Neural Dysfunction in Postpartum Depression: *An fMRI Pilot Study*

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ABSTRACT

Introduction: With ~4 million births each year in the United States, an estimated 760,000 women annually suffer from a clinically significant postpartum depressive illness. Yet even though the relationship between psychiatric disorders and the postpartum period has been documented since the time of Hippocrates, fewer than half of all these cases are recognized.

Objective: Because postpartum depression (PPD), the most common complication of childbearing, remains poorly characterized, and its etiology remains unclear, we attempted to address a critical gap in the mechanistic understanding of PPD by probing its systems-level neuropathophysiology, in the context of a specific neurobiological model of fronto-limbic-striatal function.

Methods: Using emotionally valenced word probes, with linguistic semantic specificity within an integrated functional magnetic resonance imaging (fMRI) protocol, we investigated emotional processing, behavioral regulation, and their interaction (functions of clinical relevance to PPD), in the context of fronto-limbic-striatal function.

Results: We observed attenuated activity in posterior orbitofrontal cortex for negative versus neutral stimuli with greater PPD symptomatology, increased amygdala activity in response to negative words in those without PPD symptomotology,

Needs Assessment

Greater than 50% of the 760,000 women who suffer from a clinically significant postpartum psychiatric illness each year go unrecognized. Postpartum illnesses account for the largest cause of maternal death, with suicide rates of up to 5% and infanticide rates of nearly 4%. Because untreated mood disorders place the mother at risk for recurrent disease and maternal depression is associated with diminished enrichment behavior, which is known to result in long-term cognitive, emotional, and behavioral problems in the child, characterizing the behavioral and neurobiological features of postpartum depression is important for early diagnosis and intervention. This study addresses a critical gap in the mechanistic understanding of postpartum depression by probing its systems-level neuropathophysiology, in the context of a specific neurobiological model of fronto-limbic-striatal function.

Learning Objectives

At the end of this activity, the participant should be able to:

- List the various mechanisms hypothesized to be responsible for postpartum depression to date.
- Understand the application of functional neuroimaging toward informing clinical and cognitive disorders associated with affective dysregulation.
- Comprehend key components of the fronto-limbic-striatal network associated with the neuropathophysiology of emotional dysregulation in postpartum depression.

Target Audience: Neurologists and psychiatrists

CME Accreditation Statement

This activity has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Mount Sinai School of Medicine and MBL Communications, Inc. The Mount Sinai School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

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This activity has been peer-reviewed and approved by Eric Hollander, MD, chair at the Mount Sinai School of Medicine. Review date: October 15, 2007. Dr. Hollander does not have an affiliation with or financial interest in any organization that might pose a conflict of interest.

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and attenuated striatum activation to positive word conditions with greater PPD symptomotology.

Conclusion: Identifying the functional neuroanatomical profile of brain systems involved in the regulation of emotion and behavior in the postpartum period will not only assist in determining whether the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* psychiatric diagnostic specifier of PPD has an associated, unique, functional neuroanatomical profile, but a neurobiological characterization in relation to asymptomatic (postpartum nondepressed) control subjects, will also increase our understanding of the affective disorder spectrum, shed additional light on the possible mechanism(s) responsible for PPD and provide a necessary foundation for the development of more targeted, biologically based diagnostic and therapeutic strategies for PPD.

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INTRODUCTION

Considerable evidence exists suggesting that mood disorders are twice as prevalent in women compared to men.[1] While the dissociation between gender and affective disorders can be first observed at menarche (prior to puberty prevalence is equal among males and females), the preponderance of mood disorders occurs in women during the childbearing years,[2] with peak lifetime prevalence for psychiatric disorders and hospital admissions for women occurring in the first 3 months after childbirth.[3]

Postpartum depression (PPD), the most common complication of childbearing,[4] is a prevalent disorder in the spectrum of affective illness associated with significant morbidity. Traditionally viewed as a time of emotional well-being, the weeks that follow childbirth are, in fact, more often a time of heightened psychic vulnerability. Indeed, mood and behavioral symptoms during the puerperal period reportedly affect up to 85% of all new mothers.[4] With an onset usually between 3 and 14 days (although possibly up to 1 year[5,6]) postpartum symptoms of anxiety, exhaustion, alternating mood, and an inability to concentrate are usually short-lived. However, up to 20% of all postpartum women will go on to develop a more severe mood disorder that meets criteria for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*[7] depression characterized by impairment in functioning with symptoms, including neurovegetative dysregulation and ideation of harm to the self or the baby.[3] While these episodes account for a seven-fold increase in psychiatric hospital admissions compared with pre-pregnancy,[8] <50% of all of these cases will be recognized.

PPD is a cross-cultural health concern with significant public health consequences. Postnatal psychiatric illness is not only the largest cause of maternal death in the United Kingdom (statistics are difficult to obtain in the United States due to current documenting standards),[9,10] it is associated with nearly 60% of all infanticides occurring in the first 3 month postpartum.[11] Despite its suspected prevalence, PPD remains under-diagnosed and under-treated, possibly because controversy still exists about how to characterize the depression that occurs in the postpartum period. For example, while the *DSM-IV* utilizes "postpartum onset" as a modifier defined as an episode of depression within the first 4 weeks of childbirth, the American College of Obstetricians and Gynecologists[12] defines the postpartum period as extending for 1 year.

Even though numerous theories have been advanced to explain the well-documented and frequent co-occurrence of depression and childbirth, the etiology of PPD remains unclear. For example, recent research has suggested causal mechanisms, such as postpartum estrogen and progesterone shifts[13-15] thyroid disease and thyroid antibodies,[16] inflammatory responses,[17] situational triggers, such as traumatic obstetric experiences,[18] low socioeconomic status,[19] infant health[20] and psychological stress.[21] Yet, because the hormonal changes observed in childbirth are unprecedented among all other reproductive cycle events,[22] the most prevalent theories of PPD genesis relate to the effects of sex hormones on brain regions mediating mood and cognition.

Sex hormones have been shown to influence the central nervous system in a large number of varied ways, including effects on neurogenesis, gliagenesis, cell survival, ion-channel modulation, neurochemical modulation, transcription, neural excitation, and neural inhibition.[23-31] Unfortunately, the neuroedocrinology of PPD

remains poorly understood and studies exploring PPD symptomotology[22,23] do not seem to correlate well with absolute differences in hormone levels between affected and unaffected women with multiple and contradictory findings. Rather, it is quite possible that the observed symptoms may correspond to differences in the way the central nervous system responds to various (and possibly interactive) hormonal and immunologic fluctuations. Nevertheless, although brain response to sex hormones in PPD patients appears central to a neurobiological understanding of PPD's psychopathology, to date, a specific hormonal mechanism has remained elusive.

Because the clinical characterization and neurobiologic mechanisms of this evolving condition remain inadequately defined, the aim of this work was to probe and begin identifying the systems-level neuropathophysiology of PPD, in the context of a specific neurobiological model of fronto-limbic-striatal function. Using functional magnetic resonance imaging (fMRI) methods with specific neuropsychological probes of emotional processing and behavioral regulation (functions of clinical relevance to the symptomatology of PPD), and their interaction, in well-characterized patient samples, we tested mechanistic hypotheses concerning fronto-limbic-striatal circuit dysfunction in PPD in comparison to asymptomatic postpartum female control subjects. Such a neurobiological characterization in relation to non-depressed postpartum control subjects is hoped to increase our understanding of the affective disorder spectrum and shed additional light on the mechanism(s) responsible for PPD. Given the increased prevalence of mood and anxiety disorders in females, it is also hoped that this research will also provide a deeper foundation for the development of more targeted, biologically based diagnostic and therapeutic strategies for PPD.

METHODS

Subjects

Participants consisted of eight postpartum women (mean age: 28 years). Subjects gave informed consent before study participation (part of a Mount Sinai Medical Center Institutional Review Board-approved protocol). All subjects were right-handed, native English speakers, with a history free of psychiatric difficulty (including antepartum depression), head trauma, neuropsychiatric complication, illicit substance abuse, or chemical/alcohol dependence. No subjects were actively taking birth control or psychoactive medication at the time of screening or scanning. The Structured Clinical Interview for *DSM-IV* Axis I Disorders[33] was used to ensure that comparison subjects did not have any Axis I psychiatric diagnoses and that depressed participants were free of any Axis I comorbidity. The Hamilton Depression Inventory[34] was used to identify specific symptoms of depression as delineated by the *DSM-IV*. The Edinburgh Postnatal Depression Scale (EPDS),[35] a 10-item 4-point inventory with a maximum score of 30, was used to determine eligibility. Because a multinational review of the EPDS[36] demonstrated that scores of 8.5–12 points had a specificity of 49% to 100% and sensitivity of 65% to 100%, subject groups were based on the EPDS as follows: those scoring >12 were included in the depressed group (n=4), whereas those subjects scoring <6 were included in the normal comparison group (n=4). The EPDS was re-administered immediately prior to entering the MRI and an average of the two scores was taken (depressed group mean: 15.33; range: 12–19; normal comparison mean: 1.33; range: 0–4). The change of the EPDS score between administrations never varied >2 points. All scans occurred between weeks 7 and 8 postpartum.

Neuropsychological Activation Paradigm

The fMRI activation paradigm consisted of an emotional word probe, with linguistic-semantic specificity, allowing for a complementary higher-level examination of the hypothesized fronto-limbic-striatal circuitry. This paradigm employs stimuli whose emotional qualities are incidental relative to the explicit nature of the word/non-word determination behavioral task demand (2-alternative forced choice method [2AFC]). By using this technique, the evocation of potentially confounding cognitive processes (eg, semantic categorization) are hoped to be minimized.

Stimuli consisted of positive, negative (both threat and non-threat), and neutral words (adjectives, nouns, and verbs) balanced across categories for frequency, length, and part of speech, with the exception that, within the neutral list, verbs were substituted for adjectives. This was done because adjectives, comprising an important component of the valence categories, are by nature generally not free of valence. Verbs were substituted, rather than nouns, as their image-

ability is more similar to that of adjectives. Stimuli were rated for suitability as defined by Bradley and Lang.[37] Examples include positive-success, admired, praise; negative-worthless, murder, burn; neutral-transfer, trunks, fasten.

Behavioral responses were based on word/non-word judgment cues, such that subjects were instructed to perform a right index finger button-press immediately upon presentation of a word (eg, MURDER) and to perform a right middle finger button press upon presentation of a random letter string (eg, DSKDFA). Corresponding button presses were counterbalanced across subjects. Subjects were not pre-informed of the emotional nature of the stimulus words.

The task was presented in a block design. Presentation was counterbalanced to control for order and time effects. Each block was comprised of 10 stimuli words/non-words (trials) of the same valence; there 100 trials per condition, 400 total trials per complete study session. Blocks included 90%, 80%, or 70% words (compared to random letter-strings). Each stimulus appeared for 1.5 seconds, followed by a jittered interstimulus interval averaging 1,900 milliseconds, for a total block duration of 34 seconds (not including intertrial interval rest). Each block was followed by 12 seconds of rest. Each run was preceded and followed by an additional 36 second rest periods. During rest periods, subjects were instructed to look at a cross at the center of the screen, with their minds either blank or floating freely. Stimulus presentation and response collection were performed within the E-Prime environment (Psychology Software Tools, Inc., Pittsburgh, Penn.). Stimuli were presented in white against a black background subtending an average visual angle of ~2 degrees in height by 6 degrees in width.

We designed a factorial paradigm with a block (rather than event-related) design for several reasons: to maximize operationalization of sustained emotional tone; to facilitate factorial comparison of various permutations of emotion and response conditions; to exploit the imaging sensitivity bestowed by block design; and to minimize potentially confounding extraneous cognitive-behavioral functions.

There were two objectives associated with the neuropsychological tasks. First, by giving subjects a task, we ensure that they were focusing on the stimuli presented to them. In turn, this enhances the likelihood that blood-oxygen level dependent (BOLD) response changes are related to the relevant stimuli. Thus, the first objective was to present subjects a "probe" that would activate relevant brain circuitry. The second objective was to measure differences in motor response performance by condition. It is well documented that emotion-inducing stimuli can generate cognitive and/or behavioral task processing interference.[38,39]

Immediately after imaging, subjects were removed from the scanner and presented via computer with a list of words consisting of the stimuli seen during scanning (targets) randomly interspersed with an equal number of new words (distractors) divided equally into each stimulus category, and balanced for the same qualities as the targets. Subjects were asked to indicate which words they believe were presented during the scanning session using a 2AFC button press. Accuracy was measured for later analysis. Following the completion of this task, subjects were asked to rate a similarly counter-balanced subset of target words presented on a touch-screen monitor along a Likert-like scale using the subjective-assessment mannequin[37] according to emotional valence (strongly positive, neutral, or strongly negative, ranging in value from +3 to –3, respectively).

Image Acquisition

Imaging data were acquired with a research-dedicated Seimens Allegra Magnetron 3 Tesla head-dedicated MRI scanner). T1-weighted spoiled gradient (MP-RAGE) MRI whole brain anatomical scans (208 slices; 8 mm in-plane resolution, 0.8 mm slice thickness, contiguous slices) were acquired followed by T2-weighted turbo spin echo axial whole-brain images (3 mm slice thickness) to explore potential pathology. Finally, gradient echo planar imaging–blood-oxygen level dependent (EPI-BOLD) fMRI were acquired (repetition time: 2,000 milliseconds, time to echo: 30, 32 slices; 3 mm thickness; 1 mm gap) as an index of neuronal activity during the neuropsychological activation paradigm.

Image Processing and Data Analysis

Prior to statistical analysis, the first two volumes of each run were discarded to allow the magnetic resonance signal to reach steady state. The remaining images in each participant's time series were motion corrected using the Motion Correction using the FMRIB Linear Image Registration Tool (MCFLIRT) module of the Functional Magnetic Resonance Imaging of the Brain (FMRIB) Center's Software Library, v 3.3) package (available at www.fmrib.ox.ac.uk/

fsl). Images in the data series were then spatially smoothed with a three-dimensional Gaussian kernel (full width at half maximum: x 8 x 8 mm^3), and temporally filtered using a high-pass filter (320 seconds). The FMRIB Expert Analysis Tool (FEAT) module of the FMRIB Software Library package was used for these steps and later statistical analysis.

Customized square waveforms were generated for each individual. These waveforms were convolved with a double γ-hemodynamic response function. For each participant, we used FMRIB's Improved Linear Model (FILM), with local autocorrelation correction, to estimate the hemodynamic parameters for four explanatory variables (neutral, positive, negative, and threat) and generate statistical contrast maps of interest. The six movement parameters (ie, translation and rotation of x, y, and z axes) were modeled as covariates.

Each of the five runs for each participant was analyzed separately and the average of these five runs for each individual was obtained through a higher-level analysis using the FMRIB's Local Analysis of Mixed Effects (FLAME) module (stage 1 only). Contrast maps were warped into common stereotaxic space before mixed-effects group analyses were performed. The normalization procedure involved registering the average EPI image to the MP-RAGE image from the same participant, and then to the International Consortium for Brain Mapping 152 T1 template,[40] using the FMRIB's Linear Image Registration Tool (FLIRT) module.

To identify the regions of brain activation, we defined the regions of interest (ROI) by clusters of ≥30 contiguous voxels[41] in which there was significant difference in brain activity across conditions ($Z>2.81$, $P<.005$ two-tailed). Using the Mintun peak algorithm,[42] we further located the local peaks (maximal activation) within each ROI. Additional ROI analyses were performed using the average signals extracted from these clusters.

RESULTS

Word Valence Ratings

Analysis of the post-scan ratings of all stimulus words (positive, negative threat/non-threat, and neutral) confirmed our assignment of word stimuli to negative, neutral, or positive categories. Subjects rated negative, neutral, and positive words as significantly negative, neutral, and positive, respectively. Therefore, it is fair to assume that the emotional word categories employed in this study were reasonable probes of emotional linguistic-stimulus processing within the participating subject population.

Neuropsychiatric Activation Paradigm Findings (Reaction Time)

A two-way repeated measures analysis of variance of reaction times of the 2AFC word/non-word judgment task performed during scanning revealed significant valence by diagnosis interactions ($F=4.61$, $P<.01$). Further analysis of these differences revealed that while affective stimuli were associated with enhanced responsivity (positive word vs neutral words; $P<.01$, and negative word vs neutral word; $P<.01$) to the word/non-word judgment task in the non-depressed control subjects (no difference was found between the two affective word conditions; positive vs negative; not significant), those with PPD tended to take significantly longer to make word/non-word judgments during the positive word condition compared with negative ($P<.03$) and neutral ($P<.01$) word conditions (differences observed between negative and neutral word conditions were not significant). Therefore, not only was enhanced processing of negative stimuli not observed in our PPD subjects, as is regularly reported in the depression literature,[43,44] reaction times were increased in the positive word condition as compared to neutral word condition. That is, positive words seemingly had the effect of inhibiting responsivity in those with PPD.

Functional Imaging Findings of Hypothesized Regions

Orbital Frontal Cortex

Consistent with findings reported in the literature[45] demonstrating attenuated activity in posterior reported in the literature demonstrating diminished activity in posterior orbitofrontal cortex regions in general depression, we found that in the negative word conditions BOLD-related activity was also diminished in PPD (Figure 1). These decreases in frontal activity relative to non-depressed postpartum women can be interpreted in the context of emerging conceptualizations orbitofrontal cortex function in emotional inhibitory regulation[46-49] as well as emotion-influenced decision-making.[50-52] Indeed, postpartum depressed patients are prone to disadvantageous decision-making.[22]

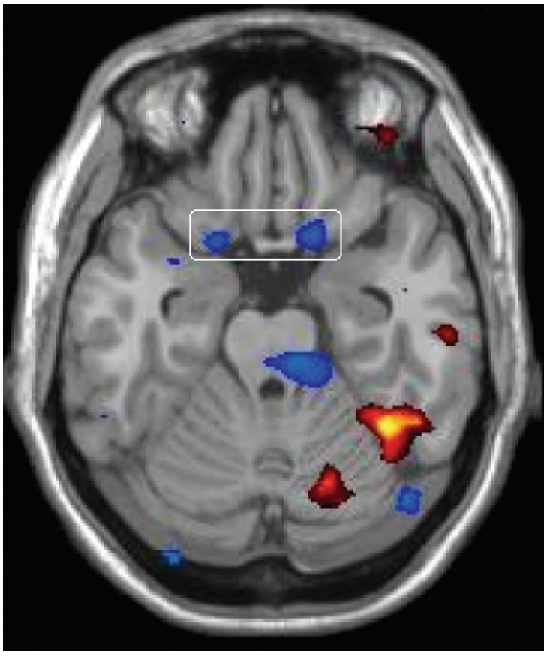
Amygdala

The amygdala has long been associated with emotional processing especially arousal.[53] It is known that glucose metabolism in the amygdala is abnormally elevated in depressives with familial pure depressive disease, bipolar II disorder and nonpsychotic bipolar I disorder.[54,55] This abnormality, however, was not found in more severe psychotic type bipolar disorder subjects or in major depressive disorder samples meeting Winokur criteria[56] for depression spectrum disease. The results from the present study demonstrate greater amygdala activity in response to negative words in non-depressed postpartum subjects compared with depressed subjects (Figure 2). That PPD subjects had significantly less activation to negatively valenced stimuli than did controls stands in contrast to a number of other imaging studies[57,58] of general depression and may point toward a specific phenotype of depressive function in PPD. The possibility that the absence of elevations in amygdala activity may be due to volume loss similar to that observed in first-episode bipolar disorder[59] and may occur within a neuroanatomical reduction of other limbic areas observed in the postpartum period, such as the hippocampus,[60] requires further exploration.

Insula

The insular cortex is regularly implicated in imaging studies of human emotion[61] as a key integration and relay center for heteromodal sensory, visceral, autonomic, and limbic information processing.[62] Comparing PPD with non-depressed postpartum subjects, we found increased BOLD activations in bilateral insula in contrasts of negative versus neutral emotion conditions and right greater than left insula BOLD activation in all emotion conditions collapsed versus neutral emotion conditions (Figure 3). These findings are particularly relevant to emerging neurocognitive models[63] implicating the insula in the neural circuitry of the subjective emotional experience of depression.

FIGURE 1.
Decreased activation to negative words in bilateral posterior OFC regions with increased PPD symptomatology (*P*<.05 uncorrected, for visualization)



OFC=orbitofrontal cortex; PPD=postpartum depression.

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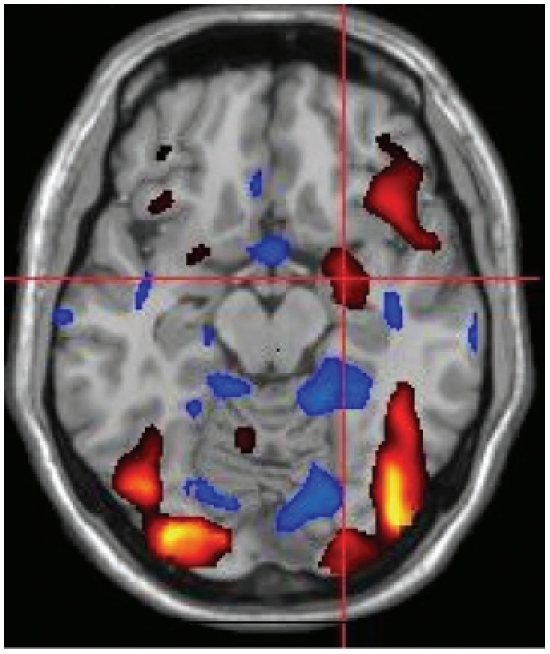
FIGURE 2.
Increased right amygdala activity in response to negative words in non-depressed postpartum subjects compared to depressed subjects (*P*<.05 uncorrected, for visualization)



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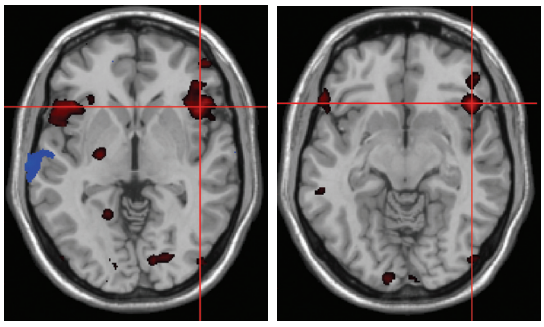
Striatum

In subjects diagnosed with major depression or bipolar disorder, cerebral blood flow and metabolism have been shown to be abnormally decreased in the caudate,[54,64] a region implicated in motivation and action.[41] While the phenomenology of depression consists of an accentuation of negative affective processing it also consists of an inability to experience pleasure or positive motivation. Consistent with this, a recent fMRI study[65] found that depressed patients demonstrated significantly less ventral striatum activation (an area implicated in reward/motivational processing) to positive stimuli. Notably, the findings from our study similarly demonstrate decreased BOLD striatal activation to positive stimuli in those diagnosed with PPD compared with non-depressed postpartum women (Figure 4). This observation of diminished striatum activity in those with PPD supports a pathophysiological model of PPD that includes reward/motivational pathway dysfunction, suggesting a possible neural substrate responsible for the phenomenological experience of diminished responses to positive extraneous stimuli, in general.

FIGURE 3.
Increased bilateral insula activity in those with PPD compared with non-depressed postpartum subjects in contrasts of negative emotion versus neutral emotion conditions (left), and right > left insula BOLD activation in all emotion conditions collapsed versus neutral emotion conditions (right; *P*<.05 uncorrected, for visualization)



PPD=postpartum depression; BOLD=blood-oxygen level dependent.

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Additional Functional Magnetic Resonance Imaging Data

Table 1 lists additional regions of differential BOLD activity observed during the emotional linguistic activation paradigm.

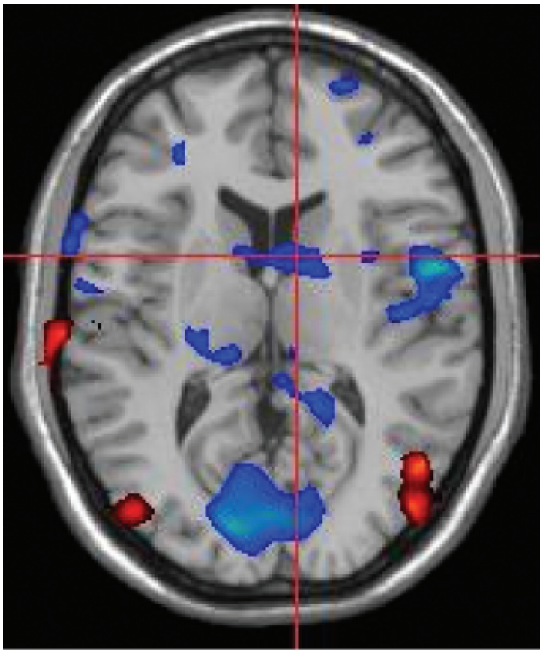
Memory

Incidental recognition memory for each of the three word types (positive, negative threat/non-threat, and neutral) is reported in Table 2. Notably, even though subjects were not informed of a post-scan recognition assessment prior to scanning, consistent with the literature on depression, PPD subjects demonstrated enhanced memory for stimulus words presented during the negative condition. Conversely, PPD participants also showed diminished incidental memory for positive words compared to non-depressed postpartum, control subjects.

DISCUSSION

The etiology of PPD, a potentially catastrophic complication of childbearing, is unclear. We

FIGURE 4.
Decreased striatum activation with increased PPD symptomatology to positive stimuli (*P*<.05 uncorrected, for visualization)



PPD=postpartum depression.

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believe this to be the first neuroimaging study specifically designed to identify neural activity changes in unmedicated postpartum depressed women carefully characterized as having no previous history of psychiatric symptomatology. The reported preliminary findings begin to shed light on the neural mechanisms responsible for mood dysregulation frequently observed in the postpartum period, extending previous reports of valence dissociations in fronto-limbic-striatal subregion response to emotional stimuli to a group of psychologically well-characterized female sub-

TABLE 1.
Other Selected Cortical Regions

Region	BA	Cluster size	x	y	z	Z value	Change
Negative Condition (correlation with EPDS)							
Fusiform	37	30	–42	–52	–22	2.82	Increase
Rolandic	48	45	–56	4	12	2.88	Decrease
Supramarginal gyrus	39	51	–48	–50	32	2.83	Decrease
Superior temporal gyrus	21	30	–56	0	–6	2.68	Decrease
Negative Condition (Non-depressed > depressed)							
Precentral gyrus	6	2,021	–36	–12	60	3.74	Increase
	6	192	44	0	28	3.11	Increase
	4	279	–54	0	40	3.21	Increase
Cingulate		405	–6	–4	52	3.47	Increase
Putamen		2,536	–26	–6	0	3.43	Increase
Inferior temproal gyrus	37	76	46	–68	–10	3.16	Increase
Pallidum		745	20	6	4	3.12	Increase
Fusiform	37	63	38	–54	–18	3.06	Increase
Insula	48	159	46	6	–2	3.01	Increase
Precuneous		2,489	0	–60	38	3.22	Decrease
DLPFC	9	156	26	34	48	2.91	Decrease
	9	62	–28	34	42	2.86	Decrease
Superior temporal gyrus	22	44	72	–18	2	2.87	Decrease
Frontal	10	105	–2	54	–4	2.84	Decrease
ACC			2	34	–6	2.67	Decrease
Positive Condition (Non-depressed > depressed)							
Precentral gyrus	6	247	–32	–10	62	3.58	Decrease
	6	99	–58	6	28	3.05	Decrease
	6	49	56	6	34	2.88	Decrease
Cingulate gyrus	24	550	–4	6	48	3.46	Increase
Parietal	40	57	–36	–48	42	3.17	Increase
Pallidum		133	–20	2	4	3.03	Increase
		85	–16	4	6	2.84	Increase
DLPFC	9	185	26	30	46	3.16	Decrease
Precentral gyrus	6	267	26	–18	72	3.04	Decrease

* $P<.01$; cluster size: >30

EPDS=Edinburgh Postnatal Depression Scale; BA=Brodmann area; DLPFC=dorsolateral prefrontal cortex; ACC=anterior cingulate cortex.

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jects studied during the postpartum period. This characterization of the systems-level neuropathophysiology of PPD, extends our understanding of the neurobiological spectrum of affective disorders in women across the lifecycle and provides a foundation for future investigations of the mechanisms involved in the dysregulation of emotion and behavior in PPD and the translational potential for informing development of more targeted therapies.

Despite the projects design and analysis, a primary limitation of this study is the small-sample, which inevitably results in less reliable estimates. Due to this limitation the results reported need to be considered preliminary and any firm conclusions must await additional recruitment and replication.

CONCLUSION

Accordingly, the neural mechanisms related to PPD observed thus far appear somewhat different than those of non-postpartum-related depression. For certain, differences among neuropsychiatric activation paradigms, depression subtypes (ie, bipolar vs unipolar, primary vs neurological), as well as the heterogeneous nature of clinical expression across individuals, are likely responsible for much of the variance reported across the literatures. Therefore, although it may be premature to conclude that PPD is a unique depression phenotype, these preliminary findings suggest the potential to identify an empirically based neural characterization of PPD that will provide a necessary cornerstone for developing more targeted, biologically based diagnostic and therapeutic strategies specific to mood changes as a consequence of reproductive health. ***CNS***

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TABLE 2.
Signal Detection Analysis of Incidental Encoding to Presented Valenced Stimuli During the Post-scanning Assessment of Recognition*

	Positive PPD	Positive Non-depressed	Negative PPD	Negative Non-depressed	Neutral PPD	Neutral Non-depressed
Hit	73.3%	77.4%	76.4%	69.8%	71.2%	71.2%
FA	31.9%	24.8%	22.2%	22.8%	31.8%	29.5%
A'	.794	.845	.852	.821	.782	.794
B'	–.05	–.03	.02	.09	–.03	.01
Acc	70.4%	76.3%	77.1%	72.9%	69.6%	70.8%

* This Table also shows that PPD subjects were less accurate at remembering words, except for those in the negative valence condition.

PPD=postpartum depression; Hit =correct identification; FA=false alarm (incorrectly reporting the recognition of a distractor); A'=sensitivity; B'=Bias; Acc=Accuracy (corrected).

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