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The Ties That Bind: Maternal-Infant Interactions and the Neural Circuitry of Postpartum Depression

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Little is known about the pathophysiology of postpartum depression. While the same can be said for many (if not most) psychiatric illnesses, in the case of postpartum depression the need for pathophysiological studies to guide the development of novel treatments is particularly pressing because the illness affects not only the woman who experiences it, but also her newborn and other members of her family (1).

But while pathophysiological studies of postpartum depression are particularly important, they are also very difficult to conduct, given the biological and logistical complexities that characterize the postpartum period. Therefore, the study by Moses-Kolko et al. (2) in this issue of the *Journal* is a welcome addition to the literature. The authors used functional magnetic resonance imaging (fMRI) to study 16 healthy women and 14 unmedicated unipolar depressed women within 12 weeks of giving birth. While being scanned, subjects completed a task that included shape and face matching blocks, with the latter including angry and sad faces. This task is designed to probe between-group differences in amygdala activity. Previous fMRI studies using similar tasks in patients with depression demonstrate abnormalities in amygdala activity and amygdala-medial prefrontal cortex connectivity in response to negatively valenced emotional faces (3). However, the precise nature of those abnormalities, and the extent to which they differ in unipolar versus bipolar depression, remains unclear.

Given the previous literature, Moses-Kolko et al. focused their analysis on activity in the amygdala and the medial prefrontal cortex. Their major finding was a group-by-condition interaction in the dorsomedial prefrontal cortex (the finding was specifically in Brodmann's area 32). While both depressed and comparison mothers activated this region more in response to faces than to shapes, depressed mothers activated more in response to shapes than comparison mothers, and comparison mothers activated more in response to faces than depressed mothers. As discussed below, the dorsomedial prefrontal cortex is known to mediate important aspects of social cognition. Therefore, it is notable that depressed mothers, relative to comparison mothers, show decreased activation in this region in response to the social stimulus of a face. Moses-Kolko et al.'s finding indicates that it is important to focus research and treatment strategies not only on a mother's depression, but also on her ability to engage affectively with her infant.

A hallmark of depression is increased self-focus, particularly in the form of self-referential negative thoughts; research suggests that this symptom may be mediated by the dorsomedial prefrontal cortex. For example, Johnson et al. (4) found associations between activity in the

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dorsomedial prefrontal cortex (as well as posterior medial prefrontal cortex), rumination, and difficulty disengaging from self-referential thoughts in subjects with major depressive disorder. There is an extensive body of literature indicating that the dorsomedial prefrontal cortex is activated when subjects are asked to perform “theory of mind” or “mentalizing” tasks (5). These tasks require subjects to focus not on their own thoughts but instead on the thoughts, beliefs, or feelings of other individuals.

As any parent who has tried to calm a fussy baby can attest, parenting a preverbal child is arguably the ultimate challenge to one’s mentalizing abilities. Considerable research documents the elegant interplay that occurs within healthy infant-mother dyads as they communicate using mutual gaze, vocalizations, and nonverbal expressions of affect (6). Observational studies of mother-child interactions show that, on average, depressed mothers demonstrate less positive affect toward their child than nondepressed mothers, engage with their child less often, and are less sensitive to the child’s cues (1). Further, such parenting difficulties are associated with subsequent deficits in the infant’s social engagement and emotion regulation abilities (1).

In a depressed mother, are difficulties interacting with her infant mediated by dorsomedial prefrontal cortex dysfunction? The design of the study by Moses-Kolko et al. does not provide an answer to this question, and it is clearly an important topic for further work. Future studies could use paradigms that assess depressed and comparison mothers’ neural responses to verbal or auditory cues from their own infant (versus that of other infants and noninfant stimuli) and could correlate such neural responses with observational measures of mother-infant interactions. A few fMRI studies in healthy mothers have tested neural responses to their infant’s cues, but results have been inconsistent because of differences in paradigms and analytic strategies as well as small sample sizes (even in healthy women, postpartum studies are challenging). However, activation in Brodmann’s area 32 has been noted when healthy mothers hear their infant cry (7) or watch a video of their infant crying after separation (8).

Ultimately, research on the circuitry mediating postpartum depression and/or maternal-child interactions in healthy and depressed women will have the greatest impact if it suggests new treatment strategies for the illness. When testing treatments for postpartum depression, both the mother’s depressive symptoms and adverse mother-infant interactions should be considered important targets for intervention. Importantly, we do not know whether successfully treating a mother’s depression will necessarily improve parenting interactions, although preliminary evidence suggests that it may not (9). Psychopharmacologic studies in postpartum depression tend to assess the impact of treatment on the mother’s depression but not on mother-infant interactions (10, 11). Several trials of interpersonal psychotherapy have used depressive symptoms as the primary outcome but have also assessed the impact of treatment on parenting. However, parenting assessment has been accomplished with self-report scales, which provide less detail (and perhaps less reliability) than observational measures (e.g., 12, 13). One study found that parenting classes are less effective than interpersonal psychotherapy for the symptoms of postpartum depression (14), but the impact of the parenting classes on mother-infant interactions was not assessed.

The most effective strategies for treatment development in postpartum depression would therefore combine expertise in clinical trials, observational studies of mother-infant interactions, and neuroimaging. fMRI, in combination with carefully designed behavioral paradigms, could be used to delineate the neural mechanisms that compromise a depressed mother’s ability to respond to her baby optimally. For example, investigators could test whether infant-related stimuli are less emotionally salient for depressed mothers than for nondepressed mothers, with emotional salience assessed by behavioral measures (e.g.,

reaction times) and the degree to which such stimuli engage “bottom-up” attentional circuitry, including the amygdala and ventral prefrontal cortex. Also, given the anhedonia characteristic of major depression, one could test the hypothesis that women with postpartum depression would be less likely than unaffected women to experience interactions with their infant as rewarding, with the latter assessed by self-report, behavioral measures, and striatal activation. The degree to which attentional versus reward-based deficits contribute to parenting difficulties can inform the development of new psychotherapeutic approaches and thus has direct treatment implications.

Parenting a newborn is a challenging endeavor, even for mothers (and fathers) not burdened by the pain and symptoms of acute depression. For those with depressive illness, parenting an infant can be quite daunting. Our obligation is to both relieve the suffering of women with postpartum depression and to support their ability to parent lovingly and effectively. To fulfill that goal, we need to learn much more about the pathophysiology of postpartum depression and about how to treat this devastating illness effectively.

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