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Emotional memory in pregnant women at risk for postpartum depression

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ABSTRACT

Postpartum depression (PPD) is associated with debilitating effects on mothers and their infants. A previous history of depression is considered the strongest risk factor for PPD. Depressed individuals recall more negative than positive content and higher levels of stress hormones released during encoding are associated with enhanced recall of emotional stimuli. This study examined the impact of a previous history of major depressive disorder (MDD) and pregnancy on emotional memory. Seventy-seven participants completed the study [44 pregnant women in the second trimester of pregnancy with and without a lifetime history of MDD and 33 non-pregnant women with and without a lifetime history of MDD]. All completed an encoding task and provided salivary cortisol (sCORT) and alpha-amylase (sAA) samples. Participants returned one week later for a surprise incidental recognition memory task. Women with a history of MDD had worse recognition than women without a history of MDD for negative, but not positive images; this effect was independent of sCORT and sAA levels. Pregnancy did not affect emotional memory. Considering that several previous studies found enhanced memory bias for negative content during depressive states, our results suggest that clinical remission may be associated with an opposite cognitive processing of negative emotional content.

1. Introduction

Postpartum depression (PPD) is a common and preventable disorder associated with a debilitating effect on mothers and their infants (Wisner et al., 2006). Women have approximately a 50% higher risk of developing depression postnatally than at any other time in their lives (Vesga-Lopez et al., 2008). Longitudinal studies have shown that children born to mothers who suffered from PPD may display elevated cortisol and noradrenaline levels, and developmental deficits in language, intelligence, and memory compared to children of non-depressed mothers (Cogill et al., 1986; Essex et al., 2002; Grace et al., 2003). Moreover, studies examining maternal depression and risk for child psychopathology have consistently found an association between mothers with recurrent depression and co-morbid psychiatric disorders including anxiety or alcohol abuse and heightened risk for future psychiatric illness in offspring (Sellers et al., 2012). A number of psychosocial and environmental risk factors for the mother developing PPD have been identified including poor marital and social support, major stressful life events, low self-esteem, anxiety and depression during pregnancy, and difficult temperament of the child (Milgrom et al., 2008; O'Hara, 2009). In addition, previous history of MDD, especially depression during pregnancy, is considered the strongest risk factor for PPD (Heron et al., 2004; Milgrom et al., 2008). PPD is estimated to affect between 7% and 15% of women in the general population (Gaynes et al., 2005), but this rate increases to 25% among women with previous postpartum episodes, putting pregnant women with a history of MDD at significantly greater risk for PPD (Cooper and Murray, 1995; Wisner et al., 2002; Wisner et al., 2004). Despite increasing awareness of PPD and its debilitating effects on both mother and child, its neurobiology remains unclear.

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1.1. Emotional memory in depression

In humans, emotional information is better remembered than non-emotional information, likely because stimuli that evoke positive or negative emotional and physiological arousal are more crucial and relevant to human survival than neutral stimuli (Pratto and John, 1991). It is well established that individuals with MDD display emotion-related cognitive biases in attention and memory. For instance, depressed individuals have difficulty inhibiting or disengaging attention from negatively valenced information (De Raedt and Koster, 2010; Gotlib and Joormann, 2010) and display better memory for negative than positive content (Watkins et al., 1992; Bradley et al., 1995). In contrast, healthy controls display enhanced memory for positive relative to negative content (Bradley et al., 1995). This mood-congruent memory bias is theorized by some to be a maladaptive cognitive schema that contributes to depressive states (Hasler et al., 2004; Kovacs and Beck, 1978; Ridout et al., 2003; Watkins et al., 1992). Hamilton and Gotlib (2008) examined the neural correlates of enhanced emotional recall for negative content in individuals with MDD. They found that individuals with acute depression displayed a greater memory bias than healthy controls for negative images, but not for positive or neutral images. Enhanced memory for negative images at retrieval was associated with greater amygdalar activation at encoding. In contrast, individuals with no lifetime history of depression recalled positive images more accurately than the negative images (Hamilton and Gotlib, 2008). These results suggest that there is greater activation of the amygdala for content that is emotionally arousing, but not for neutral content, and that this memory effect is selective for individuals with depression when encoding negative content (Hamilton and Gotlib, 2008).

The majority of previous studies on memory biases have investigated individuals who were currently depressed or individuals with remitted depression using a sad mood induction. Less is known about memory biases in individuals with a history of depression who are currently euthymic as previous studies have produced inconsistent results. While some studies have failed to find any differences in memory retrieval of negative content between remitted individuals and healthy controls (Arnold et al., 2011; Gotlib and Cane, 1987; Teasdale and Dent, 1987; Wilkinson and Blackburn, 1981), some studies have found a memory bias for negative content in remitted individuals compared to healthy controls, but only following a sad mood induction (for review see Scher et al., 2005). More recently, Romero et al. (2014) have found that euthymic individuals with a history of MDD displayed increased recall of negative self-referent adjectives and decreased recall of positive self-referent adjectives compared to individuals with no lifetime history of MDD on an incidental recall task.

Using functional magnetic resonance imaging (fMRI), Arnold et al. (2011) provided evidence for a neural bias during encoding of positive words in euthymic individuals with remitted depression. They presented remitted MDD participants and healthy controls with positive, neutral, and negative words in a scanner and subsequently tested their memory for these emotional words using a free recall test. Results showed that there were no differences between healthy controls and remitted individuals in memory performance or neural processing during successful encoding of negative or neutral words. They only found group differences in neural processing during successful encoding and memory for positive words; remitted individuals over-recruited brain regions known to be involved in enhancing emotional memory, including the cingulate gyrus, right inferior- and left-medial-frontal gyrus as well as the right anterior hippocampus/amygdala. The results of this study indicate the presence of a processing bias for positive content and an absence of valence-specific memory biases in currently euthymic MDD individuals. This is in contrast to previous findings of reduced memory for positive content in remitted individuals (Teasdale and Dent, 1987).

Evidence from animal studies suggest that glucocorticoids facilitate memory enhancement of emotional information along with endogenous noradrenergic activation in the basolateral nucleus of the amygdala (BLA) in response to arousing emotional events (Roozendaal, 2000). The amygdala appears to mediate glucocorticoid effects on memory consolidation of emotional experiences via interactions with the hippocampus, which is dense with glucocorticoid receptors (Roozendaal, 2000). In humans, a study by Segal and Cahill (2009) showed that higher levels of salivary adrenergic and glucocorticoid release during encoding of an emotional memory task was correlated with enhanced memory for emotional stimuli at retrieval compared to non-emotional stimuli.

1.2. Memory during pregnancy

Although pregnant women often report memory difficulties including forgetfulness, absentmindedness, difficulty concentrating, and decreased attention (Sharp et al., 1993), empirical studies have yielded inconsistent results. Contrary to this common perception, past research has shown that cognitive performance in the domain of recognition (Mickes et al., 2009) and word list learning (Silber et al., 1990) was actually enhanced during pregnancy. A study investigating recognition for emotional faces in early (7–14 weeks) and late gestation (33–39 weeks) found that pregnant women in late gestation had an enhanced ability to recognize facial expressions displaying fear, disgust, and anger compared to women in early gestation, but no change in the ability to recognize sad or happy facial expressions (Pearson et al., 2009). Overall, studies suggest that there are less objective memory deficits during pregnancy than what is subjectively reported by pregnant women (Crawley, 2002; Crawley et al., 2008). In addition, previous studies that examined the possibility that cortisol, low mood or increased anxiety may account for the memory difficulties reported in pregnancy have not found much evidence to support this theory (Buckwalter et al., 1999).

1.3. Objectives and hypotheses

To the best of our knowledge, no studies have investigated emotional memory in pregnant women at increased risk for PPD (e.g., those with a history of MDD). Thus, the main objectives of the present study were to (1) compare emotional memory between euthymic pregnant women with a history of MDD and pregnant women considered to be at lower risk (those with no lifetime history of MDD), and (2) determine the relation between salivary cortisol (sCORT) and salivary alpha-amylase (sAA) and emotional memory performance in pregnant women. To control for potential pregnancy effects on emotional memory, a group of non-pregnant women with and without a lifetime history of MDD were also recruited. We hypothesized that women with a history of MDD would exhibit enhanced memory for negative stimuli as compared to women with no lifetime history of MDD. We also hypothesized that memory for negative images would significantly correlate with increased sCORT and sAA levels in women with a history of MDD. Based on the above literature (Crawley, 2002; Crawley et al., 2008), we predicted that pregnancy itself would not affect emotional memory performance.

2. Method

2.1. Sample

Eighty-six women were recruited through the Women's Health Concerns Clinic (WHCC) at St. Joseph's Healthcare Hamilton, the Community Midwives Clinic and local advertisements in Hamilton, Ontario, Canada. All participants gave written informed consent and the study was approved by St. Joseph's Healthcare Hamilton Research Ethics Board in accordance with the Declaration of Helsinki.

Inclusion criteria for individuals with a past history of MDD included: (1) lifetime history of Major Depressive Disorder and (2) being currently euthymic according to the Structured Clinical Interview for the Diagnostic and Statistical Manual for Mental Disorders Research Version (SCID-I/P) (First et al., 2002). Participants were excluded if they met current criteria for any other Axis I disorder according to the (SCID-I/P). Additional exclusion criteria included: (1) presence of any neurological disease; (2) history of head trauma with loss of consciousness for more than five minutes; (3) estimated IQ less than 70; (4) unstable medical condition; (5) history of any anxiety disorder in the past six months; (6) history of lifetime alcohol or substance dependence, or alcohol or substance abuse in the last 6 months; (7) Edinburgh Postnatal Depression Scale (EPDS) scores greater than 12. Of the individuals initially enrolled in the study, 4 were deemed not eligible after administering the SCID-I/P and meeting lifetime criteria for an eating disorder and/or current criteria for Generalized Anxiety Disorder (GAD). Therefore, a total of 77 participants between the ages of 18–44 (mean age: 27.3 ± 6.2 yo) successfully completed the study. This included 14 pregnant women with a history of MDD, 13 non-pregnant women with a history of MDD, 30 pregnant women with no lifetime depression, and 20 non-pregnant women with no lifetime depression. Pregnant participants were studied in the second trimester (between 12 and 22 weeks gestation) as this period is associated with the least reported physical discomfort and pain complaints and less sleep disturbance, which are known to negatively impact memory (Orff and Parry, 2013). Given that the presence of depressive symptoms is also associated with impaired memory, all women with a diagnosis of MDD had to be euthymic for at least 3 months prior to study participation. All non-pregnant women had regular menstrual cycles and were tested during the follicular phase of the menstrual cycle to avoid potential influence of premenstrual symptoms on emotional memory (Ertman et al., 2011). Non-pregnant participants were not taking any hormonal agents for the entire duration of the study as oral contraceptives have been shown to wash out the influence of cortisol on memory retrieval (Kuhlmann and Wolf, 2005). All participants were free from psychotropic medications, except for 4 participants (2 pregnant with MDD and 2 non-pregnant with MDD) who were taking antidepressants (Escitalopram or Venlafaxine) at the time of the study. All study participants had an estimated Intelligence Quotient (IQ) of 70 or greater.

2.2. Measures

The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/P) (First et al., 2002) was used to evaluate psychiatric diagnosis. Current depressive symptoms were assessed in the pregnant participants with the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987). Current depressive symptoms in the non-pregnant subjects were assessed with the Montgomery–Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979). The State-Trait Anxiety Index (STAI) (Spielberger and Lushene, 1970) was administered to measure current anxiety symptoms. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The Postpartum Depression Predictors Inventory-Revised (PDPI-R) (Beck, 2002) was used to determine risk factors present during the second trimester (12–22 weeks of GA) in the pregnant sample. The PDPI-R assesses risk factors that have been consistently reported as predictors of PPD (Beck, 2002). Baseline intellectual capacity (estimated IQ) was assessed with two sub-scales of the Wechsler Abbreviated Scale of Intelligence (WASI): vocabulary (i.e., word knowledge, verbal concept formation) and matrix reasoning performance (i.e., visual information processing, abstract reasoning skills) (Psychological Corporation, 1999).

2.2.1. Emotional memory task

Incidental encoding and recognition memory tasks included images selected from the International Affective Picture System (IAPS) (Lang et al., 1997), which are divided into positive, neutral, and negative categories based on normative valence ("the positive or negative nature of a stimulus") and arousal ("the stimulating or calming nature of a stimulus") (Mickley Steinmetz et al., 2010). Positive pictures had a mean normed valence of 7.53 with a range between 6.56 and 8.59, and a mean normed arousal of 5.28; neutral pictures had a mean normed valence of 5.17 with a range between 4.53 and 5.76, and a mean normed arousal equal to 3.42; negative pictures had a mean normed valence of 2.66 with a range between 1.29 and 4.23, and a mean normed arousal of 5.65. As the current study sample included members of potentially vulnerable populations (i.e., pregnant women and women with a history of depression), images were chosen with caution so as to not cause undue distress or mental anguish. The incidental tasks were adapted from a similar methodology used by Canli et al. (2000) and more recently by Hamilton and Gotlib (2008). Stimulus presentation, timing, and recording of behavioral data during the incidental tasks were generated by an ASUS K53SV laptop with $37.8 \times 25.3 \times 2.83$ cm^3 dimensions and 15.6 in. display. The incidental tasks were coded using E-prime v1.2 software and administered according to Van Stegeren et al. (2005).

2.2.2. Salivary cortisol and alpha-amylase

Sorbettes (Salimetrics LLC, State College, PA, USA) were used to collect the sCORT and sAA saliva samples. The fraction of free cortisol was measured by an expanded range high sensitivity salivary cortisol enzyme immunoassay kit and alpha-amylase concentrations were determined using a kinetic enzyme assay kit, both with proven reliability and validity (Salimetrics LLC, State College, PA, USA).

2.3. Study visits

In the first session, consent was obtained and participants were assessed using the SCID-I/P (First et al., 2002) by a certified psychiatrist (BNF) or trained graduate student (MEW). Participants completed self-report questionnaires (EPDS and STAI) and were professionally administered diagnostic depression and sleep quality questionnaires (MADRS, PDPI-R, PSQI). The WASI was then administered by a trained graduate student (MEW). Cortisol and alpha-amylase in saliva were collected at four different times during the first visit: 10 min before the incidental encoding task (time −1), immediately before the task (time 0), immediately after the task (time 1), and 10 min after the task (time 2). Participants were asked to refrain from consuming caffeine or alcohol, or participating in cardiovascular exercise 24 h prior to both study visits to control for diurnal hormonal variations (Segal and Cahill, 2009; Walsh et al., 1999). Testing was conducted between the hours of 10:00 and 19:00. At each time point, a saliva sample was collected by inserting a Sorbette under the participant's tongue, which is the best placement for simultaneous collection of alpha-amylase and cortisol (Salimetrics LLC, State College, PA, USA), for a minimum of 90 s. After the first saliva sample was collected, participants were shown instructions on screen and completed a practice run before beginning the incidental encoding task. Immediately after the second saliva sample, the encoding task began. Participants viewed a total of 144 images in random order, consisting of 48 neutral pictures, 48 negative pictures, and 48 positive pictures. A fixation cross was shown on screen for 500 ms before each image, which participants were instructed to focus on. Each picture was presented for 3000 ms. Participants were instructed to view each picture for the entire time that it was on the screen. After the presentation of each picture, participants were asked on screen to indicate their perception of emotional intensity of the picture on a 7-point likert scale where 1 represented "not emotional at all" and 7 represented "extremely emotional". Immediately after completing the encoding task, the third saliva sample was collected, then after 10 min the final saliva sample was collected. All saliva samples were frozen at −80 °C within two hours after collection until assayed. Participants were not aware at any time during the first visit that their memory would be assessed in the subsequent week. Rather, they were told that they would return the following week to perform "a similar task". Participants returned one week later for the second session and once again completed the EPDS, MADRS, STAI, and PSQI questionnaires. Then, participants then took part in an incidental recognition memory task (Segal and Cahill, 2009) where they viewed a total of 216 images, which included the 144 original images shown during the first session, and 72 foil pictures (24 pictures for each valence category) that were not previously shown. Foil pictures were matched for average valence and arousal to the original 144 images. Participants viewed each image and were then asked on screen to indicate whether they had seen the picture previously by pressing one of three buttons. Participants were instructed to press the number "1" key if they had not seen the picture before, the number "2" key if the picture looks familiar, but they are not sure, or the number "3" key if they are sure they had seen the picture before. Participants were debriefed on the purpose of the task and asked if they had any further questions following completion of the task.

2.4. Data analysis

Statistical analyses were performed using the Statistical Package for Social Sciences version 21.0 for Windows (IBM Corp., Armonk, NY, USA). Differences between groups in age, education, intellectual capacity (IQ score from WASI), and weeks of GA were analyzed using a one-way analysis of variance (ANOVA). Since number of previous MDEs, for those with a history of depression, was not normally distributed, a Kruskal–Wallis non-parametric test was used. Mean emotional intensity ratings were calculated for each participant group for each of the three valence categories. A multivariate general linear model included intensity ratings with participant group (pregnancy status or MDD history) as the between-subjects factor and intensity ratings as a function of valence (negative, neutral, positive) as the within-subjects factor. Here, "pregnancy status" refers to whether participants are pregnant or non-pregnant and "MDD history" refers to whether participants have a history of MDD or no history of MDD. A main effect of group (pregnancy status or MDD history) and their interaction (pregnancy status by MDD history)

was analyzed. Age and total number of educational years were included as covariates in the model. For the incidental recognition memory task, "Hits" were counted as the number of correctly identified original pictures rated as 2 ("familiar") or 3 ("with certainty") for each valence category. "False alarms" were counted as incorrectly recognizing a foil picture as having been shown during the first session (assigning a rating of "2" or "3"). Hit and False Alarm rates were calculated for each individual participant by dividing the number of hits and false alarms, respectively, by the total number of "2" and "3" responses for each category of emotional valence (Hamilton and Gotlib, 2008). These rates were then used to calculate the sensitivity indexes (d′). Valence specific sensitivity indexes (positive and negative) were calculated by dividing the d′ for positive and d′ for negative information by the d′ for neutral information, respectively, to control for variance explained by decreased overall memory in depressed individuals compared to non-depressed individuals (Burt et al., 1995). A multivariate general linear model included these resultant memory sensitivity indexes and d′ for neutral information with participant group (pregnancy status or MDD history) as the between-subjects factor and valence (positive, neutral, negative) as the within-subjects factor. A main effect of group (pregnancy status or MDD history) and the group interaction (pregnancy status by MDD history) was examined. Age, total number of years of education, and area under the cortisol curve (AUC_G), which is the plot of cortisol versus time, were included as covariates in the model. Significance of post hoc comparisons between groups was calculated with the Bonferroni correction. All tests were based on a 95% confidence interval corresponding to an α of 0.05 to indicate statistical significance. Area under the curve with respect to ground (AUC_G) was used to incorporate the four time points of hormonal collection and detect individual and group changes in sCORT and sAA over time (Pruessner et al., 2003). Total release (AUCG) was calculated from the four sCORT and four sAA measures using 10 min (between time −1 and time 0, between time +1 and time +2) and 30 min intervals (between time 0 and time +1) between measurements. The interval between measurements at time 0 and time +1 was 30 min as this was the duration of the incidental encoding task. The formula used to calculate AUC_G for each individual participant is as follows:

$$AUC_G = (m_2 + m_1)*t_1/2 + (m_3 + m_2)*t_2/2 + (m_4 + m_3)*t_3/2$$

With t_1–t_3 denoting the time intervals between the single measurements and m_1–m_4 representing the single measurements. The relation between total salivary free cortisol and alpha-amylase secretion (AUC_G) and subsequent recognition memory was estimated using multiple linear regression. For each participant group, recognition memory for negative images was the dependent variable and education, age, intellectual capacity (IQ score on WASI), and all original AUC_G values for cortisol and alpha-amylase were included as predictors in the model.

3. Results

3.1. Demographic and clinical characteristics

Demographic and clinical characteristics are shown in Table 1. The four groups did not differ with respect to intellectual capacity (IQ score) ($F(3,74)=1.0$, $p=0.40$). A Kruskal–Wallis test showed that there was no statistically significant difference in previous number of MDEs between the pregnant with a history of MDD group and the non-pregnant with a history of MDD group $\chi^2(1)=0.02$, $p=0.89$, with a mean rank of 13.68 for the pregnant with a previous history of MDD group and 13.29 for the pregnant with no lifetime history of MDD group. However, there were significant differences between groups on age ($F(3,76)=6.97$, $p<0.001$) and total number of years of education ($F(3,76)=5.68$, $p=0.002$). A post hoc Bonferroni test revealed that the non-pregnant with no lifetime history of MDD group was younger and had fewer years of education completed than the pregnant with a history of MDD ($p=0.001$) and the pregnant with no lifetime history of MDD ($p=0.002$) groups. Thus, age and education were included as covariates in all statistical analyses. There were significant differences between groups on STAI state ($F(3, 76)=6.71$, $p<0.0001$) and STAI trait ($F(3,76)=5.80$, $p=0.001$) scores, but not on PSQI ($F(3,76)=0.97$, $p=0.41$) or MADRS ($F(3,76)=2.02$, $p=0.12$) scores. A post hoc Bonferroni test revealed that the non-pregnant with a history of MDD had higher STAI state scores than non-pregnant with no lifetime history of MDD ($p=0.045$) and pregnant with no lifetime history of MDD ($p<0.0001$) groups. Similarly, the non-pregnant with a history of MDD group had higher STAI trait scores than the pregnant with no lifetime history of MDD group ($p=0.001$).

Table 1
Demographic and clinical characteristics of participant groups.

Variable	Group				
	Pregnant and history of MDD	Non-pregnant and history of MDD	Pregnant healthy	Non-pregnant healthy	*p* Value
Age, years	31 (4.4)	27 (7.6)	29 (4.2)	23 (6.9)	0.001[***a,b]
Education, years	17.3 (3.5)	16.4 (3.5)	16.9 (3.1)	13.5 (2.7)	0.006[**,a] 0.003[**,b]
Gestational age, weeks	18.4 (2.9)	N/A	17.6 (2.5)	N/A	0.94
Number of MDEs	2.9 (5.0)	2.8 (4.0)	N/A	N/A	0.89
EPDS	5.0 (2.7)	N/A	2.56 (2.1)	N/A	0.02[*,e]
MADRS	3.4 (2.7)	4.1 (4.3)	2.45 (1.9)	2.0 (2.4)	0.12
STAI, state score	27.8 (5.5)	32.7 (7.6)	25.1 (3.2)	27.7 (5.1)	0.001[***,c] 0.04[*d]
STAI, trait score	35.3 (6.3)	38.3 (9.2)	30.5 (3.4)	32.8 (6.2)	0.001[**,c]
PSQI Global score	4.4 (2.8)	5.7 ± 3.7	4.6 (2.2)	4.2 (1.9)	0.41
IQ score, WASI	114.6 (7.4)	109.9 (16.1)	111.2 (11.6)	107.7 (13.7)	0.40

EPDS = Edinburgh Postnatal Depression Scale; MADRS = Montgomery-Asberg Depression Rating Scale; PSQI = Pittsburgh Sleep Quality Index; STAI = State-Trait Anxiety Inventory; WASI = Wechsler Adult Intelligence Scale.
Mean differences are reported with standard deviations in parentheses.

[*] The mean difference is significant at the 0.05 level.
[**] The mean difference is significant at the 0.01 level.
[***] The mean difference is significant at the 0.001 level.
[a] Difference between pregnant with a history of MDD and non-pregnant healthy groups is significant.
[b] Difference between pregnant healthy and non-pregnant healthy groups is significant.
[c] Difference between pregnant healthy and non-pregnant with a history of MDD groups is significant.
[d] Difference between non-pregnant with a history of MDD and non-pregnant healthy groups is significant.
[e] Difference between pregnant with a history of MDD and pregnant healthy groups 12–22 weeks of gestational age is significant.

3.2. Emotional intensity ratings

The mean intensity ratings for emotional valence categories across all participant groups are displayed in Fig. 1a. A multivariate analysis of covariance (MANCOVA) revealed that the main effect of pregnancy status was not significant; pregnant and non-pregnant groups did not differ on intensity ratings for negative ($F(1,71)=0.17$, $p=0.68$, $d=0.24$), neutral ($F(1,71)=0.16$, $p=0.70$, $d=0.25$) or positive ($F(1,71)=0.01$, $p=0.91$, $d=0.34$) images. There was a significant interaction between pregnancy status and MDD history on emotional ratings for negative ($F(1,71)=4.52$, $p=0.04$, $d=0.24$) and positive ($F(1,71)=8.68$, $p=0.004$, $d=0.34$), but not neutral ($F(1,71)=0.83$, $p=0.37$, $d=0.25$) images. In pregnant women, having a previous history of MDD was associated with higher intensity ratings for negative and positive images. In non-pregnant women, history of MDD was associated with lower intensity ratings for these same emotional categories of images. Observed effect sizes for the analysis of emotional intensity ratings were found to be small.

3.3. Memory sensitivity (d′)

The mean normalized memory sensitivity indexes (d′) for emotional valence categories across all groups are shown in Fig. 1b–d. A MANCOVA revealed that the main effect of pregnancy status was not significant; pregnant and non-pregnant groups did not differ in recognition memory for negative ($F(1,71)=1.02$,

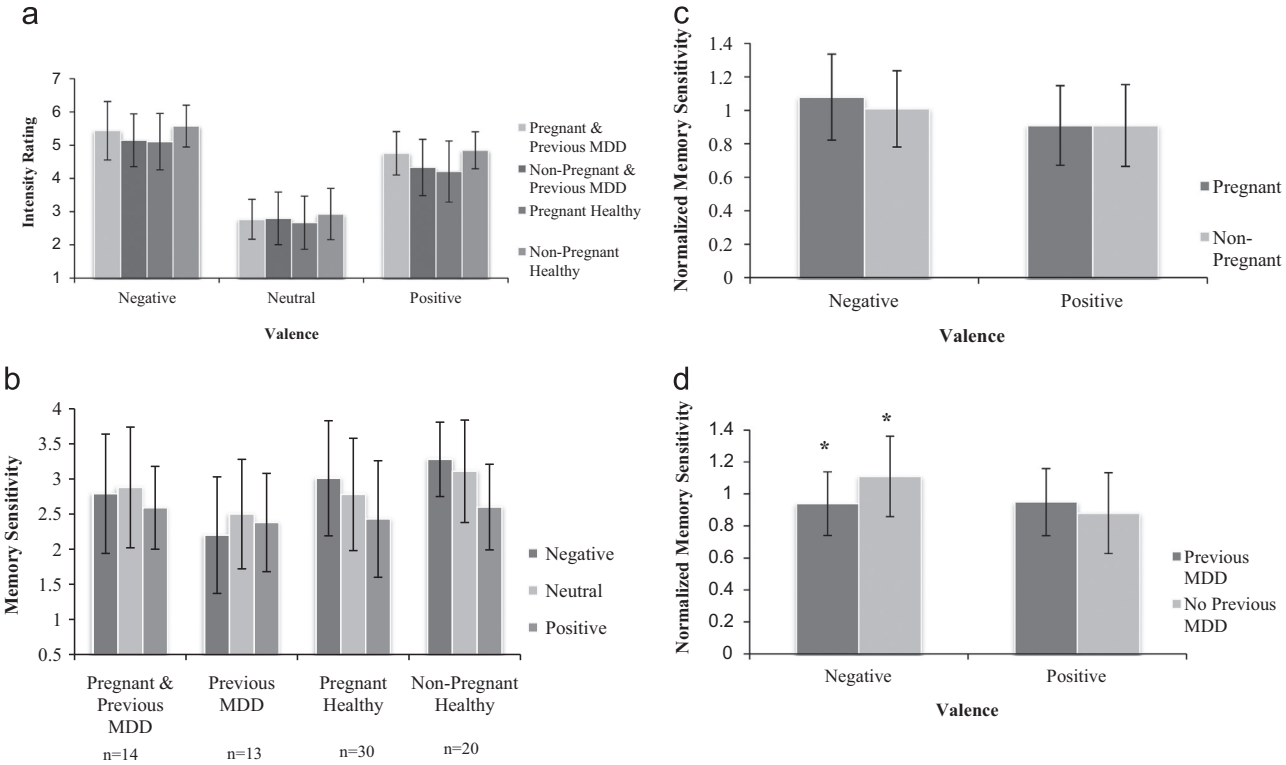

Fig. 1. (a) Mean intensity ratings for emotional valence categories across all participant groups. (b) Mean memory sensitivity indexes (d′) and standard deviations for emotional valence categories across all participant groups. (c) Mean normalized memory sensitivity scores and standard deviations for emotional valence categories across pregnant ($N=44$) and non-pregnant ($N=33$) participant groups. (d) Mean normalized memory sensitivity scores and standard deviations for emotional valence categories across participants with ($N=27$) and without ($N=50$) a history of MDD. *The mean difference is significant at the 0.05 level.

$p=0.32$, $d=-0.29$), neutral ($F(1,71)=0.98$, $p=0.33$, $d=0.07$), or positive ($F(1,71)=0.002$, $p=0.96$, $d=0.04$) images. However, there was a main effect of MDD history: women with a history of MDD had worse recognition memory than women without a history of MDD for negative ($F(1,71)=8.04$, $p=0.01$, $d=0.80$), but not neutral ($F(1,71)=0.67$, $p=0.42$, $d=0.26$) or positive ($F(1,71)=2.40$, $p=0.13$, $d=-0.35$) images. The observed effect size for this analysis ($d=0.80$) was found to be large despite the smaller sample size. In contrast, there was no difference in emotional memory between pregnant women with a history of MDD and pregnant women without a history for negative ($F(1,42)=2.63$, $p=0.11$, $d=-0.47$), neutral ($F(1,42)=0.06$, $p=0.81$, $d=0.12$) or positive ($F(1,42)=0.17$, $p=0.69$, $d=0.14$) images. The interaction between pregnancy status and MDD history on recognition memory was not significant for negative ($F(1,71)=0.33$, $p=0.57$, $d=-0.29$), neutral ($F(1,71)=2.86$, $p=0.10$, $d=0.07$) or positive ($F(1,71)=1.04$, $p=0.31$, $d=0.00$) images.

3.4. Salivary cortisol and alpha-amylase

Of the 77 participants, data were missing due to insufficient saliva collection in two (2.5%) participants. The relation between recognition memory for negative images and salivary hormones (cortisol and alpha-amylase AUCG) was estimated using multiple linear regression. Recognition memory for negative images was not predicted by area under the cortisol curve (AUC_G), $b=0.05$, t (0.42), $p=0.67$ or area under the alpha-amylase curve (AUC_G), $b=-0.03$, t(-0.22), $p=0.82$. In this model, a history of MDD significantly predicted worse recognition memory for negative images, $b=-0.31$, $t(-2.57)$, $p=0.01$; MDD history explained 13% of variance in recognition memory for the negative stimuli, $R^2=0.13$, $F(6,67)=1.61$, $p=0.01$. These results suggest that the association between history of MDD and worse memory for negative stimuli is independent of sCORT and sAA.

4. Discussion

This is the first study to investigate emotional memory in pregnant women with and without a history of MDD. Contrary to our primary hypothesis, we found that women with a history of MDD displayed worse recognition memory for negative images compared to women with no history of MDD, with no differences in recognition memory for positive images. Therefore, past history of MDD predicted a selective impairment in recognition memory for negative images. Previous research examining memory biases during remission have been inconsistent, with some studies reporting no differences between remitted individuals and healthy controls with no lifetime history of depression on memory retrieval for negative content (Gotlib and Cane, 1987; Teasdale and Dent, 1987; Wilkinson and Blackburn, 1981), and other studies reporting a memory bias for negative content in remitted individuals compared to healthy controls, but only following a sad mood induction (Scher et al., 2005). Our finding is supported by a recent neuroimaging study reporting no valence-specific memory biases in currently euthymic MDD individuals (Arnold et al., 2011). A potential explanation for our finding may be that the previously depressed individuals blocked or supressed negative content during the encoding task before it triggered a negative mood state, which would lead to less memory for negative images. Whether this cognitive profile protects against future relapse in these individuals is unknown (Lethbridge and Allen, 2008; Preiss et al., 2009). It is also possible that the negative images selected from the IAPS were below the threshold for valence (pleasant to unpleasant) and/or arousal (calm to excited) to elicit negative emotion and therefore, may have reduced the impact of the negative stimuli. As the current study sample included members of potentially vulnerable populations (i.e., pregnant women and women with a history of depression), negative images were selected

with caution so as to not cause undue distress or mental anguish and this may have affected the results.

We also found that pregnant and non-pregnant women did not differ in recognition memory for negative and positive images. Moreover, there were no differences in recognition memory between pregnant women with a history of MDD and pregnant women without a lifetime history. Previous studies investigating memory performance during pregnancy have primarily studied healthy (e.g., no history of depression) pregnant women in the third trimester, with very few studies to date investigating emotional memory in the second trimester. A recent study by Farrar et al. (2014) compared cognitive function in pregnant women during each trimester of pregnancy and non-pregnant women using the Cambridge Neuropsychological Automated Test Battery (CANTAB) and found that the pregnant group scored significantly lower than the non-pregnant group only on the Spatial Recognition Memory (SRM) test during the second trimester. Overall, most studies have shown that although pregnant women frequently report more memory difficulties than non-pregnant women (Brindle et al., 1991; Crawley et al., 2008; Sharp et al., 1993), this is not observed with objective cognitive testing (Logan et al., 2014). As predicted, our finding suggests that pregnancy does not influence emotional memory. This finding is supported by previous studies showing that recognition performance is normal or sometimes enhanced during pregnancy (Mickes et al., 2009; Pearson et al., 2009; Sharp et al., 1993). However, it is worth noting that these previous studies were conducted in the third trimester of pregnancy, when cortisol levels are higher and pain, physical discomfort, and sleep disturbances are more common.

We found no relation between sCORT and sAA during encoding and subsequent recognition memory in any of the study groups. Moreover, memory for negative images did not correlate with sCORT or sAA levels in pregnant women with a history of MDD and pregnant women with no lifetime history of MDD groups. This finding is contrary to previous studies showing that elevated levels of sCORT and sAA during incidental encoding are associated with enhanced memory for emotional content (Buchanan and Lovallo, 2001; Segal and Cahill, 2009) and suggests that the memory impairment of negative images in women with a history of MDD is independent of sCORT and sAA. It is conceivable that the physiological rise in cortisol during pregnancy could have caused a ceiling effect.

4.1. Limitations

Some limitations must be considered when interpreting the results of our study. First, a large number of pregnant participants in the study ($N=34$, or 51% of the total sample size) were recruited from a community midwives clinic. Women who choose midwifery care may be qualitatively different than women treated in tertiary obstetric care centers, leading to a more homogenous sample. Second, the non-pregnant healthy group was significantly younger and also had fewer years of education compared to the other three groups. To control for this, age and total number of years of education were included as covariates in all statistical models. Third, non-pregnant participants verbally reported having regular menstrual cycles and being in the follicular phase of their cycle at the time of study participation. We did not measure hormone levels to confirm this; however, we believe that not confirming menstrual cycle phase by objective measures is unlikely to have affected memory recall overall. In fact, we think knowing the approximate menstrual cycle phase may be one of the strengths of our study since most previous studies do not account/control for this, even though menstrual cycle phase is known to affect memory performance. Finally, the relatively small sample size per group may have limited our statistical power. However, our sample size is very much comparable with recent studies looking at hormones, MDD and emotional memory (e.g., Cahill et al., 2003; Hamilton and Gotlib, 2008).

4.2. Future directions

Future longitudinal studies are needed to establish whether the selective impairment in memory recognition for negative images is associated with differential risk for PPD in pregnant women with a history of MDD. Future studies should also aim to identify a reliable biological marker for PPD. In this context, two independent fMRI studies have found that women with PPD have blunted activation of the amygdala in response to negative emotional stimuli (Moses-Kolko et al., 2010; Silverman et al., 2011), which is the opposite of what has been widely found in non-postpartum depressed samples. The finding that women with PPD have a blunted affect to negative stimuli provides important insight into the potentially different neurophysiologic mechanisms responsible for depression in the postpartum period. It is, therefore, conceivable that such neurobiological differences may explain why we found a decreased, as opposed to increased negative memory bias in pregnant women with a history of MDD.

4.3. Conclusion

Our results show that a previous history of MDD selectively impaired the recognition memory of negative images, which was independent of salivary cortisol and alpha-amylase. This study provides a basis for future investigation of neuroanatomical abnormalities associated with dysregulated emotion from pregnancy to the postpartum period, which may help to characterize the brain correlates of the development of PPD.

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