

Indiscriminate Amygdala Response to Mothers and Strangers After Early Maternal Deprivation

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Background: In altricial species, maternal stimuli have powerful effects on amygdala development and attachment-related behaviors. In humans, maternal deprivation has been associated with both “indiscriminate friendliness” toward non-caregiving adults and altered amygdala development. We hypothesized that maternal deprivation would be associated with reduced amygdala discrimination between mothers and strangers and increased parent report of indiscriminate friendliness behaviors.

Methods: Sixty-seven youths (33 previously institutionalized; 34 comparison; age-at-scan 4–17 years) participated in a functional magnetic resonance imaging experiment designed to examine amygdala response to mother versus stranger faces. In-scanner behavior was measured. Indiscriminate friendliness was assessed with parental report.

Results: Comparison youth showed an amygdala response that clearly discriminated mother versus stranger stimuli. Previously institutionalized youths, by contrast, exhibited reduced amygdala discrimination between mothers and strangers. Reduced amygdala differentiation correlated with greater reports of indiscriminate friendliness. These effects correlated with age-at-adoption, with later adoptions being associated with reduced amygdala discrimination and more indiscriminate friendliness.

Conclusions: Our results suggest that early maternal deprivation is associated with reduced amygdala discrimination between mothers and strangers, and reduced amygdala discrimination was associated with greater reports of indiscriminate friendliness. Moreover, these effects increased with age-at-adoption. These data suggest that the amygdala, in part, is associated with indiscriminate friendliness and that there might be a dose–response relationship between institutional rearing and indiscriminate friendliness.

Key Words: Affective salience, amygdala development, attachment, indiscriminate friendliness, institutional rearing, maternal deprivation

The impact of maternal deprivation in the formation of attachment-related behaviors has been explored in the animal (1–4) and human literature (5–8). Early maternal separation and institutional rearing (e.g., orphanages) has implications for mental health outcomes (9–12). One common outcome in previously institutionalized (PI) children is a behavior often called “indiscriminate friendliness,” which includes reduced reticence and atypical approach behaviors toward all adults, including strangers (13). It is important to note that the term is a misnomer, as the behavior in these children has been noted to be “neither ‘friendly’ nor ‘sociable’” (14). Tizard and Hodges (15) note that this behavior was the greatest source of complaints from teachers, because the children engaged in attention-seeking behaviors, attempting to engage in social approach toward teachers too frequently and at inappropriate times, in a way that disrupted the classroom environment. This common phenotype after deprivation might be associated with reactive attachment disorder, indiscriminate type (16), or might be present in the absence of dysfunctional attachment (17–20).

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Under most circumstances, the early human environment is highly constrained in that a caregiver will typically remain present. Caregiver presence is a necessary and species-expected environmental agent (21), which instantiates a developmental learning process that includes: 1) approaching the caregiver; 2) learning to recognize the caregiver; and 3) forming a preference for the caregiver and avoiding non-caregiver adults (2). Thus, experience with a primary caregiver facilitates a process whereby infants show preference for that caregiver over and above all other adults. In contrast, indiscriminate friendliness is characterized by attenuated affective discrimination between caregiver and strangers. Caregiver preference development is profoundly influenced by stability of care. Several factors work against this process in an institutional environment, including fluctuating staff, lack of caregiver sensitivity, and physical deprivation (22). If presence of a stable caregiver is required for typical attachment-related behaviors, including discrimination between mothers and strangers, then it is not surprising that PI children are at elevated risk for displaying indiscriminate behaviors (23).

Work in humans and nonhuman animals suggests that the amygdala plays an important role in representing affective relevance of the caregiver. Maternal absence alters the trajectory of amygdala development (24–26). In its broader role, the amygdala represents motivational salience of stimuli (27–31). For this reason, the amygdala might be well-suited to mediate affective discrimination of attachment figures (i.e., the role of the amygdala in detecting affective salience and motivating behavior might also serve to represent the importance of the maternal stimulus). Work in nonhuman primates has demonstrated that the amygdala is necessary for expression of caregiver preference; infants with amygdala lesions showed lack of maternal preference after maternal separation, despite initially demonstrating species-typical bonding behaviors with mothers (32,33). Similarly, the amygdala of the child is preferentially engaged by the mother

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stimulus over and above that for an unfamiliar adult, and this amygdala response has been found to mediate specific approach behaviors to caregivers (21). These findings suggest that amygdala response is associated with intense emotional relationships. The hypothesis that amygdala activity supports attachment-related behaviors is substantiated by findings that mothers also show increased amygdala activation to their own child, an effect that does not seem to merely reflect familiarity (34,35). Taken together, these data suggest a role for amygdala in the dyadic and intense interaction between mother and child, perhaps in recognizing affective salience of the primary caregiver.

Notwithstanding evidence for the involvement of the amygdala in human attachment representation, little is known about the mechanism by which deprivation-induced brain development gives rise to indiscriminate friendliness behaviors. Of note, PI children have been shown to have atypical amygdala development, with children adopted later having larger amygdala volumes, compared with early-adopted/non-adopted children (36,37). In addition, PI children have been shown to exhibit amygdala hyperactivation to emotionally arousing faces (38). These findings with human samples mirror the effects of maternal deprivation observed in several other altricial species (24,25,39,40).

We used a previously published functional magnetic resonance imaging (fMRI) paradigm (21) to examine neural responses to mother and stranger stimuli in PI youth and a typically raised comparison (Comp) group. Given the role of the amygdala in selectively representing affective/motivational salience of caregivers (21,41), we hypothesized that children with a history of maternal deprivation would show indiscriminate amygdala response to all social stimuli that would mirror the indiscriminate friendliness seen both by parents and in laboratory settings in this population. We predicted that, unlike typically raised children who show more robust amygdala response to their mothers relative to strangers (21), PI children would show reduced amygdala discrimination between mothers and strangers, a prediction based on previous work showing hyperactivity of the amygdala (38). We anticipated that amygdala reactivity would be atypically high to strangers in the PI group, despite the nonfearful nature of our stimuli. Moreover, we anticipated that children with less amygdala discrimination would exhibit more indiscriminate friendliness. On the basis of previous findings of age-at-adoption associations with indiscriminate friendliness (10,42), we hypothesized that children adopted at a later age would show more indiscriminate friendliness and less differential amygdala response to mothers and strangers.

Methods and Materials

Participants

Functional MRI data were collected from 75 youths. Comp youth ($n = 37$), living with biological parents, and PI youth ($n = 38$) with a history of institutional rearing and resultant deprivation were studied. All PI youths were adopted by families in the United States via international adoption. Although all youths in institutional care experience maternal deprivation (43), institutional care is also commonly associated with physical, nutritional, and sensory deprivation in addition to adverse prenatal exposures (43).

Of the 75 participants for whom data were collected, 67 were included in our study (Comp $n = 34$, mean age-at-scan = 11 ± 4 years, range 4–17 years; PI $n = 33$, mean age-at-scan = 10 ± 3 years, range 6–15 years). Twenty-five Comps have been

previously published (21), whereas all PI data have never been published. There was no significant difference in number excluded or reason for exclusion by group (Comp = 3, PI = 5, $p > .05$): motion artifacts (Comp = 0, PI = 1, $p > .05$); clinical imaging findings (Comp = 0, PI = 1, $p > .05$); imaging outliers (Comp = 3, PI = 2, $p > .05$)¹. Parents completed a series of questionnaires, including an indiscriminate friendliness questionnaire (detailed in the following), the Security Scale to assess attachment-related behaviors (44), the Child Behavior Checklist (45), and a telephone interview with regard to medical and psychiatric history. Relevant demographic data, including country of origin (Table 1) and age-at-orphanage/adoption (Table 2) were collected for each PI participant. To address variability in pre-adoption quality of care and possible prenatal exposure to alcohol, we included additional data (Figure S1 in Supplement 1) related to preadoption parameters in our PI population: 1) measures of orphanage quality of care (Table 2); and 2) prevalence of typical fetal alcohol dysmorphological facial features by photographs (Figure S1 in Supplement 1), that might suggest prenatal alcohol exposures. Modified version of the Hoyme criteria (46) as well as the Astley photographic scale (47) were used to quantify upper lip and philtrum characteristics on a scale of 1–5. However, no definitive Fetal Alcohol Syndrome diagnoses can be made on the basis of these data alone (47).

Youths with a history of serious medical illness, including head trauma, seizure disorder, or borderline intellectual functioning (IQ < 70) were excluded from the study. All participants were right-handed. Families had incomes above the US median annual household income (\$48,451) (United States Census Bureau, 2006). This study was approved by the University of California Los Angeles Institutional Review Board, and informed consent and assent were obtained.

Questionnaires

Indiscriminate Friendliness Scale. To examine stranger-related behaviors, we adapted indiscriminate friendliness measures of multiple laboratories (13,15,17,42), which have been shown to have convergent validity (19). Previous work has shown that parental report of indiscriminate friendliness correlates well with observation of children and families by clinical psychology staff (10). Parent-administered questionnaire (1–10 scale) assessed the following: 1) How likely do you think it is that your child would willingly go home with a stranger?; 2) How likely do you think it is that your child would wander off (and not be distressed)?; and 3) How trusting is your child with new adults?

Attachment Security. To examine mother-related behaviors in our sample, youths completed the Security Scale (44), which provides a continuous measure of their perception of security in parent-child relationships in middle childhood and early adolescence. Although frequency and intensity of caregiver-directed attachment-related behaviors decline after infancy, these behaviors continue to be observed during childhood and adolescence, particularly during stress (44). Items are rated on a 4-point scale, with higher scores signifying more secure attachment. The instrument provides scores for three subscales: 1) belief of the child that attachment figure is responsive and available; 2) reliance of the child on attachment figure in times of stress; and 3) ease and interest of the child in communicating with

¹In the supplemental analysis with anatomical region of interest (ROI), there were two additional imaging outliers from PI group excluded for >2.5 SD from mean.

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