Complex post-traumatic stress disorder

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Complex post-traumatic stress disorder (complex PTSD) is a severe mental disorder that emerges in response to traumatic life events. Complex PTSD is characterised by three core post-traumatic symptom clusters, along with chronic and pervasive disturbances in emotion regulation, identity, and relationships. Complex PTSD has been adopted as a new diagnosis in the ICD-11. Individuals with complex PTSD typically have sustained or multiple exposures to trauma, such as childhood abuse and domestic or community violence. The disorder has a 1–8% population prevalence and up to 50% prevalence in mental health facilities. Progress in diagnostics, assessment, and differentiation from post-traumatic stress disorder and borderline personality disorder is reported, along with assessment and treatment of children and adolescents. Studies recommend multicomponent therapies starting with a focus on safety, psychoeducation, and patient-provider collaboration, and treatment components that include self-regulatory strategies and trauma-focused interventions.

Introduction

The 11th version of WHO's *International Classification of Diseases*[1] (ICD) has introduced a new disorder—complex post-traumatic stress disorder (complex PTSD)—in addition to post-traumatic stress disorder (PTSD) under the parent category of "Disorders specifically associated with stress". Exposure to a traumatic event is a prerequisite for consideration of either disorder. The diagnostic criteria for PTSD consist of three symptom clusters that relate specifically to the traumatic event, including re-experiencing in the here and now, avoidance of traumatic reminders, and heightened sense of threat. The diagnosis of complex PTSD is comprised of six symptom clusters, the three PTSD clusters and three symptom clusters representing pervasive and chronic disturbances in self-organisation; affect dysregulation, extremely negative self-concept, and difficulties in forming and maintaining relationships.

ICD-11 introduced complex PTSD as a diagnosis distinct from PTSD to recognise the effect that chronic or repeated trauma can have on self-organisation-related mechanisms. Exposure to particular traumatic events such as repeated childhood sexual or physical abuse, domestic violence, prolonged combat exposure, torture, and genocide campaigns is associated with substantially greater risk for complex PTSD as compared with PTSD. The often unsatisfactory therapeutic and clinical management procedures used for these patients in the past have steadily improved in recent decades. This Seminar summarises the current state of knowledge regarding diagnosis, epidemiology, cause, and treatment options, including sections on complex PTSD during childhood and adolescence.

Search strategy and selection criteria

We searched PubMed, PsycINFO, and Embase for entries on complex post-traumatic stress disorder (PTSD) between May 1, 2013 (first publications of current complex PTSD concept[135]) and Oct 15, 2021. In each database, we used a combined search strategy of controlled vocabulary (including abbreviations like C-PTSD and cPTSD) and text words (including truncation wildcards and synonyms). The number of systematic reviews, meta-analyses, and randomised controlled trials are few, therefore, primary studies were the main sources of this Seminar. We restricted the systematic search exclusively to studies using the ICD-11 complex PTSD definition as earlier definitions are different and did not reach a critical mass of systematic research. However, additional research using earlier conceptualisations of symptom clusters (eg, Disorder of Extreme Stress Not Otherwise Specific) that were incorporated in the ICD-11 complex PTSD definition or descriptions of people who have experienced traumas, which could initiate ICD-11 complex PTSD (eg, aversive childhood experiences and complex trauma) were discussed by and selected for inclusion by consensus. We also searched for relevant evidence-based practice guidelines (eg, the British National Institute for Health and Care Excellence)[95] for related areas (eg, chronic trauma or child adversity consequences). There were no restrictions on language or publication format.

Clinical presentation

The following cases provide examples of the wide-ranging presentation of complex PTSD. The cases differ by age, gender, sexual orientation, traumatic exposures, and service context in which they are likely to be seen.

Case 1

A 36-year-old female who has escaped from the Islamic State enslavement comes to the health service in a refugee camp for help with poor sleep, problems eating, and general agitation. The primary health-care worker provides help for these problems and in addition completes a screen for complex PTSD. The woman reports witnessing the deaths of many people, including a family member. She has lost contact with her two children and is uncertain of where they are. She reports nightmares, a chronic sense of threat, and avoidance of activities that remind her of her enslavement (eg, the smell of foods she was forced to cook). Since arriving at the camp, she has felt depressed, lethargic, and helpless, alienated by daily routines, and full of self-reproach regarding the loss of her children and her inability to

protect them. She finds herself losing time over the course of the day, noticing she has not moved for minutes, and sometimes an hour can go by without her having any awareness of her environment. She feels like a failure because she allowed herself to be enslaved and feels worthless to her community. She avoids all social contact in part due to her shame but also because she has lost all sense of trust in others, including people of her own culture.

Case 2

A 45-year-old married female arrives at the emergency department with neck bruises consistent with strangulation, although she reports that she tripped and fell. After a careful review of her psychosocial history, she reveals a history of repeated physical and sexual abuse by her husband. An initial screen for complex PTSD is completed. The woman endorses a chronic sense of threat, nightmares, avoidance of thinking about her situation, and avoidance of conversations about her personal life with friends for fear of slipping up and revealing her experiences. She experiences radical shifts in emotional state, sometimes experiencing rage at the simplest difficulties (eg, vegetables unavailable at the market) and dissociative states when her partner comes home. She reports that she feels entirely despicable and that she avoids all relationships except for her husband as she believes he is the only person necessary for her survival.

Case 3

A 25-year-old gay male visits a drop-in consultation at the local LGBTQ clinic. 2 years earlier, he had been taunted by a group of men, severely physically and sexually assaulted, and left for dead. He had flashbacks and nightmares about the event, which he thought would subside but have not. In fact, this event had triggered memories of being physically and verbally bullied in middle school (ages 10–14 years). He feels more and more ashamed of what happened and shamed by his identity. He breaks off relationships as soon as a sense of emotional closeness develops, fearing he might have to reveal his sexual assault history. He is chronically moody and reacts to the smallest provocations at his job. He has begun dabbling in drugs and alcohol and unprotected sex as a way of distracting himself.

Diagnosis

Complex PTSD is listed in ICD-11 under the category "Disorders specifically associated with stress" (code 6B41). The diagnosis builds on the preceding diagnosis in ICD-10 "Enduring personality change after catastrophic experiences" (EPCACE code F62.0), which highlighted the effects of prolonged exposure to life-threatening situations (eg, concentration camp experiences). Of note, the DSM-IV[2] considered the inclusion of a complex PTSD diagnosis called Disorder of Extreme Stress, Not Otherwise Specific but the proposal was rejected on the grounds that there was no sufficient empirical support. A similar decision was made in 2013 for the DSM-5.

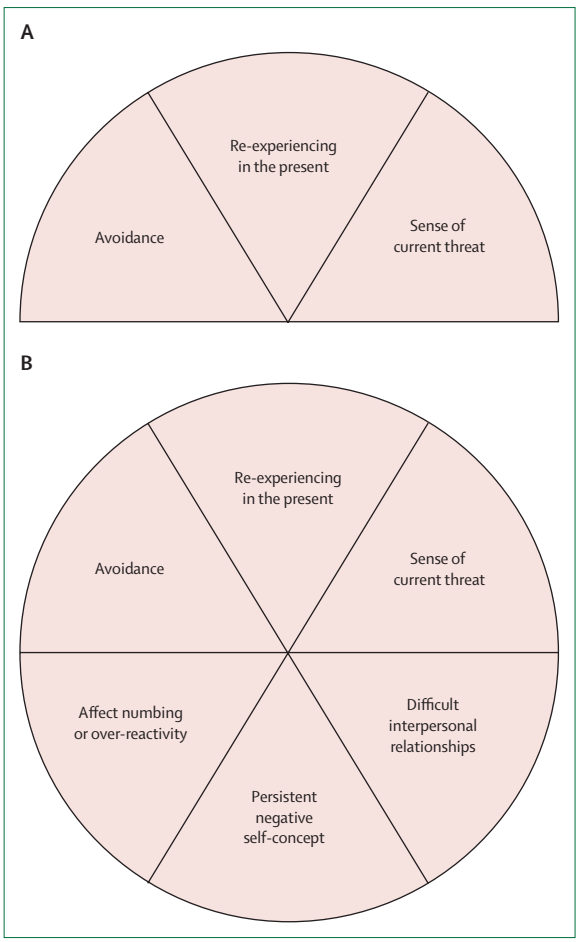

Figure: **Symptom patterns of post-traumatic stress disorder (A) and complex post-traumatic stress disorder (B)**

The complex PTSD diagnosis requires the presence of a traumatic stressor, defined as an extremely threatening or horrific event or series of events, and endorsement of at least one symptom from each of the six symptom clusters: (1) re-experiencing in the present; (2) avoidance of traumatic reminders; (3) a sense of current threat (the PTSD triad); (4) affective dysregulation; (5) negative self-concept; and (6) difficulties in forming and maintaining interpersonal relationships (the disturbances in self-organisation triad; figure). A complex PTSD diagnosis requires that these symptoms cause substantial impairment in functioning. Onset of symptoms can occur across the lifespan and are typically related to exposure to chronic or repeated traumatic events, or victimisation that has continued for a period of months or years.

Importantly, unlike previous formulations of complex PTSD,[3] the type of trauma is a risk factor and not a requirement for consideration of the complex PTSD

Panel 1: **Important teaching points for clinicians**

Maintain sensitivity to possible trauma as indicated by:

Verbal remarks by the patient suggesting:

- Childhood experiences of violence in or from a close social environment, such as harsh punishment as a child
- Unpleasant or coerced sexual experiences

Signs of exposure to violence from domestic, interpersonal, or man-made sources:

- Scars or deformities that can indicate torture or sustained physical abuse
- Local or systemic chronic deficiency symptoms

Be aware of the disturbance in self-organisation symptoms that distinguish complex post-traumatic stress disorder

- Easily resolvable irritability and rapid anger reaction
- So-called depressive appearance without typical phased progressions as in unipolar or bipolar depression
- Marked feelings of worthlessness
- Few or no social relationships or withdrawal from relationships since the traumatic experience, including break-off of family relationships

Recognise the effect of symptoms on clinical interview and interactions

- Emotional reactivity could produce high patient impulsivity, readiness for anger and rage, or verbal accusations directed towards the doctor in the case of any irritation
- Patient is likely to have low self-regard, believe that they are permanently damaged, and improvement is impossible or unlikely
- Distrust in relationships can lead to the patient searching for indications that the doctor has also led a life marked by losses and experiences of trauma; patient might want to test the doctor in this regard

Approach patient and patient interactions in a trauma-sensitive manner to establish safety and trust

- A calm attitude and sustained attention to the patient's statements
- Respect for the individual's trauma history
- Acceptance of their perspectives regarding their experiences and problems
- Explicit description of assessment and treatment planning activities
- Clear statements that effective treatment options exist

It is recommended that services with a high proportion of trauma-exposed patients provide training for all staff (clinicians, administrators, and support personnel) to create a supportive and trauma-informed environment. Staff awareness of the prevalence of trauma, its manifestation in patients, and appropriate responses will create service environments that support routine screening, accurate detection, and appropriate treatment of complex post-traumatic stress disorder patients.

diagnosis. This notion recognises the role of personal (eg, genetic or dispositional) and environmental (eg, social stressors and support) risk and protective factors for vulnerability to the disorder. For example, a person who has experienced sustained childhood sexual abuse might develop PTSD rather than complex PTSD, or might not develop any trauma-related disorder, depending on dispositional strengths and the presence of protective resources in the environment, such as having had loving and attentive caregivers or ongoing social support. Alternatively, an individual who experiences a single highly distressing traumatic event in adulthood (eg, witnessing the murder of their child) might develop complex PTSD given dispositional vulnerabilities, poor social support, negative social environment, or a history of adverse childhood events.

In contrast to the ICD-11, the most recent version of the DSM-5 does not include a complex PTSD diagnosis but rather has recognised the heterogeneity of symptoms observed among various trauma populations by expanding the number and types of symptoms under the PTSD diagnosis. For example, DSM-5 introduces a symptom cluster of negative alternations in mood and cognitions along with a dissociative subtype to address some aspects of affect disturbance and self-perception. These extensions have led to concerns about the utility of the disorder regarding the large number of symptom profiles that can be generated under a single diagnosis and difficulties in translation from diagnosis to treatment planning.[4]

Assessment

An atmosphere of calm and safety supports the completion of the initial assessment (panel 1). Extensive details of the trauma do not need to be collected during screening (a full trauma account will be taken by the clinician who will deliver ongoing therapy). Rather, assessment should focus on determining the effect of the trauma on the individual. For specific assessment, the current literature has primarily used the newly developed partner instruments, the clinician-administered International Trauma Interview (ITI)[5] and the self-report International Trauma Questionnaire (ITQ).[6] The validity and reliability of the ITI needs to be investigated more extensively, whereas the ITQ has been validated and studied and used across many languages, cultures, and regions of the world.[7,8]

Assessment should include a broad range of biopsychosocial aspects, with a particular focus on dissociation, suicidal ideation, and substance abuse. Physical health problems are common among individuals with trauma exposure, and chronic or repeated exposure increases the risk for general health problems.[9] Rates of cardiometabolic diseases, particularly cardiovascular disease and type 2 diabetes are significantly elevated.[10] Environmental risk factors and stressors must be identified, such as ongoing domestic violence or homelessness, and referrals should be provided to services

that address these needs as a first step in treatment (figure).

Comorbidity

Highly relevant comorbidities exist with dissociative and somatic symptom disorders, quasi-psychotic symptoms, drug and alcohol use disorders, and depressive and anxiety disorders. Dissociative disorders such as dissociative neurological symptom disorders, dissociative amnesias, depersonalisation-derealisation disorder and (partial) dissociative identity disorder are aetiologically co-determined to a large extent by aversive and traumatic childhood experiences.[11] To date, there are no studies on the overlap of these diagnoses with complex PTSD as defined by ICD-11; however, several studies have shown that the general tendency to dissociate is considerably higher in ICD-11 complex PTSD than in PTSD, and this finding has been consistent despite the use of various measures of ICD-11 complex PTSD.[12–14] When differentiating between dissociative symptoms that relate more to bodily experience (somatoform dissociation) and symptoms that relate to perceptual and cognitive processes (psychogenic dissociation), the former have been more strongly associated with the occurrence of PTSD.[15]

Quasi-psychotic symptoms should also be evaluated; most notably, ego-dystonic auditory or visual illusions of varying clinical severity.[16] When presented with these symptoms in individuals from a refugee or migrant background, assessment of complex PTSD should be considered, particularly if the individual is from a different cultural background. In one study, approximately 30% of refugees seeking treatment for PTSD in a Danish outpatient psychiatric clinic also experienced psychotic symptoms, with approximately 50% of these individuals also experiencing disturbances in self-identity and personal relationships, as required for diagnosis of complex PTSD.[17]

The long-established comorbidity between chronic PTSD and drug and alcohol dependence is also likely to apply to complex PTSD. In one population-level study, a point prevalence of 46% for alcohol dependence was shown among those with complex PTSD, relative to 22% in traumatised people without complex PTSD (odds ratio [OR] 2·2).[18] For drug dependence, the OR increased to 3·4.[19] Finally, complex PTSD is associated with an increased risk for both anxiety and depressive disorders, relative to individuals with PTSD and to those without either PTSD or complex PTSD in both clinical and community samples.[7,18,20]

Major differential diagnoses

Complex PTSD versus PTSD

ICD-11 PTSD is conceptualised as a conditioned response of fear and horror to a highly threatening experience, and symptoms most often occur upon exposure to reminders of the trauma. The complex PTSD diagnosis includes the PTSD symptoms, and, consistent with them, the associated fear conditioning conceptualisation. The additional disturbances in self-organisation symptoms are proposed to result predominantly from the effect of chronic or repeated traumatic exposure on basal mechanisms of affect regulation, sense of self, and interpersonal relationships. Unlike the intermittent PTSD symptoms, disturbances in self-organisation symptoms are persistent and pervasive, and occur across a variety of contexts regardless of proximity to a traumatic stressor, although the presence of a stressor can exacerbate their expression and intensity.

Given that complex PTSD is comprised of a greater number and types of symptoms relative to PTSD, it is unsurprising that it is associated with greater functional impairment and poorer quality of life.[9,21,22] The diagnoses of PTSD and complex PTSD are mutually exclusive. If a person is diagnosed with complex PTSD, they cannot also have a diagnosis of PTSD.

Complex PTSD versus borderline personality disorder (BPD)

BPD is recognised as a personality disorder and is a categorically defined diagnosis in ICD-11.[23] A formal diagnostic distinction is that complex PTSD requires the presence of a traumatic stressor whereas BPD does not. Although individuals with BPD often report a traumatic stressor, this is not part of the criteria for diagnosis nor is it a focus of traditional BPD treatment. Complex PTSD and BPD share conceptual overlap with three types of problems; namely, difficulties in affect regulation, self-concept, and interpersonal relationships. The particular expression of the symptoms, however, is largely distinguishable. Although there is substantial overlap in affective symptoms, research to date indicates that impulsivity, suicidal, and self-injurious behaviours are more common in BPD.[21,24] Indeed, self-harming behaviours are part of the diagnostic criteria for BPD but not for complex PTSD. In BPD, self-concept difficulties reflect an unstable sense of self,[25] whereas in complex PTSD, individuals reflect a persistent negative sense of self. Relational difficulties in BPD are characterised by volatile patterns of interactions and intense engagement in relationships, whereas in complex PTSD, they reflect a persistent tendency to avoid relationships and to distance when intense emotions arise. The characteristics of the disorders are such that individuals with BPD could endorse many complex PTSD symptoms (eg, negative view of self) but those with complex PTSD will not endorse many BPD symptoms (eg, negative and positive view of self).

Diagnosis in children and adolescents

Diagnosis of complex PTSD in young individuals follows the same criteria as in adults, with consideration that symptom expression is sensitive to the developmental

stage.[1] For example, in a child with complex PTSD, affective dysregulation could be expressed in tantrums, relationship difficulties could be observable as resistance to their teacher, and dissociation could appear to be daydreaming or failing to pay attention. Some symptoms such as tantrums or little interactive play might be age appropriate, thus the presence of these symptoms before the traumatic stressor needs to be taken into account and identified as worsening. Factor analyses have supported the distinction between ICD-11 PTSD and complex PTSD in children and adolescents.[22,26,27] At least one alternative diagnostic formulation concerning the effect of complex trauma in children has been proposed for the DSM.[28] The DSM includes a greater number and diversity of symptoms than complex PTSD with a particular focus on behavioural and cognitive difficulties. Research is needed to evaluate the reliability and validity of the disorder, and, in particular, the variance of symptoms across cultures other than the USA.

Assessment of complex PTSD symptoms in young people can be conducted with the ITQ Child and Adolescent version (ITQ-CA),[29] which has adapted wording on the items appropriate to age 9 years reading level. The ITQ-CA has been validated for use for individuals aged 10–17 years[25] and internal reliability and convergent validity were established with foster children aged 10 years and older.[30] However, to date, the ITQ-CA does not have operationalised diagnostic thresholds and validation with children aged under 10 years. The development of diagnostic interviews and caregiver report assessments for younger children is also needed.[31] As in adults, childhood complex PTSD relative to PTSD is associated with higher rates of comorbidity[32,33] including the co-occurring presence of depression, anxiety, and externalising disorders, which should be considered to minimise misdiagnosis.

Epidemiology, culture specific profiles, and causes

Since complex PTSD is a relatively new diagnosis, prevalence studies to date are based on self-report questionnaires through which one can only determine a probable complex PTSD diagnosis. In numerous European countries and in Israel and the USA where prevalence has been investigated in the general population, the one-month prevalence of complex PTSD has varied between just under 1% (Germany) and just under 8% (Ireland). For comparison, PTSD prevalence ranged in the same order of magnitude between 1·5% and 9%.[20,34–36] For the UK, lifetime prevalence—which is always higher than point prevalence—was reported as 13% for complex PTSD and 5% for PTSD.[18] In three African countries (Ghana, Kenya, and Nigeria), initial estimates of one-month prevalence have ranged from 13% to 20% for complex PTSD, and from 17% to 19% for PTSD.[37] National prevalence differences could reflect between-country differences in the extent of violence, war, and use of physical violence against children.[38,39] In addition, there are methodological differences between studies, such as representativeness of samples included and differences in cultural attitudes when completing questionnaires. A systematic review of age and gender differences found that although PTSD rates were consistently higher among women than men and consistently lower among the older age groups (65+ years) than in middle-aged adults, complex PTSD rates tended to be equivalent across men and women, and were not consistently lower among individuals in older age groups versus younger age groups.[40] Racial or ethnic differences have not yet been systematically studied.

In mental health services, complex PTSD prevalence rates are high, with suggestions of up to 50%.[18,41] Other high-risk samples indicate a prevalence of 16–38% in refugees and asylum seekers[42] and approximately 15% in former political prisoners.[43] In British firefighters and police, approximately 15% exhibit complex PTSD in addition to approximately 7% experiencing PTSD.[44,45]

In former soldiers or veterans, prevalence estimates have varied from country to country. Approximately 13% of US veterans have been reported as experiencing complex PTSD relative to 21% with PTSD.[46] An Australian study[47] of treatment-seeking veterans found a complex PTSD diagnosis in 49% and a PTSD diagnosis in an additional 14%. Higher prevalence was found for Croatian veterans with 64% experiencing complex PTSD.[48] These different rates could indicate the need to consider causes, but are also likely to be influenced by between-study variation in assessment methods and sample selection.

For low-income and middle-income countries, two particularities of clinical presentations have been described thus far. The first is a victim–perpetrator overlap for (former) child soldiers, child terrorists, and gang members, which is a presentation common in several regions of the world. Here, the consequences of complex trauma often include strong dissociation tendencies and emotional numbing.[49] The second presentation is in contexts in which there are very high levels of ongoing violence, which frequently have political or war-related origin (eg, townships in South Africa) in which symptomatology includes persistent alertness and fear of highly probable peril to oneself and loved ones.[50]

A starting point for the causes of complex PTSD is the seminal models underlying the three symptom clusters of re-experiencing, avoidance, and heightened sense of threat, along with models accounting for dysregulation of memory encoding and retrieval to avoid psychophysical alarm responses at recall.[51] Models of complex PTSD as a disorder focus on the groups of traumatic experiences and biopsychosocial factors. Studies have consistently indicated that polytraumatisation, that is, repeated or long-term traumatic experiences in the interpersonal sphere, is highly correlated with complex PTSD. Polytraumatisation has been proposed to drive complex PTSD-related changes in self-organisation,

relational capacities, difficulties in emotion regulation, and other functions including memory and attention that can contribute to threat management and the organisation and coherence of trauma memories.[52–54] Such complex PTSD-relevant polytraumatisation occurs mainly in childhood and young adulthood. Related event dynamics can contribute to a sense of cumulative trauma. For example, coercive caretaking measures in childhood might be accompanied by physical abuse in childhood and repeated sexual violence in adolescence. When the number of traumatic or adverse single events are summed, an increasing number of stressors is associated with heightened complex PTSD risk, especially for childhood trauma.[20,55] This dose–response effect has been repeatedly shown in large-scale studies examining adverse childhood experiences, which includes both experiences formally recognised as traumatic events (eg, sexual abuse) and other aversive factors such as maltreatment, poverty, and parental substance dependence, which increase risk for the psychological consequences that are now recognised as part of complex PTSD.[56–58]

Various biopsychosocial factors across the lifespan could also be relevant.[54] There is evidence that trauma exposure creates risk for complex PTSD in ways that are sensitive to the developmental epoch in which the trauma has occurred. For example, trauma in childhood can adversely affect attachment patterns and mental integration capabilities.[59–62] This includes, for instance, an adverse effect during adolescence on the formation of one's own social identity and the acquisition of morality and values, and in early adulthood, taking responsibility for people and assignments,[63] all of which are accompanied by emotion regulation and relationship skills development.[64] Such findings lead to comprehensive lifespan cascade models, such as that observed among older survivors of institutional child maltreatment.[65] Additionally, protective social factors for survivors are relevant, namely the ability to disclose the trauma and to gain social acknowledgment of their victim status.[66–68]

Underlying neurobiological mechanisms

Given the insufficient research on complex PTSD consistent with the ICD-11 conceptualisation, in this section, we include investigations of the neurobiological underpinnings of PTSD related to prolonged and repetitive childhood traumas (eg, sexual or physical abuse), and aversive childhood experience (adverse childhood experiences [eg, emotional abuse, neglect, and mental illness in the family]).

There is ample evidence that adverse childhood experiences are linked to deleterious effects on neurocognitive functioning (namely, working memory and inhibitory control), mirrored in substantial functional and structural alterations in stress-sensitive and emotion-sensitive brain regions in the amygdala and hippocampus, along with the anterior cingulate cortex.[69] It has been hypothesised that the emotion-sensitive brain regions are particularly vulnerable to the effect of adverse childhood experiences due to a high density of glucocorticoid receptors, hence prolonged release of glucocorticoids is stated to cause damage, dendritic atrophy, and neurogenesis suppression.[70] Research in both animal models and human participants has revealed that the brain is not only shaped by the level of distress, but also by type and timing of adverse childhood experiences during brain development.[71,72] So-called active maltreatments challenging the physical integrity of the self (eg, physical and sexual abuse) have been shown to result in different neurobiological alterations than so-called passive maltreatments, which challenge the basic needs of a child (eg, emotional and physical neglect).[73] Neuroplasticity, as defined by the ability of the brain to adapt its structure and function in response to environmental demands, varies during maturation between different brain areas.[74] Accordingly, research revealed that adverse childhood experiences have a differential effect on sensitive brain areas, especially within the limbic circuit, during specific maturation phases.[75,76] For instance, sensitive periods for the limbic circuit (including the amygdala and hippocampus) and areas involved in stress regulation (such as the prefrontal cortex) are during preadolescence (approximately 9–12 years) and early adolescence (approximately 13 years).[76] This could contribute to the heterogeneity of study results in different PTSD populations based primarily on cross-sectional diagnoses.

In general, meta-analyses of structural imaging of individuals with complex PTSD have reported reduced volume in the hippocampus, parahippocampal gyrus, amygdala, insula, and anterior cingulate cortex.[77–79] On a functional level, across several studies, individuals with complex PTSD have shown increased activity in the hippocampus, parahippocampal gyrus, insula, prefrontal cortex, and anterior cingulate cortex compared with healthy controls.[80–85] The first neuroimaging study[86] to directly contrast functional activity during threat processing between individuals with ICD-11 complex PTSD compared with ICD-11 PTSD suggested that individuals with complex PTSD experienced increased activity in the amygdala and insula relative to those with PTSD. No significant group differences were observed in prefrontal and anterior cingulate regions.

Neuroendocrine research on ICD-11 complex PTSD is currently missing. Research in hypothalamic–pituitary–adrenal axis reactivity in individuals with PTSD has been inconsistent with studies reporting hypocortisolism,[87] hypercortisolism,[88] or no difference in cortisol level,[89,90] relative to healthy controls. In childhood abuse-related PTSD, one study observed a reduced basal cortisol level.[90] Further, studies investigating the neuroendocrine stress reactivity in abused women have revealed an enhanced hypothalamic–pituitary–adrenal axis responsiveness under challenging conditions.[91–94]

Psychotherapeutic interventions

Treatment guidelines for complex PTSD offered by professional organisations have been cautious about how best to proceed with treatment for this population given that the disorder is new and there are insufficient data to guide recommendations. Recommendations have generally proposed the use of evidence-based treatments for PTSD, which include both trauma-focused interventions and multicomponent therapies (International Society for Traumatic Stress Studies [ISTSS] Guidelines Committee Position Paper, Guidelines Committee, Australian Guidelines on Complex PTSD, and The German-speaking Society for Traumatic Stress Studies).[95-97] The National Institute for Health and Care Excellence guidelines[98] recommend that this patient group could require a higher number of sessions to develop trust and stabilise acute symptoms relative to individuals with PTSD. ISTSS have highlighted the importance of attention to general functioning given the substantial level of impairment associated with complex PTSD.[95] Given there is inadequate evidence specific to this population, it is appropriate to tailor the treatment according to patient needs and symptoms.

Two meta-analyses of treatment trials were conducted to assess whether current evidence-based therapies for PTSD are effective for patient populations with trauma histories and symptoms representative of individuals who might meet criteria for the newly established complex PTSD diagnosis.[99,100] One study reported that trauma-focused therapies provided better outcomes compared with non-trauma-focused treatments regarding all complex PTSD symptoms. However, analyses also indicated that treatment outcomes were consistently less positive for individuals with childhood trauma, a type of trauma that is strongly associated with complex PTSD. The results suggest that although trauma-focused treatments are likely to be effective for complex PTSD, treatment outcomes are not optimal.

The second meta-analysis evaluated different kinds of treatment for complex trauma samples (eg, childhood abuse, refugees, and military veterans), that is, populations who are representative of those likely to meet complex PTSD diagnosis. Results provided some evidence that multicomponent interventions including distress tolerance and emotional self-regulatory strategies along with trauma-focused strategies provided the strongest reductions in PTSD symptoms, emotion dysregulation, and interpersonal problems.

Two multicomponent, sequential approaches have been studied intensively. First, Skills Training in Affect and Interpersonal Regulation (STAIR) with narrative therapy[101] has been evaluated in three randomised controlled trials among individuals with complex traumas (eg, childhood abuse and multiple types of interpersonal violence). STAIR plus narrative therapy has been shown to be superior to waiting list[101] and superior to either STAIR plus non-specific supportive counselling or narrative therapy plus non-specific supportive counselling.[102] Another randomised controlled trial evaluated a 16-week treatment of STAIR plus exposure (eight sessions for each component) compared with either 16 weeks of sustained trauma-focused work, or 16 sessions of intensive exposure work conducted over 4 weeks.[103] All three conditions resulted in significant and equivalent improvement in PTSD, emotion regulation, interpersonal functioning, and self-esteem, suggesting that multicomponent therapies and extended trauma-focused therapies are effective. Such results potentially pave the way for individualised treatment choices for individuals with complex PTSD.

Second, Dialectical Behaviour Therapy for PTSD has been specifically designed for clients with complex PTSD following aversive childhood experiences. This treatment programme combines trauma-specific exposure-based intervention with techniques from dialectical behavioural therapy and compassion-focused therapy.[104-106] The intervention has shown effectivity in two randomised controlled trials with female childhood abuse survivors presenting with PTSD and symptoms of borderline personality disorder, yielding large effect sizes (d=1·4) under both residential and outpatient conditions.[107,108]

In addition, alternative multicomponent intervention approaches have been proposed, which include flexible ordering of components based on patient-identified and clinician-identified treatment targets, or trauma-focused programmes that integrate additional interventions (eg, meaning making—ie, making sense of life events), or target particular groups (eg, refugees).[109–111] These remain to be more intensively investigated.

The meta-analyses and clinical studies described above have relied on patient populations that were diagnosed with complex forms of PTSD or have symptom profiles representative of populations likely to have complex PTSD. These studies provide preliminary guidance for treatment; however, randomised controlled trials with individuals formally diagnosed with complex PTSD are crucially needed. In addition, as suggested by a meta-analysis of treatment dropout rates in complex trauma populations,[112] there could be a risk of high attrition rates among individuals with complex PTSD, and strategies for patient engagement is an important topic for further research.

Treatment management

Exposure to trauma is a common occurrence, and its presence and psychological consequences should be included as part of an individual's history and symptom assessment in medical environments such as the emergency department and internal medicine, in addition to mental health services. Screening for trauma and its psychological effect, including complex PTSD, should be normalised as an integral part of health evaluations for both adults and children. The clinician's attitude should convey awareness of the ubiquity of

traumatic exposures, compassion for the individual's experiences and suffering, and a sense of hopefulness regarding resolution of problems given the emerging evidence regarding effective treatment. Assessments should be conducted in a calm, straightforward, sympathetic, and supportive manner with time taken as needed for the patient to gather their thoughts and manage distress (panel 1).

Assessment and treatment planning should be implemented in a collaborative manner that attends to the individual's concerns and follows a shared decision-making model.[108,113] Following a thorough assessment of mental, physical, and basic social resource needs, a treatment plan should include coordination of psychosocial therapies, medication, physical health monitoring, and social services. Personal strengths and relational resources of the individual are integrated into treatment to support a sense of mastery and efficacy, which is particularly valuable for chronically traumatised patients. If there is ongoing abuse (eg, intimate partner violence) or risk of suicidal behaviours, safety planning is introduced as a priority goal preceding but overlapping with the implementation of other treatment activities. It might be appropriate to involve a mental health professional (eg, social worker) in safety planning to ensure supportive networks (eg, emergency housing and mental health crisis teams) when the individual leaves the treatment facility. Panel 2 summarises the steps within a treatment from assessment onwards.

Psychoeducation about complex PTSD is provided with the goal of normalising the patient's experience of their symptoms and reducing stigma. People with complex PTSD often consider their problems a sign of weakness and the chronicity of symptoms as the result of a characterological or inborn personality defect. Individuals who experience exposure to trauma sustained over many years, either in childhood (eg, sustained physical or sexual abuse, or both) or adulthood (eg, sustained exposure to violence related to race or ethnicity) understandably view these environments as normal or the world as it is, leading to the conclusion that the source of their problems is a disturbed individual make-up rather than a disturbed or disturbing environment. Identifying the well known effect of trauma on emotional and relational capacities, disruptions in thought processes, in the shaping of belief systems, and on physical health status can alleviate guilt and shame and generate hope for the opportunity to recover and change.

Treatment for children and adolescents

For children aged 5 years and older, international treatment guidelines recommend trauma-focused CBT for treating complex PTSD.[95] Two randomised controlled trials have evaluated the effect of trauma-focused CBT for children with probable complex PTSD for whom complex PTSD diagnosis was determined using questionnaire responses and interview-based assessment of PTSD.[27,114] Core PTSD and self-organisation disturbance symptoms were reduced to moderate-to-large degrees. A third randomised controlled trial has evaluated cognitive processing therapy[115] for individuals aged 14–21 years with probable complex PTSD. Results suggested large treatment effects for individuals with probable complex PTSD, with effect sizes being similar to participants with PTSD.[114] Notably, one common characteristic in each of these studies is that patient groups with probable complex PTSD began with more severe symptoms and ended treatment with more symptoms compared with PTSD. Treatments specifically designed for complex PTSD or the addition of treatment components that specifically address disturbances in self-organisation symptoms have yet to be examined in children, although recommendations have been made for how trauma-focused CBT could be tailored for youth with complex trauma histories (eg, greater emphasis on coping skills[116]). It is therefore uncertain whether disturbances in self-organisation

Panel 2: **Summary of assessment, management principles, and treatment of complex post-traumatic stress disorder (complex PTSD)**

Assessment

- Complete diagnostic assessment
- Conduct differential diagnosis particularly versus post-traumatic stress disorder and borderline personality disorder
- Identify strengths, resources, and support systems
- Provide referrals to services (eg, medical and social) as needed

Treatment management principles

- Focus on safety; describe patient's rights, clarify roles and responsibilities, and describe known outcomes for various treatment interventions
- Explain complex PTSD symptoms with the goal of normalising reactions and de-stigmatising diagnosis
- Support collaboration and patient self-efficacy; decisions regarding prioritising targets of interventions are patient-driven, and patient strengths and resources are identified and incorporated into treatment

Intervention approach

- Recommend a flexible, multicomponent treatment with a trauma-focused component
- For children, recommend trauma-focused cognitive behavioural therapy
- Collaborate with the patient to develop a treatment plan consistent with preferences and values
- Consider comorbid symptoms (eg, depression and dissociation) in selection of treatment components
- Include focus on psychosocial functioning
- Coordinate services as needed including medications, physical health assessment and monitoring, and social services

symptom-specific treatment components, or, perhaps, completion of extra sessions, could further improve treatment outcomes for children with complex PTSD.

There are treatment management considerations for children and adolescents. One barrier to the delivery of these treatments for children with complex PTSD is therapist reservations, particularly therapist hesitation to complete trauma-focused or exposure work with children. It is important to emphasise that trauma-focused interventions, which include exposure, improve the functioning and wellbeing of children with complex trauma histories (including sexual abuse[117]) and have successfully treated children as young as 3 years.[118] Further, acceptability ratings and completion rates in these studies indicate that children do recognise the importance of therapy and its trauma-focused approach.[119,120] If hesitation is evident after psychoeducation for both the therapist and the patient on the benefits of exposure, there are trauma-focused CBT manuals that include minimal exposure work, instead placing a greater emphasis on challenging negative beliefs.[119]

Given the small number of treatment studies to date, further evaluation of treatment components for complex PTSD in children is needed as pharmacological intervention is not recommended for children experiencing PTSD.[121]

Pharmacotherapy

All treatment guidelines and meta-analyses conclude that there should be a preference for psychological treatment, and that although pharmacotherapy should not be used as a standalone treatment, it might be used to address stability issues that prevent engagement with psychological treatment.[122–123] As very little specific effect of medication has been shown on complex PTSD symptoms, routine medication for issues such as emotional instability or cognitive disruption are not recommended unless there is a comorbidity that justifies its use.[122–123]

Psychopharmacological interventions, particularly SSRIs and venlafaxine, have been frequently used in the treatment of PTSD. However, meta-analyses have indicated that effect sizes for SSRIs are inferior to those obtained for trauma-focused treatment.[100,124] Meta-analyses or large-scale studies of prazosin have produced mixed findings regarding PTSD symptom clusters and especially nightmares.[125,126] The literature on pharmacotherapy of borderline personality disorder suggests that the disturbances in self-organisation symptoms of complex PTSD, which are similar to BPD, do not respond to the antipsychotics (eg, quetiapine) and anticonvulsants (eg, lamotrigine) that are routinely used with these patients.[127]

Regarding sleep disorders comorbid to trauma consequences, there is no meta-analytical evidence for the efficacy of any of the drugs routinely used, so psychotherapeutic interventions are recommended here as well.[124] For the frequent comorbidity with major depression, the relevant pharmacological recommendations should be followed;[128] however, it has been repeatedly shown that SSRIs are consistently less effective in individuals with depression with childhood abuse than in individuals with depression without childhood abuse.[129]

Controversies and outstanding research questions

As noted earlier, DSM-5 of the American Psychiatric Association[130] has not recognised the diagnosis of complex PTSD but rather has included symptoms that somewhat overlap with disturbances in self-organisation symptoms (eg, alterations in mood and cognition) into the PTSD diagnosis. The literature supporting the presence of distinct PTSD and complex PTSD symptom profiles as described in ICD-11 is strong,[7,131] and impressively, has been observed across different countries and cultures.[132,133] Evidence of reliability and validity of ICD-11 PTSD and complex PTSD diagnosis is substantial, as is that for the DSM-5 PTSD diagnosis. An important topic of research is to determine whether the presence of two diagnoses (as represented in ICD-11) as compared with one diagnosis (as represented in DSM-5) will advance treatment development and lead to better and more efficient treatments and better functional outcomes for patients.

There is an ongoing debate regarding common and differential characteristics of traumatised individuals with BPD and those with complex PTSD. For example, it has been argued that the described overlap and comorbidity between complex PTSD and BPD suggests that these disorders can be moved closer together under the classificatory heading of "trauma- and stress-related disorders".[107] There is some data suggesting that BPD is in fact a trauma generated disorder and could only differ from complex PTSD due to the timing of when the trauma occurs. Recent research from the past 5 years, considering the effect of type, timing, and age at traumatic experiences on the differential symptom characteristics, finds initial evidence that severe borderline disorder involves very early, chronic trauma combined with severe social rejection and neglect, whereas complex PTSD without BPD is more likely to involve trauma later in life.[76] In addition, the multicomponent therapies that appear appropriate for complex PTSD share many treatment elements in common with BPD. Lastly, an alternative view to the classifications systems[107] suggests that the disorders have shared underlying psychopathology that are phenomenologically represented in different ways. In this framework, a focus on individual symptoms or a formulation-based approach might be an appropriate and flexible strategy for treatment planning.

There is a need for more neurobiology research. Future research is needed to investigate the differences between PTSD and complex PTSD, and between complex PTSD and BPD. Although some of this work has begun,[86,134] additional studies can take into consideration the effect of trauma type and timing on brain maturation. This effect might lead to findings that

contribute to a better understanding of the differences and similarities across these disorders. The identification of brain circuits underlying ICD-11 PTSD, complex PTSD, and BPD might help improve differential diagnostic processes and the treatment of these disorders.

The development and evaluation of treatment approaches for complex PTSD is still at an early stage, and there are several key questions that are not yet settled. Interventions from the psychodynamic, attachment, and mindfulness frameworks remain to be investigated as standalone interventions or components within treatment programmes. A much-discussed controversy is whether multicomponent, multimodal therapies as compared with trauma-focused unimodal approaches are more effective for people with complex PTSD. Although head-to-head comparisons are likely to be investigated, some caution needs to be taken as these two polarised characterisations of trauma treatments could be more theoretical than real, given that some unimodal approaches incorporate diverse interventions and multi-component therapies rarely exclude trauma-focused work.[135]

The optimal duration of treatment is unknown as the length of successful treatment of complex trauma populations has varied from 4 months to 12 months. Assessment of a wide range of outcomes including functional impairment is important to determine if particular symptoms take longer to resolve than others, and how change in one symptom cluster effects change in others. This information has implications for determining whether and how to introduce flexibility in sequencing of interventions. It will also provide important information to the therapist and patient in the context of developing a treatment plan that supports the patient's treatment goals and preferences regarding the problems that they want to target.

Contributors

All authors contributed equally to the manuscript and were involved in the literature search, interpretation of the studies, and writing. All authors approved the final version of the manuscript.

Declaration of interests

AM has received revenues by book publications on the topic from publishing houses Springer/Nature and Hogrefe. MC has received revenues by book publications from publishing houses Guilford and Springer. MB has received revenues by book publications from publishing houses Springer, Hogrefe, Schattauer, Klett Cotta, and Guilford. AM, MC, YRS, MB, RB, and BK have received occasional speaker honoraria at conferences and workshops (pharma-free). CH declares no competing interests.

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