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Changes in sleep duration and sleep difficulties from adolescence to young adulthood and the risk of obesity: Bidirectional evidence in the GINIplus and LISA studies

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ABSTRACT

Objective: This study aimed to assess the association of changes in sleep behaviors from adolescence to young adulthood with the risk of overweight/obesity, and the reverse relationship.
Methods: Data of 1978 participants was obtained from the 15- and 20-year follow-ups of the GINIplus and LISA birth cohorts. Insufficient sleep was defined as reported sleep duration <8 h for adolescents, <7 h for adults, and sleep difficulties as reported having sleeping difficulties. Logistic regression models were used to assess bidirectional associations of changes in insufficient sleep and sleep difficulties with overweight/obesity. The polygenic risk scores (PRS) for body mass index (BMI) was tested in a subsample (n = 918).
Results: Compared with sufficient sleep in both adolescence and young adulthood, insufficient sleep only in young adulthood was associated with an increased risk of overweight/obesity (odds ratio = 1.85, 95% confidence interval = [1.27–2.69]). Compared with no sleep difficulties at both time-points, only persistent sleep difficulties was associated with a higher risk of overweight/obesity (2.15 [1.22–3.77]). The PRS for BMI was associated with overweight/obesity (1.41 [1.17–1.70]), but no significant gene-sleep interaction effect was observed. Reversely, only persistent overweight/obesity was associated with increased risks of insufficient sleep (1.81 [1.21–2.70]), and sleep difficulties (1.77 [1.18–2.66]), respectively.
Conclusions: Insufficient sleep only presented a cross-sectional association with overweight/obesity in young adulthood, while long-term sleep difficulties from adolescence to young adulthood was associated with young adult overweight/obesity. Reversely, long-term overweight/obesity from adolescence to young adulthood was associated with insufficient sleep and sleep difficulties in young adulthood.

1. Introduction

The prevalence of pediatric insufficient sleep and insomnia has greatly increased over the past decades [1,2]. Insufficient sleep and insomnia have detrimental effects on health and well-being among children and adolescents [3], especially on overweight/obesity in adulthood [4–6]. However, the cause and direction of the

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association between sleep behaviors and overweight/obesity remain unclear, and few longitudinal studies have investigated the relationships between changes in sleep behaviors (insufficient sleep or sleep difficulties) from adolescence transitioning to young adulthood and the risk of young adult overweight/obesity [5,7].

The transition from adolescence to young adulthood is an important developmental period when individuals undergo substantial physiological and psychological changes, which might lead to changes in sleep behavior, in turn impacts health [8,9]. Previous prospective studies analyzed a different number of follow-up time-points and sleep assessment methods in childhood and adolescence [4,10–12] to predict subsequent obesity or fat mass, but these had not considered the changes in sleep duration at different time-points. Additionally, only a few studies investigated changes in sleep duration and obesity in children and adolescents [7,13]. One study found that girls with insufficient sleep at 11 years but sufficient sleep at 18 years had an increase in body mass index (BMI) z-scores at 18 years compared to those with sufficient sleep at both time-points [7], while another study observed that change in total sleep duration was not significantly associated with changes in BMI over 2 years in adolescence [13].

Insufficient sleep has been identified as an important risk factor for the development of obesity [3,4,6,14], but as a reverse direction of association cannot be ruled out, the association may be bidirectional [15–17]. It might be plausible that obesity predisposes people to poor sleep quality, such as sleep apnea disrupting sleep [18]. Only a few studies examined the potential bidirectional longitudinal associations between sleep duration and obesity in children and adolescents with inconsistent findings [12,19,20]. Some studies discovered that higher BMI was associated with subsequent shorter sleep during adolescence to adulthood [19], or in infancy and early childhood [20], but not vice versa. However, another study revealed a bidirectional association between sleep duration and adiposity among South Asian children [12].

The application of polygenic risk scores (PRS), as an estimate of a participant's genetic liability to a trait or disease, represents a possibility to study gene-environment interaction effects on obesity with increased power [21]. A few gene-environment interaction studies have investigated the interactions of sleep duration with PRS on obesity in adults, which indicated that short sleep duration accentuated the effect of PRS on obesity [22,23]. However, the research on gene-sleep interactions in children and adolescents is rare, and previous PRS only focused on several common adult BMI single nucleotide polymorphisms (SNPs) [24,25] and were not based on the latest comprehensive loci for BMI [26].

In the present study, we assessed the associations of changes in sleep duration and sleep difficulties from adolescence to young adulthood, with overweight/obesity in young adulthood, considering genetic risk variants, using data from two prospective German birth cohorts. In parallel, we examined the relationships of the changes in overweight/obesity status with insufficient sleep and sleep difficulties from adolescence to young adulthood.

2. Methods

2.1. Study participants

Data in the present study was obtained from the 15- and 20-year follow-up examinations of two ongoing German birth cohort studies, GINIplus (German Infant Study on the influence of Nutrition Intervention PLUS environmental and genetic influences on allergy development) and LISA (Influence of Lifestyle factors on the development of the Immune System and Allergies in East and West Germany). In brief, a total of 5991 mothers and their newborns were recruited into the GINIplus study between 1995 and 1998 in Munich and Wesel, which consisted of the intervention arm (n = 2252), and the observation arm (n = 3739). The intervention study arm was a double-blind, randomized, intervention trial using three hydrolyzed formula nutrition and cow's milk formula, and was carried out among newborns with at least one allergic parent and/or sibling during the first 4 months, while breastfeeding was not wished or feasible. Newborns without a family history of allergic disease, and those with a family history whose parents refused to participate in the trial were followed-up in the observation arm. For the LISA study, a total of 3094 healthy, full term neonates were recruited between 1997 and 1999 in Munich, Leipzig, Wesel and Bad Honnef and surrounding areas. Four study centers were selected to represent different living areas across Germany, with Munich and Leipzig being considered more urban, and Wesel and Bad Honnef more rural areas. The study designs and recruitments have been described in more detail elsewhere [27–29].

Finally, a total of 1978 participants with complete information on variables of interest at both 15- and 20-year follow-ups were included for the main analysis, and a sub-sample of 918 participants with genotype data available in Munich and Wesel study centers were included for the genetic analysis (Fig. 1). Both studies were approved by the respective local ethics committees (Bavarian Board of Physicians, University of Leipzig, Board of Physicians of North-Rhine-Westphalia), and written informed consents were given from participants and their families.

2.2. Unfavorable sleep behaviors

Two unfavorable sleep behaviors, insufficient sleep duration and sleep difficulties, were assessed in the questionnaires at the 15- and 20-year follow-up examinations of both cohorts. In the 15-year follow-up, participants' parents were asked to answer the sleep duration related question “How many hours in total during the day and night does the child sleep on average?” and the sleep difficulties related question “Does the child have sleeping difficulties? (answer: yes; no)”. In the 20-year follow-up, participants responded to the sleep duration related questions “How many hours do you sleep on average on school/working days?” and “How many hours do you sleep on average on days off from school/work?”. Information on sleep difficulties was collected by the question “Do you have sleeping difficulties? (answer: yes; no)”. Average sleep duration in the 20-year follow-up was calculated as [(sleep duration on school/working days * 5 + sleep duration on days off from school/work * 2)/7]. Insufficient sleep was defined as sleep duration of <8 h for adolescents (15-year follow-up) [30] and < 7 h for young adults (20-year follow-up) [31]. Sleep difficulties were defined as parent-reported or self-reported sleeping difficulties.

To investigate the changes in insufficient sleep between adolescence and young adulthood, the participants were categorized into four groups according to insufficient sleep at both follow-ups, describing presence/absence at both time-points or at either time-point:

1) persistent sufficient sleep at both time-points (No/No, n = 1372)
2) insufficient sleep in adolescence but sufficient sleep in young adulthood (Yes/No, n = 259)
3) sufficient sleep in adolescence but insufficient sleep in young adulthood (No/Yes, n = 267)
4) persistent insufficient sleep at both time-points (Yes/Yes, n = 80).

For the changes in sleep difficulties over time, the participants were also divided into four groups:

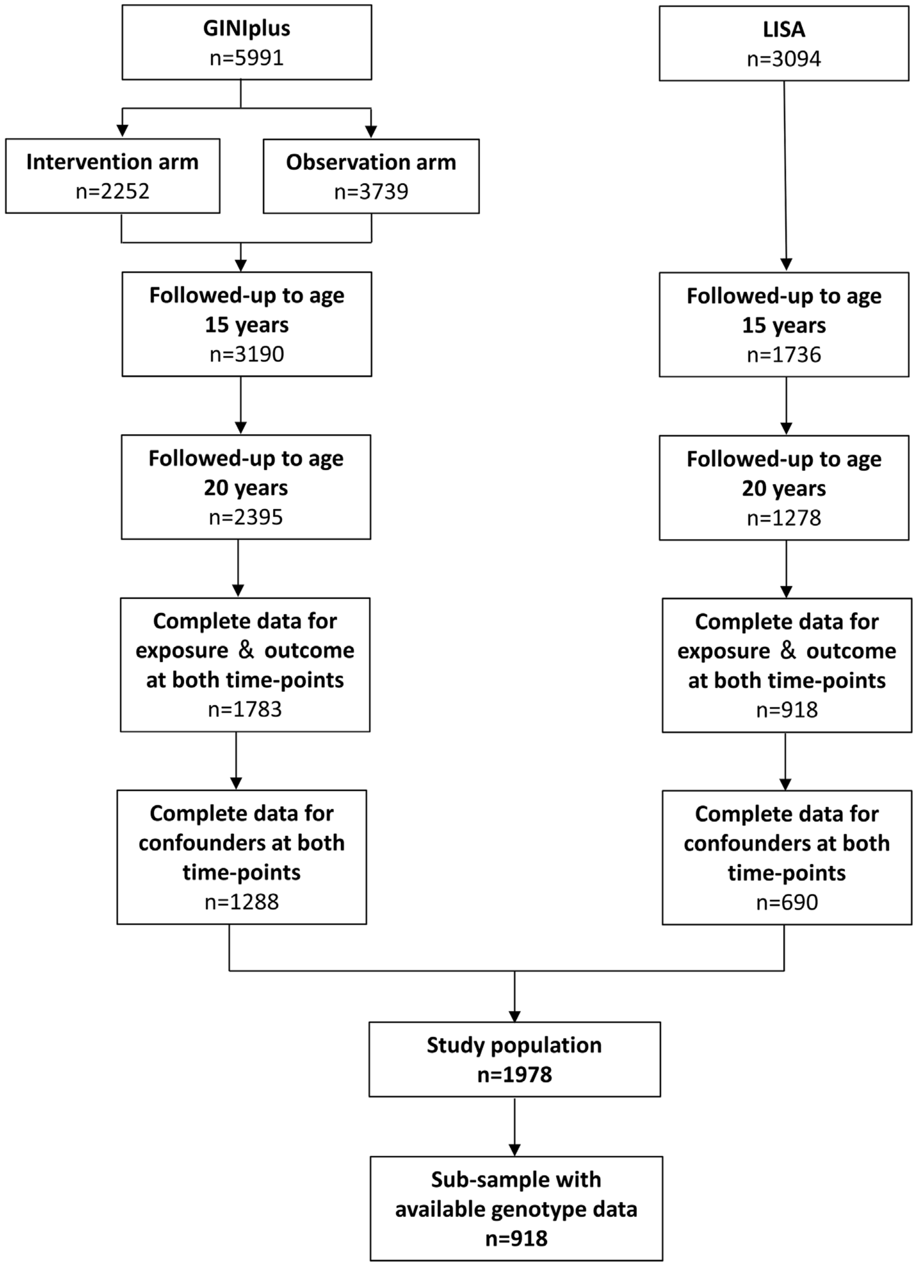

Fig. 1. Flow chart of participants.

1) persistent no sleep difficulties at both time-points (No/No, n = 1412)
2) sleep difficulties in adolescence but no sleep difficulties in young adulthood (Yes/No, n = 162)
3) no sleep difficulties in adolescence but sleep difficulties in young adulthood (No/Yes, n = 293)
4) persistent sleep difficulties at both time-points (Yes/Yes, n = 111).

2.3. Overweight/obesity

The weight and height of participants were reported by the parents at the 15-year follow-up, and by the participants at the 20-year follow-up. BMI was calculated as weight (kg)/height's square (m^2). For the 15-year follow-up, BMI z-scores were calculated based on the World Health Organization (WHO) growth reference for school-aged children and adolescents [32]. BMI was categorized into overweight/obesity (BMI z-scores ≥1 for adolescents [32] and BMI ≥25 kg/m^2 for young adults [33]) and normal weight (BMI z-scores <1 for adolescents and BMI <25 kg/m^2 for young adults).

To elucidate the changes in weight status from adolescence transitioning to young adulthood, participants were categorized into four groups, describing the presence/absence of overweight/obesity at both time-points or at either time-point:

1) persistent normal weight at both time-points (No/No, n = 1581)
2) overweight/obesity in adolescence but normal weight in young adulthood (Yes/No, n = 72)
3) normal weight in adolescence but overweight/obesity in young adulthood (No/Yes, n = 172)

4) persistent overweight/obesity at both time-points (Yes/Yes, n = 153).

2.4. Calculation of PRS

Genotyping for GINIplus and LISA was performed in 1511 samples using the Affymetrix Chip 5.0 and 6.0 (Thermo Fisher, USA) in the Munich study center and 883 samples using the Infinium Global Screening Array GSA v2 MD (Illumina, USA) in the Wesel study center. After quality control and genotype imputation, genome-wide data available for 918 participants in Munich and Wesel study centers with complete information on variables of interest was included in the present study. The quality control and genotype imputation have been described in detail previously [34,35].

PRS for adult BMI, as genetic determinants, were calculated based on previously published genome-wide association studies (GWAS) results on 97 significant BMI-associated loci ($P < 5 \times 10^{-8}$) [26]. The individual number of effect alleles of the selected SNPs were extracted for each participant and were weighted with the determined GWAS effect size [26]. For the Munich study center, of the 97 SNPs [26], only 96 SNPs were available, where 2 more were excluded due to low imputation quality ($R^2 < 0.4$) but one proxy with $R^2 > 0.7$ was added to replace one of the missing SNPs, and 95 SNPs in total were finally included in the calculation of the PRS. For the Wesel study center, 96 SNPs were available to be calculated into a PRS, but there was no proxy available for the missing variant. All PRS were normalized for the final analysis. The lists of SNPs for Munich and Wesel datasets can be found in the Supplemental Table S1.

2.5. Potential confounders

Potential confounders were sex, study (GINI observation arm, GINI intervention arm, and LISA study), study center (Munich, Leipzig, Bad Honnef, and Wesel), a parental highest education level (low: <10th grades; medium: 10th grades; and high: >10th grades), puberty stage (at 15-year follow-up) as well as exact age, physical activity, screen time, traffic noise and education/occupation types at the 20-year follow-up. Puberty stage was obtained from a self-rated scale for pubertal development: 1) prepubertal, 2) early pubertal, 3) midpubertal, 4) late pubertal, 5) postpubertal [36], and then was combined into 3 groups for the final analysis: 1) pre-/early/mid-pubertal, 2) late pubertal, and 3) postpubertal. Participants were asked how many hours per week (h/week) they spent in moderate physical activity (slight sweating, slightly increased breathing e.g. cycling, swimming, skating) in summer and winter, respectively; and how many hours they spent in vigorous physical activity (a lot of sweating, rapid breathing, e.g. ball games, training) in summer and winter, respectively. Then the average number of hours in moderate physical activity (summer and winter), and in vigorous physical activity (summer and winter), in h/week were calculated, respectively; followed by the sum of average moderate activity and average vigorous activity in h/week, which was defined as moderate to vigorous physical activity (MVPA). Physical activity was classified as low (MVPA <7 h/week), medium (7 h/week ≤ MVPA <10.5 h/week; MVPA ≥10.5 h/week but vigorous physical activity <3.5 h/week), high (MVPA ≥10.5 h/week and vigorous physical activity ≥3.5 h/week), according to Janssen (2007) [37]. Participants were asked how many hours they spent in front of a screen (television, computer, video games) per working/school day in summer and winter, respectively: 1) < 1 h, 2) 1–2 h, 3) 3–4 h, 4) 5–6 h, 5) 7–8 h, 6) 9–10 h, 7) > 10 h. Screen time was categorized into ≤2 h in summer and winter, and >2 h in summer or winter. Traffic noise was the self-reported degree to which the participant was disturbed by traffic noise at home when the window is open, from 0 (does not disturb) to 10 (unbearable), and was defined as no (0) and yes (>0). Participants were asked about the activity they currently mainly carried out: 1) school, 2) job training (a dual system accompanied with school attendance), 3) voluntary social/environmental year, 4) university, 5) employed, 6) unemployed, 7) housewife/househusband, 8) other. Then, education/occupation types were categorized into five types: 1) university, 2) job training, 3) school, 4) employed, and 5) other activities (voluntary social/environmental year, unemployed, housewife/househusband, and other).

2.6. Statistical analysis

The characteristics of the study participants were described in the total population and by sex, using mean value and standard deviation (SD) for continuous variables, and frequency (n) and percentage (%) for categorical variables. T-test for continuous variables and Chi-square test for categorical variables were used to explore differences between males and females.

In order to investigate the effects of changes in sleep behaviors on overweight/obesity, unfavorable sleep behaviors changes from adolescence to young adulthood, insufficient sleep and sleep difficulties, respectively, were modelled as exposures, and overweight/obesity in young adulthood as the outcome in multivariable logistic regression analyses. Three models were developed to adjust for potential confounding variables and PRS: Model 1 with adjustment for age, sex, study, study center, parental education, puberty (in adolescence), physical activity, screen time, traffic noise and education/occupation types in young adulthood; Model 2 with adjustment for covariates in Model 1 plus overweight/obesity in adolescence to test the effect of pre-existing overweight/obesity; and Model 3 with adjustment for covariates in Model 1 plus the PRS for BMI, followed by Model 3a that further added the interaction term with PRS. The insufficient sleep changes and sleep difficulties changes were mutually adjusted for in the same models.

In parallel, to determine the impact of the changes in overweight/obesity on unfavorable sleep behaviors, the exposures and outcomes were reversed. In the multivariable logistic regression models, the overweight/obesity status changes from adolescence to young adulthood were included as independent variables, and unfavorable sleep behaviors in young adulthood, insufficient sleep and sleep difficulties, respectively, as dependent variables. Two models were conducted to assess the effects of potential confounders. Model 1 included age, sex, study, study center, parental education, puberty (in adolescence), physical activity, screen time, traffic noise, education/occupation types, and sleep difficulties (for insufficient sleep) or insufficient sleep (for sleep difficulties) in young adulthood. Model 2 additionally included insufficient sleep and sleep difficulties in adolescence to examine the impact of pre-existing unfavorable sleep behaviors.

Furthermore, the interaction effects with sex were tested, and if the interaction term reached nominal significance, followed by sex-stratified analyses. Three sensitivity analyses were used to examine the robustness of our findings: first, excluding participants with overweight/obesity in adolescence; second, excluding those who had insufficient sleep or sleep difficulties in adolescence; third, using insufficient sleep defined only on school/working days in young adulthood.

3. Results

A total of 1978 participants with available data in adolescence and young adulthood were included in the final analyses. Table 1 presents the characteristics of the participants in the total

Table 1
Characteristics of participants in adolescence and young adulthood.

Variable	Total (n = 1978)	Male (n = 864)	Female (n = 1114)	*P*-value
Study, %				0.081
GINI observation	715 (36.1)	289 (33.4)	426 (38.2)	
GINI intervention	573 (29.0)	257 (29.7)	316 (28.4)	
LISA	690 (34.9)	318 (36.8)	372 (33.4)	
Study center, %				0.176
Munich	1080 (54.6)	495 (57.3)	585 (52.5)	
Leipzig	152 (7.7)	66 (7.6)	86 (7.7)	
Bad Honnef	69 (3.5)	29 (3.4)	40 (3.6)	
Wesel	677 (34.2)	274 (31.7)	403 (36.2)	
Parental education, %				0.219
Low	79 (4.0)	40 (4.6)	39 (3.5)	
Medium	454 (23.0)	186 (21.5)	268 (24.1)	
High	1445 (73.1)	638 (73.8)	807 (72.4)	
Adolescence (15-year follow-up)				
Age, years	15.0 ± 0.3	15.0 ± 0.2	15.1 ± 0.3	0.180
BMI, kg/m^2	20.1 ± 2.8	20.1 ± 2.9	20.1 ± 2.6	0.982
BMI z-score	−0.1 ± 1.0	0.0 ± 1.0	−0.2 ± 0.9	0.011
Sleep duration, hours	8.2 ± 0.8	8.3 ± 0.7	8.1 ± 0.8	<0.001
Overweight/obesity[a], %				<0.001
No	1753 (88.6)	735 (85.1)	1018 (91.4)	
Yes	225 (11.4)	129 (14.9)	96 (8.6)	
Insufficient sleep[b], %				<0.001
No	1639 (82.9)	752 (87.0)	887 (79.6)	
Yes	339 (17.1)	112 (13.0)	227 (20.4)	
Sleep difficulties, %				0.009
No	1705 (86.2)	765 (88.5)	940 (84.4)	
Yes	273 (13.8)	99 (11.5)	174 (15.6)	
Puberty, %				<0.001
Pre-/early/mid-pubertal	406 (20.5)	359 (41.6)	47 (4.2)	
Late pubertal	1376 (69.6)	499 (57.8)	877 (78.7)	
Postpubertal	196 (9.9)	6 (0.7)	190 (17.1)	
Young adulthood (20-year follow-up)				
Age, years	20.3 ± 0.4	20.3 ± 0.4	20.2 ± 0.4	<0.001
BMI, kg/m^2	22.4 ± 3.4	22.9 ± 3.4	22.1 ± 3.4	<0.001
Sleep duration, hours	7.6 ± 0.8	7.6 ± 0.8	7.7 ± 0.8	0.005
Overweight/obesity[a], %				0.032
No	1653 (83.6)	704 (81.5)	949 (85.2)	
Yes	325 (16.4)	160 (18.5)	165 (14.8)	
Insufficient sleep[b], %				0.409
No	1631 (82.5)	705 (81.6)	926 (83.1)	
Yes	347 (17.5)	159 (18.4)	188 (16.9)	
Sleep difficulties, %				0.001
No	1574 (79.6)	716 (82.9)	858 (77.0)	
Yes	404 (20.4)	148 (17.1)	256 (23.0)	
Physical activity, %				<0.001
Low	872 (44.1)	322 (37.3)	550 (49.4)	
Medium	589 (29.8)	263 (30.4)	326 (29.3)	
High	517 (26.1)	279 (32.3)	238 (21.4)	
Screen time, %				0.380
≤ 2 h	322 (16.3)	133 (15.4)	189 (17.0)	
> 2 h	1656 (83.7)	731 (84.6)	925 (83.0)	
Traffic noise, %				0.039
No	788 (39.8)	367 (42.5)	421 (37.8)	
Yes	1190 (60.2)	497 (57.5)	693 (62.2)	
Education/occupation types, %				0.096
University	1119 (56.6)	480 (55.6)	639 (57.4)	
Job training	436 (22.0)	184 (21.3)	252 (22.6)	
School	80 (4.0)	42 (4.9)	38 (3.4)	
Employed	191 (9.7)	97 (11.2)	94 (8.4)	
Other activities	152 (7.7)	61 (7.1)	91 (8.2)	

[a] Overweight/obesity: BMI z-score ≥1 according to WHO for adolescents; BMI ≥25 kg/m^2 for adults.
[b] Insufficient sleep: sleep duration <8 h for adolescents; <7 h for adults.

population and by sex in adolescence and young adulthood. Overall, the prevalence of insufficient sleep and sleep difficulties in adolescence was 17.1% and 13.8%, respectively, and the corresponding prevalence in young adulthood was 17.5% and 20.4%, respectively. The range of sleep duration in adolescence and young adulthood was 5.0–12.0 and 4.6–12.1 h, and the number of participants sleeping more than 10 h was 7 (0.3%) and 6 (0.3%), respectively. In addition, the prevalence of insufficient sleep on school/working days and on days off from school/work in young adults was 22.2% and 1.6%, respectively. The prevalence of sleep difficulties in participants with insufficient sleep was significantly higher than that in those with sufficient sleep in adolescence (25.4% vs 11.4%), and in young adulthood (32.6% vs 17.8%), respectively. However, no significant interaction effect between sleep difficulties and insufficient sleep on overweight/obesity was observed (data not shown).

In adolescence, 225 (11.4%) participants were overweight or obese, and in young adulthood, 325 (16.4%) were overweight or obese. Regarding the difference between sexes, female adolescents had a significantly higher prevalence of insufficient sleep and sleep difficulties than males, while the prevalence of overweight/obesity in females was lower than in males. In young adulthood, a similar pattern was found, although the difference in the prevalence of insufficient sleep between males and females was non-significant.

3.1. Associations between unfavorable sleep behaviors changes and overweight/obesity

Table 2 shows the associations from multivariable logistic regression models analysing changes in unfavorable sleep behaviors from adolescence to young adulthood with overweight/obesity in young adulthood. In Model 1, sufficient sleep in adolescence but insufficient sleep in young adulthood, and persistent sleep difficulties at both time-points were associated with increased risks of young adult overweight/obesity (odds ratio (OR) = 1.80, 95%confidence interval (CI) = [1.29–2.51] and 1.76 [1.05–2.94]), respectively. In Model 2, the effects were consistent with further adjustment for overweight/obesity in adolescence, and corresponding OR [95%CI] were 1.85 [1.27–2.69] and 2.15 [1.22–3.77], respectively. In contrast, participants with insufficient sleep or sleep difficulties in adolescence transitioning to be favorable in young adulthood, had no increased risk of young adult overweight/obesity (1.26 [0.82–1.95] and 1.12 [0.66–1.89]; respectively, Model 2). In Model 3, additionally including the PRS for BMI, the PRS was independently associated with the risk of young adult overweight/obesity (1.41 [1.17–1.70]), but the effect of persistent sleep difficulties on overweight/obesity attenuated to statistical non-significance (2.05 [0.95–4.42]). However, there was no significant interaction effect between PRS and the changes in insufficient sleep or sleep difficulties (Model 3a).

For the interaction analyses with sex, there was a significant interaction effect between sex and the group with sufficient sleep in adolescence but insufficient sleep in young adulthood (*P*-value interaction = 0.029). In the sex-stratified analyses, insufficient sleep only in young adulthood was associated with an increased risk of young adult overweight/obesity among males (2.62 [1.58–4.35]), but no such association was found in females (Table S2). However, females with persistent sleep difficulties at both time-points had a higher risk of young adult overweight/obesity (2.29 [1.09–4.81], Table S2). In the sensitivity analyses excluding those who were overweight/obese in adolescence, the overall findings did not change (Table S3).

3.2. Associations between overweight/obesity status changes and unfavorable sleep behaviors

Participants with persistent overweight/obesity at both time-points had higher risks of insufficient sleep (1.81 [1.21–2.70]), and sleep difficulties (1.77 [1.18–2.66]), respectively, compared to those who had normal weight at both time-points, including adjustment for insufficient sleep and sleep difficulties in adolescence (Table 3, Model 2). In contrast, the risk of young adult insufficient sleep or sleep difficulties did not seem to increase, when overweight/obesity in adolescence transitioned to normal weight in young adulthood (1.08 [0.56–2.09] and 0.54 [0.25–1.19]; respectively).

No significant interaction effect between sex and weight status changes was observed. In females, persistent overweight/obesity in both periods was associated with an increased risk of sleep difficulties (2.47 [1.42–4.27]) in young adulthood, but there was no association between weight status changes and insufficient sleep (Table S4). However, among males, no significant association between weight status changes and sleep difficulties was found, but overweight/obesity only in young adulthood was associated with a higher risk of insufficient sleep (2.06 [1.17–3.60]) (Table S4). In additional sensitivity analyses, after exclusion of those who had insufficient sleep or sleep difficulties in adolescence, the risk of sleep difficulties in the group with persistent overweight/obesity at both time-points was attenuated and not significant (1.59 [0.96–2.64], Table S5).

In further sensitivity analyses, the overall findings remained robust and unchanged, when using the definition of insufficient sleep restricted on school/working days only (Table S6).

4. Discussion

In the present study, we assessed the changes in unfavorable sleep behaviors and the risk of young adult overweight/obesity, and

Table 2
Associations between unfavorable sleep behaviors changes from adolescence to young adulthood and young adult overweight/obesity.

Outcome	Exposure		Model 1 (N = 1978)			Model 2 (N = 1978)		Model 3 (N = 918)			Model 3a
	Adolescence	Young adulthood	n (%)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	n (%)	OR (95% CI)	*P*-value	*P-value interaction*
Overweight/obesity	**Insufficient sleep**										
	No	No	201 (14.7)	1.00		1.00		92 (14.5)	1.00		
	Yes	No	42 (16.2)	1.10 (0.75–1.61)	0.639	1.26 (0.82–1.95)	0.289	20 (15.7)	0.99 (0.55–1.75)	0.960	0.767
	No	Yes	65 (24.3)	1.80 (1.29–2.51)	0.001	1.85 (1.27–2.69)	0.001	34 (27.4)	2.18 (1.34–3.56)	0.002	0.844
	Yes	Yes	17 (21.2)	1.22 (0.66–2.24)	0.520	0.83 (0.39–1.77)	0.634	8 (23.5)	1.36 (0.55–3.37)	0.503	0.090
	Sleep difficulties										
	No	No	216 (15.3)	1.00		1.00		101 (15.3)	1.00		
	Yes	No	27 (16.7)	1.18 (0.74–1.87)	0.488	1.12 (0.66–1.89)	0.678	10 (14.7)	0.97 (0.46–2.06)	0.945	0.705
	No	Yes	57 (19.5)	1.32 (0.93–1.86)	0.117	1.16 (0.78–1.72)	0.476	31 (22.0)	1.37 (0.84–2.25)	0.212	0.930
	Yes	Yes	25 (22.5)	1.76 (1.05–2.94)	0.030	2.15 (1.22–3.77)	0.008	12 (25.5)	2.05 (0.95–4.42)	0.066	0.575
	PRS								1.41 (1.17–1.70)	<0.001	

Model 1: Adjusted for age, sex, study, study center, parental education, puberty (in adolescence), physical activity, screen time, traffic noise, and education/occupation types in young adulthood.
Model 2: Model 1 + overweight/obesity in adolescence.
Model 3: Model 1 + PRS for BMI.
Model 3a: Model 3 + interaction term between unfavorable sleep behaviors and PRS.
n (%): number of cases (prevalence). OR: odds ratio; 95%CI: 95% confidence interval. PRS: polygenic risk scores. The insufficient sleep changes and sleep difficulties changes were mutually adjusted for in the same models.

Table 3
Associations between overweight/obesity status changes from adolescence to young adulthood and unfavorable sleep behaviors in young adulthood.

Outcome	Exposure		n (%)	Model 1 (N = 1978)		Model 2(N = 1978)	
	Adolescence	Young adulthood		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Insufficient sleep	**Overweight/obesity**						
	No	No	253 (16.0)	1.00		1.00	
	Yes	No	12 (16.7)	1.07 (0.56–2.06)	0.838	1.08 (0.56–2.09)	0.813
	No	Yes	39 (22.7)	1.46 (0.98–2.16)	0.060	1.45 (0.98–2.15)	0.067
	Yes	Yes	43 (28.1)	1.81 (1.21–2.70)	0.004	1.81 (1.21–2.70)	0.004
Sleep difficulties	**Overweight/obesity**						
	No	No	314 (19.9)	1.00		1.00	
	Yes	No	8 (11.1)	0.55 (0.26–1.19)	0.129	0.54 (0.25–1.19)	0.126
	No	Yes	35 (20.3)	1.06 (0.71–1.59)	0.784	0.99 (0.65–1.50)	0.959
	Yes	Yes	47 (30.7)	1.74 (1.17–2.58)	0.006	1.77 (1.18–2.66)	0.006

Model 1: Adjusted for age, sex, study, study center, parental education, puberty (in adolescence), physical activity, screen time, traffic noise, education/occupation types, and sleep difficulties (for insufficient sleep) or insufficient sleep (for sleep difficulties) in young adulthood.
Model 2: Model 1 + insufficient sleep and sleep difficulties in adolescence.
n (%): number of cases (prevalence). OR: odds ratio; 95%CI: 95% confidence interval.

the reverse association of changes in overweight/obesity with the risk of young adult unfavorable sleep behaviors, using data from the 15- and 20-year follow-ups of the GINIplus and LISA cohorts. We found that insufficient sleep only had a cross-sectional association with overweight/obesity in young adulthood, while persistent sleep difficulties from adolescence to young adulthood was associated with overweight/obesity. Reversely, persistent overweight/obesity had impacts on young adult insufficient sleep and sleep difficulties.

The risk of overweight/obesity in young adulthood was associated with current insufficient sleep, independent of insufficient sleep in adolescence. Participants who favourably altered their insufficient sleep between adolescence and young adulthood had a similar risk of overweight/obesity to those with persistent sufficient sleep at both time points. To our knowledge, only one other study assessed the relationships between combinations of the presence or absence of insufficient sleep at two time-points and BMI or BMI z-scores from childhood to young adulthood among 3974 Brazilian participants [7]. In contrast to the findings of the present study, compared to those with adequate sleep duration at both time-points, girls who altered the inadequate sleep duration at 11 years to adequate sleep duration at 18 years, had an increase in BMI z-scores ($\beta = 0.39$, 95%CI = 0.13–0.65) and fat mass index (FMI) z-scores ($\beta = 0.30$, 95%CI = 0.07–0.53) [7]. In addition, a study reported that the change in total sleep duration was not associated with changes in BMI or percent body fat (PBF) over 2 years in 723 US adolescents [13]. On the contrary, another prospective study comprising 14800 US participants found that cumulative exposure to short sleep from adolescence to young adulthood had a dose-response association with the odds of obesity [4].

Unlike the cross-sectional association between insufficient sleep and overweight/obesity in young adulthood, sleep difficulties exhibit a long-term relationship with overweight/obesity throughout adolescence and young adulthood. While the cross-sectional association of BMI with sleep duration is well known, the association of sleep difficulties with overweight/obesity is less clear. A meta-analysis mostly comprising cross-sectional studies including 25,082 children, adolescents, and young adults found that poor sleep quality (subjectively reported) was significantly associated with a higher odds of overweight/obesity (1.46 [1.24–1.72]), independent of sleep duration [38]. In contrast, 233 German patients with a confirmed diagnosis of insomnia (mean age 52 years old) showed a lower BMI (23.8 kg/m^2 versus 27.1 kg/m^2; $P < 0.05$), compared to the representative population matched by age and sex [39]. Varying findings between previous studies might be due to different study designs, age groups, and sample sizes.

In addition to previous studies, we also considered genetic risk variants and found that PRS for BMI was independently associated with overweight/obesity in young adulthood, while there was no interaction effect with unfavorable sleep behaviors. This is different from the previous studies related to the interaction effects between genetic risk scores (GRS) with sleep duration in children and adolescents. For example, in a Chinese cohort study of 3211 children and adolescents aged 6–18 years, Fu et al. [25] revealed that a GRS consisting of six leptin-related SNPs had an interaction with sleep duration, where GRS was robustly associated with a higher BMI and overweight/obesity among short sleepers (<8 h/day). Similarly, Prats-Puig et al. [24] reported that a GRS of three common SNPs in the obesity genes (*FTO*, *TMEM*18, and *NRXN*3) had a greater effect on the negative association between short sleep duration and BMI in 297 Caucasian children aged 5–9 years. Unlike the previous few studies of gene-sleep interactions in children and adolescents [22], our study utilized the most comprehensive SNPs (96 SNPs in Munich center and 95 SNPs in Wesel center) for BMI to analyse the gene-sleep interaction on the risk of overweight/obesity in young adults. The discrepancy between the above studies may be due to the different study approaches, where we evaluated the genetic risk using GWAS-selected SNPs, but other studies focused on specific pathways, as well as different sample sizes and ethnicities [22].

Our study also found that associations vary between sexes, where females with persistent sleep difficulties from adolescence to young adulthood had a higher risk of overweight/obesity, yet males with insufficient sleep only in young adulthood was associated with an increased risk of overweight/obesity. This finding related to short sleep among males was consistent with the majority of previous research. Several studies have reported a stronger association between short sleep and overweight/obesity in boys than in girls among adolescence [40,41]. For example, a US study composed of a nationally representative sample found that short sleep presented a cross-sectional association with obesity in adolescent boys but not in girls, while exhibiting a longitudinal association with obesity in both young adult males and females [41]. In contrast, Lytle et al. [13] did not observe a significant association between change in sleep duration and change in BMI or PBF over 2 years during adolescence in either girls or boys. The evidence about the sex discrepancy in association between sleep difficulties and overweight/obesity is rare. Our findings suggested that females with sleep difficulties between adolescence and young adulthood are more susceptible to develop overweight/obesity than males, which might be due to different physiologic mechanisms and sex hormones between sexes during adolescence [41,42].

While exploring the direction of unfavorable sleep behaviors with overweight/obesity, we observed that overweight/obesity had long-term impacts on insufficient sleep and sleep difficulties from adolescence to young adulthood. Our finding regarding the bidirectional associations of sleep duration with overweight/obesity was similar to the results in children observed by Collings et al. [12], where sleep duration was inversely associated with total and abdominal adiposity, and higher adiposity was also associated with shorter sleep duration among South Asian children, using data at 4 time-points from 12 to 36 months of age. However, Sokol et al. [19] found that higher BMI was associated with subsequent shorter sleep during adolescence to adulthood, but sleep duration was not associated with subsequent BMI. Until now, longitudinal studies on obesity and sleep difficulties, as well as their bidirectional associations were very rare in children and adolescents. A meta-analysis conducted in adults based on three prospective studies found that the odds of developing future insomnia symptoms among participants with obesity at baseline were not significantly higher than among those with normal-weight at baseline (1.07 [0.91, 1.26]) [43].

Regarding the bidirectional relationships between insufficient sleep, sleep difficulties, and overweight/obesity, it is hard to distinguish what comes first [44,45], and it might be that there are also shared risk factors. In our sensitivity analyses, after exclusion of adolescents who were overweight/obese at baseline, persistent sleep difficulties was still associated with the risk of developing new-onset young adult overweight/obesity (2.04 [1.11–3.73]). However, persistent overweight/obesity was no longer statistically related to the risk of developing new-onset young adult sleep difficulties (1.59 [0.96–2.64]) after the exclusion of participants with insufficient sleep/sleep difficulties at baseline, although the p-value (0.071) was borderline significant. The mechanism of sleep restriction leading to obesity may be that sleep deprivation influences physiological, autonomic nervous system, hormonal system, and food preferences, further promoting the increased dietary intake, decreased physical activity, and weight gain [44–46]. On the other side, the relationship that obesity could cause sleep loss or sleep disorders should also be worth noting. The biological mechanisms regarding this association might involve the changes in pro-inflammatory cytokines levels, diet food components, and vitamin D deficiency [44,47,48].

Our study has several strengths. We investigated the relationships between the changes in sleep difficulties from adolescence transitioning to young adulthood and the risk of overweight/obesity for the first time. Our data also allowed us to consider the role of genetic variants for BMI on the associations. In addition, we explored the bidirectional associations between unfavorable sleep behaviors and overweight/obesity in adolescence and young adulthood. The limitations of the present study should also be noted. Firstly, the information on sleep behaviors, including sleep duration and sleep difficulties, were obtained by parent-reported questionnaire at 15-year follow-up and self-reported questionnaire at 20-year follow-up. Although there is a potential bias between subjective sleep and objective sleep, some evidence showed that parent-reported and self-reported sleep data were moderately correlated with objective sleep data [49,50]. However, self-reported sleep duration has been used by several previous studies, but applied different methodology with regards to number and time-points of sleep assessment as well as age and follow-up period which limits comparability [4,10–12]. Secondly, the weight and height of participants were reported by parents at the 15-year follow-up, and by participants at the 20-year follow-up. Despite males tend to overestimate their heights and females tend to underestimate their weights, self-reported height and weight has been confirmed to be statistically associated with actual measures and can be calculated for BMI and weight categories in young adults [51]. Thirdly, we could not account for other sleep characteristics, such as sleep timing, sleep efficiency, sleep onset latency, and day-to-day variability in sleep duration, which could also have impacts on weight status in adolescents [52,53]. Fourthly, our study used the average sleep duration in the 15-year follow-up and average sleep duration [(sleep duration on school/working days * 5 + sleep duration on days off from school/work * 2)/7] in the 20-year follow-up to represent participants' average and habitual sleep duration, and was unable to consider the weekend catch-up sleep. Our results showed that the prevalence of insufficient sleep in a week and on school/working days were similar, but the prevalence of insufficient sleep was much lower on days off from school/work. However, the sensitivity analyses restricting the definition of insufficient sleep only on school/working days showed robust results. Fifthly, we were not able to distinguish sufficient sleep and hypersomnia, due to missing information about the daytime sleepiness in the study. Sixthly, we could not differentiate sleep difficulties from other sleep disorders, especially insomnia and delayed sleep phase syndrome, which are common sleep disorders in adolescents [54].

5. Conclusions

Long-term sleep difficulties between adolescence and young adulthood were associated with young adult overweight/obesity, and vice versa, indicating a bidirectional association. Insufficient sleep only showed a cross-sectional relationship with young adult overweight/obesity, while overweight/obesity had a longitudinal association with young adult insufficient sleep. In contrast, the risk of young adult overweight/obesity did not seem to increase when unfavorable sleep behaviors in adolescence transitioned to be favorable in young adulthood. Our study highlighted the impacts of long-term sleep difficulties on young adult obesity, and emphasized the importance of maintaining a healthy sleep from adolescence to young adulthood through future public health interventions to prevent obesity later in life.

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Declaration of competing interest

None

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Appendix A. Supplementary data

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