Conceptual and Methodological Issues in Neuroimaging Studies of the Effects of Child Maltreatment

THE EXTENSIVE SCIENTIFIC LITERATURE ON child maltreatment (CM) has provided strong evidence of the globally negative effects of abuse, neglect, and emotional maltreatment on healthy development and of the remarkable resilience of individuals who manage to prosper even in the face of these adverse experiences.[1,2] Yet, after many decades of CM research, the underlying mechanisms by which risk and resilience are conferred are just beginning to be understood. In recent years, there has been an acceleration of progress in this area, owing largely to advances in developmental cognitive neuroscience methodologies that are allowing researchers an unprecedented opportunity to understand the manner by which these experiences get "under the skin"[3] to affect the development of neurobiological systems.[4-6] These findings (from animal and human studies) document structural and functional changes in the developing brain associated with CM[7,8] and yield strong support for the role of CM in subsequent psychopathology in childhood and across the life span.[9] Edmiston et al[10] followed this recent trend of neuroscientific investigations of CM but broke new ground in 4 important ways.

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First, by examining adolescents, Edmiston et al[10] revealed linkages between the neurobiological effects of CM previously observed in children and adults. Specifically, Edmiston et al[10] showed that gray matter (GM) volume is decreased across several cortical, striatal, and limbic regions in adolescents reporting prior CM. The results cited in Edmiston et al[10] demonstrate that GM volume decreases in adults and children. However, whereas volumetric hippocampal reductions are the most frequent finding in previous research on adults with CM, this pattern is absent in children with CM, raising the question of whether it emerges in adolescence. Edmiston et al[10] suggested that such volumetric hippocampal reductions are present in some adolescents.

Second, whereas prior neuroscience researchers have treated CM as a unitary construct (without distinguishing subtypes or severity of CM) or have focused on a single type of CM (eg, physical abuse), Edmiston et al[10] examined differences on measures of brain morphometry according to CM subtypes. For example, the noted decreased hippocampal volume in the CM sample was primarily observed in those reporting emotional neglect. Similarly, the authors noted other regional effects that were common across CM subtypes (specifically, GM reductions in the rostral prefrontal cortex), and they provided logical (albeit speculative) hypotheses about how these differences might explain parallel differences in previously reported behavioral sequelae of specific CM subtypes.

Third, Edmiston et al[10] examined sexually dimorphic CM effects on brain morphometry. Specifically, the regions most effected in male patients with prior CM appear to be more strongly associated with impulse control, including the caudate and rostral prefrontal cortex. In contrast, the female patients showed alterations in multiple areas associated with emotion reactivity and regulation, including the amygdala, orbitofrontal cortex, subgenual cingulate cortex, insula, and hippocampus. Similar to the results for CM subtypes, the sex analyses provide evidence of concordance between previously observed behavioral phenomena (specifically, differential vulnerability to psychopathology) and underlying neurobiological effects.

Fourth, and perhaps the most noteworthy characteristic of the study, the sample consisted of individuals who did not meet criteria for a mental health disorder. The morphometric differences that were noted and that were associated with particular CM subtypes existed among individuals who appeared behaviorally unscathed by their experiences of prior adversity. As Edmiston et al[10] noted, these results might be evidence of future vulnerabilities and/or evidence of adaptations that have allowed compensatory processes to facilitate healthy development in the face of adversity. Additional work in this area is particularly important to meeting the needs of this population because understanding future risk in the absence of behavioral difficulties would greatly assist in the development of screening and prevention programs. Furthermore, knowledge about compensatory processes that help to support resiliency could be leveraged in the development of treatment programs to mitigate CM effects.

Given the importance of the study by Edmiston et al,[10] we believe that an expansion of research on the developmental neurobiology of CM subtypes is warranted. One particularly relevant new mind-set would consider the regional developmental trajectories of GM and white matter (WM) in a movement toward thinking about these effects at the level of networks rather than isolated regions. Anatomical integration between remote brain regions is accomplished by WM tracts, and measures of WM integrity such as diffusion tensor imaging have illustrated that WM development steadily increases into adulthood.[11,12] In particular, WM fibers connecting the prefrontal cortex to subcortical limbic and striatal structures (including those found to be affected by CM in the study by Edmiston et al[10]) continue to mature into young adulthood.[13] Another relevant element of brain development

is that of functional connectivity, which is complementary to, but not synonymous with, anatomical connectivity. Functional connectivity can be estimated in a task-independent fashion (ie, at rest),[14] and such methods have led to the identification of multiple networks, some of which are developed by puberty, although network metrics continue to evolve with further development.[15]

Therefore, to fully understand the effect of the GM reductions observed in individuals with CM across various cortical, striatal, and limbic regions (including those reported in the study by Edmiston et al[10]), it would be useful to consider the following:

- Are the precise locations of GM reductions in adults with CM consistent across studies? Meta-analyses conducted using tools such as GingerALE could provide insight beyond summary reporting of labeled regions.[16]
- Given the answer to the preceding question, does the trajectory of GM development in each of the regions effected by CM predict the age during which GM reductions attributable to CM are first observed? The regionally specific patterns of maturation in the cortical and subcortical regions and the WM that connects them[13,17,18] have been increasingly documented. Furthermore, changes in WM are known to be associated with changes in GM.[19,20]
- Can we use typically developing patterns of anatomical or functional connectivity between cortical, limbic, and striatal regions to identify particular networks or additional regions that are placed at risk by CM in a "downstream" fashion, according to the earliest-emerging affected regions?
- Finally, can we use information about these networks' functional contributions to better understand the behavioral consequences of these atypical patterns of neurodevelopment? Because any given brain region is responsible for multiple functions, it is important to be cautious about making strong claims that depend on reverse inference.[21,22] Network-wide analyses and searches for selective associations should be more robust in regard to this issue.[23-25]

Research in these areas has great potential to address the needs for more effective prevention and treatment programs for individuals with specific CM subtypes.

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Author Contributions: *Study concept and design:* Fisher and Pfeifer. *Drafting of the manuscript:* Fisher and Pfeifer. *Critical revision of the manuscript for important intellectual content:* Fisher and Pfeifer. *Obtained funding:* Fisher. *Administrative, technical, and material support:* Fisher.
Financial Disclosure: None reported.
Funding/Support: Support for this article was provided by grant MH078105 from the National Institute of Mental Health, grants DA023920 and DA021424 from the National Institute on Drug Abuse, grant R324A080026 from the US Department of Education, and grant HD045894 from the National Institute of Child Health and Human Development.

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