The association between obesity and hyperactivity/anxiety among elementary school students in Japan

Yohei Suzuki, MD¹, Ai Ikeda, PhD¹, Koutatsu Maruyama, PhD², Naoko Sakamoto, PhD³, Hiroo Wada, MD¹, Takeshi Tanigawa, MD¹

¹ Department of Public Health, Graduate School of Medicine, Juntendo University. Tokyo, Japan. ²Department of Bioscience, Graduate School of Agriculture, Ehime University. Ehime, Japan. ³Department of Epidemiologic Research, Toho University. Tokyo, Japan.

Address for correspondence:

Prof. Takeshi Tanigawa, MD, PhD

Department of Public Health, Graduate School of Medicine, Juntendo University. 2-1-1

Hongo, Bunkyo-ku, Tokyo, Japan.

Phone: +81 (3) 5802-1049 Fax: +81 (3) 3814-0305 Email: <u>tataniga@juntendo.ac.jp</u>

Word counts: 3753 words (excluding references and tables).

Acknowledgements

We gratefully acknowledge the contribution of all the children, their parents, and the members of the educational committee in Matsuyama City who took part in this study. This study was supported by MEXT/JSPS KAKENHI Grant Number JP2640844 and a research grant from Juntendo University.

Conflict of interest Declaration

The authors declare that they have no conflict of interest.

Abstract

Background

We aimed to evaluate the association between hyperactivity/anxiety and obesity among elementary school students in Matsuyama City, Japan.

Methods

We conducted a cross-sectional study of all 46 elementary school students (24, 296 students) in Matsuyama City. The questionnaire included question items from the Strengths and Difficulties Questionnaire (SDQ), as well as questions about height and weight. The students were classified into two groups according to Rohrer index. After separating the data by gender, we examined the association between (1) obesity and hyperactivity, (2) obesity and anxiety, and (3) obesity and combination of hyperactivity and anxiety, by estimating relative risk using Poisson regression model. We also conducted stratified analyses to examine the effect modification by age groups and unbalance of diet on those associations. Moreover, we calculated relative excess risk due to the interaction (RERI) to examine whether there was an additive interaction between hyperactivity and anxiety.

Results

Sixteen thousand forty-eight students were included in the present analysis. The prevalence ratio (PR) of being obese in girls who had both hyperactivity and anxiety was higher compared to girls without those symptoms (PR = 1.80; 95% CI 1.04–3.13). There was no significant difference in the prevalence ratio for obesity in boys, whether they were hyperactive, anxious, or neither. RERI was 0.00 for boys and 0.18 for girls.

Conclusion

We found a significant association between obesity and co-existence of hyperactivity and anxiety among elementary school girls. Our findings strengthen the need to further explore the association between childhood obesity, hyperactivity, and anxiety.

Keywords

Anxiety, Children, Hyperactivity, Obesity

Introduction

Obesity among schoolchildren has become a major problem in Japan. According to a national survey, the number of obese children aged between 6 and 12 has increased by about three-fold compared to the number reported 30 years ago [1]. In 2017, the prevalence ratio for obesity was 9.69% for Japanese boys and 8.72% for Japanese girls in the sixth grade of elementary school [2]. Obesity in childhood may be associated with various physical problems, such as hypertension [3], hyperinsulinemia [3], and hyperlipidemia [3]; it may also be associated with various mental health problems, such as hyperactivity and anxiety.

The problem of hyperactivity in children is generally known as one of the main symptoms of attention deficit hyperactivity disorder (ADHD). The prevalence of ADHD has been reported to be between 1 and 20%, differing by country [4]. In Japan, Sugawara et al. reported the prevalence to be 10.5% for 114 children aged between 7 and 9 [5]; but their sample size was relatively small; thus, prevalence in Japan has not been revealed yet. According to one study using meta-analysis, the inattentive subtype seemed to be the most common subtype of ADHD. Nevertheless, the result did not deny the importance of the hyperactive subtype, since hyperactive symptoms will significantly affect children's daily lives. Previous studies in hospital settings have examined the association between hyperactivity/ADHD and childhood obesity [6–8]. In these studies, several mechanisms, such as eating behavior or genomic background, have been suggested to explain the association between hyperactivity and obesity. However, the generalizability of these studies has been limited due to the study design. Only a few studies have examined the association between hyperactivity/ADHD and obesity among the general pediatric population worldwide [9–11].

Anxiety disorders are a group of mental disorders characterized by significant feelings of anxiety and fear [12]. Anxiety disorders are also often seen among children and are associated with impairment and disability in daily life. The prevalence of anxiety disorders (i.e., generalized anxiety disorder, social anxiety disorder, and agoraphobia) in children and adolescents ranged from 2.2 to 9.5% among a total of six studies reported from the USA and the UK [13]. In Japan, no previous studies have reported the prevalence of anxiety disorders in children. Only a few cross-sectional studies have examined the association between anxiety symptoms/anxiety disorder and obesity in general children's population worldwide [14–17]. Although a causal relation has not yet been established, previous studies have suggested that anxiety symptoms may lead to obesity by involving the endocrine system [18] or sleep dysregulation [19]. On the other hand, other studies have found that being obese may lead to anxiety symptoms due to the social environment (e.g., the social pressure to be thin) [16].

Despite of the fact that obesity is associated with hyperactivity and anxiety through separate etiologic pathways, hyperactivity and anxiety together could exacerbate obesity and its related effects. A previous study found that children with both hyperactivity and anxiety had poorer quality of life and functioned poorly both at home and at school, compared to children with ADHD or anxiety alone [20]. Moreover, children with comorbid hyperactivity and anxiety tended to have higher level of epinephrine excretion, potentially aggravating hyperactivity and anxiety, compared to children with just one or the other [21]. However, the combination impact of hyperactivity and anxiety on child obesity remains poorly understood.

We would also like to emphasize that no studies have conducted a city-wide survey to examine hyperactivity and anxiety in relation to obesity among elementary school children in an Asian population. The average body mass index (BMI) of boys and girls aged 6–11 years in the USA was 16.0 in 2001 [22]. On the other hand, the average BMI of boys and girls aged 6–11 years in Japan was 17.3 in 2001 [1]. Due to the magnitude of the numbers, we may assume that there seems to be no significant difference in the BMI between US children and Japanese children, but that there is a significant difference in the proportions of obesity between these two countries. For instance, the percentage of children in Japan who were 20% or more above the standard weight was 8–10% in 2013 [1]. On the other hand, the percentage among US children was 30– 35% in 2007–2008 [23]. Therefore, we may conclude that the proportion of obese children is relatively small among Japanese children compared to that among US children, thus giving our study a clinical significance of examining an association between obesity and hyperactivity/anxiety in the population in which the proportion of obese children is relatively small. Examining this association in a relatively non-obese population is important because the occurrence of hyperactivity and anxiety may differ between obese populations and non-obese populations.

Based on the above considerations, we focused our research on hyperactivity, which is one of the typical symptoms of ADHD, and anxiety; accordingly on 26,960 children from all 46 elementary schools in Matsuyama City, a regional city in Japan with an approximate population of 500,000, to examine the association between (1) obesity and hyperactivity, (2) obesity and anxiety, and (3) obesity and the combination of hyperactivity and anxiety.

Methods

Subjects

A questionnaire was distributed to 26,960 children from all 46 elementary schools in Matsuyama City. Children and their parents signed an informed consent form before participating in the survey. The parents filled out the questionnaire, and the response rate was 90.0%. Of the 24,296 children who responded to the questionnaire, children whose gender were not able to be determined were excluded; thus, 22,035 children remained. Moreover, children who did not answer or did not answer correctly to questions for height, weight, grade, usual bedtime hour, total hours of sleep, existence of tonsil and adenoid hypertrophy, existence of an unbalanced diet, past existence of seizure or asthma, and questions related to sleep were excluded; therefore, a final total of 16,048 children were included in the analysis. In Appendix 1, we showed the characteristics of children which were included in the analysis and excluded from the analysis. Although the characteristics of both children were similar, children who were excluded had smaller mean sleep time, and also had higher percentage of having hyperactivity.

Methods

Baseline questionnaire

The questionnaire included height, weight, grade, usual bedtime hour, total hours of sleep, existence of tonsil and adenoid hypertrophy, existence of an unbalanced diet, past existence of seizure or asthma, and questions related to sleep. Height and weight were not estimated directly from children but obtained from answers by their parents. For unbalanced diet, we simply asked whether child had an unbalanced diet or not. It is well known that obesity causes respiratory abnormalities during sleep, such as apnea pauses [24–26]; therefore, we included usual bedtime hour, total hours of sleep, and existence of tonsil and adenoid hypertrophy as key covariates. For questions related to sleep, we translated the previously validated sleep-disordered breathing questionnaire into Japanese for use in this study (shown in Table 1) [27].

A total of five questions regarding to hyperactivity and five questions regarding to anxiety were also included in the questionnaire (shown in Tables 2 and 3, respectively). The questions were referred to translated version of Strengths and Difficulties Questionnaire (SDQ), which has been widely used in European countries such as England and Germany [28]. The validity of using translated version of SDQ toward Japanese children is already examined by Moriwaki et al. [29] and Matsuishi et al. [30]. The original SDQ is composed of 25 question items, extending over five fields including prosocial behavior problems, emotional symptoms, hyperactivity symptoms, conduct problems, and peer relationship problems.

In the present study, we only used the items regarding to hyperactivity and emotional symptoms in SDQ. Each question was answered as follows: 0 for "No," 1 for "Somewhat yes," and 2 for "Yes." According to the study toward Japanese children conducted by Matsuishi et al., we chose the same cut-off point for hyperactivity and anxiety [30]. When scores for the items regarding hyperactivity were 7 or more, the subjects were considered as hyperactive. Subjects with scores that were less than 7 were not classified as hyperactive. When scores for the items regarding to emotion were 5 or more, they were considered as anxious. Subjects with scores that were less than 5 were not classified as anxious.

We estimated their gender from their given names, and the children whose gender could not be estimated were excluded from the analysis. Although estimating children's gender from their given names may have caused misclassifications, we would like to note that it is culturally easier to estimate gender from given name in Japan [31]. Therefore, we believe that misclassifications for gender were relatively few. After children were classified to either boys or girls, unlinkable anonymizing was processed to the data for afterwards analysis in order to guarantee the privacy of children. For the levels of obesity measurement, we used the Rohrer index based on the discussion from a previous study [32]. In the study by Sugiura et al., they discussed that BMI increases as height increases in puberty children with the optimal weight for their sex and age. Therefore, a considerable variation in the range of BMI is observed in normal individuals of the same degree of fatness, and from this viewpoint, distinguishing the respective healthy weight, overweight, and obese groups based on cut-off points using BMI percentile during puberty is difficult [32].

Rohrer index was calculated by the following formula:

Rohrer index = Weight (kg) \div Height (cm) $^{3} \times 10000000$.

Statistical methods

In general, a Rohrer index equal to 130 (SD \pm 15) is considered as a normal weight for children, and children who have a Rohrer index greater than 145 are considered as obese. Therefore, we defined children as obese if they had a Rohrer index > 145,and non-obese if they had a Rohrer index \leq 145.

We estimated prevalence ratio (PR) by using Poisson regression model for each gender to examine the association between hyperactivity/anxiety and weight according to the combination of hyperactivity and anxiety, using the non-hyperactive and nonanxious group as a reference. In the multivariate model, we included hyperactivity, anxiety, and factors that were associated with SDQ (p < 0.05). We used three following models: ① model including children with only hyperactivity, ② model including children with only anxiety, and ③ model including children with both hyperactivity and anxiety. Age, levels of snoring, existence of past history of asthma, and existence of an unbalanced diet were adjusted in the multivariate model as the confounding factors in boys, whereas age, levels of snoring, existence of past history of seizure, existence of past history of asthma, and existence of an unbalanced diet were adjusted in the multivariate model as the confounding factors in girls.

We also conducted stratified analyses to examine the effect modification by age groups ($\leq 8, 9$ to 10, 11 \leq) and diet (balanced or unbalanced) on the association between SDQ and obesity.

Moreover, we examined whether there was an additive interaction between hyperactivity and anxiety. The relative excess risk due to interaction (RERI) is the excess risk as a result of joint exposure [33]. RERI was calculated by using the following formula:

RERI = exponent $(\beta 1 + \beta 2 + \beta 3)$ – exponent $(\beta 1)$ – exponent $(\beta 2)$ + 1

(β 1, β 2, and β 3 are the coefficients from the models for estimating prevalence ratios according to combination of hyperactivity and anxiety.)

RERI = 0 means no interaction or exactly additivity, RERI > 0 means positive interaction or more than additivity, and RERI < 0 means negative interaction or less than additivity. RERI may go from – infinity to + infinity.

We also calculated attributable proportion due to interaction (AP), which is the proportion of obesity among those having both hyperactivity and anxiety that is attributable to interaction. AP was calculated by using the following formula:

AP = [RERI/PR (hyperactivity + anxiety)]

AP = 0 means no interaction or exactly additivity, AP > 0 means positive interaction or more than additivity, and AP < 0 means negative interaction or less than additivity. APmay go from -1 to +1.

We used SAS Version 9.0 for the statistical analysis.

The study was approved by the Ethics Committee of Juntendo University.

Results

The numbers of children having hyperactivity and anxiety are shown in Table 4. The mean age of total children was 9.6 (SD 1.7) years, and the mean score of the Rohrer index of total children was 124.7 (SD 17.4).

Table 5 shows the basic characteristics according to hyperactivity. Boys with hyperactivity had a slightly higher average score in the Rohrer index compared to those who did not have the symptoms, and the same tendency was observed in girls. Moreover, boys with hyperactivity were relatively younger compared to those who did not have the symptoms, and the same tendency was observed in girls. Average time of sleep was almost the same in boys and girls regardless of having hyperactivity.

Table 6 shows the basic characteristics according to anxiety. In boys, average score for Rohrer index among children with anxiety was slightly higher compared to those without the symptom, and same tendency was observed in girls. Also, average hour of sleep was same between boys with and without anxiety, but average hour of sleep was slightly less among girls with anxiety compared to girls without anxiety.

Table 7 shows sex-specific prevalence ratio for obesity and 95% confidence interval (95% CI) in children according to hyperactivity and anxiety, which were calculated from three models mentioned before. Among boys, we did not observe a significant

difference in prevalence ratio. On the other hand, prevalence ratio was higher among girls who had both hyperactivity and anxiety compared to girls who had none (PR = 1.80 [95% CI 1.04-3.13]). Prevalence ratio was also higher among girls who had only hyperactivity compared to girls who had none (PR = 1.40 [95% CI 1.01-1.92]).

RERI was 0.00 (95%CI–0.88–0.88) for boys and 0.18 (– 1.47–1.83) for girls, indicating that combination of hyperactivity and anxiety did not have a significant supra-additive effect on obesity. AP was 0.00 for boys and 0.10 for girls.

We did not find any significant effect modifications by either age or unbalanced diet on the association between hyperactivity or anxiety and Rohrer index in boys and girls (not shown in table).

Discussion

In our study, the existence of both hyperactivity and anxiety was significantly associated with obesity among girls but not among boys. There was no interaction by age and an unbalanced diet in relation to hyperactivity/anxiety and obesity. The combination of hyperactivity and anxiety did not have a significant supra-additive effect on obesity among boys, indicating that hyperactivity and anxiety are independently associated with obesity by different pathways. By contrast, considering that the RERI was 0.18 for girls, the supra-additive effect seemed to exist among girls. This may have been the reason why we found the existence of both hyperactivity and anxiety to be significantly associated with obesity among girls.

To our knowledge, this is the first study to conduct a city-wide survey to examine hyperactivity/anxiety in relation to obesity among elementary school children in an Asian population. A previous study with a similar research design was conducted in the USA [9]. Approximately 60,000 children were included in the study to examine the association between ADHD and obesity. However, only a single question was used to identify ADHD in the study, which may have led to a misclassification of ADHD. By contrast, we used question items that were extracted from the SDQ, which is recommended for the screening of ADHD in the clinical primary care field [34, 35].

Agranat-Meged etal. Pointed out that the specific difficulty in behavioral regulation found in ADHD may lead to the development of abnormal eating behaviors linked to obesity [6]. The association between anxiety and obesity may also be explained from the standpoint that anxiety could affect diet or activity levels, such as an increase in emotional eating, an elevation in sedentary behavior, and a decrease in exercise [36].

In our present study, we did not find any significant effect modification by an unbalanced diet on the association between hyperactivity/anxiety and obesity. We only asked a single question regarding diet, and there was also a discrepancy between the number of children with a balanced diet and those without a balanced diet, which may have influenced the results of our study. Further research is needed to identify the effect modification of eating behavior on the association between hyperactivity/anxiety and obesity.

It is well known that obesity causes respiratory abnormalities during sleep, such as apnea pauses [24–26]. As Cortese et al. stated, sleep apnea syndrome produces symptoms that resemble those of ADHD [37]. Daytime drowsiness and diminished alertness are associated with three characteristic symptoms: irritability (which may be confused with motor restlessness), mental restlessness, and inattention. Previous studies have also discussed the association between anxiety and sleep problems [19, 38]. Some clinical studies that compared different anxiety subtypes have even suggested that sleep difficulties may be more strongly associated with certain subtypes, such as generalized anxiety disorder [39,40]. In our present study, adjusting for the presence of snoring did not alter the association between obesity and hyperactivity/anxiety. A more precise investigation, such as one using nighttime polysomnography, is required to validate this issue.

Some studies have shown that girls tend to have a stronger association between hyperactivity and obesity compared to boys [41,42]. One study reported that the odds ratio of obesity for girls with unmedicated ADHD is higher compared to the ratio of those without ADHD but that this tendency was not observed in boys [43]. The study suggested that this incident might be related to the higher prevalence of the inattentive subtype of ADHD observed in females versus the hyperactive-impulsive subtype that is more prevalent among males. Another study reported that having ADHD symptoms is associated with an increased risk for obesity only in girls aged between 6 and 17 [44]. The study suggested some reasons for this finding. First, girls are under the cultural pressure to be thin and are therefore most prone to dieting [45], but ADHD symptoms have been shown to be strong negative predictors of intentional weight loss in several studies [44–46]. Thus, while adolescent girls with low ADHD symptoms may have better chances to achieve a normal weight, those with high ADHD symptoms may have the tendency to fail and remain overweight. Second, the prevalence of binge eating is highest in adolescent females; ADHD symptoms have been shown to be associated with an increased risk of binge eating among adolescents. Moreover, Dumith et al. suggested that an earlier age-dependent decrease in physical activity and relatively lower muscle mass may limit activity energy expenditure in girls [47]. In addition, girls show relatively less energy-consuming hyperactive and impulsive behavior in relation to inattentive behavior than boys.

Environmental factors may also contribute to the association between anxiety and obesity. Adolescent girls in Japan are under the social pressure to be thin [48], which may explain the result in our study in which the prevalence ratio for obesity tended to increase when girls had anxiety. On the other hand, a previous study in Iran reported no significant association between anxiety and being overweight among young girls, which may be due to the positive attitude of family and peers to fatness in adolescence as noted in the study [16].

The strengths of our study are the large sample size, as a result of recruiting all the elementary school students in Matsuyama City, and the very high response rate (90%). Therefore, we may generalize our findings to the Japanese population, which should

have a lower percentage of obese children compared to the populations in western countries.

Our study has some limitations. First, we did not use the Diagnostics and Statistical Manual of Mental Disorder-5 [12] for the diagnosis of hyperactivity/anxiety. Nevertheless, SDQ has diagnostic validity for parents to identify hyperactive symptoms, as mentioned by Croft et al. [34] and Muris et al. [35], and to identify anxiety symptoms, as mentioned by Silva et al. [49]. Second, we could not exclude children with a medical history of ADHD or anxiety disorder. Thus, it could be possible that those who were diagnosed with ADHD/ anxiety disorder and prescribed medication were included in the subject, leading to an underestimation of the association between hyperactivity/anxiety and obesity. Third, we focused on hyperactivity, which is one of the sub-components of ADHD; thus, our study may not apply to the inattentive subtype of ADHD. Fourth, symptoms of hyperactivity and anxiety were parent-reported. Considering the inter-rater reliability between child- and parent-reported symptoms, there may have been an overestimation or underestimation of the association between hyperactivity/anxiety and obesity. Fifth, we assumed the children's gender from their names. Although the children whose gender could not be determined were excluded from the analysis, there still may have been misclassification of gender, thus leading to

unprecise analysis. Nevertheless, as we have mentioned in the methods section, we believe that misclassification of gender occurred infrequently, due to the cultural easiness of estimating the gender from a given name in Japan. Lastly, our study used a cross-sectional design; therefore, we could not reveal the true causal relation between hyperactivity/anxiety and obesity.

In conclusion, we found that the existence of both hyperactivity and anxiety increased the prevalence ratio of obesity among elementary schoolgirls in Matsuyama City, which has a lower percentage of obese children compared to that in western countries. Although our results were from a cross-sectional study, the combination of hyperactivity and anxiety did not have a significant supra-additive effect on obesity, indicating that hyperactivity and anxiety may be independently associated with obesity by different pathways. Several factors, such as social environment and behavioral tendency, which is specific to girls, may explain our results of finding the association only in girls. Although further studies are needed to explore the associations among childhood obesity, hyperactivity, and anxiety to clarify the true causal relation and identify the target of intervention, our findings have suggested that it is important for pediatricians, psychiatrists, and school officials to be aware of possible obesity risks associated with hyperactivity and anxiety or vice versa among children.

Compliance with Ethical Standards

Ethical approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional committee and have been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

References

1. Ministry of Education, Culture, Sports, Science and Technology; Japan.

http://www.mext.go.jp/b_menu/toukei/chousa05/hoken/kekka/1268813.htm

Accessed on June 30, 2019.

- Ministry of Education, Culture, Sports, Science and Technology; Japan.
 <u>http://www.mext.go.jp/b_menu/toukei/chousa05/hoken/kekka/k_detail/1399280.htm</u> Accessed on June 30, 2019.
- Dietz WH. Overweight in childhood and adolescence. N Engl J Med 2004 Feb 26;
 350 (9): 855-7.
- Faraone SV, Sergeant J, Gillberg C, Biederman J. The worldwide prevalence of ADHD: is it an American condition? World Psychiatry 2003 June; 2 (2): 104–113.
- Sugawara M, Mukai T, Kitamura T, Toda MA, Shima S, Tomoda A, Koizumi T, Watanabe K, Ando A. Psychiatric disorders among Japanese children. J Am Acad Child Adolesc Psychiatry. 1999 Apr;38(4):444-52.
- Agranat-Meged AN, Deitcher C, Goldzweig G, Leibenson L, Stein M,
 Galili-Weisstub E. Childhood obesity and attention deficit/hyperactivity disorder: a newly described comorbidity in obese hospitalized children. Int J Eat Disord 2005; 37 (4): 357–359.

- Curtin C, Bandini LG, Perrin EC, Tybor DJ, Must A. Prevalence of overweight in children and adolescents with attention deficit hyperactivity disorder and autism spectrum disorders: a chart review. BMC Pediatr 2005; 5: 48.
- Lam LT, Yang L. Overweight/obesity and attention deficit and hyperactivity disorder tendency among adolescents in China. Int J Obes (Lond) 2007; 31 (4): 584-590.
- Waring ME, Lapane KL. Overweight in children and adolescents in relation to attention-deficit/hyperactivity disorder: results from a national sample. Pediatrics 2008 Jul; 122 (1): e1-6.
- 10. Halfon N, Larson K, Slusser W. Associations between obesity and comorbid mental health, developmental, and physical health conditions in a nationally representative sample of US children aged 10 to 17. Acad Pediatr 2013 Jan-Feb; 13 (1): 6-13.
- 11. Erhart M, Herpertz-Dahlmann B, Wille N, Sawitzky-Rose B, Hölling H, Ravens-Sieberer U. Examining the relationship between attention-deficit/ hyperactivity disorder and overweight in children and adolescents. Eur Child Adolesc Psychiatry 2012 Jan; 21 (1): 39-49.
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (5th ed.). Arlington: American Psychiatric Publishing. 2013. pp. 189–195.

- Merikangas K, Nakamura E, Kessler R. Epidemiology of mental disorders in children and adolescents. Dialogues Clin Neurosci. 2009; 11(1): 7-20.
- Esposito M, Gallai B, Roccella M. Anxiety and depression levels in prepubertal obese children: a case-control study. Neuropsychiatr Dis Treat. 2014 Oct 3; 10: 1897-902.
- 15. Anderson SE, Cohen P, Naumova EN. Adolescent obesity and risk for subsequent major depressive disorder and anxiety disorder: prospective evidence. Psychosom Med. 2007 Nov; 69(8): 740-7.
- 16. Jari M, Qorbani M, Motlagh ME. Association of Overweight and Obesity with Mental Distress in Iranian Adolescents: The CASPIAN-III Study. Int J Prev Med.
 2014 Mar; 5(3): 256-61.
- Burke NL, Storch EA. A meta-analysis of weight status and anxiety in children and adolescents. J Dev Behav Pediatr. 2015 Apr;36(3):133-45.
- Pervanidou P, Chrousos GP. Stress and obesity/metabolic syndrome in childhood and adolescence. Int J Pediatr Obes. 2011 Sep; 6 Suppl 1: 21-8.
- Hansen BH, Skirbekk B, Oerbeck B. Comparison of sleep problems in children with anxiety and attention deficit/hyperactivity disorders. Eur Child Adolesc Psychiatry. 2011 Jun; 20(6): 321-30.

- 20. Sciberras E, Lycett K, Efron D, Mensah F, Gerner B, Hiscock H. Anxiety in children with attention-deficit/hyperactivity disorder. Pediatrics. 2014 May;133(5):801-8.
- 21. Pliszka SR1, Maas JW, Javors MA, Rogeness GA, Baker J. Urinary catecholamines in attention-deficit hyperactivity disorder with and without comorbid anxiety. J Am Acad Child Adolesc Psychiatry. 1994 Oct;33(8):1165-73.
- 22. Centers for Disease Control and Prevention.

https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm

Accessed on June 30, 2019.

- Ogden CL, Carroll MD, Curtin LR, Lamb MM, Flegal KM. Prevalence of high body mass index in US children and adolescents, 2007-2008. JAMA 2010; 303(3): 242-249.
- 24. Andersen IG, Holm JC, Homøe P. Obstructive sleep apnea in children and adolescents with and without obesity. Eur Arch Otorhinolaryngol. 2019 Mar;276(3):871-878.
- 25. Kang KT1, Lee PL, Weng WC, Hsu WC. Body weight status and obstructive sleep apnea in children. Int J Obes (Lond). 2012 Jul;36(7):920-4.

- 26. Lam YY1, Chan EY, Ng DK, Chan CH, Cheung JM, Leung SY, Chow PY, Kwok KL. The correlation among obesity, apnea-hypopnea index, and tonsil size in children. Chest. 2006 Dec;130(6):1751-6.
- 27. Spruyt K, Gozal D. Screening of pediatric sleep-disordered breathing: a proposed unbiased discriminative set of questions using clinical severity scales. Chest. 2012 Dec;142(6):1508-1515.
- 28. Ministry of Health, Labor and Welfare; Japan.

http://www.mhlw.go.jp/bunya/kodomo/boshi-hoken07/

Accessed on June 30, 2019.

- 29. Moriwaki A, Kamio Y. Normative data and psychometric properties of the strengths and difficulties questionnaire among Japanese school-aged children. Child Adolesc Psychiatry Ment Health. 2014 Jan 21; 8(1): 1.
- 30. Matsuishi T, Nagano M, Araki Y, Tanaka Y, Iwasaki M, Yamashita Y, et al. Scale properties of the Japanese version of the Strengths and Difficulties Questionnaire (SDQ): a study of infant and school children in community samples. Brain Dev. 2008 Jun;30(6):410-5.

- 31. Malmasi S, Dras M. A Data-driven Approach to Studying Given Names and their Gender and Ethnicity Associations. Proceedings of Australasian Language Technology Association Workshop. 2014 145-149.
- 32. Sugiura R, Murata M. Problems with body mass index as an index to evaluate physical status of children in puberty. Pd International 2011; 53: e634-642.
- 33. Richardson DB, Kaufman JS. Estimation of the Relative Excess Risk Due to Interaction and Associated Confidence Bounds. Am J Epidemiol. 2009 Mar 15; 169(6): 756–760.
- 34. Croft S, Stride C, Maughan B, Rowe R. Validity of the Strengths and Difficulties Questionnaire in Preschool-Aged Children. Pediatrics 2015 May; 135 (5): e1210e1219.
- 35. MurisP, Meesters C, van den Berg F. The Strengths and Difficulties Questionnaire (SDQ)--further evidence for its reliability and validity in a community sample of Dutch children and adolescents. Eur Child Adolesc Psychiatry. 2003 Jan; 12(1): 1-8.
- 36. Rofey D, Kolko R, Losif A. A longitudinal study of childhood depression and anxiety in relation to weight gain. Child Psychiatry Hum Dev. 2009 Dec; 40(4): 517-26.
- 37. Cortese S, Moreira-Maia CR, St Fleur D, Morcillo-Peñalver C, Rohde LA, Faraone

SV. Association Between ADHD and Obesity: A Systematic Review and Meta-Analysis. Am J Psychiatry 2016 Jan; 173 (1): 34-43.

- Alfano CA, Beidel DC, Turner SM. Preliminary evidence for sleep complaints among children referred for anxiety. Sleep Med. 2006 Sep; 7(6):467-73.
- 39. Alfano CA, Zakem AH, Costa NM. Sleep problems and their relation to cognitive factors, anxiety, and depressive symptoms in children and adolescents. Depress Anxiety. 2009; 26(6):503-12.
- Gregory AM, Sadeh A. Sleep, emotional and behavioral difficulties in children and adolescents. Sleep Med Rev. 2012 Apr; 16(2):129-36.
- 41. Byrd HC, Curtin C, Anderson S. Attention-deficit/hyperactivity disorder and obesity in US males and females, age 8-15 years: National Health and Nutrition Examination Survey 2001-2004. Pediatr Obes 2013 Dec; 8 (6): 445-53.
- 42. van Egmond-Fröhlich A, Widhalm K, de Zwaan M. Association of symptoms of attention-deficit/hyperactivity disorder with childhood overweight adjusted for confounding parental variables. Int J Obes 2012 Jul; 36 (7): 963-8.
- 43. Neumark-Sztainer D, Wall M, Larson NI, Eisenberg ME, Loth K. Dieting and disordered eating behaviors from adolescence to young adulthood: findings from a 10-year longitudinal study. J Am Diet Assoc 2011 Jul; 111 (7): 1004-11.

- 44. Nederkoorn C, Braet C, Van Eijs Y, Tanghe A, Jansen A. Why obese children cannot resist food: the role of impulsivity. Eat Behav 2006 Nov; 7 (4): 315-22.
- 45. Nederkoorn C, Jansen E, Mulkens S, Jansen A. Impulsivity predicts treatment outcome in obese children. Behav Res Ther 2007 May; 45 (5): 1071-5.
- 46. van Egmond-Fröhlich A, Claussnitzer G, Dammann D, Eckstein E, Bräuer W, de Zwaan M. Parent reported inattention and hyperactivity/impulsivity as predictor of long-term weight loss after inpatient treatment in obese adolescents. Int J Eat Disord 2013 Jan; 46 (1): 39-46.
- 47. Dumith SC, Gigante DP, Domingues MR, Kohl HWIII. Physical activity change during adolescence: a systematic review and a pooled analysis. Int J Epidemiol 2011 Jun; 40 (3): 685-98.
- 48. Nagata K. Does an excessive thin wish influence university student and school child's subjective symptoms? The Kwassui review. 2007; 50: 31-41.
- 49. Silva TB, Osório FL, Loureiro SR. SDQ: discriminative validity and diagnostic potential. Front Psychol. 2015 Jun 10; 6: 811.

Table 1. Questions about sleep

- 1. Do you ever shake your child to make him/her breathe again when asleep?
- 2. Does your child stop breathing during sleep?
- 3. Does your child struggle to breathe while asleep?
- 4. Are you ever concerned about your child's breathing during sleep?
- 5. Does your child snore?
- 6. Does he/she have problems with bed wetting?
- 7. Is your child easy to wake up in the morning?
- 8. Does your child need time to feel completely awake in the morning?
- 9. Does your child fall asleep suddenly in the daytime?
- 10. Does your child look tired?
- 11. How loud is the snore of your child?

Table 2. Questions about the expression of hyperactivity

- 1. Restless, overactive, cannot stay still for long.
- 2. Constantly fidgeting or squirming.
- 3. Easily distracted, concentration wanders.
- 4. Acting before thinking enough.
- 5. Lacking sufficient attention span, unable to see work through to the end.

Ref. Manual for noticing and supporting mild development disorder children (Ministry of Health, Labor and Welfare, Japan)

Table 3. Questions about the expression of anxiety

- 6. Often complains of headaches, stomach-aches or sickness
- 7. Many worries or often seems worried
- 8. Often unhappy, depressed or tearful
- 9. Nervous or clingy in new situations, easily loses confidence
- 10. Many fears, easily scared

Ref. Manual for noticing and supporting mild development disorder children (Ministry of Health, Labor and Welfare, Japan)

	Boys			Girls		
	Total	hyperactivity	anxiety	Total	hyperactivity	anxiety
	Ν	N, %	N, %	N	N, %	N, %
First grade	1236	100 (8.1)	63 (5.1)	1162	58 (5.0)	47 (4.0)
Second grade	1308	152 (11.6)	64 (4.9)	1251	55 (4.4)	51 (4.1)
Third grade	1328	130 (9.8)	38 (2.9)	1190	55 (4.6)	56 (4.7)
Fourth grade	1395	118 (8.5)	51 (3.7)	1354	55 (4.1)	63 (4.7)
Fifth grade	1480	118 (8.0)	65 (4.4)	1455	34 (2.3)	59 (4.1)
Sixth grade	1474	59 (4.0)	43 (2.9)	1415	27 (1.9)	53 (3.7)

Table 4. The numbers of children having hyperactivity and anxiety

	Boys			Girls		
	Hyper-	Hyper-	p value for	Hyper-	Hyper-	p value for
	activity (+)	activity (-)	difference	activity (+)	activity (-)	difference
Total number; N	677	7544		284	7543	
Mean Rohrer index (SD)	127.5 (18.8)	125.3 (17.7)	0.32	128.2 (17.7)	123.4 (16.6)	<0.001
Mean age; years (SD)	9.3 (1.6)	9.6 (1.7)	<0.001	9.1 (1.6)	9.6 (1.7)	<0.001
Mean hours of sleep;	8.4 (0.7)	8.4 (0.7)	0.90	8.3 (0.8)	8.4 (0.7)	0.33
hours (SD)						
Loud snoring; N (%)	118 (17.4)	681 (9.0)	<0.001	52 (18.3)	531 (7.0)	<0.001
Adenoid hypertrophy; N (%)	96 (14.2)	942 (12.5)	0.20	36 (12.7)	718 (9.5)	0.08
PH of seizure; N (%)	8 (1.2)	44 (0.6)	0.06	7 (2.5)	62 (0.8)	0.003
PH of asthma; N (%)	59 (8.7)	496 (6.6)	0.03	22 (7.7)	369 (4.9)	0.03
PH of HA; N (%)	4 (0.6)	53 (0.7)	0.74	3 (1.1)	42 (0.6)	0.27
Unbalanced diet; N (%)	239 (35.3)	1425 (18.9)	<0.001	93 (32.7)	1393 (18.5)	<0.001

Table 5. The characteristics of each group of children according to hyperactivity

PH = past history HA = hypoferric anemia

	Boys			Girls		
			p value for			p value for
	anxiety (+)	anxiety (-)	difference	anxiety (+)	anxiety (-)	difference
Total number; N	324	7897		329	7498	
Mean Rohrer index (SD)	128.0 (22.4)	125.4 (17.6)	0.13	125.0 (18.2)	123.5 (16.6)	0.005
Mean age; years (SD)	9.4 (1.7)	9.6 (1.7)	0.008	9.6 (1.7)	9.6 (1.7)	0.52
Mean hours of sleep;	8.4 (0.7)	8.4 (0.7)	0.43	8.2 (0.8)	8.4 (0.7)	<0.001
hours (SD)						
Loud snoring; N (%)	58 (17.9)	741 (9.4)	<0.001	49 (14.9)	534 (7.1)	<0.001
Adenoid hypertrophy; N (%)	60 (18.5)	978 (12.4)	0.001	40 (12.2)	714 (9.5)	0.15
PH of seizure; N (%)	2 (0.6)	50 (0.6)	0.85	7 (2.1)	62 (0.8)	0.006
PH of asthma; N (%)	28 (8.6)	527 (6.7)	0.30	18 (5.5)	373 (5.0)	0.83
PH of HA; N (%)	4 (1.2)	53 (0.7)	0.44	1 (0.3)	44 (0.6)	0.18
Unbalanced diet; N (%)	124 (38.3)	1540 (19.5)	<0.001	122 (37.1)	1364 (18.2)	<0.001

Table 6. The characteristics of each group of children according to anxiety

PH = past history HA = hypoferric anemia

	Boys			Girls		
	N (%)	PR		N (%)	PR	
Total	8221			7827		
HA(-)/A(-)	7312 (88.9)	1.00		7265 (92.8)	1.00	
HA(+)/A(-)	585 (7.1)	1.03	(95%CI 0.82-1.29)	233 (3.0)	1.40	(95%CI 1.01-1.92)*
HA(-)/A(+)	232 (2.8)	1.14	(95%CI 0.83-1.59)	278 (3.6)	1.34	(95%CI 0.98-1.84)
HA(+)/A(+)	92 (1.1)	1.16	(95%CI 0.70-1.93)	51 (0.7)	1.80	(95%CI 1.04-3.13)*
RERI	0.00		(95%CI -0.88-0.88)	0.18		(95%CI -1.47-1.83)
AP	0.00			0.10		

Table 7. Prevalence ratio for obesity regarding to hyperactivity and anxiety

HA = hyperactivity, A = anxiety PR = prevalence ratio, RER I= relative excess risk due to interaction, AP = attributable proportion due to interaction Age, Levels of snoring, Past history of asthma, and Existence of an unbalanced diet were adjusted for boys. Age, Levels of snoring, Past history of seizure, Past history of asthma, and Existence of an unbalanced diet were adjusted for girls. *p<0.05.

Appendix 1. Characteristics of children included in and excluded from the analysis

Characteristics of children included in the analysis

Male: 8221 Female: 7827

Mean age: 9.6

Mean Rohrer index: 124.6

Mean sleep time: 8.4

Percentage of children having hyperactivity: 6.0% (961/16048)

Percentage of children having anxiety: 4.1% (653/16048)

Characteristics of children included excluded from the analysis

Male: 3172 Female: 2748 Unknown: 2261 Mean age: 9.3 Mean Rohrer index: 119.0 Mean sleep time: 6.8 Percentage of children having hyperactivity: 9.0% (739/8181) Percentage of children having anxiety: 4.9% (397/8181)

	Boys		Girls	
	PR		PR	
HA(-)/A(-)	1.00		1.00	
HA(+)/A(-)	1.03	(95%CI 0.82-1.29)	1.40	(95%CI 1.01-1.92)*
HA(-)/A(+)	1.15	(95%CI 0.93-1.43)	1.13	(95%CI 0.89-1.42)
HA(+)/A(+)	1.10	(95%CI 0.75-1.61)	1.76	(95%CI 1.13-2.72)*

Appendix 2. Prevalence ratio for obesity regarding to hyperactivity and anxiety (excluding questions about depressive state)

*p<0.05.

Boys		Girls			
PR		PR	PR		
1.00		1.00			
1.03	(95%CI 0.82-1.29)	1.40	(95%CI 1.01-1.92)		
1.14	(95%CI 0.83-1.59)	1.34	(95%CI 0.98-1.84)		
1.16	(95%CI 0.70-1.93)	1.80	(95%CI 1.04-3.13)*		
	Boys PR 1.00 1.03 1.14 1.16	Boys PR 1.00 1.03 (95%CI 0.82-1.29) 1.14 (95%CI 0.83-1.59) 1.16 (95%CI 0.70-1.93)	Boys Girls PR PR 1.00 1.00 1.03 (95%CI 0.82-1.29) 1.40 1.14 (95%CI 0.83-1.59) 1.34 1.16 (95%CI 0.70-1.93) 1.80		

Appendix 3. Prevalence ratio for obesity regarding to hyperactivity and anxiety (including questions about depressive state)

*p<0.05.

	obesity	hyperactivity	anxiety	age	sleep	diet
obesity	1	0.01 (0.32)	0.02	-0.02	-0.06	0.08
			(0.13)	(0.13)	(<0.01)	(<0.01)
hyperactivity	0.01	1	0.15	-0.06	0 (0.9)	0.08
	(0.32)		(<0.01)	(<0.01)		(<0.01)
anxiety	0.02	0.15 (<0.01)	1	-0.03	-0.01	0.06
	(0.13)			(0.01)	(0.40)	(<0.01)
age	-0.02	-0.06 (<0.01)	-0.03	1	-0.39	-0.01
	(0.13)		(0.01)		(<0.01)	(0.42)
sleep	-0.06	0 (0.9)	-0.01	-0.39	1	-0 (0.98)
	(<0.01)		(0.40)	(<0.01)		
diet	0.08	0.08 (<0.01)	0.06	-0.01	-0 (0.98)	1
	(<0.01)		(<0.01)	(0.42)		

Appendix 4. correlation matrix for boys

	obesity	hyperactivity	anxiety	age	sleep	diet
obesity	1	0.04 (0)	0.03	-0.07	0.01	0.07
			(0.01)	(<0.01)	(0.43)	(<0.01)
hyperactivity	0.04 (0)	1	0.13	-0.06	-0.01	0.08
			(<0.01)	(<0.01)	(0.33)	(<0.01)
anxiety	0.03	0.13 (<0.01)	1	-0 (0.68)	-0.04 (0)	0.06
	(0.01)					(<0.01)
age	-0.07	-0.06 (<0.01)	-0 (0.68)	1	-0.43	-0.02
	(<0.01)				(<0.01)	(0.15)
sleep	0.01	-0.01 (0.33)	-0.04 (0)	-0.43	1	-0.01
	(0.43)			(<0.01)		(0.49)
diet	0.07	0.08 (<0.01)	0.06	-0.02	-0.01	1
	(<0.01)		(<0.01)	(0.15)	(0.49)	

Appendix 5. correlation matrix for girls