Longitudinal Study of Depressive Symptoms and Progression of Insulin Resistance in Youth at Risk for Adult Obesity

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OBJECTIVE—The purpose of this study was to determine whether having childhood depressive symptoms is a risk factor that prospectively predicts impairment in glucose homeostasis.

RESEARCH DESIGN AND METHODS—A non–treatment-seeking sample of 115 children (aged 5–13 years), oversampled for being at risk for adult obesity, was assessed at baseline and again ~6 years later. Children self-reported depressive symptoms using the Children's Depression Inventory at baseline. Insulin resistance was assessed at baseline and follow-up with the homeostasis model assessment of insulin resistance index (HOMA-IR).

RESULTS—Children's depressive symptoms were a significant predictor of follow-up HOMA-IR, fasting insulin, and fasting glucose in models accounting for baseline HOMA-IR, insulin, or glucose values; sex; race; baseline age; baseline BMI; change in BMI at follow-up; family history of type 2 diabetes; and time in the study ($P < 0.01$).

CONCLUSIONS—In this study, depressive symptomatology at baseline predicted the progression of insulin resistance during child and adolescent development independent of changes in BMI. Research is needed to determine whether early intervention to decrease elevated depressive symptoms in youth ameliorates later development of insulin resistance and lessens the risk of type 2 diabetes.

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Worsening insulin resistance, in concert with impaired insulin secretion, is a major physiological precursor of type 2 diabetes. Insulin resistance often develops through excessive gain of body weight or adiposity. Among youth, those who are obese (BMI [kg/m^2] ≥95th percentile) have greater insulin resistance than their nonobese peers.

Psychological factors also may play a role in the development of insulin resistance and consequent type 2 diabetes. In particular, evidence from adult studies suggests that symptoms of depression may be a risk factor for insulin resistance and type 2 diabetes, independent of BMI (1). Depressive symptoms and perceived psychosocial stress are positively associated with insulin resistance in women, even after accounting for body weight (2,3). Furthermore, in adult women and men, elevated depressive symptoms or the presence of major depressive disorders predict type 2 diabetes onset after accounting for measures of body weight or adiposity (4–8). A meta-analysis of prospective adult studies concluded that elevated depressive symptoms were associated with a 37% increased risk of developing type 2 diabetes at a later point in time, and this effect did not seem to be significantly diminished by confounders such as BMI (9). Although the mechanisms that explain depression's impact on insulin resistance are not well understood, depressive symptoms may promote worsening insulin resistance through affecting behavioral patterns, such as increased total energy or carbohydrate intake and lowered voluntary energy expenditure. Depressive symptoms also may activate underlying physiological stress pathways, distress-induced upregulation of counterregulatory hormone systems like the hypothalamic-pituitary-adrenal axis, sympathetic nervous system activation, alteration of insulin signaling in the brain, and/or an increase in proinflammatory factors (10).

Despite the strong evidence linking depressive symptoms and insulin resistance or type 2 diabetes in adults, there are limited data on the relationship between symptoms of depression and insulin resistance during childhood and adolescent development. Given the possible role that adult studies suggest for depression in the development of type 2 diabetes, understanding how depressive symptoms are linked to insulin resistance during childhood and adolescence may be important for identifying early risks for potentially adverse health outcomes. In a large community study of youth aged 6–18 years, parents' perceptions of their children's negative emotionality were associated cross-sectionally with children's fasting insulin, particularly among boys (11). Among healthy nonoverweight and overweight adolescents aged 12–17 years, depressive symptoms were positively related to poorer insulin sensitivity cross-sectionally, even after adjusting for body composition (12). Depressive symptoms also were associated cross-sectionally with higher fasting insulin among overweight middle-school children with a

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family history of type 2 diabetes (13). However, it remains to be determined whether depressive symptoms are prospectively related to worsening progression of insulin resistance among youth.

We therefore sought to evaluate whether children's depressive symptoms predicted worsening insulin resistance over time. Understanding the link between depressive symptoms and insulin resistance during the transition from childhood to adolescence is important. Normative endocrine changes associated with the onset of puberty produce increased insulin resistance relative to childhood. Moreover, entry into adolescence marks a peak time for increases in elevated depressive symptoms. These marked biological and psychological shifts render the transition from childhood to adolescence an important developmental window for understanding how symptoms of depression are associated with insulin resistance. On the basis of adult longitudinal data (9) and cross-sectional studies in youth (12,13), we hypothesized that children's depressive symptoms at a baseline assessment would be related to greater insulin resistance when followed-up in adolescence, independent of initial BMI and BMI change over time.

RESEARCH DESIGN AND METHODS

—Participants were a non–treatment-seeking sample of children taking part in a longitudinal study designed to investigate risk factors for excessive weight gain and adverse metabolic outcomes (clinical trial reg. nos. NCT00001522 and NCT00001195, clinicaltrials.gov) between July 1996 and November 2010. By design, the sample was oversampled to include children at increased risk for the development of adult obesity by virtue of either the child's overweight status (BMI ≥85th percentile) or a parental history of being overweight (BMI ≥25 kg/m^2). Participants were recruited through mailings to pediatricians, family physicians, and two waves of notices to families with elementary school–aged youth in Maryland and the Washington, DC, metropolitan area. Advertisements requested the participation of children willing to undergo phlebotomy and X rays for studies investigating hormones and metabolic functioning in children. All recruitment materials specified that no treatment would be offered. Approximately 7% of families responded to each of the school mailings, and subjects recruited directly from these mailings constituted 88% of all subjects studied. Youth were in good general health and were not taking medications known to affect body weight or metabolism for at least 2 weeks prior to study entry. Exclusion criteria included a significant medical health problem, such as renal, hepatic, most endocrinologic (e.g., hyperthyroidism, Cushing syndrome, or type 2 diabetes), or pulmonary disorders (other than mild asthma not requiring chronic medication) or major psychiatric illnesses requiring treatment. Children provided written assent and parents gave written consent to participate. Children were financially compensated for their participation at baseline ($120) and follow-up ($120). All study procedures were approved by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Institutional Review Board.

Assessment

At a baseline assessment visit, participants underwent a physical examination that included pubertal staging by a pediatric endocrinologist or trained pediatric or family nurse practitioner. Parents reported the child's and the family medical history, including parental height and weight and family history of type 2 diabetes. Children's height and weight measurements were obtained after an overnight fast. Participants were clothed but with shoes removed. Each child's height was measured three times to the nearest millimeter by a stadiometer (Holtain, Crymmych, Wales, U.K.) that was calibrated before each child's measurement. Weight was measured to the nearest 0.1 kg with a calibrated digital scale (Scale-Tronix, Wheaton, IL). Participants' height and weight were used to compute BMI (kg/m^2). BMI *z* (SD) scores for sex and age were calculated according to the Centers for Disease Control and Prevention 2000 standards.

Participants completed the 27-item Children's Depression Inventory (CDI) to assess the extent and severity of depressive symptoms (14). Younger children (aged ≤8 years) had the questions read to them so that any difficult concepts could be explained. A total raw score, ranging from 0 to 54, is derived from the sum of its items. A total score that exceeded 12 was proposed as the cutoff for screening for at risk for clinical depression (15). We examined the CDI total score both as a continuous variable and as a dichotomous variable (lower depressive symptoms [CDI <13] vs. elevated depressive symptoms [CDI ≥13]). The CDI is reliable and well validated (14), and the total score has demonstrated adequate internal reliability in studies oversampled to include youth aged ≤14 years who were at risk for adult obesity in our laboratory (α = 0.79). Any child who endorsed active suicidal ideation was referred for an immediate psychiatry consultation at the National Institutes of Health Clinical Center and was excluded from participation in the current study.

Each participant provided fasting blood samples for serum insulin and glucose after an overnight fast. Children were asked at least twice about caloric consumption before blood was drawn. A fasted state was encouraged to be reported truthfully by providing compensation for the visit even if subjects reported not having fasted. Youth consumed their habitual diet (invariably reported on a food-frequency questionnaire as ≥35% energy from carbohydrates) during the week before they were studied. Glucose was measured using a Hitachi 917 analyzer using reagents from Roche Diagnostics (Indianapolis, IN). Insulin concentrations were determined using a commercially available immunochemiluminometric assay purchased from Diagnostic Product Corporation (Los Angeles, CA) and calibrated against insulin reference preparation 66/304. The insulin assay uses a monoclonal anti-insulin antibody and was run on an Immulite2000 machine (Diagnostic Product Corporation). The cross-reactivity of the insulin assay with proinsulin was <8% and with C-peptide was <1%, sensitivity was 2 μU/mL, and the mean inter- and intra-assay coefficients of variation were 5.8 and 3.6%, respectively. Insulin resistance was estimated with the homeostasis model assessment of insulin resistance (HOMA-IR) index, calculated as follows: (fasting insulin [μU/mL] × fasting glucose [mmol/L])/22.5. Although HOMA-IR as a continuous variable was considered the primary outcome measure in the current study, secondary outcomes included insulin resistance defined dichotomously (absence [HOMA-IR <3.16] vs. presence [HOMA-IR ≥3.16]), impaired fasting glucose (absence [fasting glucose <100 mg/dL] vs. presence [fasting glucose ≥100 mg/dL]), and hyperinsulinemia (fasting insulin ≥15 μU/L).

At a follow-up appointment intended to take place 5 years later, participants' height and weight were reassessed to calculate BMI, as completed at baseline. Participants again provided fasting blood samples for serum insulin and glucose,

which were used to reassess HOMA-IR. For ~2% of participants, plasma glucose (collected in tubes containing powdered sodium fluoride) was used in place of serum glucose when the latter was not available. For participants who did not complete a 5-year follow-up, available anthropometric and phlebotomy data were used either from a somewhat shorter or longer follow-up period, whenever such data were available.

Statistical analysis

Analyses were conducted using SPSS 18.0. Study variables were examined to determine whether the assumptions of univariate and multivariate analyses were met. The skew and kurtosis were satisfactory on all variables, and outliers (<3% of all data points) were adjusted to fall 1.5 times the interquartile range below or above the 25th or 75th percentile. This strategy was used because it minimizes outliers' influence on the characteristics of the distribution, minimally changes the distribution overall, and avoids potential bias associated with eliminating outliers altogether. Missing data patterns were characterized to test baseline differences in study variables between children who did and those who did not complete a follow-up assessment. Correlations or independent-sample *t* tests were used to examine the bivariate associations among baseline demographic and anthropometric characteristics, depressive symptoms, and insulin resistance. Hierarchical multiple regressions were conducted regressing follow-up insulin resistance on baseline depressive symptoms, including in the model baseline insulin resistance, sex, race (non-Hispanic white vs. other), first- or second-degree family history of type 2 diabetes (presence vs. absence), baseline age (years), baseline BMI (kg/m^2), change in BMI from baseline to follow-up, and time in study (years between baseline and follow-up). Baseline pubertal staging was considered to be a covariate but was removed because it was nonsignificant in all models ($P > 0.65$). Parallel analyses also were conducted for the secondary outcomes of fasting insulin and fasting glucose. ANCOVA was used to test whether similar relationships between depressive symptoms and insulin resistance, fasting insulin, or glucose were observed if depressive symptoms were considered categorically as children with lower depressive symptoms (CDI total score <13) versus elevated symptoms (CDI total score ≥13). Logistic regressions were conducted to test whether depressive symptoms predicted greater odds of categorical outcomes of insulin resistance (absence [HOMA-IR <3.16] vs. presence [HOMA-IR ≥3.16]), hyperinsulinemia (fasting insulin ≥15 μU/L), and impaired fasting glucose (absence [fasting glucose <100 mg/dL] vs. presence [fasting glucose ≥100 mg/dL]). Parallel sets of covariates were used in these analyses. Differences and associations were considered significant when *P* values were ≤ 0.05. All tests were two tailed.

As a result of a large missing data fraction, we also reran the primary analyses using multiple imputation with SAS 18.0 to handle missing data. Ten imputed datasets were produced (16). Following standard multiple imputation procedures, each dataset was analyzed separately, and then the effects were combined using the SAS MIANALYZE procedure. Because these results did not significantly differ from the nonimputed findings, results obtained in the nonimputed analyses are presented.

RESULTS—A total of 198 children (51.9% female) aged 8.6 ± 1.7 years (range 6–13) completed a baseline assessment visit. Three children were excluded because of medical illnesses identified at their baseline visit. Fifty percent of participants were obese (BMI ≥95th percentile), 16% were overweight (BMI ≥85th and <95th percentile), and 34% were nonoverweight (BMI <85th percentile) but had at least one overweight parent. Demographic, anthropometric, and metabolic characteristics of the study participants by depressive symptom status are described in Table 1. Compared with children with lower depressive symptoms ($n = 160$), children with elevated depressive symptoms ($n = 38$) were slightly, but significantly, younger (aged 8.1 ± 1.5 years vs. 8.7 ± 1.6 years, $P = 0.03$), were more likely to have hyperinsulinemia (31.6 vs. 14.4%, $P = 0.01$), and were more likely to have elevated insulin resistance (HOMA-IR ≥3.16; 34.2 vs. 16.9%, $P = 0.02$) at baseline. Fifty-eight percent of children ($n = 115$) returned for a follow-up phlebotomy appointment an average of

Table 1—*Participant characteristics at baseline assessment*

Variable	Lower depressive symptoms CDI total score <13	Elevated depressive symptoms CDI total score ≥13	*P*
n	160	38	
Sex (% female)	51.3	55.3	0.66
Race (%)*			0.11
Non-Hispanic black	30.6	47.4	
Non-Hispanic white	66.9	52.6	
Hispanic	2.5	0	
Family history of type 2 diabetes (% presence)	58.5	55.9	0.79
Baseline BMI (kg/m^2)	22.0 ± 5.9 (13.2–40.1)	23.7 ± 7.8 (13.2–40.1)	0.21
Baseline BMI *z* score	1.4 ± 1.1 (−1.9 to 3.2)	1.6 ± 1.2 (−1.9 to 3.4)	0.27
Baseline fasting insulin (μU/L)	9.1 ± 6.3 (1.0–26.1)	11.6 ± 7.9 (2.0–26.1)	0.07
Hyperinsulinemia (% presence)†	14.4	31.6	0.01
Baseline fasting glucose (mg/dL)	88.1 ± 6.7 (70.5–106.5)	89.1 ± 6.3 (79.0–103.0)	0.38
Impaired fasting glucose (% presence)‡	3.8	5.3	0.67
Baseline HOMA-IR	2.0 ± 1.4 (0.2–5.9)	2.6 ± 1.8 (0.4–5.9)	0.07
Elevated HOMA-IR (% presence)§	16.9	34.2	0.02

Data are means ± SD (range), unless otherwise indicated. $n = 176–198$. *When race/ethnicity was defined dichotomously as non-Hispanic white vs. other, its association with depressive symptoms status remained nonsignificant ($P = 0.10$). †Hyperinsulinemia defined as fasting insulin ≥15 μU/L. ‡Impaired fasting glucose defined as fasting glucose ≥100 mg/dL. §Elevated HOMA-IR defined as ≥3.16.

5.8 ± 1.3 years (range 3.1–8.3) later. Mean age at follow-up was 14.6 ± 2.3 years (range 8.9–20.3). One child had confirmed type 2 diabetes at follow-up. Youth who did not complete a follow-up appointment had greater baseline depressive symptoms (8.4 ± 6.5 vs. 6.8 ± 5.2, $P = 0.05$), higher baseline fasting insulin (11.0 ± 7.7 vs. 8.5 ± 5.6, $P = 0.01$), and higher baseline insulin resistance (2.5 ± 1.8 vs. 1.9 ± 1.3, $P = 0.01$) than youth who did return for a follow-up. There were no differences between completers and noncompleters on any other variable.

Table 2 summarizes the analyses examining baseline depressive symptoms as a predictor of follow-up insulin resistance, fasting insulin, and fasting glucose. Controlling for all other variables in the models, children's baseline depressive symptoms predicted greater insulin resistance and higher fasting insulin and glucose at follow-up ($P < 0.01$). Baseline depressive symptoms explained 8% of the variance in follow-up insulin resistance ($P < 0.001$), 7% of the variance in follow-up fasting insulin ($P < 0.001$), and 4% of the variance in follow-up fasting glucose ($P = 0.019$), after accounting for the other variables in the model. An identical pattern of results was observed when depressive symptoms were considered categorically. Youth with elevated depressive symptoms at baseline ($n = 17$) had higher insulin resistance, fasting insulin, and fasting glucose at follow-up than youth with lower depressive symptoms at baseline ($P \leq 0.001$) (Fig. 1). As an exploratory analysis, we also tested whether baseline insulin resistance predicted follow-up depressive symptoms, accounting for baseline depressive symptoms and a parallel set of covariates. Insulin resistance was not a significant predictor of follow-up depressive symptoms ($P = 0.99$).

At follow-up, 43 (37.4%) children met the criteria for elevated insulin resistance, 43 (37.4%) for hyperinsulinemia, and 4 (3.8%) for impaired fasting glucose. Table 3 presents a summary of analyses examining baseline depressive symptoms as a predictor of elevated insulin resistance, hyperinsulinemia, and impaired fasting glucose. Accounting for all other variables in the model, each one-unit increase in CDI total score at baseline was associated with a 1.14 greater odds of elevated insulin resistance at follow-up (95% CI 1.01–1.28, $P < 0.05$). Depressive symptoms did not significantly predict follow-up hyperinsulinemia or impaired fasting glucose. When depressive symptoms were considered categorically, those with and without elevated depressive symptoms at baseline did not significantly differ in their odds of elevated insulin resistance ($P = 0.10$), hyperinsulinemia ($P = 0.52$), or impaired fasting glucose ($P = 0.98$), adjusting for all of the same covariates.

CONCLUSIONS—The current study provides evidence that children's depressive symptoms are a prospective risk factor for worsening insulin resistance. Even when accounting for known additional risk factors, including family history of type 2 diabetes, children's baseline BMI, and changes in children's BMI over time, depressive symptoms were associated with greater insulin resistance ~6 years later. Depressive symptoms' impact on insulin resistance was clinically meaningful such that depressive symptoms were associated with a significantly greater likelihood of developing clinically elevated HOMA-IR (defined as ≥3.16). Of note, children's degree of insulin resistance is a significant predictor of type 2 diabetes onset in young adulthood, even after accounting for BMI (17).

The current findings are consistent with previous cross-sectional studies demonstrating a link between depressive symptoms or negative affect and insulin resistance in youth independent of body composition (12,13). Moreover, the present results are consistent with adult data demonstrating that depressive symptoms are related to greater odds of developing type 2 diabetes (9). The mechanisms explaining the relationship between depressive symptoms and insulin resistance are not well understood. Symptoms of depression, including fatigue, lack of energy, or anhedonia (referring to loss of pleasure over activities that one previously found enjoyable), may prompt behavioral decreases in voluntary energy expenditures, such as exercise, which, in turn, may heighten insulin resistance. Consistent with this notion, adolescent depressive symptoms are

Table 2—*Multiple hierarchical regressions examining children's baseline depressive symptoms as a predictor of follow-up insulin resistance, fasting insulin, and fasting glucose*

	Follow-up								
	HOMA-IR			Fasting insulin			Fasting glucose		
Predictor	B	SE	β	B	SE	β	B	SE	β
Sex (female)	0.87	0.31	0.22*	4.27	1.36	0.23*	−2.26	1.35	−0.15†
Race (black or Hispanic)	−0.48	0.32	−0.12	−2.25	1.40	−0.12	−1.67	1.39	−0.11
Family history of type 2 diabetes (present)	0.64	0.31	0.16‡	3.23	1.37	0.17‡	−1.09	1.36	−0.07
Baseline age (years)	−0.24	0.10	−0.20‡	−1.03	0.43	−0.19‡	−1.04	0.43	−0.23‡
Baseline BMI (kg/m^2)	0.04	0.04	0.11	0.17	0.18	0.12	−0.13	0.12	−0.10
BMI change	0.09	0.04	0.22*	0.46	0.16	0.24*	−0.11	0.16	−0.07
Time in study (years)	−0.27	0.11	−0.19‡	−1.28	0.50	−0.20*	−0.45	0.49	−0.09
Baseline HOMA-IR	0.52	0.17	0.40*	—	—	—	—	—	—
Baseline fasting insulin (μU/L)	—	—	—	0.59	0.17	0.43§	—	—	—
Baseline fasting glucose (mg/dL)	—	—	—	—	—	—	0.22	0.10	0.20‡
		$R^2 = 0.37$§			$R^2 = 0.43$			$R^2 = 0.11$	
Baseline depressive symptoms	0.10	0.03	0.29§	0.44	0.11	0.28§	0.29	0.12	0.23*
		$R^2 = 0.45$§			$R^2 = 0.50$§			$R^2 = 0.15$‡	
		$\Delta R^2 = 0.08$§			$\Delta R^2 = 0.07$§			$\Delta R^2 = 0.04$‡	

$n = 98$–102. *$P \leq 0.01$. †$P \leq 0.10$. ‡$P \leq 0.05$. §$P \leq 0.001$.

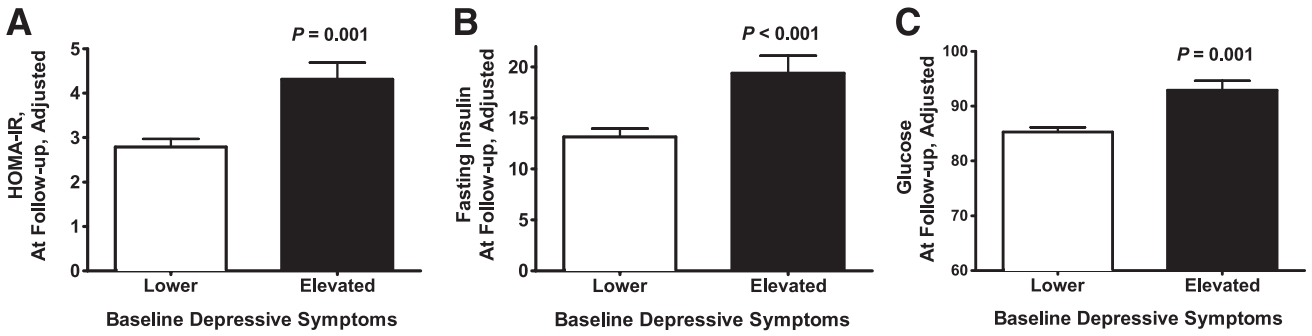

Figure 1—*Compared with children with lower depressive symptoms at baseline* (n = *97; CDI total score <13), youth with elevated depressive symptoms at baseline* (n = *18; CDI total score ≥13) had greater follow-up: insulin resistance (HOMA-IR: [means ± SE] 2.8 ± 0.2 vs. 4.3 ± 0.4,* P < *0.001)* (A)*, fasting insulin (13.2 ± 0.8 μU/L vs. 19.4 ± 1.7 μU/L,* P = *0.001)* (B)*, and fasting glucose (85.3 ± 0.8 mg/dL vs. 92.9 ± 1.7 mg/dL,* P < *0.001)* (C)*, adjusting for the respective baseline values, sex, race, family history of type 2 diabetes, baseline age, baseline BMI, BMI change, and time in study.*

associated with poorer cardiorespiratory fitness (18). Depressive symptoms also have been concurrently related to emotional eating patterns (19), which possibly may promote insulin resistance independent of weight gain. From a neurohumoral framework, depressive symptoms are hypothesized to promote insulin resistance by upregulating cortisol and enhancing its downstream effects, including increasing the production of the neurotransmitter neuropeptide Y (10,20,21).

Strengths of the current investigation include the longitudinal nature of data, the examination of depressive symptoms and insulin resistance in a sizeable sample of children, and the adjustment for important covariates, including measured BMI and BMI change. Study limitations include the use of surrogate measures for assessing insulin resistance and depression. The measure of insulin resistance was derived from fasting values, which, although highly related to clamp-derived measures, is not considered as precise an assessment. Likewise, although the CDI is a widely used, reliable, and valid measure of depressive symptoms, it does not provide a diagnostic assessment of clinical depression. Future longitudinal studies examining the impact of depressive symptoms on insulin resistance using criterion measures are warranted. Another significant study shortcoming was the very high degree of attrition that diminished the sample size at follow-up. Although the greater likelihood of dropout among youth with greater baseline depressive symptoms and higher insulin resistance could be expected to attenuate the significance of the results, this pattern, as well as the nature of the sample being oversampled to include youth at risk for adult obesity, may limit the generalizability of the findings. In addition, the effect of depressive symptoms on insulin resistance was small relative to the effect of anthropometric variables. Youth with major depression or active suicidal ideation were excluded from participation. Examination of the depression-insulin resistance relationship in samples of adolescents with clinically elevated symptomatology may shed more light on the magnitude of the depression-insulin relationship.

Adolescence marks a developmental period notable for a normative increase in insulin resistance that typically resolves by the end of puberty (22–25). Yet, youth vulnerable for type 2 diabetes may display the largest increases in insulin resistance and continued progression of worsening insulin resistance throughout late adolescence and possibly into young adulthood. Therefore, investigation of the impact of child or adolescent depressive symptoms on the progression of insulin resistance during an even longer follow-up interval would be important to clarify the role of pediatric depressive symptoms in the development of type 2 diabetes. An equally important task for future research is to elucidate the mechanisms by which

Table 3—***Children's baseline depressive symptoms as a predictor of follow-up elevated insulin resistance, hyperinsulinemia, and impaired fasting glucose***

	Follow-up		
Predictor	Elevated HOMA-IR ≥3.16	Hyperinsulinemia ≥15 μU/L	Impaired fasting glucose >100 mg/dL
Sex (female)	2.75 (0.83–9.08)	0.90 (0.29–2.78)	0.56 (0.01–61.65)
Race (black or Hispanic)	0.53 (0.13–2.16)	0.83 (0.23–2.99)	0.00 (0.00–0.00)
Family history of type 2 diabetes (present)	1.69 (0.57–5.01)	1.86 (0.68–5.14)	41.61 (0.45–3,819.55)
Baseline age (years)	0.88 (0.57–1.36)	1.00 (0.66–1.50)	5.10 (0.39–66.33)
Baseline BMI (kg/m^2)	1.11 (0.95–1.28)*	1.07 (0.93–1.23)	0.83 (0.57–1.21)
BMI change	1.17 (1.00–1.37)	1.19 (1.03–1.39)†	0.88 (0.45–1.72)
Time in study (years)	0.67 (0.39–1.17)	0.84 (0.50–1.40)	1.80 (0.07–45.28)
Baseline HOMA-IR	1.65 (0.83–3.26)	—	—
Baseline fasting insulin (μU/L)	—	1.16 (1.00–1.35)†	—
Baseline fasting glucose (mg/dL)	—	—	0.88 (0.60–1.28)
Baseline depressive symptoms‡	1.14 (1.01–1.28)†	1.03 (0.92–1.14)	2.23 (0.95–5.19)*

Data are odds ratios (95% CIs). *n* = 98–102. *$P \leq 0.10$. †$P \leq 0.05$. ‡CDI total score (continuous).

depressive symptoms may impact insulin resistance. An understanding of the putative behavioral and/or physiological factors that explain how depression relates to insulin resistance is crucial to the design of effective interventions.

In the current study, we observed that depressive symptoms begin to exert an impact on insulin resistance early in life. Among adults, interventions targeting depressive symptoms among adults with type 2 diabetes and/or major depression have been shown to improve indices of glucose impairment or insulin resistance even without altering body weight or adiposity (1). Research is needed to determine whether early interventions to decrease youths' depressive symptoms will ameliorate worsening insulin resistance and consequently lessen the risk of developing type 2 diabetes. If treating or preventing the onset of major depression in adolescents improves insulin resistance, routine depression screening in primary care settings, especially among youth at risk for type 2 diabetes, might have the potential to delay or possibly prevent type 2 diabetes onset in a considerable subset of individuals.

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