Chapter 4.1

Review of the literature on the association between depressive symptoms in childhood and adolescence and overweight in later life

Eryn T. Liem
Pieter J.J. Sauer
Albertine J. Oldehinkel
Ronald P. Stolk

ABSTRACT

Objective: To present an overview of the association between depressive symptoms in childhood and adolescence and subsequent overweight in later life.

Data sources: MEDLINE, EMBASE, and Web of Science for all indexed journals from January 1, 1997, to May 30, 2007.

Study selection: Abstracts of 514 articles were reviewed manually. Studies were excluded if unrelated to depressive symptoms and overweight (n=460), if they were conducted in an adult population (n=10) or in a population of all age groups (n=2), or performed in clinic-based populations of overweight participants. In total, 32 articles were reviewed including 21 cross-sectional and 11 longitudinal reports.

Main exposure: Depressive symptoms in childhood and adolescence.

Main outcome measure: Overweight.

Results: Four cross-sectional studies that satisfied our quality criteria revealed an association between depressive symptoms and overweight in girls aged 8 to 15 years, reporting different effect sizes including a correlation coefficient of 0.14 and a regression coefficient of 0.27. Four longitudinal studies in accord with our quality criteria suggest that depressive symptoms in childhood or adolescence are associated with a 1.90- to 3.50-fold increased risk for subsequent overweight (95% confidence intervals varying from 1.02 to 5.80, respectively).

Conclusion: These results support a positive association between depressive symptoms at age 6 to 19 years and overweight in later life, assessed after a period of 1 to 15 years.

INTRODUCTION

Worldwide, the prevalence of childhood overweight has increased. In the United States between 2002 and 2004, the prevalence of overweight in 6- to 19-year-old individuals was 31.8% among males and 30.3% among females.[1] In Europe numbers vary from 10-20% in the northern areas to 20-35% in the Mediterranean areas.[2] This results in an increased prevalence of complications of overweight, such as hypertension, dyslipidemia, and diabetes mellitus type 2. For example, the Centers for Disease Control and Prevention (CDC) estimates that one-third of the children born in the United States in 2000 will eventually develop diabetes.[3] Thus, prevention of overweight is a major public health concern. Targeted and tailored preventative strategies that consider cost-effectiveness need to be developed, and, therefore, important predictors of overweight in childhood and adolescence need to be determined. Predictors of childhood and adolescent overweight are also appropriate to identify groups at high risk. A recent review identified both somatic factors, such as dietary intake and parental overweight and psychosocial predictors such as life style, temperament, socioeconomic status, and parental control of feeding as possible predictors of overweight.[4] Depressive symptoms have been described as a predictor and as a consequence of overweight, primarily in adults but also in adolescents.[5] Identifying treatable predictors such as depressive symptoms could lead to better strategies for prevention of overweight.

Adolescence is a decisive period in human life because of the multiple changes that occur between childhood and adulthood. Puberty is the primary neurohormonal determinant of both physiological and psychological changes, although social and behavioral factors must also be considered in this process.[6] In adolescence, both overweight and depressive symptoms become more common, increasing the likelihood of a simultaneous occurrence. This raises questions about a possible association or common cause, as described in an early review article on obesity-depression associations in the population.[5] In contrast to the common idea that overweight might lead to unhappiness and consequently to depressive symptoms, recent reports suggest that depressive symptoms could also precede overweight[5] and thereby could be a risk factor for the development of overweight.

In particular, atypical depression has been considered related to the development of overweight.[7] Despite the term “atypical”, it is a common form of depression.[8] Atypical depression is characterized by mood reactivity and reversed neurovegetative symptoms such as weight gain, hyperphagia, and hypersomnia, which renders it interesting in the association between depressive symptoms and overweight. Atypical depression has been described in children and adolescents, although it is not a very distinct entity in this age group.[9]

The objective of this review was to evaluate the evidence for the role of depressive symptoms in childhood and adolescence as a risk factor for overweight. Because we were interested in early risk factors for overweight, we focused on studies with a baseline measurement in childhood or adolescence, in which at least one follow-up measurement was

performed. We defined childhood as age 1 to 12 and adolescence as age 13 to 19 years. To introduce the existing literature, assessment of depressive symptoms and overweight are briefly explained. Current hypotheses about the mechanisms involved in the relationship between depressive symptoms and overweight are also discussed.

METHODS

Study retrieval

A preliminary search of PubMed revealed that before 1997 no longitudinal studies in children and adolescents had been published that examined the association between depressive symptoms and overweight. Moreover, most of the cross-sectional reports have been published in the last 10 years. Therefore, we performed searches of MEDLINE, EMBASE, and Web of Science in May 2007 for all indexed journals from January 1, 1997, to May 30, 2007. Keywords included "depression", "depressive disorder", "internalizing disorders", "mental disorders", "obesity", and "overweight", limited to "all child". Additional studies were identified in the bibliographies of the articles. Only English-language articles that were peer reviewed were considered. This resulted in 514 articles, of which abstracts were reviewed manually. Most articles concerned a different topic (n=460), such as "Exercise therapy as a treatment for psychopathological conditions in obese and morbidly obese adolescents: a randomized controlled trial,"[10] and "The link between sleep duration and obesity: we should recommend more sleep to prevent obesity."[11] Studies were excluded if conducted in an adult population (n=10) or in a population of all age groups (n=2). Reviews (n=5) were excluded as well. In addition, clinic-based populations of obese children and adolescents seeking treatment (n=5) were excluded because populations seeking treatment differ from population-based samples and, therefore, were considered beyond the scope of this article. In view of the limited number of published articles on longitudinal research, cross-sectional studies were reviewed as well to support the existence of an association between depressive symptoms and overweight. We extracted age, sex, and sample size of the population; measure of depressive symptoms; assessment of weight and height (measurement or self-report); main result (positive, negative, or no association), and effect size. If available, odds ratios (ORs) or β levels were used as indicators of the effect size. If not, other available measures such as correlations and maximum explained variances were extracted. First, we included all studies that satisfied the inclusion and exclusion criteria (n=32, including 21 cross-sectional and 11 longitudinal reports). Second, we focused on the quality of the various studies. Quality was determined by four criteria, namely whether studies were based on questionnaires specifically validated for depressive symptoms; whether investigators measured BMI (calculated as weight in kilograms divided by height in meters squared) rather than using self-reported values; whether they

also evaluated important confounding variables, specifically sex, ethnicity, and socioeconomic status;[5] and whether investigators reported an effect size. Four cross-sectional and 4 longitudinal studies were in accord with these criteria.

Assessment of depressive symptoms and overweight

Depressive symptoms can be assessed with the use of various methods, depending on the perspective and taxonomic system but also on the nature of the sample under investigation. Various definitions of adolescent depressive symptoms have been adopted, specifically depressed mood, syndromes that include depressive symptoms, and depressive disorder according to the *Diagnostic and Statistical Manual of Mental Disorders*.[12] These 3 approaches entail different measurement tools. Depressed mood and depressive syndromes are generally assessed with the use of questionnaires that result in continuous measures, whereas *Diagnostic and Statistical Manual of Mental Disorders* depressive disorders are usually ascertained by diagnostic interviews, resulting in dichotomous outcomes. Despite differences in the various measurement tools, previous research has shown consistencies in the identification of depressed mood and depressive symptoms.[13] Nevertheless, not all studies included in this review use questionnaires which have been validated for assessment of depressive symptoms. Especially in large epidemiological surveys, questions regarding depressive symptoms are commonly part of a broader evaluation of general psychosocial health. This implies that these surveys should be cautiously interpreted. To this extent, we evaluated the use of validated questionnaires in a quality assessment.

For the assessment of overweight in large epidemiological surveys, BMI is recommended. This is not a direct measure of body fatness because it does not differentiate between muscle tissue and fat tissue, contrary to, for example, dual-energy X-ray absorptiometry.[14] However, weight and height measurements for BMI are practical and show a low measurement error and high reliability.[14] It has been reported that BMI is more accurate when weight and height are measured clinically than when obtained by self-reported measurements at home. Overweight and obesity are defined by BMI cut-off values based on large population-based surveys.[15,16]

RESULTS

Cross-sectional studies

Sixteen population-based cross-sectional studies in children and adolescents[17-32] suggest a positive association between depressive symptoms and overweight (Table 1). Of these, eight studies reported ORs ranging from 1.67 to 3.72, and 95% confidence intervals (CIs) from 1.08 to 10.2. Four cross-sectional studies reported effect sizes based on continuous measures.[18,22,26,27] Statistically significant betas varied from 0.07 to 0.27, with SEs of 0.02 to 0.10.

Pine and colleagues reported no significant result from the linear regression analysis, but a significant result from the logistic regression analysis.[27] Two studies reported correlations, of 0.14 and 0.20, respectively.[17,28] One study reported maximum explained variances of 0.003 and 0.005 (P = 0.001 and 0.01 respectively).[25] Two studies did not report any effect size.[21,24]

We found 4 studies that reported no association between overweight and depressive symptoms.[33-36] This could be explained by a small sample size in 1 study [33] and the use of a single item questionnaire to evaluate depressive symptoms in another.[35] Moreover, 3 studies did not provide any measure to quantify their findings.[33-35] One study based on self-reported weight and height reported a negative association.[37]

Four of the 20 cross-sectional studies satisfied our quality criteria (Table 1a). In a population of 868 children aged 8 to 9 years, Erickson and colleagues reported a correlation of 0.14 between BMI and depressive symptoms in girls and no association in boys.[17] Xie and colleagues, who conducted their study in a population of 1655 Chinese adolescents aged 11 through 15 years, also found an association (regression coefficient 0.27) only in girls.[26] Wardle and colleagues actually described 2 studies; however, a validated questionnaire for depressive symptoms was used only in the smaller study in 1824 adolescents aged 14 to 15 years.[25] Analysis of variance revealed a positive association ($F_{(2, 4231)} = 6.97$; P = 0.001).

Table 1. Cross-sectional studies correlating youth depressive symptoms and overweight.
Table 1a. Cross-sectional studies correlating youth depressive symptoms and overweight in accordance with quality criteria.

Study	Population	Measure of depressive symptoms	BMI (weight and height from self-report or measured)	Main result	Effect size
Erickson et al (2000)[17]	n=868 Age: 8-9 yrs	CDI*	Measured continuous	+	r = 0.14 (P < 0.01) ♀
Xie et al (2005)[26]	n=1655 Age: 11-15 yrs	CES-D*	Measured continuous	+	Beta = 0.27, SE 0.10 (P < 0.05) ♀
Wardle et al (2006)[25]	n=4320 Age: 11 yrs	SDQ-ES	Measured overweight and obesity (Cole)	+	R^2 = 0.003 (P = 0.001)
	n=1824 Age: 14-15 yrs	CES-D*	Measured overweight and obesity (Cole)	+	R^2 = 0.005 (P = 0.01)
Ozmen et al (2007)[37]	n=2101 Age: 15-18 yrs	CDI*	Measured overweight: BMI (Cole)	0	OR = 1.74 (0.96 – 3.23)

+ = positive association; - = negative association; 0 = no association.
CDI = Children's Depression Inventory (questionnaire); CES-D = Center for Epidemiological Studies Depression scale (questionnaire); SDQ-ES = Strengths and Difficulties Questionnaire – Emotional Symptoms scale (non validated questionnaire.
r = correlation coefficient; Beta = regression coefficient; SE = standard error; R^2 = maximum explained variance; OR = odds ratio (95% confidence interval).
* Validated questionnaire / interview.

Table 1b. Other cross-sectional studies correlating youth depressive symptoms and overweight.

Study	Population	Measure of depressive symptoms	BMI (weight and height from self-report or measured)	Main result	Effect size
Pine et al (1997)[27]	n=644 Age: 22 yrs	DIS*	Self-report - continuous - cut-off: 80th percentile	+ 	 Beta = 0.40, SE 0.22 (NS) ♂, Beta = - 0.92, SE 0.27 (NS)♀ OR = 1.54 (1.09 – 2.17) ♀
Neumark-Sztainer et al (1997)[32]	n=31122 Age: 12-18 yrs	Validated questionnaire*	Self-report - overweight: BMI ≥ 85th percentile - obesity: BMI ≥ 95th percentile	+ 	 NS OR = 1.32 (1.09 – 1.60) ♂ OR = 1.24 (1.01 – 1.55) ♀
Renman et al (1999)[33]	n=116 Age: 14-18 yrs	YSR* (internalizing subscale)	Measured - severe obesity BMI ≥ 30 or ≥ 99.6th percentile	0 	Non reported
Pesa et al (2000)[36]	n=3197 (♀) Age: 12-18 yrs	Validated questionnaire*	Self-report - overweight: BMI > 25	- 	 DFC = -0.096 (P = 0.011)
Falkner et al (2001)[30]	n=9943 Age: 12-17 yrs	Non validated questionnaire	Self-report - overweight: BMI ≥ 85th percentile (NHANES I) - obesity: BMI ≥ 95th percentile (NHANES I)	+ 	 OR = 0.98 – 1.09 (0.65 – 1.65) (depending on subscale of questionnaire) OR = 1.38 – 1.79 (1.08 – 2.65) (depending on subscale of questionnaire)
Lamertz et al (2002)[34]	n=2939 Age: 14-24 yrs	M-CIDI* SCL-90-R*	Self-report - obesity: BMI ≥ 95th percentile	0 	Non reported
Mustillo et al (2003)[31]	n=991 Age: 16 yrs	CAPA	Measured - trajectories	+ 	 OR = 3.72 (1.27 – 10.2) ♂
Datar et al (2004)[23]	n=9949 Age: 5 yrs	SRS	Measured - overweight: BMI ≥ 95th percentile	+ 	 OR = 1.54 (1.09 – 2.17) ♀
Berg et al (2005)[21]	n=989 (all male) Age: 15 yrs	Non validated questionnaire	Self-report - overweight: BMI (Cole) - obesity: BMI (Cole)	+ 	Non reported

Table 1b. continued

Study	Population	Measure of depressive symptoms	BMI (weight and height from self-report or measured)	Main result	Effect size
Daniels (2005)[35]	n=7993 Age: 16-18 yrs	Non validated questionnaire	Self-report - overweight: BMI ≥ 85th percentile (CDC) - obesity: BMI ≥ 95th percentile (CDC)	0	Non reported
Needham et al (2005)[18]	n=18924 Age: 12-18 yrs	CES-D*	Self-report - continuous	+	Beta = 0.08, SE 0.02 (P < 0.01)
Sjöberg et al (2005)[19]	n=4703 Age: 15-17 yrs	DSRS*	Self-report - overweight: BMI (Cole) - obesity: BMI (Cole)	+ 	 OR = 0.96 (0.77 – 1.12) OR = 1.67 (1.12 – 2.49)
Richardson et al (2006)[20]	n=3101 Age: 11-17 yrs	SCL-90*	Self-report - obesity: BMI ≥ 95th percentile (CDC)	+ 	 OR 2.17 (1.25 – 3.77) ♀ OR 1.95 (1.19 – 3.18) ♂
Sweeting et al (2006)[24]	n=2127 Age: 11-15 yrs	- KDS* - DISC* (age 15)	Measured - obesity: BMI > 95th percentile	+ (♂, age 11)	Non reported
Ter Bogt et al (2006)[22]	n=1826 Age: 11-16 yrs	YSR* (internalizing subscale)	Self-report - overweight: BMI ≥ + 1.1 SD	+ 	 Beta = 0.07, SE not reported (P < 0.01)
Viner et al (2006)[29]	n=2789 Age: 11-14 yrs	SDQ	Measured - obesity: BMI ≥ 95th percentile (CDC)	+ 	 OR = 1.5 (1.1 – 2.1)
Young-Hyman et al (2006)[28]	n=164 Age: mean 11.9, SD 2.5	CDI*	Measured - continuous: SDS (based on CDC)	+ 	 r = 0.20 (P < 0.01)

+ = positive association; - = negative association; 0 = no association.

DIS(C) = Diagnostic Interview Schedule for Children (layperson interview); YSR = Youth Self Report (questionnaire); M-CIDI = Munich – Composite International Diagnostic Interview; SCL-90-R = Symptoms Checklist Revised 90 (questionnaire); CAPA = Child and Adolescent Psychiatric Assessment (interview); SRS = Social Rating Scale (questionnaire); CES-D = Center for Epidemiological Studies Depression scale (questionnaire); DSRS = Depression Self Rating Scales of the DSM-IV A (questionnaire); KDS = Kandel Depression Scale (questionnaire); SDQ = Strengths and Difficulties Questionnaire (non validated questionnaire); CDI = Children's Depression Inventory (questionnaire).

r = correlation coefficient; Beta = regression coefficient; SE = standard error; R^2 = maximum explained variance; OR = odds ratio (95% confidence interval); NS = not statistically significant; DFC = discriminant function coefficient.

* Validated questionnaire / interview.

However, logistic regression analysis showed that the OR (95% CI) for having a score on the Depressive Symptom Scale in the top quintile in obese adolescents compared with normal weight was not significant for either sex (girls, 0.89 (0.44 - 1.81), and boys, 1.25 (0.27 – 5.66)). The authors concluded that their findings provided limited support for an association between depressive symptoms and overweight. In 2101 Turkish adolescents aged 15 to 18 years, no statistically significant association was found (OR, 1.74; 95% CI, 0.96 – 3.23). However, this could have been because of the low prevalence of overweight (9.0%).[37]

Thus, differences according to sex were found in the studies by Erickson and colleagues and by Xie and colleagues. In 1 study in which subgroup analyses were performed according to race/ethnicity, significant differences were found between ethnic groups. Erickson and colleagues reported an effect in Asian American girls only, compared with white, Hispanic, and African American girls.[17] Whereas most studies were conducted primarily in white populations, 1 study was performed in a Chinese population.[26] This study by Xie and colleagues found a positive association in girls. Thus, racial/ethnic differences have been found, but the results are inconsistent. However, a positive association was found in both Asian populations studied. Socioeconomic status was adjusted for, but did not change the associations. In addition to these covariates, pubertal status could be important in pediatric research. Puberty was not studied as a potential effect modifier in the mentioned studies.

Longitudinal studies

We found 11 reports on the longitudinal association between depressive symptoms in childhood[38-42] and adolescence[38-48] and subsequent overweight in adolescence and young adulthood in which a correction was made for overweight at baseline (Table 2). Two studies did not find such an association,[39,47] which could have been because of a limited sample size of a young age group in 1 of the studies.

Nine longitudinal studies reported a positive association between depressive symptoms in childhood and adolescence and subsequent overweight.[38,40-46,48] Odds ratios, reported in 7 studies, varied from 1.30 to 4.62 and 95% CIs ranged from 1.0 to 12.74.[38,41-46] Hasler and colleagues reported a hazard ratio of 11.52 in females, which might be an overestimation because only retrospective data on childhood depressive symptoms were available, potentially resulting in recall bias.[48] Two studies reported results from linear regression analyses with regression coefficients varying from 0.02 to 0.11.[43,44] Linear mixed models revealed greater yearly gains in BMI SDS of 0.09 units/yr in girls with a history of depression.[40] Another study reported a higher adult BMI in participants who had major depressive disorder in childhood compared with an adult population without childhood depression (mean ± SD difference, 1.9 ± 4.7 kg/m^2).[41]

Four of the 11 longitudinal studies were in accord with our quality criteria (Table 2a). These included 1 study which did not find an association. Tanofsky-Kraff and colleagues studied 146 children at risk for adult overweight, defined as being overweight (65.1% at

Table 2. Longitudinal studies on the association between depressive symptoms and overweight.

Table 2a. Longitudinal studies on the association between depressive symptoms and overweight in accordance with quality criteria.

Study	Population	Age at baseline (follow up period)	Measure of depressive symptoms	BMI (weight and height from self-report or measured)	Main result	Effect size
Pine et al (2001)[41]	n=177	Age 6-17 yrs, (10-15 yrs)	K-SADS*	Measured and self-report: - continuous - overweight: BMI > 25	+	 BMI 1.9 ± 4.7 higher (P < 0.01) OR 1.90 (1.02 – 3.40)
Goodman et al (2002)[44]	n=9374	Age 12-19 yrs (1 yr)	CES-D*	Measured and self-report - continuous: SDS - obesity: 95th percentile (CDC)	+	 Beta = 0.11, SE 0.05 (P = 0.045) OR = 2.39 (1.05 – 5.45)
Franko et al (2005)[43]	n=1554 (all female)	Age 16.5 yrs (2 yrs and 5 yrs)	CES-D*	Measured and self-report - continuous - obesity: 95th percentile (CDC)	+	 Beta = 0.03, SE 0.009 (P = 0.002) (W1 – W3) Beta = 0.02, SE 0.008 (P = 0.01) (W2 – W3) OR = 3.11 (1.13 – 5.12) (W1 – W3) OR = 3.50 (1.26 – 5.80) (W2 – W3)
Tanofsky-Kraff et al (2006)[39]	n=146	Age 6-12 yrs (4.2 ± 1.8 yrs)	CDI*	DEXA: fat mass	0	Beta = 0.004 (95% CI = -0.07 – 0.014)

+ = positive association; - = negative association; 0 = no association.

K-SADS = Schedule for Affective Disorders and Schizophrenia for School-Age Children (interview); CES-D = Center for Epidemiological Studies Depression scale (questionnaire); CDI = Children's Depression Inventory (questionnaire).

OR = odds ratio (95% confidence interval); Beta = regression coefficient; SE = standard error; W1 = assessment point 1; W2 = assessment wave 2; W3 = assessment wave 3.

* Validated questionnaire / interview.

Table 2b. Other longitudinal studies on the association between depressive symptoms and overweight.

Study	Population	Age at baseline (follow up period)	Measure of depressive symptoms	BMI (weight and height from self-report or measured)	Main result	Effect size
Bardone et al (1998)[47]	n=459 (all female)	Age 15 yrs (6 yrs)	DIS*	Measured: - continuous	0	Beta 0.06, NS (SE and P not reported)
Barefoot et al (1998)[45]	n=4726	Age 17-25 yrs (21-23 yrs)	OBD* NEO*	Measured and self-report: - weight change	- if lean + if heavy	OR = 2.2 ♀, OR = 1.3 ♂
Richardson et al (2003)[38]	n=881	Age 11-15 yrs Age 18-21 yrs (7-13 yrs, at age 26 yrs)	DIS*	Measured - cut-off: BMI 30	+	OR = 2.32 (1.29 – 3.83)
Hasler et al (2004)[46]	n=591	Age 19 yrs (20 yrs)	SPIKE*	Self-report - overweight: BMI > 79th percentile	+ (atypical depression)	OR = 2.9 (1.3 – 6.5) ♀ OR = 2.0 (1.0 – 4.2) ♂
Hasler et al (2005)[48]	n=591	Age < 19 yrs (20 yrs)	SPIKE*	Self-report - obesity: BMI ≥ 30	+	HR = 11.52, SE 1.24 (P < 0.05) ♀ HR = 1.10, SE 0.66 (P = 0.88) ♂
Stice et al (2005)[42]	n=496 (♀)	Age 11-15 yrs (4 yrs)	K-SADS*	Measured - obesity: 95th percentile (CDC)	+	OR = 4.62 (1.67 – 12.74)
Anderson et al (2006)[40]	n=820	Age 9-18 yrs (2.5 yrs, 9.5 yrs, and 19 yrs)	DIS* SCID*	Self-report - continuous: SDS	+	BMI SDS change greater by 0.09 (95% CI = 0.03 – 0.15) units/yr (P < 0.05) ♀

+ = positive association; - = negative association; 0 = no association.

DIS = Diagnostic Interview Schedule (layperson interview); OBD = Obvious Depression subscale of the MMPI (questionnaire); NEO = NEO Personality Inventory (questionnaire); SPIKE = Structured Psychopathological Interview and Rating of Social Consequences for Epidemiology (expert interview); K-SADS = Schedule for Affective Disorders and Schizophrenia for School-Age Children (interview); SCID = Structured Clinical Interview for DSM-IV-TR (layperson interview).

OR = odds ratio (95% confidence interval); Beta = regression coefficient; SE = standard error; NS = not statistically significant; HR = hazard ratio.

* Validated questionnaire / interview.

the first measurement wave) or having at least 1 overweight parent.[39] In this population, depressive symptoms at age 6 to 12 years did not significantly predict increase in body fat mass as measured by BMI and dual-energy X-ray absorptiometry 4 years later. That the sample size was limited (n=146 children), most children were already overweight, and most of the children (n=111) were younger than 10 years at baseline, could have been responsible for these outcomes. The authors hypothesized that depressive symptoms might be a more potent predictor of fat gain in older children. In a longitudinal study assessing depressive symptoms in both early and in late adolescence, a significant association was found only between late adolescent depressive symptoms and adult overweight.[38]

An association was found in the 3 other studies. Goodman and Whitaker reported a 2.39-fold (95% CI, 1.05 – 5.45) increased risk of subsequent overweight in children with depressive symptoms. Their study was performed in a population of 9374 children aged 12 to 19 years at baseline who were reassessed after 1 year.[44] Franko and colleagues performed a study in a cohort of 1554 female participants who were evaluated at 3 assessment waves (at mean ages of 16.5, 18.6, and 21.4 years).[43] They reported an OR (95% CI) of 3.11 (1.13 – 5.12) for the association between depressive symptoms at assessment point 1 and overweight at point 3, and of 3.50 (1.26 – 5.80) for the association between points 2 and 3. A cohort of 177 children aged 6 to 17 years at baseline were followed up for 10 to 15 years by Pine and colleagues.[41] They concluded that depressive disorder predicted adult overweight with an OR of 1.90 (95% CI, 1.02 – 3.40). Adults who suffered from childhood depressive symptoms had, on average, a higher BMI (1.9 (4.7) kg/m^2). The studies by Goodman and Whitaker[44] and Pine and colleagues[41] both refuted sex distinctions, and the study by Franko was performed in a cohort of girls only.[43] Ethnicity was adjusted for in all three studies,[41,43,44] but none performed subgroup analyses. All four longitudinal studies that satisfied our quality criteria adjusted for socioeconomic status, which did not influence the results.[39,41,43,44]

COMMENT

Most cross-sectional and longitudinal research that satisfies our quality criteria supports an association between depressive symptoms in childhood and adolescence and subsequent overweight. Evidence from the 4 longitudinal studies suggests that depressive symptoms in childhood or adolescence are associated with a 1.90- to 3.50-fold increased risk for overweight in later life (95% CIs vary from 1.02 to 5.80). In the 4 cross-sectional studies , a correlation coefficient of 0.14 and a regression coefficient of 0.27 were reported in girls, which supports the findings from the few longitudinal studies.

Strengths and limitations

The main strength of our review is the systematic search we performed of all available literature on the specific association between depressive symptoms in childhood and adolescence and subsequent overweight, evaluated longitudinally. Earlier reviews included studies regarding both adult and childhood depressive symptoms.[5,49-52] In addition, they were not systematic [5,49,52] and did not focus on depressive symptoms specifically, describing well-being,[52] mood disorders,[50] or psychopathologic conditions in general.[49]

Two limitations must be addressed. First, it is difficult to compare the included studies. Both the cross-sectional and the longitudinal studies differed with regard to assessment methods. Body mass index was included in the analyses either as a continuous variable or dichotomized with the use of cut–off values for overweight according to various criteria. Only 1 longitudinal study evaluated body fat measurements with the use of DEXA. This study did not find an association between depressive symptoms and body fat percentage, possibly because the sample size was limited, most of the children were already overweight, and most of the children were younger than 10 years at baseline.[39] Second, few studies have evaluated the presence of depressive symptoms in preadolescent children and the development of overweight in adolescence. Clearly, more studies are needed, not only regarding the association between depressive symptoms in adolescence and overweight in adulthood, but also regarding the association between depressive symptoms and overweight at a younger age.

Mechanisms

Hypotheses about mechanisms having a role in the association between depressive symptoms and subsequent overweight include various social and biological risk factors for overweight, that have been previously associated with depressive symptoms.[41] These include factors that could mediate or moderate the association and factors that could influence both depressive symptoms and overweight at different time points. These third factors include neurobiological mechanisms that could be implicated through 2 different pathways, specifically, serotonin and its metabolites, and the hypothalamic-pituitary-adrenal (HPA) axis. Central serotonergic pathways have been implicated in disturbances in mood and appetite,[53] and various studies suggest that both depressive symptoms and overweight are related to dysregulation of the HPA axis.[54-56]

Factors that possibly mediate or moderate include reduced physical activity and use of anti-depressant agents. Depressive symptoms are often accompanied by lethargy and social withdrawal, which could lead to reduced physical activity levels and, therefore, to increased risk of becoming overweight. However, this was considered a covariate in the studies by Needham and Crosnoe,[18] by Goodman and Whitaker,[44] by Barefoot and colleagues,[45] and Hasler and colleagues[46,48] to control for possible confounding. Physical activity was assessed with the use of a questionnaire [18,44,45] or interview.[46,48] Adjusting for physi-

cal activity did not change the positive association found in these studies. Moreover, the study by Stice and colleagues evaluated physical activity, assessed by the Past Year Leisure Physical Activity Scale, as a predictor of overweight onset in adolescent girls.[42] They did not find a significant longitudinal association, possibly because of reporting bias or highly fluctuating exercise behaviors over time. In accord with their findings, Berg and colleagues did not report different frequencies of physical activity, assessed using a questionnaire, in groups of adolescent boys with normal weight, overweight, or obesity.[21] Inasmuch as all measures of physical activity were dependent on self-report, these results must be interpreted with caution. Reporting bias could have a role in the unaltered association between depressive symptoms and overweight when correcting for physical activity.

Use of anti-depressants could also have a role in the association between depressive symptoms and overweight.[57] However, this was corrected for in the longitudinal studies by Pine and colleagues[41] and by Richardson and colleagues,[38] which did not change the positive association found in these studies. Moreover, prescription of anti-depressants is not common in pediatric populations.

It is also possible that an association between depressive symptoms and overweight is present in subtypes of depression. For example, atypical depression is characterized by, among other factors, increased appetite and excessive sleeping,[8] which could underlie later weight problems. Another possible mechanism is that in subgroups depressive symptoms are associated with developing binge eating disorder. This disorder is characterized by binge eating episodes accompanied by distress, loss of control and absence of compensatory behaviors such as vomiting. The prevalence of binge eating in community-based studies has been reported to be 2% in German children aged 5 to 6 years,[58] 8% to 26% in Northern American (i.e., Canada and the United States) and British adolescent girls,[59-62] and 3 to 13%[60] in US adolescent boys. Regular binge eating, defined as twice a week or more, was prevalent in 3 to 8%, respectively, of US and British adolescent girls[59,62] and in nearly 1% of American adolescent boys. A higher prevalence of approximately 30% has been reported in obese youngsters seeking treatment.[63] Results from a prospective study in adolescents confirm earlier reports that binge eating disorder is associated with onset of overweight.[64] Depressive symptoms have been described as a risk factor for onset of binge eating disorder in 2 studies in adolescent girls and young females (age range, 17-38 years).[64,65] This could be explained by the affect-regulation model, stating that binge eating provides relief of depressive symptoms.

Clinical implications

Insofar as clinical implications, we can only draw tentative conclusions, because further research that satisfies all quality criteria is needed. However, treatment programs for depressive symptoms should consider that depressive symptoms might have a role in the onset of increase in body weight. Specifically, binge eating and possibly even BMI

should be evaluated. Treatment programs should be adapted to include prevention and treatment of overweight. On the other hand, in treating overweight individuals, it should be kept in mind that depressive symptoms could underlie the increase in body mass. Assessing depressive symptoms and binge eating warrants consideration, especially if overweight treatment fails. When assuming a causal pathway, evaluating and treating depressive symptoms in children and adolescents could lead to a reduction in the occurrence of overweight.

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Chapter 4.2

Associations between depressive symptoms in childhood and overweight and its metabolic complications in adolescence

Eryn T. Liem
Ronald P. Stolk
Albertine J. Oldehinkel
Johan Ormel
Pieter J.J. Sauer

ABSTRACT

Objective: We aimed to assess whether childhood depressive symptoms are related to overall and abdominal adiposity in adolescence, and to associated metabolic characteristics.

Study design: In a population-based cohort of 800 girls and 720 boys, depressive problems (measured by questionnaires), BMI, and sum of skinfolds were assessed at mean ages 11.1 and 16.2 years. Percentage BF, waist circumference, blood pressure, glucose, insulin, and lipid profile, were obtained at age 16.2 years.

Results: At age 11.1 years, median BMI was 17.22 (IQR, 15.84 – 19.22) and 11.1% of participants had depressive problems (according to an 85th percentile criterion). Adjusting for age and sex, depressive problems at age 11.1 years were associated with higher BMI (B=0.65; 95% confidence interval (CI), 0.18 – 1.13 kg/m^2), %BF (B=1.50; 95% CI, 0.74 – 2.25 %), waist circumference (B=1.62; 95% CI, 0.35 – 2.91 cm), lower HDLC (B=-0.10; 95% CI, -0.16 – -0.04 mmol/l), and an increased risk of overweight/obesity (odds ratio (OR)=1.81 (95% CI, 1.22 – 2.70) at age 16.2 years. There was a trend for higher sum of skinfolds (B=2.8; 95% CI, -0.2 – 5.9 mm). We found no associations with change in BMI or skinfold thicknesses over time. Persistent depressive problems from age 11.1 to 16.2 years were associated with higher BMI (B=0.91; 95% CI, 0.15 – 1.69 kg/m^2) and %BF (B=1.46; 95% CI, 0.26 – 2.67 %), and an increased risk of overweight/obesity (OR=2.89; 95% CI, 1.64 – 5.09) at age 16.2 years.

Conclusions: Depressive problems at age 11.1 years were associated with increased overall and abdominal adiposity at age 16.2 years. They did not predict increases in BMI or sum of skinfolds over time, suggesting that the association between depressive problems and BMI remains stable during adolescence. Persistent depressive problems were associated with increased BMI and risk of overweight.

INTRODUCTION

Prevention of overweight is a major public health concern. Targeted and tailored preventive strategies that take cost-effectiveness into account need to be developed and therefore, predictors of overweight in childhood and adolescence need to be determined. Depressive symptoms have been described both as a predictor and as a consequence of overweight, mostly in adults but in adolescents as well.[1] In a review of the literature, we found that depressive symptoms in childhood or adolescence are associated with a 1.90 to 3.50 increased risk for subsequent overweight.[2] Depressive symptoms were measured with various scales, but most studies dichotomized their scales into a measure of clinically relevant depressive problems. The use of such a dichotomized measure of depressive symptoms improves the comparability of the effect sizes reported. Overweight was assessed by BMI in most longitudinal studies, whereas only one study specifically assessed body fat.[3] Although overall body fat is an important indicator of weight-related diseases, distribution of body fat is even more important. Epidemiological studies have demonstrated that, already in childhood, especially abdominal fat appears to be associated with an unfavorable metabolic profile, including insulin resistance, elevated LDLC concentrations, and decreased HDLC concentrations.[4,5] Interestingly, in adults a longitudinal association between depressive symptoms and type 2 diabetes has been described.[6] In the elderly, depression has been related to cardiovascular morbidity and mortality.[7,8] In addition, an association between depressive symptoms and the metabolic syndrome (a cluster of cardiovascular risk factors consisting of increased waist circumference, triglycerides, blood pressure, and glucose; and decreased HDLC) was found in a population-based cohort of young adults.[9] Especially associations with waist circumference were consistent, in contrast to the other components of the metabolic syndrome, underlining the importance of abdominal adiposity. It is therefore important to know if such associations are already present in childhood and adolescence, i.e. if childhood depressive symptoms are associated with abdominal adiposity and its related metabolic characteristics in adolescence.

The aim of this study was to assess whether depressive symptoms in childhood are associated with both overall and abdominal adiposity in adolescence. In addition, we evaluated the association between depressive symptoms and metabolic characteristics related to overweight, specifically glucose, insulin, triglycerides, LDLC, HDLC, blood pressure; and a composite metabolic syndrome score.

METHODS

Study population

Our study was performed within the TRAILS study, an ongoing population-based cohort study assessing psychosocial and physical health from preadolescence into adulthood. Sample selection has been described elsewhere.[10] In short, children were recruited through community registers of 5 communities in the 3 northern provinces of the Netherlands to obtain a representative sample. Home interviews with parents were conducted; children filled out questionnaires and were measured at their schools. The present study included data from the first and third assessment visits, which were performed in 2001-2002 at mean (± SD) age 11.1 ± 0.6 and in 2005-2007 at age 16.2 ± 0.7 years. We included participants with complete data on depressive symptoms and BMI at age 11.1 years and at age 16.2 years, which were 1520 (70.5%) of the 2155 participants of whom data on depressive symptoms and BMI were available at age 11.1 years. Participants who were lost to follow-up had a higher BMI and higher sum of skinfold thicknesses (median differences 0.6 kg/m^{2,} $p<0.001$; and 3 mm, $p=0.01$ respectively) at age 11.1 years. However, the median difference in depressive symptoms SDS at age 11.1 years was not significantly different ($p=0.11$). All procedures were approved of by the Dutch Central Committee on Research Involving Human Subjects (CCMO). Written informed consent was obtained from participants and their parents or custodians.

Measures

Depressive symptoms were assessed by the Depressive Problems scale[11] of the Child Behavior Checklist (CBCL, parent questionnaire),[12,13] and of the Youth Self-Report (YSR, child questionnaire).[14] The mean of standardized parent and child scores was used as a measure of depressive symptoms because a composite score is less vulnerable to context and perspective.[15,16] This depressive symptoms score was dichotomized using a cut-off of 1.04 (sex-specific 85th percentile within the whole population), creating a subgroup with 'depressive problems' to allow for comparison with other studies in which such cut-offs were used.[17]

At both assessment visits, weight and height were measured with the use of regularly calibrated equipment (Model 770 and Model 214, respectively; Seca, Hamburg, Germany). We also obtained triceps, biceps, subscapular, and supra-iliac skinfold thicknesses using standardized protocols and calibrated equipment, i.e. a Harpenden skinfold caliper (CMS instruments, London, UK). We performed all measurements in duplicate and if the difference exceeded a predefined value, a third measurement was performed. All available measurements were used to calculate means. BMI was calculated in kg/m^2, and the sum of four skinfolds in mm. Overweight and obesity were defined according to international age- and sex-adjusted BMI criteria (equivalent to the Dutch 94th and 99.7th percentile in 1980

for overweight and obesity, respectively).[18] At age 16.2 years, additional measurements were obtained. A hand-to-foot BIA (BIA 101, Akern®, Italy) was performed from which %BF was calculated with the use of the Deurenberg equation.[19,20] We measured waist circumference, again in duplicate or triplicate, at the mid-point between the lower costal margin and the iliac crest. SBP and DBP were measured with a Dinamap Critikon 1846SX (Critikon Inc., Tampa, FL, USA) and the mean of the two readings was calculated. We obtained a fasting blood sample for measurement of glucose (Roche Diagnostics, Basel, Switzerland), insulin (Diagnostic Systems Laboratories Inc., Texas, USA), triglycerides, total cholesterol and HDLC (Roche Diagnostics, Basel, Switzerland).[21,22] LDLC was calculated according to Friedewald's equation.[23] A composite score for the metabolic syndrome was calculated as the mean of insulin, glucose, HDL, triglycerides, waist circumference and mean blood pressure SDSs, calculated within our population after ln-transformation of all not normally distributed variables.[24]

Questionnaires were filled out by parents and child to assess ethnicity, pubertal stage (Tanner and Physical Development Scale[25] questionnaire), and socioeconomic status (SES). SES was calculated as the mean of SDSs on family income, mother's and father's level of education, and occupation based on the International Standard Classification of Occupations.[26] The lowest 25%, intermediate 50%, and 25% highest were considered to represent low, medium, and high SES, respectively.

Data analysis

Differences between participants with and without depressive problems were tested with the use of T-tests and Mann-Whitney U tests for continuous variables and chi-square tests for dichotomous variables.

To assess the association between depressive problems at age 11.1 years and overweight at age 16.2 years, we performed multivariate linear and logistic regression analyses for BMI, sum of skinfolds, %BF, waist circumference, and overweight/obesity (in which overweight and obese participants were defined together as cases). We also evaluated the associations between depressive problems at age 11.1 years and metabolic characteristics at age 16.2 years in linear regression analyses for SBP, DBP, glucose, insulin, HDLC, and LDLC levels separately; and for the composite score of the metabolic syndrome. Weight, BMI, skinfolds, waist circumference, SBP, triglycerides, and insulin were ln-transformed, to obtain a better approximation of the normal distribution. In all models, we used the dichotomized 'depressive problems' variable as independent variable. We adjusted for age and sex; and in a second step for socioeconomic status (SES) as it is an important confounder.[2] Adjustment for pubertal stage instead of age did not substantially change the results. Based on previous literature,[27] we evaluated sex as a potential effect modifier by adding a multiplicative term to the models. Mean effect sizes for ln-transformed outcomes were back-transformed to report them on their original scale. They were calculated

as mean increase in the average value of the outcome measure per unit increase in the predictor: *mean effect size = median* $_{outcome\ measure}$ ** (e^{β} -1).* [28]

To assess the longitudinal association between depressive problems and overweight we used two strategies. First, we evaluated the influence of depressive problems on change in BMI and sum of skinfolds from age 11.1 to age 16.2 years in linear mixed models. We adjusted for the same confounders included in the regression analyses. If depressive problems actually precede overweight, we would expect depressed children to have a steeper increase in BMI and sum of skinfolds, i.e. a significant interaction between depressive problems and time on the outcomes. Second, we divided all participants in 4 groups according to differences in persistence of depressive problems: (1) no depressive problems at both assessment visits (n=1232, 81.1%), (2) depressive problems at age 11.1 but not at age 16.2 years (n=107, 7.0%), (3) depressive problems at age 16.2 years only (n=119, 7.8%), (4) depressive problems at both age 11.1 and age 16.2 years (n=62, 4.1%). We entered this 'difference in persistence of depressive problems'-variable consisting of 3 dummy variables as predictor in regression analyses to evaluate the influence of these different trajectories on overweight measures at age 16.2 years.

All statistical analyses were performed using SPSS version 16.0 (SPSS, Chicago IL, USA). The level of statistical significance was set at a probability of <0.05.

RESULTS

Descriptives

Our study population consisted of 800 girls and 720 boys. Mean (± SD) age at the first measurement visit was 11.1 ± 0.6 years; and 169 participants (11.1%) had depressive problems according to the 85th percentile criterion (Table 1). This was less than expected because the criterion was applied to the whole study population whereas not all children participated in the weight and height measurements. At age 11.1 years, 16% of participants were overweight or obese. At the follow-up assessment visit, median age was 16.2 ± 0.7 years and 14.6% was overweight or obese (Table 2).

Depressive problems at age 11.1 years and overweight / metabolic characteristics at age 16.2 years

BMI and sum of skinfolds did not differ significantly between subgroups with and without depressive problems at age 11.1 years (Table 1). However, the subgroup with depressive problems was significantly more obese at age 11.1 years. At the follow-up assessment visit, the subgroup with depressive problems at age 11.1 years had significantly higher %BF at age 16.2 years, a higher prevalence of overweight and obesity, and a lower HDLC.

Table 1. Characteristics at age 11.1 years according to subgroups of participants with and without depressive problems at age 11.1 years.

	n	All	No depressive problems at age 11.1 yrs (SDS < 1.04)	Depressive problems at age 11.1 yrs (SDS ≥ 1.04)	P-value
Sex (% girls)	1520	52.6	52.9	50.3	0.52
Ethnicity (% Caucasian)	1520	88.8	89.1	86.4	0.29
SES (% in 3 categories)*	1500	21.1/49.1/29.7	20.2/49.7/30.1	28.3/44.6/27.1	0.06
Age (yrs)	1520	11.1 ± 0.6	11.1 ± 0.5	11.0 ± 0.6	0.03
Pubertal stage (% in 3 categories)**	1460	86.3/10.7/3.0	86.5/10.6/2.9	84.8/11.5/3.6	0.82
Weight (kg)	1520	40.0 (35.0 – 46)	40.0 (35 .0– 46.0)	40.0 (35 .0– 46.0)	0.74
Height (cm)	1520	151.8 ± 7.8	151.8 ± 7.8	151.7 ± 7.7	0.92
BMI (kg/m^2)	1520	17.22 (15.84 – 19.22)	17.21 (15.83 – 19.20)	17.35 (15.89 – 19.63)	0.52
Overweight/obese (%)	1520	13.4/2.6	13.4/2.1	13.0/6.5	0.01
Sum of four skinfolds (mm)	1026	36 (26 – 53)	35 (26 – 52)	37 (28 – 55)	0.25

All data are means ± SD or median (interquartile range) unless otherwise indicated.

* Socioeconomic status was based on questionnaires and classified as low, medium, and high SES.

** Determined by a Tanner questionnaire, divided into pre/early pubertal, midpubertal and late/post pubertal.

After adjustment for age and sex, depressive problems at age 11.1 years were associated with higher BMI, %BF, waist circumference; and a trend for higher sum of skinfolds at age 16.2 years (Table 3). Adjustment for SES yielded slightly weaker, but similar results.

Depressive problems at age 11.1 years were also associated with a 1.81 increased risk of being overweight or obese at age 16.2 years; and with a significantly lower HDLC at age 16.2 years, which persisted after adjustment for SES (Table 3). Further adjustment for BMI did not attenuate the association (B=-0.09; 95% CI, -0.14 – -0.03). No significant associations were found with the other metabolic characteristics or with the composite metabolic syndrome score. Interaction with sex was not significant in any of the associations (p-values 0.68 to 0.97).

Because the 85th percentile criterion to define depressive problems is an arbitrary cut-off, we also performed analyses using lower (82nd percentile) and higher (88th percentile) cut-off values, which did not change the results substantially. Certain medications are known to influence body composition, so we performed all analyses after exclusion of participants using anti-depressants (n=3) and participants whose medication is not known (n=15). Results were comparable. Results excluding the second of all siblings (n=15) or all non-Caucasian participants (n=170) also provided similar results.

Table 2. Characteristics at age 16.2 years according to subgroups of participants with and without depressive problems at age 11.1 years.

	n	All	No depressive problems at age 11.1 yrs (SDS < 1.04)	Depressive problems at age 11.1 yrs (SDS ≥ 1.04)	P-value
Age (yrs)	1520	16.2 ± 0.7	16.2 ± 0.6	16.2 ± 0.7	0.79
Pubertal stage (% in 3 categories)*	1448	15.3/28.5/56.2	14.9/29.1/56.0	18.4/24.1/57.6	0.30
Depressive symptoms (SDS)	1520	-0.24 (-0.65 – 0.39)	-0.31 (-0.65 – 0.29)	0.68 (0.06 – 1.46)	<0.001
Weight (kg)	1520	62.8 (57.1 – 69.8)	62.8 (57.0 – 69.7)	63.1 (57.7 – 71.0)	0.18
Height (cm)	1520	173.9 ± 9.0	173.8 ± 9.0	174.0 ± 9.1	0.88
BMI (kg/m^2)	1520	20.75 (19.13 – 22.59)	20.74 (19.12 – 22.53)	20.86 (19.24 – 23.58)	0.14
Overweight/obese (%)	1520	11.8/2.8	11.1/2.5	17.3/4.8	0.03
Sum of four skinfolds (mm)	1520	47 (32 – 65)	47 (32 – 64)	48 (33 – 68)	0.35
Body fat (%)	1476	28.3 (24.0 – 32.3)	28.1 ± 5.6	28.9 ± 6.4	0.01
Waist circumference (cm)	1514	73.7 (69.9 – 78.5)	73.5 (69.8 – 78.3)	74.8 (70.6 – 80.1)	0.06
Systolic blood pressure (mmHg)	1500	116 (109 – 127)	117 (109 – 127)	115 (108 – 125)	0.24
Glucose (mmol/l)	1042	4.5 ± 0.4	4.5 ± 0.4	4.6 ± 0.4	0.50
Insulin (mUl/l)	1032	12.0 (9.1 – 16.0)	12.0 (9.1 – 16.0)	12.0 (8.9 – 16.0)	0.63
Triglycerides (mmol/l)	1040	0.68 (0.51 – 0.92)	0.69 (0.52 – 0.94)	0.66 (0.51 – 0.87)	0.47
HDLC (mmol/l)	1040	1.46 ± 0.31	1.47 ± 0.31	1.37 ± 0.26	0.004
LDLC (mmol/l)	1040	2.20 (1.80 – 2.65)	2.22 (1.84 – 2.65)	2.14 (1.80 – 2.66)	0.34
Metabolic syndrome score (SD)	1025	-0.02 ± 0.53	-0.03 ± 0.53	0.02 ± 0.53	0.34

BMI= body mass index; HDLC = high density lipoprotein cholesterol; LDLC = low density lipoprotein cholesterol.
All data are means ± SD or median (interquartile range) unless otherwise indicated.
* Measured by the Physical Development Scale questionnaire, divided into pre/early pubertal, midpubertal and late/post pubertal.

Longitudinal association between depressive problems and overweight

Linear mixed models showed that depressive problems at age 11.1 years were associated with increased BMI (estimate=0.57; 95% CI, 0.16 – 0.98 kg/m^2) and sum of skinfolds (estimate=3.8; 95% CI, 0.7 – 6.8 mm). Interaction between depressive problems and time was not significant (p-values 0.12 and 0.17), which suggests that the association of depressive problems with BMI and sum of skinfolds was stable over time. No significant interaction between depressive problems and sex was found (p-values 0.31 and 0.54).

Differences in persistence of depressive problems were associated with BMI at age 16.2 years, after adjustment for age and sex (F=2.77, p=0.04). In this model, the group with depressive problems at both 11.1 and 16.2 years had a higher BMI compared with the other groups (B=0.91; 95% CI, 0.15 – 1.69) (Table 4). Differences in persistence of depressive problems were also related to %BF (F=5.11, p=0.002) at age 16.2 years. This model

Table 3. Associations between depressive problems at age 11.1 years and overweight related measures at age 16.2 years.

		Depressive problems B (95% CI)	
	no adjustments	**+ adjustment for age and sex**	**+ adjustment for SES[§]**
Overweight	**1.79 (1.21 – 2.67)****	**1.81 (1.22 – 2.70)****	**1.73 (1.16 – 2.60)****
BMI (kg/m^2) [‡]	**0.59 (0.12 – 1.08)***	**0.65 (0.18 – 1.13)**	**0.59 (0.12 – 1.07)***
Sum of skinfolds (mm) [‡]	2.1 (-1.3 – 5.8)	2.8 (-0.2 – 5.9)	2.5 (-0.4 – 5.6)
Body fat (%)	**1.34 (0.42 – 2.26)****	**1.50 (0.74 – 2.25)**	**1.41 (0.67 – 2.16)****
Waist circumference (cm) [‡]	**1.53 (0.26 – 2.82)***	**1.62 (0.35 – 2.91)**	**1.46 (0.20 – 2.74)***
SBP (mmHg) [‡]	-1.15 (-3.05 – 0.79)	1.39 (-3.19 – 0.43)	-1.56 (-3.35 – 0.26)
Glucose (mmol/l)	0.03 (-0.06 – 0.11)	0.02 (-0.06 – 0.11)	0.02 (-0.06 – 0.11)
Insulin (mU/l) [‡]	-0.40 (-1.46 – 0.75)	-0.38 (-1.44 – 0.77)	-0.49 (-1.54 – 0.65)
HDLC (mmol/l)	**-0.10 (-0.16 – -0.04)****	**-0.10 (-0.16 – -0.04)****	**-0.09 (-0.15 – -0.03)****
LDLC (mmol/l)	-0.05 (-0.18 – 0.07)	-0.04 (-0.16 – 0.09)	-0.05 (-0.18 – 0.08)
Triglycerides (mmol/l) [‡]	-0.02 (-0.08 – 0.05)	-0.02 (-0.08 – 0.05)	-0.02 (-0.08 – 0.04)
Metabolic syndrome score (SD) [¶]	0.05 (-0.06 – 0.16)	0.05 (-0.06 – 0.16)	0.03 (-0.08 – 0.14)

BMI = body mass index; SBP = systolic blood pressure; HDLC = high density lipoprotein cholesterol; LDLC = low density lipoprotein cholesterol.

Results from regression analyses with dichotomized depressive problems variable as predictor and overweight measures and metabolic characteristics as outcomes.

Significant associations are in bold; * p < 0.05; ** p < 0.01.

[§] Socioeconomic status was based on questionnaires and classified as low, medium, and high SES.

[‡] Ln-transformed in view of not normally distributed residuals; back-transformed using: *mean effect size = median $_{outcome\ measure}$ * (e^{β} -1).*[28]

[¶] Metabolic syndrome score: mean SDS including glucose, insulin, HDL, triglycerides, waist circumference and mean blood pressure.

showed a significantly higher %BF in the group with depressive problems only at age 11.1 years (B=1.53; 95% CI, 0.61 – 2.46 %) and in the group with depressive problems at both assessment visits (B=1.46; 95% CI, 0.26 – 2.67 %). There were no significant associations with sum of skinfolds (F=0.003, p=0.13) and waist circumference (F=2.48, p=0.06). Differences in persistence of depressive problems were associated with overweight/obesity

Table 4. Mean BMI (kg/m^2) in girls according to presence of depressive problems at age 11.1 and 16.2 years.

		BMI (kg/m2) median (interquartile range)	
	n	**Age 11.1 yrs**	**Age 16.2 yrs**
No depressive problems	620	17.46 (19.32 – 15.92)	21.18 (22.85 – 19.48)
Depressive problems at age 11.1 years only	49	17.65 (19.87 – 15.52)	21.41 (23.93 – 19.61)
Depressive problems at age 16.2 years only	95	17.67 (20.18 – 16.14)	21.17 (22.75 – 19.68)
Depressive problems at both age 11.1 & 16.2 years	36	17.50 (18.79 – 16.23)	22.05 (24.96 – 19.11)

(Wald=14.1, p=0.003). In this model, the group with depressive problems at both 11.1 and 16.2 years had an increased risk of being overweight or obese (OR=2.89; 95% CI, 1.64 – 5.09). Results were slightly weaker albeit similar after adjustment for SES.

DISCUSSION

Our results suggest that childhood depressive problems at age 11.1 years are related to overall body fat and abdominal fat in adolescence, at age 16.2 years. Depressive problems did not significantly predict changes in BMI or skinfold thicknesses between age 11.1 and age 16.2 years. The persistence of depressive problems from childhood to adolescence was associated with a higher BMI and higher risk of overweight/obesity in adolescence.

Our results are in line with several previous reports which studied the influence of childhood depressive symptoms on subsequent overweight. Although these studies vary in ages and time periods studied, all[29-37] but two studies[3,38] found a significant influence. For example, Goodman and colleagues reported results from a population of 9374 children. Depressive problems in children aged 12 to 19 were associated with a 2.39-fold (95% CI, 1.05 – 5.45) increased risk of overweight a year later.[30] From their cohort study in 177 participants, Pine and colleagues concluded that depressive disorder at age 6 to 17 was related to adult overweight (10 to 15 years later) with an OR of 1.90 (95% CI, 1.02 – 3.40).[31] A meta-analysis of all longitudinal studies on depressive symptoms and subsequent overweight, reported an OR of 1.47 (1.16 – 1.85).[27] These reported odds ratios are similar to our findings (OR=1.81; 95% CI, 1.22 – 2.70).

To our knowledge, this is the first study evaluating associations between depressive symptoms and various measurements of overall and abdominal fat in adolescence. In line with our findings, a study in young adults also found an association between high levels of depressive symptoms and waist circumference.[9] Assessing associations with more specific measurements of overall and abdominal adipose tissue is important because these confer increased risk of later metabolic complications such as diabetes and cardiovascular disease. We did not find an association between depressive problems at age 11.1 and overweight associated metabolic characteristics at age 16.2 years, except for a lower HDLC. Moreover, no association was found with the metabolic syndrome score. This finding is in contrast to a population-based study in young adults, which did show such an association.[9] It is possible that the difference in age explains these contrasting findings.

The fact that no association was found with changes over time in BMI and sum of skinfolds, implies that participants with depressive problems already tended to have a higher BMI at age 11.1 years, although not significantly. This hypothesis is supported by our finding that although children with depressive problems at age 11.1 years did not differ regarding BMI, they had a significantly higher prevalence of overweight/obesity.

This could be because of an association between depressive problems and the high end of the BMI spectrum instead of the whole BMI range. Stable associations over time have also been reported by others,[34] who found an association between depressive symptoms and overweight, but no association with change in BMI.

Mechanisms which might have a role in the association between depressive symptoms and subsequent overweight include decreased physical activity, increased appetite, and use of anti-depressants. Depressive symptoms are often accompanied by lethargy and social withdrawal, which could lead to reduced physical activity levels and therefore to an increased risk of becoming overweight. However, various studies included physical activity in their analyses, but did not find support for this hypothesis.[30,33-35] Increased appetite has been described as a symptom in atypical depression.[39] Finally, use of anti-depressants could have a role in the association between depressive symptoms and overweight.[40] In our study, only 3 participants used anti-depressants and their exclusion, expectedly, did not change our results.

A major strength of our study is that we evaluated overall adiposity and fat distribution, and their associated metabolic characteristics in a large population-based cohort of adolescents. In addition, depressive symptoms have been assessed through validated questionnaires including parent and child perspectives. We were also able to adjust for important covariates such as SES.

Several limitations need to be addressed. First, we were not able to reassess all participants at age 16.2 years. Additional analyses showed that participants who were lost to follow-up years had significantly higher BMI and sum of skinfolds at age 11.1 years. However, the median difference in depressive symptoms SDS at age 11.1 years was not significantly different. Second, we do not have information on depressive symptoms and overweight prior to age 11 years. It is therefore not possible to establish if depressive problems actually precede overweight.

In conclusion, our results support an association between depressive problems in childhood and overweight in adolescence. This association is stable from childhood to adolescence. It is therefore important that treatment programs for depression take into account that depressive problems can be associated with increased body weight. Treatment programs should be adapted to include treatment of overweight, if necessary. Because the pathway remains to be established, future longitudinal research should focus on younger children to evaluate whether depressive problems actually precede overweight.

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