Childhood Maltreatment and Psychopathology Affect Brain Development During Adolescence

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Objective: The hippocampus and amygdala have received much attention with regard to the deleterious effects of childhood maltreatment. However, it is not known if and when these effects emerge during adolescence and whether comorbid psychopathology is more likely to explain these effects. This study investigated whether childhood maltreatment was associated with hippocampal and amygdala development from early to midadolescence and whether the experience of psychopathology during this period mediated the relation. **Method:** One hundred seventeen (60 male) adolescents, recruited as part of a broader adolescent development study, participated in magnetic resonance imaging assessments during early and midadolescence (mean age at baseline 12.62 years, SD 0.44 years; mean follow-up period 3.78 years, SD 0.20 years), and completed self-report measurements of childhood maltreatment and diagnostic interviews assessing *DSM-IV* mental disorders. **Results:** Childhood maltreatment was associated with larger baseline left hippocampal volumes and retarded growth of the left amygdala over time and was indirectly associated, through the experience of psychopathology, with retarded growth of the left hippocampus and accelerated growth of the left amygdala over time. Exploratory cortical analysis showed that maltreatment influenced thickening of the superior parietal region through the experience of psychopathology. **Conclusions:** Childhood maltreatment was associated with altered brain development during adolescence. The experience of Axis I psychopathology during adolescence may be one mechanism by which childhood maltreatment has continuing effects on brain development during the adolescent years. These findings highlight the importance of early intervention for individuals who have experienced childhood maltreatment. J. Am. Acad. Child Adolesc. Psychiatry, 2013; 52(9):940–952. **Key Words:** adolescence, amygdala, brain development, hippocampus, maltreatment

It is well recognized that childhood maltreatment represents an important risk factor contributing to the development of psychopathology later in life.[1,2] The high prevalence of childhood maltreatment in the general community (up to 40%)[3] highlights the importance of understanding the mechanisms that influence its relation with poor mental health outcomes. There is growing evidence to suggest that maltreatment may alter the functioning of neurobiological stress systems, and that this may be one mechanism by which maltreatment contributes to the development of psychopathology.[4,5]

Supplemental material cited in this article is available online.

The hippocampus and amygdala play critical roles in stress reactivity,[6,7] and as such these brain regions have received much attention with regard to the deleterious effects of stress, trauma, and maltreatment.[4,8] Regarding the hippocampus, studies of adult humans have consistently found decreased volumes in those with a history of childhood maltreatment (see McCrory *et al.*,[4] Tottenham and Sherdan,[8] Dannlowski *et al.*,[9] and Teicher *et al.*[10]). Interestingly, similar studies of children and adolescents who have experienced maltreatment have produced mixed results, with some studies finding smaller volume (e.g., Edmiston *et al.*[11]) and many studies reporting no effects on hippocampal volume[12,13] or increased volume.[14] This discrepancy between studies of adults versus children and adolescents suggests that the

effects of childhood adversity on the hippocampus may not be static but rather changes across the lifespan. Early adversity may have protracted or delayed effects on hippocampal structure that do not emerge until many years after the experience of adversity.[15] Regarding the amygdala, findings have been inconsistent in all age groups studied, with some studies finding smaller volume,[13,16] some finding increased volume,[17] and many not identifying any effects.[9,18-20] Thus, it is even less clear if, and when, the effects of maltreatment on amygdala structure might emerge.

A marked gap in the current literature is the lack of studies assessing the effects of childhood maltreatment on patterns of hippocampal and amygdala development (i.e., longitudinal change) over time. In 1 of only 2 human longitudinal studies conducted to date, although the amygdala was not investigated, elevated cortisol levels in children who were maltreated (8–14 years old) and had posttraumatic stress disorder (PTSD) predicted a hippocampal volume decrease over a subsequent 12- to 18-month interval.[21] Another study of children (10–13 years old) with maltreatment-related PTSD failed to find any changes in hippocampal or amygdala volume over the late childhood to early adolescent period.[19]

Although these studies make an important contribution to the knowledge of if, and when, the effects of childhood maltreatment on hippocampal structure emerge, one marked limitation of these studies, and indeed most cross-sectional studies, is that participants in clinical groups have a history of maltreatment and some form of psychopathology (e.g., PTSD, depression). This means that it is often not possible to detect the unique effects of maltreatment on brain morphology. Indeed, several maltreatment-related mental disorders also have been consistently associated with altered hippocampal and amygdala volumes, and there is some evidence that these alterations are the consequence of experiencing the disorder.[22-24]

The aims of this study were to examine the effects of childhood maltreatment on hippocampal and amygdala development in a community sample of adolescents and whether the experience of psychopathology mediated or explained this relation. The authors predicted that childhood maltreatment would be associated with decreases in the volume of the hippocampus from early to midadolescence. They also predicted that the experience of psychopathology would mediate this relation. Predictions regarding the amygdala were less clear, but given the available evidence, they hypothesized that maltreatment would not be associated with volume change over time. In addition, the authors performed an exploratory whole-brain analysis to identify any direct and indirect effects of maltreatment on cortical development.

METHOD

Participants

Participants were a community sample of 139 adolescents (76 male; male mean age 12.64 years, SD 0.46 years; female mean age 12.61 years, SD 0.42 years) recruited from schools across metropolitan Melbourne, Australia as part of a larger cohort study (the Orygen Adolescent Development Study [ADS]). The aim of the ADS was to prospectively examine biopsychosocial risk and resilience factors for emotional and behavioral problems during adolescence. To maximize the ability to examine risk and resilience, the ADS screened a large number (i.e., 2,453) of early adolescents from primary schools in and around metropolitan Melbourne and selected a smaller sample of adolescents (i.e., 415) who represented those with extreme scores on key affective temperaments known to promote risk and resilience for psychopathology (see Yap *et al.*[25] for further details). Participants were excluded from entering the study if there was any evidence of current or previous depressive, substance-use, or eating disorder and were excluded from neuroimaging if there was evidence of chronic illness, language or learning disabilities, or use of medicines known to affect nervous system functioning. The 139 adolescents in the present study represented those who, from the selected sample of 415, consented to participating in baseline neuroimaging and an assessment of childhood maltreatment. Of this sample, 117 of the 139 participants (84%; 60 male) completed a follow-up assessment (mean follow-up period 3.78 years, SD 0.20 years).

At baseline and follow-up, the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime interview[26] was used to assess lifetime history of *DSM-IV* Axis I psychopathology. During the follow-up period (i.e., baseline to follow-up), 45 participants experienced at least 1 *DSM-IV* Axis I disorder. Comorbid disorders were common (71%); 51% developed at least 1 internalizing disorder (i.e., mood or anxiety), 18% developed at least 1 externalizing disorder (e.g., conduct disorder, substance use disorder), and 31% developed comorbid internalizing and externalizing disorders. For 22 of these participants, disorder episode(s) occurred during the follow-up period (i.e., from baseline to follow-up assessments, with offset before the follow-up assessment). For 8 of these participants, disorder episodes were current at the follow-up assessment. The remaining 15 participants had episodes during the follow-up period (i.e., with offset before the follow-up