The Role of Stress and Fear in the Development of Mental Disorders

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KEYWORDS

• Fear • PTSD • Stress • Extinction • Conditioning

KEY POINTS

- Stress and fear, in response to actual or possible threat, enhance the possibility of forming trauma-related memories leading to posttraumatic stress disorder (PTSD).
- Excessive fear responses in PTSD can be seen as physiologic reactions to trauma cues and alterations in arousal and reactivity increasing fear conditioning capacity.
- Predisposing factors such as childhood abuse increase the risk of fear conditioning, renewal, and reconsolidation.
- Studies on fear learning, extinction, and neuroimaging support the notion that increased fear is related to amygdala hyperresponsivity and dysfunctions in neural circuitry, specifically in the areas of the ventromedial prefrontal cortex that regulate fear.
- Severity of PTSD is associated with the inability to inhibit fear generalization, poor cognitive emotion regulation, and hippocampal damage affecting the memory processing of fear.
- Findings on fear have led to the identification of effective treatment modalities to reduce fear alterations in PTSD, such as effective pharmacotherapy including propranolol and selective norepinephrine reuptake inhibitors, cognitive behavior therapy, and exposure therapy.

Exposure to stress can lead to different psychiatric manifestations depending on the individual. One possible pathologic manifestation after a stressor is posttraumatic stress disorder (PTSD). Developing PTSD is closely related with predisposing factors such as genes and early traumatic experiences.[1] The Diagnostic and Statistical

This work was funded by National Center for Research Resources U54RR026139-01A1 and NIMHHD 8U54MD007587-03 (K.G. Martinez).
Disclosures: None.
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Psychiatr Clin N Am 37 (2014) 535–546
http://dx.doi.org/10.1016/j.psc.2014.08.010 **psych.theclinics.com**
0193-953X/14/$ – see front matter

Abbreviations	
BDNF	Brain-derived neurotrophic factor
CBT	Cognitive behavior therapy
CR	Conditioned response
CS−	Safety signal
CS+	Threat signal
CS	Conditioned stimulus
DI	Dorsolateral
DSM-IV-TR	Diagnostic and statistical manual of mental disorders, fourth edition, text revision
DSM-V	Diagnostic and statistical manual of mental disorders, fifth edition
fMRI	Functional MRI studies
HPA	Hypothalamic-pituitary-adrenal
NMDAR	*N*-Methyl-D-aspartic acid receptor
PTSD	Posttraumatic stress disorder
SCR	Skin conductance response
UR	Unconditioned response
US	Unconditioned stimulus
vmPFC	Ventromedial prefrontal cortex

Manual of Mental Disorders, Fifth Edition, (DSM-V) includes a category of trauma-related and stressor-related disorders that encompasses the variable clinical expressions of stress.[2] One of the most recognized expressions after a stressful stimulus is fear. Although fear is a natural response that protects against threats, when fear is excessive or expressed inappropriately it can become pathologic. Fear elicits natural autonomic responses such as increased heart rate, increased skin conductance, and activation of facial muscles that prepare the body to react to threat.[3] A possible pathologic manifestation of excessive fear after a stressor is PTSD.

The diagnosis of PTSD describes the cluster of symptoms that emerge after exposure to actual or threatened death, serious injury, or sexual violence. The person then develops intrusion symptoms associated with the trauma such as intrusive memories, distressing dreams, flashbacks or distress, or physiologic reactions on exposure to cues of the trauma. There is also the avoidance of the reminders of the trauma, alterations in memories or mood associated with the trauma, and marked alterations in physiologic arousal and reactivity. Projected lifetime risk for PTSD according to DSM-V is 8.7% in the United States, with lower prevalence in other countries. PTSD is a serious problem in certain samples such as war veterans, emergency medical personnel, and survivors of rape.[2]

FEAR EXPRESSION

In PTSD, a traumatic event causes a fear reaction that is excessively expressed. Based on DSM-V criteria, excessive fear can be seen as the physiologic reactions to trauma cues and the alterations in physiologic arousal and reactivity. Increased fear can be studied by evaluating the autonomic responses that are elicited, such as increased heart rate or skin conductance and activation of facial muscles, such as the startle response. Initial studies of fear responses in patients exposed to trauma showed increases in all of these autonomic responses to non–trauma-related stimuli.[4,5] Increased startle has even been reported in veterans with subthreshold PTSD symptoms.[6] These heightened responses seemed to be acquired as an effect of trauma exposure, as shown by twin studies in which the twin exposed to combat developed the increased physiologic responses, whereas the non–combat-exposed twin did not.[7] There is