investigated. For this purpose, 'ADHD', 'Attention deficit hyperactivity disorder', 'inattentive', 'hyperactivity', 'impulsivity', 'obesity' and 'overweight' keywords were scanned in a variety of combinations using PubMed medium. Case reports, systematic review and meta-analyzes were not taken into account. Studies for both children and adults have been included.

According to PubMed database research (January 1990-December 2017) the numbers of the results were the following; ADHD and obesity: 136 references; attention deficit hyperactivity and obesity: 133 references; inattention and obesity: 2 references; hyperactivity and obesity: 212 references; impulsivity and obesity: 222 references; ADHD and overweight: 63 references; attention deficit hyperactivity and overweight: 67 references; inattention and overweight: 1 reference; hyperactivity and overweight: 110 references; impulsivity and overweight: 163 references. As a result of the screening, a total of 1,109 studies were achieved. A total of 1,059 studies, which were examined according to the headings and excluded from this study of 976 studies because of having not related context, of 72 study in different languages and of 11 systematic review-meta-analysis studies. Of the remaining 50 studies, 14 were found to be identical studies from different keyword scans. Consequently, a total of 36 studies were included in the study (Figure 1).

## Results

Among the 36 studies included in our systematic review, 24 of them evaluated the weight status of individuals with ADHD and 12 evaluated the prevalence of ADHD in obese patients. The studies in our systematic review are as follows:



**Figure 1. Algorithm of the studies included in this study**

### *Studies Assessing the Weight Status of Individuals with ADHD*

In this field, the study conducted by Spencer et al. (1996) was the very first study and it evaluated the height and weight of 124 male and adolescent and 109 normal control groups diagnosed with ADHD (diagnosed according to DSMIII-R criteria) between the ages of 6-17. In this study, it was stated that 89% of the patients received pharmacological treatment in their lives for a while including stimulants, 53 of them received stimulants (may have anorexigenic effects), while 66 patients did not receive any stimulant treatment in the last two years. Although the mean BMI of the patients with ADHD was higher than the controls (age- and height-corrected weight index:  $109 \pm 15$ ), there was no significant difference between ADHD and control group according to age and height-adjusted weight indices. Age and height-adjusted weight index of the untreated ADHD patients were found to be 115. However, this result should be considered with caution when considering a limited number of untreated cases ( $N = 13$ ) and the initial (prior to treatment) height and weight are not present. While some psychotropic agents may have anorexigenic effects, age- and height-adjusted weight indices of untreated ADHD cases may be significantly higher than the baseline controls. The authors did not report the effects of psychiatric comorbid disorders (such as depressive disorders) on age- and height-adjusted weight index. In another similar study (Biederman et al. 2003), weights and height of 140 girls diagnosed with ADHD and 122 control groups aged 6-17 years were compared. While the values of the patients diagnosed with ADHD were above average (although not indicative of overweight or obesity), no significant difference was found between the ADHD and the control group in the treated and untreated cases. Interestingly, age and height-corrected weight index were significantly higher in patients with major depression (MD) associated with ADHD than those without MD (for MD  $N = 21$ ,  $126 \pm 31,3$  vs. not MD  $N = 103$ ,  $109 \pm 25.7$ ;  $p = 0.011$ ).

**Table 1. Weight studies of subjects with ADHD**

Author (s), Year	Sample	Age ( $\pm$ SD)	Main outcome
Spencer et al. (1996)	124 male ADHD, 109 control	6-17 years	BMI levels of ADHD higher than controls (age- and height-corrected weight index: $109 \pm 15$ ); but there was no difference between ADHD and controls.
Biederman et al. (2003)	140 female ADHD, 122 control	6-17 years	Age-corrected weight index was higher although it was not point out obesity or overweight (1.1). ADHD with Major depression (MD) had higher age-corrected weight indices than that of ADHD without MD aptanmıştır ( $p=0.011$ ).
Holtkamp et al. (2004)	97 ADHD	10 ( $\pm 2$ ) years	Mean BMI of ADHD was higher than age-corrected references ( $p=0.038$ ). Obesity (7.2%) and overweight (19.6%) rates were higher than that of same-age population samples' obesity or overweight rates ( $p=0.0008$ and $p=0.0075$ , respectively).
Farone et al. (2005)	568 ADHD	6-12 years	Basal weight levels were higher than normality scores (BMI z score 0.41).
Hubel et al. (2006)	39 male ADHD, 30 control	8-14 years	Mean BMI value of ADHD was higher than controls ( $0.29 \pm 1.01$ vs. $0.05 \pm 0.94$ ).
Anderson et al. (2006)	655 cases (general population)	<16.6 years	Mean BMI was higher in ADHD for all age groups than that of subjects with no any disruptive behavior disorder ( $0.21$ (%95 CI, $0.07-0.35$ )).
Spencer et al. (2006)	178 OROS MPH treatment of ADHD cases	6-13 years	Weights of subjects were slightly higher than that of what was expected.
Swanson et al. (2006)	140 ADHD	3-5.5 years	Mean BMI value was 16.9 (86 percentile).
Lam and Yang (2007)	1,429 cases (general population)	13-17 years	Obesity risk was higher in subjects with had high-risk for ADHD as 1.4 times than that of subjects with had low-risk for ADHD.
Pagoto (2009)	6,735 cases (general population)	18-44 years	Obesity was higher in adult with ADHD (29.4%) than those who had ADHD in childhood but not adulthood (23.7%) and both were higher than subjects with no ADHD history (21.6%).
De Zwaan (2011)	1.633 cases	18-64 years	Obesity risk in ADHD was higher twice (22.1%) compared to the general population (10.2%).
Yang et al. (2013)	158 ADHD children or adolescents	9.2 ( $\pm 2$ ) 6-16 years	Obesity was 12%, overweight was 17.1% (higher than that of population as 2.1% and 4.5%). Risk was higher in combined-ADHD and with ADHD of adolescence-beginning.
Cortese et al. (2013a)	Total=34,653 Lifetime ADHD=616, Persistent ADHD=340, Treated ADHD=276, Not-ADHD=34,037	>20 years	Obesity rates and BMI values were significantly higher in adults with persistent ADHD compared to the not-ADHD subjects (obesity: OR=1.44, %95 CI=1.06-1.95; BMI: $p=0.015$ ).
Cortese et al. (2013b)	Childhood ADHD=111, No-ADHD in childhood=111, ADHD persistent=24, ADHD treated=87	>20 years	Males diagnosed with ADHD when they were children had risk for obesity two times than that of no-ADHD (41.4% vs. 21.6%, $p=0.001$ ).
Fliers et al.	372 ADHD	5-17 years	Male ADHD aged 10-17 years and female ADHD

(2013)			aged 10-12 years, had heavier than that of general Netherlands population with girls had lower risk of being overweight.
Pauli Pott et al. (2014)	144 pure ADHD, 63 ADHD+ODD/CD, 50 pure ODD/CD, 103 control	6-12 years	Obesity rates was the following, 5.7%, 11.8%, 11.5% and 3.9%, respectively. ODD/CD associated with higher impulsivity, addictive behavior, psychosocial stress.
Turkoglu et al. (2015)	300 ADHD, 75 control	10.1 ( $\pm$ 2.5) 7-17 years	Being overweight and/or obese was higher in ADHD compared to the controls ( $p<0.001$ ).
Ozcan et al. (2015)	30 ADHD, 40 control	9.3 ( $\pm$ 1.78)	Being overweight or obese in ADHD group was 30% whereas it was 10% in controls.
Hanc et al. (2015a)	215 ADHD, 396 control	6-18 years	ADHD was related with increased overweight rate (un-adjusted OR=2.31, 95%CI=1.40-3.81, $p=0.001$ ).
Hanc et al. (2015b)	212 ADHD, 308 control	6-18 years	At 2-year-old (retrospective analysis), children with ADHD had lower weight/obesity (ADHD 10.71%, control 20.13%, $p=0.02$ ). At 6-year-old (retrospective analysis), children with ADHD had more lower weight (8.93% vs. 3.25%, $p=0.02$ ).
Racicka et al. (2015)	408 ADHD	7-18 years	Overweight (14.81% vs. 12.83%, $p<0.001$ ) and obesity (6.3%, 9.45, $p<0.001$ ) in ADHD was higher than general population counterparts.
Güngör et al. (2016)	362 ADHD, 390 control	5-15 years	Obesity and overweight rates of ADHD subjects were higher than that of controls (24.8% vs. 18.9%, $p<0.0001$ ).
Kummer et al. (2016)	23 ADHD, 19 Control	ADHD 8.5 ( $\pm$ 2.4) Control 8.6 ( $\pm$ 2.9)	The frequency of obesity and being overweight in ADHD was significantly higher than the controls ( $p=0.04$ ).
Aguirre Castenada et al. (2016)	336 ADHD, 665 Control. BMI data obtained after 20 years later: ADHD=285, Control=450	ADHD 26.4 ( $\pm$ 5.7) Control 23.4 ( $\pm$ 7.1)	Obesity risk higher in ADHD than that of control at 1.23 times (95% CI=1.00-1.50; $p<0.05$ ). 20-year-follow-up, obesity rate was 34.4% in ADHD and 25.1% in control ( $p=0.01$ ). Stimulants treatment did not effect the outcomes.

SD: Standard deviation, ADHD: Attention deficit hyperactivity disorder, MPH: methylphenidate, BMI: Body-mass index, OR: odds ratio

In a study conducted in Germany (Holtkamp et al. 2004), it was found that the mean BMI of 97 children with ADHD (based on DSM-IV criteria) were significantly higher than the 97 children who were treated inpatient or outpatient clinics according to the age-matched reference values ( $p = 0.038$ ). In addition, the rate of obese (7.2%) and overweight (19.6%) cases was significantly higher in the same age group than the prevalence of obese and overweight in the German population ( $p = 0.0008$  and  $p = 0.0075$ , respectively). The presence of somatic, neurological and psychiatric disorders (such as depression) and the use of anorexigenic drugs apart from methylphenidate (MPH) were determined as exclusion criteria for the study. Only conduct disorder (CD) was accepted as a psychiatric comorbidity (57.7% of the participants) and nonetheless, there was no significant difference in the mean BMI standard deviation scores (SD) between participants with and without CD. In addition, 14.4% of the patients were treated with MPH for an average of five months (they may have anorexigenic effects), but no significant difference was found between participants who did not and did not use drugs. As stated by the authors, only the clinical sample and the use of male

gender, the socioeconomic status and the BMI of the parents were not controlled as they were this study's limitations. In another study of 568 patients aged 6-12 and with ADHD (Farone et al. 2005), the basal measurements were found to be more severe than the average (BMI z score 0.41). Hubel et al. (2006) compared 39 patients diagnosed with ADHD according to DSM-IV and 30 healthy controls between the ages of 8-14 years. In the study, non-CD comorbidities were excluded. 24 of the ADHD cases were combined-subtype and 15 of them were hyperactive-impulsive type. It was found that BMI was higher in patients with ADHD than that of control group ( $0.29 \pm 1.01$  and  $0.05 \pm 0.94$ , respectively), and this difference became more evident as the age increased. No difference was found between ADHD subtypes. In addition, the rate of obese and overweight in the ADHD group (17.95% and 7.69%, respectively) was similar to that of Holtkamp et al. (2004). In a prospective study conducted by Anderson et al. (2006) with 655 cases younger than 16.6 years, psychiatric disorders were assessed by a structured diagnostic interview with parents and participants according to DSM-III-R (APA, 1987) criteria applied separately by trained interviewers and BMIs were obtained using CDC's BMI table for age range reference. In this study, the mean BMI values of all ages were higher in subjects with ADHD than in patients without any disruptive behavior disorder (DBD) (0,21 (95% CI, 0.07-0.35)). The results were not significantly changed after ADHD, Oppositional defiant disorder (ODD), and CD were evaluated separately or after those using drugs were excluded.

Three studies investigating the effects of stimulants on growth in children with ADHD (Faraone et al. 2005; Spencer et al. 2006; Swanson et al. 2006) found that baseline BMI z-score of patients with ADHD was  $> 0$ , indicating that the cases were more severe than expected. However, these studies did not provide information about psychiatric comorbid disorders (such as depressive disorders) which may affect obesity prevalence and BMI in children with ADHD. In a larger population survey, Lam and Yang (2007) investigated the potential relationship between ADHD and overweight /obesity in a sample of 1,429 students aged with 13-17 years. ADHD diagnosis was determined according to DSM-IV (APA, 1994) criteria, however, given the number of participants, structured interviews were only given to students and no information was received from parents or teachers. Therefore, rather than the clinical diagnosis of ADHD, a 'predisposition to ADHD' has been mentioned. It was found that patients with high tendency to ADHD tend have a 1.4-fold higher risk of obesity than those with low tendency to ADHD. As in the aforementioned studies, the effect of potentially comorbid psychiatric disorders in this study has not been controlled.

**Table 2. Prevalance studies of ADHD in subject with overweight/obese**

Author (s), Year	Samples	Age ( $\pm$ SD)	Main outcome
Altfas et al. (2002)	215 obese adults, bariatric surgery clinics	43.9 ( $\pm$ 10.9)	ADHD prevalence in obese adults was 27.4%, grade III obesity with ADHD rate (42.6%) was higher than that of grade I-II obesity and overweight groups (22.8% and 18.9%) ( $p=0.002$ ).
Mustillo et al. (2003)	991 cases, general pediatric population	9-16 years	ADHD was not related with any type of obesity (not-obese, childhood obesity, adolescence obesity, or chronic obesity).
Eremis et al. (2004)	30 obese, 30 control Clinical and Non-clinical samples	13.8 ( $\pm$ 2.0)	Clinically obese subjects had higher ADHD rate (13.3%) compared to other groups (3.3% and 3.3%).

Fleming et al. (2005)	75 adults obese women	40.4 ( $\pm$ 10.8)	Wender Utah Rating scales ADHD cut-off was 38.6%, this rate was higher than normal population ( $p < 0.001$ ).
Agranat-Meged et al. (2005)	26 obese children, eating disorders unit	13.04 ( $\pm$ 2.78)	ADHD rates in obese children were higher compared to their population counterparts (57.7% vs. 10%, $p < 0.0001$ ).
Rojo et al. (2006)	35,403 participants 2,879 obese, 78 morbid obese, population-based study	13-15 years	Morbid obese males and females had higher inattention/hyperactivity symptoms but they were not statistically significant.
Braet et al. (2007)	65 overweight children (clinic), 53 healthy controls	10-18 years	Overweight children had higher impulsivity, inattention and hyperactivity scores in some tests but ADHD prevalence not high.
Gruss et al. (2012)	124 morbid obese adults, prebariatric surgery clinics	38.6 ( $\pm$ 10.5)	Adult ADHD rate was 12.1%, higher than normal population but there was no difference in comparison with morbid obese population (14.3%).
Alfonsson et al. (2012)	187 adults, bariatric surgery clinics	41.04 ( $\pm$ 11.07)	10% of adults had ADHD positive and ADHD symptoms were correlated with anxiety, depression and irregular feeding.
Halfon et al. (2013)	43,297 cases	10-17 years	Obese children with no stimulant medication had more ADHD diagnosis than with normal weight counterparts (OR=1.93, %95 CI 1.26-2.94; aOR 1.85, % 95CI 1.18-2.92).
Pe´rez Bonaventura et al. (2015)	Longitudinal design; 3 age $\rightarrow$ 611 cases 4 age $\rightarrow$ 596 cases 5 age $\rightarrow$ 564 cases	All subjects were tested at 3, 4 and 5 years of age	Increased BMI at 3rd years old was associated with hyperactivity, peer relational issue, higher ADHD in their 4; increased BMI at 4th was related with ADHD; increased BMI at 5th was related with peer relation problems.
Colpan et al. (2018)	49 obese adolescents 47 controls	Obese 14 ( $\pm$ 3) Control 15 ( $\pm$ 3)	Perceived mood expression, emotional and behavioral problems, inattention, hyperactivity, peer relation problems, social skills were more effected in obese adolescents than that of control ( $p < 0.001$ ).

SD: Standard deviation, ADHD: Attention deficit hyperactivity disorder, BMI: Body-mass index, OR: odds ratio, aOR: adjusted odds ratio

In a study conducted with 6,735 patients from general population between the ages of 18-44 (Pagoto et al. 2009), obesity was higher in adult ADHD patients (29.4%) than that of those who had still no ADHD but had in their childhood (23.7%) and both cases were higher than those without ADHD (21.6%). In a study conducted with 1,633 adults in Germany, the prevalence of ADHD was found to be 9.3% in obese individuals, and no such high prevalence was observed in overweight (3.8%) and normal weight (4.3%) individuals. The risk of being obese was reported to be doubled in participants with ADHD (22.1%) compared to the general population (10.2%). In another study with 158 children aged 6-16 years and with ADHD (Yang et al. 2013), the prevalence of obesity was higher in patients with ADHD and those who have ADHD-combined subtype was found to be more obese or overweight than that of ADHD-inattention or ADHD-hyperactive-impulsive subtypes.

In a study conducted by Cortese et al. (2013a), one of the largest population-based studies showing the relationship between ADHD and obesity, obesity rates and BMI values were found to be significantly higher in adults with persistent ADHD than in those with persistent ADHD (obesity: OR = 1.44, 95% CI = 1.06- 1.95; BMI:  $p = 0.015$ ). Obesity rates were not significantly higher in adults with lifetime ADHD than

those without ADHD. There was no significant relationship between persistent, life-long or improved ADHD and obesity in the corrected model for sociodemographic factors and psychiatric comorbidities. In the same study, the number of ADHD symptoms in childhood and the presence of obesity in adulthood were significantly associated only with women. This study was extended as a longitudinal study (Cortese et al. 2013b) and it was found that the risk of obesity was twice as high in men with ADHD as childhood (41.4%, 21.6%;  $p = 0.001$ , respectively). In a study conducted with 372 ADHD children in the Netherlands (Fliers et al. 2013), it was reported that boys aged 10-17 years with ADHD and girls aged 10-12 years with ADHD were more heavier than Netherlands population with the result of girls were found to have a lower risk of being overweight. Pauli-Pott et al. (2014) reported obesity rates in 144 children of pure ADHD, 63 of ADHD plus ODD/CD, 50 of pure ODD/CD and 103 of controls, as 5.7%, 11.8%, 11.5% and 3.9%, respectively).

ODD/CD were associated with increased impulsivity, addiction behavior and psychosocial stress. Turkoglu et al. (2015) found that the rate of being overweight and obese was significantly higher in the 300 children with ADHD compared to 75 controls, aged with 7-17 years. Conners' Parenting Rating Scale (CPRS) inattention and behavior subscales were also found to be predictors of BMI elevation. Özcan et al. (2015) studied with 30 ADHD and 40 healthy controls (mean age  $9.3 \pm 1.78$ ) and being overweight and /or obese was found in the ADHD group as 30% whereas 10% in the control group. In a study conducted in 2015 by Hanc et al. (2015a), ADHD was associated with an increased rate of overweight (uncorrected OR = 2.31, 95% CI = 1.40-3.81,  $p = 0.001$ ). In a retrospective analysis conducted by the same author (Hanc et al. 2015b), the data of this study were 2 years old children with ADHD were less overweight/obese than the control group (ADHD 10.71%, control group 20.13%,  $p = 0.02$ ) and when they were 6, children with ADHD were less overweight than those without ADHD (8.93%, 3.25%,  $p = 0.02$ , respectively). In a study conducted by Racicka et al. (2015) with 408 ADHD patients, overweight (14.81% vs. 12.83%,  $p < 0.001$ ) and obese (6.3% vs. 3.45%,  $p < 0.001$ ) was significantly higher in children with ADHD than in the general population.

In the study performed by Gungor et al. (2016) with 362 ADHD and 390 controls between the ages of 5 and 15, both malnutrition and obesity rates were significantly higher in the ADHD group. In ADHD group, the rate of being overweight was found to be 9.4% and the rate of being obese was 7.1% and these rates were significantly higher than the control group (1.5% and 0.2%, respectively). Kummer et al. (2016) studied with 23 ADHD and 19 controls and found that the prevalence of overweight and obese patients with ADHD was significantly higher than that of controls ( $p = 0.04$ ).

Finally, in a longitudinal study investigating the relationship between ADHD and obesity (Aguirre Castenada et al. 2016), the risk of obesity was found to be 1.27 times higher in the patients with ADHD than in controls (95% CI = 1.00-1.50,  $p < 0.05$ ). In 20 years of follow-up, 34.4% of ADHD cases and 25.1% of controls were obese ( $p = 0.01$ ) and only girl gender was reported to be significantly related to ADHD and obesity. Stimulant use did not significantly affect the results (Table 1).

### *Studies Evaluating the Prevalence of ADHD in Obese Individuals*

The first study investigating the prevalence of ADHD in obese subjects was performed by Altfas et al. (2002). In this study, the prevalence of ADHD was found to be 27.4% in obese adults, and the grade III obesity (42.6%) was significantly higher in patients with ADHD than in those with grade I-II obesity and overweight (22.8% and 18.9%,  $p = 0.002$ ). In addition, patients with ADHD had significantly higher BMI than those without ADHD (39.2 and 34.6,  $p = 0.01$ , respectively). Weight loss was reported to be higher in obese adults treated with ADHD. The lack of a control group (ADHD rates in obese individuals were compared with only the general population) and comorbidities such as obstructive sleep apnea, depression and anxiety disorders that they did not account for were among the limitations of the study.

In a longitudinal study conducted by Mustillo et al. In 2003, ADHD diagnosis was not associated with any obesity status (obesity, childhood obesity, adolescent obesity and chronic obesity). Considering the studies conducted in this field in our country, 30 obese adolescents and 30 healthy controls from the clinical and non-clinical sample was evaluated by Erermis et al. (2005) and ADHD rate was found significantly higher in clinically obese group as 13.3%, while 3.3% in not-clinical obese group and 3.3% in control group. In another study of 75 adult obese women (Fleming et al., 2005) was evaluated with Wender Utah Rating Scale (WURS) and 38.6% of the participants had cut-off point for ADHD and this rate was found significantly higher than 4% of normal population rate ( $p < 0.001$ ). The lack of a formal ADHD diagnosis, the absence of control of other psychiatric comorbid disorders and the lack of a control group were main limitations of the study.

In a study conducted in obese children in the eating disorder unit (Agranat-Meged et al. 2005), the rate of ADHD in obese children was significantly higher than the general population (57.7% and 10.0%, respectively,  $p < 0.0001$ ). In addition, obese patients with ADHD were reported to have predominantly inattention-symptom. A population study of 35,403 participants (Rojo et al. 2006) using Strength and Difficulties Questionnaire (SDQ) showed that there was a statistically insignificant increase in the inattention/hyperactivity symptoms of men and girls with morbid obesity compared to those with obese, overweight and normal weight. Braet et al (2007) showed in a study that children who are overweight revealed more impulsivity, hyperactivity and inattention symptoms in some tests than that of controls; however, ADHD prevalence was not high.

In a study conducted by Alfnsson et al. (2012) with 187 adult bariatric surgical patient, 10% of patients were screened positively for adult ADHD, and adult ADHD symptoms were significantly correlated with anxiety, depression, and irregular eating. Gruss et al. (2012) reported in a study of 124 morbid obese adult patients that adult ADHD rate was 12.1% and although this rate was significantly higher than the general population sample rate, there was no significant difference when compared with a group of morbid obese samples (14.3%) in the general population sample.

In a large cross-sectional study with 43,297 adolescents (Halfon et al. 2013), obese children who did not use stimulants were diagnosed with ADHD more than those with normal weight (OR = 1.93, 95% CI 1.26-2.94; OR 1.85, 95% CI 1,18-2,92). This finding was not found to be significant in obese children using stimulants. In a longitudinal study conducted in Spain (Pelarirez Bonaventura et al. 2015) revealed that increa-

sed BMI in 3-years-old age was found associated with hyperactivity, peer relationship problems, and high ADHD risk when they were 4-year-old; whereas increased BMI in 4-years-old age was associated with ADHD and increased BMI of 5-years-old children was significantly related with peer relationship problems. Finally, in a recent study conducted by Colpan et al. (2018), 49 obese patients in the adolescent age group and 47 control groups were taken. Significant differences were found between obese adolescents' perceived feelings of expression, emotional and behavioral problems, attention deficit hyperactivity disorder, peer relationship problems and social skill levels compared to the control group ( $p < 0.001$ ) (Table 2).

## Discussion

In recent years, evidence from literature indicates a two-way relationship between ADHD and obesity. Understanding the relationship between obesity and ADHD, both of which are common conditions, is very important in terms of preventive mental health and public health studies. There is increasing evidence suggesting a higher prevalence of obesity in ADHD patients. The literature data of our review shows that children with ADHD have higher BMI than expected. However, in most of the surveys in our review study, the potential impact of possible contributors, such as low socioeconomic status and comorbid psychiatric disorders, and the age, gender, pattern of study, or country of study is unclear. This situation makes generalization difficult.

A wide range of possibilities are discussed from a single explanation of the underlying mechanisms of ADHD and obesity (Cortese et al. 2011). These explanations include that 'ADHD can increase the risk of obesity', 'obesity and related factors can cause ADHD' and 'ADHD and obesity may have common behavioral and neurobiological risk factors'.

The first explanation states that ADHD can increase the risk of obesity. Impulsivity, which is present in a large subset of individuals with ADHD, is an expression of a lack of inhibitory control and can reinforce abnormal eating behaviors that may increase the likelihood of obesity (Kim et al. 2014, Ptacek et al. 2014). Especially in dopaminergic pathways in the inferior frontal cortex and anterior cingulate cortex, dysfunction-induced 'inhibition disorder' may make it difficult for an individual to control their own actions and increase unhealthy food consumption, exhibit abnormal eating behaviors (secret eating, over-eating, night-eating, binge eating) consequencing an increase in obesity. In addition, compulsive eating behaviors may also be a mechanism to compensate for the frustration associated with attention difficulties. Inattention and poor planning are reported to cause obesity by leading to regular eating habits and difficulties in adhering to the diet, lack of awareness of food intake (Schweickert et al. 1997, Davis et al. 2006). This may be due to dysfunction in executive functions due to mesocortico-limbic dopaminergic dysfunction. Inattention could reduce the organization of eating and social habits, and therefore the person may not be able to perceive internal hunger and satisfaction cues. In addition, people with ADHD may exhibit excessive eating behavior when they are not over-focused and they do not when they are over-focused, a symptom of extreme focusing on things whar are loved and not frequently needed.

Another view is that individuals with ADHD are less likely to participate in sports activities than their healthy peers, and due to reduced physical activity, the risk of developing obesity may be increased (Lingineni et al. 2012, Khalife et al. 2014, Cook et al.

2015). It can be thought that this is due to the symptoms that cause social problems such as difficulty in following the rules in regular games and activities, impatience and recklessness, all seen in ADHD. There are also studies supporting the view that common skipping and snacking in ADHD may contribute to the development of obesity in the easy-to-obtain high-calorie fast food style foods (Cortese et al. 2013). It is reported that there is a significant link between ADHD and abnormal diet style (eating junk food instead of traditional three meals). It has been shown that patients with ADHD are more likely to jump breakfast and dinner and eat more than five meals a day. It was also found that the consumption of fruits and vegetables decreased and the consumption of sugar drinks increased (Ptacek et al. 2016). Consumption of these foods, which are perceived as small but rapid rewards, and directed towards impulsive eating behaviors, can be considered as a behavior similar to self-medication behavior to increase decreased dopamine levels in individuals with ADHD.

The second explanation emphasizes that obesity and related factors may cause ADHD. It is thought that attention problems that may be seen in obese patients may occur with recurrent division of daily activities of abnormal eating and binge eating behavior in some obese individuals (Cortese et al. 2007). Frequent division of daily activities may lead to focus problems and shortening of attention time. Another explanation is that attention problems can be caused by daytime somnolence and hypoxemia due to Obstructive Sleep Apnea Syndrome (OSAS) which is one of the frequent comorbidity/sleep problems of obesity (Bass et al. 2004). Sleepiness may cause attention problems not due to OSAS, but also due to chronic inflammatory processes of obesity. In a study, it was reported that excessive daytime sleepiness might help explain the relationship between obesity and ADHD (Odent 2010). Patients with ADHD who are experiencing excessive daytime sleepiness may be considered to be overactive and impulsive to compensate for this and to be alert. Daytime excessive sleepiness may be a sleep disorder or it may also develop due to obesity's metabolic or circadian rhythm anomaly.

The last view states that ADHD and obesity may have common behavioral and neurobiological risk factors. There are some opinions that 'reward deficiency syndrome (RDS)', which is known as a dopaminergic system dysfunction, can play a role in the common etiology of many diseases such as alcohol dependence, substance use disorders, pathological gambling, ADHD, obesity, via especially DRD2 and DRD4 receptors and other dopaminergic pathways (Cortese et al. 2010). It is also known that RDS is associated with various chemical imbalances in a large brain area including basal ganglia, mesolimbic brain regions, especially the nucleus accumbens (NAC), prefrontal cortex, hypothalamus and amygdala (Sahpolat et al. 2014). Changes occurring in major neurotransmitters that are modifying DA such as serotonin, noradrenaline (NA), gamma-aminobutyric acid (GABA), opioid and cannabinoids, and also DA itself could cause RDS and these neuropsychological pathways, neurotransmitters and related receptors might have an etiological relationship between ADHD and obesity. In the first of two studies focusing on the underlying genetic mechanisms (Albayrak et al. 2013), 32 risk alleles associated with increased BMI in obesity patients were investigated with Genome Wide Association Studies (GWAS) and in the German population rs206936 NUDT3 gene was associated with ADHD and related factors (inattention, hyperactivity/impulsivity).

The fat mass and obesity-related gene (FTO) are located in chromosome 16 and known as obesity genes thought to play a role in the modulation of neurobiological system. Different studies have shown that single nucleotide polymorphisms (SNPs) in the first intron of the FTO gene are associated with obesity (Dina et al. 2007, Frayling et al. 2007). In the second study focusing on genetic mechanisms, a significant relationship was found between FTOSNP rs8050136 allele and ADHD (Choudhry et al. 2013).

In another study (Kernie et al. 2000), dysfunction of brain derived neurotrophic factor (BDNF) which has crucial role in neuronal development was found to play a role in common etiology of hyperphagia, obesity and hyperactivity. In MCR4R deficiency syndrome, the fasting/satiety pathway was affected and abnormal eating behaviors were observed. It has been reported that the same gene may play a role in the etiology of ADHD (Agranat-Meged et al. 2008). Leptin-Melenocortin pathway is composed of leptin, leptin receptor, proopi melanocortin, prohormone convertase 1, melanocortin 4 receptor (melanocortin 4 receptor, MC4R) and plays a role in food intake. It is reported that mutations in this pathway cause obesity and MC4R gene dysfunction is the most common dysfunction in this area (Beckers et al. 2009). In MC4R deficiency, modification of appetite may be impaired, but other regulatory mechanisms in the brain may also be affected and it could cause obesity in susceptible individuals by developing abnormal eating behavior, or it may result in ADHD by causing deterioration in organization, planning and regulation skills. In addition, the neurobiological etiology of ADHD and obesity may be associated with common immunosuppressive and neuroinflammatory processes, perinatal risk factors and fetal processes.

Using only PubMed from online search, not utilizing other medium, indexed journals not included in PubMed, and not having the relevant theses scanned in our county are the limitations of our review article.

## Conclusion

On the whole, considering the findings of studies related to ADHD and obesity, the association of these two diseases can be considered as a public health problem. Assessment of obesity risk in clinical practice should become a part of ADHD clinical evaluation and management. In addition, evaluation of obese individuals who are followed by psychiatric and non-psychiatric clinicians, especially those who have failed weight loss attempts, could be useful in terms of solving ADHD. From an academic point of view, it is clear that further research on ADHD and obesity, both of which are morbidly high diagnoses, are needed in the future. In some of the studies we have reviewed, we have noticed the some sort of limitations as the following; uncontrolling the effect of potential comorbid psychiatric disorders, not the use of a formal ADHD diagnosis, lack of control group, use of only clinical sample and male gender, not controlling the factors such as socioeconomic status and BMI of parents, not taking into account the initial height and weight. Designing future research taking into account the limitations we have specified, with prospective design, interview and follow-up as well as treatment options to evaluate, the role of neurobiological mechanisms and neurotransmitters in the discussion that may play a role in the etiology would crucial support and contribution to better understanding of the relationship between ADHD and obesity and the

underlying mechanisms, as consequence of, that will contribute to better understanding of the underlying health policies.

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