Developmental Epidemiology of PTSD

Self-Regulation as a Central Mechanism

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ABSTRACT: Epidemiologic and meta-analytic studies point to consistent effects of pretrauma factors on risk for posttraumatic stress disorder (PTSD). However, our understanding of why only some individuals are vulnerable to the adverse effects of traumatic events remains limited. This article argues that a developmentally informed approach to the epidemiology of PTSD is needed to move this understanding forward. However, there are many challenges to such an approach including the historic conceptualization of PTSD as a normative response to traumatic events, the almost exclusive reliance on retrospective self-report of PTSD risk factors, and the lack of attention to current knowledge of human development in selecting risk factors for epidemiologic studies. The developmental construct of self-regulation may provide a key mechanism for understanding the effects of pretrauma factors on the vulnerability to PTSD. Pretrauma factors shown to have consistent effect on risk for PTSD in meta-analytic studies include familial psychopathology, child abuse, and preexisting psychopathology. A preliminary framework integrating these pretrauma factors with self-regulation as a central mechanism in the etiology of PTSD is presented. The implications of a developmentally informed epidemiologic approach to PTSD for theory, research, and practice are discussed.

KEYWORDS: posttraumatic stress disorder (PTSD); developmental epidemiology; self-regulation; trauma; child development

INTRODUCTION

Posttraumatic stress disorder (PTSD) occurs following exposure to a potentially traumatic life event and is defined by three symptom clusters:

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reexperiencing, avoidance and numbing, and arousal.[1] The past two decades have witnessed an explosion in epidemiologic studies of PTSD.[2–10] This research has identified PTSD as a important public health problem, with a lifetime prevalence rate of 8% in the general population and costing the United States $3 billion per year.[7,11] One of the major findings of epidemiologic research on PTSD is that although the majority of Americans will be exposed to a traumatic event at some point in their lives, only a minority of those exposed will develop PTSD. This disparity between the prevalence of exposure to traumatic events and the prevalence of PTSD has led more recent epidemiologic studies to search for true risk factors for the disorder among exposed persons.

This article argues that a developmentally informed approach to the epidemiology of PTSD is needed to increase our understanding of why only some individuals are vulnerable to the adverse effects of traumatic events. Two meta-analyses of PTSD risk factors have argued for the primacy of trauma-related factors such as characteristics of the traumatic event (e.g., life threat), peritraumatic response (e.g., dissociation), and posttrauma factors (e.g., social support) in PTSD etiology.[12,13] However, both meta-analyses also state that current risk factor models only explain a small proportion (approximately 20%; see Ref. 13) of the variance in PTSD.[12,13] In addition, Brewin *et al*.,[12] acknowledge that the effects of pretrauma factors on risk for PTSD may in fact be underestimated. In fact, the effect of pretrauma factors on PTSD may be mediated by trauma-related factors and therefore appear to have weak effects when such factors are controlled. Moreover, the pretrauma factors examined in most epidemiologic studies tend to be "very general ones"[12] (p. 756) and their selection is not driven by any etiologic model for the disorder. Thus, our "understanding of vulnerability to PTSD is at an early stage"[12] (p. 756). A developmental epidemiologic approach to PTSD is necessary to move this understanding forward.

DEVELOPMENTAL RISK FACTORS FOR PTSD

The absence of a developmental epidemiologic approach to studies of adult PTSD is striking given the consistent evidence for the role of pretrauma factors, and particularly childhood factors, in the etiology of the disorder. This evidence first emerged in studies of World War II (WWII) veterans. Eliot Slater, a psychiatrist at the Maudsley Hospital of the Institute of Psychiatry in London, who conducted one of the largest studies of WWII veterans observed:

> There was evidence that the terrifying stresses of war tended to provoke anxiety states to a significantly preferential extent, but they did so far from regularly. A more important determinant of the type of response was the constitution of the individual, as shown by his family history, previous life, and personality (p. 217).[14]

It should be noted that Dr. Slater was not writing about PTSD *per se*; the diagnosis did not exist at that time. But it is noteworthy that the extant literature is consistent with Dr. Slater's observations and points to relatively small but significant effects on risk for PTSD for both within-individual characteristics, such as pretrauma psychological adjustment, and environmental factors, such as child abuse and general childhood adversity.[2–4,7,8,12,13,15,16] These findings support both "stress vulnerability" and "stress sensitization" models for the development of PTSD. Within-individual capacities, such as psychopathology, make some individuals more vulnerable to the adverse effects of a potentially traumatic experience. However, there is also evidence that early environmental conditions, such as exposure to environmental adversity and child abuse, sensitize individuals to the effects of such experiences. The single epidemiologic study of PTSD that assessed a wide range of childhood risk factors, albeit retrospectively, was the National Vietnam Veterans Readjustment Study.[8] Data from this study indicated that childhood antisocial behavior, unstable family environment, and prior trauma history were significantly associated with increased risk of PTSD in male veterans. The authors argued that "more attention should be given to critical developmental conditions, especially family instability and earlier trauma exposure, in conceptualizing PTSD in adults" (p. 520).[17]

CHALLENGES TO A DEVELOPMENTAL EPIDEMIOLOGY OF PTSD

Developmental epidemiology has been one of the dominant approaches to studies of mental disorders such as schizophrenia and major depression.[18] Why not for PTSD? One challenge to a developmental epidemiology of PTSD is conceptual; PTSD was originally viewed as a "normative" response to an extreme event. For example, in Diagnostic and Statistical Manual of Mental Disorders Version III (DSM-III) (1980), a trauma was defined as, ". . . a recognizable stressor that would evoke significant symptoms of distress in *almost anyone.*"[19] Thus, much of the original focus of epidemiologic PTSD research was on the characteristics of the traumatic event in predicting who develops the disorder; for example, on average, the conditional risk of developing PTSD is greater following a rape than following a car accident.[7] This research also supports a dose-response relation between the severity of the trauma exposure and risk of developing PTSD; for example, the prevalence of PTSD increases with the severity of combat exposure.[8] Although PTSD is no longer considered a normative response to trauma, this former conceptualization has directed research away from pretrauma influences on PTSD risk.

A second challenge to a developmental epidemiology of PTSD is the almost exclusive reliance on retrospective self-report measurement of risk factors in epidemiologic studies. This limitation has become especially concerning as evidence has accumulated that reports of risk factors, such as severity of trauma

exposure, may be biased by current symptomatology.[20–23] A few studies have examined prospective data in relation to specific risk factors such as child abuse,[24] prior trauma exposure,[15] pretrauma intelligence,[25,26] personality,[27] heart rate,[28] and family environment.[29] However, I know of no published study with prospective data on a wide range of childhood risk factors starting from birth plus diagnostic data on lifetime PTSD in participants followed through early adulthood. Follow-up through early adulthood at minimum is necessary when identifying risk factors for PTSD as the incidence of certain potentially traumatic events, such as interpersonal violence, peaks around the of age 20 years.[3]

A third challenge to a developmental epidemiology of PTSD is that even the best-designed epidemiologic studies are not informed by current knowledge of human development. Risk factors chosen for study tend to be the usual suspects in psychopathology—socioeconomic status, race, gender, parental separation—and not driven by current understandings of the developmental processes that might underlie PTSD. One such process that has received a great deal of attention in developmental research is self-regulation. Self-regulation encompasses a set of skills most broadly defined as the "ability to modulate behavior according to the cognitive, emotional, and social demands of a particular situation"(p. 479).[30] These skills appear highly relevant to how individuals differ in exposure and response to trauma exposure, are moderately heritable, are endophenotypes for a range of later psychopathology, and their development appears to be modified by early adverse environmental experiences.[31] Understanding self-regulation has been called "the single most crucial goal for understanding development and psychopathology" (p. 427).[31] However, the relation between the mechanisms of self-regulation and etiology of PTSD has not been explicitly examined. This is surprising given that potentially traumatic events are extreme "environmental demands" that activate self-regulatory systems.

SELF-REGULATION AND PTSD

A review of the self-regulatory systems relevant to PTSD vulnerability is beyond the scope of this article. However, there are systems that appear to be particularly relevant— emotion processing (EP) and executive functioning (ExF). Adults with PTSD show deficits in both EP[32] and ExF.[33] EP includes registration of a stimulus, assessment of the degree of threat, and the regulation of arousal in response to that threat.[34] Individual variation in EP has been well documented[34] as have genetic influences on the variation in many constructs intimately related to EP including emotionality, personality, and temperament.[35] The putative importance of EP in PTSD is codified in Criterion A2 of the DSM-IV PTSD diagnosis whereby the traumatic event must invoke the subjective response of "fear, helplessness, or horror."[1] Thus, the A2 requirement

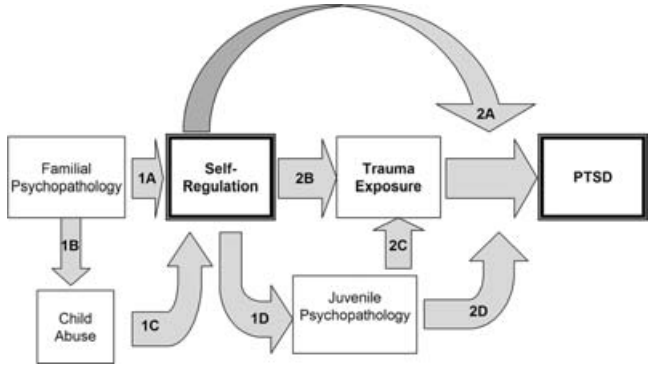

FIGURE 1. Conceptual framework for integrating epidemiologic findings with self-regulation as a central mechanism in PTSD etiology.

proposes that an intense emotional response to the event is necessary for it to result in PTSD. Although the A2 requirement remains controversial, research supports the role of acute emotional response in the etiology of PTSD.[13] Individual differences in EP may, therefore, influence the development of PTSD.

ExF is another component of self-regulation believed to play a role in PTSD etiology.[36] ExF is a higher-order cognitive construct involved in the planning, initiation, and regulation of goal-directed behavior. Specific cognitive abilities considered aspects of ExF include inhibitory control, working memory, and strategic goal planning.[37] ExF deficits are associated with a wide range of psychopathology, particularly conduct disorder and substance dependence,[38–40] which also increase the risk of trauma exposure and PTSD.[16,41,42] Genetic studies influences on ExF have been demonstrated.[43]

Neurocognitive models for PTSD suggest that individual differences in self-regulation, particularly EP and ExF, influence risk for the development of the disorder. The amygdala, as the brain structure that mediates fear conditioning,[45] is central to these models. When an individual is confronted with a traumatic event, sensory information is sent to the amygdala via the "low road," the thalamo–amygdala pathway, and the "high road," the cortico–amygdala pathway.[45] Either amygdala overactivation (EP) in response to threat or frontal (ExF) deficits resulting in the lack of amygdala inhibition could potentially influence acute trauma response and the development of PTSD. Positron emission tomography (PET) and magnetic resonance imaging (MRI) studies comparing PTSD probands and normal controls implicate both processes in the disorder[46,47] (see also Shin, this volume). Deficits in EP and ExF appear to be mediated by the interconnections between the limbic, particularly the amygdala, and frontal brain systems. Such deficits may represent vulnerabilities for the development of PTSD and that only become apparent after exposure to a traumatic event.

FIGURE 1 presents one possible framework for integrating epidemiologic findings with self-regulation as a central mechanism in the etiology of PTSD. Testable hypotheses extend from this framework as follows:

1. Well-established risk factors for PTSD influence the development of self-regulation. 1A. Familial psychopathology has genetically mediated adverse effects on the development of self-regulation. 1B–1C. Child abuse environmentally mediates the adverse effects of familial psychopathology on the development of self-regulation. 1D. Self-regulation deficits mediate the relationship between familial psychopathology, child abuse, and the development of pretrauma psychopathology.
2. Self-regulation deficits influence risk for PTSD. 2A. Self-regulation directly influences peri-traumatic response and thereby risk for PTSD. 2B. Self-regulation influences risk for PTSD through increasing risk of trauma exposure. 1D–2C. Self-regulation indirectly influences risk for PTSD through increasing risk of psychopathology and substance abuse, which then increase risk of trauma exposure. 1D–2D. Self-regulation indirectly influences the risk for PTSD through the increasing risk of psychopathology and substance abuse, which then increases the risk of PTSD among the exposed.

A review of the vast literature that may be brought to bear on this framework is beyond the scope of this article. However, an attempt to integrate some of the most relevant studies is presented below.

Familial Psychopathology

Parents with psychopathology may pass self-regulation deficits to their children through genetic (1A) and environmental (1B–1C) mechanisms. The evidence for the effect of genetic factors on self-regulation is supported by both animal models and human correlational studies. For example, genetically distinct mouse strains reared in identical environments show variation in response to fear conditioning.[48] Functional MRI (fMRI) studies show an association between variation in the serotonin transporter gene and differential amygdala responding to fear stimuli[49] and cingulate–amygdala interaction[50] in human subjects. Polymorphisms in FKBP5, co-chaperone of stress proteins, predict peritraumatic dissociation in medically injured children.[51] Genetic influences on PTSD have also been well documented. Twin studies have documented that exposure to certain types of traumatic events and to PTSD are moderately heritable.[16,52–55] Three of four molecular genetic association studies have found significant associations between genetic variation in the dopaminergic system, which is implicated in fear conditioning, and PTSD diagnosis.[56–59] A developmentally informed epidemiologic approach to the etiology of PTSD must, therefore, take the role of genetic influences into account.

Child Abuse

Because parental psychopathology increases risk of child abuse (1B), this offers another pathway for the transmission of deficits from parents to children.[60,61] How might child abuse impair the development of self-regulation (1C)? Animal models suggest a mechanism for the relation between such unpredictable environmental conditions in childhood and sensitization to the effects of later stress exposure. Offspring reared under stressful conditions are insecurely attached, emotionally dysregulated,[62,63] and show persisting alterations in functioning of the hypothalamic-pituitary-adrenal (HPA) axis.[64,65] Dysregulation of the HPA axis is implicated in the etiology of PTSD.[66] As stated above, exposure to trauma activates the amygdala, which is intimately connected with three self-regulatory systems. If the flexible responding and fight/flight systems are overwhelmed, dysregulation in these systems occur. Such dysregulation is thought to be more likely in young children because inhibitory connections from the prefrontal cortex to the amygdala are still developing.[67] According to the developmental traumatology model, dysregulation negatively affects brain development through neuronal loss, and inadequate energy resources.[68,69] Areas of the brain that mature postnatally, such as the orbitofrontal cortex, are particularly sensitive to environmental influences, and show diminished or impaired growth in the presence of dysregulated stress–response systems.[67,68] Damage to the development of the orbitofrontal cortex further contributes directly to problems in ExF. Such damage also contributes to problems in EP due to disinhibition of the amygdala. The result is a feedback loop that, without intervention, perpetuates disruptions to the developing child's ability to respond to later stress, and thus makes the child more vulnerable to the later development of PTSD.[68,70]

Juvenile Psychopathology

Self-regulation deficits are implicated in the development of many forms of psychopathology, including conduct disorder (1D). One of the most consistent epidemiologic findings is that preexisting psychopathology increases risk of trauma exposure and PTSD among the exposed (2C, 2D).[71] The association between conduct disorder and risk of PTSD is particularly well documented.[2,7,8,16,42] Conduct disorder is a manifestation of poor self-regulation that may place the individual at increased risk of trauma exposure. Moreover, individuals with conduct disorder may be more likely to develop PTSD, once exposed to trauma, because they have difficulty with affect tolerance necessary for processing the traumatic event. Instead, they are likely to angrily act out, or to engage in avoidance, strategies that may contribute to the development of PTSD. High levels of anger have been shown to interfere with recovery from PTSD in community[72] and clinical samples.[73]

CONCLUSIONS AND IMPLICATIONS

Epidemiologic research has made seminal contributions to our understanding of PTSD in the past decade. However, the extant literature only explains a minority of the variance in PTSD.[13] A developmental epidemiologic approach to PTSD is needed to improve our understanding of the within-individual capacities and environmental conditions that make some individuals more vulnerable to the adverse consequences of traumatic events.

A developmental epidemiologic approach to studying the etiology of PTSD has implications for theory, research, and practice. Such an approach challenges our understanding of the disorder as solely a response to trauma. Rather, PTSD may, instead, be viewed as one potential endpoint in a lifelong trajectory of risk that begins at conception when an individual's genotype is determined. In terms of research, developmental epidemiology relies on longitudinal designs, particularly those involving large birth cohorts. Incorporating assessments of trauma and PTSD into such designs would go a long way to addressing a major limitation of epidemiologic research in PTSD; the almost exclusive reliance on retrospective self-report of risk factors. By integrating current understandings of the developmental processes with epidemiologic methods, developmental epidemiologic studies can test specific mechanisms by which pretrauma factors increase risk for PTSD. Self-regulation may represent a key developmental process to be considered in such studies. In terms of practice, clinicians who serve clients with PTSD may find their treatment approach informed by a developmental perspective, particularly one that assesses self-regulation deficits. In fact, psychotherapy that combines a developmentally informed approach with addressing deficits in clients' self-regulatory capacities with more traditional trauma-focused treatment has been shown to be highly effective in reducing PTSD symptoms in adult women.[74] Prevention efforts aimed at addressing developmental risk factors and self-regulatory deficits may ultimately reduce the risk of PTSD.

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