DEPRESSION AND ANXIETY 28:737–749 (2011)

Review

CLASSIFICATION OF TRAUMA AND STRESSOR-RELATED DISORDERS IN DSM-5

Matthew J. Friedman, M.D. Ph.D.,[1,2] Patricia A. Resick, Ph.D.,[3,4] Richard A. Bryant, Ph.D.,[5] James Strain, M.D.,[6] Mardi Horowitz, M.D.,[7] and David Spiegel, M.D.[8*]

This review examines the question of whether there should be a cluster of disorders, including the adjustment disorders (ADs), acute stress disorder (ASD), posttraumatic stress disorder (PTSD), and the dissociative disorders (DDs), in a section devoted to abnormal responses to stress and trauma in the DSM-5. Environmental risk factors, including the individual's developmental experience, would thus become a major diagnostic consideration. The relationship of these disorders to one another is examined and also their relationship to other anxiety disorders to determine whether they are better grouped with anxiety disorders or a new specific grouping of trauma and stressor-related disorders. First how stress responses have been classified since DSM-III is reviewed. The major focus is on PTSD because it has received the most attention, regarding its proper placement among the psychiatric diagnoses. It is discussed whether PTSD should be considered an anxiety disorder, a stress-induced fear circuitry disorder, an internalizing disorder, or a trauma and stressor-related disorder. Then, ASD, AD, and DD are considered from a similar perspective. Evidence is examined pro and con, and a conclsion is offered recommending inclusion of this cluster of disorders in a section entitled "Trauma and Stressor-Related Disorders." The recommendation to shift ASD and PTSD out of the anxiety disorders section reflects increased recognition of trauma as a precipitant, emphasizing common etiology over common phenomenology. Similar considerations are addressed with regard to AD and DD. Depression and Anxiety 28:737–749, 2011.

Key words: *trauma; stress; stressor; dissociation; dissociative disorders; anxiety disorders; adjustment disorders; PTSD; ASD; posttraumatic stress disorder*

INTRODUCTION

Should the DSM-5 include a section on Disorders Related to Environmental (Traumatic and Other) Stressors, ranging in severity from adjustment disorders

[1]National Center for PTSD, US Department of Veteran Affairs, VA Medical Center, White River Junction, Vermont
[2]Departments of Psychiatry and Pharmacology & Toxicology, Dartmouth Medical School, Hanover, New Hampshire
[3]VA Center for National Center for PTSD, White River Junction, Vermont
[4]Boston University, Boston, Massachusetts
[5]School of Psychology, University of New South Wales, Sydney, Australia
[6]Department of Psychiatry, Mt Sinai School of Medicine, New York, New York
[7]Department of Psychiatry, University of California, San Francisco, California
[8]Department of Psychiatry and Behavioral Sciences, Stanford, California

*Correspondence to: David Spiegel, Department of Psychiatry, Stanford University School of Medicine, Stanford, California. E-mail: dspiegel@stanford.edu

The authors report they have no financial relationships within the past 3 years to disclose.

Received for publication 4 February 2011; Revised 28 April 2011; Accepted 4 May 2011

DOI 10.1002/da.20845
Published online 16 June 2011 in Wiley Online Library (wiley onlinelibrary.com).

(ADs) to acute stress disorder (ASD), posttraumatic stress disorder (PTSD), and dissociative disorders (DDs)? Currently, these possibly related disorders are classified under different categories in DSM-IV (anxiety disorders, DDs, and ADs). This review examines the spectrum of stress-related and posttraumatic and symptomatology, the relatedness of these disorders, and how they might be classified in DSM-5 under a heading as Trauma and Stressor-Related Disorders. This review emphasizes that there is both clinical utility and heuristic value in clustering specific diagnoses within broad diagnostic categories. Such a method of classification enables clinicians to distinguish one diagnosis from another, despite overlapping symptoms or clinical presentations. Broad diagnostic categories also generate testable theoretical explanations for specific groups of psychiatric disorders which can be systematically evaluated in research. The hypothesized stress-induced fear-circuitry disorders, and dissociative subtype of PTSD, discussed below, are good examples of how laboratory results with neuroimaging suggest a distinct classification scheme for some, but not all, anxiety disorders.

BACKGROUND

Poets, dramatists, and novelists (e.g., Homer, Shakespeare, Dickens) were the first to record the profound impact of traumatic stressors on cognitions, feelings, and behavior. Medicalization of such invisible wounds began during the mid-Nineteenth Century on both sides of Atlantic during the American Civil and Franco-Prussian Wars. Psychological trauma among civilians was most conspicuous following train accidents and became known as "Railway Spine." Such syndromes have embodied many, if not all, current PTSD symptoms although a variety of explanatory models have been invoked to account for such clinical observations. Some explanations focused on the heart (e.g., soldier's heart, Da Costa's syndrome, neurocirculatory asthenia); others on the nervous system (e.g., railway spine, shell shock) and others on the psyche (e.g., nostalgia, traumatic neurosis). From a theoretical perspective different explanatory models for these various syndromes have been derived from: psychoanalytic theory, Pavlovian fear conditioning models, Mowrer's two factor theory, Selye's theories of stress and adaptation, Horowitz's information processing cognitive-dynamic theories, cognitive theories, and neurobiology.[1–3]

By contrast, earlier editions of the DSM were steadfastly descriptive and atheoretical, presumably as a reaction against psychodynamic theorizing about the etiology of psychopathology, and to gain a greater opportunity for reliability in the diagnostic process. The One necessary exception was posttraumatic stress disorder, because it was by definition caused, at least in part, by exposure to a traumatic stressor. (Other exceptions included the, AD (which required a more than normal response to a stressor), organic mental disorders, and substance abuse disorders, where the etiological agent was specified.) Of course, like the etiology of any disorder, biopsychosocial factors combine, and traumatic events have an impact based on preexisting neural, genetic, personality, and contextual factors, including prior identity and relationship capacities and attitudes. Some would like to base most diagnoses, even PTSD, upon genetic, developmental, and personality differences,[4,5] although data suggest that the severity and frequency of trauma exposure is the most important variable.[6] Clearly, the underlying premise is that there are a variety of pathological responses to exposure to a range of stressors, from mild to severe and traumatic, and there is some association between the severity of the stressor, the individual stressed, and the nature of the response.[7] Therefore, it makes sense to consider a grouping of disorders within DSM-5 that ranges from adjustment through acute and posttraumatic stress disorders, and possibly others that constitute the range of reactions to environmental stressors. (This is not to say that onset of a depressive or anxiety disorder episode may not be preceded by exposure to stress, but a specified stressor does not constitute a required criterion for the diagnosis). It is noted that a specified stressor is also not required for DD; however, these conditions often exist following adverse experiences, and so the merits and limitations of including DD along with PTSD, ASD, and AD in this diagnostic cluster are considered. This issue is addressed later.

HISTORY OF DSM AND STRESS RESPONSES

In DSM-I,[8] "gross stress reaction" was an ill-defined diagnosis for classifying individuals who had been psychologically altered by exposure to military or civilian experiences. It was a useful diagnosis for initially classifying military veterans, ex-prisoners of war, rape victims, and Nazi Holocaust survivors. From a DSM-III[9] perspective, however, the major problem was that gross stress reaction was considered a "temporary diagnosis" which would be changed to a "neurotic reaction" if the condition persisted.

DSM-II[10] eliminated this diagnosis, leaving practitioners with no diagnostic option by which to classify clinically significant and persistent reactions to catastrophic experiences. "Situational Reaction" was the only diagnostic alternative. Because it included the full spectrum of adverse events from traumatic events to unpleasant experiences, it was seen as trivializing the impact of traumatic exposure. Furthermore, as with the DSM-I gross stress reaction, it was also considered a temporary and reversible clinical condition. By the mid-to-late 1970s many mental health clinicians recognized the need for a new diagnosis for patients suffering from severe, chronic and sometimes irreversible syndromes

following exposure to catastrophic events. Although not included in DSM-II, a number of syndromes had been described in the professional literature by that time, all named after the traumatic event itself such as: rape trauma syndrome, post-Vietnam syndrome, prisoner-of-war syndrome, concentration camp syndrome, war sailor syndrome, child abuse syndrome, battered women's syndrome, etc. The exciting new formulation that emerged during the DSM-III process[9] was that all of these discrete syndromes could be adequately characterized by the specific symptoms proposed in the PTSD diagnostic criteria.

There have been some alterations of the original DSM-III[9] PTSD criteria. The number of possible symptoms has increased from 12 to 17. The original three symptom clusters (e.g., reexperiencing, numbing, and miscellaneous) have been shuffled slightly to the present triad (e.g., reexperiencing, avoidance/numbing, and hyperarousal). But the fundamental construct, built into the diagnostic criteria, that exposure to overwhelming stress may precede the onset of clinically significant and persistent alterations in cognitions, emotions, and behavior has endured. Epidemiological studies have confirmed the DSM-III perspective and shown that exposure to extreme stress sometimes precedes severe and long-lasting psychopathology.[11–15]

It has also become apparent that although specific PTSD symptoms (e.g., intrusive thoughts, unbidden imagery repetitions, nightmares, avoidance behavior, hypervigilance, etc.) often are seen in the temporary distress exhibited by acutely traumatized individuals, e.g., bereavement, who recover normal functioning within days or weeks,[16] it is the persistence or re-emergence of such symptoms that characterizes what is pathological about PTSD.[17] In short, it appears that PTSD reflects a failure of adaptation or recovery, whereby most normal acute reactions to extreme stress do correct themselves over time.[17]

PTSD

Three different sets of organizing principles which have been invoked to classify PTSD and to cluster it with other diagnoses with common properties will now be considered. The arguments for placing PTSD within each specific category will be examined. First, designating PTSD as an "anxiety disorder," as has been the convention adopted in DSM-III and maintained in DSM-IV, is considered. This classification is based on clinical phenomenology with specific emphasis on disorders characterized by fear or anxiety reactions to environmental stimuli or circumstances. Second, disorders from the perspective of neurocircuitry are discussed. Specifically, disorders characterized by excessive amygdala reactivity and prefrontal cortex hypo-reactivity in response to stressful or fearful situations are examined. Third, results from confirmatory factor analysis of symptoms associated with a variety of diagnoses, with specific reference to the three subclasses of "internalizing disorders" identified within mood and anxiety disorders are evaluated. The question addressed is one of "goodness-of-fit": whether PTSD is best classified as an anxiety, a stress-related fear-circuitry, an internalizing disorder, or whether it should be classified elsewhere.

IS PTSD AN ANXIETY DISORDER?

Phenomenologically, PTSD shares a number of symptoms (especially from its Hyperarousal/D Criterion cluster) with other anxiety disorders such as insomnia, irritability, poor concentration, and startle reactions. PTSD avoidance behavior is similar to phobic and anxious avoidance. Physiological arousal and dissociation (e.g., derealization and depersonalization) also occur in panic disorder. Persistent intrusive thoughts or memories are commonly observed across anxiety disorders, including generalized anxiety disorder (GAD), obsessive–compulsive disorder (OCD), panic disorder, and social phobia.[18–20] Hypervigilance is superficially similar to the persistent apprehension seen in GAD, whereas in PTSD it has a focus on threat-related stimuli. In GAD it is usually an unrealistic worry about a number of life domains. PTSD is primarily a disorder of reactivity, along with specific and social phobia, rather than a syndrome with a consistent alteration of the tonic/basal state, such as depression and GAD However, PTSD is also often associated with unwanted, persistent, and depressed mood[21,22] (see below).

Furthermore, anxiety is present in most psychiatric disorders. It is not a particularly sensitive and specific index to posttraumatic reactions, normal or abnormal. Certain personality temperaments and character structures render some people to have more fear responses than others over a lifetime, depending on the development of personality strengths as compensations. According to Craske et al.[23] individuals with anxiety disorders exhibit a sensitivity to threat that is expressed in terms of both fear and anxiety responding. Specifically, anxiety disorders are associated with inordinately and abnormally (1) elevated fear responding to cues that signal threat; (2) elevated fear responding to cues that signal no threat when presented in the context of threat, and to cues that formerly signaled threat (i.e., extinction trials); (3) elevated anxiety in contexts and during periods in which aversive stimuli are anticipated; (4) equivalent acute responses to nonspecific stressors/unconditioned stimuli; and (5) elevated responses to disorder-specific (personally relevant) stressors. These features are shared with PTSD, supporting the notion that PTSD can be conceptualized as an anxiety disorder. Similarly, Jones and Barlow have argued that PTSD is most closely linked to other anxiety disorders because of "the presence of alarms and the general process of anxious apprehension," including intrusive recollections of trauma and nightmares.[24]

In contrast, there are reasons to question whether PTSD is appropriately understood simply as an anxiety

disorder. The diagnostic frames in DSM-IV, and intended for DSM-5, are not yet based on etiological understanding, and need to have an anchor in syndromic description. This standard requires specificity of symptoms within a disorder, and also within a cluster of disorders. A number of symptoms observed in PTSD, such as numbing, alienation, and detachment, are frequent depressive symptoms, and can be responsible for the high co-morbidity between the two disorders.[25] Although there is overlap between other anxiety disorders and depression, as well, this pattern suggests that PTSD is more than simply an anxiety disorder.

IS PTSD A STRESS-RELATED FEAR CIRCUITRY DISORDER?

In preparing for the DSM-5 process, the American Psychiatric Association (APA) examined the evidence favoring a proposed diagnostic cluster characterized by abnormalities in the neural circuitry that mediates the processing of threatening or fearful stimuli. Other disorders considered for this diagnostic group (or subgroup) are panic disorder, specific phobia, and social phobia.[26] In brief, the rationale is based on the role played by the amygdala and fiber tracts to and from the frontal cortices and other limbic areas in processing threatening, fearful, or intense emotional stimuli. Such neural circuitry coordinates the brain's reaction to such stimuli and (with respect to PTSD) mediates and moderates the afferent processing, appraisal, encoding, and retrieval of trauma-related information.[27,28] The pathophysiological problem in PTSD is currently hypothesized to possibly involve disinhibition of the amygdala and insula from normal medial prefrontal cortex (mPFC) restraint. Indeed, evidence showing disrupted anterior cingulate and orbitofrontal function is completely consistent with this model[2,29,30] but similar data have been found in other psychiatric disorders. Thus, relatively unrestrained amygdala activation is understood to increase the likelihood of recurrent fear conditioning, threat appraisals, and maladaptive protective behaviors.[2,28]

Although no biomarker has been found, there is some evidence for a biological profile that might be associated with PTSD, panic disorder, social phobia, and specific phobia (fear circuitry disorders) marked by greater brain activation in the amygdala and insula, along with decreased activation of the dorsal and rostral anterior cingulate. In contrast to those with social or specific phobias, however, in a small, unreplicated study only PTSD patients exhibited altered activation in ventromedial prefrontal cortex.[31] Furthermore, relative to control and depressed groups, PTSD patients demonstrate greater sensitivity to correctly recognized stimuli in the left amygdala and ventral striatum, and in the right occipital cortex, frontal gyrus, and bilateral insula. Such findings suggest that there might be different patterns of neural activation underlying PTSD versus depression.[17] Thus, at this time there is tentative evidence for common neural circuitry across the so-called fear circuitry disorders that is distinct from circuitry underlying nonfear conditions.

There is also evidence to challenge the proposed stress-induced fear-circuitry classification scheme. Opposite findings have been observed when individuals with PTSD exhibit prominent dissociative symptoms such as depersonalization, derealization, and fragmented thoughts. Such individuals exhibit excessive (rather than reduced) frontal activity that is associated with reduced (rather than increased) amygdala arousal.[32] Whether this should be considered a dissociative subtype of PTSD or whether it suggests that the neurocircuitry of PTSD is more variable than suggested by aforementioned findings, remains to be seen. Furthermore, neurocircuitry similarities are greatest between PTSD and panic disorder but not as pronounced with social and specific phobia. Finally, the relative prominence of hippocampal activity differs from one disorder to the next, appearing to be most prominent in PTSD.[33] Accordingly, whereas the fear circuitry hypothesis is intriguing, the weight of evidence from neuroimaging studies is mixed.

Neurocircuitry aside, there is a long tradition of psychological theory and research supporting the idea that primary symptoms might, in part, represent Pavlovian fear conditioning.[1,34–37] Specifically, there is overwhelming evidence for hyperreactivity (e.g., heart rate, skin conductance response) in PTSD in comparison to nonaffected individuals in response to reminders of the traumatic experiences[38,39]—this evidence does provide strong support for the proposal that PTSD functions as a fear circuitry condition. It needs to be acknowledged, however, that, in addition to fear, PTSD also includes a wide range of other emotions, such as guilt, anger, and shame, which are not readily explained by associative learning models.[40,41] Thus, it appears that an exclusive focus on fearful stimulation of the neural circuitry underlying PTSD cannot comprehensively account for the breadth of PTSD presentations.

IS PTSD AN INTERNALIZING DISORDER, AN EXTERNALIZING DISORDER, OR BOTH?

Watson[42] has argued that there is a lack of coherence in the current affective and anxiety diagnoses, which is one reason why there is so much comorbidity within and between these two diagnostic categories. He has proposed collapsing mood and anxiety disorders into an overarching class of "internalizing" disorders which contains three subclasses: the bipolar disorders (bipolar I, bipolar II, cyclothymia), the distress or "anxious misery" disorders (major depression, dysthymia, GAD, PTSD), and the fear disorders (panic, agoraphobia, social phobia and specific phobia). A fourth cluster, "externalizing" disorders,[43] consists of alcohol dependence, drug

dependence, adult antisocial personality disorder, and childhood conduct disorder.

Although PTSD was omitted from the original analyses that contributed to the development of this scheme, a reanalysis of DSM-III-R data from the National Comorbidity Study,[44] as well as analysis of DSM-IV data from the Australian National Survey of Mental Health and Well-Being[45] showed that it loaded with the distress/anxious-misery disorders but to a lesser extent than did depression, dysthymia or GAD.[42] These results suggest that PTSD can be characterized by anhedonic mood and anxious rumination rather than by pathological fear or externalizing behavior.[46]

Considering PTSD as an internalizing disorder within the distress/anxious-misery domain has the heuristic advantage of providing a rationale for the high comorbidity between PTSD and depression, although the comorbidity of both with substance abuse disorders, which would be classified as externalizing disorders, would be less easily accommodated, as noted previously. Furthermore, when data is considered from confirmatory factor analysis,[47] this formulation is consonant with the finding in some studies of a dysphoria factor within the latent structure of PTSD. However, other research has indicated that PTSD can fall on either the internalizing or the externalizing dimension or not fall on either dimension.[48–51] Indeed, PTSD can be understood as a disorder of dysregulation of affect and motor activity, ranging from overcontrol to undermodulation.[32,40] The fact that many people exhibit an externalizing, angry and aggressive form of PTSD, argues against the fear circuitry and anxiety disorder models of PTSD.[46]

Together, these findings suggest that PTSD can be understood in terms of both the internalizing and externalizing spectrum. Extrapolating from host–vector infectious disease models, PTSD could be conceptualized as the product of an environmental pathogen, e.g., a traumatic stressor) operating on individual diatheses that span the spectrum of human variation in vulnerability (and resilience) to psychopathology.[43] This diathesis–stress interaction can result in extensive heterogeneity in the phenotypic expression of psychopathology, with depression/anxiety being just one manifestation of the process.[46] The available evidence suggests that the most appropriate location for PTSD in DSM-5 would be among a class of disorders whose onset was preceded by exposure to serious adverse life events, i.e., a spectrum of traumatic-stress disorders.

WHERE DOES PTSD BELONG?

A crucial issue for DSM-5 is the extent to which trauma specifically precedes the onset of PTSD, as distinct from a range of other mood and anxiety disorders that arise following traumatic events.[52–55] For example, sexual abuse is associated with an increased risk of lifetime anxiety, depression, eating disorders, sleep disorders, and suicide attempts,[56] as well as DD (Dalenberg et al., 2011; under review), whereas child maltreatment is associated with an increased risk of depression, suicide attempts, alcohol problems, and behavior problems during childhood and adolescence.[57] Although exposure to stressful events may precede the onset of affective and anxiety disorders besides PTSD, ASD, and AD,[58] according to DSM-IV, such exposure is not a necessary condition for their occurrence. There is a useful distinction between those disorders that are precipitated (directly dependent upon) by a traumatic stressor and those that may be exacerbated by one. Indeed, it should be of great clinical utility to document a stressor/trauma history for all psychiatric disorders because such a stressor/trauma history might help to focus treatment issues more usefully than the current Axis IV which only addresses current stressors. For diagnostic purposes, however, what distinguishes PTSD, ASD, and AD from all other disorders is the requirement that symptom onset be precipitated by a specific stressor or traumatic event, and not that they just be associated with one.

The fear circuitry model holds that anxiety disorders occur when fear conditioning persists and there is a failure of extinction learning. Although there are some data suggesting that aversive or traumatic experiences do precede onset of panic disorder[59,60] and social phobia,[61] this evidence is mixed.[62] Further, with the exception of panic disorder and PTSD, most anxiety disorders have a gradual onset.[63] Although it is very common for a range of disorders to develop following trauma, the key question is the extent to which occurrence of a disorder is specific to a traumatic trigger. For example, the majority of cases of depression, GAD, social phobia, panic disorder, and specific phobia are not precipitated by a stressful event. Nor are the majority of OCD[64] or psychotic episodes.[65] Perhaps the most important argument for the exclusivity of a trauma/stress related grouping is that stress is necessary, even if not sufficient for the outbreak of the disorder.

To summarize, it is by no means obvious where PTSD best fits within the current and proposed classification schemes, which have been based upon symptom description rather than etiology. In this sense psychiatry has diverged from most other medical specialties' emphasis on causation as a critical component of diagnosis, e.g. "myocardial infarction" rather than "chest pain syndrome," and "epilepsy" rather than "loss of consciousness and motor control." At the time of this writing, it has not been finally determined what the groupings of disorders will be in DSM-5 or which disorders will be categorized in each grouping. There is an indication that there may be an "Anxiety and Stressor-Related Disorders" section that would include Trauma and Stressor-Related Disorders, including ASD, PTSD, AD, and DD in one subsection and "Anxiety (Fear) Disorders" in another, including Panic, Phobias, Social Anxiety Disorder, and Avoidant Personality Disorder. On the other hand, it is also possible

that DSM-5 will place Trauma and Stressor-Related Disorders in a category by themselves and will place Anxiety (Fear) Disorders in their own separate category. Depending on the choice of model selected, one comes to very different conclusions with regard to a proper place of PTSD within or outside the anxiety or anxiety/affective disorders. Although a stress-related fear circuitry model that would place PTSD alongside panic disorder, specific phobia, and social phobia has support from neuroimaging and fear conditioning studies, this approach is limited by the increasing evidence that PTSD encompasses a wider range of emotions than fear-based anxiety. An internalizing model that places PTSD within the distress/anxious-misery cluster alongside depression, dysthymia, and GAD ignores consistent evidence that PTSD is sometimes expressed as an externalizing disorder. Therefore, it is proposed to classify PTSD within an entirely separate category in which each disorder was precipitated by a serious adverse life event.

SUBTYPES OF PTSD

As indicated by Resick and Miller,[46] PTSD exhibits a variety of clinical manifestations that are best understood within a stress diathesis model. Because of the heterogeneity and wide spectrum of different individual diatheses, traumatic exposure may be followed by a variety of clinical presentations including the predominance of: fear-based anxiety, dysphoric/anhedonic, aggressive/substance abusing, guilt or shame, or dissociative symptoms, as well as combinations of any or all of the above. Therefore, on balance, the available evidence suggests that PTSD should be classified within a separate category of stress response syndromes or stress event or trauma-related disorders along with ASD, AD, and DD.

Another way of conceptualizing PTSD is not so much based on symptom overlap per se but rather in the range of possible maladaptive responses to disruptive input, ranging from stress to traumatic stress to repeated and severe trauma. The sudden intrusive occurrence of trauma or a stressor requires a response. This can challenge affect regulation systems, and trigger a variety of reactions that include, numbing, avoidance, and dissociation at one extreme to, flashbacks, irritability, impulsiveness, and aggression at the other.[5,66] The core of stress response syndromes is not so much any given symptom, but rather a varying pattern of either under or over-modulation of emotional, cognitive, and behavioral responses.[67]

Two recent studies suggest two types of PTSD response to traumatic stress, one involving overmodulation of emotion, a so-called dissociative subtype, affecting about 1/3 of those with PTSD, and the more traditional intrusion/irritability subtype with emotional undermodulation.[32,68] The former is associated with hyperactivity of mPFC in response to trauma stimuli coupled with inhibition of the amygdala, whereas the hyperarousal subtype shows the converse, medial prefrontal hypo-activation and amygdala activation. These variations of response within PTSD highlight the heterogeneity of the condition, and different presentations are associated with distinct neural circuitries. This heterogeneity suggests that PTSD cannot be understood by a single model because different mechanisms are probably underpinning both the etiology and maintenance of the variants of PTSD. The possibility of a dissociative subtype for PTSD is another example of the relationship between ASD/PTSD and DD. Adoption of such a subtype in DSM-5 would be consistent with the recommendation that PTSD, ASD, and AD be merged with DD to form a single diagnostic cluster in DSM-5. It would at the same time acknowledge the heterogeneity within them, for example, because there is evidence that the dissociative subtype of PTSD requires more extensive stabilization and interpersonal support before exposure-based treatments can be helpful.[32,69]

ACUTE STRESS DISORDER

There is a similarly strong argument to be made that ASD belongs in a stress response syndromes category, and is strongly linked to both PTSD and DD through the etiology of a significant traumatic stressor and symptoms. (The DSM-IV-TR symptomatology included the same A stressor criterion as for PTSD, one intrusion, one avoidance, and one hyperarousal symptom from PTSD, and in addition three of five dissociative symptoms: derealization, emotional numbing, depersonalization, a lack of awareness for one's surroundings, and psychogenic amnesia).[70] It therefore, by design, placed increased emphasis on the dissociative aspects of trauma response during the first month after trauma. These dissociative symptoms were included in the ASD in DSM-IV diagnosis because they were found to be highly associated with other ASD symptoms, provided good sensitivity and specificity, and have proven to be predictive of PTSD symptoms.[71–79] However, not all studies show that the dissociative symptoms add to the predictive power of the overall ASD diagnosis.[19,80] This may be due in part to the fact that there are fewer dissociative symptoms in PTSD (amnesia, flashbacks, numbing: 3 of 17), limiting the similarity of symptom comparisons. The proposed diagnostic criteria for ASD in DSM-5[19] does not require dissociative symptoms to be present, recognizing that ASD may or may not include dissociative reactions. In essence, all the arguments made above in terms of PTSD are equally applicable to the ASD diagnosis.

DISSOCIATIVE DISORDERS

Pierre Janet was the first to propose an etiological relationship between trauma exposure and dissociation.

He proposed (1904; see[81,82] that when the mind is unable to integrate posttraumatic "vehement emotions, the mind may not be able to match what is going on with existing cognitive schemes. As a result, memories of the experience …are split off (dissociated) from conscious awareness and voluntary control";[3] p 23). Dissociative symptoms (e.g., flashbacks, amnesia, and numbing) have remained within PTSD and ASD diagnostic criteria (more so for the latter than the former) although they have taken a back seat to symptoms that are more consonant with a fear-conditioning model. Recent fMRI research suggesting that there may be a distinct dissociative subtype of PTSD,[32] however, has brought this issue to the forefront.

It is acknowledged at the outset that DD, composed of Dissociative Identity Disorder (DID), Dissociative Amnesia and Fugue, and Depersonalization Disorder, differ from all other proposed diagnoses for the Trauma and Stressor-Related Disorders diagnostic cluster because prior exposure to a traumatic or stressful event has not been listed explicitly as a diagnostic criterion. The argument for including DD in this group hinges on the relationship of trauma to dissociation. There is considerable evidence that traumatic experiences, especially in childhood, predispose to dissociative symptoms, including disturbances in identity (DID and Dissociative Fugue), memory (Dissociative Amnesia), and consciousness (Depersonalization Disorder).[83–92] These traumatic experiences are not explicitly required for the diagnosis, and are more often chronic, repeated experiences of physical and sexual abuse in childhood rather than single traumatic events. The dissociative symptoms are often related to the trauma, as flashbacks that involve reliving episodes of abuse, amnesia about those episodes or periods of life during which it occurred, or symptoms of depersonalization or derealization occurring in relation to reminders of traumatic situations or perpetrators. These symptoms are associated with both functional and structural brain changes in neural systems regulating cognition, mood, and affect.[93–98]

Specifically, patients diagnosed with DID have been found to have smaller hippocampal volume[98] and hyperactivity of frontal cortex associated with limbic inhibition.[32] The underlying idea is that integration of sensory, motor, cognitive, and affective experience is an achievement, not a given, and that traumatic input disrupts the ability to perform such integration, leading to dissociative amnesia, disruption of identity, depersonalization, and derealization.[5,91,99–104] This understanding of DD relies on a bottom-up rather than a top-down model of information management, known in information systems as parallel distributed processing.[105,106] Integration of experience into memory, identity, somatic perception, and consciousness can be disrupted by stress, especially of a traumatic, repeated, or severe nature, leading to a reflection of the external discontinuity in inner experience[85] From this perspective, dissociation can be understood as having both intrusive (flashbacks, shifts in identity) and avoidant (amnesia, detachment) aspects:

> "an involuntary response with subjective loss of integration of information or control over mental processes that, under normal circumstances, are available to conscious awareness or control. Dissociative symptoms can manifest in all areas of psychological functioning, including memory, identity, emotion, perception, body representation and behavior. Symptoms are characterized either by (a) unbidden and unpleasant intrusions into awareness and behavior, with an accompanying loss of continuity in subjective experience (so-called positive dissociation); and/or (b) an inability to access information or control mental functions that are normally amenable to such access/control (so-called negative dissociation)." ([107], p 3.)

The very ability to put aspects of traumatic experience out of conscious awareness may make it more difficult for the person to process and put the traumatic events into perspective. Dissociative amnesia, as a symptom in PTSD, and in DID and Dissociative Amnesia, facilitates avoidance of traumatic memories, disconnecting them from mood states that may trigger them. This further confuses such individuals about the source of their dysphoria, leading them to misattribute it to some personal defect rather than to their abuse experiences. In a path-analytic study of 50 women with abuse history, Low et al. identified two pathways connecting abuse events to suicide: increased dissociative symptoms and reduced self-esteem.[108]

Such an understanding of pathological dissociation provides some justification for considering DD alongside ASD, as well as AD. As noted below, however, there is an important conceptual and empirical difference between the relationship of a stressful/traumatic event to ASD/PTSD on the one hand, and early life trauma to subsequent DD. Whereas the former is an immediate *precipitant* of the disorder, the latter appears to establish a long-term *vulnerability* factor for a diverse range of adult psychopathology, including but not limited to dissociative symptomatology.

In considering a category of trauma and stressor-induced disorders, it is important to recognize that it is problematic to include stressors that have a distal influence on psychiatric onset because these factors diffuse and lack specificity in terms of impact on later disorders. Childhood trauma and adversity has been linked to a very wide range of psychopathologies, potentially because it contributes to a generic emotional or cognitive vulnerability to mental disorder. On the other hand, delayed-onset PTSD has been documented after a long latency following the traumatic event, which raises questions about the importance of

the proximal/distal distinction; delayed-onset cases are uncommon, however, and the latency tends to be several months rather than years.[109] Although DDs, especially DID, are typically diagnosed some time after the traumatic event, they do sometimes occur within a proximal timeframe. There is evidence that the risk for many adult psychiatric conditions is increased with early life stress,[110] which may occur because of influences on neuronal development, coping style, cognition, or via gene and environment interactions. For example, a history of childhood trauma interacts with polymorphisms of the FKBP5 gene (a co-chaperone of the glucocorticoid receptor) in predicting vulnerability to the development of PTSD.[111] This finding builds on earlier work showing that early life trauma predicts hypothalamic-pituitary-adrenal axis hypersensitivity to stressors in adult life.[112] These findings provide a physiological rationale for delay in symptom onset as well as vulnerability to relapse among those with prior PTSD. They also underscore the fact that such symptoms may occur in response to a traumatic stressor long after exposure to it. At the same, there is evidence that carriers of the short allele of the serotonin transporter gene (5HTT) may develop depression, rather than PTSD, when exposed to multiple adverse life events,[113] although the evidence supporting this link has been questioned.[114] This pattern highlights that interactions of life stressors with genetic influences predispose people to a range of disorders beyond PTSD or DD. Herein lies the major challenge for including disorders with a distal contribution to the condition, such as many DD, because the same stressful causal agent has been documented for a range of other psychiatric conditions.

ADJUSTMENT DISORDERS

ADs are generally milder, more vaguely defined maladaptive responses to stressors that are broader in range than the A criterion of ASD and PTSD, from relatively mild to severe. The symptoms are likewise less specifically delineated, and include: (1) malfunctioning at work, at school, in relationships, or in other areas of living; and (2) the magnitude of distress and/or functional impairment is, not infrequently, excessive and out of proportion to the degree of the stress. Unlike PTSD and ASD, there is less emphasis on the nature and severity of the stress(ors) which do not have to reach the traumatic level, than on maladaptation and distress. AD subtypes have generally been understood as subsyndromal mood, anxiety, and conduct disorders. In that regard, they have provided a residual diagnosis for individuals whose distress and/or functional capacity warrants clinical attention although they do not exceed a diagnostic threshold for a more discrete or major psychiatric disorder. In DSM-5, ADs have been reconceptualized as stress response syndromes. Within that context, they provide a diagnostic option for people whose problems are clearly related to a nontraumatic, stressful event with which the individual is unable to cope.[115]

In addition, an ASD/PTSD subtype of AD has been proposed for DSM-5 to provide a specific diagnostic niche for individuals exposed to a traumatic event who do not meet ASD or PTSD criteria. Indeed, the proposed ASD/PTSD subtype is more specific than any other AD subtype (regarding anxiety depression, conduct or combinations of the above). It may, in effect, serve as a subsyndromal ASD or PTSD diagnosis.[115]

What separates nonspecific ADs from the new ASD/PTSD subtype is that whereas traditional subtypes are characterized entirely by their designation (e.g., depression, anxiety, mixed, conduct disorder), the new ASD/PTSD subtype is much more specific as a number of discrete symptoms are required to allow placement in this new category. Furthermore, for diagnostic purposes, nonspecific ADs which occur following adverse nontraumatic (e.g., interpersonal, vocational, financial, health) events are diagnostically equivalent to those which foillow traumatic events. In both cases individual vulnerability or inability to cope with the demands of the situation (resilience) is the critical factor rather than the specific characteristics of the event itself.

Many questions remain with regard to the concept of the AD diagnosis: the role of stressors and vulnerability of the patient; the place of specific stressors; the importance of age; and the relative contributions of concurrent psychiatric and medical morbidity. Although there are important disagreements about the boundaries between normal states, problems of living, (i.e., V-Codes), ADs and NOS categories of anxiety and depression, there is no disagreement that ADs are reactions to significant stressors and therefore belong in a stressor/trauma-related diagnostic category.

CONCLUSION

Any categorical clustering contains decisions that weigh certain factors more than others in determining inclusion and exclusion from that category. There is also inevitable arbitrariness in the conversion of variables on a continuum, such as the number and severity of anxiety, depressive, dissociative, and other symptoms, to categories. Pathological responses to stress and trauma have commonalities with anxiety disorders, including phobias (fearfulness, hyperarousal, avoidance) and OCD (intrusive thoughts), and panic disorder (hyperarousal), but also with depression (rumination, dysphoria) and DD (amnesia, depersonalization, derealization). What AD, ASD, PTSD, and most cases of DD have in common is a history of stress and/or trauma exposure.

The syndromes discussed have in common their participation in the framework of trauma and stress-related disorders. These disorders share in having characteristics indicating the importance of the

external events as a partial but important factor in evoking problems, symptoms, and signs. One factor is that the causal event is often known and can be verified as an actual, high impact episode and this connects thoroughly with a second factor, which is that memories related to the particular external event are often a central component in the symptoms presented, such as nightmares of an automobile accident, flashbacks of a combat scene, intrusive worries about the return of a rapist to the apartment complex.

It is proposed that there is heuristic value in grouping these disorders as a stress-related category because of the purported common etiological (mechanism) agent. In this regard, establishing a separate category for these disorders is more in keeping with the heterogeneous clinical phenomenology of PTSD. Indeed, the primary traumatic stress-related disorder, PTSD, is characterized by a variety of clinical presentations including: fear-based anxiety, dysphoric/anhedonic, aggressive/substance abusing behavior, guilt and shame, and dissociative responses. It should also be noted that the World Health Organization's 10th edition of its International Classification of Diseases (ICD-10) has a distinct category, Reaction to Severe Stress and Adjustment Disorders (F43) that includes ASD, PTSD, and AD. These disorders are distinct among other diagnoses insofar as they have the triggering event recognized in the diagnostic criteria—this factor alone is a major justification for clustering these conditions together. DDs are the next adjacent category in ICD-10 (F44), and both F43 and F44 are in a section entitled "Neurotic, Stress-Related, and Somatoform Disorders."

In proposing this clustering for DSM-5, it is acknowledged the utility of alternate frameworks, including an anxiety grouping, fear circuitry propositions, and internalizing/externalizing dimensions. There is sound evidence for each of these. However, each also has limitations because they fail to recognize the heterogeneity of responses following an adverse event. By grouping these disorders into a category on the basis of a precipitating event, it is possible to understand these disorders as being related to an environmental toxin but also acknowledging the diversity of responses and the contribution of different etiologies.

In summary, there is a need to distinguish between disorders that are *precipitated* by traumatic stressors and disorders in which traumatic exposure is a *predisposing* factor. Putting biological, social, and cognitive etiological mechanisms aside, and simply focusing on the convenience of categorizing disorders that by definition precipitated by a stressful event, there is a logical grouping of PTSD, ASD, and AD. The logic of including DD into this category is less clear in that a stressor or traumatic event is not required for the diagnosis, and there is not a clear connection established between trauma and DD in all cases. Although many DD can be linked to adverse childhood events, the same association can be made for many other psychiatric disorders, and in this sense the inclusion of distally related stressor conditions into this category comes at the cost of reduced specificity. Conversely, most people exposed to a traumatic or nontraumatic stressor do not develop any mental disorder. In this context, it needs to be noted that the DSM-5 approach to grouping different disorders in categories is influenced by several factors, one of which is the motivation to limit the number of categories. This approach will probably result in various disorders being grouped together based upon multiple criteria approaching similarity rather than identity. In this sense, it is important to acknowledge that some groupings in DSM-5 may not be optimal and that the DSM-5 text will need to explicitly recognize the limitations of certain groupings. For example, placing DD in a grouping that is titled "Trauma and Stressor-Related Disorders" may convey the idea that all DDs are sequelae of traumatic or adverse life events: it will be important for DSM-5 to inform the reader that the evidence does not indicate this relationship in all cases. This has important forensic implications as well as inclusion of DD in this diagnostic cluster does not necessarily imply that they are caused by a traumatic event.

The key question is the heuristic or clinical utility to clustering trauma or stress-related disorders together in the DSM-5. The specific mechanisms that function to lead an individual to develop one of these disorders rather than another or not developing any psychiatric disorder at all following a traumatic or stressful event will continue to be a major focus of research. It is already apparent that processes occurring in the wake of a severe traumatic event are qualitatively different from those observed in the aftermath of milder stressful events. It is for this reason that it is argued that a grouping of disorders related to a precipitating traumatic or stressful event explicitly acknowledges their qualitative differences and probable variations in etiology. If DDs are to be included in this category, it is especially important to recognize the multifactorial pathways to a DD, and there are cases in which these pathways do not involve apparent trauma. On face value, it appears a reasonable umbrella-term under which a range of different disorders can be described. It raises the possibility of presuming commonalities among disorders that may not exist, and most centrally, the role of exposure to traumatic or other stressors.

On the other hand, there is clear clinical utility for such a classification because it will encourage clinicians to inquire specifically about premorbid experiences and will provide a spectrum of diagnostic options to characterize subjective distress or functional impairment that was not present before exposure to aversive experiences. This spectrum ranges from proximate stress followed by milder (AD) or more severe (ASD) reactions, through more distal stress (at least one month) with more severe reactions (PTSD), to severe early life stress and more severe reactions (DD).

In addition, if such a change in classification is approved, it will definitely precipitate research on these disorders, which will enable us to determine whether or not such a diagnostic cluster should be retained in DSM-6.

Acknowledgments. This paper was commissioned by the DSM-5 Anxiety, Obsessive-Compulsive Spectrum, Post-Traumatic, and Dissociative Disorders Work Group. It represents the work of the authors for consideration by the work group. *Recommendations provided in this paper should be considered preliminary at this time; they do not necessarily reflect the final recommendations or decisions that will be made for DSM-5, as the DSM-5 development process is still ongoing.* It is possible that this paper's recommendations will be revised as additional data and input from experts and the field are obtained. In addition, the categorization of disorders discussed in this review needs to be harmonized with recommendations from other DSM-5 workgroups and the DSM-5 Task Force for the overall structure of DSM-5.

REFERENCES

1. Monson CM, Friedman M, La Bash HAJ. A psychological history of PTSD. In: Friedman MJ, Keane TM, Resick PA, editors. PTSD: Science and Practice—A Comprehensive Handbook. New York: Guilford; 2007;37–52.
2. Charney DS. Psychobiological mechanisms of resilience and vulnerability: implications for successful adaptation to extreme stress. Am J Psychiatry 2004;161:195–216.
3. van der Kolk BA. The history of trauma in psychiatry. In: Friedman MJ, Keane TM, Resick PA, editors. Handbook of PTSD: Science and Practice. New York, NY: Guilford Press; 2007;19–36.
4. Afifi TO, Asmundson GJ, Taylor S, Jang KL. The role of genes and environment on trauma exposure and posttraumatic stress disorder symptoms: a review of twin studies. Clin Psychol Rev 2010;30:101–112.
5. Butler LD, Duran RE, Jasiukaitis P, Koopman C, Spiegel D. Hypnotizability and traumatic experience: a diathesis-stress model of dissociative symptomatology. Am J Psychiatry 1996;153:42–63.
6. Roy-Byrne P, Arguelles L, Vitek ME, et al. Persistence and change of PTSD symptomatology—a longitudinal co-twin control analysis of the Vietnam Era Twin Registry. Soc Psychiatry Psychiatr Epidemiol 2004;39:681–685.
7. Horowitz MJ. Stress Response Syndromes: PTSD, Grief, and Adjustment Disorders. Northvale, NJ: Jason Aronson; 1997.
8. American Psychiatric Association. Dianostic and Statistical Manual of Mental Disorders (DSM I). Washington, DC: American Psychiatric Association; 1952.
9. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 3rd ed. Washington, DC: American Psychiatric Association; 1980.
10. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 2nd ed. Washington, DC: American Psychiatric Association; 1968.
11. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Arch of Gen Psychiatry 1995;52:1048–1060.
12. Norris FH, Slone LB. The epidemiology of trauma and PTSD. In: Friedman MJ, Keane TM, Resick PA, editors. Handbook of PTSD: Science and Practice. New York, NY: Guilford Press; 2007:78–98.
13. Morgan L, Scourfield J, Williams D, Jasper A, Lewis G. The Aberfan disaster: 33-year follow-up of survivors. Br J Psychiatry 2003;182:532–536.
14. Neria Y, Nandi A, Galea S. Post-traumatic stress disorder following disasters: a systematic review. Psychol Med 2008;38:467–480.
15. Whalley M, Brewin C. Mental health following terrorist attacks. Br J Psychiatry 2007;190:94–96.
16. Galea S, Ahern J, Resnick H, et al. Psychological sequelae of the September 11 terrorist attacks in New York City. New Engl J Med 2002;346:982–987.
17. Brewin CR, Lanius RA, Novac A, Schnyder U, Galea S. Reformulating PTSD for DSM-V: life after Criterion A. J Trauma Stress 2009;22:366–373.
18. Hackmann A, Clark DM, McManus F. Recurrent images and early memories in social phobia. Behav Res Ther 2000;38:601–610.
19. Bryant RA, O'Donnell M, Creamer M, McFarlane AC, Silove D. Posttraumatic intrusive symptoms across psychiatric disorders. J Psychiatric Res 2011;45:842–847.
20. Salkovskis PM. Obsessional-compulsive problems: a cognitive-behavioural analysis. Behav Res Ther 1985;23:571–583.
21. Thomas JL, Wilk JE, Riviere LA, McGurk D, Castro CA, Hoge CW. Prevalence of mental health problems and functional impairment among active component and National Guard soldiers 3 and 12 months following combat in Iraq. Arch Gen Psychiatry 2010;67:614–623.
22. Ikin JF, Creamer MC, Sim MR, McKenzie DP. Comorbidity of PTSD and depression in Korean War veterans: prevalence, predictors, and impairment. J Affect Disord 2010;125:279–286.
23. Craske MG, Rauch SL, Ursano R, Prenoveau J, Pine DS, Zinbarg RE. What is an anxiety disorder? Depress Anxiety 2009; 26:1066–1085.
24. Jones JC, Barlow DH. The etiology of posttraumatic stress disorder. Clin Psychol Rev 1990;10:299–328.
25. Blanchard EB, Penk WE. Posttraumatic stress disorder and comorbid major depression: is the correlation an illusion? J Anxiety Disord 1998;12:21–37.
26. Andrews G, Charney DS, Sirovatka PJ, Regier DA. Stress-Induced and Fear Circuitry Disorders: Advancing the Research Agenda for DSM-V. Arlington, VA: American Psychiatric Publishing, Inc.; 2009.
27. Davis M, Whalen PJ. The amygdala: vigilance and emotion. Mol Psychiatry 2001;6:13–34.
28. Neumeister A, Henry S, Krystal JH. Neurocircuitry and neuroplasticity in PTSD. In: Friedman MJ, Keane TM, Resick PA, editors. Handbook of PTSD: Science and Practice. New York, NY: Guilford Press; 2007:151–165.
29. Vermetten E, Bremner JD. Circuits and systems in stress. I. Preclinical studies. Depress Anxiety 2002;15:126–147.
30. Woodward SH, Kaloupek DG, Streeter CC, Martinez C, Schaer M, Eliez S. Decreased anterior cingulate volume in combat-related PTSD. Biol Psychiatry 2006;59:582–587.
31. Etkin A, Wager T. Functional neuroimaging of anxiety: a meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. Am J Psychiatry 2007;164:1476–1488.
32. Lanius RA, Vermetten E, Loewenstein RJ, et al. Emotion modulation in PTSD: clinical and neurobiological evidence for a dissociative subtype. Am J Psychiatry 2010;167:640–647.
33. Rauch SL, Drevets WC. Neuroimaging and neuroanatomy of stress-induced and fear circuitry disorders. In: Andrews G, Charney DS, Sirovatka PJ, Regier DA, editors. Stress Induced and Fear Circuitry Disorders: Refining the Agenda for DSM-V. Arlington, VA: American Psychiatric Association; 2009:215–254.
34. Foa EB, Kozak MJ. Emotional processing of fear: exposure to corrective information. Psychol Bull 1986;99:20–35.

35. Keane TM, Zimering RT, Caddell JM. A behavioral formulation of posttraumatic stress disorder in Vietnam veterans. Behav Therapist 1985;8:9–12.
36. Kolb LC, Ciccone PE, Burstein A, Greenstein RA. Heterogeneity of PTSD. Letter to the editor. Am J Psychiatry 1989;146: 811–812.
37. Lang PJ. Imagery in therapy: an information processing analysis of fear. Behav Ther 1977;8:862–886.
38. Orr SP, Lasko NB, Metzger LJ, Berry NJ, Ahern CE, Pitman RK. Psychophysiologic assessment of women with posttraumatic stress disorder resulting from childhood sexual abuse. J Consult Clin Psychol 1998;66:906–913.
39. Orr S, Metzger L, Lasko N, Macklin M, Peri T, Pitman R. De novo conditioning in trauma-exposed individuals with and without posttraumatic stress disorder. J Abnorm Psychol 2000; 109:290–298.
40. Krupnick JL, Horowitz MJ. Stress response syndromes. Recurrent themes. Arch Gen Psychiatry 1981;38:428–435.
41. Horowitz MJ. Understanding and ameliorating revenge fantasies in psychotherapy. Am J Psychiatry 2007;164:24–27.
42. Watson D. Rethinking the mood and anxiety disorders: a quantitative hierarchical model for DSM-V. J Abnorm Psychol 2005;114:522–536.
43. Krueger RF, Markon KE, Patrick CJ, Iacono WG. Externalizing psychopathology in adulthood: a dimensional-spectrum conceptualization and its implications for DSM-V. J Abnorm Psychol 2005;114:537–550.
44. Cox BJ, Clara IP, Enns MW. Posttraumatic stress disorder and the structure of common mental disorders. Depress Anxiety 2002;15:168–171.
45. Slade T, Watson D. The structure of common DSM-IV and ICD-10 mental disorders in the Australian general population. Psychol Med 2006;36:1593–1600.
46. Resick PA, Miller MW. Posttraumatic stress disorder: anxiety or traumatic stress disorder? J Trauma Stress 2009;22:384–390.
47. Friedman MJ. PTSD and other posttraumatic syndromes. In: McKay D, Abramowitz JS, Taylor S, Asmundson GJG, editors. Current Perspectives on the Anxiety Disorders: Implications for DSM-V and Beyond. New York, NY: Springer Publishing Co.; 2009:377–409.
48. Miller MW, Greif JL, Smith AA. Multidimensional Personality Questionnaire profiles of veterans with traumatic combat exposure: externalizing and internalizing subtypes. Psychol Assess 2003;15:205–215.
49. Miller MW, Kaloupek DG, Dillon AL, Keane TM. Externalizing and internalizing subtypes of combat-related PTSD: a replication and extension using the PSY-5 scales. J Abnorm Psychol 2004;113:636–645.
50. Miller MW, Resick PA. Internalizing and externalizing subtypes in female sexual assault survivors: implications for the understanding of complex PTSD. Behav Ther 2007;38:58–71.
51. Sellbom M, Bagby RM. Identifying PTSD personality subtypes in a workplace trauma sample. J Trauma Stress 2009;22:471–475.
52. Blanchard EB, Hickling EJ, Taylor AE, Loos W. Psychiatric morbidity associated with motor vehicle accidents. J Nerv Ment Dis 1995;183:495–504.
53. Mayou R, Bryant B, Ehlers A. Prediction of psychological outcomes one year after a motor vehicle accident. Am J Psychiatry 2001;158:1231–1238.
54. O'Donnell ML, Creamer M, Pattison P, Atkin C. Psychiatric morbidity following injury. Am J Psychiatry 2004;161:507–514.
55. Shalev AY, Freedman S, Peri T, et al. Prospective study of posttraumatic stress disorder and depression following trauma. Am J Psychiatry 1998;155:630–637.
56. Chen LP, Murad MH, Paras ML, et al. Sexual abuse and lifetime diagnosis of psychiatric disorders: systematic review and meta-analysis. Mayo Clin Proc 2010;85:618–629.
57. Widom CS, Czaja SJ, Paris J. A prospective investigation of borderline personality disorder in abused and neglected children followed up into adulthood. J Pers Disord 2009;23:433–446.
58. Bryant RA, O'Donnell ML, Creamer M, McFarlane AC, Clark CR, Silove D. The psychiatric sequelae of traumatic injury. Am J Psychiatry 2010;167:312–320.
59. Manfro GG, Otto MW, McArdle ET, Worthington III JJ. Relationship of antecedent stressful life events to childhood and family history of anxiety and the course of panic disorder. J Affect Disord 1996;41:135–139.
60. Faravelli C. Life events preceding the onset of panic disorder. J Affect Disord 1985;9:103–105.
61. McCabe RE, Antony MM, Summerfeldt LJ, Liss A, Swinson RP. Preliminary examination of the relationship between anxiety disorders in adults and self-reported history of teasing or bullying experiences. Cogn Behav Ther 2003;32:187–193.
62. Rapee RM, Litwin EM, Barlow DH. Impact of life events on subjects with panic disorder and on comparison subjects. Am J Psychiatry 1990;147:640–644.
63. Rapee RM, Bryant RA, Andrews G, Charney DS, Sirovatka PJ, Regier DA. Stress and psychosocial factors in onset of fear circuitry disorders. In: Andrews G, Dennis S, Charney, Paul J, editors. Stress-Induced and Fear Circuitry Disorders: Advancing the Research Agenda for DSM-V. Arlington, VA: American Psychiatric Publishing, Inc.; 2009:195–214.
64. McKeon JP, Roa B, Mann A. Life events and personality traits in obsessive-compulsive neurosis. Br J Psychiatry 1984; 144:185–189.
65. Tessner KD. Longitudinal study of the influence of psychosocial stress and cortisol on symptoms in adolescents with schizotypal personality disorder. US: Dissertation Abstracts International: Section B: The Sciences and Engineering, ProQuest Information & Learning; 2009.
66. Spiegel D, Hunt T, Dondershine HE. Dissociation and hypnotizability in posttraumatic stress disorder. Am J Psychiatry 1988;145:301–305.
67. Horowitz MJ, Field NP, Classen CC. Stress response syndromes and their treatment. In: Goldberger L, Breznitz S, editors. Handbook of Stress: Theoretical and Clinical Aspects. 2nd ed. New York, NY: Free Press; 1993:757–773.
68. Felmingham K, Kemp AH, Williams L, et al. Dissociative responses to conscious and non-conscious fear impact underlying brain function in posttraumatic stress disorder. Psychol Med 2008;38:1771–1780.
69. Cloitre M, Stovall-McClough KC, Miranda R, Chemtob CM. Therapeutic alliance, negative mood regulation, and treatment outcome in child abuse-related posttraumatic stress disorder. J Consult Clin Psychol 2004;72:411–416.
70. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association; 2000.
71. Kleim B, Ehlers A. Reduced autobiographical memory specificity predicts depression and posttraumatic stress disorder after recent trauma. J Consult Clin Psychol 2008;76:231–242.
72. Classen C, Koopman C, Hales R, Spiegel D. Acute stress disorder as a predictor of posttraumatic stress symptoms. Am J Psychiatry 1998;155:620–624.
73. Marmar CR, Weiss DS, Metzler T. Peritraumatic dissociation and posttraumatic stress disorder. In: Bremner JD, al CRMe, editors. Trauma, Memory, and Dissociation. Washington, DC: American Psychiatric Press, Inc.; 1998:229–247.

74. Marmar CR, Weiss DS, Metzler TJ, Delucchi KL, Best SR, Wentworth KA. Longitudinal course and predictors of continuing distress following critical incident exposure in emergency services personnel. J Nerv Ment Dis 1999;187:15–22.
75. Marmar CR, Weiss DS, Schlenger WE, et al. Peritraumatic dissociation and PTSD in male Vietnam theater veterans. Am J Psychiatry 1994;151:902–907.
76. Koopman C, Classen C, Cardena E, Spiegel D. When disaster strikes, acute stress disorder may follow. J Trauma Stress 1995;8: 29–46.
77. Spiegel D. Dissociative disorders. In: Hales RE, Yudofsky SC, eds. The American Psychiatric Press Synopsis of Psychiatry. Washington, DC: American Psychiatric Association; 1996; 583–604.
78. Shalev AY, Peri T, Canetti L, Schreiber S. Predictors of PTSD in injured trauma survivors: a prospective study. Am J Psychiatry 1996;153:219–225.
79. Walde L, Koopman C, Rierdan JDS. Symptoms of acute stress disorder and posttraumatic stress disorder following exposure to disastrous flooding. J Trauma Dissociation 2001;2:37–52.
80. Ginzburg K, Solomon Z, Koifman B, et al. Trajectories of posttraumatic stress disorder following myocardial infarction: a prospective study. J Clin Psychiatry 2003;64:1217–1223.
81. van der Kolk B, van der Hart O. Pierre Janet and the breakdown of adaptation in psychological trauma. Am J Psychiatry 1989;146: 1530–1540.
82. van der Kolk BA, van der Hart O. Pierre Janet and the breakdown of adaptation in psychological trauma. Am J Psychiatry 1989;146:1530–1540.
83. Coons PM. Iatrogenic factors in the misdiagnosis of multiple personality disorder. Dissociation Prog Dissociative Disord 1989;2:70–76.
84. Spiegel D. Dissociating damage. Special Issue: dissociation. Am J Clin Hypnosis 1986;29:123–131.
85. Spiegel D, Cardena E. Disintegrated experience: the dissociative disorders revisited. J Abnorm Psychol 1991;100:366–378.
86. Spiegel D, Yehuda R, McFarlane AC. Trauma, dissociation, and memory. In: Yehuda R, editor. Psychobiology of posttraumatic stress disorder. New York, NY: New York Academy of Sciences; 1997:225–237.
87. Kluft RP. The natural history of multiple personality disorder. In: Kluft RP, editor. Childhood Antecedents of Multiple Personality. Washington, DC: American Psychiatric Press; 1985;197–238.
88. Low J. The structures of suffering: Tibetan Buddhist and cognitive analytic approaches. In: Watson G, Batchelor S, Claxton G, editors. The Psychology of Awakening: Buddhism, Science, and Our Day-To-Day Lives. York Beach, ME: Samuel Weiser; 2000:250–270.
89. Akyuz G, Kugu N, Akyuz A, Dogan O. Dissociation and childhood abuse history in epileptic and pseudoseizure patients. Epileptic Disord 2004;6:187–192.
90. Lewis-Fernandez R. Culture and dissociation: a comparison of ataque de nervios among Puerto Ricans and possession syndrome in India. In: Spiegel D, editor. Dissociation: Culture, Mind, and Body. Washington, DC: American Psychiatric Association; 1994:123–167.
91. Spiegel D. Editorial: recognizing traumatic dissociation. Am J Psychiatry 2006;163:566–568.
92. Spiegel D. Multiple personality as a posttraumatic stress disorder. Psychiatr Clin North Am 1984;7:101–110.
93. Ehling T, Nijenhuis ER, Krikke AP. Volume of discrete brain structures in complex dissociative disorders: preliminary findings. Prog Brain Res 2008;167:307–310.
94. Sar V, Unal SN, Ozturk E. Frontal and occipital perfusion changes in dissociative identity disorder. Psychiatry Res 2007; 156:217–223.
95. Hopper JW, Frewen PA, van der Kolk BA, Lanius RA. Neural correlates of reexperiencing, avoidance, and dissociation in PTSD: symptom dimensions and emotion dysregulation in responses to script-driven trauma imagery. J Trauma Stress 2007;20:713–725.
96. Lanius RA, Williamson PC, Bluhm RL, et al. Functional connectivity of dissociative responses in posttraumatic stress disorder: a functional magnetic resonance imaging investigation. Biol Psychiatry 2005;57:873–884.
97. Shin LM, Orr SP, Carson MA, et al. Regional cerebral blood flow in the amygdala and medial prefrontal cortex during traumatic imagery in male and female Vietnam veterans with PTSD. Arch Gen Psychiatry 2004;61:168–176.
98. Vermetten E, Schmahl C, Lindner S, Loewenstein RJ, Bremner JD. Hippocampal and amygdalar volumes in dissociative identity disorder. Am J Psychiatry 2006;163:630–636.
99. Bremner JD, Vermetten E, Vermetten E, Dorahy M, Spiegel D. Psychiatric approaches to dissociation: integrating history, biology, and clinical assessment. In: Vermetten E, Dorahy MJ, Spiegel D, editors. Traumatic Dissociation: Neurobiology and Treatment. Arlington, VA: American Psychiatric Publishing, Inc.; 2007:239–258.
100. Foote B, Smolin Y, Kaplan M, Legatt ME, Lipschitz D. Prevalence of dissociative disorders in psychiatric outpatients. Am J Psychiatry 2006;163:623–629.
101. Chu A, DePrince AP. Development of dissociation: examining the relationship between parenting, maternal trauma and child dissociation. J Trauma Dissociation 2006;7:75–89.
102. Lewis-Fernandez R, Garrido-Castillo P, Bennasar MC, et al. Dissociation, childhood trauma, and ataque de nervios among Puerto Rican psychiatric outpatients. Am J Psychiatry 2002;159: 1603–1605.
103. Simeon D, Guralnik O, Schmeidler J, Sirof B, Knutelska M. The role of childhood interpersonal trauma in depersonalization disorder. Am J Psychiatry 2001;158:1027–1033.
104. Birmes P, Carreras D, Ducasse J-L, et al. Peritraumatic dissociation, acute stress, and early posttraumatic stress disorder in victims of general crime. Can J Psychiatry/La Revue canadienne de psychiatrie 2001;46:649–651.
105. Li D, Spiegel D. A neural network model of dissociative disorders. Psychiatr Ann 1992;22:144–147.
106. Rumelhart DJM. Parallel Distributed Processing: Explorations in the Microstructure of Cognition. Cambridge: The MIT Press; 1986.
107. Spiegel D, Lewis-Fernandez R, Loewenstein R, et al. Dissociative disorders in DSM5. Depress Anxiety; under review.
108. Low G, Jones D, MacLeod A, Power M, Duggan C. Childhood trauma, dissociation, and self-harming behaviour: a pilot study. Br J Med Psychol 2000;73:269–278.
109. Andrews B, Brewin CR, Philpott R, Stewart L. Delayed-onset posttraumatic stress disorder: a systematic review of the evidence. Am J Psychiatry 2007;164:1319–1326.
110. McLaughlin KA, Hatzenbuehler ML. Mechanisms linking stressful life events and mental health problems in a prospective, community-based sample of adolescents. J Adolesc Health 2009;44:153–160.
111. Binder EB, Bradley RG, Liu W, et al. Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults. J Am Med Assoc 2008;299: 1291–1305.

112. Heim C, Newport DJ, Heit S, et al. Pituitary-adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. J Am Med Assoc 2000;284:592–597.
113. Caspi A, Sugden K, Moffitt TE, et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science 2003;301:386–389.
114. Risch N, Herrell R, Lehner T, et al. Interaction between the serotonin transporter gene (5-HTTLPR), stressful life events, and risk of depression: a meta-analysis. J Am Med Assoc 2009; 301:2462–2471.
115. Strain J, Friedman M. Considering adjustment disorders as stress response syndromes for DSM-5. Depress Anxiety 2011;1–6.