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Research Domain Criteria and the Study of Trauma in Children: Implications for Assessment and Treatment Research

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Abstract

By definition, the Diagnostic and Statistical Manual (DSM) diagnosis of posttraumatic stress disorder (PTSD) requires exposure to a traumatic event. Yet, the DSM diagnostic requirements for children and adolescents for PTSD may fail to capture traumatized youth with significant distress and functional impairment. Many important studies have utilized PTSD diagnosis as a mechanism for grouping individuals for comparative studies examining brain functioning, neuroendocrinology, genetics, attachment, and cognition; however, focusing only on those with the diagnosis of PTSD can miss the spectrum of symptoms and difficulties that impact children who experience trauma and subsequent impairment. Some studying child trauma have focused on examining brain and biology of those with exposure and potential impairment rather than only those with PTSD. This line of inquiry, complementary to PTSD specific studies, has aided our understanding of some of the changes in brain structure and neuroregulatory systems at different developmental periods following traumatic exposure. Application of the Research Domain Criteria (RDoC) framework proposed by NIMH to the study of child trauma exposure and subsequent impairment is an opportunity to examine domains of function and how they are impacted by trauma. Research to date has focused largely in the areas of negative valence, regulatory, and cognitive systems, however those studying complex or developmental trauma have identified an array of domains that are impacted which map onto many of the RDoC categories. This paper will review the relevant literature associated with child trauma as it relates to the RDoC domains, outline areas of needed research, and describe their implications for treatment and the advancement of the field.

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Contributors

Dr. Stover was responsible for the overall design of the manuscript. Both Dr. Stover and Keeshin contributed to the literature review and writing of the manuscript. Both authors contributed to and have approved the final manuscript.

Conflict of Interest

There are no conflicts of interest to report.

Focus on the study of trauma, defined here as resulting from an event, series of events, or set of circumstances that is experienced by an individual as physically or emotionally harmful or threatening and that has lasting adverse effects on the individual's functioning and physical, social, emotional, or spiritual wellbeing (SAMHSA, 2012), has greatly advanced understanding of the myriad of ways these experiences can impact the functioning of children and adolescents. The Research Domain Criteria (RDoC) proposed by the National Institute of Mental Health (NIMH) was designed to create a framework for research on pathophysiology to inform classification schemes (Insel et al., 2010). This framework seems particularly relevant to the study of pediatric trauma to inform the mechanisms whereby exposure to a potentially traumatic event results in impairment.

The nature, intensity, duration, and developmental timing of trauma exposure have all been linked to child outcomes (Buka, Stichick, Birdthistle, & Earls, 2001), and the field is beginning to understand the mechanisms through which trauma impacts youth across a wide range of domains. However, additional research is needed to further understanding of who is at risk for impairment in which domains of functioning at what developmental period. The current paper will: 1) provide an overview of the RDoC domains that have amassed the most research to date related to child trauma and posttraumatic stress disorder (PTSD), 2) review illustrative trauma and PTSD relevant research using the RDoC proposed elements of analysis, 3) explore how study of domains of functioning can advance assessment and treatment for those exposed to potentially traumatic events, 4) review complications to using the RDoC approach, and 5) propose areas of future research using RDoC in the field of pediatric trauma and PTSD.

Approach to Current Review

The RDoC outlined by NIMH currently contains five domains and covers a broad array of areas. These domains include: Negative Valence Systems, Positive Valence Systems, Cognitive Systems, Systems of Social Processes and Arousal/Regulatory Systems (NIMH Research Domain Criteria (RDoC), 2011). All of these domains have some relevance to pediatric trauma, but some are more salient and have already amassed some research, while others have not yet been the focus of much study. Many of the domains are relevant to the cognitive, adaptive and social impairment that can result from trauma exposure. This paper focused on literature that included symptom level analysis, which included studies of children at risk for trauma symptoms following a potentially traumatic event, as well as, those studies that required a PTSD diagnosis. This approach was chosen because together these studies have advanced our understanding of how different events are associated with symptoms.

Studies that took a broad definition of trauma exposure, reflective of the transition to DSM-5 diagnostic criteria for PTSD were also included. For example, criteria A-1 for PTSD was revised from DSM-IV to DSM-5 to remove the requirement of feelings of intense fear, helplessness or horror right after the event. More specific details have also been added about the types and nature of potential exposure that were not included previously (American Psychological Association, 2013). These changes evolved from the field's increased understanding of what constitutes a trauma that may result in posttraumatic symptoms.

Continued exploration of potentially traumatic events and their association to symptoms and functioning may further refine understanding in the future for PTSD and other disorders.

Further, the focus was on RDoC domains that were most closely associated with trauma related reactions. The pediatric PTSD and child trauma/maltreatment literature was reviewed, searching specifically for studies that had performed sub-analyses that are the same or similar to RDoC constructs. The following sections will review literature on pediatric trauma and PTSD that is demonstrative of both the ease and challenges that would be encountered for pediatric trauma science to incorporate RDoC principles in future research studies. The literature reviewed is meant to be illustrative and is in no way exhaustive.

Overview of RDoC Domains

Social Processes

The RDoC domain of social processes contains four constructs: affiliation and attachment, social communication, understanding of self and understanding of others. Although all of these areas are relevant to pediatric trauma, most research has focused on affiliation and attachment and understanding of self.

Affiliation and attachment—Early exposure to childhood maltreatment (e.g. physical abuse, sexual abuse, psychological abuse), especially in infancy and early childhood, has been shown to be associated with insecure attachment (Cicchetti & Barnett, 1991; Braer & Martinez, 2006). Young maltreated children may develop attachment related disorders such as reactive attachment disorder (Stafford, Zeanah, & Scheeringa, 2003). Lack of focus on attachment and affiliation in the study of trauma symptoms misses an important component related to recovery (Scheeringa & Zeanah, 2001). The developmental context of trauma, the nature of attachment relationships at the time of the trauma and the subsequent impact on attachment systems are important to understanding the symptoms and psychopathology that develop.

Not only can trauma impact attachment security, but attachment security may impact an individual's response to new traumas. In a study of prisoners of war, secure attachment of survivors was significantly associated with lower PTSD symptoms (Dieperink, Leskela, Thuras, Engdahl, 2001). Similar findings were found in studies of adults exposed to the September 11th terrorist attacks with secure attachment associated with lower PTSD symptoms (Fraley, Fazzari, Bonanno Dekel, 2006). Specific to youth, insecure attachment has been shown to be associated with severity of internalizing and externalizing symptoms in preschoolers following sexual abuse (Beaudoin & Bernier, 2013).

Interpersonal traumas such as sexual assault are the most consistently associated with PTSD in adults (Frans et al., 2005). Although non-interpersonal trauma such as automobile accidents have been the least associated with PTSD (Frans et al., 2005), a study by Shalev and Freeman (2005) found that terror survivors who developed PTSD did not statistically differ from motor vehicle accident survivors at one-week post trauma on symptoms of depression, trauma, anxiety or dissociation. This is additional evidence that some other

process such as attachment may moderate the association between trauma type and resulting longer term symptoms.

Moreover, studies have indicated caregiver responses play a critical role in determining children and adolescents' successful post-trauma adaptations. For example, caregivers can provide important social and emotional support, direct guidance in adaptive coping, help with safety planning and the avoidance of future traumatization, and can provide access to mental health treatment (Kliewer, Cunningham, Diehl, Parrish, Walker, Atiyeh, et al, 2004; Kliewer, Parrish, Taylor, Jackson, Walker, & Shivy, 2006; Ozer, 2005; Ozer & Weinstein, 2004; Stallard, Velleman, & Baldwin, 2001). These studies highlight the important role attachment and affiliation can play in resilience and the development of a range of symptoms indicating the need to further incorporate this construct in studies of pediatric trauma.

Understanding of self—Emotional awareness is described as the capacity to be aware of and describe one's own emotions as well as those of others (Fridja, 2007; Lambie & Marcel, 2002). Emotional awareness can be considered a form of understanding of the self. Individuals with PTSD often have difficulty identifying and labeling emotions (their own and those of others), as well as understanding and expressing emotions in healthy ways (Ehring & Quack, 2010; Frewen, Dozois, Neufeld, & Lanius, 2008, 2012). Research on children exposed to potentially traumatic events reveals subsequent deficits in emotional awareness (Cloitre, Miranda, Stovall-McClough, & Han, 2005). As will be described later, these deficits in emotional awareness and regulation are the focus of many trauma and PTSD specific treatments for youth.

Negative Valence and Arousal/regulatory Systems

Negative valence—The Negative Valence System includes five constructs: response to acute threat (fear), responses to potential harm (anxiety), responses to sustained threat, frustrative non-reward and loss (NIMH Research Domain Criteria (RDoC), 2011). This system is relevant for children exposed to trauma whether they develop PTSD or not; however of particular relevance to PTSD is the responses to potential harm construct, which is consistent with the increased arousal criteria of PTSD. The response to sustained threat construct is more consistent with the types of changes described in youth with chronic exposure whereby they experience changes in affect, cognition, physiology and behavior, as a result of exposure to sustained or repeated traumas, that continue in the absence of those threats (Cook et al., 2005). The construct of loss has also been studied in the context of trauma exposure and PTSD and may moderate clinical course and treatment response. For example, studies following hurricanes Andrew and Katrina found loss of loved ones, homes and resources due to the hurricane were associated with increased severity of symptoms and the onset of PTSD in the months and years following the disasters (Ironson et al., 1997; Osofsky, Osofsky, Kronenberg, Brennan, & Hansel, 2009).

Regulatory system—The regulatory systems domain relates to trauma exposure in multiple ways. This domain contains three constructs: arousal, sleep wakefulness and circadian rhythms. Although there is evidence that circadian rhythms and sleep can be disrupted in children exposed to trauma (Kovachy, O'Hara, Hawkins, Gershon, Primeau,

Madej, & Carrion, 2013), literature in this area is not well developed and could lead to new understandings of the neurobiology of trauma. Regarding arousal constructs, a heightened fear potentiated startle response in anticipation of emotionally charged test procedures (shock) has been identified in adults with PTSD (Morgan III, Grillon, Southwick, Davis, & Charney, 1995). In children, abnormal acoustic startle has been noted, with a significant loss of the normal inhibitory modulation of startle response in children with PTSD compared to controls (Ornitz & Pynoos, 1989).

Importantly, there is also evidence that those who previously met criteria for PTSD but no longer do, still show failure of habituation of the abnormal startle response (Van der Kolk, 2004), and a prospective study suggests this heightened response may be pre-existing. Pole and colleagues (Pole et al., 2009) found hypersensitivity to context (greater fear under low threat), elevated sympathetic nervous system reactivity to explicit threat (larger responses under high threat), and failure to adapt to repeated aversive stimuli (evidenced by slower habituation) are all unique preexisting vulnerability factors for greater PTSD symptom severity following a trauma exposure. These findings are quite compatible with an RDoC framework that would allow for the examination of domains of functioning prospectively without specificity of disorder, leading to alternative potential assessment and early intervention targets for those exposed to trauma, such as the evaluation of a pre-existing heightened startle response.

Links from Social Processes to Regulatory System Domains

There are interconnections between the RDoC domains of social processes and the negative valence/regulatory systems. Disruptions in attachment born from early childhood maltreatment can have profound impact on the developing brain and neurobiological systems. The maturation of the stress regulating systems, part of the limbic-autonomic circuits (Rinaman, Levitt, & Card, 2000), is experience dependent and vulnerable to relational trauma. Schore (2001) has described that early trauma alters the development of the right brain, which processes social-emotional information and bodily states. The internal working model of the early attachment relationship is thought to be stored in the right cerebral cortex (Schore, 1994, 2000; Siegel, 1999). Developmental impairment of this system would severely impact a child's ability to cope with stress. Such a limitation of the right brain impacts the ability to regulate affect. Loss of the ability to regulate the intensity of feelings has been described as the most extensive effect of early trauma exposure (Van der Folk & Fisler, 1994).

Attachment may impact the immediate and enduring stress regulating biological systems, and social ties and social perceptions modulate fear reactivity in the brain (Charuvastra & Cloitre, 2008). These links are important because examination of how trauma impacts attachment and the neuroendocrine system have led to advancements in treatment for traumatized children in foster care (Dozier, Peloso, Lewis, Laurenceau, & Levine, 2008; Dozier et al., 2006). Children who experience trauma in infancy and early childhood have atypical patterns of diurnal cortisol throughout the day (Dozier et al., 2006). This dysregulation in normal biological patterns is believed to have the potential for long term impacts. An intervention developed to target both the attachment of a foster child to a foster

mother and biological dysregulation reduces cortisol levels and behavior problems (Dozier, Laurenceau & Levine, 2008). This type of integrated work that targets multiple domains can guide future intervention development.

RDoC Elements of Analysis, Trauma and Pediatric PTSD

With an understanding of some of the RDoC domains most relevant to pediatric trauma, we now turn to elements of analysis. Included in the RDoC matrix are specific elements of analysis that could be used to study the domains described above. Studies of brain changes, genetics and neuroendocrine functioning in child trauma that are associated with the negative valence and arousal domains fall into some of these categories. Studies examining units of analysis such as genes, molecules, cells, circuits and physiology have all been applied to trauma, however, for the most part, these studies have yielded inconsistent results with regards to pediatric PTSD. Some of that variation is likely due to small, heterogeneous populations at various developmental stages that have experienced a variety of types of traumatic experiences with a wide range of trauma burden. However, it is also possible that RDoC domains, when used in conjunction with PTSD diagnostic criteria, may be more likely to result in consistent results when examining changes in structure and/or function of the brain or the stress response system. Some examples of the current state of pediatric PTSD research in RDoC elements of analysis are included below to illustrate the complementary potential for utilizing both PTSD diagnosis and RDoC designs.

Imaging Research

The hippocampus, associated with memory acquisition and retrieval, has long been associated with PTSD. In the adult literature, decreased size of hippocampus is consistently associated with PTSD (Teicher & Samson, 2013). However, twin-twin studies have demonstrated decreased hippocampal volume with both twins, regardless of PTSD (Gilbertson et al., 2002), suggesting that smaller hippocampal volumes might be a risk factor for the development of PTSD after traumatic exposure rather than a result of exposure. Importantly, decreased hippocampal volume has also been found in adults with diagnoses of depression (Bremner et al., 2000; Vakili et al., 2000; Vythilingam et al., 2002), schizophrenia (Nelson, Saykin, Flashman, & Riordan, 1998), and substance abuse (De Bellis et al., 2000) with subsequent adult studies revealing decreases in hippocampus volume associated with exposure to maltreatment and adversity in childhood, irrespective of diagnosis of PTSD (Teicher, Anderson, & Polcari, 2012). These findings suggest decreased hippocampal volume is not disorder specific and may be a risk factor for changes in domains that cross a variety of diagnoses experienced by traumatized individuals.

The pediatric literature is inconsistent with regards to hippocampus findings, with non-significant findings suggesting both increased and decreased volume and function in both PTSD and trauma exposed youth. It is possible that associations are dependent on the chosen units of analysis when interpreting imaging findings in pediatric PTSD, and an RDoC approach examining specific domains in trauma exposed children may help clarify current hippocampal findings. For example, in a secondary cross-sectional analysis of children with

and without PTSD, both PTSD as well as externalizing behaviors were positively associated with increased hippocampal size (Tupler & De Bellis, 2006).

Furthermore, a longitudinal study of maltreated children with PTSD observed changes in hippocampal size over a 12-18 month period, where increased arousal was negatively associated with hippocampal growth over time (Carrion, Weems, & Reiss, 2007). However, when functional activity (rather than size) of the hippocampus was examined using a cross-sectional cohort of violence exposed children with at least some symptoms of posttraumatic stress, arousal was not associated with changes in function, but rather avoidance/numbing was associated with a decreased activation of the right hippocampus during a verbal declarative memory task (Carrion, Haas, Garrett, Song, & Reiss, 2010). These findings suggest that, depending on the units of analysis of focus, specific domains, rather than PTSD, may be correlated with hippocampal changes in traumatized children.

Corpus callosum studies—Another region of interest in pediatric brain imaging research is the corpus callosum, responsible for inter-hemispheric communication. Changes in size of the corpus callosum are associated with emotional and arousal responses to external stimuli (De Bellis, Keshavan, et al., 1999b). In studies of children (mostly latency age and adolescents), decreases in size of the corpus callosum as well as function have been noted in both children with PTSD as well as children exposed to (chronic) trauma regardless of diagnosis (Teicher & Samson, 2013). When explored further, symptoms of hyperarousal, which map onto constructs within the negative valence and arousal domains, have been independently associated with decreased size of segments of the corpus callosum in maltreated children with PTSD (De Bellis, Keshavan, et al., 1999b).

The specificity of decreased corpus callosum size to certain negative valence constructs may be questioned, as studies have also shown decreased size to be associated with other constructs outside of negative valence and arousal domains, such as dissociative symptoms, which likely correspond more with constructs within the cognitive systems domain (De Bellis, Baum, et al., 1999a). Furthermore, when the traumatized group is matched to the control group based on social economic status, although the general finding that PTSD is related to decreased size of the corpus callosum remains, the unique association between specific PTSD criteria (hyperarousal) or associated symptoms (dissociation) disappears (De Bellis et al., 2002). Interestingly, many published studies examining group differences in traumatized or PTSD populations do not specify or examine the severity or extent of PTSD symptoms or presence of comorbidity, limiting the capacity to hypothesize how RDoC constructs might be related to current imaging research findings.

Cortex regions and volume related studies—Specific areas of the cortex, as well as global brain volume, have been examined in the context of exposure to maltreatment-associated trauma, with and without PTSD. Areas most reported in the literature include the prefrontal cortex, anterior cingulate cortex and temporal cortex. Studies have examined overall volume of the cortex and different substructures, as well as singling out the gray matter components of structures of interest. Results generally demonstrate an overall decrease in cortex volume, with some studies showing preferential increases or decreases in specific regions of the cortex (Teicher & Samson, 2013). Differences in age of child and age

of exposure(s) to trauma are possible reasons for variable and inconsistent findings. Some studies have correlated individual symptoms of PTSD with lateral ventricle size, an easily measurable proxy for loss of cortex in pediatric maltreatment related PTSD. That finding has not been consistently replicated in all studies (De Bellis, Keshavan, et al., 1999b; De Bellis et al., 2002), and there is a paucity of data linking symptom specific criteria with overall cortex size or function.

Amygdala studies—The amygdala is implicated in RDoC domains such as fear conditioning, emotional processing and memory. Two separate meta-analyses demonstrate that there are no differences in right amygdala volume in PTSD versus trauma exposed without PTSD individuals or controls, and that there may be a small (and potentially significant) decrease in left amygdala size (Karl et al., 2006; Woon & Hedges, 2009). However, functional changes in the amygdala may be more consistent, where task oriented studies using fMRI have demonstrated that relative to controls, youth with PTSD show greater activation in the amygdala when exposed to angry faces. This indicates an association with heightened negative valence such as acute or potential threat (Garrett et al., 2012).

Neuroendocrine Research

The autonomic nervous system (ANS) is one of several systems responsible for the homeostatic regulation of stress responses, and dysregulation has been established in constructs that fall within the negative valence and arousal domains. ANS functional changes are associated with PTSD, where cerebral spinal fluid (CSF) norepinephrine (NE) is generally elevated and correlates with increased intrusive and hyperarousal symptoms (Strawn & Geraciotti, 2008; Weiss, 2007). However, studies of peripheral NE in adults have demonstrated both elevated levels of NE and no difference between patients with and without PTSD, and the correlation between peripheral NE and central NE is unclear. In children with recent trauma who later develop PTSD, plasma NE levels are elevated within 6 months of a trauma (Pervanidou et al., 2007). Additionally, pediatric victims of maltreatment related trauma with or without PTSD also demonstrate greater 24 hour urinary catecholamine excretion compared to non-maltreated individuals (De Bellis, Keshavan, et al., 1999b; De Bellis, Lefter, Trickett, & Putnam, 1994).

Within the HPA axis, the hypothalamic secretion of corticotropin releasing hormone (CRH) is regulated by a number of factors, including acute and chronic stress, resulting in altered peripheral cortisol concentrations commonly associated with PTSD. In children, salivary cortisol concentrations are elevated following traumatization in those youth who subsequently develop PTSD when compared to traumatized youth who did not develop PTSD at 6 months following traumatization (Pervanidou et al., 2007). That same analysis hypothesized that daytime hyperarousal symptoms might drive increases in baseline cortisol, especially during the evening. Some studies have found an associated blunting of the cortisol awakening response among individuals with PTSD, and in the pediatric population, that association appears to be most impacted by intrusive and hyperarousal symptoms (Keeshin, Strawn, Out, Granger, & Putnam, 2014). However, although PTSD, as well as negative valence and arousal domains, may correlate with aberrations in HPA-axis activity, it is not at

all clear if these changes are domain specific or trauma specific. For example, in children chronically exposed to stress but without a clear trauma, blunting of diurnal cortisol variation has been observed in the absence of psychopathology (Bernard, Butzin-Dozier, Rittenhouse, & Dozier, 2010). Further, among individuals with a history of sexual abuse there is an initial hypercortisolemia followed by an eventual hypocortisolemia irrespective of trauma specific symptoms (Trickett, Noll, Susman, Shenk, & Putnam, 2010).

Genetic Research

A growing body of literature examines the gene x environment impact of childhood adversity on subsequent psychopathology. This method of investigation, pioneered through investigations of the serotonin transporter gene and its relationship to depression risk following prior and current life stressors (Caspi et al., 2003), has led to large, often population based studies of alleles involved in the production or regulation of neurotransmitters hypothesized to be involved in negative valence and arousal domains. Additionally, epigenetic research, which focuses on gene expression, has also been examined in the context of PTSD, examining the impact of stressors in both animal as well as human populations (Meaney & Szyf, 2005; Yang et al., 2013). Few genetic studies look at childhood trauma and pathology risk among children.

The dopamine transporter (DAT) gene has been evaluated in adult and pediatric traumatized patients with posttraumatic stress disorder. This gene is especially relevant to the pediatric population, as dopamine regulation is likely implicated in other common pediatric conditions such as attention deficit hyperactivity disorder (ADHD), and therefore some of the clinical overlap between ADHD and PTSD could be explained by common pathway mechanisms. Several studies have now demonstrated that certain DAT alleles are associated with the development of PTSD (Drury, Theall, Keats, & Scheeringa, 2009; Segman et al., 2002). Examining PTSD criteria in children exposed to trauma, one study demonstrated that hyperarousal was independently associated with the presence of a specific 9 repeat allele DAT haplotype. This finding builds on the prior research demonstrating group associations, and suggests specific domains and constructs that overlap known disorders (Drury, Brett, Henry, & Scheeringa, 2013).

Epigenetics—Recently researchers have begun to examine epigenetics changes in PTSD. In general, the available studies focus on adults with PTSD compared to controls, and have examined epigenetic changes associated with genes that regulate the immune and stress response systems (Voisey, Young, Lawford & Morris, 2014). As an example, Yehuda and colleagues found methylation of FKBP5 in adults to be associated with PTSD severity as measured by the Clinician Administered PTSD Scale (Yehuda et al., 2013). However, no studies to date have examined epigenetic differences in children with PTSD or have used a more deconstructive approach consistent with RDoC. Further study of these areas applying RDoC negative valence and regulatory systems domains, as well as possible inclusion of other domains, may enhance our understanding of how specific alleles and epigenetic changes are associated with risk of functional impairment or responsiveness to treatment following trauma exposure.

Implications for Treatment of Traumatized Youth

The field of child trauma treatment has been burgeoning over the last several decades with multiple new treatments developed and tested. Trauma Focused Cognitive Behavioral Therapy (TF-CBT; Cohen et al., 2012), Child Parent Psychotherapy (CPP; Lieberman, Ghosh Ippen, & Van Horn, 2007), Structured Psychotherapy for Adolescents Responding to Chronic Stress (SPARCS; Habib et al., 2013), Trauma Affect Regulation Guide for Education and Therapy (TARGET; Ford et al., 2013), Attachment, Self-Regulation, and Competency (ARC; Kinniburgh, Blaustein, Spinazzola, & van der Kolk, 2005) and the Child and Family Traumatic Stress Intervention (CFTSI; Berkowitz, Stover, & Marans, 2011) are some of the treatments that have been developed that are in various stages of developing their status as evidence based treatments. These treatments have been designed based on the current science of PTSD and other symptoms associated with childhood trauma with careful consideration of child developmental process.

The efficacy of TF-CBT has been studied in many randomized controlled trials and it is widely disseminated both nationally and internationally as a leading treatment for childhood PTSD and trauma related psychopathology (e.g. Cohen et al., 2012; Mannarino, Cohen, Deblinger, Runyon, & Steer, 2012). The treatment is designed to move children and their caregivers through a set of components intended to reduce symptoms of PTSD (e.g. hyperarousal and avoidance), but also to target some of the key domains outlined by RDoC. The relaxation and affective regulation skills components directly target the negative valence, regulatory systems and social process domains. The trauma narrative portion of the treatment, in which the child writes a story about their trauma with the guidance of the therapist, is likely targeting multiple domains as well. The repeated retelling of the trauma narrative in greater detail targets negative valence and regulatory systems as well as cognitive and social processes. The goals of narrative development are to reduce arousal and anxiety related to the trauma details, reduce symptoms of re-experiencing (unwanted thoughts about the trauma), and process cognitive distortions about the self and others as related to the trauma. Following the development and processing of the narrative with the therapist, the child shares their story with a non-offending caregiver. These conjoint sessions with a prepared and supportive caregiver likely impact the affiliation and attachment domains. In addition, a treatment application of TF-CBT for traumatic grief specifically targets the loss construct within the negative valence domain (Cohen, Mannarino, & Staron, 2006).

This is one example of how an evidence based trauma treatment may be applied to RDoC to open up areas of future study. Does TF-CBT result in changes in those specific domains and if so, are those changes associated with more positive outcomes? If changes do not occur in certain areas, does that result in less successful treatment results? One area of future study is the examination of which components of the RDoC matrix are targeted by child trauma interventions and whether they might facilitate improvement in other components. Many trauma interventions start with psychoeducation (teaching) and then move into providing skills. These skills often target negative valence and regulatory systems domains (e.g. decrease arousal, improve sleep). Some treatments then move on to other target areas (e.g. avoidance by developing a narrative or attachment through conjoint sessions), but others

focus more exclusively in the negative valence/regulatory areas. What is unclear is whether these “early” components of longer treatments that influence negative valence and regulatory systems may then impact other systems and allow for improvement in other capacities such as social processes. This may then allow for briefer or more targeted treatments.

One brief intervention for youth exposed to traumatic events has been developed that provides some evidence to support this notion. CFTSI (Berkowitz et al., 2011) is a five to eight session intervention for children aged seven through 18 developed specifically to fill the gap that exists between crisis intervention and longer-term evidence-based trauma treatments designed to address traumatic stress symptoms which have become established. Implemented in the peritraumatic period, CFTSI goals are to: 1) improve screening and initial assessment of children impacted by traumatic stress; 2) reduce traumatic stress symptoms and prevent chronic PTSD; and 3) assess need for longer-term treatment. Several of the central features of CFTSI work to: 1) increase communication between caregiver and child about the child's traumatic stress reactions through conjoint sessions; 2) provide skills and strategies to families to help cope with traumatic stress reactions (e.g. relaxation skills, sleep hygiene and other coping skills); and 3) reduce external stressors resulting from the trauma (e.g. loss of housing or resources) through case management.

In terms of RDoC constructs, CFTSI targets areas of negative valence and regulatory systems through psychoeducation, teaching coping skills and enhancing affiliation and attachment through focus on communication with caregivers during conjoint sessions. This brief intervention has been shown to reduce the onset of both full and partial PTSD compared to a psychoeducational/support comparison condition (Berkowitz, Stover, & Marans, 2011). In an open trial chart review study of CFTSI, number of previous traumas experienced prior to the new incident that prompted implementation of CFTSI and severity of posttraumatic symptoms assessed at the outset of intervention were significantly associated with post-treatment outcomes (Hahn, Oransky, Epstein, Stover, & Marans, 2016). Broadening exploration of genetic and neurobiological markers (e.g. cortisol, acoustic startle) of negative valence, regulatory systems and attachment in addition to emotional/behavioral and symptom indicators in future studies of CFTSI could aid in determining how the intervention is impacting or interacting with these systems, leading to better identification of those youth who can most benefit from a brief early intervention and those that need to go directly into longer term trauma treatment.

Others have proposed the idea of stepped care for psychiatric problems (Bower & Gilbody, 2005). Zatzick and colleagues (2004, 2011, 2013) developed a stepped care intervention approach for PTSD for injured adult trauma survivors preventing worsening PTSD symptoms, but results in pediatric populations have been mixed. Kassam-Adams and colleagues did not show significant improvement for a stepped care approach over treatment as usual for children referred after a hospital visit due to an unintentional injury (Kassam-Adams et al., 2011).

In a community mental health setting, Salloum and colleagues did find positive outcomes for their parent trained, clinician assisted stepped care model for youth who had experienced a range of trauma types. Their studies assessed a phased approach to determine whether

longer term treatment was needed by delivering an initial step of treatment first to determine if the child recovered (Salloum et al., 2014; Salloum, Scheeringa, Cohen, & Storch, 2013; Salloum & Storch, 2011). In their pilot study, Step One included 3 therapist lead sessions that accompanied an at home parent-child workbook. They found that 56% of the sample responded to this intervention without need for Step Two (implementation of TF-CBT) (Salloum et al., 2014). Additional studies designed with RDoC domains in mind could facilitate understanding of which children need all parts of a longer treatment intended to address PTSD or complex trauma versus those who need only some parts (e.g. psychoeducation and coping skills) in this kind of stepped approach.

Dismantling Study Approaches

Some intervention studies have begun to examine specific components of evidence based trauma treatments to determine if all parts are needed in every case or if some youth may benefit from some components, but may not need all. These dismantling studies can further our understanding of how treatments work and for which children they will be most effective. A study designed to compare a short (8 sessions) and long version (16 sessions) of TF-CBT with and without the trauma narrative component, found that all studied interventions reduced symptoms (Deblinger, Mannarino, Cohen, Runyon, & Steer, 2011). The authors hypothesized that trauma as the focus of intervention may be important to optimize outcomes, but it may not require a detailed written narrative in all cases to achieve PTSD recovery. Instead they proposed, there may be alternative TF-CBT methods and varying lengths of treatment needed to attain optimal outcomes. These variations in treatment implementation could be designed and provided depending on children's initial symptom presentations, which could be assessed using RDoC domains rather than for a specific psychiatric disorder.

This is consistent with the work of treatment developers studying treatments for youth exposed to complex trauma. These therapies do not require a detailed disclosure and telling of the traumatic events, but instead focus on providing a relational foundation and teach skills to help youth and their caregivers recognize stress reactions and to regulate their emotions and behaviors (Ford et al., 2013). Randomized comparative studies that examine how differing treatment approaches (e.g. TF-CBT, ARC, SPARCS) impact the range of domains affected by trauma could provide a wealth of information about the best treatment approaches for youth exposed to a variety of traumas presenting with differential attachment, neurobiological and symptom pictures at the time of treatment initiation.

Domain Analysis and Treatment Resistance

Many interventions that have been developed to treat child trauma and PTSD specifically target emotion awareness and regulation skills (Cohen, Mannarino, & Deblinger, 2012; Cohen, Mannarino, Kliethermes, & Murray, 2012; Ford, Blaustein, Habib, & Kagan, 2013; Habib, Labruna, & Newman, 2013; Lieberman & Van Horn, 2004) consistent with the understanding of the self and arousal domains. Further understanding of the neurobiology of emotional awareness and self-perception can aid in intervention development especially for those who struggle to gain emotional awareness and regulation during already developed trauma specific interventions.

For example, study of changes to the right pre-frontal cortex in children who experienced interpersonal trauma in infancy, and how these changes are associated with HPA axis functioning and attachment could play a significant role in our understanding of youth who experience extreme difficulties in emotion regulation making implementation of treatments specific to PTSD difficult. Broadening the lens to an expansive understanding of problems experienced by youth exposed to trauma has already led to the development of multiple treatments. These treatments emphasize an understanding of how a wide range of impairments can be resolved by learning how to modify the adaptations the body and mind make in feelings, thinking and behaviors in order to endure and survive exposure to trauma (Ford et al., 2013).

Challenges in the Use of RDoC in Pediatric Trauma Research

Despite advantages of an RDoC approach, there are also inherent challenges. A challenge within the RDoC matrix is the omission of two primary aspects of fundamental importance to the research and treatment of childhood trauma, specifically, development and environment. Mentioned within the RDoC framework as two important areas not specifically included within the RDoC matrix, the RDoC framework strongly encourages a systematic and careful focus on developmental and environmental aspects as they relate to specific circuits and functions.

Developmental Context

Within the world of pediatric trauma, several disorders are partially defined by the developmental period at which they occur. At one end of the spectrum, young children who experience trauma, especially those that are preverbal or in the early stages of effective language communication, will often have social processing issues. These challenges in attachment, often related to early childhood abuse (Cyr, Euser, Bakermans-Kranenburg, & Van Ijzendoorn, 2010), fall outside of the traditional view of pediatric PTSD. Older, chronically traumatized teens are more likely to have derangements in the domain of social processes, leading to overrepresentation of personality disorders in traumatized populations. This mechanism, too, likely has underlying molecular and circuit underpinnings that explain the well described association between child abuse and personality disorders (Tyrka, Wyche, Kelly, Price, & Carpenter, 2009).

In comparing these two pathologies, the phenotypic similarities and differences between aspects of attachment disorders and personality disorders may be explainable by different underlying mechanisms on the matrix. However, it is also possible that differences may be more related to a development $\times$ trauma interaction that the matrix, in its current form, is ill prepared to address. In addition, it is quite possible that constructs on the matrix, when viewed from a developmental perspective, are the very units of analysis that moderate or directly increase the risk for subsequent constructs, such as attachment mediating subsequent psychopathology (McGoron et al., 2012).

Even within the same disorder, development can make diagnosis challenging. Most studies in pediatric PTSD focus on severity of symptoms or presence of diagnosis, and do not further evaluate specific domains. And there is some good reason for this – prior to the

creation in DSM-5 of a PTSD that is more specific for children under 7, the diagnosis of PTSD was not developmentally sensitive (Scheeringa & Zeanah, 2001). Through the work of Terr and others who raised awareness that it is possible for children to develop PTSD, children were still being forced into constructs that were designed for survivors of experiences such as war and battle. Therefore the three primary criteria of PTSD prior to DSM-5, intrusive experiences, avoidance and hypervigilance were not defined in a developmentally sensitive manner. The field may need to move forward in applying the RDoC domains to trauma while carefully considering the impact of developmental period on each of the areas being assessed. For example, attachment looks quite different behaviorally at age two than it does at age 12 and trauma impacts the attachment system differently at these varying ages. In addition, the extent of previous trauma exposures also plays an important role in how a new trauma is experienced (Breslau, Chilcoat, Kessler, & Davis, 1999; Goslin et al., 2013; Winston et al., 2003). A systematic approach that incorporates development will be essential to clarifying the impact of trauma on various constructs.

Environmental Context

Environment is another component not systematically incorporated within the RDoC matrix. Although the environment may impact many disorders, in an area such as pediatric PTSD where the core component of the risk for developing the disorder is environmental, care must be given to defining how both positive and negative environmental exposures should be systematically recorded and included in ongoing studies. In adult studies, a social environment with one type of childhood adversity or trauma is a significant risk factor for subsequent adversities, with 87% of all respondents reporting any adversity reporting more than one (Dong et al., 2004). Multiple and prior traumatization may constitute a significant portion of an individual's allostatic load, or total combined stressors experienced by the individual over time (McEwen, 2000), which may be a significant moderator of poor health and behavioral problems. This may be particularly true for children who experience maltreatment (Rogosch, Dackis, & Cicchetti, 2011).

Conversely, understanding environmental factors that contribute to resiliency is equally important when examining how adverse events and traumas contribute to symptoms of posttraumatic stress in children. Although factors such as social support and community resources are considered to promote resiliency in recently traumatized children (Bonanno & Mancini, 2008), a study specific to child sexual abuse questioned the efficacy of social support post trauma (Bolen & Gergely, 2014). High quality and systematic methods of measuring environmental factors that may contribute to resiliency are necessary to understand how the environment contributes to the effects of trauma on various domains.

Additional Directions for Future Research

Large scale retrospective and prospective studies could be designed to examine the impact of trauma exposure (differing types, duration, etc.) on a set of constructs given the literature reviewed above. This could aid in our understanding of the differential impact of traumas on both development and impairment in a broad array of areas. These findings would inform developmentally appropriate assessment measures that are not based solely on diagnoses but

on a wider set of domains relevant to trauma. Additionally, and potentially most important, studies of this type could result in the identification of a set of phenotypes that are defined by the impact of trauma on the domains of negative valence, positive valence, cognitive systems, social processes, and regulatory systems based on neuroscience and emotional/behavioral indicators, allowing for the development of new interventions and treatments.

There are also several avenues in which RDoC constructs could be incorporated into current research with trauma-exposed youth. First, recognizing the heterogeneity of children who all meet criteria for PTSD, published data should include, at a minimum, breakdown of severity of specific PTSD criteria, acting as a bridge to a more formalized RDoC framework for future studies in traumatized children. By publishing and making available to researchers severity of PTSD symptom criteria and specific co-morbidity results (e.g. severity of depression symptoms), even non-significant findings can be hypothesis generating for future RDoC centered research.

Second, often studies designed to focus on a cohort of children with PTSD exclude conditions where participants have some symptoms of posttraumatic stress but do not meet full criteria. However, excluding children with some symptoms of posttraumatic stress is not representative of many children who experience trauma, where some posttraumatic stress symptoms are quite common (Scheeringa et al., 2012). This is the advantage of the RDoC system. Rather than recruit children with PTSD, samples of trauma exposed children can be entered into intervention or prevention studies, and specific constructs can be measured and followed during the course and after treatment, agnostic of any particular disorder. This method provides a greater opportunity for researchers to relate therapeutic interventions to particular systems of interest in the field.

Third, as has been highlighted throughout the research reviewed, future RDoC studies should strive to focus on specific developmental periods when studying the impact of trauma on children. Applying adult centered criteria to a wide range of pediatric developmental stages has been a challenge for pediatric PTSD in general, and RDoC constructs within the different domains may have different phenotypes depending on the developmental period. Consideration of age and development of the brain and neurophysiology is key to understanding the results of pediatric studies. Careful selection of age of the child at the time of trauma, for instance, is needed to understand the meaning of neurobiological findings as well as, cognitive, social and behavioral symptoms.

Fourth, unlike adult studies that examine remote or childhood trauma, pediatric RDoC studies should strive to control for time since exposure and exposure chronicity when evaluating traumatized children. Systematically controlling for time, as well as other covariates such as allostatic loading prior to the most recent trauma, will help determine the time x development x exposure interface, which is not currently well understood.

Last, by exploring specific constructs in large research studies without specification of disorder, the field can uncover neurobiological and other changes that cut across disorders. A study that measures structural and functional changes in the brain and regulatory systems, attachment, cognition and understanding of the self, as well, as the spectrum of psychiatric

symptoms could uncover etiology and targets for prevention and treatment across a range of current disorders.

Conclusion

A great deal has been learned in the last several decades about the broad impact of trauma on children. In addition to studies that explore differences in children with and without PTSD, examination of cohorts of trauma exposed children and the resulting outcomes have led to a clearer understanding of factors associated with psychiatric difficulties and functional impairment after trauma exposure. Using this knowledge and applying constructs from RDoC to further the understanding of neurobiological domains impacted by trauma has the potential to greatly advance the field. Increased identification of the ways in which pre-existing factors (e.g. attachment, DAT genes) and neurobiological changes following trauma (e.g. HPA activity, startle response) lead to impairment following trauma exposure at different developmental stages will have direct implications for treatment through: a) identification of those at greatest risk for significant impairment following exposure to a wide array of trauma types allowing for development of the best possible early assessment approaches; and b) identification of the ways in which treatments are influencing neurobiological systems impacted by trauma resulting in decreased symptoms and dysfunction and better outcomes for children and youth.

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Highlights

We give a rationale for use of Research Domain Criteria(RDOC) to study child trauma.

We review existing research in the RDOC domains related to childhood trauma exposure.

Much research is still needed in RDOC domains related to childhood trauma.

Review how new RDOC studies can guide intervention development and evaluation.

Suggestions of how RDOC can enhance the field's understanding of childhood trauma