Predicting the Development of Posttraumatic Stress Disorder from the Acute Response to a Traumatic Event

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Posttraumatic stress disorder (PTSD) is a psychiatric condition that is directly precipitated by an event that threatens a person's life or physical integrity and that invokes a response of fear, helplessness, or horror. In recent years it has become clear that only a proportion of those exposed to fear-producing events develop or sustain PTSD. Thus, it seems that an important challenge is to elucidate aberrations in the normal fear response that might precipitate trauma-related psychiatric disorder. This paper summarizes the findings from recent studies that examined the acute and longer term biological response to traumatic stress in people appearing to the emergency room immediately following trauma exposure. In the aggregate, these studies have demonstrated increased heart rate and lower cortisol levels at the time of the traumatic event in those who have PTSD at a follow-up time compared to those who do not. In contrast, certain features associated with PTSD, such as intrusive symptoms and exaggerated startle responses, are only manifest weeks after the trauma. The findings suggest that the development of PTSD may be facilitated by an atypical biological response in the immediate aftermath of a traumatic event, which in turn leads to a maladaptive psychological state. Biol Psychiatry 1998;44:1305–1313

Key Words: Posttraumatic stress disorder, animal models, startle, cortisol, acute stress response, longitudinal studies

Introduction

According to recent estimates, approximately 18% of all women and 10% of all men in the United States will develop posttraumatic stress disorder (PTSD), defined according to the DSM-IV, at some time in their lives (Breslau et al 1998a). The high prevalence of this disorder reflects not only a fairly violent society in which exposure to events such as rape, child abuse, crime, and other forms of interpersonal violence are common, but also a reasonably dangerous environment that offers several opportunities for exposure to other kinds of man-made (e.g., motor vehicle accidents, plane crashes, or toxic waste exposure) or naturally occurring (e.g., earthquake, flood, avalanche) hazards. About 90% of citizens in the United States are exposed to at least one potentially life-threatening event (as defined by the DSM-IV) in the course of their lives (Breslau et al 1998). A great many individuals are exposed to more than one traumatic event in their lives (Kessler et al 1995).

By definition, PTSD can only be diagnosed following exposure to a traumatic event. According to the most current definition in the Diagnostic and Statistical Manual, 4th edition, a traumatic event is one that "results in a threat of death or physical integrity and in a subjective response of fear, helplessness, or horror" (American Psychiatry Association 1994). This definition states the obvious: that fear is an essential component of the response to an overwhelming, life-threatening event. Based on the prevalence of these events in our society it could easily be concluded that the fear response is something that all persons experience at some time in their lives.

Relationship between Trauma and PTSD

In considering the relationship between trauma exposure and PTSD it is useful to distinguish between the acute and chronic response to a traumatic event. Most individuals who are exposed to traumatic events develop symptoms in the early aftermath of the event; however, as time goes on, the intensity of the initial response, and the number of individuals who manifest these responses, substantially decreases (Rothbaum and Foa 1993; McFarlane and Papay 1992; Grace et al 1993). Posttraumatic symptoms become chronic only in a subgroup of trauma survivors.

One of the most salient predictors of chronic PTSD is the nature of the traumatic event that has been experienced. Events associated with torture or prolonged victim-

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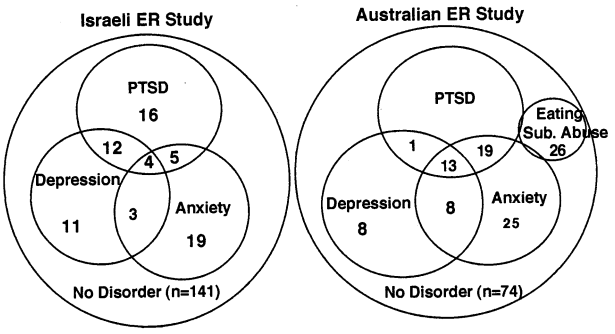

Figure 1. Overlap between PTSD, depression and anxiety disorders following trauma exposure. The Israeli ER study data are from Shalev and Yehuda (1998) (n = 211); the Australian ER study data are from McFarlane et al unpublished (n = 174). Sub., substance. The left panel is reproduced, with permission, from Shalev and Yehuda (1998).

ization are associated with the highest estimates for chronic PTSD. The prevalence of chronic PTSD among torture survivors such as prisoners of war and concentration camp survivors is about 50% (Kluznick et al 1986; Goldstein et al 1987; Yehuda et al 1995a). In contrast, the prevalence rate of chronic PTSD in survivors of natural disasters is about 4% (Shore et al 1989); however, even among those who are exposed to very severe and prolonged trauma, there is usually a substantial number of individuals who do not develop PTSD. Thus, PTSD can best be considered a possible, but not inevitable, outcome following trauma exposure.

One of the consequences of the establishment of the diagnosis of PTSD was that the relationship between stress and the development of other psychiatric disorders was deemphasized. From 1980 until recently, very few studies examined the development of psychiatric disorders other than PTSD following exposure to trauma; however, it is becoming clear that trauma exposure precipitates the development of many different psychiatric disorders, which may or may not co-occur with a PTSD.

In a recent study, Shalev et al (1998a) examined a group of consecutive admissions to the Hadassah Emergency Room (ER) immediately following trauma exposure. These subjects were subsequently followed up 4 months later and given complete diagnostic assessments. Of the 211 survivors that were available for follow-up, 141 of them—two thirds of the sample—had no psychiatric disorder 4 months after trauma exposure. Of the remaining subjects, 17% (n = 37) met diagnostic criteria for PTSD, 14% (n = 30) met diagnostic criteria for major depression, and 15% met diagnostic criteria for another anxiety disorder such as generalized anxiety disorder or simple phobia (Figure 1). About one quarter of the subjects meeting diagnostic criteria for one psychiatric disorder met criteria for another disorder. Thus, of the 17% of subjects with PTSD, only 7.5% (n = 16) did not meet criteria for another psychiatric disorder. Of the 14% with major depression, only 5% (n = 11) did not meet criteria for another disorder, and of the 15% with other anxiety disorder, only 9% (n = 19) did not also meet criteria for PTSD or depression. This is a landmark study in clarifying that PTSD is no more probable an outcome following trauma exposure than major depression or other mood disorders. Furthermore, the likelihood of developing both a mood and an anxiety disorder following trauma exposure is comparable to the likelihood of developing only one such condition.

The above findings are similar to those recently obtained (but not yet published) in an Australian cohort of consecutively admitted motor vehicle accident victims (preliminary data are described in McFarlane 1997). In this study, 174 motor vehicle accident victims, with no previous psychiatric disorder, were studied within 24 hours after their admission to the hospital following a severe motor vehicle accident and were followed up at 6 and 18 months. Figure 1 provides a breakdown of the psychiatric disorders at the 6-month follow-up in this sample (McFarlane, Atchison, Yehuda, unpublished data). About 42% of the subjects in this sample (n = 74) did not have a psychiatric disorder at follow-up; however, 19% (n = 33) had PTSD, 17% (n = 30) had major depressive disorder, and 37% percent of the subjects (n = 65) met criteria for one or more anxiety disorder (panic, generalized anxiety disorder, and/or simple phobia). A substantial number of subjects also developed other disorders, such as alcohol abuse or dependence (n = 22), drug abuse or dependnece (n = 11), eating disorder (n = 8), and/or obsessive–compulsive disorder (n = 4).

In the Australian motor vehicle accident study, the percentage of subjects showing psychopathology, and the number and range of diagnoses, were greater than in the Israeli cohort. One explanation for this is that the study of Shalev and colleagues examined civilians who were exposed to a broader range of traumatic events that may have been more random (e.g., being present in a marketplace during a terrorist bombing). In contrast, exposure to a motor vehicle accident provides a narrower range of subjects, who have more circumscribed and specific risk factors, such as being intoxicated at the time of the accident. Furthermore, the subjects in the Australian study may have been more injured, since they were only included for study if their injuries were severe enough to require hospitalization. In Shalev's study, many trauma victims returned to their homes after presenting to the emergency room. Nonetheless, the similarity between these data and those of Shalev and colleagues is in the high rate of diagnostic comorbidity and the fact that numerous

diagnoses—not just PTSD—could be present at several months posttrauma.

These studies show that there is no simple relationship between exposure to a traumatic event and the subsequent development of PTSD. This is an important consideration in determining the relevance of initial fear reactions and the development of subsequent psychopathologies. Indeed, an understanding of the universal fear response will not provide an answer to the question of how the initial response is transduced into *different* psychiatric disorders. Rather, the data reviewed above raise the question of why the fear response precipitates an anxiety disorder in some trauma survivors, whereas others develop mood disorders, and still others—the majority—develop a mood and an anxiety disorder.

What Predicts the Development of PTSD following Exposure to a Traumatic Event?

The idea that PTSD is simply one of several possible long-term outcomes following exposure to a traumatic event would not strike most mental health workers as a particularly unusual revelation. After all, the notion that stress causes or exacerbates psychopathology is one of the cornerstones of the biopsychosocial model of mental illness. It seems obvious that trauma could precipitate a whole host of mental health problems; however, given the emphasis on the link between trauma and PTSD implied by the DSM (American Psychiatric Association 1980), and on the concept of PTSD as a "natural consequence" of exposure to traumatic stress (e.g., Yehuda and McFarlane 1995), the finding of numerous psychiatric disorders following trauma is challenging. But to the extent that this observation does surprise us, this may be due to the fact that PTSD in and of itself is a post hoc formulation of the effects of trauma.

The diagnosis of PTSD was established by evaluating symptomatic individuals who had been previously traumatized and inferring that the traumatic event sustained years earlier was the cause of their current symptoms. The conclusions that were drawn were not erroneous in linking past trauma to the current PTSD. Rather, because of the retrospective nature of the evaluation, it was difficult to determine that trauma could have also resulted in other consequences including recovery, since individuals with other or no diagnoses were not similarly questioned about whether a trauma may have been a precipitating factor in their conditions. Certainly the data summarized above from both the above-mentioned prospective studies compel us to address the question of what factors predict the specific response of PTSD, and this is best done in the context of a prospective design.

The major advantage of prospective, longitudinal studies is that they allow an investigation of the variables affecting the development of PTSD without the distortions that occur from retrospective analyses. In both the above studies, numerous data were collected regarding characteristics of the traumatic event, prior history of the trauma survivor, and psychological and biological responses to the traumatic event, both in the immediate aftermath and at subsequent time points following exposure.

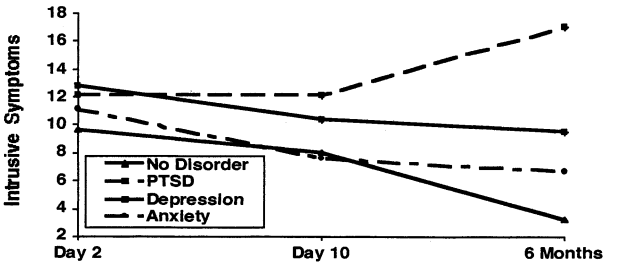

Figure 2. Intrusive symptoms in the acute aftermath of a motor vehicle accident, and at follow-up. This graph demonstrates group means for symptoms on the Intrusion subscale of the Impact of Event Scale (Horowitz et al 1979). At Day 2, there was no significant difference in intrusive symptoms among any of these groups ($F = 0.82$; df = 3,173; ns). Similarly, on Day 10 there are no significant differences between groups ($F = 2.56$; df = 3,173; $p = .06$), even though subjects with PTSD are becoming somewhat more elevated on this subscale. By 6 months, however, it is clear that PTSD subjects have significantly higher intrusion scores than other groups ($F = 35.99$; df = 3,174; $p < .0001$). Subject numbers are for no disorder ($n = 73$), for PTSD ($n = 36$), for depression ($n = 16$), and for other anxiety disorder ($n = 49$).

In the study of motor vehicle accident victims described by McFarlane (1997), discriminant function analysis failed to demonstrate a significant effect of gender, age, past psychiatric history, prior trauma, injury severity, pain severity, or intrusive, avoidance, and dissociative symptoms in the immediate aftermath of the trauma (canonical coefficient for first function: .34, $p = .29$; second function .18, $p = .78$). These results are noteworthy because they suggest that variables that have emerged as salient predictors of PTSD in retrospective studies—which use a more narrow range of subjects that are classified based on the dichotomy of presence or absence of PTSD—actually have very little predictive value in determining the development of this disorder when gauged from a prospective vantage point. Similarly, a careful analysis of psychometric predictors of PTSD (Shalev et al 1997a) has shown that early intrusive, avoidance, or hyperarousal symptoms were poor predictors of PTSD.

Figure 2 demonstrates that when subjects in the motor vehicle accident study are subdivided according to their primary diagnostic classification at 6 months posttrauma, there are no significant group differences in intrusive thoughts on the day following the motor vehicle accident

(Day 2). This means that in the acute aftermath of a traumatic event, it is not really possible to differentiate between individuals who will subsequently develop a PTSD and those who will it not. Over time it becomes clear that intrusive symptoms intensify in those who will subsequently develop PTSD, and abate in those who develop another psychiatric disorder or in those who will not develop any disorder. The data imply that a pathological process develops between Day 2 and Day 10, and again between Day 10 and subsequent months later. To date, the nature of this process has not been elucidated. Regardless, it appears that the passage of time is a major ingredient in the expression of PTSD.

At first glance, the above data might lead to the conclusion that the development of PTSD is influenced by factors or adaptations occurring at least several days following the event; however, there also appear to be some salient predictors of PTSD that are manifest within hours after the traumatic event. These are not psychological variables, but rather biological ones. To fully appreciate the significance of these findings, and place them into context, we present a brief overview of the relevant neuroendocrine and sympathetic nervous system (SNS) alterations in chronic PTSD, and then describe alterations in the acute aftermath of trauma.

The Hypothalamic–Pituitary–Adrenal (HPA) Axis in Chronic PTSD

In response to stress, neuropeptides in the brain stimulate the release of corticotropin-releasing hormone and other secretagogues from the hypothalamus. These stimulate the release of adrenocorticotropic hormone from the pituitary, which in turn stimulates the release of cortisol from the adrenal glands (Rivier and Plotsky 1986; Selye 1936). As this cascade is initiated, numerous biological reactions are also set in motion. The major function of cortisol is to contain these stress-activated reactions (Munck et al 1984). The HPA stress response is ultimately terminated by the negative feedback inhibition of cortisol at the pituitary, hypothalamus, and extrahypothalamic brain sites.

The neuroendocrine profile observed in chronic PTSD is somewhat paradoxical because the alterations observed in the hypothalamic–pituitary–adrenal axis are almost diametrically different to that observed in studies of acute and chronic stress and major depressive disorder (Chrousos and Gold 1992). Whereas the classic descriptions of stress and major depression have demonstrated increased levels of circulating cortisol (e.g.,Mason et al 1986), decreased concentrations and responsiveness of glucocorticoid receptors (e.g.,Lowy et al 1989; Yehuda et al 1993), a decreased sensitivity of the HPA negative feedback (APA Task Force on Laboratory Tests in Psychiatry 1987; Carroll et al 1981), and a progressive desensitization of the entire HPA axis (Yehuda et al 1996a), PTSD is characterized by decreased levels of circulating cortisol (Yehuda et al 1995b), increased concentration and responsiveness of glucocorticoid receptors (Yehuda et al 1995c), an increased sensitivity of the HPA negative feedback inhibition (Yehuda et al 1996b), and a progressive sensitization of the entire HPA axis (Yehuda 1997, Yehuda 1998).

The current working understanding of HPA axis alterations in PTSD is that the HPA axis is hypersensitive to negative feedback due to a primary increase in the number and sensitivity of glucocorticoid receptors (Yehuda et al 1995c; Yehuda 1998). Until recently, these alterations were thought to be characteristic of chronic PTSD; however, it may be that there are fundamental differences in the way the HPA axis is normally regulated that determine how an individual will respond to traumatic stress.

Cortisol Responses in the Acute Aftermath of Trauma

Resnick et al (1995) obtained blood cortisol levels from 39 women during an emergency room visit within hours after being raped. Significantly lower cortisol levels were present in the subgroup of women with a previous sexual assault history compared to those without such a history. The former subgroup of women subsequently demonstrated a threefold greater probability of developing PTSD at a 4-month follow-up compared to women who had no previous sexual assault history. The data raise the possibility that the prior traumatization was the cause of attenuated hypothalamic–pituitary–adrenal axis responses to the subsequent rape, and that the attenuated cortisol response consequently increased the risk for developing PTSD from that rape. Although this study marked the first prospective biological investigation in PTSD, it was limited by the fact that follow-up investigations asked only about the presence and absence of PTSD, but not other psychiatric disorders.

McFarlane et al (1997) obtained blood cortisol levels in a subset of the motor vehicle accident victims described above. As illustrated in Figure 3, when subjects from that study were subdivided based on their diagnostic grouping at 6 months, cortisol levels obtained in the immediate aftermath were significantly different based on this later subdivision. In contrast to the failure to observe differences in intrusive or other symptoms in the immediate aftermath of the trauma, individuals who subsequently developed PTSD had lower cortisol levels, and those who subsequently developed major depression had higher cortisol levels than those who did not develop a psychiatric disorder. The group differences were significant when

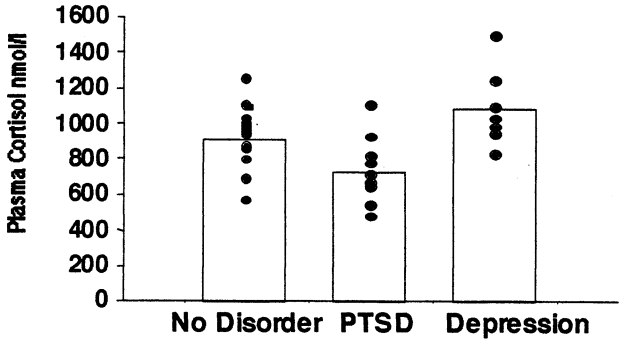

Figure 3. Cortisol levels in trauma survivors in the immediate aftermath of a motor vehicle accident. Data from 38 subjects are shown and are redrawn from McFarlane et al 1997. Results of a two-way analysis of variance (group × gender) revealed a main effect of diagnosis ($F = 4.59$; df = 2,35; $p = .02$), but no main effect of gender or group × gender interactions. Covariates were minutes postaccident, time of day, severity of trauma, and past PTSD. No covariate was significant.

controlling for variables such as time of day, minutes posttrauma, and accident severity (see Figure 3 legend).

The studies by Resnick et al (1995) and McFarlane et al (1997) suggest that a paradoxically lower cortisol response is present in trauma survivors who subsequently develop PTSD compared to those who either develop depression or those who do not develop a psychiatric disorder. It is important to note that neither of these studies examined cortisol levels before the trauma, and therefore, no statement can be made about the cortisol response relative to the trauma survivor's baseline. Nonetheless, Resnick et al's observations raise the possibility that the biological response to a traumatic event may be predicted by pretrauma characteristics related to cortisol reactivity.

Sympathetic Nervous System Activity in Chronic PTSD

Alterations of the SNS have also been characterized in persons with chronic PTSD. In response to stress, SNS activation results in the release of the catecholamines norepinephrine and epinephrine (Mountcastle 1973). These hormones increase heart rate and blood pressure, thereby allowing increased muscle perfusion, and also mobilize glucose as a quick energy source for the "fight or flight" reaction described by Cannon (1914).

The link between traumatic stress responses and the SNS was made relatively early, in 1918, when investigators noticed greater heart rate responses to combat sounds in combat veterans with "shell shock" compared to healthy control subjects (Meakins and Wilson 1918) Grinker and Spiegel (1945) described combat soldiers as appearing as if they had "received an injection of adrenaline" and who suffered from chronic stimulation of the SNS. Contemporary research on PTSD has substantiated these initial observations by demonstrating increased heart rate responses during provocation (for review, Shalev and Rogel 1994). Some studies have also demonstrated increases in baseline heart rate in combat veterans with PTSD.

Shalev et al (1998b) collected heart rate data from the trauma survivors described above, who appeared at the Haddassah emergency room in the immediate aftermath of a traumatic event, including in this study only subjects without significant physical injury. Of 86 such subjects, 20 (23.4%) developed PTSD, as determined during a 4-month follow-up. Mean heart rate levels at the time of the trauma were significantly higher in subjects who had developed PTSD at 4 months compared to those who did not develop PTSD. The mean heart rate in the PTSD group remained higher at the 1-week follow-up; however, by 1 month and 4 months, there were no group differences. These data are graphed in Figure 4. Importantly, subjects who did not develop PTSD also had elevated heart rate (83.2 beats per minute) at the emergency room, because they were expressing a stress response. The groups did not differ in initial blood pressure. The results remained significant when adjusted for age, event severity, response intensity, and peritraumatic dissociation.

In contrast, when Shalev et al (1997b) examined auditory startle responses, a very different finding emerged. Auditory startle responses obtained 1 week following the traumatic event were not significantly different in subjects with PTSD at the 4-month follow-up compared to those

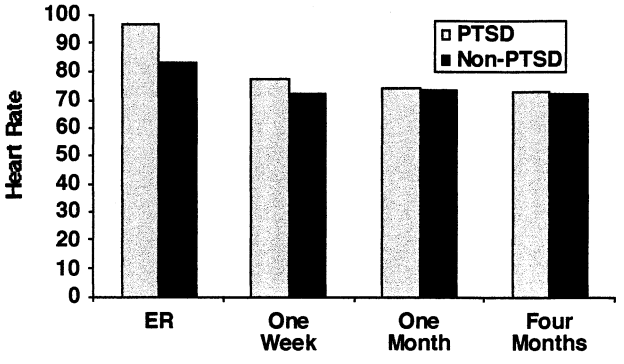

Figure 4. Mean heart rate data in trauma survivors in the emergency room and at follow-up. These are data redrawn from Shalev et al (1998) that demonstrate a significant difference in heart rate in the emergency room (ER) and at 1-week follow-up in Israeli trauma survivors who subsequently developed PTSD compared to those who did not. Mean heart rate levels were significantly higher in subjects who developed PTSD 4 months later compared to those who did not at the ER and at the 1-week follow-up, $t(84) = 4.4$, $p < .001$; $t(84) = 2.3$, $p < .03$. Repeated-measures analysis of variance for heart rate showed a significant group main effect [$F(1,84) = 5.7$, $p < .02$], a significant time main effect [$F(3,252) = 62.2$, $p < .0001$], and a significant group × time interaction [$F(3,252) = 8.7$, $p < .001$]. Differences at 1 month and 4 months are not significant.

who did not have PTSD. Rather, startle responses became clearly differentiated at the 1-month posttrauma assessment (i.e., for number of trials to habituation $F = 1.03$, df = 1,216; $p < .0001$ and for mean heart rate $F = 5.60$, df = 1,216; $p < .001$). These data suggest that there is a progressive development of the abnormal startle response that occurs somewhere between the first and fourth week following trauma exposure in those who develop chronic PTSD. This finding is extremely important to the question of how preclinical or human studies of startle relate are applicable to PTSD. Clearly, PTSD involves a process in which the startle response progressively changes over time.

SNS–HPA Interactions

In chronic PTSD there appear to be low cortisol levels in the presence of high catecholamine levels (e.g., Yehuda et al 1992, press). Yehuda et al (1990) have previously suggested that HPA axis abnormalities may be directly related to hyperadrenergic states in PTSD and may even represent a potential underlying mechanism for catecholaminergic dysfunction in this disorder. This is because glucocorticoid receptors are colocalized with monoaminergic neurons in several brain areas (Harfstrand et al 1986), and could therefore easily influence, excite, or inhibit (depending on whether genomic or nongenomic effects are considered) the adrenergic system (McEwen et al 1987). Indeed, glucocorticoids have been found to increase locus coeruleus firing (Avanzino et al 1987), but at the same time, adrenalectomy has been shown to increase plasma norepinephrine (Brown and Fisher 1986).

The adrenergic system, in turn, also contributes to the regulation of the HPA axis both through its direct action of corticotropin-releasing factor (CRF) release and via sympathetic innervation of the adrenal cortex (Ganong 1980; Weiner and Ganong 1978). Again, different adrenergic receptors dictate whether the actions on CRF are inhibitory or excitatory (Lanes et al 1985; Laakmann et al 1984). Catecholamines also have direct effects on the specific binding of glucocorticoid receptors (Stith and Person 1982; Tsuda et al 1982). Although a review of catecholamine–HPA interactions in stress is beyond the scope of this paper and is available elsewhere (i.e., Yehuda et al 1990), it can briefly be mentioned that during stress, the normal rise in cortisol is accompanied by an immediate release of norepinephrine (NE), followed by a transient decrease in NE levels (Laakmann et al 1984). When normal rise in glucocorticoids is prevented by adrenalectomy, acute stress results in an even greater elevation of plasma NE (Brown and Fisher 1986).

The interaction between the HPA axis and catecholamines system appears to be particularly important when it comes to stress-related memory acquisition; however, again, these interactions are quite complex and multidetermined. There is substantial evidence that catecholamines, particularly epinephrine, enhance memory consolidation in laboratory rats (Bohus 1984; Cahill et al 1994; De Wied 1984; De Wied and Croiset 1991; McGaugh 1985). This effect appears to be at least in part modulated by adrenal steroids, since adrenalectomized animals are more sensitive to the enhanced effects of epinephrine on memory consolidation (Bohus 1984; De Wied 1984). When adrenalectomized animals are given high doses of glucocorticoids, they became less sensitive toward the memory-enhancing effects of epinephrine (Borrell et al 1983).

Pitman (1989) hypothesized that PTSD results from exposure to a traumatic event that results in an exaggerated response of neuropeptides and catecholamines. The increased levels of these stress hormones initiate a process in which memories of the traumatic event might be "overconsolidated" or inappropriately remembered due to an exaggerated level of distress. Indeed, one of the ways that catecholamines facilitate memory formation is by maintaining organisms in a heightened state of arousal (De Wied and Croiset 1991). The increased heart rate observed in the emergency room in individuals who subsequently develop PTSD certainly is consistent with the idea that PTSD or the formation of distressing memories of the trauma occur while the SNS is in a hyperactive state.

The neuroendocrine results suggest that what may ultimately lead to PTSD is that the SNS remains hyperactive because of a failure of cortisol to contain this response (Yehuda and Harvey 1997). Because cortisol's role in stress is to antagonize catecholamine elevations in the acute aftermath of stress (Munck et al 1984), it is plausible that an attenuated cortisol response to stress might facilitate a process that results in an inappropriate memory consolidation. In support of this idea, Yehuda et al (1998b) recently demonstrated that there was a positive correlation ($r = .69$; $n = 9$; $p = .04$) between 3-methoxy-4-hydroxyphenylglycol (MHPG) and cortisol levels in the immediate aftermath of a rape (i.e., in a subset of subjects reported in Resnick et al 1995); whereas in the group who subsequently developed PTSD, there was a lack of correlation ($r = .05$; $n = 11$, ns)—or a biological dissociation—between the MHPG and cortisol response to the rape trauma. These preliminary results are tantalizing because they suggest a possible mechanism for why only some individuals would develop a PTSD-like response. They also offer a testable hypothesis: that there are risk factors that determine whether or not there will be an attenuated cortisol response to a traumatic event. Individuals who have these risk factors may respond to a traumatic event by failing to release sufficient levels of

cortisol for a long enough period of time to shut down the SNS (Yehuda and Harvey 1997). The increased SNS activity would disrupt normal memory processing, and particularly, would sustain distress associated with reexperiencing and reprocessing the traumatic event in the initial posttrauma stages. This disrupted reexperiencing process would initiate a cascade of events that would result in an escalation of intrusive symptomatology and a resultant disruption in neurocircuits of fear and anxiety, and these (currently unspecified) events would ultimately lead to the development of an enhanced startle response. According to this view, the development of PTSD occurs in individuals predisposed to biological hyperresponsiveness, and incubates in a progressive sensitization affecting multiple systems. The appeal of this idea is that it explains how the experience of trauma may culminate in a PTSD-like response in some individuals, but also leaves open the opportunities for a diverse range of stress responses, which is more consistent with the empirical reality.

Summary

PTSD is a possible, but not inevitable, outcome following exposure to traumatic stress. The above discussion demonstrates that it is possible to feel terrorized in the face of a life-threatening or potentially life-threatening event and not develop PTSD, or any long-term psychiatric disorder. Furthermore, it is possible to develop a posttraumatic psychiatric disorder other than PTSD.

One of the fundamental challenges in determining the applicability of the neurocircuitry of the fear response to the specific pathophysiology of PTSD is to address why not all fear responses culminate in a chronic PTSD response. It may ultimately be determined that the PTSD involves a process in which the experience of fear becomes transduced into anxiety disorder because of disruptions in the normal cacade of the fear response and its resolution. The above discussion raises the possibility that this disrupted process may result from pretraumatic vulnerability factors.

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