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ORIGINAL PAPER

Fear of Hypoglycemia and Self Reported Posttraumatic Stress in Adults with Type I Diabetes Treated by Intensive Regimens

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Abstract This study investigated the prevalence of hypoglycemic fear (FH) and hypoglycemia-specific posttraumatic stress (PTS) among individuals with Type I diabetes. Over 25% of participants met diagnostic criteria for current PTSD. High percentages of participants endorsed PTS symptom clusters, suggesting that individuals may be experiencing distress without necessarily meeting diagnostic criteria. Hierarchical multiple regression analyses revealed that perceived threat of death from hypoglycemia and FH were significantly related to PTS. Number of recent hypoglycemic episodes did not predict PTS/PTSD. Depression and nonspecific anxiety did not contribute to the statistical prediction of PTSD, suggesting that symptomatology endorsed represents hypoglycemia-specific anxiety rather than global psychological distress. The hypothesis that greater PTS symptomatology would relate to poorer glycemic control was unsubstantiated. Perceived death-threat from hypoglycemia and nonspecific anxiety were the only variables that contributed to prediction of glycemic control, suggesting that PTS did not represent a significant barrier for glycemic control in this sample.

Keywords Diabetes · Posttraumatic stress · Hypoglycemia · Glycemic control · Hypoglycemic fear

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Diabetes Mellitus (DM) and its subsequent complications are the third leading cause of death in the United States (Strauss, 1996). Since most diabetes-related morbidity and mortality are associated with persistent hyperglycemia, or elevated blood glucose (BG) levels, the therapeutic goal of glycemic control is to maintain BG within the normative range (Diabetes Control and Complications Trial Research Group, 1993). For individuals with Type I diabetes, administration of exogenous insulin is necessary to achieve these normative levels (Rubin & Peyrot, 2001). Recent advances in treatment options that facilitate maintenance of "tight control" of BG levels include Multiple Daily Injection regimens (MDI) using Glargine with per-meal Lispro or Aspart insulin in a basal/bolus format, and Continuous Subcutaneous Insulin Infusion (CSII) using an insulin pump (American Diabetes Association, 2001). Results from the DCCT (Diabetes Control and Complications Trial Research Group, 1993) showed that intensive therapy regimens, defined as either (a) three or more daily injections of insulin (MDI), or (b) treatment with an insulin pump (CSII), effectively delayed the onset and slowed the progression of diabetic complications. These results suggested that intensive therapy (MDI or CSII) as compared to the conventional therapy was significantly better at preventing complications associated with DM. These intensive therapies also showed improved glycemic control as measured by glycosylated hemoglobin. One adverse effect associated with intensive insulin therapies was an increased likelihood of having a severe hypoglycemic episode.

However, there were no significant differences between the conventional and intensive therapies with regard to acute medical complications directly related to a severe hypoglycemic state leading the DCCT to conclude that the benefits associated with intensive therapy outweighed the risks.

One shortcoming of the DCCT study is that no distinctions were made within the intensive therapy regimen group regarding differences that may be related to regimen choice. Specifically, the intensive regimen condition was a combined sample of individuals who either utilized multiple daily self-injections (MDI) or insulin pumps (CSII). No within group comparisons were made between these two intensive management regimens to clarify whether there were any systematic differences related to choice of intensive regimen that may have influenced the outcome of the study.

There are no set criteria establishing which individuals should use MDI or insulin pumps. The National Institute for Health and Clinical Excellence (2006) suggests that CSII therapy should be used for those individuals who have failed multiple-dose insulin therapy. However, the American Diabetes Association (2006) suggests that insulin pumps are a good choice for almost any person who is willing to monitor their diabetes management closely. Regardless of regimen choice, both methods require frequent BG monitoring and have similar feedback methods for BG. In the present study, both MDI and CSII participants were instructed by their diabetes educator to monitor BG four times daily, suggesting that there were no differences in the amount of BG feedback between the two intensive regimens.

CSII therapy has been associated with increased flexibility and lifestyle advantages (Wolf, Jacober, Wolf, Cornell, & Floyd, 1989), more accurate insulin delivery (American Diabetes Association, 2006), and improved/tighter glycemic control (Champion, Sheperd, Rodger, & Dupre, 1980; Diabetes Control and Complications Trial Research Group, 1993). Clinical follow-up studies have also reported decreased rates of severe hypoglycemia for those using CSII methods. However, randomized studies have not confirmed this finding and less severe hypoglycemia has been found to be more common with pump use (Hanas & Ludvigsson, 2006).

In general, tight glycemic control may increase the risk of hypoglycemia (Irvine, Cox, & Gonder-Frederick, 1994). Hypoglycemic episodes can be physically aversive, create negative mood states, and are potentially life threatening (Gold, MacLeod, Frier, & Deary, 1995; Gonder-Frederick, Cox, Bobbitt, & Pennebaker, 1989; Polonsky, Davis, Jacobson, & Anderson, 1992; Taylor & Rachman, 1988). Many individuals with DM are knowledgeable that the symptoms of hypoglycemia may signal potential death (Cox, Irvine, Gonder-Frederick, Nowacek, & Butterfield, 1987; Strauss, 1996).

Studies have shown fear of hypoglycemia (FH) to relate to poorer glycemic control (Cox, Irvine, Gonder-Frederick, Nowacek, & Butterfield, 1987), to higher trait anxiety, and difficulty distinguishing between anxiety and hypoglycemia, and past hypoglycemic experiences (Polonsky, Davis, Jacobson, & Anderson, 1992), as well as higher perceived stress, frequency of past hypoglycemic episodes, and greater daily BG variability (Irvine, Cox, & Gonder-Frederick, 1992). Additionally, some individuals compromise their glycemic control by running their insulin levels lower/BG levels higher (Surwit, Scovern, & Feinglos, 1982), or overtreat early signs of hypoglycemia (Cox, Irvine, Gonder-Frederick, Nowacek, & Butterfield, 1987), in an attempt to avoid these hypoglycemic sensations. For these individuals, FH may induce behaviors that increase risk for the long-term medical complications associated with hyperglycemia, and reduce the efficacy of these regimens for optimal glycemic control. While an important literature has begun to investigate FH, indicating that it may interfere with self-management, more thorough investigation of this phenomenon appears warranted, and may serve to guide clinical intervention and optimize metabolic outcomes.

Taken together, these studies suggest that some individuals with Type I DM: 1) become hypervigilant and experience intrusive ideation about the risk and threat of hypoglycemia (Cox, Irvine, Gonder-Frederick, Nowacek, & Butterfield, 1987; Irvine, Cox, & Gonder-Frederick, 1992), 2) become anxious when experiencing signals of hypoglycemia and/or misconstrue anxiety symptoms as hypoglycemia (Polonsky, Davis, Jacobson, & Anderson, 1992), and 3) show excessive escape and avoidance behaviors when they perceive the threat of hypoglycemia (Cox, Irvine, Gonder-Frederick, Nowacek, & Butterfield, 1987; Surwit, Scovern, & Feinglos, 1982). This pattern, which we have observed clinically, raises questions as to whether this symptom pattern reflects the posttraumatic stress symptom clusters (intrusive ideation, anxious arousal, and avoidance) related to hypoglycemia.

Posttraumatic stress has been investigated following other life-threatening or severe medical stresses, such as cancer (Barakat, Kazak, Gallagher, Meeske, & Stuber, 2000; Boyer et al., 2002; Erickson & Steiner, 2001; Mundy et al., 2000; Neel, 2000; Pitman et al., 2001; Smith, Redd, Peyser, & Vogl, 1999; Widows, Jacobsen, & Fields, 2000), burns (Perez-Jimenez, Graell-Berna, Perez-Sales, & Santodomingo, 1993; Tarrier, 1995; Van Loey, Maas, Faber, & Taal, 2003), spinal cord injury (Boyer, Knolls, Kafkalas, Tollen, & Swartz, 2000; Boyer, Tollen, & Kafkalas, 1998; Boyer, Ware, Knolls, & Kafkalas, 2003; Kennedy & Evans, 2001; Lude, Kennedy, Evans, & Beedie, 2005; Mona, Cameron, Lesondak, & Norris, 2000; Nielsen, 2003a, 2003b; Radnitz et al., 1998; Radnitz et al., 1995), and cardiac events (Bennett, 1999; Doerfler, Pbert, & DeCosimo, 1994; Ginzburg et al., 2003). Although two studies have examined PTS among parents

of children diagnosed with Type I DM (Landolt et al., 2002; Landolt, Vollrath, Laimbacher, Gnehm, & Sennhauser, 2005), no studies have investigated whether individuals with DM exhibit the full symptoms of PTS following potentially life-threatening aspects of the disease process and management.

Present study

Individuals utilizing intensive insulin regimens (i.e., MDI and CSII) have received less empirical investigation than the more traditional insulin delivery regimens. Attention to the experience of these individuals is important, because these treatment plans are becoming more widely utilized, and most closely mimic the natural endogenous insulin release of individuals without diabetes. Since the tight control attainable with these regimens is imperative, but can pose substantial risk for hypoglycemia, and since FH may serve as a barrier to successful self-management, understanding the scope and nature of FH is critical to optimal medical outcomes. The present study sought to assess the full symptom clusters of posttraumatic stress among individuals using self-selected MDI and CSII for Type I diabetes. In order to assess for relationship of any PTS symptoms to actual hypoglycemic experiences and/or appraisal of hypoglycemic experiences, patients' number of hypoglycemic episodes were queried, as well as complications and experiences incurred during or after hypoglycemic episodes, and perceived threat of death from hypoglycemia. Self-report of depression and nonspecific anxiety were also collected, and tested for relationship to hypoglycemia-related PTS/PTSD. Our primary hypotheses were (a) experiential history, appraisal factors (perceived death threat), psychological distress, and fear of hypoglycemia may relate significantly with PTS severity, as well as diagnostic levels of PTSD, and (b) experiential history, appraisal factors, psychological distress, fear of hypoglycemia, and PTS/PTSD may relate significantly to participants' glycemic control, as measured by glycosylated hemoglobin (HbA1c). Glycosylated hemoglobin is a blood assay test that measures average BG level over the past 6 weeks to 3 months, and often serves as a stable and reliable measure of glycemic control.

Method

Participants

A total of 90 participants (65 females [72.2%] and 25 males [27.8%]) participated in the study. Seventy-seven of the 90 participants (85.5%) utilized insulin pumps. The average age for the sample was 43.2 years, and 82 participants (91.1%) classified themselves as 'Caucasian'. The mean number of months diagnosed with diabetes was 279 (23.25 years) (Range = 12-664 months, $s.d. = 162.77$) A total of 344 participants who met the inclusion criteria: (a) diagnosis of Type I DM; (b) had diabetes for at least 6 months duration; (c) were age 18 years or older; (d) were judged by their certified diabetes educator to be beyond any "honeymoon" period suggesting that the participant had stabilized with regard to their current regimen needs; and (e) used either an insulin pump or multiple daily self-injections in a basal/bolus format as their method of diabetes management were obtained from Integrated Diabetes Services located in a suburban location. The Integrated Diabetes Services (IDS) is a for-profit organization that provides individualized diabetes education and management services to children and adults, specializing in intensive blood glucose management and insulin pump services. Response rate was 26.1% of the eligible patients. A series of t-tests and chi-square tests were conducted to assess whether there were significant differences among the responder and non-responder groups. The *t*-test comparing the responder and non-responder groups on age was significant [t-test $(1, 332) = 6.67, p < .001$] with the responders being older than the non-responders. Chi square tests revealed a significant statistical difference for gender [$\chi^2 = 9.711, p < .002$]. The responder group contained a significantly higher number of females compared to the non-responder group.

Procedure

Each of the patients who met inclusion criteria was mailed a letter from the IDS, describing the study and requesting their participation. Verbal consent was attained by telephone before identities of patients were disclosed to non-IDS collaborators. A written Informed Consent Form and the questionnaire packet were then sent to those who had verbally consented. A follow-up telephone call was made 2 weeks after the original mailing date to all individuals who had not returned study materials, prompting them to participate if they so chose. The study protocol was approved by the university Institutional Review Board.

Measures

Demographics questionnaire

The demographics questionnaire is a self-report measure developed specifically for this study. Participants were instructed to provide information regarding their gender, age, ethnicity, date of DM diagnosis, general DM information including significant medical complications and/or hospitalizations, pump use/injection regimen, last glycosylated hemoglobin value, and history of hypoglycemic episodes.

Hypoglycemic Fear Survey-98

The original Hypoglycemic Fear Survey (Cox, Irvine, Gonder-Frederick, Nowacek, & Butterfield, 1987) is a 27-item self-report questionnaire that contains two subscales. The HFS-Worry subscale consists of 17 items which measure worries about hypoglycemia. The HFS-Behavior subscale is 10 items and focuses on behaviors designed to avoid hypoglycemia. Psychometric data on the measurement indicate good internal reliability and temporal stability (Cox, Irvine, Gonder-Frederick, Nowacek, & Butterfield, 1987). Responses to each item of the HFS items are on a 5 point Likert scale ranging from *never* (1) to *very often* (5). Individual items are summed to produce each subscale score. A revised version of the HFS was developed in 1998 (HFS-98), and was provided to the present study by the authors of the instrument (Cox, 2001). The HFS-98 contains similar items to the original form, however, six additional items are included. Five additional items have been included to the original Behavior subscale, and one additional item to the Worry subscale. Similar to the original HFS, the HFS-98 is also on a 5 point Likert scale. However, items range from *never* (0) to *always* (4). No published psychometric data are yet available on the HFS-98. For the purposes of this study, the Total Score for the HFS-98 was used.

Posttraumatic Diagnostic Scale

The Posttraumatic Diagnostic Scale (PDS) (Foa, 1995) is designed specifically to correspond with DSM-IV criteria for PTSD. Each of 18 items asks respondents to rate on a 4 point Likert scale how bothered they have been over the past month by the DSM-IV PTSD criteria. In addition, nine dichotomous items assess the degree to which the symptoms have interfered with functioning. Symptom Severity Scores range from 0–51, with higher scores representing higher severity of symptomatology. Participants were oriented to complete the items regarding their experience with hypoglycemia only. Participants were not instructed to complete the PDS items for other trauma experiences such as rape or victimization. Symptom cluster scoring, subjecting the responses to the DSM-IV diagnostic criteria, was used to determine symptoms consistent with current PTSD, and to avoid false positives that occur more frequently when cut-off scores are used with self-report measures of PTSD (Manne, Du Hamel, Gallelli, Sorgen, & Redd, 1998). The PDS shows good internal consistency (.78–.92) (Foa, Cashman, Jaycox, & Perry, 1997), test-retest reliability of PTSD diagnosis (kappa = .74) and Total Symptom Severity (kappa = .83), and showed 82% agreement with the Structured Clinical Interview for the DSM-III-R (SCID) (Foa, Cashman, Jaycox, & Perry, 1997). Overall, the psychometric properties of the PDS indicate that it is a valid and reliable instrument for assessing both PTSD diagnoses and symptom severity in a self-report format. While the PDS offers an exceptional self-report format for assessing posttraumatic stress symptoms, the adjunctive use of a clinical interview is necessary for determining an actual diagnosis of PTSD. Clinical interviews were not utilized in this study to avoid extra burden for individuals who chose to participate, and lifetime prevalence rates for PTSD were not assessed.

Beck Depression Inventory-II

The Beck Depression Inventory-II (BDI-II) is a 21-item self-report measure of depression. Each item is rated on a 4 point scale ranging from 0 to 3. The psychometric properties of the BDI-II are sound (Beck, Steer, Ball, & Ranieri, 1996). The psychometric evaluation of the BDI-II with primary care medical patients has been demonstrated (Arnau, Meagher, Norris, & Bramson, 2001), as well as with individuals with diabetes (Lustman, Clouse, Griffith, Carney, & Freedland, 1997).

Beck Anxiety Inventory

The Beck Anxiety Inventory (BAI) is a 21-item self-report instrument that assesses the severity of anxiety in adults and adolescents. The BAI has demonstrated good psychometric properties (Beck, Epstein, Brown, & Steer, 1988).

Glycosylated hemoglobin scores

Values from the last Glycosylated hemoglobin (HbA1c) blood assay were collected by participants' self-report and IDS chart reviews, representing the average blood glucose value across a 6-week to three-month period. HbA1c represents a more stable and meaningful measure of glycemic control than individual blood glucose tests, and is utilized by most providers as the best measure of overall glycemic control (American Diabetes Association, 2002; Sacks et al., 2002).

Results

Hypoglycemia-related experiences

One of the goals of this study was to assess the impact of hypoglycemia-related experiences that may relate to posttraumatic stress (see Table 1). During the course of their lifetime, over 97% of the sample reported having a low BG episode, and 81.1% reported requiring assistance from someone else during a low BG episode. More than 46% of the sample required paramedic assistance during a low BG episode, and over 45% reported a loss of consciousness.

Table 1 Participants' endorsement of hypoglycemia-related experiences

	Percentages		
	Total sample	MDI	CSII
Ever had a low BG episode	97.8%	100%	97%
Needed help from others	81.1%	84.6%	80.5%
Paramedic assistance	46.7%	46.2%	46.8%
Loss of consciousness	45.6%	38.5%	46.8%
Trip to the ER	38.9%	15.4%	42.9%
Fear of death from low BG	30%	46.2%	27.3%
Hypoglycemic seizure	25.6%	23.1%	26.0%
Hypoglycemic hospitalization	18.9%	15.4%	19.5%
Automobile accidents	11.1%	7.7%	11.7%

Note. MDI = Multiple Daily Injections; CSII = Continuous Subcutaneous Insulin Infusion.

Thirty percent of the total sample reported fear of death from hypoglycemia, 25.6% experienced a hypoglycemic seizure, 38.9% required a trip to the emergency room, 18.9% reported a hypoglycemia-related hospitalization, and 11.1% reported having an automobile accident when BG was low.

Posttraumatic stress

A total of 23 participants (25.5%) met criteria for current posttraumatic stress disorder based on symptom cluster scoring of the PDS. Five individuals who utilized the self-injection method (38.4%) and 18 individuals who utilized insulin pumps (23.3%) met criteria for posttraumatic stress disorder as measured by the PDS diagnostic score. Fifteen individuals (23.1%) were women and eight participants (32%) were men (see Table 2). The percentage of participants meeting the diagnostic criteria for one or more re-experiencing symptom, three or more avoidance symptoms, or two or more arousal symptoms are presented in Table 2. Within the total sample, 65.5% met criteria on the re-experiencing cluster, 31.1% met criteria for avoidance symptoms, 54.4% met criteria for the arousal cluster, and 95.5% reported interference in functioning in at least one of the life domains of the PDS. Simple correlations comparing time since diagnosis with the PDS total severity and PDS diagnosis scores, as well as fear of hypoglycemia were non-significant (Myers, Boyer, Herbert, & Scheiner, 2004), therefore, time since diagnosis was excluded as a predictor variable in the main regression analyses.

Gender differences have been noted with regards to posttraumatic stress endorsement. Prevalence data suggest higher rates of PTSD in women than men (Tolin & Foa, 2002). Research suggests that men experience more trauma events, but women are more likely to develop PTSD (Gavranidou & Rosner, 2003), and that prevalence rates of PTSD in men compared to women has been higher for certain types of traumas (Resick & Calhoun, 2001). Chi-square analyses showed no significant differences between genders on PTSD criteria in the current sample $\chi^2(1, N=90)=.756$, $p=.385$ or the three symptoms clusters: re-experiencing, avoidance, and arousal endorsement [$\chi^2(1, N=90)=.037$, $p=.847$, χ^2 (1, $N=90)=.013$, $p=.908$, $\chi^2(1, N=90)=1.274$, $p=.259$, respectively], and gender was, therefore, not entered into the subsequent regression equations.

Hypothesis A

A 2 × 2 chi square analysis was conducted to test whether MDI and CSII users differed regarding diagnostic levels of PTSD. In addition, a t-test was conducted with method of insulin delivery as an IV, and PDS total severity score as DV. The chi-square and t-tests assessing differences between participants using CSII and MDI were nonsignificant, suggesting that there were no statistically significant differences in PTS/PTSD related to methods of insulin administration. No significant differences were found for PTSD endorsement $\chi^2(1, N=90)=1.339$, $p=.247$, or on the three PTSD symptom clusters [χ^2 (1, $N=90)=.091$, $p=.763$, χ^2 (1, $N=90)=.678$, $p=.410$, χ^2 (1, $N=90)=1.339$, $p=.247$] and insulin regimen. For this reason the entire sample was aggregated for the analyses for hypotheses b and c.

Hypothesis B

It was hypothesized that experiential history (number of hypoglycemic episodes in last month), appraisal factors (perceived life-threat from hypoglycemia), psychological distress (nonspecific anxiety, depression), and fear of hypoglycemia may relate significantly to PTS severity, as well

Table 2 Participants' posttraumatic stress symptomatology

	Percentage of participants				
	Total sample	MDI	CSII	Men	Women
Current PTSD criteria	25.5%	38.4%	23.3%	32.0%	23.1%
PTSD symptom clusters					
Re-experiencing symptoms	65.5%	69.2%	64.9%	64.0%	66.1%
Avoidance symptoms	31.1%	38.4%	29.8%	32.0%	30.7%
Arousal symptoms	54.4%	69.2%	51.9%	64.0%	50.7%
Interference in functioning	95.5%	100%	94.8%	96.0%	95.4%

Note. MDI = Multiple Daily Injections; CSII = Continuous Subcutaneous Insulin Infusion.

as diagnostic levels of PTSD. Two hierarchical multiple regressions were conducted, with IVs for each entered in the following order: number of previous hypoglycemic episodes, perceived life-threat from hypoglycemia, anxiety, depression, and fear of hypoglycemia. Number of episodes and fear of death from low BG were entered first into the regression due to the salience these factors may have on psychological distress and FH endorsement. FH was placed last in the analyses because it was conceptualized that it may uniquely contribute to PTS endorsement beyond the influence of the other predictors. Subscale scores of the HFS-98 were not included in the analysis because the subscales were not independent of one another and the total HFS outcome, and were significantly correlated with one another with a strong magnitude ($R = .65$–$.85$, $p = .001$) (Cohen, 1988). One analysis used hierarchical regression with PDS total severity score as the dependent variable, and the other used hierarchical logistic regression with the PDS score as the dependent variable. Hierarchical regressions were chosen based on criteria suggested by Tabachnick and Fidell (1996) that specify hierarchical regressions should be chosen in order to 1) elucidate the proportion of variance attributable to each predictor variable after controlling for the variance accounted for by other predictor variables already in the equation, and 2) test specific hypotheses for a specific theoretical model. Since gender, method of insulin administration, and other non-PTSD related demographic variables (Myers, Boyer, Herbert, & Scheiner, 2004) were not significantly related to PTS\PTSD, these variables were not included in the regression analyses. The full hierarchical regression equation accounted for 64% of the variance in PTS total severity score ($F = 29.5$, $p = .001$) (see Table 3). However, perceived death threat from hypoglycemia ($\beta = .25$, *partial* $R = .35$, $p = .001$) and FH ($\beta = .47$, *partial* $R = .48$, $p = .001$) were the only variables to significantly contribute to the prediction of PTS total severity scores. By Cohen's standards, R^2 values between 0.2 and 0.49 are small effects, R^2 values between 0.5 and 0.79 are medium effects, and large effects are represented by R^2s 0.8 and higher (Cohen, 1988; Rosnow & Rosenthal, 1996). The effect sizes for the first hierarchical analysis ranged from $R^2 = .002$ to .640. The effect size for previous hypoglycemic episodes was small ($R^2 = .002$), however, the other variables had large effects. The full hierarchical regression equation accounted for 53.6% of variance in PTSD diagnosis scores ($F = 19.2$, $p = .001$), with perceived death threat from hypoglycemia ($\beta = .22$, *partial* $R = .28$, $p = .009$) and HFS total score ($\beta = .45$, *partial* $R = .42$, $p = 001$) contributing significantly to the prediction of PTSD diagnosis score. Effect sizes for this analysis ranged from $R^2 = 0.000$ to 0.536, with the majority of the predictor variables demonstrating large effects (see Table 4).

A *t*-test was conducted to compare individuals' current PTSD diagnosis on measures of depression and anxiety [*t*-test (1, 88) $= -4.69$, $p = .001$]. Individuals who met current PTSD according to the PDS symptom cluster and severity scores criteria reported significantly higher BDI-II and BAI scores than participants who did not meet current PTSD criteria. Additional correlations between the PDS total severity score and both the BDI-II and BAI were statistically significant [$r_{(BDI-II)} = .499$, $p = .001$; $r_{(BAI)} = .633$, $p = .001$]. This suggests that there is a positive correlation between

Table 3 Hierarchical regression analysis summary for experiential history, appraisal factors, psychological distress, and fear of hypoglycemia predicting PTS severity ($N = 89$)

Measure	*B*	*SEB*	β	R^2	$\triangle R^2$	$\triangle F$
Step 1[a]						
Previous hypoglycemic episodes	.012	.073	.011	.002	.002	.217
Step 2[b]						
Perceived life threat	5.039	1.481	.251*	.278	.275	32.73*
Step 3[c]						
Anxiety	.171	.102	.167	.520	.242	42.87*
Step 4[d]						
Depression	.107	.079	.112	.528	.008	1.422
Step 5[e]						
Fear of hypoglycemia	.223	.044	.473*	.640*	.112	25.83*

[a]Number of low blood glucose episodes in last month, [b]Endorsed whether believe would die from a hypoglycemic event, [c]Total score on the Beck Anxiety Inventory, [d]Total score on the Beck Depression Inventory, [e]Total score of the Hypoglycemia Fear Survey.

*$p < .01$.

Table 4 Hierarchical regression analysis summary for experiential history, appraisal factors, psychological distress, and fear of hypoglycemia predicting PTS diagnosis ($N = 89$)

Measure	*B*	*SEB*	β	R^2	$\triangle R^2$	$\triangle F$
Step 1[a]						
Previous hypoglycemic episodes	−.0276	.043	−.049	.000	.000	.016
Step 2[b]						
Perceived life threat	2.344	.871	.225*	.219	.219	24.09*
Step 3[c]						
Anxiety	.101	.060	.197	.434	.215	32.36*
Step 4[d]						
Depression	.0112	.047	.023	.435	.000	.050
Step 5[e]						
Fear of hypoglycemia	.110	.026	.451*	.536*	.102	18.21*

[a]Number of low blood glucose episodes in last month, [b]Endorsed whether believe would die from a hypoglycemic event, [c]Total score on the Beck Anxiety Inventory, [d]Total score on the Beck Depression Inventory, [e]Total score of the Hypoglycemia Fear Survey.

*$p < .01$.

higher scores on the PDS and higher scores on the BDI-II and BAI.

Hypothesis C

It was expected that the same factors may relate significantly to participants' glycemic control, as measured by HbA1c. A hierarchical regression was conducted with IVs entered in the following order: number of previous hypoglycemic episodes, perceived life-threat from hypoglycemia, anxiety, depression, and fear of hypoglycemia, and total PTS severity score, and HbA1c as the DV. Although the full model accounted for 18.8% of the variance in HbA1c, and remained a significant prediction of HbA1c scores ($F = 3.12$, $p = .008$), only perceived death-threat from hypoglycemia (F change $= 4.46$, $p = .038$) and BAI score (F change $= 10.2$, $p = .002$) accounted for significant F change in prediction of HbA1c ($R^2 = .154$, $F = 5.12$, $p = .003$), and only BAI score contributed significantly to the prediction ($\beta = .34$, partial $R = .33$, $p = .002$). Effect sizes for this analysis ranged from $R^2 = 002$ to 0.188, with the majority of variables demonstrating medium and large effects (see Table 5).

Discussion

This study represents the first attempt to evaluate the full scope of PTSD symptom clusters among individuals with Type I diabetes. Based upon findings regarding FH, and upon clinical observations regarding the role of anxious arousal in the fearful avoidance of low BG, the explicit focus was on reactions to hypoglycemia. Since hypoglycemia represents a potentially life-threatening experience associated with salient and distressing symptoms, a hypoglycemic episode may easily be perceived as life-threatening, even if not conceptualized as meeting criteria A of the PTSD diagnosis (American Psychiatric Association, 2000). These data indicate that one out of four participants reported symptoms consistent with current PTSD in response to hypoglycemic experience, and that a high proportion of individuals met re-experiencing, avoidance, and arousal criteria for PTSD. These results suggest that for a subset of individuals with Type I diabetes, the medical sequelae of diabetes, particularly hypoglycemia, may be sufficient to induce PTSD symptoms. In addition, nearly two-thirds (65.5%) met criteria on the re-experiencing symptom cluster, nearly one-third (31.1%) met criteria for avoidance symptoms, and over half (54.4%) met criteria for the arousal symptom cluster. Additionally, over 95% of the sample reported interference in functioning in at least one of the life domains of the PDS. This suggests that a large percentage of the total sample may be experiencing emotional distress in each of these domains, but may not meet full current diagnostic criteria.

Furthermore, individuals reporting a perceived threat of death from hypoglycemia and reporting specific FH were more likely to meet diagnostic criteria for PTSD, and reported more severe PTS symptomatology. In contrast, the number of hypoglycemic episodes reported within the past month did not predict either PTS/PTSD. This finding parallels results regarding PTS and cancer, in which subjective appraisal showed stronger relationship to PTS than did medically-determined severity of the treatment conditions (Barakat, Kazak, Gallagher, Meeske, & Stuber, 2000; Tedstone & Tarrier, 2003). The greater relationship between PTS/PTSD and perceived death threat than between PTS/PTSD and number of hypoglycemic experiences appears dramatic, since 38.9% of patients had required emergency room services, 46.7% had required paramedic services, 45.6% had lost consciousness, and 25.6% had experienced a hypoglycemia-related seizure within the past month. Even though the actual acuity of hypoglycemic experiences was high, the appraisal of impending death from hypoglycemia showed more potent association with PTS/PTSD symptomatology.

It is also noteworthy that, whereas perceived death threat and FH related significantly to PTS/PTSD, depression and nonspecific anxiety were not significantly associated with PTS/PTSD. It appears that despite significant simple correlations between anxiety and PTS, and between depression and PTS, these phenomena are not accounting for the hypoglycemia-related PTS when subjected to more rigorous

Table 5 Hierarchical regression analysis summary for experiential history, appraisal factors, psychological distress, and fear of hypoglycemia predicting glycosylated hemoglobin ($N = 88$)

Measure	*B*	*SEB*	β	R^2	$\triangle R^2$	$\triangle F$
Step 1[a]						
Previous hypoglycemic episodes	−.0069	.016	−.043	.002	.002	.163
Step 2[b]						
Perceived life threat	.450	.355	.151	.052	.050	4.465*
Step 3[c]						
Anxiety	.0547	.023	.366*	.154	.103	10.20*
Step 4[d]						
Depression	.0244	.018	.023	.174	.015	1.536
Step 5[e]						
Fear of hypoglycemia	−.0037	.011	−.055	.178	.009	.865
Step 6[f]						
PTS severity	−.0235	.024	−.162	.188*	.009	.934

[a]Number of low blood glucose episodes in last month, [b]Endorsed whether believe would die from a hypoglycemic event, [c]Total score on the Beck Anxiety Inventory, [d]Total score on the Beck Depression Inventory, [e]Total score of the Hypoglycemia Fear Survey, [f]Total Severity score on the Posttraumatic Diagnostic Scale.

*$p < .05$.

multiple regression analyses. The appraisal of lethality of hypoglycemia and FH showed the strongest association with PTS, and were the only variables to contribute significantly to the statistical prediction of PTS. Therefore, the symptomatology presented here represents hypoglycemia-specific anxiety, rather than representing global psychological distress. This finding adds more data to the controversy regarding PTS/PTSD as a legitimate symptom expression subsequent to medical stressors (Andrykowski, Manne, Cordova, & Coyne, 2003). Investigators have questioned whether symptoms reported in inquiries of PTSD are better accounted for by general distress, such as depression and nonspecific anxiety (Coyne, Palmer, & Cook, 2003).

The relationship between HFS and PDS total score raises methodological questions regarding the nature of this relationship. FH may represent a developmental precursor, acting as a risk factor for the development of full PTSD symptomatology. In contrast, HFS may be measuring a subset of the same symptoms assessed by the PDS. If the latter were the case, the relationship between HFS and PDS scores would represent a measurement confound rather than an association between two distinct constructs. A content analysis of the HFS and PDS items suggest that nearly all the HFS items represent a more detailed inquiry of hypoglycemia-specific avoidance and intrusive ideation, paralleling only two symptom clusters of the PDS. For a more rigorous investigation of this issue, future research should subject the HFS and PDS items to factor analytic assessments to test for item clustering. If, however, HFS scores represent measurement of a subset of the PTSD symptoms, similar to the Revised Impact of Events Scale's (Weiss & Marmar, 1997) measurement of intrusive ideation and avoidance but not arousal, then the regression results presented here require different interpretation. That is, if FH and PTS represent aspects of the same phenomenon, then perceived death-threat emerges as the primary predictor of PTS/PTSD.

Nonetheless, investigators and clinicians must be cautious regarding the interpretation of these preliminary data, and further investigation of PTS/PTSD among individuals with diabetes appears warranted. Reviews of issues important for consideration in the diagnosis of PTSD are available (Herbert & Sageman, 2004; McNally, 2003), and have noted that general distress may inflate the endorsement of PTSD items (McNally, 2003). The findings presented here, indicating stronger relationships between perceived death-threat from hypoglycemia than between general distress (i.e., depression and nonspecific anxiety), suggest a hypoglycemia-specific phenomenon. In addition, the finding of a stronger relationship between perceived death-threat and PTS than between actual hypoglycemic history and PTS emphasizes the cognitive processing elements in the emotional processing of the hypoglycemic experience (Foa & Riggs, 1995; Foa & Rothbaum, 1998).

Another issue relevant to PTSD diagnostic conceptualization involves the phenomenon of an ever present, potentially life-threatening event, such as hypoglycemia for those with diabetes. Individuals with Type I diabetes face the threat of hypoglycemia for the duration of their insulin treatment across the course of their life. As such, these data raise a more phenomenological question. Does this PTS represent "posttraumatic stress" or rather ever-present "peri-traumatic stress?" Just as the diagnostic criteria for adjustment disorders have been revised to respect the fact that "stressors" to which one must adjust may be chronic and ongoing, PTSD scholars are currently grappling with the issue of how best to conceptualize individuals' response to ongoing life threat and trauma.

It is also noteworthy that the percentage of participants reporting diagnostic levels for the avoidance symptom cluster was the lowest of the three PTSD symptom clusters. This finding raises several questions. First, does the medical necessity of DM management and the guidance of the medical treatment team serve to prevent avoidance of hypoglycemia-related triggers? Second, as discussed below, this sample represents individuals utilizing the most advanced of all available regimens, and may represent the least avoidant patients. Greater levels of avoidance symptoms might be found among those who are less pursuant of intensive basal/bolus regimens (i.e., those employing traditional regimens like R and NPH or Lente insulins). Third, would the patients who are most avoidant in response to stimuli that trigger hypoglycemia-related distress be less likely to complete the questionnaires and participate in the study? If the answer to this third question is "yes," then the PTS prevalence reported here may be an underestimation of the actual levels of symptomatology in this population.

Either way, it is clear that PTS/PTSD symptoms need to be investigated more thoroughly among varied patient populations, and contrasted among those using different regimens or displaying different initiative in pursuit of advanced or intensive regimens.

Although it was hypothesized that greater PTS symptomatology would relate to higher HbA1c values (i.e., poorer glycemic control), this was not found. Of all the variables considered, only perceived death-threat from hypoglycemia and nonspecific anxiety (i.e., BAI score) contributed to prediction of HbA1c. It is unclear why FH did not impact glycemic control. Fear of hypoglycemia has been, in other studies, a major barrier for appropriate diabetes management with intensive therapies. However, these results suggest a lack of impact. Furthermore, only nonspecific anxiety accounted for a significant change in variance accounted for by the regression equation. As such, the strength of the PTS → HbA1c relationship did not represent an important barrier for glycemic control among these participants.

Therefore, the potential interference of PTS/PTSD on glycemic control requires further investigation.

Limitations

Limitations of this study include the discrepancy in the number of responders versus non-responders and the reliance on a convenience sample. Convenience samples can yield small, non-representative groups, and mailed survey studies have a poor response rate. Only 26% of the original solicitation sample chose to participate in this study. This suggests that the representativeness of this sample to the overall Type I diabetes population is limited, and draws into question the generalizability of these findings. This study also did not measure previous trauma history or adherence with self-management activities, preventing assessment of these factors' possible role in the findings. Despite these limitations, there were notable strengths. This study assessed the experiences of persons with diabetes using the most current regimens for tight control of blood glucose. Although these findings may not be generalizable to the entire Type I population, it addressed a subpopulation of persons with Type I diabetes receiving less attention in the literature.

Conclusion and clinical and research implications

These findings highlight the extent of the intrusive experiences caused by hypoglycemic episodes among individuals with diabetes using intensive insulin regimens. These data indicate that 25.5% of individuals using CSII or MDI basal/bolus regimens report symptoms consistent with current PTSD specific to hypoglycemia. Sixty-five percent reported diagnostic levels of intrusive re-experiencing symptoms, 54.4% reported diagnostic levels of arousal symptoms, 31.1% reported diagnostic levels of avoidance symptoms, and over 95% reported that their hypoglycemia-specific anxiety interfered in at least one area of life functioning (e.g., occupational, interpersonal). In multiple regression analyses, perceived death-threat from hypoglycemia and fear of hypoglycemia statistically predicted PTS/PTSD, while depression and nonspecific anxiety did not contribute significantly to the prediction of PTS/PTSD.

Research should further investigate hypoglycemia-specific PTS/PTSD among a broader population of individuals with diabetes, the potential relationship between PTS and glycemic control, and the relationships among general anxiety, depression, PTS, and perceived threat from hypoglycemia. These data raise the question of whether fear and anxiety specific to hypoglycemia should be screened carefully among individuals using intensive basal/bolus insulin regimen. To date, interventions to reduce FH, or related PTS, have been largely uninvestigated, leaving clinicians with limited empirical data to guide intervention. It may be, however, that perceived threat from hypoglycemia, hypoglycemia fear and PTS should be a high priority for assessment and treatment among those with diabetes, as is the case for depression and general anxiety. Until the relationships among perceived threat, general anxiety, hypoglycemia-specific anxiety, and glycemic control are more well-investigated, however, it appears warranted to assess these phenomena on an individual basis among patients, in order to prevent any potential negative impact upon both psychological adjustment and medical outcomes.

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