Maternal Depression Across the First Years of Life Impacts the Neural Basis of Empathy in Preadolescence

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Objective: Exposure to maternal depression across the first years of life markedly increases children's susceptibility to psychopathology, yet no study has tested its effects on the maturation of children's social brain.

Method: Using a birth cohort of mothers with no contextual risk (N = 1,983), families were followed at 7 time points from birth to 11 years and repeatedly assessed for maternal depression across the first 6 years to form 2 cohorts: mothers continuously depressed from birth to 6 years and controls without depression. At 11 years of age, children's (n = 72; depressed, n = 27; nondepressed, n = 45) brain response to others' pain was measured by magnetoencephalography.

Results: Preadolescents displayed a unique oscillatory pattern with higher alpha power to pain versus no pain expressing as alpha rebound, not alpha suppression, at a late time window (1,100–1,300 ms post-stimulus) in the supplementary motor area. This suggests that top-down processing in areas of the pain matrix can underpin the maturation of vicarious empathy. Children of mothers with depression showed enhanced alpha rebound to pain in the right posterior superior temporal gyrus, which was unrelated to emotion detection abilities, pointing to decreased late processing of others' overwhelming experiences in socio-cognitive areas. Alpha power in the posterior superior temporal gyrus was predicted by higher maternal intrusiveness and lower synchrony across early childhood.

Conclusion: These findings, from the first study to examine maternal depression and early caregiving as long-term predictors of children's neural empathic response, pinpoint a decrease in top-down socio-cognitive mechanisms as potential pathways for the cross-generational transfer of vulnerability from mothers with depression to their offspring and highlight the need for early interventions focused on enhancing maternal attunement.

Key words: maternal depression, mother–child interaction, empathy, magnetoencephalography, alpha oscillations

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Exposure to maternal depression has long been known to negatively affect children's social and emotional development, including increased social withdrawal,[1] compromised peer relationships,[1] poor emotion regulation,[2] and decreased empathy.[3,4] When the onset of maternal depression occurs during the child's first months of life and the disorder is of a chronic course, the risk for maladaptive outcome significantly increases.[5,6] However, although maternal depression is a common psychiatric disorder affecting 15% to 18% of parturient women in industrial societies[7] and up to 30% in developing countries,[8] no study to date has tested its long-term effects on children's social brain.

Children of mothers with depression show disruptions in the development of empathic response to the distress of others. Preschool-age children of mothers with depression have been found to exhibit less concern for the distress of their mother and an experimenter[9] and less helping behavior to infant crying.[4] A study on guilt found that school-age children of mothers with depression responded with aborted and unresolved narratives to others' distress compared with controls' expression of responsibility and reparation,[3] suggesting that the immature mechanisms for processing others' distress could relate to the encounter with distress in oneself. This indicates that the reported deficits in empathic behavior in children of mothers with depression[4,9] do not stem from their inability to correctly assess interpersonal situations but from disruptions to emotion regulation mechanisms and difficulties in modulating the high arousal associated with observing others' distress. Such deficits can block the child's engagement in overwhelming situations, leading to premature withdrawal or over-excitability that can impede vicarious empathy.[10] However, because not all children reared by mothers with depression show similar social and emotional difficulties, understanding the pathways leading from exposure to maternal depression in early life to the neural and behavioral underpinnings of social adjustment and empathy is critical for early detection and for the construction of individually tailored interventions.

One pathway repeatedly shown to mediate the effects of maternal depression on child outcome is the mother–child

This article is discussed in an editorial by Dr. Tony W. Wilson on page 8.

Supplemental material cited in this article is available online.

relationship and its specific disruptions in cases of maternal depression. Child empathy develops based on attuned parenting; higher maternal synchrony with the infant's nonverbal signals has been shown to predict greater empathy at 6 and 13 years of age,[11] and maternal response to preschoolers' distress has been shown to predict empathy to the distress of others.[12] Mothers with depression are more intrusive and less synchronous during interactions with their infants and young children,[13-16] and these maladaptive patterns have been associated with deceased empathy to others' distress in their offspring.[9,17] However, the effects of these relational impairments on the neural mechanisms underpinning the expression of empathy have not yet been studied in prospective longitudinal research. Understanding the impact of maternal depression on social brain development can shed new light on the mechanisms implicated in the lifetime vulnerability to psychopathology, social withdrawal, and loneliness observed in offspring of mothers with depression. Moreover, because the ability to process others' distress signals and respond in prosocial ways is critical for social learning and psychological adjustment,[18] charting the pathways by which maternal care supports the brain basis of empathy and its disruptions in cases of maternal depression is of theoretical and clinical importance.

In assessing the effects of maternal depression on the brain basis of empathy, it is important to understand how the age-appropriate neural response to others' pain is expressed. Empathic response to the distress of others involves a multidimensional constellation of processes ranging from automatic increase in sensorimotor arousal, an evolutionary ancient process observed in rudimentary form in rodents,[19] to higher-order mechanisms implicating emotion regulation, cognitive appraisal, and the capacity to engage multiple perspectives and oscillate between first- and third-person viewpoints.[10] Developmental studies have indicated that although empathic response to others' distress is observed already in early infancy,[20] the ability to show empathic concern, not only personal distress, unfolds gradually across childhood and adolescence and requires maturation of emotion regulation capacities.[21,22] Functional magnetic resonance imaging studies testing developmental changes in children's neural response to others' pain have shown an age-related decrease in amygdala activation and increase in frontal regions' activations alongside increased prefrontal-amygdala connectivity that correlate with the degree of perceived pain.[23,24] An electroencephalographic (EEG) study of children's and adults' event-related brain potentials to others' pain has found that children display stronger response in the early components combined with weaker response in the later components,[25] suggesting that age-related changes in neural responsivity to others' pain stem from maturation of top-down control mechanisms.[23]

In light of these findings, the present study examined, for the first time, the long-term effects of early and chronic maternal depression on preadolescents' neural response to others' pain using magnetoencephalography (MEG). MEG uniquely combines high temporal resolution with good spatial localization and is particularly suited to examine the integration of automatic and higher-order processing implicated in vicarious empathy. To specify pathways by which maternal depression shapes the brain basis of empathy, we used a large birth cohort (N = 1,983) of women with no comorbid contextual risk who were repeatedly assessed for maternal depression across the first years of life (Figure 1 presents a description of the cohort). At 9 months and at 6 years, mother–child interactions were observed and relational behaviors were examined as predictors of children's neural response at 11 years.

MEG studies assessing adults' brain response to others' pain have found greater alpha suppression in response to painful compared with nonpainful stimuli in the sensorimotor cortex.[26,27] Alpha oscillation is the predominant frequency in humans during rest and is suppressed while processing relevant information[28,29]; thus, greater alpha suppression to painful stimuli is believed to index greater processing in areas of the brain's pain matrix.[26] Only 1 study examined developmental changes in alpha suppression to others' pain using EEG and found that up to 9 years of age children show no differentiation in alpha suppression to pain versus no pain within the first post-stimulus second.[25] This is surprising in light of brain and behavioral studies using other techniques that showed that school-age children exhibit differential response to others' pain.[21-24] Because age-related improvements in empathic response during preadolescence depend on maturation of regulatory processes,[22,23,30] examination of later time windows that reflect top-down cognitive control of the initial non-differentiated response might be required. Thus, we hypothesized that differences between response to pain and no pain would emerge at later post-stimulus time windows in areas repeatedly shown to comprise the brain's pain matrix: the anterior cingulate cortex, the anterior insula, the supplementary motor area (SMA), and the sensorimotor cortex.[31] Consistent with behavioral studies,[4,9,17] we expected a less mature response to others' distress in children exposed to maternal depression across the first 6 years. Zahn-Waxler *et al.*[3] found that children of mothers with depression are more distressed by the pain of others, which decreases their other-oriented response, but are no less cognizant of it. Thus, we hypothesized that group differences might be found in socio-cognitive areas, such as the temporal pole, posterior superior temporal sulcus, posterior superior temporal gyrus (pSTG), and medial prefrontal cortex,[32] and that it might be dissociable from children's emotion detection abilities.[3] Further, we expected that mother–child relational patterns across the first 6 years of life, particularly increased maternal intrusiveness and decreased synchrony,[9,17] would predict the altered neural response to others' pain in children of mothers with depression.

METHOD

Participants

Participants were recruited in 7 waves of data collection (Figure 1), and a detailed description of recruitment appears in Supplement 1 (available online). During the second day after birth, 1,983 women who were healthy, completed high school, were older than 21 years, above the poverty cutoff, cohabitating, and whose infants were at