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Depressive symptoms during childhood and adult obesity: the Zurich Cohort Study

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Depression and obesity have become major health problems with increasing prevalence. Given the limited effectiveness of treatment for weight problems, the identification of novel, potentially modifiable risk factors may provide insights on new preventive approaches to obesity. The purpose of this study was to test the hypothesis that depressive symptoms during childhood are associated with weight gain and obesity during young adulthood. Participants were from a prospective community-based cohort study of young adults ($N=591$) followed between ages 19 and 40 years. The sample was stratified to increase the probability of somatic and psychological syndromes. Information was derived from six subsequent semistructured diagnostic interviews conducted by professionals over 20 years. The outcome measures were body mass index (BMI) and obesity (BMI > 30). Among women, depressive symptoms before age 17 years were associated with increased weight gain (4.8 *vs* 2.6% BMI increase per 10 years) representing greater risk for adult obesity (hazard ratio = 11.52, $P<0.05$). Among men, only after controlling for confounders, depressive symptoms before age 17 years were associated with increased weight gain (6.6 *vs* 5.2% BMI increase per 10 years) in adulthood but not with occurrence of obesity. These associations between childhood depressive symptoms and adult body weight were adjusted for baseline body weight, a family history of weight problems, levels of physical activity, consumption of alcohol and nicotine, and demographic variables. As the magnitude of the associations was high, and depression during childhood is a prevalent and treatable condition, this finding may have important clinical implications for the prevention and treatment of obesity. Whether the results of this study are limited to populations with elevated levels of psychopathology remains to be tested.
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Overweight and obesity have become major health problems.[1] These conditions cause multiple medical consequences such as increased risk for coronary heart disease, high blood pressure, high blood cholesterol level, type 2 diabetes mellitus, gallbladder disease, osteoarthritis, and overall mortality.[2] In addition, being overweight is associated with important social and economic consequences,[3] and weight-related morbidity is estimated to account for 6.8% of US health-care costs.[4] Given the limited availability of effective treatment of weight problems, one approach to prevention involves the identification of potentially modifiable risk factors for pathological body weight. Prior research considers a range of such risk factors, including levels of activity and diet. However, the identification of other potentially novel risk factors might provide insights on other possible preventative approaches to overweight. For example, since major depression represents a highly treatable condition, demonstrating a longitudinal relationship between prior depression and later weight problems might encourage efforts to consider the benefits of treating depression for weight-related morbidity.

While depressive disorders are associated with changes in body weight in clinical studies,[5–7] this association may reflect referral bias or treatment effects. Consistent with this possibility, epidemiological studies document weak and inconsistent cross-sectional associations between depression and body mass index (BMI).[8,9] Nevertheless, recent epidemiological studies suggest that relatively strong longitudinal associations may emerge between psychopathology and BMI, particularly when psychopathology involves the presence of depressive symptoms during childhood and adolescence in women,[10–13] and when follow-up assessment expands beyond age 21 years.[13,14]

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While previous longitudinal studies on body weight and depression followed study subjects up from childhood to young adulthood, this is the first study using long-term follow-up data into middle age. Based on prior longitudinal studies,[10–12] we test the hypothesis that depressive symptoms present during childhood predict increased weight gain and an increased incidence of obesity in adulthood. In addition, we examine associations after testing and controlling variables considered in previous studies to be potential mediators, moderators, or confounders. These include a history of conduct disorder symptoms, a family history of weight problems, parity (in women), socioeconomic status, educational level, household income, physical activity, levels of self-esteem, adult psychopathology, consumption of alcohol and nicotine, and antidepressant use.[10,15,16]

Materials and methods

Sample

The Zurich Cohort Study comprises a cohort of 4547 subjects (2201 males; 2346 females) representative of the canton of Zurich in Switzerland, who were assessed in 1978 with a psychological symptom questionnaire, the Symptom Checklist 90-R,[17] and a questionnaire for sociodemographic data. The study is based on a stratified sample with an over-representation of risk cases for psychiatric disorders. In order to increase the probability of somatic and psychological syndromes, a subsample of 591 subjects (292 males, 299 females) was selected for interview, with two-thirds consisting of high scorers (defined by the 85th percentile or more of the SCL-90-R) and a random sample of those with scores below the 85th percentile. To account for the nonrandom sample over-representing psychiatric conditions, we adjusted all analyses for the level of psychological symptoms at screening (0 = SCL-90-R low scorer sample; 1 = SCL-90-R high scorer sample).

After complete description of the study to the subjects, informed consent was obtained from subjects according to the requirements of the Swiss National Science Foundation. The screening took place in 1978 at age 19 years, the first and second interviews in 1979 and 1981, the third and fourth interviews in 1986 and 1988, the fifth interview in 1993, and the sixth in 1999.

Across 20 years, 62.1% of the original sample continued to participate in the study and the following proportions participated in specific numbers of interviews: 47% in all six interviews; 63% in five interviews; 74% in four interviews; 82% in three interviews; and 91.4% in at least two interviews. Those who dropped out did not differ significantly from the 1999 participants regarding the risk group at study entry and most demographic characteristics.[18]. Also, they did not differ on the major variables of this study assessed in 1979 including childhood depression, BMI, physical activity, and smoking (analyzed by χ^2 tests and *t*-tests).

Diagnostic interview

The diagnostic instrument used in the Zurich study was the SPIKE (Structured Psychopathological Interview and Rating of the Social Consequences for Epidemiology), a semistructured interview for psychiatric and medical conditions and health habits that was developed for epidemiological studies.[19] Psychiatric residents and clinical psychologists with extensive clinical training administered the SPIKE in the participants' homes.[20] This interview schedule assesses a number of somatic syndromes, including insomnia; headache; gastrointestinal, cardiovascular, respiratory, perimenstrual, and sexual syndromes; and psychological syndromes, including depression, hypomania, anxiety, phobia, obsessive–compulsive disorder, eating disorder, post-traumatic stress disorder, substance abuse, and suicidality.

Screening probes based solely on the major phenomenological features of each syndrome (eg depressed, irritable, sad mood) were administered for each diagnostic category. Positive endorsement of the entry probe was followed by queries, first, about specific symptoms and, second, about their duration, frequency and severity, and treatment history and impairment. Categorical ratings of treatment use, medications, and impairment in work, social, and leisure activities were included in each diagnostic section. Personal and family histories of the syndromes were assessed for all subjects, irrespective of endorsement of the diagnostic screening question for each section. The childhood/adolescence section of the interview assessed several aspects of behavior and emotional function retrospectively, including conduct disorder symptoms and symptoms of major depression presenting during childhood and adolescence. The level of physical activity was assessed by interview in the first three interviews based on frequency ratings of sports activity, walking, and watching television. Self-esteem was assessed by self-report at each interview with the scale of Pearlin and Schooler.[21]

Diagnostic definitions

The SPIKE was designed to assess DSM-III-R and DSM-IV diagnoses. Data on the reliability and validity of the SPIKE are reported in Merikangas *et al*.[22] We used diagnostic information from all interviews.

The diagnostic criteria for the atypical depressive subtype included the diagnosis of a major or minor depressive disorder plus 'atypical features' such as rejection sensitivity, overeating, and oversleeping; for further details, see Angst *et al*.[23] At least four binges (ie eating, in a discrete period of time, an amount of food that is definitely larger than most people would eat with a sense of lack of control and subsequent distress) over 1 year were required for binge eating.[24] The 12 subjects with bulimia were included in the 'binge eating' diagnosis; none of the subjects met the criteria for anorexia. Given that childhood sexual abuse was found to be associated with the development and persistence of obesity in adulthood,[25,26] and

thus being a potential confounder of depression–obesity associations, we defined adverse sexual experience during childhood as one or more self-reported negative sexual experiences before age 17 years and used it as covariate. A family history of weight problems was defined as having one or more overweight or obese first-degree relatives.

Assessment of childhood depressive symptoms

At the first interview, subjects were given a detailed description of the depressive syndrome (depressed mood, sadness, loss of energy, feelings of worthlessness, loss of interest in almost all activities, lack of reactivity to usually pleasurable stimuli, suicidal ideation) about which they were encouraged to ask questions. Irrespective of diagnostic status, subjects were asked about the presence of past depressive symptoms. If subjects endorsed past symptoms of depression, the interviewers carefully determined the age when the first depressive symptoms occurred and collected data on impairment and treatment of these symptoms. Prior studies[10–13] find that major depression in adolescence emerges as a particularly potent predictor of obesity in women. As a result, we defined childhood depressive symptoms as those with an onset before age 17 years (dichotomous exposure variable).

Assessment of BMI

BMI is frequently used to estimate body fat in clinical practice and epidemiological research, partially because of the ease with which it is measured.[27] Among middle-aged adults, BMI is strongly correlated with fat mass measured densitometrically and adjusted for height (r is approximately 0.9 for both men and women).[28]

Overall, studies show that people tend to exaggerate their height and underestimate their weight, which would underestimate BMI. However, a Swiss national survey showed that BMI under-reporting is age dependent and is minimal in young adults between ages 20 and 40 years.[29] Moreover, any such biases associated with depressive symptoms would be expected to operate most strongly in cross-sectional analyses. Since the current study is devoted to an examination of longitudinal associations, such biases are unlikely to influence the reported findings.

For the Zurich Cohort Study, height was determined by self-report in 1979, and weight was determined by self-report at each interview. Following the US guidelines for healthy weight,[27] we defined obesity as having a BMI ≥ 30. Table 1 shows the mean BMI of the sample at each interview over 20 years (body weight was not assessed in 1978 and 1980). To evaluate for the impact of missing observations on BMI, we calculated differences in average BMI at each interview between the whole sample as indicated in Table 1, and in the sample consisting only subjects without missing data differences were small, ranging from 0.0 to 0.2.

Table 1 Sample and design of the Zurich Cohort Study

Year	*N*	*Age (years)*	*Mean BMI (SD)*	*Assessment*
1978	4547	19	—	Screen
1979	591	20	21.2 (2.5)	Interview
1980	501	21	—	Questionnaire
1981	456	22	21.6 (2.7)	Interview
1986	457	27	21.8 (2.9)	Interview
1988	424	29	22.0 (3.0)	Interview
1993	407	34	22.5 (3.4)	Interview
1999	367	40	23.3 (3.8)	Interview

SD = standard deviation.

Statistical analyses

Based on results in previous studies regarding gender differences in the associations between childhood depression and body weight,[10,13] we expected stronger associations among women than men. Therefore, we modeled the interaction between gender and childhood depression, and we analyzed the data for women and men separately. The level of psychological symptoms at screening (0 = SCL-90-R low scorer sample; 1 = SCL-90-R high scorer sample) was included as covariate in all analyses as covariate. All statistical analyses were completed by using SAS for Windows release 8.02 (SAS Institute Inc., Cary, NC, USA).

For the separate unilevel analyses of mean BMI, BMI trend over time, and BMI variability, only subjects with (1) BMI measures of at least three different time points and with (2) at least one BMI measure between ages 29 and 40 years were included ($N = 458$) to reduce differences across unilevel analyses due to missing data (Table 2). The mean BMI was calculated for each subject as the mean of all his or her assessed BMI values over 20 years. To estimate the BMI trend over time, we applied a simple linear regression model for each subject in which his or her assessed BMI values was the dependent variable and the age at the time of the BMI assessments the independent variable; we used the slope coefficient of this model as an individual's BMI change trend of direction and magnitude (BMI slope). We used the standard deviation around this slope, root mean square error, as estimate for the BMI variability magnitude (BMI variability). In addition, mean BMI and BMI slope were used to calculate average BMI change per 10 years ((BMI slope $\times$ 10)/mean BMI; indicated in %) to offer a more clinically relevant picture of the results (Table 2). For between-group comparisons of mean BMI, BMI slope, and BMI variability, we compared least-squared means adjusted for stratified sampling as covariate.

For the longitudinal analyses using repeated measures, we used mixed models (ie including both random and fixed effects) with subject as random effect, subject as cluster, and a first-order autoregressive within-cluster correlation structure; exposure

Table 2 BMI level, BMI slope, and BMI variability in subjects with and without childhood depressive symptoms

	Subjects without childhood depressive symptoms	*Subjects with childhood depressive symptoms*	*Difference (95% CI)*
Women (N = 233)			
Mean BMI[a]	20.6 (0.3)	21.9 (0.3)	1.2 (0.5, 2.0)*
BMI slope (change/year)[a]	0.056 (0.019)	0.117 (0.015)	0.061 (0.014, 0.107)*
% BMI (change/10 years)	2.56 (0.78)	4.83 (0.62)	2.27 (0.36, 4.18)**
BMI variability[a]	0.87 (0.06)	0.90 (0.05)	0.03 (−0.12, 0.18)
Men (N = 225)			
Mean BMI[a]	22.8 (0.3)	22.8 (0.2)	0.0 (−0.7, 0.6)
BMI slope (change/year)[a]	0.125 (0.016)	0.152 (0.016)	0.028 (−0.016, 0.071)
% BMI (change/10 years)	5.22 (0.69)	6.59 (0.65)	1.37 (−0.44, 3.17)
BMI variability[a]	0.79 (0.06)	0.80 (0.06)	0.01 (−0.14, 0.17)

[a]Least-squared means (SE) adjusted for stratified sampling (SCL-90-R high scorer *vs* SCL-90-R low scorer).
*$P<0.01$.
**$P<0.05$.

variable, stratified sampling, and potential confounders, moderators, and mediators as fixed effects, including all available BMI measures of all study subjects (women: $N=299$; men: $N=292$) as dependent variable. The form of the mixed model is identical to that used in ordinary multiple regression, but the methods used to estimate the regression coefficients are modified to account for the correlation between repeated measures on the same subject.

For determining the 'best' model, we followed the modeling strategy guidelines developed by Kleinbaum and Klein.[30] We initially specified clinically and biologically meaningful independent variables based on the literature[10,15,16] and on a previous study using the same data set.[31] We defined childhood depressive disorder as exposure variable and selected the following covariates: age at BMI assessment, adult depressive disorders related to weight change (major depression; the atypical depressive subtype; depressive symptoms presenting with a seasonal pattern), levels of physical activity, educational level, socioeconomic status, household income, family history of weight problems, parity (in women), level of self-esteem, use of antidepressants (as time-dependent indicator variable), anxiety disorders (composite variable including panic disorder, generalized anxiety disorder and phobic disorders), binge eating, conduct disorder symptoms, adverse sexual experience during childhood, smoking (number of cigarettes a day as time-dependent covariate), alcohol consumption (number of glasses a week as time-dependent covariate), and diagnoses of drug abuse/dependence. We selected gender, age, socioeconomic status, educational level, binge eating, and atypical depression as potential effect modifiers.[32]

This analysis stage showed that there was a significant interaction between childhood depressive symptoms and age, and that age-modified depression–BMI associations were different for women and men. Other interactions between potential effect modifiers and childhood depressive symptoms were removed from the model because they did not reach statistical significance. Finally, we reduced the potentially confounding variables by backward elimination. Among the variables included in the final models, the following were associated with childhood depressive symptoms: atypical depression (OR = 2.8, 95% CI (1.6, 4.8), $P<0.001$), conduct disorder symptoms (OR = 1.8 (1.1, 2.8), $P<0.05$), and a family history of weight problems (OR = 1.5 (1.0, 2.1) $P<0.05$). Adult depressive symptoms were associated with childhood depressive symptoms (OR = 1.6 (1.1, 2.3), $P<0.05$), but they were not associated with BMI or obesity. Table 3 shows a selection of potential confounders/mediators classified by gender and childhood depression. Table 4 shows the relationship between confounders/mediators and BMI.

Following the suggestions of Kraemer *et al*,[33] we considered a variable (*B*) as mediator of the main risk factor (*A*) when (1) *A* is correlated with *B*, (2) *A* temporally precedes *B*, and (3) when considering *A* and *B* jointly, presence of either domination of *A* by *B* or codomination by *A* and *B*. In women, atypical depression and binge eating met criteria (1) and (2); in men, only atypical depression met criteria (1) and (2). Given the assessment method (body weight at the time of the interview, and potential adult mediators/confounders of body weight during the year prior to the interview), the potential mediators/confounders preceded the outcome. Including potential mediators/confounders as lagged predictors, that is, from the adjacent preceding interview, did not lead to relevant changes of the estimated effects of childhood depression and generally reduced the estimated effects of the predictors.

Table 3 Baseline and follow-up characteristics by gender and childhood depressive symptoms (CDS)

	Women (N = 299)		*Men (N = 292)*	
Variable	*With CDS N (%)*	*Without CDS N (%)*	*With CDS N (%)*	*Without CDS N (%)*
Major depression at baseline	13 (12.6%)	19 (9.7%)	4 (4.7%)	10 (4.9%)
Major depression at any interview	50 (48.5%)	65 (33.2%)	25 (29.1%)	46 (22.3%)
Atypical depression at baseline	9 (8.7%)	10 (5.1%)	3 (3.5%)	0 (0.0%)
Atypical depression at any interview	20 (19.4%)	16 (8.2%)	13 (15.1%)	12 (5.8%)
Binge eating at baseline	9 (8.7%)	9 (4.6%)	2 (2.3%)	5 (2.4%)
Binge eating at any interview	21 (20.4%)	25 (12.8%)	5 (5.8%)	15 (7.3%)
Conduct disorder symptoms	17 (16.5%)	22 (11.2%)	34 (39.5%)	46 (22.3%)
Family history of weight problems	51 (49.5%)	81 (41.3%)	44 (51.2%)	86 (41.8%)
Low educational level	32 (31.1%)	53 (27.0%)	27 (31.4%)	92 (44.7%)
Smoking at baseline	33 (32.0%)	74 (37.8%)	32 (37.2%)	64 (31.1%)
	Mean (SD)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Average number of cigarettes per day	4.7 (6.5)	4.4 (5.7)	6.1 (7.7)	5.3 (7.1)
Average glasses of alcohol per week	3.9 (4.7)	3.6 (3.7)	9.7 (11.5)	8.4 (8.5)
Sports activity (four frequency levels)	2.3 (1.0)	2.1 (1.0)	2.5 (1.1)	2.5 (1.1)
Hiking/walking (four frequency levels)	2.6 (1.0)	2.7 (1.0)	2.3 (1.0)	2.1 (0.9)
Watching TV (four frequency levels)	2.6 (1.2)	2.5 (1.2)	2.7 (1.2)	2.8 (1.1)

Table 4 BMI by clinical characteristics

Condition	*With condition Mean[a] (SD)*	*W/o condition Mean[a] (SD)*	*Difference*	*P-value*
Major depression	21.9 (2.8)	21.9 (2.7)	0.0	NS
Atypical depression	23.2 (4.5)	21.8 (2.6)	1.3	<0.05
Binge eating	23.5 (3.4)	21.7 (2.6)	1.8	<0.0001
Conduct disorder symptoms	22.5 (2.8)	21.9 (2.7)	0.6	<0.05
Family history of weight problems	22.5 (3.0)	21.6 (2.5)	0.9	<0.001
Low educational level	22.7 (3.0)	21.6 (2.5)	1.1	<0.0001
SCL-90-R high scorer sample	21.8 (2.6)	22.2 (2.9)	0.4	NS
Smoking	22.0 (2.7)	21.9 (2.7)	0.1	NS
Alcohol intake >7 glasses per week	21.9 (2.6)	22.1 (2.8)	−0.1	NS
Sports activity at least once a week	22.2 (2.4)	21.9 (3.0)	0.4	NS
Hiking/walking at least once a week	21.8 (2.6)	22.3 (2.9)	−0.4	NS
Watching television at least once a day	22.7 (3.0)	21.7 (2.6)	1.0	NS

NS = not significant.
[a]Least-squared means adjusted for gender and average age at BMI assessments.

Scoring high on the SCL-90-R at baseline appeared to be rather negatively than positively associated with BMI (Table 4). In the SCL-90-R high scorer sample, 34.5% had childhood depressive symptoms, while in the SCL-90-R low scorer sample, 26.2% had childhood depressive symptoms, reflecting a trend for an association between childhood depressive symptoms and scoring high on the SCL-90-R at baseline (OR = 1.5 (1.0, 2.2), $P = 0.06$). To evaluate the impact of the stratified sampling, we fit mixed models for subjects in the SCL-90-R low scorer sample and for subjects in the SCL-90-R high scorer sample separately. This analysis revealed a very small difference in the magnitude of the model parameter estimates between the subsamples, and scoring high on the SCL-90-R at baseline appeared to be rather protective than a risk for weight problems. To evaluate for the impact of missing data on BMI, we fit mixed models for women and men that included only subjects who participated in all interviews. This led to some minor changes in the model parameter estimates that did not alter the interpretation of the results.

To test the association between childhood depressive symptoms and the occurrence of adult obesity we used Cox's proportional hazards regression analysis based on data from the whole sample (women: $N=299$; men: $N=292$). The outcome variable was defined as the waiting time (ie the survival time) until obesity occurred. The observations were censored in the sense that for some subjects obesity had not occurred at the time of their last assessment. Using the same modeling strategy as mentioned above, we included BMI at age 20 years, the level of physical activity, level of psychological symptoms at screening (0 = SCL-90-R low scorer sample; 1 = SCL-90-R high scorer sample), socioeconomic status, and family history of weight problems as covariates in the final model. Cox's regression analysis estimates the survival probability of a given outcome at each time point that an event occurs on the basis of available data at that point of time. The benefit of this approach is that it takes maximum advantage of each subject's available data, even though subjects were tracked for different lengths of time.

Results

Univariate associations

In initial analyses, we used a full factorial model including gender, age, and childhood depressive symptoms to examine differences in BMI. This model did not generate a significant interaction between gender and childhood depressive symptoms predicting BMI; however, there was a significant gender-by-age interaction ($F(1, 1476)=7.87$, $P<0.01$). As a result of this interaction as well as prior studies on gender differences, univariate associations are examined in each gender separately. As indicated in Table 2 and displayed in Figure 1, women with a history of childhood depressive symptoms had higher mean BMI and higher average weight gain between ages 20 and 40 years than women without childhood depressive symptoms. Among men, before controlling covariates, childhood depressive symptoms were not associated with adult mean BMI or BMI slope.

Mixed model for BMI

Table 5 shows the mixed models for BMI in women and men. Among women, after controlling covariates, there was a significant interaction between childhood depressive symptoms and age at BMI assessment predicting BMI. This interaction demonstrated that the strength of the association between childhood depressive symptoms and BMI increased with age, reflecting a persistent excessive weight gain from young adulthood into middle age among individuals with childhood depressive symptoms. Excluding women with binge eating from the model led to a reduction in the main parameter estimate of 14%. Excluding subjects with atypical depression from the model also led to a reduction in the main parameter estimate of 14%. The effect of atypical depression on BMI[31] disappeared when childhood depressive symptoms were included in the model, while the effect of binge eating remained almost unchanged when childhood depressive symptoms were included.

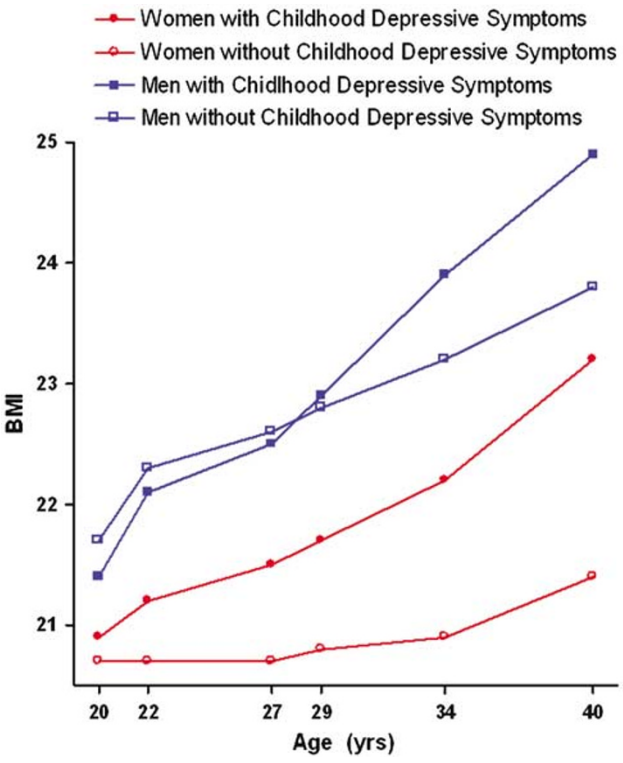

Figure 1 The course of BMI (least-squared means adjusted for stratified sampling (SCL-90-R high scorer *vs* SCL-90-R low scorer) over time in a community sample classified by gender and childhood depressive symptoms.

Among men, there was also a significant positive association between childhood depressive symptoms and BMI increasing with age, although of lower magnitude than among women. Excluding men with atypical depression or with binge eating from the model did not change the main parameter estimate.

Proportional hazards regression for obesity

Among women, after controlling for BMI at age 20 years, level of physical activity, socioeconomic status, family history of weight problems, and stratified sampling, there was a significant positive association between childhood depressive symptoms and the occurrence of adult obesity (hazard ratio = 11.52, SE = 1.24, $P<0.05$). Among men, using the same model, childhood depressive symptoms were not associated with the occurrence of adult obesity (hazard ratio = 1.10, SE = 0.66, $P=0.88$).

Discussion

Consistent with previous studies,[10–13] this 20-year prospective community study of a cohort of young adults demonstrates a longitudinal association between

Table 5 Mixed models for BMI

Fixed effects	*Estimate*	*SE*	*DF*	*F-value*	*P-value*
Women (N = 299)					
Age (years)	0.052	0.017	1, 957	9.06	0.003
Childhood depressive symptoms (CDS)	−1.136	0.718	1, 957	2.50	0.12
CDS × age interaction	0.074	0.021	1, 957	12.00	0.0006
Watching television (four frequency levels)	0.304	0.160	1, 957	3.60	0.05
Smoking (number of cigarettes/day)	−0.016	0.005	1, 957	9.48	0.002
Binge eating	1.357	0.457	1, 957	8.82	0.003
Low socioeconomic status	1.123	0.382	1, 957	8.65	0.003
Low educational level	0.978	0.411	1, 957	5.66	0.02
Family history of weight problems	0.718	0.368	1, 957	3.80	0.05
SCL-90-R high scorer sample	−0.526	0.404	1, 957	1.69	0.19
Men (N = 292)					
Age (years)	0.112	0.014	1, 828	63.25	<0.0001
Childhood depressive symptoms (CDS)	−1.156	0.631	1, 828	3.36	0.07
CDS × age interaction	0.042	0.019	1, 828	5.07	0.02
Generalized anxiety disorder	−0.930	0.337	1, 828	3.84	0.05
Alcohol consumption (glass/week)	0.007	0.003	1, 828	3.32	0.07
Binge eating	1.428	0.608	1, 828	5.51	0.02
Conduct disorder symptoms	0.519	0.365	1, 828	2.03	0.15
Low educational level	1.029	0.361	1, 828	8.13	0.005
Family history of weight problems	0.660	0.337	1, 828	3.84	0.05
SCL-90-R high scorer sample	−0.901	0.377	1, 828	5.73	0.02

DF = degrees of freedom; the variables are dichotomous when no (unit) is indicated.

childhood depression and female obesity. Moreover, the current study adds new insight into previous studies by having a longer follow-up period than previous studies and by controlling for a wide range of covariates, which were consistently assessed at each interview.

Among women, depressive symptoms before age 17 years were associated with both increased weight gain between ages 20 and 40 years, and increased occurrence of adult obesity. These associations persisted after controlling for adverse sexual experience during childhood, a history of conduct disorder symptoms, a family history of weight problems, demographic variables, adult psychopathology, consumption of alcohol and nicotine, and antidepressant use. The multivariate analysis suggested that binge eating and atypical depression mediated some of the effects of childhood depression on body weight. The current study adds to previous reports that depressive symptoms, irrespective of diagnostic status, during childhood may considerably increase the risk for female obesity; it also adds to previous studies that increased weight gain associated with childhood depressive symptoms persists from young adulthood to middle age representing a risk for female obesity that increases with age. The high magnitude of the association found in the current long-term study in combination with the high prevalence for depression in children and adolescents[34] imply an important public health impact of childhood depressive symptoms in women.

Among men, depressive symptoms presenting during childhood were associated with adult weight gain in the mixed model. The weight gain in men was smaller than the weight gain in women and did not increase the occurrence of adult obesity in men. The multivariate analysis did not provide evidence for variables mediating between childhood depression and increased adult weight gain. These results are in line with previous studies suggesting that the association between body weight and depressive disorders differs between women and men.[8,10,13] In addition to previous studies, the current study suggests that there is an association between childhood depressive symptoms and adult BMI in both genders being considerably stronger in women than in men. However, the graphic presentation in Figure 1 suggests that the effects on men might appear after the growth period, which is later in men than in women.

Growing evidence implicates common brain monoamines and peptides in depression and the regulation of food intake or body weight. These monoamines and peptides include serotonin, norepinephrine, dopamine, neuropeptide Y, and corticotropin-releasing hormone.[35,36] With respect to metabolic processes, both obesity and depression have been associated with glucose intolerance, insulin resistance, and diabetes.[37] As a result, associations between depression and body weight are not surprising. However, interpreting the specific mechanisms on the basis of the current neurobiological understanding remains speculative.

Shared genetic factors for body fat regulation and depression have been proposed,[32,38] possibly related to a common underlying central dopaminergic dysfunction,[39,40] and gender-specific genetic factors for depression[41] might explain gender differences in depression–obesity associations. The potentially mediating role of eating-related psychopathology (binge eating, atypical depression) suggests that shared genetic factors act rather at a behavioral than at a metabolic level, that is, genes might influence both depression and increased appetitive behaviors. Specifically, atypical depression has been related to female gender, a young age of onset,[23] increased appetite, and high BMI;[31,38,42] and theoretically, atypical depression has been considered as relatively homogeneous depressive subtype with respect to etiology and pathophysiology.[38,43] In addition, the temperamental factor 'disinhibition' has been implicated in early-onset depression,[44] weight change,[5] and obesity,[45] with higher scores for emotional disinhibition in adult women than in adult men[45] being consistent with the gender difference found in the current study. Since many patients with depression consume carbohydrates and fat foods to modulate states of low mood and boredom,[46] one may hypothesize that these subtle eating-related symptoms (emotional eating) may persist into adulthood even in the absence of clinical depression, and thus contribute to excessive weight gain. Finally, there is evidence that psychosocial factors operating during critical periods in childhood and adolescence may influence the development of overweight and obesity during adulthood.[47] Likewise, depressive symptoms in childhood might have an impact on mechanisms that entrain the long-term development of the body fat mass.

The relationship found in the current study between childhood depression and adult obesity may have important clinical implications because depression during childhood is a prevalent and treatable condition.[34] Therefore, this study might encourage further studies examining the effects on overweight of treatments aimed at reducing depressive symptoms during childhood among women. This may provide another potential means to reduce the burden associated with obesity and related negative health consequences. Moreover, it might encourage further studies examining the relationship between depression and obesity, because both conditions may have their origins in childhood and adolescence, and both depression and obesity show increasing prevalence for unknown reasons.[1,48]

This study has several methodological limitations that need to be addressed. The assessment of childhood depressive symptoms involved a degree of retrospective recall, and data on individual depressive symptoms or childhood depressive disorders were not available. Nevertheless, symptoms were rated prior to age 20 years, a point where symptoms are still considered 'early onset'. Moreover, recall biases cannot explain findings reflecting the relationship between symptoms recalled at age 20 years and overweight status determined in mid-life. Second, height and weight were examined by self-report, and the sample was a single age cohort. However, the strengths of this study suggest the findings are worthy of further consideration. Specifically, the sample was community based; the study design was longitudinal over 20 years; experienced well-trained clinicians administered standardized interviews; the assessment included well-established risk factors for weight problems; the hypothesis of this study relating childhood depressive symptoms to adult obesity was based on prior longitudinal studies implicating a high prior probability; and the screening method yielded a high number of subjects with childhood depressive symptoms; since psychopathology was assessed prior to the determination of overweight in mid-life, the reports of childhood psychopathology was not influenced by biases associated with weight problems present in mid-life.

In summary, this study shows a relatively strong longitudinal association between childhood depressive symptoms and adult BMI with the effect of childhood depressive symptoms on adult BMI increasing with age leading to a considerable increase in the incidence of female obesity. This relationship persisted after controlling for potentially confounding variables. As the magnitude of the associations was high, and depression during childhood is a prevalent and treatable condition, this finding may have important clinical implications for the prevention and treatment of obesity.

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