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Relationships among stressful life events and physiological markers, treatment adherence, and psychosocial functioning among youth with type 2 diabetes

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on behalf of the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) Study Group*

Abstract

Objective—To examine the relationship between stressful life events and physiological measures, medication adherence, depressive symptoms, and impaired quality of life in adolescents with recent onset type 2 diabetes (T2D).

Study design—Data were collected from 497 ethnically diverse participants (66% female) in the final year of the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) multi-center clinical trial. Exposure to 32 possible events over the prior year and rating of subsequent distress or upset were collected by self-report, and summarized in a major stressors score. The score was analyzed for relationship to glycemic control (HbA1c and treatment failure), BMI, diagnosis of hypertension or triglycerides dyslipidemia, oral medication adherence, presence of depressive symptoms, and impaired quality of life.

Results—The total number of major stressful life events was calculated, with 33% of the sample reporting none, 67% at least one, 47% at least two, 33% at least three, and 20% reporting four or more. There were no associations between major stressors score and physiological measures or diagnosis of comorbidities. The odds of medication non-adherence increased significantly from those reporting at least one major stressor (odds ratio=1.58, p=0.0265) to those reporting at least 4 (odds ratio=2.70, p=0.0009). Significant odds of elevated depressive symptoms and impaired quality of life were also found with increased reporting of major stressors.

Conclusions—Exposure to major stressful life events is association with lower adherence and impaired psychosocial functioning among adolescents with T2D.

Type 2 diabetes (T2D) in youth was an extremely uncommon clinical entity prior to the 1990s but has emerged as a rising public health concern in conjunction with increases in the rates and associated risks of pediatric obesity[1]. Although the psychosocial impact of obesity[2] as well as the behavioral sequelae associated with type 1 diabetes (T1D)[3] have been reasonably well-established, minimal findings are available concerning the psychosocial course of youth with T2D. Adolescence presents unique challenges for chronic illness management across diseases and is often characterized by deteriorating treatment adherence, lower levels of self-care, and compromised outcomes for patients with chronic illnesses[4]. In adolescents with T1D, both cross-sectional and longitudinal studies have found a relationship among exposure to stressful life events, diminished metabolic control, and adherence to treatments[5-6]. Thus, it is important to determine the extent and impact of stress exposure among adolescents with T2D. This importance is underscored by emerging research suggesting that youth with T2D face an accelerated trajectory toward metabolic deterioration and secondary comorbidities compared with patients with adult-onset T2D[7].

The Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) clinical trial provides the unique opportunity to assess psychosocial factors in youth diagnosed with T2D. The trial was a collaboration of 15 clinical centers designed to evaluate the efficacy of three treatment regimens in a large cohort of youth with recent-onset T2D[8]. The current report examined relationships between stressful life event exposure and physiological,

psychosocial, and treatment adherence factors among youth with T2D. We expected higher levels of stressful life event exposure to correspond to poorer physiological markers, specifically, diminished metabolic control, increased rates of co-morbidities, and more extreme overweight status. Moreover, we anticipated relationships between exposure to stressful life events and diminished oral medication adherence and quality of life (QOL) as well as more elevated presence of depressive symptoms. Improved understanding of the impact of stressful life events on illness outcomes and psychosocial correlates will help shape and optimize clinical practice and the development of intervention programs to maximize adherence to treatments and psychological functioning among youth with T2D.

METHODS

The TODAY study rationale, design, and methods have been previously reported[8]. Between July 2004 and February 2009, 699 multi-ethnic youth were enrolled who were ages 10-17 inclusive, diagnosed with T2D <2 years, ≥85th percentile for body mass index (BMI), negative for diabetes auto-antibodies, with fasting C-peptide >0.6 ng/mL. Exclusion criteria included the presence of another significant condition, such as a major psychiatric or developmental disorder, that investigators deemed would prevent full participation in the study protocol. The protocol was approved by an external evaluation committee convened by the NIDDK and by the Institutional Review Board for each of the participating institutions. All participants provided both informed parental consent and minor child assent. Materials developed and used for the TODAY standard diabetes education program and the intensive lifestyle intervention program are available to the public at https://today.bsc.gwu.edu/.

Participants were randomly assigned to one of three treatment arms: metformin monotherapy, metformin plus rosiglitazone, or metformin plus an intensive lifestyle intervention program. The primary objective was to compare the three treatment arms on time with treatment failure (ie, loss of glycemic control), defined as either HbA1c ≥8% over a 6-month period or inability to wean from temporary insulin therapy within 3 months following acute metabolic decompensation. Almost half of the cohort (n=319, 45.6%) reached the primary outcome after an average follow-up of 3.9 years (range 2-6.5). The metformin plus rosiglitazone combination was found to be superior to metformin monotherapy (p=0.006); metformin plus lifestyle was not statistically significantly different from metformin alone[9].

In the last year of the trial, participants completed a self-report questionnaire capturing life event exposure. The survey was based on the Yeaworth Adolescent Life Change Event Scale[10-11]. The instrument provided the ability to assess both the frequency and the self-rated level of distress associated with the occurrence of life events having to do with family, friends, relationships, job, school, etc., over the past year. The survey was modified to include several supplemental items from the Holmes and Rahe Social Readjustment Rating Scale[12]. Participants responding to the questionnaire first indicated whether the event had occurred (yes/no), and for ‘yes’ responses they rated how upsetting the event was for them (0 = not at all upset, 1 = a little upset, 2 = somewhat upset, 3 = very upset, 4 = extremely upset). There were 33 items, but one item for girls only related to menstrual cycles was

excluded from the analysis. Three composite scores were derived: (1) occurrence of discrete events, or tally score, was the number of 'yes' responses; (2) upset ratings were summed to create a severity score; and (3) a major stressors score was computed as the number of events classified as somewhat, very, or extremely upsetting[11]. The tally score was interpreted as a cumulative measure of events experienced by the participant, and the severity score was conceptualized as the level of distress caused by the events experienced. The major stressors score reflected both the frequency and the degree of severity of events reported.

Physiological measures, oral medication adherence, QOL, and depressive symptom data were also collected during the final year of the study. Height and weight were measured by trained staff using standard methods and equipment[8] and used to compute body mass index (BMI). A central study laboratory provided measurements of HbA1c. Adherence to the prescribed oral medication treatment was estimated based on pill counts; non-adherent was defined as a rate of pill use below 80% of the prescribed dose. Depressive symptoms were assessed using either the Children's Depression Inventory (CDI) for participants <16 years or the Beck Depression Inventory II (BDI-II) for those ≥16 years. Total scores were calculated for each instrument; a cut-off score ≥13 on the CDI and ≥14 on the BDI-II indicated clinically significant levels of depressive symptoms[13-15]. The Pediatric Quality of Life Inventory (PedsQL) measured youth perception of QOL, with impaired QOL defined as one standard deviation below the mean for the entire sample (74.6)[16]. BMI, HbA1c, and adherence from quarterly study visits in the final year of the study were averaged. Once treatment failure (loss of glycemic control) occurred, participants were treated with insulin and metformin; during the last year 40% of the sample had HbA1c values on this regimen. The depression inventory and PedsQL were administered at the final study visit.

The other three outcome status measures represented evaluations made once as occurred during TODAY. Treatment failure was defined above. A diagnosis of hypertension was defined as blood pressure ≥130/80 mm Hg or ≥95th percentile for age, sex, and height (based on CDC normative data) measured at two study visits 6 months apart or a previously documented elevated blood pressure that had normalized secondary to anti-hypertensive medication. A diagnosis of triglycerides dyslipidemia was made if values ≥150 mg/dL occurred at two study visits 6 months apart.

Statistical analyses

Cut-offs were applied to the major stressors score to create four categories (≥1 event, ≥2, ≥3, ≥4). Continuous measures were tested using general linear models; each category was compared with a fifth category reporting either no event or an event that was rated not at all or a little upsetting. Binary measures were tested using logistic regression to generate odds ratios (OR) and 95% confidence intervals (CI); OR for the four major stressor event accumulation categories used the category with no events or no upset rankings as a reference group. Possible covariates tested for significant differences in major stressors score were age, sex, race/ethnicity, household annual income at baseline, highest household education level at baseline, and duration of T2D; nonparametric methods were used due to lack of normal distribution. Only sex was significant ($p<.0001$). Both sex and the interaction of sex

with major stressor category were included in an initial analysis to test whether associations varied between males and females; in all cases, interaction terms were not significant and were dropped from the analysis. A p-value <.05 was considered significant without adjustment for multiple comparisons; the study was powered to perform the primary outcome only and all other analyses are considered exploratory. The Statistical Analysis Software package (SAS, version 9.2, 2008, SAS Institute Inc., Cary NC) was used for all analyses.

RESULTS

Of the 699 TODAY cohort participants enrolled, usable data were collected from 497 in the final year of the trial (71.1% completion rate); 202 were missing due to loss to follow-up, consent withdrawal, or incomplete data. Those with missing data did not differ from those included in the analysis on baseline characteristics such as BMI, sex, race/ethnicity, household annual income, and head of household's highest level of education (all p >.05; data not shown). The analysis sample (n=497) consisted of 65.8% female, 31.4% Black non-Hispanic, 40.0% Hispanic, 21.5% White non-Hispanic, and 7.1% other ethnicity. At the time of survey completion, the study sample was, on average, 18.4 years old (range 12.4-24.2) with 4.8 years since diagnosis (range 2.1-8.3). Hypertension was diagnosed in 39.8% and triglycerides dyslipidemia in 33.4%. In the last year of the study, 60.1% had an average oral medical adherence <80%, 11.7% reported depressive symptoms, and 16.4% had impaired QOL.

Participants reported on average 5.2 stressful life events (tally score) occurring in the previous year (SD 2.9, range 0-14), a mean severity score of 11.7 (SD 9.1, range 0-61), and an average of 1.9 major stressful events (SD 2.1, range 0-13). Data analyses using the tally, severity, and major stressor scores revealed similar results; we report only results using the major stressors score.

A total of 165 participants reported no major stressful events in the previous year (33.2%), 332 reported at least one major event (66.8%), 233 (46.9%) reported two or more, 166 (33.4%) reported three or more, and 100 (20.1%) reported four or more. Females reported more major stressful events than males (median [25^{th}-75^{th} percentiles] 2 [0-3] vs. 1 [0-2], respectively; p<0.0001), however associations between major stressful events and HbA1c or other clinical markers did not differ by sex.

Table I shows an increase in mean final year BMI across major stressor event accumulation categories, but no statistical difference from the mean of those who reported no major stressor event. Mean final year HbA1c, indicating glycemic control in the last year of the study, did not change across the categories with major stressor events; although means were higher than for those with no events, the differences were not statistically significant.

Table II shows the association between the number of major stressful events during the past year and physiological and metabolic outcomes (treatment failure, hypertension, triglycerides dyslipidemia), oral medication adherence, and psychosocial measures (presence of depressive symptoms, impaired QOL). As with HbA1c, treatment failure was

another indicator of poor glycemic control and was not significant. The presence of another metabolic comorbidity – either hypertension or triglycerides dyslipidemia – was not related to stress magnitude.

Measures of treatment adherence and psychosocial functioning, however, were significantly related to accumulation of major stressors. Across all categorical cut-offs of number of major stressor events, ORs were significant (one marginal significance) and rose as number of events increased, indicating that lack of satisfactory adherence to study medication, presence of depressive symptoms, and presence of impaired QOL in the final year of TODAY were related to the occurrence of major life stressors. The odds of being nonadherent were 58% higher in those reporting ≥1 major stressor than none, and the odds increased steadily as number of events increased, ending at a 70% increase in odds for those with ≥4 events. Similarly, the odds of having clinically elevated depressive symptoms or impaired QOL were associated with a two-fold increase among those reporting at least one major stressful event and rose to 4.06 and 3.51, respectively, among those reporting at least four major stressful events.

DISCUSSION

The purpose of this study was to determine whether increased exposure to stressful life events was associated with worse physiological status, lower treatment adherence, and more compromised psychosocial functioning among a cohort of adolescents with T2D.

We did not find associations between stressful life event exposure and physiological markers including glycemic status, BMI, and diagnosis with hypertension or triglycerides dyslipidemia. To our knowledge, no other studies have examined the relationship between life stressors and metabolic outcomes among youth or adults with T2DM. Although differences in study methods and design and sample characteristics limit comparability, a study among youth with T1D employing the same stressful life event assessment methodology found that stress exposure was associated with worse glycemic control concurrently and over time, and that self-care behavior partly mediated this relationship[5]. In a population-based study of adults in Finland, greater frequency of stressful life events was associated with some components of metabolic syndrome (BMI, waist circumference, and triglyceride levels) but not others (blood pressure and impaired fasting glucose)[17].

Supporting our hypotheses and comparable with other reports, we found consistently strong associations between the extent of major stress event exposure and lower treatment adherence and psychosocial functioning, with “dose-response” relationships identified for lower adherence to the oral medication regimen, worse QOL, and greater depressive symptoms[5,18-20]. Our findings suggest that measuring stressful life event exposure, both in terms of the frequency and perceived severity of events, may help elucidate barriers to illness management, depressive factors, and other potential contributors to the diminished QOL characteristic of adolescents with chronic health conditions[21-22]. The medical management of youth-onset T2D presents a host of challenges, and medical providers may feel overwhelmed by the additional complexities associated with recognizing and responding to psychosocial stressors. Utilizing interdisciplinary teams, merging expertise of

pediatricians with behavioral health providers has been shown to be an effective model of care for T1D, and should be examined systematically within T2D[23].

The greatest limitation to our current report was the single measurement of the life stressor inventory collected at end of study, which varied from 2 to 6.5 years depending on date randomized. Repeated assessments are particularly helpful in a cohort of youth experiencing rapid developmental changes and life circumstances that are often in flux, and subsequent longitudinal analyses are an important future direction. Moreover, even though participants with missing data did not differ from those with complete data on baseline characteristics, we were unable to determine stress exposure for 28.9% of the cohort. Another potential limitation was our reliance on self-report of stressful life event exposure; clinical interview tools could provide a more refined and detailed assessment[24]. Clinical interview tools, such as the Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA), could be employed to assess diagnostic stress levels associated with traumatic events[25], providing a more robust evaluation beyond the discrete event-specific questionnaire used.

Fully comprehending the relationships between stress exposure and declines in functioning among youth with T2D requires longitudinal data collection and analysis. Future efforts in this area will help to characterize the associations between life events and physiologic markers and psychosocial outcomes in patients with youth-onset T2D.

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APPENDIX

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Abbreviations

BMI	body mass index
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
QOL	quality of life
T1D	type 1 diabetes
T2D	type 2 diabetes
TODAY	Treatment Options for type 2 Diabetes in Adolescents and Youth

REFERENCES

1. Zeitler P. Considerations regarding the diagnosis and treatment of childhood type 2 diabetes. Postgrad Med. 2010; 122:89–97. [PubMed: 20463418]
2. Pervanidou P, Chrousos GP. Stress and obesity/metabolic syndrome in childhood and adolescence. Int J Pediatr Obes. 2011; 6(Suppl 1):21–8. [PubMed: 21905812]
3. Delamater AM. Psychological care of children and adolescents with diabetes. Pediatr Diabetes. 2009; 10(Suppl 12):175–84. [PubMed: 19754628]
4. Dean AJ, Walters J, Hall A. A systematic review of interventions to enhance medication adherence in children and adolescents with chronic illness. Arch Dis Child. 2010; 95:717–23. [PubMed: 20522463]
5. Helgeson VS, Escobar O, Siminerio L, Becker D. Relation of stressful life events to metabolic control among adolescents with diabetes: 5-year longitudinal study. Health Psychol. 2010; 29:153–9. [PubMed: 20230088]
6. Delamater AM, Kurtz SM, Bubb J, White NH, Santiago JV. Stress and coping in relation to metabolic control of adolescents with type 1 diabetes. J Dev Behav Pediatr. 1987; 8:136–40. [PubMed: 3597781]
7. Cefalu WT. TODAY reflects on the changing faces of type 2 diabetes. Diabetes Care. 2013; 36:1732–4. [PubMed: 23844434]
8. TODAY Study Group. Treatment options for type 2 diabetes in adolescents and youth: a study of the comparative efficacy of metformin alone or in combination with rosiglitazone or lifestyle intervention in adolescents with type 2 diabetes. Pediatr Diabetes. 2007; 8:74–87. [PubMed: 17448130]
9. TODAY Study Group. A clinical trial to maintain glycemic control in youth with type 2 diabetes. N Engl J Med. 2012; 366:2247–56. [PubMed: 22540912]
10. Yeaworth RC, McNamee MJ, Pozehl B. The Adolescent Life Change Event Scale: its development and use. Adolescence. 1992; 27:783–802. [PubMed: 1471559]
11. Yeaworth RC, York J, Hussey MA, Ingle ME, Goodwin T. The development of an adolescent life change event scale. Adolescence. 1980; 15:91–7. [PubMed: 7369013]
12. Holmes TH, Rahe RH. The Social Readjustment Rating Scale. J Psychosom Res. 1967; 11:213–8. [PubMed: 6059863]
13. Anderson BJ, Edelstein S, Abramson NW, Katz LEL, Yasuda PM, Lavietes SJ, et al. for the TODAY Study Group. Depressive symptoms and quality of life in adolescents with type 2

diabetes: baseline data from the TODAY study. Diabetes Care. 2011; 34:2205–7. [PubMed: 21836107]

14. Kovacs, M. Children's Depression Inventory. Multi-Health Systems; New York: 1992.
15. Beck, AT.; Steer, RA.; Brown, GK. Manual for the Beck Depression Inventory-II. Psychological Corporation; San Antonio, TX: 1996.
16. TODAY Study Group. Binge eating, mood, and quality of life in youth with type 2 diabetes: baseline data from the TODAY study. Diabetes Care. 2011; 34:858–60. [PubMed: 21357794]
17. Pyykkonen AJ, Raikkonen K, Tuomi T, Eriksson JG, Groop L, Isomaa B. Stressful life events and the metabolic syndrome: the prevalence, prediction and prevention of diabetes (PPP)-Botnia Study. Diabetes Care. 2010; 33:378–84. [PubMed: 19880581]
18. Leserman J, Ironson G, O'Cleirigh C, Fordiani JM, Balbin E. Stressful life events and adherence in HIV. AIDS Patient Care STDS. 2008; 22:403–11. [PubMed: 18373416]
19. Elliott-DeSorbo DK, Martin S, Wolters PL. Stressful life events and their relationship to psychological and medical functioning in children and adolescents with HIV infection. J Acquir Immune Defic Syndr. 2009; 52:364–70. [PubMed: 19668083]
20. Salema NE, Elliott RA, Glazebrook C. A systematic review of adherence-enhancing interventions in adolescents taking long-term medicines. J Adolesc Health. 2011; 49:455–66. [PubMed: 22018559]
21. Villalonga-Olives E, Rojas-Farreras S, Vilagut G, Palacio-Vieira JA, Valderas JM, Herdman M, et al. Impact of recent life events on the health related quality of life of adolescents and youths: the role of gender and life events typologies in a follow-up study. Health Qual Life Outcomes. 2010; 8:71. [PubMed: 20642830]
22. Mulvaney SA, Hood KK, Schlundt DG, Osborn CY, Johnson KB, Rothman RL, et al. Development and initial validation of the barriers to diabetes adherence measure for adolescents. Diabetes Res Clin Pract. 2011; 94:77–83. [PubMed: 21737172]
23. Bitsko MJ, Bean MK, Bart S, Foster RH, Thacker L, Francis GL. Psychological treatment improves hemoglobin A1c outcomes in adolescents with type 1 diabetes mellitus. J Clin Psychol Med Settings. 2013; 20(3):333–42. [PubMed: 23712594]
24. Logan DE, Claar RL, Scharff L. Social desirability response bias and self-report of psychological distress in pediatric chronic pain patients. Pain. 2008; 136:366–72. [PubMed: 17822848]
25. Newman, E.; Weathers, FW.; Nader, K.; Kaloupek, DG.; Pynoos, RS.; Blake, DD., et al. Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA). Western Psychological Services; Los Angeles: 2004.

Table 1

Comparison of BMI and HbA1c by number of somewhat, very, or extremely upsetting events reported during the past 12 months

Continuous outcomes	Number of somewhat, very, or extremely upsetting events*				
	0 (n=165)†	≥ 1 (n=332)	≥ 2 (n=233)	≥ 3 (n=166)	≥ 4 (n=100)
BMI (kg/m^2) mean (SD)	36.4 (9.2)	36.8 (7.8)	36.8 (7.8)	37.4 (8.3)	38.1 (8.2)
P-value ‡	---	*0.5134*	*0.5268*	*0.2162*	*0.1034*
HbA1c (%) mean (SD)	7.6 (2.4)	8.0 (2.5)	7.9 (2.5)	8.0 (2.5)	8.0 (2.5)
P-value ‡	---	*0.0699*	*0.1377*	*0.0909*	*0.1205*

*Category ≥ 2 is a subset of category ≥ 1, and so on.

†Combination of (a) event did not occur in past year and (b) event occurred but was rated not at all or a little upsetting.

‡P-value for comparison of category 0 versus each of the other 4 categories with sex in model as covariate.

Table 2

Associations* between number of somewhat, very, or extremely upsetting events reported during the past 12 months with medical, behavioral, and psychosocial outcomes

Binary outcomes	Number of somewhat, very, or extremely upsetting events†			
	≥ 1 (n=332)	≥ 2 (n=233)	≥ 3 (n=166)	≥ 4 (n=100)
Treatment failure (loss of glycemic control)				
OR (95% CI)	1.33 (0.91, 1.96)	1.22 (0.81, 1.85)	1.27 (0.81, 1.98)	1.41 (0.84, 2.36)
P-value	*0.1450*	*0.3395*	*0.3019*	*0.1948*
Hypertension				
OR (95% CI)	1.05 (0.69, 1.58)	1.07 (0.69, 1.67)	1.04 (0.64, 1.69)	0.94 (0.54, 1.65)
P-value	*0.8350*	*0.7544*	*0.8795*	*0.8364*
Triglycerides dyslipidemia				
OR (95% CI)	1.05 (0.69, 1.60)	0.91 (0.58, 1.44)	0.93 (0.56, 1.52)	0.83 (0.47, 1.49)
P-value	*0.8237*	*0.6918*	*0.7581*	*0.5371*
Oral medication adherence < 80%				
OR (95% CI)	1.58 (1.06, 2.38)	2.01 (1.29, 3.14)	2.33 (1.42, 3.81)	2.70 (1.50, 4.85)
P-value	*0.0265*	*0.0021*	*0.0008*	*0.0009*
Depressive symptoms				
OR (95% CI)	2.07 (1.00, 4.27)	2.43 (1.16, 5.13)	2.65 (1.22, 5.75)	4.06 (1.81, 9.11)
P-value	*0.0503*	*0.0193*	*0.0134*	*0.0007*
Impaired quality of life				
OR (95% CI)	1.77 (0.94, 3.35)	2.04 (1.05, 3.96)	2.28 (1.13, 4.61)	3.51 (1.66, 7.41)
P-value	*0.0793*	*0.0368*	*0.0209*	*0.0010*

*Odds ratios (OR) and 95% confidence interval, and p-values from a model adjusted for sex. The reference category for number of upsetting events is combination of (a) event did not occur in past year and (b) event occurred but was rated not at all or a little upsetting.

†Category ≥ 2 is a subset of category ≥ 1, and so on.