Peritraumatic and Post-Traumatic Stress Among Individuals with Diabetes Mellitus

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Contents

Abstract

Diabetes mellitus is typically not experienced as immediately life-threatening, and represents a disease requiring long-term self-management. The degree to which patients experience severe or life-threatening symptoms at diagnosis varies, however, and this may represent a factor predicting greater fear and perceived threat. Data have begun to demonstrate that PTSD may increase risk for individuals developing diabetes. As a stressor, diabetes also may engender PTSD. This has been found for parents of children diagnosed with type 1 diabetes, for adults with type 1 diabetes related to their experience with hyperglycemic

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episodes and related to hypoglycemia episodes, and for children with type 1 diabetes related to hypoglycemia. The onset, course, and lifelong self-management of diabetes create the possibility of chronic threat for the most threatening experiences related to diabetes, rather than a discrete or time-limited threat. A taxonomy is suggested to organize and facilitate the study of PTSD regarding diabetes and other medical stressors, with three categories of study foci to clarify the pursuit of each empirical investigation. The developing research literature is reviewed, and the disease and treatment elements of diabetes are discussed with regard to hypotheses about interrelationship and PTSD risk over life-span development.

List of Abbreviations

BG	Blood glucose
CGM	Continuous glucose monitor
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
FH	Fear of hypoglycemia
HbA1c	Hemoglobin A1c (test of glycemic control)
PTS	Post-traumatic stress
PTSD	Post-traumatic stress disorder
T1D	Type 1 DM
T2D	Type 2 DM

Introduction

Diabetes mellitus (DM) affects more than 347 million people worldwide (Danaei et al. 2011) and is anticipated to be the seventh leading cause of death in the world by 2030 (WHO 2011). For several reasons, which will be explored in detail throughout this chapter, DM has received less investigation with regard to post-traumatic stress (PTS) and post-traumatic stress disorder (PTSD) than other medical stressors that are more commonly perceived as immediately life-threatening. Within the last decade, however, data suggesting PTS/PTSD related to various aspects of the DM experience have been reported. These data are here reviewed, and discussed in the context of the overarching literature about PTS/PTSD and medical stressors. An organizational taxonomy is presented and suggested as a tool to systematize the pursuit of the ongoing empirical study and presentation of emerging evidence. This taxonomy is used to organize the review of PTSD increasing risk for DM, disease factors of DM inducing PTSD, DM treatment regimen factors inducing PTSD, as well as a full integration and discussion of these findings with respect to PTSD and DM. Note that, throughout the chapter, the term post-traumatic stress disorder (PTSD) is used to denote a severity and scope of symptoms that meet diagnostic criteria, while post-traumatic stress (PTS) refers to the continuum of PTS symptoms, regardless of whether they constitute PTSD diagnosis.

Taxonomy for Classifying Studies

In order to guide the expanding exploration of PTS/PTSD related to medical stressors, a taxonomy is here proposed, offering three categories to define studies with identifiably different foci (see Fig. 1). Category 1 studies investigate whether preexisting PTSD places individuals at greater risk for subsequently developing particular medical conditions. In these studies, the medical stressor is not hypothesized as the traumatic stressor, but as an outcome, for which the previous traumatization may increase risk. Other studies investigate whether a particular medical condition acts as a stressor that may induce PTS/PTSD related to that experience. These studies, in contrast to Category 1 studies, investigate the medical condition as the potentially traumatic stressor. Investigations of the traumatogenic nature of medical conditions can be further divided into two categories. Category 2 studies investigate the development and diagnosis of the medical condition as the stressor, exploring whether the disease onset, symptoms, the diagnosis of the condition, or the patient's appraisal of threat from the disease may engender PTS/PTSD. Category 3 studies investigate whether experiences related to the treatment of the condition may induce PTS/PTSD. Treatment may be aversive due to several reasons. These include the possibility that the treatment is painful, frightening, or threatening, or induces significant side effects. Patients may also feel pressure to effectively self-manage their treatment, and perceive management failures as threats. This taxonomy distinguishes studies of PTS/PTSD resulting from the disease factors of the experience (Category 2) from PTS/PTSD resulting from the regimen factors of the experience (Category 3; Boyer 2008a). This typology will be utilized to explore PTS/PTSD related to DM. Although the study of PTS/PTSD related to DM is in its infancy, DM involves diagnostic and treatment phenomena that highlight important factors regarding how individuals respond to potentially traumatizing aspects in the experience of chronic medical conditions.

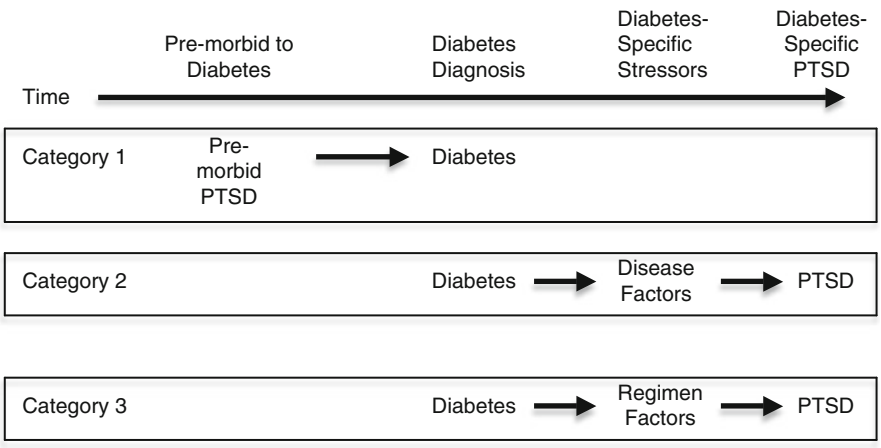

Fig. 1 Taxonomy for PTSD and diabetes studies

While a complete overview of the disease and psychosocial research related to DM is beyond the scope of this chapter (see Boyer 2008b), it is imperative to understand several important diagnostic and treatment differences relevant to DM. Each of these will be described, with particular focus on how they relate to patients' perceptions of risk and threat, and how these may relate to development and maintenance of PTS/PTSD.

Type of Diabetes and Disease Factors

Type 1 DM (T1D) produces symptoms that occur more acutely (noticeable within weeks of onset), usually at younger ages, and requires the immediate application of exogenous insulin as the primary treatment. Type 2 DM (T2D) usually begins at older ages than T1D and is associated with obesity and sedentary lifestyles, and symptoms develop more slowly over time. T2D may be present but unnoticed for extended periods before getting diagnosed, and is usually diagnosed during routine physician visits, sometimes with the patient experiencing little or no perceptible or distressing symptoms. T2D can often be controlled with either diet and exercise, or with oral medications rather than requiring insulin regimen. Over time, however, T2D may progress and eventually require administration of exogenous insulin, similar to the treatment regimen for T1D.

At diagnosis, diabetes is typically characterized as a condition requiring long-term self-management, rather than a condition with immediate life threat. In addition, the evidence that successful self-management of blood glucose over time reduces subsequent complications that constitute risk of mortality (Diabetes Control and Complications Trial Research Group 1993) is typically communicated to patients and their families. For these reasons, the diagnosis of DM may not routinely be perceived by patients as life-threatening, especially not immediately life-threatening.

While DM usually has a less life-threatening onset, and patients may receive less fear-inducing diagnostic, treatment, and prognostic information from medical professionals at diagnosis than for cancer or cardiac events, this is not always the case. Some individuals may only receive a DM diagnosis when they experience acutely distressing and dangerous symptoms, such as diabetic ketoacidosis (DKA, dangerous levels of acidic ketones, produced by the breakdown of fat, subsequent to insufficient endogenous insulin; Fajans 1973). For individuals who experience this type of onset, with extreme DKA symptoms requiring emergency care and/or intensive care services, compared to those who have little or no symptoms and receive the diagnosis during routine medical care, the topography of the diagnostic experience includes elements much more likely to constitute immediate threat to life. To describe this contrast from the patient's perspective, consider the two following examples. One person may experience almost no distressing physical symptoms (e.g., more thirsty and urinating more frequently than usual), go to their outpatient physician, discover in blood testing during a medical visit that their blood glucose (BG) is elevated, and receive the DM diagnosis in a discussion with their medical

providers. Another individual may develop headache, nausea and vomiting, and severe subjective distress, experience "diabetic coma," be taken to the emergency room, awaken in an intensive care unit with intravenous lines providing insulin, be informed that they have DKA and are at risk for death, and receive the DM diagnosis in a flurry of emergency medical services. The description of these two extremes in the diagnostic experience highlights that the onset and diagnosis may range from a low risk for perception of life threat, in which the diagnosis appears more related to long-term treatment, to a high risk for perception of immediate risk for death.

Treatment/Regimen Factors

Insulin regimens, whether for T1D or T2D, require either the subcutaneous injection of insulin by syringe and needle or the use of a continuous subcutaneous insulin infusion pump to deliver and dose insulin. In addition, the calculation of carbohydrates in food consumption, matching of insulin doses to those carbohydrate quantities, monitoring of blood glucose by "finger sticks" and/or by wearing a continuous glucose monitor (CGM), and other self-care activities are required.

In turn, the treatment regimen is multifactorial and complex, requires constant self-management and is therefore burdensome, and represents a lifelong demand for self-management effort (Boyer 2008b). All these factors pose significant risk for patients to experience difficulty successfully executing these self-management treatment regimens (Boyer 2008a), and differences among each type of treatment regimens pose different regimen-specific risk factors for PTS/PTSD. Most important is the risk of certain treatments unintentionally producing episodes of excessively low BG, or hypoglycemia. These typically produce distressing symptoms, and can be fatal if not corrected quickly by ingestion of carbohydrates. Furthermore, since the lifelong self-management of DM places patients at ongoing risk for the most distressing experiences of the disease, potentially traumatizing DM experiences are not limited to a particular time frame in the course of diagnosis and treatment. These differences among DM types and onset, and among the various treatment regimens, are important elements that frame the experiential landscape of the DM diagnosis and treatment, and the risk for possible PTS/PTSD.

Relationship of PTSD to Development of Diabetes: Category 1 Studies

There are several studies assessing the effect of PTSD on the development and course of DM. Although there is no evidence to suggest that PTSD increases one's risk of developing T1D, there are mixed results regarding whether a previous diagnosis of PTSD causes one to be more susceptible to developing T2D. One study found that PTSD related to an increased risk for subsequent T2D in both military service workers and a primary care sample (Boyko et al. 2010). Investigators of this study noted several biological markers that associated with both PTSD

and DM, including higher levels of inflammatory markers, increased endothelial dysfunction, and lower hippocampal volume. This relationship between PTSD and later T2D was confirmed by another study using civilian participants, even after controlling for metabolic risk factors and other psychological conditions (Lukaschek et al. 2013). Another study, also using a civilian population, found that the experience of trauma, but not the diagnosis of PTSD, increased the risk of developing T2D in males only (Norman et al. 2006). Although it is unclear why trauma, and not a PTSD diagnosis, should be influential in the development of T2D, it may result from using the dichotomous diagnostic variable of PTSD and thereby losing the sensitivity and statistical power afforded by considering PTS as a continuum of severity. While the evidence regarding the overall link between PTSD and DM remains quite mixed (Dedert et al. 2010; Keyes et al. 2013), there appears to be enough preliminary evidence to warrant further, rigorous investigation.

Individuals diagnosed with PTSD are more likely to report ever having DM, with one study reporting an odds ratio of 1.3 (Pietrzak et al. 2011). Another study found that this relationship disappeared after controlling for lifestyle factors, such as exercise and tobacco use (Weisberg et al. 2002). These associations, however, do not capture the direction of influence between PTSD and DM, as the studies were cross-sectional with no evidence to suggest which disorder preceded the other.

There is evidence to suggest that the development of metabolic syndrome may constitute a biological mechanism by which PTSD increases one's risk for T2D (Dedert et al. 2010; Weiss et al. 2011). Metabolic syndrome is associated with several medical conditions, including DM. In addition to possible biological mechanisms, having PTSD may increase individuals' risk of DM through an alteration in lifestyle factors. There is extensive evidence that those with PTSD have poorer health habits, including increased use of tobacco and alcohol, less physical exercise, greater caloric intake, and poorer self-care in general (Whiteman et al. 1997; Del Gaizo et al. 2011; Fu et al. 2007), and these habits are closely linked to risk for T2D. Male veterans with comorbid T2D, PTSD, and depression had higher rates of substance abuse than those with either disorder only or no psychiatric diagnosis. These patients also had higher cholesterol than those with depression only and had higher body mass index than those with neither diagnosis. Lastly, among those with DM, those with comorbid PTSD and depression were more likely to have poor glycemic control than those with only PTSD (Trief et al. 2006).

Relationship of Diabetes to Development of PTSD

The study of PTS/PTSD related to diabetes as a potentially traumatic stressor is in its infancy. It is important to note, however, that the few existing studies differ with regard to which aspects of the DM experience they orient participants to consider as they report PTS symptoms. Some inquire about PTS symptoms related to the diagnosis or overall DM experience, or related to experiences with hyperglycemia, representing Category 2 studies of disease-related PTS, while others have queried

PTS specifically related to hypoglycemia, representing Category 3 studies regarding PTS and treatment regimen factors.

Category 2 Studies

Studies evaluating whether DM can generate PTS/PTSD are few. In addition, the first to assess for PTS/PTSD following DM began with investigation of PTSD among parents of children diagnosed with T1D. Landolt and colleagues (2002) reported 22.2 % of fathers and 24.3 % of mothers endorsing symptoms consistent with PTSD in the 6 weeks following the T1D diagnosis in their child. Their prospective follow-up at 6 weeks, 6 months, and 12 months following the child's T1D diagnosis indicated PTSD symptoms in 22.4 % of mothers at 6 weeks, 16.3 % at 6 months, and 20.4 % at 12 months, with fathers reporting 14.6 %, 10.4 %, and 8.3 % at the same time intervals (Landolt et al. 2005). A subsequent study, comparing PTSD between mothers of children diagnosed with T1D and of children diagnosed with pediatric cancer (Stoppelbein and Greening 2007), found no significant difference in PTSD rates between mothers of these two diagnostic groups. Among the 46 mothers of children with T1D diagnoses, 6.5 % of mothers reported symptoms consistent with current PTSD, measured by structured interview, and 17 % reported symptoms that met the cutoff score for likely PTSD on self-report inquiry, with 25 % of mothers meeting two of three PTSD symptom clusters (Stoppelbein and Greening 2007). Based on the description of methodology in these articles, it appears that none of these studies instructed parents to rate PTSD symptoms specific to any particular aspect of their child's DM. As such, it is unclear to which aspects of the DM experience parents developed these PTS symptoms.

Another study, of 60 mothers whose children aged 16 or younger were diagnosed with T1D within the previous 1 month to 5 years, reported 10 % of mothers meeting criteria for full PTSD and 15 % meeting criteria for partial PTSD (Horsch et al. 2007). In this study, mothers were asked to identify the most distressing aspect of their child's T1D diagnosis. Sixty-five percent of mothers reported that being informed that their child had diabetes was most distressing, with 16.7 % citing a severe hypoglycemic episode and 6.7 % citing each of the following stressors: the experience of giving the first insulin injection to their child, their child's symptoms before being diagnosed, and the child's initial hospitalization. Forty-one percent of mothers described the chronic stress of worrying about their child's long-term health being impaired as most stressful. A follow-up study investigated the contribution of cognitive and noncognitive factors to the PTSD reported by mothers following their child's T1D diagnosis (Horsch et al. 2012). All of the cognitive factors assessed in the study (negative cognitive appraisals, dysfunctional cognitive appraisals) positively correlated with mothers' PTSD. Among the noncognitive variables (trauma severity, mother's psychiatric history, social support), only social support accounted for a significant amount of variance in PTSD. The cognitive variables accounted for significant variance beyond that accounted for by all the noncognitive factors. While this finding emphasizes the role of cognitive processing in the adjustment or

traumatization following the T1D stressor, it is noteworthy that most of the noncognitive factors in the study, namely, social support and psychiatric history, represent psychosocial factors rather than factors characterizing the topography of the potential trauma, such as the trauma severity variable. As discussed in more detail below, in the Summary of Research section, this greater relationship between cognitive appraisals and PTS/PTSD parallels the findings in studies of PTS/PTSD among adults with T1D.

Since most of these studies did not indicate exactly what element of the parents' experience constituted the traumatizing stressor, and since one (Horsch et al. 2007) reports both disease factors (news of diagnosis, disease symptoms) and regimen factors (hypoglycemic episodes, administering injections, hospitalization) as critical stressors, it is unclear whether these studies represent Category 2 or Category 3 studies. These articles are listed here as Category 2 studies, since their query of PTSD symptoms appeared framed to the global event of the participants' child's T1D diagnosis.

The above Category 2 studies all assessed PTS/PTSD among parents and did not investigate PTS/PTSD among the actual patients. Among the few studies investigating PTS/PTSD experienced by those diagnosed with DM, there appear to be no studies evaluating PTS/PTSD related to T2D. Only one Category 2 study has assessed PTS/PTSD among adults with T1D, directly orienting participants to report PTS symptoms related to their experience with hyperglycemia, which is a disease factor rather than a treatment regimen factor (Powlus et al. 2012). This study found 31 % of participants reporting symptoms consistent with current PTSD. Of note, 73.6 % met criteria for the intrusive re-experiencing symptom cluster, 60.3 % for the hyperarousal cluster, but only 39.3 % met criteria for the avoidance symptom cluster. Nearly 63 % reported that these symptoms interfered with daily functioning. The strongest predictors of PTS/PTSD were cognitive appraisals, particularly perceived helplessness and death threat, and DM-management factors, such as self-management activities and glycemic control. Those appraising greater helplessness and threat to life, with poorer self-management and glycemic control, showed greater PTS/PTSD. It is interesting that the number and severity of DKA episodes, the most common distressing acute complication of hyperglycemia, did not relate significantly to PTS/PTSD in regression analyses.

Category 3 Studies

One of the studies regarding parents of children with DM1, described above, cited several acute stressors representing treatment procedures (administering injections, hospitalization) or side effects (hypoglycemic episodes) as mothers' most stressful experiences (Horsch et al. 2007), characteristic of Category 3 studies. The first study of PTSD in actual patients diagnosed with DM, specifically adults with T1D, was inspired by research investigating fear of hypoglycemia (FH).

The use of intensive insulin regimens, while effective in optimizing tight glycemic control, continues to pose the risk for acute hypoglycemia (Irvine et al. 1992).

For most individuals, these episodes of low BG produce distressing physical and emotional reactions, and can represent immediate risk of death (Gold et al. 1995; Gonder-Frederick et al. 1989; Polonsky et al. 1992; Taylor and Rachman 1988). Most individuals with DM and their families know that hypoglycemic episodes can be life-threatening (Cox et al. 1987; Strauss 1996), and require immediate ingestion of carbohydrates to counteract the symptoms and avoid possible death. Given the immediate and distressing symptoms of hypoglycemia, it is not surprising that some individuals developed a focal fear of these episodes (Irvine et al. 1992; Polonsky et al. 1992). Studies suggest that individuals with high FH often overreacted to concerns about low BG, overtreated the hypoglycemia by ingesting excessive carbohydrates and driving BG to elevated rather than normative levels (Cox et al. 1987), or would intentionally reduce their dosing of insulin to keep BG at higher than optimal levels, in attempt to reassure themselves that BG levels would not become low (Surwit et al. 1982; Wiebe et al. 1994).

In the first investigation of the full PTSD symptom clusters related to hypoglycemia, among adults with T1D, 25.5 % of participants reported symptoms consistent with current PTSD (Myers et al. 2007). Sixty-five percent of participants met diagnostic criteria for the intrusive re-experiencing symptom cluster, with 54.4 % meeting criteria for the hyperarousal and 31.1 % meeting criteria for the avoidance cluster. Ninety-five percent of the sample reported that the PTS symptoms related to hypoglycemia interfered significantly in at least one function of daily living. Multiple regression indicated that, while number and severity of previous hypoglycemic episodes did not relate significantly to PTS symptomatology, perceived death threat from hypoglycemia related significantly to both PTS severity and to current PTSD diagnosis.

A replication of this study demonstrated that 29.8 % of adults with T1D met criteria for current PTSD related to hypoglycemia. Sixty-nine percent of these individuals met criteria for the intrusive re-experiencing cluster, 61 % for the hyperarousal, and 40.9 % for the avoidance cluster, with 73.8 % indicating that these symptoms interfered with life functioning (Boyer and Renna 2015). Age, total severity of hypoglycemic episodes in the past month, and appraisals of fear related to hypoglycemia were most strongly related to PTSD. Age, last HbA1c, total severity of hypoglycemic episodes, and perceived helplessness about hypoglycemia were associated significantly with severity of PTS. When an overall appraisal factor was created to reflect appraisals of fear, helplessness, and perceived threat of death from hypoglycemia, this factor showed the strongest relationship to current PTSD and a stronger correlation with PTS severity (partial $R = 0.43$) than age or last HbA1c (Boyer and Renna 2015).

In the only Category 3 study investigating PTS among children (aged 8–18 years) with T1D, assessing PTS related to hypoglycemia, 33.3 % reported PTS symptoms in the moderate range, with 16.7 % in the severe and 1.9 % in the very severe range (Sismanlar et al. 2012). Multiple regression found a number of hypoglycemic episodes in the previous month to be the only variable related to PTS severity. This study reported only severity of PTS symptoms and did not calculate the number of participants reporting symptoms consistent with PTSD diagnosis.

Across the Category 1 and Category 2 studies with adults, the rates of patients meeting criteria for intrusive re-experiencing, hyperarousal, and interference with daily functioning are notably higher than those meeting criteria for avoidance. The reasons for the lower rates of avoidance symptoms remain unclear. It may be that, for some with T1D, PTS symptoms involve avoidance of DM self-management activities rather than other more general domains of avoidance, and they did not endorse avoidance items on self-report measures. The fact that, in the few studies that have measured self-management behaviors, there were no strong relationships between self-care scores and PTS/PTSD provides no support for this hypothesis. It may also be that patients understand the medical danger from avoidance of dealing with their DM and feel unable to permit the manifestation of avoidance symptoms. If this is true, the lower avoidance may indeed exacerbate their experience of the intrusive re-experiencing and hyperarousal PTS symptoms that avoidance symptoms sometimes mitigate.

The Category 2 and 3 studies that have investigated relationship of PTS/PTSD to other factors indicate some emerging consistency between studies. While a number of hypoglycemic episodes correlated with PTS for children with T1D (Sismanlar et al. 2012) and severity of recent hypoglycemic episodes related significantly to PTS/PTSD in adults with T1D (Boyer and Renna 2015), cognitive factors show a relationship to PTS/PTSD as strong or stronger than did factors more indicative of the topography of the stressful experience. That is, cognitive appraisals of helplessness and perceived death threat related more strongly to hyperglycemia-related PTS/PTSD than did experiences with DKA and, along with fear, were among the strongest statistical predictors of hypoglycemia-related PTS/PTSD. Understanding the interrelationship among individual and temperamental factors (e.g., age, global fearfulness), topographical stress factors (e.g., actual hypoglycemia/hyperglycemia experiences, previous HbA1c), cognitive appraisal factors (e.g., fear, helplessness, perceived threat), and PTS/PTSD, as well as DM self-management and medical outcomes (e.g., glycemic control, DM complications), require further investigation and longitudinal study.

Diabetes and PTSD in the Context of Medical Stressors and Life-Span Development

Several phenomena seem to distinguish the experience of DM diagnosis and self-management from other medical conditions that have received more attention with regard to PTSD. We here discuss DM experiences regarding the perceived threat regarding the onset and diagnosis of DM symptoms, the self-management treatment regimen and side effects, and the temporal nature of lifelong exposure to perceived threat for individuals with DM. These elements offer important opportunities for understanding the interplay between specific factors of physical health and PTS symptomatology and are discussed here. The other important aspect in the study of PTSD and DM represents a life-span developmental perspective that may highlight ongoing reciprocal relationships between multiple risk factors.

For the majority of individuals diagnosed with DM, the symptoms experienced before the diagnosis are relatively minor. This, however, is not always the case, since some individuals develop DKA, with severe physical symptoms and frightening emergency and/or intensive care medical services as the onset and diagnostic context. Although this has not been extensively investigated by empirical studies, this difference between cases of DM with severe and distressing initial symptoms, versus cases with mild symptoms leading to diagnosis, probably constitutes a noteworthy factor regarding experiential threat. The developing data suggest that individuals' appraisal (fear, perceived helplessness, perceived life threat) appears more strongly related to PTS/PTSD than the actual historical events of hyperglycemic symptoms or DKA. It is not well investigated or clear, however, whether the participants' PTS/PTSD, report of DKA, and appraisal of hyperglycemia experiences were related to those at the onset and diagnosis of T1D or experiences with hyperglycemia or DKA over time. Differences in development and maintenance of PTS/PTSD related to onset and diagnosis require further investigation.

The fact that there is no cure currently, for most individuals with DM, is also different than some other medical conditions for which PTSD has been more thoroughly investigated. While DM is often perceived as less immediately threatening to mortality by comparison, treatment requires a commitment to lifelong behavioral and lifestyle changes to self-manage BG. The temporal nature of the threat related to hyperglycemia, as the primary disease factor, and hypoglycemia, as the primary regimen factor, has not been well discussed in the existing literature. With typical information, most individuals with DM know several things: (1) the risk of death from DM is not acute, unless one actually declines treatment; (2) most people experience diabetic complications or death from diabetes from persistently high BG, and it is their own self-management efforts that may prevent such disability and death; and (3) the degree and persistence of hyperglycemia that one experiences *now* and *going forward in time* may be fatal, but not until a later time. In contrast, the threat of hypoglycemia is acute, and excessively low BG may kill the person *now*. Stated another way, "low BG now can kill me now; high BG now can kill me later!" Because of this temporal expectation, along with the more immediately distressing symptoms of hypoglycemia, PTS related to hypoglycemia may be more observable in family, social, or clinical situations than PTS related to hyperglycemia. However, hyperglycemia presents an interesting experience, in which frequent indicators of hyperglycemia, such as daily BG monitoring results on glucometers or CGM, and HbA1c values, may be perceived as a threat, but the danger of the threat is delayed. This appears supported by the finding that previous HbA1c scores related significantly with PTS/PTSD related to hyperglycemia (Powlus et al. 2012). The lifelong course of treatment is thereby peppered with episodic data that, when indicating significant hyperglycemia, may represent information that constitutes ongoing threat for impending but uncertain disability or death.

The other temporal factor regarding the threat of hyperglycemia or hypoglycemia is that it is not limited but persistent. The self-management regimen for DM is such that hyperglycemia may occur on any given day. For those using insulin regimen or oral antihyperglycemic medications that can induce low BG, hypoglycemia may also

occur on any given day. For this reason, the PTS reactivity from actual previous events, the PTS reactivity regarding the constant possibility of the threat, and the anticipatory anxiety about potential high or low BG episodes in the future constitute a rather inextricable landscape of potential threat. Myers and colleagues pondered whether the term post-traumatic stress was less representative of this anxiety than an "ever-present 'peri-traumatic stress'?" (Myers et al. 2007, p. 18). Another phenomenon about perceived threat and PTS/PTSD from hypoglycemia is the emerging evidence that the severity of hypoglycemic episodes may be more important than the frequency of the episodes (Boyer and Renna 2015; Myers et al. 2007). Given that mild episodes of low BG can be quickly and readily corrected with carbohydrate ingestion, and may not interrupt daily activity, mild hypoglycemic episodes may not be distressing or may even engender greater self-efficacy to manage low BG and reduced perceived threat, while episodes inducing unconsciousness, disorientation, need for help, or seizure constitute significant threat.

Furthermore, patients' primary protection from these episodes is their own self-management behaviors. Research has begun to investigate whether PTSD relates significantly to DM self-management, but is far from determining whether DM-related PTSD may interfere with DM self-management behaviors, or vice versa. Since self-management success is crucial to optimal medical outcomes, this will be imperative to explore.

In addition to the above factors related to onset, diagnosis, treatment regimen, and course of DM, life-span developmental aspects of the interrelationship between DM and PTSD appear important. For some other diseases, there appears to be little to no evidence that PTS/PTSD increases risk. T2D, which is very affected by physical activity and food consumption, has in some Category 1 studies been shown to develop among those with PTSD regarding other previous traumas. The Category 2 and 3 studies indicate that experiences with, and cognitive appraisals of, hyperglycemia and hypoglycemia may constitute stressors that generate PTS. While these phenomena are not yet fully explored, and extant studies show PTSD increasing risk of T2D (but not T1D) and T1D (with no current evidence regarding T2D) inducing PTS/PTSD for some individuals, a developmental perspective raises some hypotheses about important possibilities. Considering current empirical findings, as well as clinical observation, judgment, and theory, multiple interlocking links may exist to pose accumulative risks over the lifetime of an individual. Considered sequentially:

1. PTS/PTSD may increase the likelihood of developing DM;
2. Preexisting PTS/PTSD regarding other traumas may increase the risk of an individual experiencing increased fear, helplessness, or perceived threat to life from DM or DM self-management regimen after DM diagnosis;
3. The previous two phenomena (#1 and #2) may increase risk of PTS/PTSD reactivity to DM diagnosis and ongoing self-management;
4. PTS related to DM may interfere with self-management success if self-management behaviors trigger intrusive re-experiencing and hyperarousal PTS symptoms, and this may indeed be most likely for those with pre-DM PTSD and/or more severe PTS related to DM;

5. PTS avoidance may decrease success of DM self-management;
6. Anxious hyperarousal may increase blood glucose via stress-related metabolic changes accompanied by sympathetic nervous system arousal;
7. The two previous phenomena (#5 and #6) may result in poorer glycemic control over time;
8. Patient awareness of poorer glycemic control, such as higher HbA1c values in routine blood work, may increase the perceived threat of the DM and perceived helplessness regarding hyperglycemia and hypoglycemia;
9. Since DM has no curative treatment, and currently requires lifelong self-management of BG, these factors may reciprocally influence each other over time.

This chapter provides an overview of the extant data regarding PTSD and DM. It offers a taxonomy for categorizing and organizing the pursuit of these investigations. Finally, the life-span developmental perspective regarding possible interplay of multiple risk factors for PTSD and its impact on disease management suggests an overview of many elements in this domain of study that remain imperative to investigate to fully understand PTSD and DM.

Practice and Procedures

The empirical study of PTSD and DM is truly in its infancy. For this reason, the scant research offers very little for guiding clinical practice. However, this research may offer important recommendations to guide research practices. The taxonomy for differentiating Category 1, 2, and 3 studies of PTSD and medical stressors may assist in organizing ongoing research pursuits, so as to make the process more focused and productive. The Category 1 studies need to more clearly evaluate and report the time frame for PTSD and for DM diagnosis in cross-sectional studies, and optimally initiate longitudinal studies to explore the degree to which PTSD increases DM risk, and by what particular mechanisms. Category 2 and 3 studies will benefit by including factors related to individual differences; onset and diagnosis of DM; history, timing, and severity of hyperglycemic and hypoglycemic events; cognitive appraisal and perceived threat regarding these events; self-management behaviors and glycemic control; and explore how these factors interact over time to explicate the development and maintenance of any DM-related PTSD. Toward this goal, Category 2 and 3 studies will benefit from very explicit inquiry as to which aspects of the participants' DM experiences constitute the fearful and threatening factors related to PTSD and/or specifically orient participants' to consider PTSD symptoms related to predetermined aspects of the potentially traumatizing factors, so as to focus the testing of particular hypotheses. While this appears to always represent the hallmarks of good scientific investigation, the first generation of PTSD studies of DM has produced results to guide the ongoing focus. As the empirical evidence develops, it seems imperative to measure how self-management behavior and glycemic control relate to perceived threat and are in turn affected by perceived

threat and PTS symptoms. Furthermore, the accumulative and possibly reciprocal influence of the lifelong course of the risk factors outlined in this chapter will need to be explored with longitudinal multifactorial research.

Key Facts of Diabetes

- Over 347 million people have DM worldwide; DM is projected to be the seventh leading cause of death worldwide by 2030.
- Diabetes has no cure, and treatment involves lifelong self-management of blood glucose.
- T1D and T2D have characteristically different age of onset and onset symptoms, with T1D onset more acute and T2D onset more insidious and with few noticeable symptoms.
- T1D requires immediate use of insulin for DM management, and this is generally accompanied by risk for hypoglycemia (dangerously low blood glucose).
- T2D may be treated without medication, or with oral medications that either do or do not produce hypoglycemia. When T2D is treated with insulin, this has greater risk for hypoglycemia.
- Hyperglycemia usually has less acute and distressing symptoms than hypoglycemia, but the accumulative threat of hyperglycemia is related to delayed complications, disability, and death.

Summary Points

- PTSD appears to place individuals at greater risk for developing type 2 diabetes, but this evidence is not consistent across studies.
- Diabetes is typically not characterized by medical providers or experienced by patients as immediately life-threatening, but this is affected by the exact circumstances of onset, side effects of treatment.
- PTSD has been documented in both parents of children diagnosed with type 1 diabetes and adults with type 1 diabetes.
- Individuals have reported PTSD regarding hyperglycemia experiences (disease factors) and related to hypoglycemia (treatment regimen factors).
- Cognitive appraisals (fear, perceived helplessness, perceived life threat) appear strongly related to PTSD across studies.

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