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Posttraumatic stress disorder and incidence of type-2 diabetes: A prospective twin study

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ABSTRACT

Growing evidence has linked posttraumatic stress disorder (PTSD) to insulin resistance and type-2 diabetes, but most previous studies were cross-sectional. We examined the association between PTSD and incidence of diabetes in a prospective study of middle-aged male twins from the Vietnam Era Twin Registry. Lifetime PTSD was diagnosed at baseline with the Diagnostic Interview Schedule (DIS) according to *DSM-III-R* criteria. Subthreshold PTSD was defined by meeting some, but not all, criteria for PTSD. A total of 4340 respondents without self-reported diabetes at baseline were included. Of these, 658 reported a new diagnosis of treated diabetes over a median of 19.4 years of follow-up. At baseline, twins with PTSD showed more behavioral and metabolic risk factors such as overweight and hypertension. The age-adjusted cumulative incidence of diabetes was significantly higher in twins with PTSD (18.9%) than those without PTSD (14.4%), [odds ratio (OR) = 1.4, 95% confidence interval (CI) 1.03–1.8], and intermediate in those with subthreshold PTSD (16.4%) (OR = 1.2, 95% CI 0.9–1.5, p for trend = 0.03). Adjustment for military, lifestyle and metabolic factors diminished the association. No significant association was found comparing twin pairs discordant for PTSD. In conclusion, PTSD was prospectively associated with a 40% increased risk of new-onset type-2 diabetes which was partially explained by a cluster of metabolic and behavioral risk factors known to influence insulin resistance. Shared biological or behavioral precursors which occur within families may lead to both PTSD and insulin resistance/diabetes. Thus, PTSD could be a marker of neuroendocrine and metabolic dysregulation which may lead to type-2 diabetes.

1. Objectives of the study and background

Posttraumatic stress disorder (PTSD) is a psychiatric condition that is common among Veterans and results from exposure to severe psychological stress, such as exposure to combat. Among Vietnam Veterans who served in the war zone, the lifetime prevalence is 15%–19% (Dohrenwend et al., 2006; Thompson et al., 2006). Reported prevalence estimates of PTSD are even higher in combat-exposed Veterans from the recent Iraq and Afghanistan wars (Hoge et al., 2004; Hoge et al., 2007).

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Although the comorbidity of PTSD and other psychiatric disorders is well characterized, its impact on physical health is less well understood. Many studies have documented a higher prevalence of physical health problems among persons with PTSD, but most used cross-sectional designs and self-reported symptoms (Dedert et al., 2010; Glaesmer et al., 2011; Schnurr and Jankowski, 1999). Evidence of a possible link between PTSD and type-2 diabetes—a growing public health problem and a major risk factor for cardiovascular disease and all-cause mortality (Danaei et al., 2011) — has received increased attention (Boyko et al., 2010; Goodwin and Davidson, 2005; Norman et al., 2006). PTSD has also been associated with the metabolic syndrome, a cluster of risk factors characterized by insulin resistance and elevated risk of diabetes (Heppner et al., 2009; Jin et al., 2009; Weiss et al., 2011). The mechanisms underlying these associations are ascribed to chronic perturbations of the hypothalamic-pituitary-adrenal (HPA) axis in those with PTSD, potentially leading to increased visceral adiposity, inflammation, and insulin resistance (Brunner et al., 2002; Chrousos, 2000; Friedman and McEwen, 2004). PTSD may also influence diabetes risk through adverse health behaviors, such as sedentary lifestyle, poor dietary habits, sleep problems, and excessive alcohol consumption (Breslau et al., 2003). Finally, genetic and familial factors may play a role. Genetic predisposition is substantial for obesity and other metabolic syndrome risk factors (Diamond, 2003; Jowett et al., 2009), as well as health behaviors, such as physical inactivity and diet (Heitmann et al., 1999; Lauderdale et al., 1997). Therefore, shared genetic pathways could potentially confound the association between PTSD and diabetes, as previously described for depression and cardiovascular disease (Kendler et al., 2009; Vaccarino et al., 2009).

A major limitation of most previous studies linking PTSD to type-2 diabetes and other metabolic risk factors is their cross-sectional design, which limits the ability to demonstrate a temporal relationship between PTSD and diabetes. Using a prospective twin study design, this study examines the association between PTSD and the incidence of treated type-2 diabetes.

2. Materials and methods

2.1. Setting

The Vietnam Era Twin (VET) Registry is the source of Vietnam-era Veterans for this study. The Registry was constructed from computerized military discharge records and is a national sample of male twin pairs from all branches who served on active duty during the Vietnam era (1964–1975). Members of the Registry were born from 1939 through 1957. The process of identifying twin pairs involved a matching algorithm based on last name, date of birth, and similar Social Security numbers. A military record search confirmed an individual was a member of a twin pair by matching parental names and place of birth. The Registry was assembled in the 1980s and has subsequently seen extensive use as a platform for genetic epidemiological studies of both physical and mental health. A complete description of the VET Registry has been published previously (Goldberg et al., 2002).

2.2. Design

A Twin Study of the Course and Consequences of PTSD in Vietnam Era Veterans [Veterans Administration (VA) Cooperative Studies Program (CSP) #569] is a prospective, observational study of physical and mental health among Veterans who are members of the VET Registry. The study used data collected at the Registry's inception that included socio-demographic data and military experience, as well as physical and mental health information collected in 1992 that included self-reported diabetes and PTSD. These measures constituted baseline data for the present study, and were combined with newly collected follow-up data from 2010 through 2012. In this analysis, we examined the association between PTSD assessed in 1992 and incident treated type-2 diabetes through 2012 among Veterans who were free of diabetes at the time PTSD was assessed.

2.3. Subjects

All members of the Registry who were known to be alive and had not withdrawn their Registry membership were recruited to participate in CSP #569. For these analyses, we restricted participants to those for whom PTSD was assessed in 1992 and who did not self-report diabetes at that time. Informed consent was obtained from all participating Registry members, and the VA Central Institutional Review Board approved the study protocol.

2.4. Measures

2.4.1. Socio-demographic and military service factors

Information on socio-demographic and military service factors were available from the military service records of members of the VET Registry. These data were abstracted at the time the VET Registry was established in the 1980s and included date of birth, race, marital status at enlistment, educational attainment at the time of enlistment, date of enlistment, branch of service, and rank at enlistment.

Extensive additional information was obtained through a series of Registry-wide surveys that were conducted from 1987 through 1992. Education and marital status were updated, and information on occupational status and family income was obtained. Combat exposure was measured by asking each Veteran whether he engaged in 18 specific combat activities such as receiving incoming fire, serving as a "tunnel rat," or checking enemy base camps, yielding a global index of combat exposure ranging from 0 to 18 (Janes et al., 1991).

2.4.2. Baseline risk factors and medical conditions

Registry-wide surveys conducted from 1987 through 1992 also provided extensive information about previous medical history and risk factors, including smoking history, alcohol consumption, anthropometric measurements, and dietary habits. Physical activity was determined by a series of questions about moderate everyday activities (6 questions) or intense sports-related physical activity (5 questions) (Lauderdale et al., 1997). Physical activity was classified as a 3-level ordinal variable of "no physical activity," "moderate physical activity" (engaged in at least one moderate every day activity, such as taking the stairs, walking for exercise, etc.), and "vigorous physical activity" (engaged regularly in at least one vigorous or sports-related activity for at least the last 3 months, such as biking, running, swimming, etc.). Alcohol consumption was addressed with a series of questions asking the respondent on how many days, during the past 2 weeks, he drank beer, wine or hard liquor, and on the days he drank, how many drinks he had per day. From these questions, an average of drinks per day was calculated. Diabetes at baseline was assessed with the question: "Do you have diabetes?" which was asked in a 1992 survey. Veterans answering either affirmatively to or not answering this question were excluded from the analysis. In the same survey, previous history of cardiovascular diseases was assessed by a series of questions asking whether the respondent was ever told by a doctor that he had angina pectoris, congestive heart failure, coronary heart disease, damaged heart valves, heart attack or myocardial infarction, heart murmur, phlebitis or thrombophlebitis, or stroke, or whether the