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Circadian rhythm disruption as a link between Attention-Deficit/Hyperactivity Disorder and obesity?

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ABSTRACT

Objective: Patients with Attention-Deficit/Hyperactivity Disorder (ADHD) have a high prevalence of obesity. This is the first study to investigate whether circadian rhythm disruption is a mechanism linking ADHD symptoms to obesity.
Methods: ADHD symptoms and two manifestations of circadian rhythm disruption: sleep problems and an unstable eating pattern (skipping breakfast and binge eating later in the day) were assessed in participants with obesity (n = 114), controls (n = 154), and adult ADHD patients (n = 202).
Results: Participants with obesity had a higher prevalence of ADHD symptoms and short sleep on free days as compared to controls, but a lower prevalence of ADHD symptoms, short sleep on free days, and an unstable eating pattern as compared to ADHD patients. We found that participants with obesity had a similar prevalence rate of an unstable eating pattern when compared to controls. Moreover, mediation analyses showed that both sleep duration and an unstable eating pattern mediated the association between ADHD symptoms and body mass index (BMI).
Conclusion: Our study supports the hypothesis that circadian rhythm disruption is a mechanism linking ADHD symptoms to obesity. Further research is needed to determine if treatment of ADHD and circadian rhythm disruption is effective in the prevention and treatment of obesity in patients with obesity and/or ADHD.
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Introduction

Globally, obesity is a growing problem with serious health consequences, such as diabetes mellitus, cardiovascular diseases, musculoskeletal disorders, and cancer [1]. Worldwide, the prevalence of obesity has nearly doubled since 1980, with a current prevalence of 10% among men and 14% among women [2]. Obesity is more prevalent in psychiatric populations, including in patients with Attention-Deficit/Hyperactivity Disorder (ADHD) [3,4]. ADHD is a disorder characterized by hyperactivity, impulsivity, and/or inattention [5]. A large population-based study showed that obesity was prevalent in 29% of adult ADHD patients in the US [6]. Vice versa, around 30% of obese adults have ADHD as observed in cross-sectional studies [7]. Moreover, longitudinal studies have found an association between childhood ADHD and obesity in adolescence or adulthood [8,9].

Circadian rhythm disruption, more specifically a delayed circadian rhythm, may be a mechanism linking ADHD symptoms to obesity. In humans, behavioral and physiological processes, such as sleep and appetite hormones release, display approximately 24-hour rhythms, i.e., circadian rhythms [10]. Disturbances of these rhythms cause sleep disorders and disrupted eating patterns, among others [11,12].

ADHD has been related to a delayed circadian rhythm, as indicated by an increased prevalence of Delayed Sleep Phase Syndrome (DSPS) in comparison to controls [13]. About 78% of adults with ADHD have sleep-onset insomnia, a condition that is often present from childhood [14,15]. Some of these ADHD patients fulfill criteria for a diagnosis of DSPS, which include difficulty falling asleep at night and waking up in the morning causing impaired social and occupational functioning [16–18].

In the long term, DSPS may result in obesity in ADHD patients. DSPS often results in chronic sleep debt, especially when persons have social or work obligations in the early morning [19]. Epidemiological and clinical studies indicate that chronic short sleep is associated with a higher prevalence of obesity [20]. Specifically, a meta-analysis of 17 studies showed that adults who slept five hours or less per night had a 55% higher odds for obesity [21]. Furthermore, lower levels of the

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appetite-reducing hormone leptin and higher levels of the appetite-stimulating hormone ghrelin have been found in short sleepers, leading to increased food craving and appetite [22]. Clinically, we have observed that ADHD patients with comorbid DSPS exhibit unstable eating patterns, characterized by skipping breakfast and binge eating later in the day, which may be mediated by a disrupted release of appetite hormones. An unstable eating pattern has a prominent role in weight gain and obesity [23].

In short, there are associations between ADHD symptoms, delayed sleep, and obesity. We recently compared these relationships in adults with ADHD and a control group [24]. Associations were found between hyperactivity, delayed sleep, binge eating, and high body mass index (BMI), both in the ADHD group as well as in the control group. In the present study, we extend our previous research by adding a group of participants with obesity. Given the high prevalence of DSPS in ADHD patients, and the association of this circadian rhythm disturbance with obesity, we hypothesized that circadian rhythm disruption may be a mechanism linking ADHD symptoms to obesity. Therefore, we expect to find that (1) the obesity group will have a higher prevalence of ADHD symptoms, sleep problems, and an unstable eating pattern than the control group, but a lower prevalence of these factors than the ADHD group; and that (2) circadian rhythm disruption, as indicated by sleep duration and an unstable eating pattern, is a mechanism linking ADHD symptoms to obesity, even after controlling for known confounders such as sociodemographics and current depression/anxiety symptoms [25,26]. Although previous researchers [27,28] have hypothesized that short sleep disruption may play a role in the association between ADHD symptomatology and obesity, no one has tested this hypothesis in adult ADHD patients. If circadian rhythm disruption is involved in the association between ADHD symptoms and obesity, this may provide clinical opportunities for the development of new chronobiological treatment strategies in patients with obesity and/or ADHD, hence improving health in the long term.

Method

Participants

Obesity group

Participants were included with a diagnosis of obesity, defined as a BMI ≥ 30 kg/m^2, based on self-reported weight and height [2]. Participants who were not fluent in Dutch were excluded from the study. We recruited 114 participants with obesity aged 18 to 65 years old, between February 2011 and April 2013 from the PsyQ outpatient clinics for eating disorders and obesity, in The Hague and Rotterdam (n = 13), from the Center for Obesity Europe in Heerlen (n = 77), from a XL Fair, a lifestyle event for obese persons, in Beverwijk (n = 6), and from the Maastricht University clinics (n = 18).

The ADHD and control groups

The ADHD and control groups were the same as described in our previous study [24]. The exclusion criterion for both the ADHD and the control group was not being fluent in Dutch. In the ADHD group, a total of 202 ADHD patients aged 18 to 65 years were included after extensive diagnostic assessment at the PsyQ outpatient clinic, The Hague, between February 2009 and March 2010.

A part of the control group consisted of 75 adults who were recruited by the researchers from public locations, such as public libraries and municipal buildings, in order to create a representative sample of the general population. The control group also included 114 students from Leiden University and one of their acquaintances (aged between 30 and 65). Acquaintances were asked to participate in order to have a more balanced age and sex distribution in the control group. However, participants born between 1985 and 1989 (ages 20–24) were still overrepresented in the control group. This might have affected our sleep results, since young adults (≤30 years) have late chronotypes, which may result in late and short sleep [29]. The overrepresentation disappeared when 33 persons were randomly excluded from this age category. In addition, we excluded 2 persons who were younger than 18 years in order to have a similar age range in the three groups. In this study, the control group therefore consisted of 154 subjects.

Measurements

ADHD symptoms

Severity of ADHD symptoms was measured using the Dutch self-report version of the ADHD-Rating Scale (ADHD-RS) [30]. The validated ADHD-RS is based on the DSM-IV criteria for ADHD, and consists of 23 items on current ADHD symptoms and 23 items on childhood ADHD symptoms, all rated on a 4-point Likert scale ranging from 0 (never or rarely) to 3 (very often) [31]. A score of ≥23 in adulthood indicated high ADHD symptoms [24].

Manifestations of circadian disruption

We used manifestations of sleep problems and an unstable eating pattern to define circadian disruption. Chronotype and sleep characteristics were assessed with the "Vragenlijst Ochtend/Avondmens" (VOA, meaning 'Questionnaire Morning/Evening type'), a Dutch questionnaire based on the Horne & Östberg Morningness-Eveningness questionnaire [32–34] and the "Munich Chronotype Questionnaire" (MCTQ) [35]. On the basis of the seven items of the VOA, subjects were categorized into five chronotypes varying from extreme morning type to extreme evening chronotype. The MCTQ is a validated questionnaire on sleep duration, mid-sleep, and the subjects' self-rated chronotype. It consists of 32 items assessing sleep habits on work and free days. The mid-sleep on free days, corrected for sleep debt on work days (MSFsc) is used as a marker for chronotype [29].

Data concerning eating patterns were collected. Participants were asked if they skipped meals and, if answered positively, which meal(s) they skipped. With regard to binge eating, the participants answered the following question: "Do you have eating binges?" and, if answered positively, "At which moment of the day?". An 'unstable eating pattern' was defined as an eating pattern in which breakfast is skipped and binge eating occurs during the evening and/or at night.

Covariates

Sociodemographic data were collected, including age, gender, height, weight, vocational status, occupation status, caffeine consumption, smoking status, alcohol consumption, physical activity, and use of medication. Vocational status was defined as lower if the highest educational level was elementary school, lower vocational training, or lower secondary education. The presence of current depressive, anxiety, and stress symptoms was based on self-report by asking whether the subjects ever had psychiatric problems and, if answered positively, what kind of psychiatric problem(s) and if they still suffer from these problems at this moment.

Procedure

Obesity group

We calculated BMI using self-reported weight and height [2]. The participants filled out the questionnaires on paper.

ADHD and control groups

During diagnostic assessment, the ADHD group filled out the questionnaires with pen and paper. The control group completed an online version of the questionnaires. A more detailed procedure for the

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