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Initial Clinical Evidence of Genetic Contributions to Posttraumatic Stress Disorder

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There are few topics in the field of traumatic stress studies that clinicians approach more ambivalently than considerations of genetic factors associated with vulnerability or resistance to traumatization. Historically, individuals suffering from combat-related posttraumatic stress disorder (PTSD) received diagnoses including "soldier's heart" or "neurocirculatory asthenia," and were frequently viewed as possessing characteristics that cast them in a disparaging light, such as "constitutional inferiority" and "lack of virility" (Campbell, 1918; see Krystal *et al.*, 1989). Early studies implicated race as an important factor influencing the vulnerability to psychological stress (cf. Dunn, 1942). However, these studies attempted to use flawed clinical data to support widely held societal prejudices against minority groups, similar to early misguided efforts to characterize the inheritance of intelligence (Gould, 1981). Similarly, German authorities abused genetic arguments to justify denying the claims of Jewish survivors of the Nazi concentration camps for reparation for long-term psychiatric sequelae of their traumatization (Eisler, 1963/1964, 1967; Kestenberg, 1980). The relatively greater progress made in characterizing the environmental factors that influence subsequent stress response, such as the importance of early childhood trauma (Herman, 1992; Krystal, 1988) and the impact of parental traumatization on parent–child relationships (Danieli, 1980; Oliver, 1993; Rosenheck, 1986), further compounds concerns about overestimating genetic factors associated with PTSD.

Yet the pull to study genetic aspects of PTSD is compelling. It grows out of efforts to explain different vulnerabilities to traumatization and distinct patterns of stress response. First, there is increasing evidence that parental PTSD increases the vulnerability to PTSD in their

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children, without a validated explanatory model for this effect (Solomon, Kotter, & Mikulincer, 1988). Second, the debate over the establishment of PTSD in DSM-III (American Psychiatric Association, 1980) focused attention on the need to establish exposure to traumatic stress as the predominating etiological factor for PTSD. However, a series of excellent epidemiological studies succeeded in demonstrating the critical pathogenic role of extreme stress for PTSD (Centers for Disease Control Vietnam Experience Study, 1988; Egendorf, Kadushin, Laufer, Rothbart, & Sloan, 1981; Gleser, Green, & Winget, 1981; Kilpatrick *et al.*, 1989; Kulka *et al.*, 1990). As a result, the research focus has been shifting to other issues, including genetically transmitted risk factors for traumatization and resilience. Third, a careful exploration of genetic traits that predispose to traumatization may reveal characteristics that might be advantageous outside of the extraordinary singularity of traumatic stress, such as bravery, cautiousness, moral rigor, and artistic capacities (Campbell, 1918; Dunn, 1942). Fourth, recent research on PTSD has begun to characterize the neurobiology of this disorder, implicating neurobiological systems whose genetic regulation has been increasingly well delineated (Hyman & Nestler, 1993). Finally, human genetic studies of PTSD trail preclinical research on distinct genotypic patterns of uncontrollable stress response by almost two decades (Krystal, 1990).

Genetic epidemiological models for PTSD begin by acknowledging the multifactorial nature of this disorder (Kendler & Eaves, 1986; True *et al.*, 1993). Generally speaking, the variance in predicting who will develop PTSD (V_{PTSD}) may be explained by the sum of the variance contributed by genetic contributions to PTSD vulnerability (V_G), the variance contributed by common or shared family environmental factors (V_C), and the variance arising from unique factors associated with an individual subject (V_E). Thus the total vulnerability to PTSD may be characterized using the following equation:

$$V_{PTSD} = V_G + V_C + V_E$$

For the purposes of genetic epidemiological studies, it is important to remember that the particular traumatic stress for each individual studied potentially influences this model in two ways: as common environmental influences, and as unique factors. Thus the total environmental influence on a trait would be the sum of V_C and V_E. Family study methods examine *familial* contributions to PTSD vulnerability but do not permit determining the relative genetic and common environmental contributions, represented as the sum of V_G and V_C. However, twin studies comparing monozygotic and dizygotic twins do permit examination of the relative contributions of genetics and family environment.

Application of a genetic epidemiological approach to the study of PTSD requires consideration of the role of the exposure to the traumatic event. The requirement of a particular environmental exposure to reveal an underlying vulnerability to pathology in PTSD may be analogous to phenylketonuria, where a metabolic defect is not evident unless vulnerable individuals are exposed to a poorly tolerated amino acid. Furthermore, the multifactorial nature of PTSD has long suggested to clinicians that heritable and environmental contributions to PTSD were reciprocally related, that is, the stronger the heritable contribution to PTSD, the lower the intensity of the stress needed to cause PTSD (reviewed in Davidson, Swartz, Storck, Krishnan, & Hammett, 1985). However, because the expression of vulnerability to PTSD may not be expressed unless individuals are exposed to extreme stressors, it may be manifest in family members in other forms that could include biological, cognitive, and personality traits, as well as other psychiatric diagnoses.

This chapter reviews the growing number of clinical studies evaluating the contribution of heritable factors to vulnerability to PTSD. In doing so, it provides an initial framework for interpreting genetic contributions to this disorder. There is a growing diversity of approaches

to the study of genetic contributions to psychiatric disorders, character traits, or biological characteristics. To date, there have been no published direct-interview family studies or molecular genetic studies of PTSD patients. Thus, this chapter reviews studies employing two methodologies: family history studies and twin studies.

FAMILY HISTORY STUDIES

Family history studies evaluate the association of psychiatric diagnoses in the family members affected with PTSD in comparison with the family members of another group of patients or healthy subjects. In contrast to the family study method, where family members are interviewed directly in order to determine their lifetime diagnoses, family history studies indirectly assess the diagnoses of family members. In other words, the subject is interviewed about the psychiatric histories of his or her relatives. A validated, structured psychiatric interview for family history assessment has been developed to standardize the collection of information (Andreason, Endicott, Spitzer, & Winokur, 1977). However, family history studies may have limited sensitivity, resulting in underestimation of the occurrence of the disorder within a family and vulnerability to recall biases on the part of the interviewed subjects (Chapman, Mannuzza, Klein, & Fyer, 1994; Kendler *et al.*, 1991; Orvaschel, Thompson, Belanger, Prusoff, & Kidd, 1982).

Although scanty, the preponderance of evidence collected from family history studies suggests that there is an increased risk for PTSD in individuals with a family history of psychiatric illness. For example, one study of firefighters exposed to a brushfire disaster found that 6 of 9 (67%) firefighters who developed chronic PTSD had family histories of psychiatric illness compared to 7 of 34 (20%) firefighters who did not develop PTSD (McFarlane, 1988). In a study of World War II prisoners of war, there was a trend for veterans with a family history of alcoholism, but not other mental illnesses, to have increased likelihood of developing PTSD (Speed, Engdahl, Schwartz, & Eberly, 1989). Similarly, a study conducted in young adults suggested that a family history of anxiety was associated with a threefold increased risk for PTSD after controlling for other risk factors (Breslau, Davis, Andreski, & Peterson, 1991).

Two family history studies conducted in populations with combat-related PTSD suggest that chronic PTSD is associated with a higher rate of familial psychopathology, particularly alcoholism, depression, and anxiety disorders (Davidson *et al.*, 1985; Davidson, Smith, & Kudler, 1989). The earlier of these studies suggested that first-degree relatives of Vietnam veterans with chronic PTSD had higher rates of alcoholism or drug abuse (60%) compared to the first-degree relatives of patients with depression (26%) or generalized anxiety disorder (38%). The first-degree relatives of patients with PTSD also had higher rates of generalized anxiety (22%) compared to the relatives of depressed patients (4%), but not the relatives of generalized anxiety disorder patients (14%). The siblings of Vietnam veterans with chronic PTSD had a higher uncorrected morbidity risk for alcoholism (12%) than did patients with either depression (1.7%) or generalized anxiety disorder (0%), where there was no increased morbidity risk in the parents of these patients. In their second study, Davidson and colleagues were unable to replicate the finding that siblings and parents of patients with PTSD had more elevated rates of anxiety disorders than patients with major depression and alcoholism, or healthy control subjects. However, the parents and siblings of patients with PTSD had higher rates of anxiety disorders, particularly generalized anxiety, than did combat veterans who did not develop PTSD. Also, the children of PTSD and generalized anxiety disorder patients had higher rates of generalized anxiety than did the children of depressed patients. These studies raise the possibility that familial anxiety disorders might contribute to the vulnerability to developing combat-related PTSD.

One factor influencing the findings of family history studies of PTSD are cohort effects, that is, generations who differ with respect to the prevalence of characteristics, such as substance abuse. Given the elevated prevalence of substance abuse among soldiers in the Vietnam war (Kulka *et al.,* 1990), one might be concerned that cohort effects might influence the relative prevalence of substance-abuse disorders in the siblings of Vietnam combat veterans with PTSD. Perhaps reflecting these cohort effects, Davidson and colleagues (1989) found that alcoholism and drug-abuse rates were elevated in the parents and siblings of Vietnam veterans relative to the parents and siblings of World War II veterans. Also, the children of Vietnam veterans with PTSD had a greater risk of developing a chronic psychiatric illness. Again, these effects must be viewed as familial; that is, the study was unable to differentiate the impact of serving in the Vietnam war on parenting from the genetic traits of the veterans studied.

Nagy *et al.* (in review) recently conducted a family history study evaluating the extent to which comorbid panic disorder or vulnerability to yohimbine-induced panic attacks in PTSD patients may be explained by a familial vulnerability for panic attacks. The overlap of panic disorder and PTSD has been of interest in light of evidence that panic disorder rates are elevated in PTSD populations (Kulka *et al.,* 1988; Breslau *et al.,* 1991). This overlap is also suggested by the phenomenological similarity between naturally occurring (Mellman & Davis, 1985) and lactate-induced (Rainey *et al.,* 1987) flashbacks and panic attacks in PTSD patients. Further, yohimbine, a drug that stimulates central noradrenergic activation, provoked panic attacks and flaskbacks in a subgroup of PTSD patients (Southwick *et al.,* 1993) and panic disorder patients (Charney, Woods, Krystal, Nagy, & Heninger, 1992) even though it failed to have this effect in many other diagnostic groups, including alcoholics, schizophrenics, depressed patients, generalized anxiety disorder patients, obsessive–compulsive disorder patients, and healthy subjects. Thus, clinical and neurobiological data warranted the investigation of familial predictors of naturally occurring and yohimbine-stimulated panic in PTSD patients.

Despite the convergence of phenomenological and biological findings, the study by Nagy *et al.* (in review) did not find familial evidence of overlap between panic disorder and PTSD. This study found lower rates of panic disorder in family members of patients with PTSD and comorbid panic disorder (3.1%) or PTSD alone (2.7%) relative to the family members of patients with panic disorder (15.9%). The rates of panic disorder in relatives of patients with PTSD and healthy controls (0%) did not significantly differ. However, the rates of PTSD were elevated in the family members of PTSD patients with (7.2%) and without (12.2%) comorbid panic disorder relative to the absence of PTSD in the relatives of both panic disorder patients and healthy controls. The presence or absence of a yohimbine-induced panic attack did not differentiate the pattern of psychiatric illness in the first-degree relatives of PTSD patients.

TWIN STUDIES

There have been two reports from twin studies related to PTSD. Twin studies are a particularly powerful approach for studying the genetic and environmental contributions to the likelihood of exhibiting a particular trait. Twin studies take advantage of the fact that twins are generally raised in the same environment. Therefore, if monozygotic (identical) twins share a trait more frequently than dizygotic (fraternal twins), it is assumed that the trait is transmitted genetically rather than environmentally. There are limitations to these models. For example, monozygotic twins may not be truly identical in many cases. For example, they may develop as mirror images of each other with opposing laterality, a process that may be influenced by the timing of the separation of the identical twins during embryonic development (Faber, 1981). Al-

though not yet applied to PTSD, two strategies have been applied elsewhere that provide additional insight into genetic and environmental contributions to a particular trait, including studies of twins reared apart and cross-fostering studies (Faber, 1981; Kety, 1987).

A twin study of 4,029 twin pairs who served during the Vietnam War era suggested that genetic factors contributed to many features of their military experience that influenced the degree of likelihood that they would be involved in combat-related trauma (Lyons *et al.*, 1993). Monozygotic (MZ) twins were approximately twice as similar as dizygotic (DZ) twins in their likelihood of their volunteering for service in Southeast Asia (MZ =- .4, DZ = .22; heritability = .36), serving in Southeast Asia (MZ = .41, DZ = .24; heritability = .47), being exposed to a similar degree of combat (MZ = .53, DZ = .30; heritability = .47), and receiving combat decorations (MZ = .52, DZ = .23; heritability = .54). There were no significant effects in this study associated with the shared environment (i.e. $V_C = 0$). This study suggested that genetic factors associated with the likelihood of experiencing situations that might generate PTSD might have influenced the rates of the subsequent development of PTSD in these individuals. These findings are consistent with an increasing number of studies (Burnam *et al.*, 1988; Helzer, Robbins, & McEvoy, 1987) indicating that premorbid factors, such as personality disorder, influenced exposure to potentially traumatic stressors.

Twins from the same twin sample also provided evidence that the development of PTSD symptoms was influenced by both unique environmental (V_E) and genetic factors (V_G) (True *et al.*, 1993). In this study, combat exposure correlated strongly with the reexperiencing cluster of symptoms, the avoidance cluster of symptoms, and guilt, but not arousal symptoms, consistent with studies in Israeli combat veterans (Solomon & Canino, 1990). Among the total sample of twins, including those who had and had not served in Vietnam, both genetic and environmental factors contributed to the development of PTSD symptoms (Table 1).

Symptoms from each cluster showed greater within-pair correlations for MZ relative to DZ twins, with an identified contribution from unique environmental factors controlling for combat exposure. In contrast to familial models, the shared environment did not contribute highly to any symptom within the PTSD symptom cluster, with the exception of avoidance of activities (adjusted $d^2 = .34$). These data indicate that genetic factors contribute to PTSD vulnerability. They also strongly suggest that the elevated rates of PTSD in the relatives of combat veterans with PTSD reflect genetic influences rather than shared family environment. Consistent with these findings, a much smaller twin study found that PTSD was more prevalent in the twins diagnosed with anxiety disorders than in twins diagnosed with other diagnoses (Skre, Onstad, Torgersen, Lygren, & Kringlen, 1993). This study also found higher rates of PTSD in the small number of MZ twins with PTSD relative to DZ twins with PTSD (Skre *et al.*, 1993).

Although not explicitly related to PTSD, a recent twin study informs considerations of the interactive effects of a major stressful life event and depression (Kendler *et al.*, 1995). This study of 1,082 female twin pairs found that stressful life events, such as assault, serious marital problems, job loss, and serious illness increased risk of developing depression within 1 month of the event. Also, having an identical twin with depression was associated with a greater risk of developing depression than was having a fraternal twin with depression, while having a healthy identical twin was more protective against developing depression than was having a healthy fraternal twin. Furthermore, there were multiplicative interactive effects of having a genetic predisposition for depression in the face of a recent major life stress. The interactive effects of environmental and genetic factors from this study are illustrated in Figure 1.

Although this study did not report the prevalence of PTSD in its sample, these data support the interactive effects of stress and psychopathology.

Table 1. PTSD Symptoms in Monozygotic and Dizygotic Twins Adjusting for Combat Exposure

Symptom	Monozygotic correlations (s_1, s_2)	Dizygotic correlations (s_1, s_2)	Environment adjusted e^2	Additive genetic adjusted h^2
Reexperiencing				
Painful memories	.35	.24	.44	.13
Dreams/nightmares	.38	.19	.44	.30
Event happening again	.37	.18	.49	.28
Avoidance				
Avoided activities	.41	.11	.42	.00
Loss of interest	.32	.15	.67	.30
Felt distant	.38	.18	.59	.35
Life is not meaningful	.38	.16	.61	.34
Arousal				
Sleep disturbance	.33	.11	.67	.10
Irritable, short-tempered	.34	.16	.64	.30
Angry, aggressive	.37	.15	.62	.31
Trouble concentrating	.31	.15	.67	.28
Easily startled	.38	.20	.56	.32
Only DSM-III				
Felt guilt	.28	.15	.50	.26
Memory problems	.32	.16	.67	.30

Modified from True *et al.* (1993).
e^2 = variance from environmental influences, including the trauma.
h^2 = variance from genetic influences.

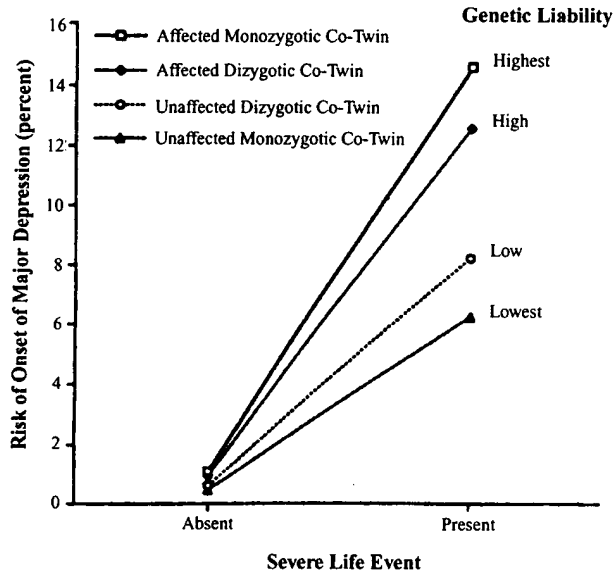

Figure 1. Risk of onset of major depression per person-month as a function of genetic liability and the presence or absence of a severe stressful life event in that month among 2,060 female twins. Genetic liability is reflected by both the zygoisty of the twin and the lifetime history of major depression in the co-twin. The results presented above are those predicted by the best-fitting logistic regression equation that contains control variables and the main effects of the life event and genetic risk factors. A severe life event is defined as assault, serious marital problems, divorce/break-up, or death of a close relative (from Kendler *et al.*, 1995, p. 837).

COMMENT AND FUTURE DIRECTIONS

A growing body of data suggests that genetic factors contribute to PTSD. PTSD appears to be associated with other anxiety disorders in a still undetermined fashion. No single diagnosis is of sufficient prevalence in the family members of patients diagnosed with PTSD to question the validity of PTSD as a distinct diagnosis. The increased risk for PTSD among individuals with anxiety disorders and the increased prevalence of anxiety disorders in the offspring of PTSD patients supports this connection but does not yet explain the nature of the relationship. Familial factors undoubtedly contribute to the rates of psychiatric problems in the offspring of combat veterans with PTSD. Consensus may emerge after the family history studies conducted in veterans with PTSD are integrated with the findings of studies that must eventually be conducted in probands with non-combat-related PTSD.

Future studies will introduce new complications. For example, it is not yet clear whether the genetic predisposing factors associated with one type of traumatic stress are similar to that associated with vulnerability to a different type of stressor. Also, we do not yet know whether the genetic factors predisposing to PTSD in males are similar to genetic factors associated with PTSD in females, and concerns about this issue have been raised for other disorders (Kosten, Rounsaville, Kosten, & Merikangas, 1991). Furthermore, it is not clear whether the genetic factors associated with vulnerability to later symptomatic presentations associated with infantile or childhood traumatization are similar to those associated with adult traumatizations. With such large and important gaps in our understanding of the genetics of PTSD, it is clearly a time for caution in the interpretation of any particular study. Perhaps it is also a time for generativity as the gaps in our knowledge base serve to stimulate future research.

Several important steps will undoubtedly be taken by the field of traumatic stress studies. One necessary step in the characterization of genetic contributions to PTSD is the completion of studies incorporating a growing number of rigorous genetic designs, such as family interview studies, that may more accurately characterize the prevalence of psychiatric disorders in the family members of PTSD patients relative to other disorders. The existing family history studies provide an important initial step but are not definitive. The family interview studies also provide a foundation for initiating molecular genetic linkage studies, incorporating a spectrum of powerful techniques that may help to identify the contributions of particular genes to traumatic stress response.

An important second step will be to characterize genetic factors associated with resilience following exposure to extreme stress. Although the prevalence of the PTSD diagnosis in 15.2% of Vietnam theater veterans speaks to the chronicity of this disorder, approximately half of the veterans with a lifetime history of this diagnosis no longer met diagnostic criteria at follow-up (Kulka *et al.,* 1990). Several factors appear to be associated with coping and recovery following traumatic stress exposure. For example, one study of American prisoners of war in Vietnam following 1969, found that successful coping was associated with introversion, whereas veterans who coped less well tended to be outgoing and extroverted (Ursano, Wheatley, Sledge, Rahe, & Carlson, 1986). Studies have found genetic contributions to introversion and extroversion (cf. Cloninger, 1991), suggesting at least one potential bridge between genetic and clinical descriptive studies. The comorbid conditions of antisocial personality, alcoholism, and substance abuse have been cited as commonly associated with chronic PTSD in combat veterans (Sierles, Chen, McFarland, & Taylor, 1983) and in the family members of combat veterans (Davidson *et al.,* 1985, 1989). These comorbid conditions with increasingly well-characterized genetic transmission (Cloninger, 1987) may predict a lack of resiliency among traumatized veterans (Cowen & Work, 1988; Garmezy, Masten, & Tellegen, 1984) or

behavior patterns, such as repetitive exposure to violence in drug-using subcultures, that may exacerbate the course of PTSD (Lyons, 1991). Because resiliency factors influence the course of PTSD, subgroups of traumatized patients may recover and, as a result, fail to be included in genetic studies of this disorder. Thus, resiliency factors may contribute significantly to the findings of studies drawn from clinical samples of PTSD patients.

A third step that may be useful in characterizing genetic contributions to traumatic stress response would be to shift the emphasis from diagnoses to specific traits. For example, it has been difficult to find a single gene that explains alcohol dependence in all affected individuals; however, a gene involved in serotonin synthesis has already been implicated in violent behavior exhibited by impulsive alcoholics (Nielsen *et al.*, 1994). Alternatively, one might focus on particular traits that might predispose individuals to a spectrum of diagnoses, the display of which depends on environmental factors during development. One trait that has received significant attention due to its association with anxiety disorders is behavioral inhibition in children (Kagan, Reznick, & Snidman, 1988). Behavioral inhibition is a laboratory-based measure of the tendency to restrict behavior in the presence of an unfamiliar environment. Behavioral inhibition was initially found to be more prevalent in the offspring of patients with panic disorder and agoraphobia (Rosenbaum *et al.*, 1988) and subsequently was found to be associated with other parental anxiety disorders as well (Rosenbaum *et al.*, 1991). These traits may have parallels in the provocative studies conducted in rhesus monkeys. These studies suggest that inherited factors producing increased reactivity to relatively mild stressors predict the pattern of response to a major stressor, maternal deprivation (see Suomi & Levine, Chapter 36, this volume). The evaluation of the patterns of inheritance of this and other well-defined and well-quantified traits could be informative in the families of patients with PTSD.

There also is an increasing need to link pathophysiological and etiological models for PTSD in the pursuit of enhancing the efficacy of pharmacotherapies for this disorder. The only current study attempting to bridge this gap to date (Nagy *et al.*, in review) did not find that responsivity to yohimbine differentiated the pattern of psychiatric disorder in family members of patients with PTSD. Yet the growing literature on the neurobiological foundations of PTSD (Charney, Deutsch, Krystal, Southwick, & Davis, 1993; Krystal *et al.*, 1989) provides new research directions that grow out of preclinical research findings. For example, a recently completed study suggested that patients with combat-related PTSD tended to respond to either yohmbine or the serotonin partial agonist, m-chlorophenyl-piperazine (*m*CPP), but not to both agents with a panic attack (Southwick *et al.*, 1997) It is not yet known whether yohimbine and *m*CPP differentiate stable subtypes of PTSD with differential involvement of noradrenergic and serotonergic systems, or whether the differential responses to these drugs reflect state-related factors.

Preclinical research suggests that different inbred mice strains respond to inescapable stress with consistent and differential involvement of monoamine neurotransmitter systems, resulting in mice strains with preferential dopaminergic, noradrenergic, and serotonergic responses to stress (Anisman, Grimmer, Irwin, Remington, & Sklar, 1979; Shanks & Anisman, 1989; Zacharko, Lalonde, Kasian, & Anisman, 1987). These mice strains respond to inescapable stress with a characteristic behavioral disruption syndrome, sometimes referred to as "learned helplessness." The rodent strains with prominent noradrenergic activation tended to be better protected from the disruptive effects of inescapable stress by prestress administration of a noradrenergic reuptake blocker than by a serotonin reuptake blocker, whereas rodent strains with more prominent serotonergic responses exhibited superior protective effects when pretreated with a serotonin reuptake blocker (Shanks & Anisman, 1989).

Information regarding genetically determined patterns of stress response could lead to a rational matching of subgroups of PTSD patients to optimally effective treatments. Currently, there is no established strategy for determining the optimal match of particular PTSD patients

with particular treatment modalities. However, if human serotenergic and noradrenergic patterns of stress response (Southwick *et al.*, 1997) parallel those reported in animals (Shanks & Anisman, 1989), then one would predict that pharmacological challenge studies and ultimately patterns of allelic expression would predict patterns of pharmacotherapy response. As a corollary, the failure to match an appropriate population of PTSD patients to an appropriate pharmacotherapy may have contributed to the lack of efficacy observed in a study evaluating desipramine treatment for PTSD (Reist *et al.*, 1989). While not yet applied to PTSD, the strategy of treatment matching based on clinically evident traits has been applied with success in other areas of psychiatry, particularly the field of alcoholism research (Kadden, Cooney, Getter, & Litt, 1989).

In closing, genetic studies of PTSD are challenged by the complexity of studying an environmentally triggered disorder and burdened by the heightened responsibility to ensure that genetic traits predisposing individuals to developing this disorder do not acquire pejorative implications. The promise of genetic studies is the better understanding of vulnerability, course, and pathophysiology of PTSD. In acquiring better predictors of vulnerability and resistance to traumatization, ultimately, clinicians and society might develop the capacity to intervene to reduce the incidence of PTSD. Understanding genetically determined patterns of stress response would illuminate all aspects of pathophysiological study of this disorder and potentially lead to more effective treatment, and treatments that are better geared to fit the needs of particular patterns of stress response. Currently, the lofty goals of genetic studies of PTSD seem quite distant within the context of a relatively small number of studies published in this area. Yet the field of traumatic stress studies awaits the development of this exciting and promising area of study.

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