Building a Model of Posttraumatic Stress Disorder

It is a given of human existence to be exposed to life-threatening events. Epidemiological studies confirm that a large majority of Americans report such exposure. Most of us weather the storms of trauma. However, a substantial unlucky minority goes on to develop posttraumatic stress disorder (PTSD). Attention to this debilitating condition has increased dramatically over the past decade, yet we still do not know why people develop PTSD, what happens when they do, or if there are different effects from different types of trauma. Four articles in this issue take us another step further in answering these important questions.

The literature that addresses vulnerability to PTSD documents higher rates in women as well as individuals with preexisting anxiety and/or depressive disorders. Lower levels of education and poorer cognitive ability also appear to be risk factors. There is a single article in the literature documenting a genetic component to risk for both combat exposure and ensuing symptoms in men. Stein and colleagues now make a major second contribution to this literature with their report on a twin study examining the heritability of PTSD symptoms in civilians. Four hundred Canadian volunteer twin pairs participated in their study; a majority were women. A questionnaire was used to obtain information about lifetime exposure to each of nine trauma types and severity of each of 17 PTSD symptoms. Of note, medical illness and medical procedures were not included in this list of traumas, in spite of the fact that PTSD was first identified in burn victims (1) and there are now a number of studies documenting PTSD in medical populations (2). Still, 75% of the Canadian twin sample indicated they had experienced trauma. Factor analysis grouped the reported traumas into assaultive and nonassaultive types. Heritability analyses, with control for age, sex, and an estimate of similarity of environment, indicated genetic effects on assaultive but not nonassaultive trauma exposure. Environmental influences appear to be different for the two trauma types. Results further suggest that effects on exposure may be gender specific. Gender differences have also been found in prevalence rates and risk factors for PTSD (3). Analyses of PTSD symptoms also showed evidence of heritability of symptoms only for assaultive trauma. Similar to the veteran study, there was a very high correlation for additive genetic correlations between assaultive trauma exposure and PTSD symptoms, implying that the genetic contribution for exposure and symptoms is the same. The authors suggest that greater emotionality could be the shared feature, with more irritability and anger comprising a risk for interpersonal violence, and greater emotional arousal a risk for symptoms in response to the assault.

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Analyses in this study are based on the premise that PTSD symptoms are on a continuum with normal reactions to trauma exposure rather than being qualitatively different. This premise is reasonable. A recent analysis of combat exposure (4) supports a dimensional model. Such continuity would be consistent with other anxiety and depressive disorders. Moreover, it is also clear that subthreshold symptoms can be clinically significant. PTSD requires a dual process of trauma exposure and response. What constitutes trauma was hotly debated in the development of the DSM criteria. The con-

servative position that trauma requires exposure to an event that is threatening to physical integrity is sensible from many standpoints, but it is likely inaccurate with respect to the development of clinically significant symptoms since this pattern of symptoms can be seen in response to other events (e.g., a lawsuit). Thus, it is possible that a clinically significant condition may be produced by subthreshold trauma exposure associated with threshold or subthreshold symptoms. Identification of the full range of symptoms may be needed to elucidate genetic mechanisms. Novel methods of assessing subthreshold and related clinical features of DSM disorders are needed (5).

Two of the articles in this issue elucidate neurobiological characteristics in patients with established PTSD. The first addresses memory impairment, a debilitating form of functional impairment. Golier et al. conducted a simple, elegant study comparing explicit and implicit memory in Holocaust survivors (63% women, mean age=69 years), suffering or not from PTSD, to healthy, nonexposed Jewish adults. Explicit memory was evaluated by a memorization task with use of moderately related and unrelated word pairs. Implicit memory was tested with word-stem completion. The PTSD group scored lower on recall of both unrelated and related words, with about one-third performing at a level suggestive of frank cognitive impairment. By contrast, there was no difference in performance on word-stem completion. Recall, but not word-stem completion, worsened with age in the PTSD group. Low levels of education and low IQ were associated with poorer recall, and the PTSD group with lower WAIS-R scores had fewer years of education. Since low IQ and low levels of education have been found to be risk factors for the development of PTSD, it is possible that the memory deficit is related to risk for—rather than the consequences of—PTSD. However, the authors point out that the PTSD group was of average intelligence and by no means uneducated. Moreover, the accelerated rate of cognitive decline in these patients, as well as other evidence for smaller hippocampal volume secondary to PTSD, suggests that at least some of the difference is a consequence rather than a cause of trauma-related symptoms.

Memory is one of our most complex and interesting mental functions. We know that explicit memory depends upon a functioning hippocampus and entails a conscious effortful process. We need explicit memory to remember where we put our keys or whether we need to buy orange juice. There is no question that frank cognitive impairment, described in almost one-third of these elderly PTSD patients, is a potentially serious complication of trauma exposure. These researchers also investigated implicit memory and found it preserved. Implicit memory is of interest in emotional disorders such as PTSD. This form of memory is not conscious. In addition to its role in procedural memory and priming effects, implicit memory has been associated with some types of emotional recollections. The mechanism for implicit memory dwells in a different part of the brain than explicit memory and sometimes affords the emotional tone of reminiscence. It may be this system that bears responsibility for Proustian remembrances that, activated by a faint sensory cue, produce a powerful wordless emotion. Implicit memory is not affected by dementing illness. Its role in PTSD remains to be elucidated but may be in the formation of intrusive images and/or disturbed dreams. The work by Golier and colleagues focuses on neutral words. McNally (6) found no implicit memory bias for trauma-related words in one study but suggested it may be present in other paradigms. It will be interesting to learn more about implicit memory in PTSD.

Lewine and colleagues also studied individuals with established PTSD. Neurobiological studies are consistent with limbic dysfunction, including smaller hippocampal volume and excessive amygdala activation in response to trauma-relevant stimuli. Electrophysiological research is further supportive of limbic dysfunction. The study of Lewine et al. examines stimulus-response intensity functions for the N100 and P200 components of the auditory event-related brain potential. Normally, there is an augmenting pattern of event-related brain response as stimulus intensity is increased. In their study, 58% of veterans with combat-related PTSD failed to augment response compared to 5%

of normal subjects. PTSD patients with the reduction pattern had less severe PTSD symptoms than PTSD patients showing augmentation. The authors conclude that this is consistent with a protective compensation mechanism that functions to reverse the normal tendency to augment response with increasing stimulus amplitude. An elevated threshold for awakening to auditory stimulation during sleep has also been found in chronic war-related PTSD (7). In this study, too, the investigators speculated that the higher threshold could be related to an active blocking effort intended to suppress response to painful stimuli.

PTSD-like symptoms occur in many individuals immediately after a trauma and progress toward resolution. However, the mechanism by which this occurs has not been elucidated. Mellman and colleagues postulate that sleep may have an important regulatory influence on arousal and on the processing of traumatic memory after trauma exposure. There is experimental evidence for the importance of sleep in optimizing learning in general; REM sleep may have a particular role in "integrating" traumatic and other distressing memories. The study they report is the first to examine polysomnographic sleep prospectively after traumatic exposure. Subjects (24% women), recruited while hospitalized for non-CNS traumatic injuries, showed differences between injured individuals who did and did not experience PTSD. The PTSD group experienced more fragmentation of REM sleep, as indicated by more REM periods and shorter average REM duration, than both traumatized and noninjured comparison subjects. REM disruption was related to follow-up PTSD severity. The authors provide some very interesting speculations about these findings. They suggest that REM sleep may be a mechanism by which details of trauma memories are incorporated into less threatening scenarios. The authors previously reported that dream content in someone with PTSD is more likely to be unmodified compared to a traumatized person without PTSD, in which trauma references are incorporated into other dreams. This very intriguing idea has additional support in the recent work of Krakow and his group (8), who have shown that PTSD symptoms can be improved by an intervention aimed at changing or revising trauma-related nightmares.

Elucidating the pathogenesis of PTSD will require identification of defects in one or more of the adaptive mechanisms used to modulate emotion after a trauma exposure. These four articles provide much new information to help carry out this task.

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