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Research report

Disorganized attachment in infancy predicts greater amygdala volume in adulthood

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HIGHLIGHTS

- Attachment disturbance in infancy predicts larger left amygdala volume in adulthood.
- Prediction is independent of later maltreatment and later attachment quality.
- Attachment disturbance also predicts adult dissociation and limbic irritability.
- Left volume mediates the relation between early attachment and limbic irritability.
- Disturbed infant attachment may affect adult amygdala volume and psychopathology.

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ABSTRACT

Early life stress in rodents is associated with increased amygdala volume in adulthood. In humans, the amygdala develops rapidly during the first two years of life. Thus, disturbed care during this period may be particularly important to amygdala development. In the context of a 30-year longitudinal study of impoverished, highly stressed families, we assessed whether disorganization of the attachment relationship in infancy was related to amygdala volume in adulthood. Amygdala volumes were assessed among 18 low-income young adults (8 M/10F, 29.33 ± 0.49 years) first observed in infancy (8.5 ± 5.6 months) and followed longitudinally to age 29. In infancy (18.58 ± 1.02 mos), both disorganized infant attachment behavior and disrupted maternal communication were assessed in the standard Strange Situation Procedure (SSP). Increased left amygdala volume in adulthood was associated with both maternal and infant components of disorganized attachment interactions at 18 months of age (overall $r = 0.679$, $p < 0.004$). Later stressors, including childhood maltreatment and attachment disturbance in adolescence, were not significantly related to left amygdala volume. Left amygdala volume was further associated with dissociation and limbic irritability in adulthood. Finally, left amygdala volume mediated the prediction from attachment disturbance in infancy to limbic irritability in adulthood. Results point to the likely importance of quality of early care for amygdala development in human children as well as in rodents. The long-term prediction found here suggests that the first two years of life may be an early sensitive period for amygdala development during which clinical intervention could have particularly important consequences for later child outcomes.

1. Introduction

Early life stress is increasingly recognized as a risk factor for psychopathology. Childhood adversity has been associated with 30–70% of the population attributable risk for depression, suicide attempts, anxiety disorders and substance abuse [1]. One central component of early adverse environments is impairment in parental regulation provided to the infant [2], with meta-analyses indicating that insecure and particularly disorganized attachment relationships in infancy predict internalizing and externalizing problems in childhood [2–5]. Impaired regulation of early stress due to poor quality care may increase risk through excessive release of glucocorticoids and associated epigenetic modifications that

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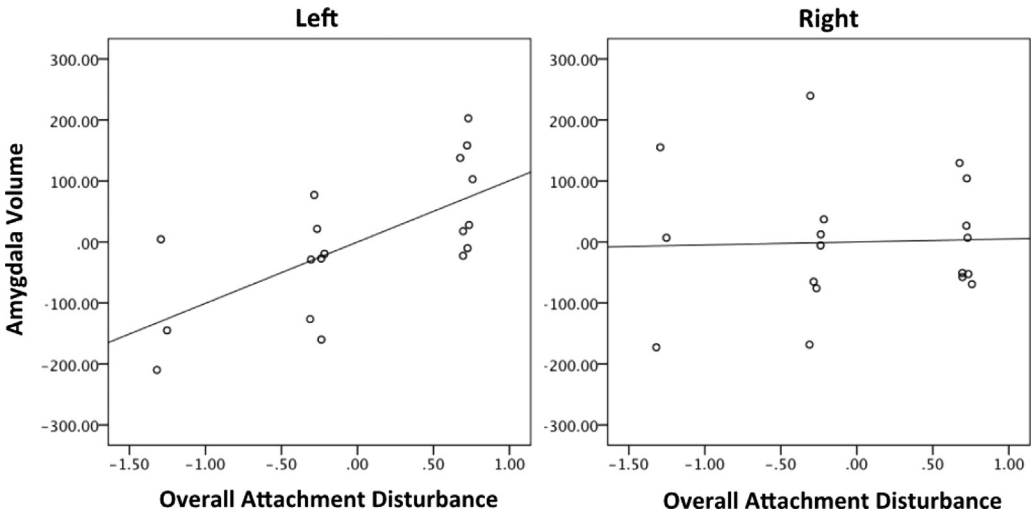

Fig. 1. Amygdala volume in adulthood and infant attachment disturbance.
Amygdala volume was normalized and adjusted for total grey matter volume and race. Left ($r = 0.679$, $p = 0.004$) but not right ($r = -0.048$, $p = 0.860$) amygdala volume was related to overall attachment disturbance.

alter critical developmental processes such as neurogenesis, synaptogenesis and myelination [6].

The amygdala may be particularly vulnerable to such effects of early stressors due to high glucocorticoid receptor density [7] and to a postnatal developmental trajectory characterized by rapid initial growth and gradual pruning [8,9]. In accord with this hypothesis, translational studies show that manipulating type and timing of early stressors leads to persistent alterations in amygdala development and function [10–12]. Both psychological stressors and stress hormone administration stimulate dendritic arborization and formation of new spines in the amygdala, increasing volume [13,14]. This pattern is opposite to stress-induced hippocampal atrophy and less reversible when the stressor is removed [15]. In particular, animal models indicate that low maternal responsiveness (LMR) during infancy is a potent stressor, associated with a host of alterations in infant development, including amygdalar effects, that persist into adulthood [10–12,16]. In rodent models, LMR has been indexed by natural or provoked variations in the responsiveness of maternal care [10,11,16].

Studies are now examining the relation between varieties of early life stress and amygdala volume among human children and adults. However, the consequences of early life stress on the human amygdala and the underlying causes (e.g., dendritic arborization) remain inconclusive [17].

First, a number of studies have found volumetric differences in relation to severe life events, including childhood maltreatment, institutional rearing, and poverty [18–26]. However, other studies have reported no differences in amygdala volume following similar types of adversity [27–37].

Second, adult volumetric differences related to childhood maltreatment have most often involved increased hemispheric volume ([18,19,38]; but see [20] for reduced volume). Increased volumes have also been reported among children exposed to institutional rearing or maternal depression [24,25,39]. However, in other studies assessing amygdala volumes in children or adolescents, effects have involved reduced volumes [21–23]. In addition, smaller amygdala volumes in adulthood were reported among individuals with childhood trauma and diagnoses of Borderline Personality [40,41] or Dissociative Identity Disorders [42,43]. Aberrant amygdala volume and function have also been reported in other psychiatric disorders marked by affective dysregulation [41,44–46].

Third, volumetric differences have varied in whether they occurred in both hemispheres or more strongly in the left or right hemisphere of the amygdala. Adults exposed to maltreatment in childhood have shown predominately right-sided differences in amygdala volume as adults [18–20,38]. Findings based on neuroimaging in childhood among children exposed to adversity (institutional rearing, maternal depression, maltreatment) have varied, with some showing overall differences or right-sided differences [24,25,39] and others showing predominately left-sided effects [21–23].

Several factors may contribute to these inconsistencies. First, the timing of adversity may be critical [17,30,38]. Given the amygdala's developmental trajectory, it may be particularly sensitive to structural changes during early childhood when it is growing at a rapid rate, and again during preadolescence when growth peaks and pruning takes over, as observed in the hippocampus [47]. Second, stress-related effects on the amygdala may be cumulative, as well as non-linear, with amygdala enlarging in response to early life stress but shrinking over time in the face of continued or overwhelming later stress [48]. Third, the amygdala may show a differential response to different types of stressors, enlarging in the face of neglect or insufficient human interaction, as with prolonged institutional deprivation, or shrinking with exposure to the types of intense abuse often reported by individuals with borderline personality or dissociative identity disorders. Thus, while there is increasing literature to suggest that the human amygdala is affected by stressful developmental experiences, it is likely that factors including timing of stressor [38], age of assessment [23], development of associated psychopathology [23], genetic loading [22], and extent of stressful life events [22] will be important to the patterning of effects on the amygdala.

While most human studies have focused on stressful events after the infancy period, a few studies have examined amygdala structure or function in relation to the effect of low maternal responsiveness in the first two years of life, including prolonged institutional deprivation or rearing by depressed mothers [21,24,25,39]. While most studies found volumetric increases [24,25,39,49] and increased activity in the amygdala [50–52], at least one study found volumetric decreases [21] and one study reported no differences [53].

To date, however, most studies have inferred low maternal responsiveness from more distal indices such as institutional care or maternal depression. One study has involved direct assessment of infant behavior, but maternal behavior was not assessed [49]. To more carefully parse how the quality of maternal care during the