Abstract

Introduction

Previous twin studies have demonstrated a strong association between the degree of combat exposure and PTSD, and the continued presence of PTSD, almost two decades after combat. Independent genetic effects have also been demonstrated for both combat exposure and PTSD vulnerability in Vietnam veterans. The current study, involving a subset of male-male twin pairs discordant for service in Southeast Asia (SEA), is a follow-up to an earlier study conducted in 1987. The purpose of this study is to examine the changes in the combat exposure-PTSD relationship over an additional decade of time. Methods

The Mississippi Scale for Combat-Related or Civilian PTSD was administered by telephone in 1997 during a follow-up survey of the Vietnam Era Twin Registry. Only twins discordant for service in Southeast Asia who originally participated in the 1987 study were included. Results of this scale and the original 1987 PTSD symptom scale were separately standardized using z-score transformations and used as dependent variables in a random effects regression model with zygosity, time and combat exposure as independent variables. Main effects and interactions were estimated to address whether there were differential effects of combat on PTSD over time, and whether there was evidence of genetic covariation between combat exposure and PTSD in 1987 that persisted to 1997.

Results

Combat exposure was strongly associated with PTSD in both 1987 and 1997. Although still highly significant, the effect sharply diminished over time. There is little evidence for a shared genetic vulnerability between combat and PTSD in either 1987 or 1997.

Conclusion

This analysis documents the continuing role of combat exposure (i.e., trauma severity) on the persistence and chronicity of PTSD. Nearly 25 years after the end of hostilities, PTSD symptoms continue to be elevated in those exposed to the highest levels of combat. There is no evidence that genetic influences on exposure to combat are shared with those inducing a genetic vulnerability to PTSD. Clinicians need to be aware of the persistent and long-term residual effects of trauma exposure.

Key words

PTSD – genetics – twins – combat

Introduction

Post Traumatic Stress Disorder (PTSD) in both combat veterans and civilians is a dynamic product of exposure to trauma (by diagnostic definition), the severity of the
trauma (Pynoos et al. 1987; Goldberg et al. 1990; Green et al. 1990), and underlying familial/genetic vulnerability (Breslau et al. 1991; Davidson et al. 1991; True et al. 1993). Studies of Vietnam era veteran twin pairs have helped to clarify the relative contributions of genetic and environmental influences to the pathogenesis of PTSD. Co-twin control studies in monozygotic (MZ) twins have demonstrated a strong association between the severity of combat exposure and PTSD (Goldberg et al. 1990). Classical twin studies involving MZ and dizygotic (DZ) Vietnam era veteran twins have found evidence supporting a genetic contribution to service in Southeast Asia and more specifically to the severity of combat exposure (Lyons et al. 1993). These findings suggest what has been termed “genetic control of exposure to the environment” (Kendler and Eaves 1986). Further, these studies have demonstrated a genetic vulnerability to PTSD symptoms that is independent of the effects of combat exposure and the genetic influences on that exposure (True et al. 1993).

The above-noted independence of genetic effects on PTSD vulnerability and combat exposure was based on a cross-sectional twin study of PTSD symptoms performed more than a decade after military service in Vietnam. Because the behavioral effects of genes can change over the life cycle (Lyons et al. 1995), it remains unknown to what extent these relationships would change over time.

The present study examines the persistence and change of PTSD symptoms in a population-based sample of veterans. Using twins from the Vietnam Era Twin Registry, a longitudinal co-twin control study was conducted that assessed PTSD symptoms at two points a decade apart (1987 and 1997). With these data, we address three questions: Do symptoms of PTSD persist over longer periods of time? Is the strength of the combat exposure-PTSD association maintained over time? Does the lack of overlap between the genes that influence exposure to combat and vulnerability to PTSD (i.e., the absence of “genetic co-variation”) change over time?

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**Subjects and methods**

**The Vietnam Era Twin Registry**

The Vietnam Era Twin (VET) Registry is one of the only national registries of twins in the US (Goldberg et al. 2002). The VET Registry was assembled from computerized records maintained by the Department of Defense (DoD), supplemented with data from Veterans Affairs (VA) computer files. A computerized record linkage methodology was developed that identified pairs of records that had a reasonable probability of being twins. The algorithm that was used involved the following criteria: males, born between 1939 and 1957, served on active duty during the Vietnam era (the interval 1965–1975), same last name, different first name, same date of birth, and similar Social Security numbers. Possible twins were identified from review of the hardcopy military records and twinship was subsequently confirmed for approximately 7,500 twins.

**Survey data collection**

In 1987, a 24-page survey was mailed to all twin pairs; after three waves of mailing, telephone follow-up was initiated. The survey collected a broad spectrum of health measures and assigned zygosity (Eisen et al. 1989) from responses to twin similarity questions. In total, 10,979 individuals responded to the mail and telephone survey for a 74% response rate; the pairwise response rate for twins was 64%, representing 4,774 pairs. Of the responding pairs, slightly more than 53% were monozygotic and 44% were dizygotic. Zygosity could not be assigned in 3% of the pairs.

In the 1987 survey, all twins were asked about their service in Southeast Asia. Based on this question, we identified 922 pairs where both twins served in SEA, 1,767 pairs where neither twin served in SEA, and 1,728 pairs where one twin served in SEA and the other twins served elsewhere. Combat exposure was assessed in those individuals who reported serving in SEA by asking each a series of 18 questions about specific military experiences (Goldberg et al. 1990). An ordinal index of combat exposure was created from these items (SEA service with no combat, and SEA service with low, medium, and high combat); this index was validated against combat-related medals and has good internal and test-retest reliability (Janes et al. 1991).

In 1997, a telephone follow-up survey of all twins who were discordant for SEA service was undertaken in preparation for a study of the origin of psychophyslogic abnormalities in PTSD (Orr et al. 2003). Out of the 1,728 SEA discordant twins identified in 1987, a total of 696 twin pairs both responded to the 1997 survey and provided complete data. These 696 pairs represent the analytic sample for the present study. Respondents to the 1997 survey were no different than non-respondents for SEA service and zygosity; however, non-respondents were significantly (p < 0.001) more likely to be older, served in combat and experienced symptoms of PTSD.

**Assessment of PTSD symptoms**

Fifteen question items in the 1987 survey collected information on PTSD symptoms (True et al. 1993). The items broadly correspond to the criteria specified in the Diagnostic and Statistical Manual of Mental Disorders, which include symptoms relating to re-experiencing, avoidance and increased arousal. Twins were asked to indicate the frequency of symptoms (very often, often, sometimes, almost never, never) during the preceding 6 months. The PTSD symptom questions were asked with reference to “your time in the military” so that twins who did not serve in Southeast Asia could also respond. In the 1997 telephone survey, PTSD symptoms were measured using the Mississippi PTSD symptom scale (Keane et al. 1988); a civilian version of the items was administered to those who did not serve in SEA (Keane et al. 1988). This 35-item, 5-point Likert, self-report scale has high internal consistency, test-retest reliability, convergent validity (with the SCID interview) and discriminant validity for identifying veterans with and without PTSD (Keane et al. 1988).

**PTSD symptom scale construction**

From the 1987 PTSD symptoms, we constructed an overall score by summing the item responses across all 15 questions. Scores ranged from 15 to 75 with a mean of 26.2 (s. d. = 10.2) and a median of 24. Cronbach’s alpha for the 1987 PTSD symptom score was 0.9 indicating a high degree of internal consistency. The same PTSD symptom questions were previously administered to a sub-sample of 150 twin pairs as part of the pilot study for the VET Registry that was conducted in 1984. From the 192 individuals who responded to both the 1984 and 1987 questionnaires, we calculated the test-retest reliability of the PTSD symptom score to be 0.6.

The Mississippi PTSD items collected in 1997 were used to create a scale by summing each of the individual items (Keane et al. 1988). The Mississippi scores ranged from 37 to 151 and had a mean of 67.6 (s. d. = 17.8); Cronbach’s alpha was 0.9 indicating a high degree of internal consistency.