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Genetic and Environmental Influences on the Relationship Among Combat Exposure, Posttraumatic Stress Disorder Symptoms, and Alcohol Use

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The role of genetic and environmental influences on the relationship between combat exposure, posttraumatic stress disorder (PTSD) symptoms, and alcohol use were examined in 4072 male–male twin pairs who served in the United States military during the Vietnam era (1965–1975). Results indicate that the relationship between combat and alcohol use and between PTSD symptom factors and alcohol use were both substantially influenced by genetic factors. Findings are most consistent with a shared vulnerability model for the etiology of the association between PTSD symptoms and alcohol use. Specific unique environmental factors were more important than genetic factors for PTSD symptoms, and both factors were equally important for alcohol use. Further support is also found for the role of the unique environment in PTSD symptoms.

KEY WORDS: posttraumatic stress disorder; alcohol use; combat; genetic; twins.

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According to the National Vietnam Veterans Readjustment Study (NVVRS), approximately 20 years following discharge from military service 15.2% of all male Vietnam theater veterans continue to suffer from PTSD and 11.2% suffer from an alcohol-related disorder (Kulka et al., 1990). Furthermore, dual diagnosis of alcohol abuse and PTSD occurs frequently (Engdahl, Dikel, Eberly, & Blank, 1998; Jelinek & Williams, 1986). The NVVRS found that 75% of male veterans with PTSD had a lifetime history of an alcohol-related disorder and 22% of those with active PTSD also met criteria for current alcohol abuse or dependence. The high rates of comorbidity between these two disorders raises the question of a shared etiology.

When considering the issue of comorbidity between two mental disorders, there are several possible hypotheses to consider (Kessler, 1995; Lyons, 1995). One possibility is that the two disorders may share an environmental risk factor or stressor that increases the possibility that they will occur together. This will be referred to as the "shared stressor hypothesis." A high rate of combat exposure is associated with increased risk for both PTSD and alcohol abuse or dependence (Card, 1987; Kulka et al., 1990; Jordan et al., 1991; Laufer, Brett, & Gallops, 1985). According to the NVVRS, a fourfold increase in PTSD was found in male veterans with high combat exposure versus those who had low or moderate combat exposure (Kulka et al., 1990). Similarly, this same study found that male veterans who had experienced high rates of combat exposure were significantly more likely to suffer from an alcohol-related disorder than those who experienced low or moderate levels of combat exposure.

The interpretation of the results of this and other studies has been hindered, however, by the lack of an adequate comparison group for high combat veterans and, therefore, the inability to control for precombat factors that might influence the relationship among combat, PTSD, and alcohol use. One approach to identifying a control group is to study monozygotic (MZ) twin pairs who are discordant on the variable of interest (Goldberg, Eisen, True, & Henderson, 1990; Goldberg, True, Eisen, & Henderson, 1990). By using MZ twin siblings as a control group, these studies accounted for the many potential confounding factors (genetic endowment, parental socioeconomic status, family discord, etc.) that may have influenced the results of previous studies. The results of this analysis were consistent with those of previous studies that found that veterans exhibited more PTSD symptoms with increasing levels of combat exposure (Goldberg, True, et al., 1990). In terms of alcohol use, however, there was only a relatively modest association between combat exposure and high levels of alcohol consumption once the relationship was adjusted for cotwin effects. This indicates that other factors, besides combat exposure, were important influences on long-term drinking patterns (Goldberg, Eisen, et al., 1990). Thus, it seems that the relationship between PTSD and alcohol use is not simply a function of their both being associated with high levels of combat exposure; some other factor seems to be important in the relationship between these two disorders.

A second hypothesis regarding the relationship between PTSD and alcohol problems is that one may develop as a consequence of the other (Kulka et al., 1990). This will be referred to as the "consequence of PTSD hypothesis." One of the most common explanations for the association of PTSD symptoms with high alcohol consumption or alcohol-related disorders or both is the self-medication hypothesis that holds that veterans use alcohol to medicate the reexperiencing and hyperarousal symptoms of PTSD (Centers for Disease Control, 1988). Many clinical accounts have proposed that disorders such as substance abuse, depression, and antisocial personality are a consequence of PTSD (see Herman, 1992; Wilson, 1988). In this context, alcohol use is an aspect of the avoidance part of the PTSD syndrome; alcohol acts as a nervous system depressant and thus allows the veteran to avoid feelings and images associated with the Vietnam experience (Kulka et al., 1990).

Given that most studies of Vietnam veterans are retrospective, the self-medication hypothesis has been difficult to test empirically. For the self-medication hypothesis to be empirically supported, however, it would seem that alcohol consumption among veterans with PTSD should be related to their level of PTSD symptomatology. In fact, evidence for a correlation between PTSD symptoms and changes in alcohol consumption is conflicting. In a study of high-combat Vietnam veterans, it was found that subjects with more PTSD symptoms as well as subjects with fewer PTSD symptoms had increased alcohol consumption after the war (Gallers, Foy, Donahoe, & Goldfarb, 1988). A longitudinal study, however, found that low self-confidence and high liquor consumption during service to be the only antecedent predictors of high PTSD in Vietnam veterans (Card, 1987). Because the behaviors occurred simultaneously, it is impossible to determine whether heavy liquor consumption was a precursor of PTSD or a consequence of ongoing combat-related problems. From these studies it is unclear whether alcohol-related disorders operate as a vulnerability for PTSD or are a consequence of acquiring the disorder.

A third hypothesis regarding the relationship between PTSD and alcohol problems is that they occur together because of a shared vulnerability that increases risk for both disorders. This will be referred to as the "shared vulnerability hypothesis." This vulnerability could be environmental (e.g., due to shared experiences within the family) or genetic in nature. Several studies support the possibility of a shared genetic vulnerability for PTSD and alcohol use. A family history study of a sample of Vietnam, Korea, and World War II veterans with chronic PTSD found that patients with PTSD had a higher prevalence of alcoholic siblings than did a control group of depressed and anxious patients (Davidson, Swartz, Storck, Krishnan, & Hammett, 1985). A recent study using data from the Vietnam Era Twin Registry (VETR) found evidence for a shared genetic vulnerability for PTSD and alcohol dependence (Xian et al., in press). This study did not, however, test whether this shared vulnerability between PTSD and alcohol dependence was related to or

independent from that for trauma exposure. Other studies have not found a familial association between PTSD and alcohol-related disorders (Davidson, Smith, & Kudler, 1989; Davidson, Tupler, Wilson, & Connor, 1998).

There is strong evidence for the important role of genetic influences in the etiology of both alcohol-related disorders and PTSD. Although the data are far too extensive to be reviewed here, many studies have observed that abuse of alcohol occurs in families, and twin studies support a genetic influence on the occurrence of alcohol abuse (Grove et al., 1990; Hrubec & Omenn, 1981; Kaij, 1960; Pickens et al., 1991). Genetic influences on the occurrence of PTSD symptoms have been described (True et al., 1993). Combat was a strong predictor only for the reexperiencing cluster and the single symptom of avoided activities. The authors concluded that genetic influences may condition the phenotypic responsiveness to certain aspects of the environment and that certain genetically influenced factors (e.g., temperament) might predispose an individual to a certain trauma response. The study also found that childhood and adolescent environmental factors shared by siblings do not substantially contribute to the susceptibility to PTSD symptoms (True et al., 1993).

The three hypotheses described earlier offer contrasting explanations for co-occurrence of alcohol problems and PTSD symptoms. The goal of this study is to use biometrical modeling to test these three hypotheses and thus provide additional information about the genetic and environmental influences on exposure to combat, PTSD symptoms, and alcohol use. The technique of biometrical modeling allows us to disentangle the genetic and environmental influences that are specific to phenotypic (observed or manifest) behaviors or symptoms and those common to a number of different behaviors and symptoms. Specifically, this technique enables us to test whether a genetic or environmental influence that is specific to one factor (alcohol use) also influences the expression of another factor (PTSD symptoms).

Each of the three hypotheses specified earlier makes different predictions with regard to the model best explaining the role of genetic and environmental influences on the phenotypic expression of combat exposure, PTSD symptoms, and alcohol use individually and in relation to each other. A model consistent with the shared stressor hypothesis would indicate that the phenotypic association between PTSD and alcohol use is primarily explained by environmental influences specific to combat. According to this model, we observe PTSD and alcohol use occurring together because they both occur in response to combat exposure. Environmental influences specific to PTSD symptoms would not influence alcohol use nor would genetic influences specific to combat influence either PTSD symptoms or alcohol use. A model consistent with the consequence of PTSD hypothesis (where alcohol use is in response to having PTSD) would indicate a significant association between environmental influences specific to PTSD symptoms and alcohol use; that is, alcohol use occurs because an individual is experiencing PTSD symptoms. The environmental or genetic influences specific to combat would not primarily explain the association between PTSD symptoms or alcohol use. Finally, a model consistent with the shared vulnerability hypothesis would indicate that combat, PTSD symptoms, and alcohol use occur together because genetic or environmental influences specific to one or more of these variables influence the others. For example, PTSD and alcohol use might occur together because of a shared genetic vulnerability; that is, genetic influences specific to alcohol use would also influence PTSD symptoms.

Method

Participants

Data were obtained from the 1987 Survey of Health that was administered to members of the Vietnam Era Twin (VET) Registry (Henderson et al., 1990). The registry consists of 7375 male twin pairs born between 1939 and 1957 in which both members of the pair served in the military during the Vietnam war. Potential twins' pairs were identified through a search of a computer file of the Department of Defense of discharged military personnel, using an algorithm that matched data entries for same last name, same birth date but different first name. Twinship was confirmed by military records. Analyses demonstrated no consistent pattern of ascertainment bias for factors related to the physical and psychosocial health of veteran pairs (Goldberg, True, Eisen, Henderson, & Robinette, 1987). The survey was administered by mail or phone (99%) or in-person interview. A casewise response rate of 74.4% and a pairwise rate of 64.7% was achieved. Reasons for nonresponse included no response to repeated mailings or telephone calls, 12.4%; refused, 9.5%; death, 2.7%; unavailable for study (either outside the United States or too ill to respond), 0.5%; and ineligible, 0.4% (Eisen, True, Goldberg, Henderson, & Robinette, 1987). Eligibility criteria in this study included survey completion by each sibling of twin pairs and sufficient accuracy in zygosity determination. Zygosity was determined using a self-report questionnaire and blood group type from military records. Self-report questionnaires offer an affordable and reliable assessment of zygosity in large samples (Eisen, Neuman, Goldberg, Rice, & True, 1989). Final analyses were based on 2249 monozygotic and 1823 dizygotic pairs.

Sample characteristics. The sample was 93.2% Caucasian, 6.3% African American; 91.8% were married, 7.2% were single; 10.7% had at least some graduate school education, 37.5% were college educated, 15.4% had post-secondary-school vocational training, 35.6% were high school educated; 90.4% were employed full time, 1.9% were employed part time, and 6.2% were not employed; 17.6% had a yearly family income in 1987 less than $20,000, 47.5% had a yearly family income between $20,000 and $40,000, 32.7% had a yearly family income over $40,000; and 39.1% of the sample served in Vietnam

Because of the large sample size and the geographic distribution of the sample, in-person interviewing was not possible. Test-retest reliability of PTSD symptoms based on a subsample of 150 twins who participated in both a pilot study and the actual study was adequate. Kappas ranged from .26 for angry and aggressive behavior to .54 for having repeated dreams about the military. Alcohol consumption measures had a weighted kappa of .55, and high consumption had a kappa of .57. Abstinence reports were found to be reliable ($\kappa = .43$).

Measures

Posttraumatic stress disorder symptomatology. Symptoms were queried with regard to traumatic exposure while in the military. Fifteen items that closely resemble *DSM-III-R* symptoms were included in the questionnaire. Each subject was asked to respond whether he had experienced each symptom in the preceding 6 months either very often, often, sometimes, almost never, or never. Two items from *DSM-III* were also included: felt guilty and memory problems (True et al., 1993).

Alcohol use. The survey gathered data on current and past alcohol consumption. Lifetime abstainers were defined as those who reported consuming fewer than 20 alcoholic drinks in their lifetime. Subjects who reported current alcohol consumption were asked the average number of days per week they currently drink and the number of drinks they consume per day on drinking days. Several categories of drinking were used for analysis (Goldberg, Eisen et al., 1990). Abstainers were defined as those who consume 0.0 ounces of ethanol per day; light drinkers, 0.01–0.21 ounces; moderate drinkers, 0.22–0.99 ounces; and heavy drinkers, 1.00 or more ounces per day. To calculate average alcohol consumption, an unspecified drink is assumed to have 0.5 ounces of ethanol.

Combat exposure. Subjects who served in Southeast Asia during the Vietnam war were queried about 18 combat roles and experiences. Reliability and validity of the combat exposure index has been demonstrated (Janes, Goldberg, Eisen, & True, 1991). Test-retest reliability of the index ($\kappa = .84$) was excellent. The validity of the measure was also high, as judged by the observation that the probability of receiving a Purple Heart, Bronze Star, Commendation Medal, and a Combat Infantry Badge increased substantially with each level of combat exposure ($p < .001$). In this study, combat was used as a continuous variable with scores ranging from 0 (*never experienced any combat*) to 18 (*experienced each category of combat at least once*).

Data Analyses

To determine how PTSD symptoms cluster together, a principal components factor analysis with Varimax rotation of the PTSD symptoms was performed. Because data derived from twin siblings are not statistically independent, separate factor analyses were performed for Twin 1 and Twin 2. Assignment of a twin as Twin 1 or Twin 2 was random and the results were indistinguishable for twin groups. The data were then pooled and factor analyses were performed again using the entire sample. The derived factors were then compared with the clusters of the PTSD diagnosis as defined by *DSM-III-R*.

The twin method compares the degree of similarity within MZ pairs with the degree of similarity within DZ pairs. For this study, a computed PTSD factor score for each twin, based on the results of the two-factor solution mentioned previously, was generated by adding the symptom scores in each factor and dividing it by the number of symptoms in the factor. Pearson product moment correlations were calculated for each PTSD factor. Pearson product moment correlations were then calculated for exposure to combat. Scores on the alcohol use scale were ordinal and therefore polyserial correlations were calculated. Comparison of MZ versus DZ twins were obtained by chi-square analyses comparing differences between the size of the correlations. When MZ twin pairs have significantly greater correlations on any outcome variable than DZ twin pairs do, it indicates a genetic influence.

Next, traditional correlation techniques were used to determine the within individual correlations between combat, alcohol, and PTSD factor scores. All subjects were included in these analyses. Alcohol scores, because they had been transformed into levels of alcohol use, were ordinal. PTSD factor scores and incidents of combat were interval variables. Correlations between interval variables were Pearson product moment correlations; correlations between ordinal variables were polychoric correlations; correlations between ordinal and interval variables were polyserial. Tests of significance calculations were by chi-square analyses.

Using the path coefficients model of univariate twin analysis, genetic and environmental estimates were obtained for each factor. Using the phenotypic correlations, univariate structural equation models can be used to estimate the proportion of phenotypic variance attributable to additive (A) and dominance (D; referring to nonadditive interactions of alleles at the same locus) genetic effects; common, shared, or family environmental effects, (C); and unique or nonshared environmental effects (E). The E term reflects influences that are specific to individuals rather than the paid and random error; these influences promote dissimilarity between pairs (Neale & Cardon, 1992). The full model is compared with reduced models that delete either additive genes or common environment.

If there is significant additive genetic variance, a model including dominant genetic effects is tested. Additive genetic effects reflect the actions of a large number of genes, each of small effect, whose influences combine in an additive fashion to produce differences at the phenotypic level. The two phenomena that produce nonadditive genetic variance are dominance and epistasis. Dominance refers to a significant influence from one specific locus. If the individual is heterozygous

for his or her alleles at that locus, the phenotype is most strongly influenced by the allele that is said to be dominant (Neale & Cardon, 1992). The other phenomenon that can produce nonadditivity is epistasis, which refers to an interaction between genes at more than one locus. That is the influence of a specific allele at one locus is altered depending on the allele present at some other locus. When the correlation between MZ twins is more than twice as large as that for DZ's, it suggests that at least some of the genetic variance in the phenotype is because of nonadditive genetic factors. Parameters are estimated by the method of weighted least squares, using the inverse of the asymptotic variances of the correlations as the weights, which ensures that appropriate chi-square values are obtained from the analysis of a correlation matrix (Neale & Cardon, 1992). In this analysis, the phenotypic outcome variable was Twin 1's (T1) score and Twin 2's (T2) score on each PTSD factor. Using a model-fitting statistical software package (LISREL) several models were tested to determine the model that best fits the data.

Relating this to our specific hypotheses, a model consistent with the shared stressor hypothesis would indicate that the phenotypic association between PTSD and alcohol use is primarily explained by environmental influences specific to combat (E_{combat}). According to this model, this hypothesis would be supported if the phenotypic (observed) association between PTSD symptoms and alcohol is explained primarily by E_{combat}. Environmental influences specific to PTSD symptoms (E_{PTSD}) would not influence alcohol use nor would genetic influences specific to combat (A_{combat}) influence either PTSD symptoms or alcohol use. A model consistent with the consequence of PTSD hypothesis (where alcohol use is in response to having PTSD) would indicate a significant association between environmental influences specific to PTSD symptoms (E_{PTSD}) and alcohol use. The environmental or genetic influences specific to combat (E_{combat}, A_{combat}) or PTSD (E_{PTSD}, A_{PTSD}) would not primarily explain the association between PTSD symptoms or alcohol use. Finally, a model consistent with the shared vulnerability hypothesis would indicate that combat, PTSD symptoms, and alcohol use occur together because common environment (C) or genetic influences (A) specific to one or more of these variables influence the observed variation in one of the others. For example, PTSD and alcohol use might occur together because of a shared genetic vulnerability; that is, genetic influences specific to PTSD (A_{PTSD}) influence alcohol use.

A chi-square difference test was used to compare the full model (ACE) with specific submodels that remove either genetic or common environmental effects (A or C). The chi-square tests evaluate the difference in the chi-square of the full versus the reduced model and is distributed as chi-square with *df* equal to *df*(reduced) minus *df*(full). If the chi-square is not significant, the reduced model is accepted.

Another method used to determine the best fitting model was the Akaike's Information Criterion (AIC) that equals the chi-square value minus twice the degrees of freedom (Neale & Cardon, 1992). The lowest value of AIC reflects the best balance of goodness-of-fit and parsimony (Kendler, Heath, Neale, Kessler, & Eaves, 1992). When the best model was determined, the parameter estimates supplied by LISREL were ascertained.

Results

Factor Analysis of PTSD Symptoms

Table 1 illustrates the two-factor solution that converged in three iterations for PTSD symptoms. Factor 1 contained symptoms primarily from the avoidance cluster (C) and increased arousal cluster (D) of *DSM-III-R*. Factor 2 included all symptoms from the reexperiencing cluster (B) and the specific symptoms avoided activities and felt guilt. Variance attributable to Factor 1 was 47% and Factor 2 was 13%.

For this sample, a two-factor solution appeared more parsimonious than for the three *DSM-III-R* clusters. Factor 1 essentially collapses the avoidance and increased arousal clusters of *DSM-III-R*. Symptoms from each cluster appear relatively equally represented within the factor. Factor 1 may best be described as the avoidance/arousal factor. Factor 2 may best be described as the reexperiencing factor.

Table 1. Rotated Factor Matrix of PTSD Symptoms: All Participants

PTSD symptom clusters	*DSM-III-R* (Cluster)[a]	Factor 1 (Probands)[b]	Factor 1 (Cotwins)[b]	Factor 2 (Probands)[c]	Factor 2 (Cotwins)[c]
Lost interest	C	80	79	17	16
Felt distant	C	77	77	27	25
Irritable and short-tempered	D	75	76	22	19
Angry or aggressive behavior	D	72	73	28	25
Trouble concentrating	D	74	72	25	25
Life is not meaningful	C	74	71	25	21
Memory problems	*DSM-III*	72	70	16	18
Easily startled	D	64	62	43	43
Trouble falling asleep, staying asleep, or sleeping too much	D	55	59	19	22
Painful memories	B	23	24	82	82
Event was happening over again	B	22	25	79	80
Avoided activities	C	19	18	77	75
Feelings or actions became stronger	B	25	27	75	76
Dreams or nightmares	B	22	23	74	77
Felt guilty	*DSM-III*	27	26	65	65

Note. Varimax Rotation converged in 3 iterations for each group of cotwins (Each score is multiplied by 100 and rounded to the nearest integer).
[a]For *DSM-III-R* diagnosis of PTSD, "B" refers to the reexperiencing cluster, "C" the avoidance/numbing cluster, "D" the arousal cluster. "Memory problems" and "feels guilt" are symptoms that are not included in the *DSM-III-R* diagnosis of PTSD but are taken from the *DSM-III*.
[b]Factor 1 is made up of "avoidance/arousal" symptoms taken mainly from Clusters C and D.
[c]Factor 2 is made up primarily of "reexperiencing" symptoms from Cluster B.

Table 2. MZ and DZ Within Twin Pair Correlations for PTSD Symptom Factors 1 and 2, Alcohol Use, and Exposure to Combat

Symptom	MZ Pairs ($N = 4498$)	DZ Pairs ($N = 3646$)
Factor 1: Avoidance/arousal	.36	.16
Factor 2: Reexperiencing	.27	.13
Alcohol use	.54	.27
Exposure to combat	.25	.12

Note. Correlations are Pearson product moment correlation, except for those involving alcohol use, which are polyserial correlations. MZ = monozygotic; DZ = dizygotic. Comparisons between MZ versus DZ used chi-square test of significance ($p < 0.001$).

Genetic and Environmental Influences on PTSD Symptoms, Alcohol Use, and Combat

Table 2 reports the cross-twin correlations between MZ and DZ twins for PTSD factors, alcohol use, and combat. Genetic and environmental influences on each PTSD item have been reported previously (True et al., 1993). Chi-square analyses confirmed that each variable had a substantial difference in MZ versus DZ correlations.

Phenotypic Correlations Between Combat, Alcohol Use, and PTSD

Table 3 illustrates the phenotypic (manifest) correlations between alcohol use, PTSD factors, and combat. All correlations were significant at the $p < .01$ level.

Genetic and Environmental Contributions to PTSD, Alcohol Use, and Combat

Two alternative methods were employed for selecting the most parsimonious model, AIC and the Maximum Likelihood Ratio Function (LR). Using AIC, several parameter estimates were below 0.10, indicating that these standardized estimates account for less than 1% of the variance. Because the sample size is large,

Table 3. Phenotypic Correlation Matrix for Combat Exposure, Alcohol Consumption, and PTSD Factors

	Combat	Alcohol	Factor 1: Avoidance/arousal	Factor 2: Reexperiencing
Combat	1.00			
Alcohol	0.06	1.00		
Factor 1: Avoidance/arousal	0.10	0.08	1.00	
Factor 2: Reexperiencing	0.46	0.06	0.10	1.00

Note. Correlations are Pearson product moment correlation, except for those involving alcohol use, which are polyserial correlations. All correlations were significant ($p <$ [illegible]

another statistical technique for model-fitting, LR, was employed (Neale & Cardon, 1992).

Table 4 gives the results for the LR method and eliminated parameters that in the AIC method were near zero. Because the LR results are statistically valid and offer more reasonable interpretive value, the focus of subsequent discussion will pertain to the results of the LR model-fitting figures. Dominant genetic factors were excluded by the model-fitting results. Therefore, the term genetic influences will be used to designate solely additive effects. Common environment was also excluded by model fitting results.

The first column in Table 4(Part A) indicates that the genes that influence combat exposure also influence alcohol consumption ($r = .21$), avoidance/arousal symptoms ($r = .36$), and reexperiencing symptoms ($r = .27$). However, the genes that influence expression of alcohol consumption did not influence expression of other phenotypes studied here. This was also true for the two PTSD factors. Regarding environmental influences on phenotype expression, with the exception of the environmental influence on combat exposure shared with the reexperiencing factor, each environmental influence had a significant effect only on its own phenotypic expression.

Unique environmental influences appeared more important than genetic influences for exposure to combat (.96 vs. .29). Unique environmental influences appeared about equally important with genetic influences on alcohol use (.68 vs. .70). Unique environmental influences appeared more important than genetic influences for each PTSD factor.

Table 4. Cholesky Analysis of Combat Exposure, Alcohol Consumption, and PTSD Symptom Factors 1 and 2 by Likelihood Ratio

A. Genetic influences

	Additive Genetic Influences Specific to:			
	Combat	Alcohol use	Factor 1: Avoidance/arousal	Factor 2: Reexperiencing
Combat	.29			
Alcohol	.21	.70		
Factor 1: Avoidance/arousal	.36	—	.47	
Factor 2: Reexperiencing	.27	—	—	.45

B. Environmental influences

	Unique Environmental Influences Specific to:			
	Combat	Alcohol use	Factor 1: Avoidance/arousal	Factor 2: Reexperiencing
Combat	.96			
Alcohol	—	.68		
Factor1: Avoidance/arousal	—	—	.80	
Factor 2: Reexperiencing	.40	—	—	[illegible]

Discussion

This study employed biometrical modeling to test hypotheses about the role of genetic and environmental factors on the relationship among combat exposure, PTSD symptoms, and alcohol use. By analyzing data from 4072 twin pairs, both of whom were in military service during the Vietnam War, we demonstrated that the same additive genetic influences that affect the level of combat exposure also influence the level of alcohol use and level of avoidance/arousal and reexperiencing symptoms. These findings are most consistent with the shared vulnerability hypothesis in that combat exposure, PTSD symptoms, and alcohol use are associated because some portion of the genes that influence vulnerability to combat also influence vulnerability to alcohol consumption and to PTSD symptoms. Specific unique environmental factors were, however, more important than genetic factors for PTSD symptoms and for current alcohol use.

Previous work by our group is also consistent with these findings. Analyzing data from the same participants, Lyons et al. (1993) found that genetic and unique environmental factors, not shared environmental ones, predispose to volunteering for military service and to exposure to combat in Vietnam. They also found that 57% of the covariance for volunteering and exposure to combat is attributable to shared genetic variance, concluding that some of the personal characteristics that lead a man to volunteer for service in a war zone might lead him to become involved in a greater number of combat-related experiences. These individual characteristics might represent some personality factor, such as impulsivity or sensation seeking, which influences a young man to volunteer for service at a younger age and to be exposed to higher levels of combat (Lyons et al., 1993; Wilson, 1988; Zuckerman, 1991). Not surprisingly, personality factors such as impulsivity or sensation seeking have been strongly associated with increased vulnerability for developing an alcohol-related disorder (Sher & Trull, 1994). These personality factors have not been studied in the context of vulnerability to developing combat-related PTSD. This and studies of other populations suggest, however, that certain familial and behavioral factors, such as a family history of antisocial behavior and childhood conduct problems, influence an individuals vulnerability to developing PTSD (Breslau, Davis, Andreski, & Peterson, 1991; Breslau & Davis, 1992; Helzer, Robins, & McEvoy, 1987; King et al., 1996). Antisocial behavior and childhood conduct problems have both been associated with the personality traits of impulsivity and sensation seeking (Zuckerman, 1991). Taken together, these data suggest that personal characteristics that are, at least in part, genetically transmitted (e.g., impulsivity), might provide a common vulnerability to combat exposure, PTSD, and alcohol use.

With regard to environmental influences, this study also provides support for the view that unique environmental influences or experiences that twins did not share (including unshared familial influences) influence combat exposure, alcohol use, and the expression of PTSD symptoms. Our study does not examine the specifics of these unique environmental influences. It does suggest that these unique environmental influences may be different for alcohol use and PTSD. For example, exposure to other types of traumatic events might influence PTSD symptoms whereas drinking patterns among peers might influence alcohol use. In addition, the environmental experiences that twins do not share are more important than genetic influences for both exposure to combat and each PTSD factor. The importance of the unique environment has previously been demonstrated in members of the VET-R with regard to combat exposure and volunteering for Vietnam service (Lyons et al., 1993), PTSD symptoms (True et al., 1993), and alcohol dependence (Xian et al., in press).

The results of this study did not support the shared stressor hypothesis in that environmental influences specific to combat were significantly associated only with reexperiencing symptoms. Environmental influences specific to combat did not influence alcohol use or avoidance/arousal symptoms. In terms of environmental influences on PTSD symptoms, the exclusion of common environment in the best fitting model for the expression of the PTSD phenotypes deserves comment. Intuitively, it might be expected that early childhood experiences effect vulnerability to future PTSD symptoms and alcohol use. The findings of this study indicate that the experiences that twins shared do not significantly influence their vulnerability to PTSD symptoms or alcohol use. For example, children who are raised by parents who foster development of effective coping styles might be expected to respond better than others to traumatic events of adulthood. On the other hand, children who share the experience of being raised in an abusive family might be expected, once exposed to combat, to be more likely to develop PTSD symptoms or increased alcohol use in adulthood. Data from this study suggested that the influence of the common environment is small at best. Instead, it seems that the influence of the shared environment on adult symptoms and behavior declines as the individual proceeds through adulthood (Lyons et al., 1995).

The results of this study were not consistent with the consequence of PTSD hypothesis for the association between PTSD symptoms and alcohol use. Environmental influences specific to PTSD symptoms were not associated with alcohol use. This may be due to relatively high levels of alcohol use and alcohol-related disorders among veterans in general (Bowman, 1986; Faustman & White, 1989; Kulka et al., 1990; Orsillo et al., 1996). Important limitations exist, however, with regard to our ability to test the consequence of PTSD hypothesis thoroughly. Because measures of PTSD symptoms and alcohol use were taken 15 to 20 years following military service, we are unable to distinguish between factors influencing onset versus course of alcohol use. In addition, it is important to note that this study examined the relationship between combat and alcohol consumption, not alcohol-related disorders. Although, in a large treatment-seeking sample of veterans, alcohol-related disorders were not associated with PTSD status

(Orsillo et al., 1996). Veterans exposed to high versus low combat may have the same levels of alcohol consumption but the former may be more vulnerable to an alcohol-related disorder.

The use of a self-report questionnaire to collect data is the primary limitation of this study. However, the size and uniqueness of this sample outweigh the disadvantages posed by self-report methodology. A further limitation of this study is the exclusive use of a continuous measure of PTSD symptoms and alcohol use rather than including *DSM* diagnoses of PTSD and alcohol abuse/dependence. Thus, the relationships discussed in this study are between PTSD symptom factors and levels of alcohol use. These relationships may not necessarily be the same for *DSM-III-R* diagnoses. Another consideration in interpretation of these results is that the PTSD symptoms and measures of alcohol use are measured up to 20 years after combat experience. Also, the possibility of a cohort effect for alcohol (Heath, Jardine, & Martin, 1989) or PTSD symptom presentation exists, limiting the generalizability of this study.

The advantages of this study relate to its twin design and use of biometrical modeling. This study employed a large cohort of twins, without regard to combat exposure or clinical status, therefore minimizing the possibility that selection bias or confounding variables are likely to explain the results. In addition, the use of biometrical modeling allows for the opportunity to test hypotheses about how the same or different sets of genetic and environmental influences affect more than one psychiatric disorder.

The findings of this study support the shared vulnerability hypothesis. That is, they indicate that the genetic influences that lead to exposure to combat also lead to increased alcohol use and PTSD symptoms. Furthermore, this study rejects the shared stressor and consequence of PTSD hypotheses regarding the relationship among combat, PTSD symptoms, and alcohol use. The results indicate that the relationship among combat exposure and alcohol use was mediated entirely by genetic influences. Instead of environmental influences specific to combat or PTSD symptoms, environmental influences specific to alcohol use (e.g., drinking patterns of peers) are important in determining an individual's level of alcohol use. Taken together, these findings suggest that the self-medication hypothesis does not explain either the association between PTSD symptoms and alcohol use or between combat and alcohol use. Instead, the covariation among combat exposure, PTSD symptoms, and alcohol use is substantially explained by common genetic influences. That is, some genetically transmitted personal characteristics influence the veteran's probability of being exposed to a high level of combat, to PTSD symptoms, and to alcohol use.

Although this study clearly demonstrates that relationship between PTSD symptoms and alcohol use is mediated by genetic influences, this does not negate the importance of environmental factors in the etiology of PTSD symptoms or alcohol use. These results suggest that environmental modification, particularly

for those individuals at risk, may have a profound impact on whether or not those individuals develop PTSD symptoms and a high level of alcohol use.

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References

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., rev.) Washington, DC: Author.

Bowman, B. (1986). Combat stress, posttraumatic stress disorder, and associated psychiatric disturbance. *Psychosomatics, 27,* 567–573.

Breslau, N., & Davis, G. C. (1992). Posttraumatic stress disorder in an urban population of young adults: Risk factors for chronicity. *American Journal of Psychiatry, 149,* 671–675

Breslau, N., Davis, G. C., Andreski, P., & Peterson, E. (1991). Traumatic events and posttraumatic stress disorder in an urban population of young adults. *Archives of General Psychiatry, 48,* 216–222.
Card, J. J. (1987). Epidemiology of PTSD in a national cohort of Vietnam veterans. *Journal of Clinical Psychology, 43*(1), 6–16.
Centers for Disease Control Vietnam Experience Study. (1988). Health Status of VietnamVeterans. I: Psychosocial characteristics. *Journal of the American Medical Society, 259,* 2701–2707.
Davidson, J. R. T., Smith, R., & Kudler, H. (1989). Familial psychiatric illness in chronic posttraumatic stress disorder. *Comprehensive Psychiatry, 30,* 339–345.
Davidson, J. R. T., Swartz, M., Storck, M., Krishnan, R. R., & Hammett, E. (1985). A diagnostic and family study of posttraumatic stress disorder. *American Journal of Psychiatry, 142,* 90–93.
Davidson, J. R. T., Tupler, L. A., Wilson, W. H., & Connor, K. M. (1998). A family study of chronic posttraumatic stress disorder following rape trauma. *Journal of Psychiatric Research, 32,* 301–109.
Engdahl, B., Dikel, T. N., Eberly, R., & Blank, A. (1998). Comorbidity and course of psychiatric disorders in a community sample of former prisoners of war. *American Journal of Psychiatry, 155,* 1740–1745.
Eisen, S., Neuman, R., Goldberg, J., Rice, J., & True, W. (1989). Determining zygosity in the Vietnam Era Twin Registry: An approach using questionnaire. *Clinical Genetics, 35,* 423–432.
Eisen, S., True, W., Goldberg, J., Henderson, W., & Robinette, C. D. (1987). The Vietnam Era Twin Registry: Method of Construction. *Acta Geneticae Medicae et Gemellologiae, 36,* 61–66.
Faustman, W. O., & White, P. A. (1989). Diagnostic and psychopharmacological treatment characteristics of 536 inpatients with posttraumatic stress disorder. *Journal of Nervous and Mental Disease, 177,* 154–159.
Gallers, J., Foy, D. W., Donahoe, C. P., & Goldfarb, J. (1988). Posttraumatic stress disorder in Vietnam combat veterans: Effects of traumatic violence exposure and military adjustment. *Journal of Traumatic Stress, 1,* 181–192.
Goldberg, J., Eisen, S. A., True, W. R., & Henderson, W. G. (1990). A twin study of the effects of the Vietnam conflict on alcohol drinking patterns. *American Journal of Public Health, 80,* 570–574.
Goldberg, J., True, W. R., Eisen, S. A., & Henderson, W. G. (1987). The Vietnam Era Twin Registry: Ascertainment bias. *Acta Geneticae Medicae et Gemellologiae, 36,* 67–78.
Goldberg, J., True, W. R., Eisen, S. A., & Henderson, W. G. (1990). A twin study of the effects of the Vietnam war on posttraumatic stress disorder. *Journal of the American Medical Association, 263,* 1227–1232.
Grove, W. M., Eckert, E. D., Heston, L., Bouchard, T. J., Jr., Segal, N., & Lykken, D. (1990). Heritability of substance use and anti-social behavior: A study of monozygotic twins reared apart. *Biological Psychiatry, 27,* 1293–1304.
Heath, A. C., Jardine, R., & Martin, N. G. (1989). Interactive effects of genotype and social environment on alcohol consumption in female twins. *Journal of Studies on Alcohol, 52,* 425–433.
Helzer, J. E., Robins, L. N., & McEvoy, L. (1987). Post-traumatic stress disorder in the general population: Findings of the epidemiological catchment area survey. *New England Journal of Medicine, 317,* 1630–1634.
Henderson, W. T., Eisen, S., Goldberg, J., True, W., Barnes, J. T., & Vitek, M. E. (1990). Vietnam era twin registry: A resource for medical research. *Public Health Report, 105,* 368–373.
Herman, J. L. (1992). *Trauma and recovery.* New York: Basic Books.
Hrubec, Z., & Omenn, G. S. (1981). Evidence of genetic predisposition to alcoholic cirrhosis and psychosis: Twin concordances for alcoholism and its biological end points by zygosity among male veterans. *Alcohol Clinical Experiments and Research, 5,* 207–215.
Janes, G. R., Goldberg, J., Eisen, S. A., True, W. R., & Henderson, W. G. (1991). Reliability and validity of a combat exposure index for Vietnam era veterans. *Journal of Clinical Psychology, 47,* 80–86.
Jelinek, J., & Williams, T. (1986). Posttraumatic stress disorder and substance abuse in Vietnam combat veterans: Treatment problems, strategies, and recommendations. *Journal of Substance Abuse Treatment, 1,* 87–97.
Jordan, B. K., Schlenger, W. E., Hough, R., Kulka, R. A., Weiss, D., Fairbank, J. A., & Marmar, C. R. (1991). Lifetime and current prevalence of specific psychiatric disorders among Vietnam veterans and controls. *Archives of General Psychiatry, 48,* 207–215.
Kaij, L. (1969). *Alcoholism in twins.* Stockholm: Almquist & Wiksell.

Kendler, K. S., Heath, A. C., Neal, M. C., Kesler, R. C., & Eaves, L. J. (1992). A population-based twin study of alcoholism in women. *Journal of the American Medical Association, 268,* 1877–1882.
Kessler, R. C. (1995). The epidemiology of psychiatric comorbidity. In M. T. Tsuang, M. Tohen, & G. E. P. Zahner (Eds.), *Textbook in psychiatric epidemiology* (pp. 179–198). New York: Wiley & Sons.
King, D. W., King, L. A., Foy, D. W., & Gudanowsli, D. M. (1996). Prewar factors in combat-related posttraumatic stress disorder: Structural equation modeling with a national sample of female and male Vietnam veterans. *Journal of Consulting and Clinical Psychology, 64,* 520–531.
Kulka, R. A., Schlenger, W. E., Fairbank, J. A., Hough, R. L., Jordan, B. K., Marmar, C. R., & Weiss, D. S. (1990). *Trauma and the Vietnam war generation: Report of the findings from the national Vietnam veterans readjustment study.* New York: Brunner/Mazel.
Laufer, R. S., Brett, E., & Gallops, M. S. (1985). Symptom patterns associated with posttraumatic stress disorder among Vietnam veterans exposed to war trauma. *American Journal of Psychiatry, 142,* 1304–1311.
Lyons, M. J. (1995). Epidemiology and personality disorders. In M. T. Tsuang, M. Tohen, & G. E. P. Zahner, *Textbook in psychiatric epidemiology* (pp. 407–436). New York: Wiley & Sons.
Lyons, M. J., Goldberg, J., Eisen, S., True, W. J., Tsuang, M. T., Meyer, J. M., & Henderson, W. G. (1993). Do genes influence exposure to trauma? A twin study of combat. *American Journal of Medical Genetics (Neuropsychiatric Genetics), 48,* 22–27.
Lyons, M. J., True, W. J., Eisen, S., Goldberg, J., Meyer, J., M., Faraone, S. V., Eaves, L. J., & Tsuang, M. T. (1995). Differential heritability of adult and juvenile antisocial traits. *Archives of General Psychiatry, 52,* 906–915.
Neale, M., & Cardon, L. R. (1992). *Methodology for genetic studies of twins and families.* Dordrecht, the Netherlands: Kluwer Academic.
Orsillo, S. M., Weathers, F. W., Litz, B. T., Stainber, H. R., Huska, J. A., & Keane, T. M. (1996). Current and lifetime psychiatric disorders among veterans with war-zone related posttraumatic stress disorder. *Journal of Nervous and Mental Disease, 184,* 307–313.
Pickens, R. W., Svikis, D. S., McGue, M., Lykken, D. T., Heston, L. L., & Clayton, P. J. (1991). Heterogeneity in the inheritance of alcoholism. *Archives of General Psychiatry, 48,* 19–28.
Sher, K. J., & Trull, T. J. (1994). Personality and disinhibitory psychopathology: Alcoholism and antisocial personality disorder. *Journal of Abnormal Psychology, 103,* 92–102.
True, W. J., Rice, J., Eisen, S. A., Heath, A. C., Goldberg, J., Lyons, M. J., & Nowak, J. (1993). A twin study of genetic and environmental contributions to liability for posttraumatic stress symptoms. *Archives of General Psychiatry, 50,* 257–264.
Wilson, J. P. (1988). Understanding Vietnam veterans. In F. M. Ochberg (Ed.), *Post-traumatic therapy and victims of violence* (pp. 227–253). New York: Brunner/Mazel.
Xian, H., Chantarujikapong, S. I., Shrerrer, J. F., Eisen, S. A., Lyons, M. J., Goldberg, J., Tsuang, M., & True, W. R. (in press). Genetic and environmental influences on posttraumatic stress disorder, alcohol, and drug dependence in twin pairs. *Drug and Alcohol Dependence.*
Zuckerman, M. (1991). *Psychobiology of personality.* New York: Cambridge University Press.