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Attention deficit/hyperactivity-disorder and obesity: A review and model of current hypotheses explaining their comorbidity

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ABSTRACT

Available meta-analyses point to a significant association between attention-deficit/hyperactivity disorder (ADHD) and obesity. The possible mechanisms underlying this relationship are unclear. Here, we overview the studies aimed at identifying the factors contributing to the comorbidity between ADHD and obesity, including genetic factors, fetal programming, executive dysfunctions, psychosocial stress, factors directly related to energy balance, and sleep patterns alterations. The bulk of current research has focused on reduced physical activity and abnormal eating patterns as possible causes of weight gain in individuals with ADHD. Further research is needed to explore the specific role of executive dysfunctions. None of the available published studies have evaluated physiological mechanisms such as hormonal and metabolic disorders or inappropriate neurobiological regulation of appetite. Research exploring the genetic basis for the coexistence of ADHD and obesity and epigenetic mechanisms, with particular emphasis on stress, both pre- and postnatal, seems particularly promising. Here, we propose a biopsychosocial model to integrate current findings and move the field forward to gain insight into the ADHD-obesity relationship.

1. Introduction

Obesity is a growing societal problem. Its prevention and treatment are one of the biggest challenges of health care worldwide (Branca et al., 2007). The increasing incidence of obesity in children and adolescents is particularly worrying, because obesity is associated with subsequent risk of other conditions, such as hypertension, diabetes type II (Wabitsch et al., 2004), sleep apnea (Arens and Muzumdar, 2010), gall bladder disease (Larsson and Wolk, 2007), and psychosocial problems (Rosen-Reynoso et al., 2011), among others. Therefore, ongoing research aims to better understand and characterize the risk factors for obesity. In this context, the previously overlooked link between attention-deficit/hyperactivity disorder (ADHD) and increased risk of obesity in children, adolescents and adults is a relatively novel and interesting line of research.

ADHD, which affects around 5% school-age children worldwide (Polanczyk et al., 2007), is characterized by age inappropriate and impairing levels of inattention and/or hyperactivity-impulsivity (American Psychiatric Association, 2000; Scahill and Schwab-Stone, 2000). Children with ADHD have lower school achievements and less satisfying relationships with peers (Hanć and Brzezińska, 2009). The etiology of ADHD is multifactorial, including a complex interplay between genetic and environmental factors. Candidate genes for ADHD are related to neurotransmission and neuroplasticity (Banaschewski et al., 2010), as well as to cell adhesion and migration, neurogenesis, synaptic plasticity, inflammation, and apoptosis (Lee and Song, 2014). Environmental risk factors include smoking during pregnancy, prematurity, and low birth weight, among others (Faraone et al., 2015; Hanć et al., 2016a).

An increasing amount of evidence has shown, albeit not consistently, a significant association between ADHD and obesity (Cortese et al., 2016a; Nigg et al., 2016). The aim of this review is to provide a synthesis of the research aimed at explaining the mechanisms underlying the ADHD-obesity association and to build a comprehensive model based on current empirical evidence. We will consider in particular the following: genetic factors, fetal programming, executive dysfunctions, psychosocial stress, factors directly related to energy balance (i.e. a physical activity, sedentary behaviors, eating patterns) and sleep

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Table 1
Research testing hypotheses to explain the relationship of ADHD and obesity.

Tested underlying mechanisms	First author and Date of publication	Main results
Genetic factors		
	Friedel et al. (2005)	No link ($p > 0.20$) between ADHD, eating disorders and obesity with genotypes of SNPs p.V66 M c-46C > T in the genomic region of *BDNF*, which was analyzed as one of the risk factors of obesity
	Velders et al. (2012)	The A allele at rs9939609 of *FTO* gene, which is strongly associated with obesity, modulates the risk of ADHD (OR:0.74, $p = 0.01$)
	Ariza et al. (2012)	Candidate genes of ADHD: *ANKK1* Taq1A ($\chi^2 = 1.05$, $p = 0.22$) and *DRD4-7R* ($\chi^2 = 1.23$, $p = 0.20$) do not differentiate groups of adults with or without obesity
	Albayrak et al. (2013)	The relationship of risk genes of obesity: rs20696 in the *NUDT3* gene (OR = 1.39, $p = 0.01$) and rs6497416 in *GPRC5B* gene ($P = 7.2 \times 10^{-4}$, $p = 0.02$) with ADHD
	Choudhry et al. (2013a)	*FTO* SNP rs8050136 was related, at the border of statistical significance, with the risk of ADHD ($Z = -1.947$, $p = 0.05$)
	Patte et al. (2016)	*ANNK1* Taq1A was significantly related with overeating (standardized estimate = 0.108, $p = 0.22$), including binge eating, emotional eating and hedonic eating. The effect of ADHD symptoms on BMI occurred in part via overeating ($p < 0.0001$)
	Hanć et al. (2016b)	Overweight in children and adolescents with ADHD was related to 4 out of 14 candidate polymorphisms: *DRD4* rs1800955 (genotype CC vs. CT + TT, OR = 0.28, CI:0.08–0.93, $p = 0.03$), *SNAP25* rs363039 (genotype GG vs. GA + GG, OR = 0.39, CI:0.15–0.99, $p = 0.04$), rs363043 (genotype CC + CT vs. TT, OR = 4.38, CI:1.25–15.41, $p = 0.02$) and *5HTR2A* rs17288723 (genotype TT vs. CT vs. CC, the Fishers test value = 4.08, p = 0.03, OR was not statistically significant: OR = 0.23, CI:0.05–1.08, $p = 0.05$)
Fetal programming		
	Hanć et al. (2015a)	ADHD-obesity relationship remained statistically significant (OR = 2.44, CI:1.38–4.29, $p = 0.002$) when birth weight was controlled for. Low birth weight was associated with a lower incidence of overweight and obesity than normal and high birth weight ($\chi^2 = 4.12$, $p = 0.04$)
Executive dysfunctions		
	Graziano et al. (2012)	Low level of executive functions in children and adolescents with ADHD, measured with the Trail Making Test, Verbal Fluency and Color-Word Interference Test from the Delis-Kaplan Executive Function System, was associated with higher BMI and higher risk of obesity and overweight (OR = 2.31, CI:10.01–5.26, $p = 0.04$)
	Choudhry et al. (2013b)	There were no significant differences in the level of executive function measured with WISC-III, WCST, Finger Widows subtest, Tower of London, Self-Ordered Pointing Test, Stroop test, CPT (mean Cohen's *d* for comparisons between normal weight and overweight groups = 0.02, and for comparisons between normal weight and obese groups = 0.09) and motivation measured with Choice Delay Task and Task-engagement Traits (mean Cohen's *d* for comparisons between normal weight and overweight groups = 0.04 and for comparisons between normal weight and obese groups = 0.00) between children with ADHD with normal weight, overweight and obesity
	Fliers et al. (2013)	Lack of significant association between inhibitory control dysfunction (measured with stop-signal task) and overweight in children and adolescents with ADHD (no additional statistics provided)
	Kerekes et al. (2015)	High extreme BMI was associated with high score on the scale of attention deficits in The Autism–Tics, ADHD and other Comorbidities (A-TAC) inventory (OR = 1.13, CI:1.07–1.19, $p < 0.001$)
	Reinblatt et al. (2015)	Children with ADHD had increased odds of loss of control eating syndrome (LOC-ES) compared with children without ADHD (OR = 12.68, CI:3.11–51.64, $p < 0.001$). Whereas, LOC-ES was related to deficits in response inhibition (OR = 1.17, CI:1.01–1.36, $p < 0.05$).
	Hanć et al. (2016b)	Overweight in children and adolescents with ADHD was not related to deficits in executive functions measured by CPT, Stroop test, TMT, MFFT, VFT, ROCF and WCST (tested with Mann-Whitney *U* test, $p > 0.05$ for all indicators differences between ADHD children with and without overweight)
Psychosocial stress		
	Pauli-Pott et al. (2017)	The psychosocial risk score was significantly correlated with the child's BMI-SDS ($r = 0.22$, $p < 0.001$) and ADHD symptoms ($r = 0.23$, $p < 0.001$). This association held after adjusting for possible confounders (psychosocial risks with ADHD symptoms: $r = 0.15$, $p = 0.003$; psychosocial risks with BMI-SDS: $r = 0.20$, $p < 0.001$)
Factors directly related to energy balance		
	Davis et al. (2006)	Overeating being the result (SEM procedure was used, factors loadings for the measurement model are presented in parenthesis) of eating in response to negative mood (0.785), eating in response to environment cues rather than hunger (0.798) and binge eating (0.610) mediates between ADHD and high BMI
	Wilhelm et al. (2011)	Children and adolescents with ADHD consume larger amounts of food during the first 30 min meal, than peers without ADHD [$F(1,89) = 3.08$, $p = 0.02$]. The amount of snacks eaten by patients with ADHD depends on the level of impulsivity
	Kim et al. (2011)	"Not riding a bike" was associated with obesity in not medicated (OR = 2.11, CI:1.22–3.67) and "not participating in organized sports" was associated with obesity in pharmacologically treated boys with ADHD and girls with ADHD (OR = 1.57, CI:1.06–2.34). Girls (age 6-17 years) with ADHD not treated pharmacologically had higher media time than peers, and it was associated with a higher incidence of obesity (OR = 2.51, CI:1.24–5.08)
	Ebenegger et al. (2012)	The symptoms of hyperactivity/inattention were associated (in unadjusted linear regression model) with lower body fat ($\beta = -0.30$, CI:-0.52 – -0.09, $p = 0.006$), higher levels of physical activity ($\beta = 9.33$, CI:-1.91 – 16.75, $p = 0.01$) and, generally, less sedentary activity ($\beta = -1.45$, CI:-2.47 – -0.43, $p = 0.005$), but also more TV viewing ($\beta = 3.34$, CI:1.18 – 5.47, $p = 0.002$) and less healthy eating habits (less fruits: $\beta = -0.05$, CI:-0.10 – -0.002, $p = 0.04$, and less vegetables: $\beta = -0.06$, CI:-0.11 – -0.001, $p = 0.04$ in the diet and more snacks in front of television: $\beta = 0.02$, CI:0.007 – 0.03, $p = 0.001$) in children aged 4-6 years

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