

Psychiatry Mental health 2017 : Neuroscience-informed interventions for youth with history of traumatic stress - Victor G Carrion - Stanford University

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35% of youth living in communities of high violence will develop significant post-traumatic stress disorder symptoms. Current treatment modalities that anchor in Cognitive Behavioral Therapy (CBT) may leave 20-50% of youth without adequate symptom relieve. New treatment modalities that address executive function, memory and emotion regulation are needed and access and dissemination should be taken into consideration. This presentation will introduce Stanford's Cue-Centered Therapy (CCT) and a school-district wide prevention effort that involves yoga and mindfulness in students' curriculum. CCT integrates elements from CBT with other empirically validated interventions for traumatized youth (psychodynamic therapy, insight, self-efficacy, education). The prevention study focuses on health and wellness through meditation and exercise. Our research identifying key brain regions (e.g.; hippocampus, amygdala, prefrontal cortex) alterations in structure and function as related to traumatic stress informed the development of CCT. CCT demonstrated effectiveness in reducing anxiety, depression and post-traumatic stress symptoms in a randomized controlled trial. We are currently engaged in treatment outcome research to demonstrate CCT's efficacy in improving brain function and cognitive and emotional outcomes. The presentation will focus on our imaging (sMRI and fMRI) and salivary cortisol studies that set the stage for the development of CCT. In addition, sleep was investigated in our prevention study. A curriculum of yoga and mindfulness improves sleep variables and these will be presented. New treatment modalities and dissemination plans need to be developed to address the highly heterogenous group of children that fall under the diagnostic umbrella of Post Traumatic Stress Disorder (PTSD). Approaching both prevention and treatment that are informed by neuroscience research promises to make our interventions more focused and targeted. Recent Publications 1. Klabunde M, Weems C, Raman M and Carrion V G (2016) The Moderating Effects of Sex on Insula Subdivision Structure in Youth with Post Traumatic Stress Symptoms. *Depression and Anxiety*; 34(1): 51-58. 2. Weems C F, Klabunde M, Russell J D, Reiss A L and Carrion V G (2015) Post-traumatic stress and age variation in amygdala volumes

among youth exposed to trauma. *Social Cognitive and Affective Neuroscience*; 10(12): 1661-7. Traumatic experiences early in life predispose animals and humans to later cognitive-behavioral, emotional, and somatic problems. In humans, traumatic experiences are strong predictors of psychiatric illness. A growing body of research has emphasized alterations in neurological structure and function that underscore phenotypic changes following trauma. However, results are mixed and imprecise. We argue that future translation of neurological findings to clinical practice will require: (1) discovery of neurobehavioral associations within a longitudinal context, (2) dissociation of trauma types and of trauma versus chronic stress, and (3) better localization of neural sequelae considerate of the fine resolution of neural circuitry. We provide a brief overview of early brain development and highlight the role of longitudinal research in unearthing brain-behavior relations in youth. We relay an emergent framework in which dissociable trauma types are hypothesized to impact distinct, rationally-informed neural systems. In line with this, we discuss the long-standing challenge of separating effects of chronic stress and trauma, as these are often intertwined. We bring to light inconsistencies in localization of neural correlates of trauma, emphasizing results in medial prefrontal regions. We assert that more precise spatial brain localization will help to advance prevailing models of trauma pathways and inform future research. Neuroimaging techniques have been central to characterization of normal brain development in domains of structure, function, and connectivity. Longitudinal structural magnetic imaging (MRI) studies show a linear increase with age in white matter that is most pronounced between early childhood and adolescence. Myelination of the corpus callosum, the primary white matter tract in the brain that controls inter-hemispheric communication, occurs in a rostral-caudal sequence and continues throughout childhood into early adulthood. In contrast, gray matter follows an inverted U-shaped pattern of change, rapidly increasing until about age 10 then decreasing thereafter. This pattern presumably reflects concurrent and complementary processes of axonal myelination and

synaptic pruning. Diffusion tensor imaging (DTI) and functional connectivity MRI (fcMRI) data highlight a transition from short-range to long-range wiring in the brain through adolescence, thought to reflect increasingly optimized brain neurocircuitry. In addition to the strengthening of long-range connections, increasing regional specialization and experience-dependent plasticity also play an intricate and commensurate role in brain maturation. Extended discussion of human brain developmental processes is available in prior influential works.

Drilling down deeper into brain maturation we find that brain maturation is linked to pubertal status that different structures in adjacent brain regions mature at different rates, and that neurodevelopmental connectional and structural trajectories differ between the sexes. Knowledge that the human brain varies along these multifaceted dimensions (age, region, sex) adds a level of complexity to consideration of the impacts of trauma in the early developing brain. By the nature of their early and upstream effects, disturbances affecting the brain in time-sensitive developmental periods can have lasting or widespread organizational impact. Increased vulnerability is ascribed to periods of rapid maturation, but empirical research is needed to unpack interactions between stress/adversity and sensitive periods in human development. Also, because adjacent brain structures mature at different rates, it is likely that individual neural regions and circuits have distinct windows of vulnerability to effects of traumatic stress. Thus, the developmental timing of traumatic events and sex of the victim are relevant to behavioral and neurological outcomes, compelling the need for longitudinal and sex-specific developmental research.

A growing body of research describes altered neurological structure and function in individuals that experience early emotional trauma. In this review, we present an overview of what has been learned and provide suggestions about next steps. We describe prior results in children and adolescents that support a model in which trauma early in life alters neural circuits consistently implicated in emotional health. That is, effects observed in individuals that experience trauma resemble those described in psychopathology. These are hyper-responsiveness in medial temporal components

of limbic circuitry, hypo-responsiveness in medial and lateral prefrontal regions associated with regulating limbic response, and decreased engagement of components of the basal ganglia involved in reward related processing. Alterations in stress regulatory pathways including the hippocampus and hypothalamus are also frequently observed in individuals that experience trauma, and most consistently in adults affected by PTSD. Overlap between neurobiological correlates of trauma-exposure and psychopathology suggests that the brain may be a conduit for the link between early adversity and development of emotional psychology. We are not the first to highlight this inference, but more research is needed to further support this conclusion.

We emphasize three areas for advancing understanding of the neurobiological bases of trauma: (1) discovery of neurobehavioral associations within a longitudinal context, (2) dissociation of trauma types and of trauma versus chronic stress, and (3) better localization of neural sequelae considerate of the fine resolution of neural circuitry. Longitudinal research can address several current limitations in the literature. Brain networks evolve, grow and adapt to changing cognitive demands, a meaningful context in which to dissect the neurobiology of trauma. Longitudinal examination is needed to evaluate prevailing theory that neural mechanisms that undergird emotional illness may mediate correspondence between severe early adversity and emergence of emotional disorder.

Biography:

Victor G Carrion is an Endowed Professor and Vice-Chair in the Department of Psychiatry and Behavioral Sciences at Stanford University and Director of the Stanford Early Life Stress and Pediatric Anxiety Program. He is in the Faculty at both Stanford University School of Medicine and Lucile Packard Children's Hospital. His multidisciplinary research on the behavioral, academic, emotional and biological late effects of experiencing trauma has led to the development and implementation of effective new interventions for treating children who experience traumatic stress.

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