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Neural responses to monetary incentives in postpartum women affected by baby blues

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ABSTRACT

Up to 50% of new mothers experience baby blues (BB) within a week of delivery, with affective disturbances being the central symptoms. Because reward processing is known to be affected in depression, this study sought to investigate whether incentive processing during the experience of BB can be altered through the monetary incentive delay (MID) task. The MID task allows reward processing to be investigated based on responses to 'anticipation' and 'feedback of reward or loss'. 60 women participated in the fMRI-based MID task within 1–6 days of delivery, and 50% of them developed BB within the first few postpartum weeks. Over a 12-week observation period, a greater number of women in the BB group (52% vs. 13%) developed psychiatric conditions, with 24% of women with BB developing postpartum depression compared to only 3% of those without BB. During the feedback trials of the MID task, women with BB, compared to those without, showed increased activation in both the winning and losing trials (the temporal areas, the insula, the midbrain, and the inferior frontal gyrus). During the anticipation trials, however, subjects affected by BB showed reduced activation in the pregenual and the subgenual anterior cingulate cortices (pg/sg ACC). Our results demonstrate, for the first time, that the BB-related time window overlaps with alterations in the brain networks associated with incentive processing. Given the involvement of pg/sgACC in the development of depressive mood, the weaker involvement of these brain regions during anticipation in participants affected by BB is of particular interest.

1. Introduction

During pregnancy, sex hormones (e.g., estradiol and progesterone) rise to unprecedented levels before dropping dramatically following delivery (Galea and Frokjaer, 2019) and remaining on very low levels for at least the first seven days (Bloch et al., 2003; Poindexter et al., 1983). Based on these hormonal changes, a particular neurochemical dysregulation is thought to be associated with this phase. It has been suggested, for instance, that the first few weeks after delivery are linked to monoamine-lowering processes and ovarian hormone deficiency, which contribute to the postpartum changes in mood (Jahangard et al., 2019; Sacher et al., 2020). Diminished progesterone release during pregnancy and the postpartum period has been associated with higher depression scores 12 weeks postpartum (Jahangard et al., 2019).

Up to 50–75% of new mothers experience 'postpartum blues' within a week of delivery (Rezaie-Keikhaie et al., 2020; Seyfried and Marcus, 2003), which is a syndrome characterized by anxiety, insomnia, irritability, and an overall depressed mood (Seyfried and Marcus, 2003). As per definition, baby blues (BB) are temporary with no particular requirement for treatment as the symptoms subside within a few days. Although most BB cases resolve themselves within about two postpartum weeks, some women may continue to experience mood disturbances beyond that period. Approximately 9–15% of new mothers develop postpartum depression (PPD), which is a clinically manifest depression developing within the first four postpartum weeks (DSM-5; American Psychiatric Association, 2013). Short-term depressive symptoms, which are longer lasting than BB, but less severe than depression, can be diagnosed as postpartum adjustment disorder (AD) in 10–15% of women (Hahn et al., 2021; Stickel et al., 2021). As opposed to PPD, AD is recognized as a stress-response and should be considered as an important differential diagnosis to PPD. As a subclinical or sub-threshold diagnosis, the associated depressive symptom severity of AD does not

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meet the criteria for clinical depression at any time point, distinguishing the condition from PPD (American Psychiatric Association, 2013).

Evolutionary models of depression aim to shed light on the functionality of the disorder. One model attributes social functionality to the depressive disorder. It postulates that when need is signaled, it results in a demand for support in social groups with a high degree of interdependence (Hagen and Anderson Thomson, 2004). Thus, postpartum mood disturbances can both pave the way for and trigger a potential redemption of resources from the social environment (Hagen, 1999).

In sum, BB represent a risk factor for postpartum affective disturbances both in terms of AD and PPD. In particular, a greater severity of postpartum blues is associated with a greater risk for PPD (e.g. Henshaw et al., 2004; Luciano et al., 2021; Reck et al., 2009).

BB have yet to be adequately investigated through neuroimaging technics. According to some preliminary studies, however, the time immediately after delivery (when BB usually occur) is associated with increased structural brain plasticity in regions involving socio-cognitive processes and emotion perception (Chechko et al., 2021a; Mitchell and Phillips, 2015), the maternal brain (Rocchetti et al., 2014), and the reward system (Chechko et al., 2021a). For instance, shortly after childbirth (on average two days postpartum), young mothers have been found to display an extensive GMV decrease in the bilateral hippocampus/amygdala, the orbitofrontal cortex/the subgenual area, the bilateral temporal lobe, the insula, the basal ganglia, and the cerebellum (Chechko et al., 2021a). In new mothers, these changes have been found to occur independently of the postpartum blues or wellbeing. In another study, Schnakenberg et al. (2021a) have shown that BB are not associated with changes in functional connectivity. As BB are short-lived and, for the most part, resolve spontaneously within the first few postpartum days, structural imaging or functional connectivity approaches are probably not as useful to uncover the differences that are still apparent on the functional level. None of the previous studies has applied functional magnetic resonance imaging (fMRI) tasks to investigate the functional correlates of BB. Becoming a mother is commonly considered to be one of life's most emotionally positive and rewarding experiences. However, in women with postpartum mood disorders, reward processing appears to be impaired, suggesting neural circuit dysfunctions in the reward system which contribute to mood problems (Post and Leuner, 2019).

The monetary incentive delay (MID) task is a widely used and validated reward processing task adapted for use in human fMRI studies to investigate motivational salience processes in health and disease (Knutson et al., 2008). The MID task allows reward processing to be parsed into at least two distinct components, namely 'anticipation' and 'feedback'. With respect to anticipations of both gain and loss, the task has been found to robustly activate the striatum and the key nodes of the salience network including the anterior insula and the anterior cingulate cortex (ACC) [Wilson et al. (2018)]. The cortico-striatal-thalamic-cortical loop, implicated in reward processing, has been suggested to be linked to maternal behavior (Atzil et al., 2017) as well as depression (Moses-Kolko et al., 2011). In response to monetary reward, depressed mothers have been found to show a rapid habituation of the ventral striatum [Moses-Kolko et al., 2011]. As incentive processing has been seen to be altered in major depression disorder (Knutson et al., 2008) and PPD (Moses-Kolko et al., 2011), the question is whether there are differences in incentive behavior pertaining to reward processing during BB.

The focus of the present study was to assess the symptoms of BB and to compare the groups with and without BB based on the MID task. The relevant risk factors, their associations with the clinical, environmental and anamnestic aspects, as well as the consequences of BB on postpartum mental health, were also assessed. Beginning shortly after childbirth, we examined the participants (after performing the MID task within six days postpartum) at several time points over 12 weeks. At 12 weeks postpartum, based on a clinical interview, the participants were separated into groups with PPD, AD and non-depressed (ND) participants. First, we sought to determine which predisposing and antecedent factors contribute to BB. Subsequently, we examined the effects of BB on postpartum psychological wellbeing, finding a higher prevalence of later AD or PPD among those affected by BB. Finally, we hypothesized that women affected by BB would show a different activation pattern during the MID task in the network related to monetary incentive processing. We postulated that, with respect to anticipations, the differences between women with and without BB would be seen in the striatum and in other key nodes of the salience network including the anterior insula and the ACC. This assumption was based on the role of these regions in the development of depressive mood (Knutson et al., 2008; Moses-Kolko et al., 2011) as well as on the fact that MID is associated with the activation of these areas (Wilson et al., 2018). In a nutshell, the major aim of the study was a better understanding of the symptoms of BB as an important risk factor for the development of PPD or AD (Hahn et al., 2021; Stickel et al., 2021). A clear understanding as to whether or not BB have functional correlates (potentially similar to the ones seen in depression) may further augment the meaningfulness of early intervention, starting with the onset of BB.

2. Methods

2.1. Participants

From the ongoing longitudinal study (Risk for Postpartum Depression [RiPoD]), we used the data of 63 postpartum women who had taken part in the fMRI-based MID task and had additionally filled out Maternity Blues Questionnaire (MBQ) (Kennerley and Gath, 1989) in the first week postpartum. Due to technical errors, the MID data of three participants were not recorded; thus, the data of 60 participants were used for the analysis.

The recruitment was performed in the Department of Gynecology and Obstetrics at the University Hospital Aachen within one to six days of childbirth. The exclusion criteria were depression at the time of recruitment, severe birth- and pregnancy-related complications (e.g., eclampsia, HELLP), alcoholic or psychotropic substance dependency or use during pregnancy, history of psychotic or manic episodes, and antidepressant or antipsychotic medication during pregnancy. In addition, only mothers of healthy children (determined by the routine German Child Health tests (U2) conducted within the first three to 10 days of life) were included. Prior to enrolment in the study, written informed consent was obtained from each participant. The study protocol was in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the Medical Faculty, RWTH Aachen University.

2.2. RiPoD study

The data in the present study originated from the longitudinal RiPoD study, which has been ongoing since 2016 at the University Hospital Aachen, resulting in several publications. Some of these publications contain information about a number of participants whose data are also included in the present study. With respect to hair cortisol and cortisone, the behavioral data of 9 participants (total = 196) from Stickel et al. (2021) and 13 participants (total n = 240) from Lang et al. (2021) have been used, revealing postpartum adjustment-related differences associated with glucocorticoid metabolism in nondepressed and depressed mothers, as well as a negative correlation between perceived stress and hair cortisone concentration in the postpartum period. The details of 21 participants (total n = 78) on brain structure in healthy postpartum women (Chechko et al., 2021a) revealed a delineation of widespread pregnancy-related gray matter volume reduction in young mothers shortly after delivery. As for the functional connectivity as an early biomarker for postpartum depression (Schnakenberg et al., 2021a), the data of 48 participants (total n = 150) have shown no differences between nondepressed and depressed mothers before the first depressive symptom onset. Other RiPoD study-related publications use data from participants who are not included in the present study (Chechko et al., 2021b; Hahn et al., 2021; Schnakenberg et al., 2021b; Stickel et al., 2019).

That being said, in none of these previous studies were baby blues part of a research question or hypothesis, with the condition having been used merely to describe the sample. The imaging data from the Monetary Incentive Delay task have never been published before. In addition, the data of 12 participants are completely new, and no information pertaining to their baby blues symptoms has yet seen the light of day.

2.3. Questionnaires

Table 1 summarizes the characteristics of the participants, including age, marital status, days of gestation and birth mode. At T0 (one to six days postpartum), the current depressive symptoms after childbirth were assessed using the EPDS (Cox et al., 1987), a 10-item self-report instrument. A cut-off score above 10 indicated possible symptoms of depression as validated and recommended for a German sample (Bergant et al., 2008). For more information on the clinical-anamnestic screening and questionnaires assessed at T0, see the Supplementary material (Table S1).

Table 1
Postpartum women's sample characteristics (means, standard deviations, and frequencies) were divided into women without and with baby blues.

	No Baby Blues Group (n = 31)	Baby Blues Group (n = 29)	Statistical test
	Mean (SD)	*Mean (SD)*	
Age	32.45(5.2)	30.9(5.62)	$t_{58} = -1.11$, p = 0.27, d= 0.28
Days of gestation	274.9(12.81)	272(15.65)	Welch $F_{1,54.22} = 0.61$, *P* = 0.43[a], $np^2 = 0.01$
MBQ score	5.71(2.4)	13.07(2.9)	$t_{58} = -10.74$, p < 0.001, d= 2.77
EPDS T0	5.19(3.53)	7.45(4.52)	BB Groups $F_{(1,54)}$ = 17.09 p < 0.001; np^2 = 0.24; Time $F_{(4216)} = 2.18$, p = 0.1, $np^2 = 0.038$; BB Groups x Time $F_{(4216)}$= 2.25, p = 0.063, $np^2 = 0.04$
EPDS T1	3.6(2.27)	8.9(4.25)	
EPDS T2	4.97(4.51)	7.52(5.28)	
EPDS T3	3.77(4.2)	7.81(4.22)	
EPDS T4	2.7(3.34)	7.43(6.08)	
MPAS T1	86.73(5.6)	83.59(8.28)	BB Groups $F_{(1,54)}$ = 2.27 p = 0.14, np^2 = 0.04; Time $F_{(3162)} = 2.5$, p = 0.072, $np^2 = 0.06$; BB Groups x Time $F_{(3162)}$= 0.35, p = 0.78, $np^2 = 0.006$
MPAS T2	86.57(7.75)	84.3(7.53)	
MPAS T3	86.67(7.59)	84.52(6.19)	
MPAS T4	87.93(6.22)	85.71(5.7)	
PSS T0	15(5.36)	14.93(5.71)	BB Groups $F_{(1,51)}$ = 2.53 p = 0.11, np^2 = 0.047; Time $F_{(4204)} = 3.75$, p = 0.006, $np^2 = 0.069$; BB Groups x Time $F_{(4204)}$= 1.21, p = 0.3, $np^2 = 0.023$
PSS T1	13.96(5.48)	16.21(5.53)	
PSS T2	14.8(6.68)	16.15(6)	
PSS T3	12.28(7.1)	16.35(7)	
PSS T4	10.97(5.6)	14.96(6.62)	
	Percent	*Percent*	
Disorder developed during the postpartum period	12.9	51.7	$Chi^2(1) = 8.71$, p = 0.003, cramer's V = 0.38
Adjustment Disorder	9.7	27.6	
Postpartum Depression	3.2	24.1	
Married	80.6	65.5	$Chi^2(1) = 1.06$, p = 0.3, cramer's V = 0.13

Note. EPDS: MBQ: Maternity Blues Questionnaire; Edinburgh Postnatal Depression Scale; MPAS: Maternal Postnatal Attachment Scale; PSS: Perceived Stress Scale; T0: 0–6 days postpartum; T1: 3 weeks postpartum; T2: 6 weeks postpartum; T3: 9 weeks postpartum; T4: 12 weeks postpartum.
For each of the continuous measures, independent sample t-tests were conducted. In case of violation of the assumption of homogeneity of variance (Levene's test), the Welch F-test was used. In case of categorical measures, Chi-square tests were conducted. The Linear Mixed analyses of variance (ANOVA) Models with repeated measures were used for the scores of the questionnaires EPDS, MPAS, and PSS, with the between factor group (BB and No BB) and within-factor time points (T0-T4).

After three weeks postpartum (T1), the participants were required to log into an online survey via an email link to help assess the symptoms of BB during the first week postpartum by means of the MBQ. According to the MBQ, a woman is seen as suffering from postpartum blues if her total score on the questionnaire is higher than the mean peak score for the whole sample. The experience of BB symptoms was assessed with a cut-off score of > 10 on the MBQ.

At 3 (T1), 6 (T2), 9 (T3) and 12 weeks (T4) postpartum, the participants were required to log into the online survey to help assess the preceding three weeks by means of the EPDS, the Maternal Postnatal Attachment Scale (MPAS; Condon and Corkindale, 1998), a 19-item self-report measure of attachment quality, hostility and pleasure in interaction, and the Perceived Stress Scale (PSS; Klein et al., 2016).

After 12 weeks of participation (T4), in a final clinical interview and, based on the DSM-5 criteria, participants with depressive mood were assigned either to the PPD group or the AD group by an experienced psychiatrist or psychologist, and those without depressive symptoms to the non-depressed (ND) group.

2.4. MID task

The MID task was adapted from the version of Votinov et al. (2014) and was presented as one run with 90 trials.

The player started the game with an initial amount of € 5. Each trial consisted of one of three geometrical cues, an anticipation period with a fixation cross, a target (black square) and immediate feedback (see Fig. 1). The cue of a potential gain of € 1 was presented as a circle, a potential loss of € 1 as a square and the control condition with no monetary outcome (€ 0) as a triangle. Each type of cue was presented 30 times in a pseudorandomized order for 250 ms. After the incentive cue, participants had an anticipation period (fixation cross) and waited for the target cue. The anticipation period was varied randomly between 2000 and 2500 ms. The participants were instructed to respond to the target with a button press as quickly as possible in order to win or to avoid losing money. The display duration of the target cue was varied (80 – 420 ms.) to ensure that participants would be able to respond in time only in 2/3 of all incentive trials. The feedback was presented for 1650 ms. immediately after the disappearance of the target, informing participants about whether they had won or lost money during that trial. An inter-trial interval followed feedback, with a fixation cross being presented between 2400 and 3200 ms.

2.5. Behavioral data analysis

All statistical analyses were conducted using an open-source statistical package: Pingouin written in Python 3 (Vallat, 2018).

The two groups (BB, with baby blues, and No BB, without baby blues) were compared with respect to various behavioral, clinical and socio-demographic parameters (see results in Table 1 and Table S1). For each of the continuous measures, independent sample t-tests were conducted. In case of violation of the assumption of homogeneity of

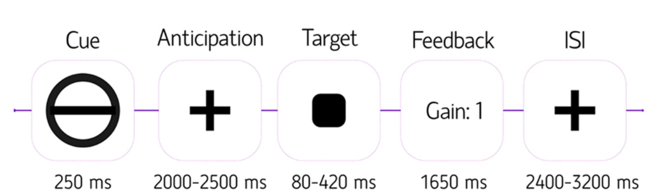

Fig. 1. Monetary Incentive Delay task (MID). Example of one trial for MID task.

variance (Levene's test), the Welch F-test was used. In case of categorical measures, Chi-square tests were conducted.

We conducted two-tailed Spearman's rank correlations between the MBQ and EPDS scores at all time points, and PSS scores at all time points, and two-tailed Pearson's correlation for the MBQ and PSS scores.

The linear mixed analyses of variance (ANOVA) models with repeated measures were used for the scores of the questionnaires EPDS, MPAS, and PSS, with the between factor group (BB and No BB) and within-factor time points (T0-T4). The same analysis was applied for reaction time (RT) extracted from the MID task with the between factor groups (BB and No BB) and within factor cue (RT gain, RT loss and RT control). The Greenhouse-Geisser correction was used to adjust degrees of freedom when significant nonsphericity was detected via the Mauchly's test.

2.6. fMRI data acquisition and data analysis

The MRI scanning was conducted on a 3 Tesla Prisma MR Scanner (Siemens Medical Systems, Erlangen, Germany) located in the Medical Faculty of RWTH Aachen University. Functional images were obtained with a single-shot echo-planar imaging (EPI) sequence. The parameters were as follows: duration 12.06 min, repetition time (TR) = 2000 ms., echo time (TE) = 28 ms., flip angle = 77°, voxel, resolution = $3 \times 3 \times 3$ mm^3, field of view (FoV) = 192×192 mm^2. For anatomical registration, we obtained high-resolution 3D T1 anatomical images using magnetization-prepared rapid acquisition gradient echo imaging sequence with these parameters: (4.12 min; 176 slices, TR = 2300 ms., TE = 1.99 ms., TI = 900 ms., FoV = 256×256 mm2, flip angle = 9°, voxel resolution = $1 \times 1 \times 1$ mm^3). All images were inspected for structural abnormalities, and scanner and motion artifacts. In case of the latter two, imaging acquisition was repeated.

Image analysis was performed using the SPM12 software package (www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB (Mathworks Inc., Natick, USA). Preprocessing included correction for slice-timing differences, realignment to the first image to adjust for movement, segmentation, normalization to standard MNI space (voxel size = $2 \times 2 \times 2$ mm^3), and smoothing with an isotropic Gaussian filter (full-width-at-half-maximum = 8 mm). All coordinates are in reference to the MNI convention (http://www.mni.mcgill.ca).

For each subject, delta functions with the time points of each type of trial presentation were convolved with the canonical hemodynamic response function (HRF) to build a regression model of the time series. Six realignment parameters of each participant were included as nuisance variables. The first level (individual subject) analyses were set up using the general linear model approach, with events of interest being modeled by regressors. The model included anticipation for three types of incentive cues: possible gain € 1 (GA), possible loss € − 1 (GL) and control € 0 (NA). The target cues and feedbacks, two for winning after gain and loss cues (GW and LW) and two for losses after gain and loss cues (GL and LL) were also modeled. The fixation crosses between trials were modeled as a baseline activity.

Contrast images of these regressors from the first level were then entered into second level random-effects analyses to allow for group-level inference, and in particular to compare the groups with and without BB.

To retest whether the MID task would reveal neural activation within the reward system during the anticipation phase, we performed single t-test analysis on the whole sample of participants using Gain Anticipation > Loss Anticipation (GA > LA) contrasts.

We performed group comparisons by using Flexible Factorial analysis. We focused on neural activation differences during the anticipation conditions, comparing anticipation phases for Gain (GA) and Loss (LA) between the BB and No BB groups.

The same analysis was performed on the feedback trials, where we compared winning (GW and LW) and losing feedbacks (GL and LL) between the BB groups.

Regions with significant activations are reported according to the automatic anatomic labeling included in the WFU PickAtlas (AAL).

3. Results

3.1. Sample characteristics of the two groups

The difference between the groups was seen based on the experience of BB (BB: n = 29; No BB: n = 31; based on the self-report and MBQ cut off score > 10). The BB and no BB participants did not differ significantly in age, gestational age, marital status and birth mode. For more information, see Table 1 and Supplementary Table S1.

A much higher number of women in the BB group (51.7% vs. 12.9% in the no BB group) developed a psychiatric condition (PPD or AD) within the first 12 postpartum weeks. 24.1% of all women in the BB group developed PPD compared to only 3.2% of participants in the group not affected by BB.

Consequently, the EPDS scores in the BB group were significantly higher during all observational time points (Table 1). A Spearman correlation for MBQ scores and EPDS T0 showed that women who were more affected by BB also had a higher depressivity score at childbirth ($r = .304$, $p = .018$; see Fig. 2). This association was seen at all time points (EPDS T1: $r = .765$, $p < .001$; EPDS T2: $r = .39$, $p = .003$; EPDS T3: r = ,56, $p < .001$; EPDS T4: $r = .54$, $p < .001$). Thus, the severity of BB shortly after delivery correlated with the wellbeing of women at all further observational time points.

There were no differences in the levels of mother-to-child attachment (MPAS) between the groups (see Table 1). However, there were significant correlations between MBQ scores and MPAS T3 ($r = -.28$, $p = .036$) and MPAS T4 scores ($r = -.3$, $p = .019$), but not those at T1 ($r = -.22$, $p = .095$) or T2 ($r = -.23$, $p = .076$).

The two groups did not differ in terms of stress experience (PSS) at any time point (Table 1). Although there was no significant interaction between the groups and the time points, the level of stress did not change much over time in BB and got lower in the No BB group. There was also some association between the MBQ scores and levels of stress at 3, 9 and 12 weeks postpartum (Pearson correlation: PSS T0: $r = .05$, $p < .67$; PSS T1: $r = .39$, $p = .002$; PSS T2: $r = .23$, $p = .09$; PSS T3: $r = .35$, $p = .01$; PSS T4 $r = 0.41$, $p = 0.001$).

3.2. Behavioral performance in the MID task

The repeated measures ANOVA revealed no main effect of group in reaction times for any of the trials. However, there was a significant effect of the factor cue ($F(1114) = 18.57$, $p < .01$), reflecting faster RT

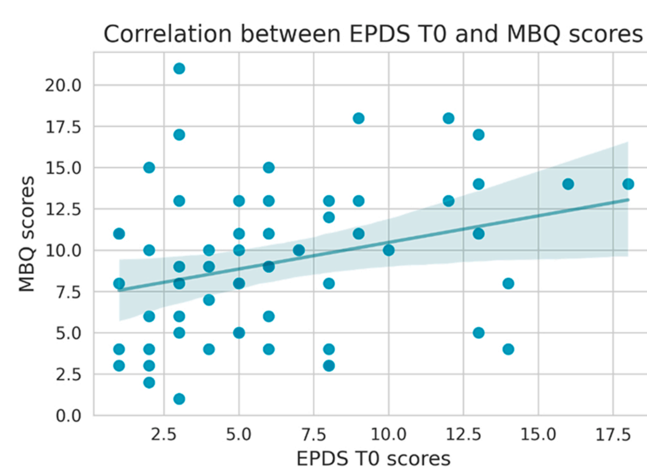

Fig. 2. Correlation between the scores of the Maternity Blues Questionnaire (MBQ) and the Edinburgh Postnatal Depression Scale (EPDS) at the time of childbirth (T0).

during the gain trials compared to the control trials (see Table 2).

4. FMRI results

4.1. Effects of GA > LA on whole-brain activation in the whole sample of participants

At the whole-brain level at $p < 0.05$ FWE correction, during GA compared to LA (independent of the experience of BB), a robust activation of the bilateral caudate extending to the bilateral thalamus was revealed. Further activation was also seen in the right midcingulate cortex and other prefrontal areas, including the bilateral supplementary motor area (SMA)/ superior frontal gyrus (SFG) and the left dorsolateral prefrontal cortex (DLPFC) (see Fig. 3). The opposite contrast LA vs GA did not reveal any results. Please see the Supplementary Table S2 for information about significant clusters, peak MNI coordinates, cluster size, and peak intensities of the volumes.

4.2. Group comparisons for gain and loss anticipation trials

The comparison between the groups in their response to GA as well as LA revealed small and negligible effects. We increased the power and combined the two anticipation phases to investigate whether the groups showed differences in activation patterns during anticipation in general, regardless of the type of anticipation. The same was done for the feedback trials.

Collapsing the GA and LA trials using a $p < 0.001$ uncorrected threshold at the voxel level, with a cluster threshold at $p < 0.05$, we found the No BB group (compared to the BB group) to demonstrate a stronger activation in the pregenual (pg) and subgenual (sg) ACC and in the right temporal lobe during the anticipation trials (Fig. 4). The opposite contrast demonstrated in the No BB group (compared to BB) less activation in the left cerebellum and the right precuneus (see Fig. 4 and Table S3 for detailed information).

4.3. Group comparison for all win trials

Using a $p < 0.001$ uncorrected threshold at the voxel level, with a cluster threshold $p < 0.05$, we collapsed all win trials (GW + LW). Participants with BB (compared to the No BB group) showed a stronger involvement of the left temporal areas involving the left superior temporal gyrus (STG)/middle temporal gyrus (MTG), the right insula/ inferior frontal gyrus (IFG) and the left midbrain (Fig. 5A and Table S4 for detailed information). The opposite contrast (No BB > BB) resulted in no significant differences.

Table 2
Mean reaction time (RT) and standard deviation (SD) of the anticipation trails in the Monetary Incentive Delay task.

	No Baby Blues Group (31)	Baby Blues Group (29)	Statistical test
	Mean (SD)	*Mean (SD)*	
Reaction Time			BB Groups $F_{(1,57)} = 0.22$
RT all trials	226.8(33.78)	229.52 (25.69)	$p = 0.63$; $np^2 = 0.004$ Cues $F_{(1114)} = 18.57$,
RT gain anticipation	221.23 (39.33)	221.92 (26.93)	$p < 0.01$, $np^2 = 0.25$ BB Groups x Cues
RT loss anticipation	226.19 (33.75)	233.19 (28.56)	$F_{(1114)}$=0.84, $p = 0.43$, $np^2 = 0.015$
RT neutral anticipation	234.51 (31.97)	237.74 (28.62)	Post-hoc (Tukey) RT Gain all> RT Neutral all, $p = 0.04$, Hedges $g = -0.45$
Total Win in €	4.96(6.89)	5.96(5.69)	Welch $F_{1,57.14} = 0.37$, $P = 0.54^a$, $np^2 = 0.006$

Note. The Linear Mixed analyses of variance (ANOVA) Models with repeated measures were used for reaction time (RT) extracted from the MID task with the between-factor groups (Baby blues and No baby blues) and within-factor cue (RT gain, RT loss and RT control). The Greenhouse-Geisser correction was used to adjust degrees of freedom when significant non-sphericity was detected via the Mauchly's test.

4.4. Group comparison for all loss trials

For all loss trials (GL + LL), at $p < .05$ FWE correction at a cluster, with an uncorrected cluster-forming threshold at voxel-level $p < .001$, the BB group showed stronger activation in the right midbrain, the right cerebellum/fusiform gyrus, and the left precuneus. Further activation was found in the left temporal lobe/MTG and in the right IFG (see Fig. 5B). The opposite contrast showed weaker activation in the BB group (compared to No BB) in the left precuneus/parahippocampal gyrus during all loss trials (see Table S5 for detailed information).

5. Discussion

The present study was designed to contrast neural and subjective responses to monetary incentives in participants with and without BB assessed by means of the MBQ. The task was performed in postpartum mothers within the first week of delivery, the time window when young mothers usually experience postpartum BB (Harris et al., 1994). In our study, 29 participants from a total of 60 who participated in the MID task, developed BB within the first postpartum week, which corresponds to a common prevalence of BB (Rezaie-Keikhaie et al., 2020).

BB have been suggested to be a risk factor for the development of a postpartum affective disorder (Hahn et al., 2021). In line with previous results, our study found a much higher number of women in the BB group to develop either PPD or AD (52% vs. 13%). In particular, a much higher number of PPD cases were found in the BB group compared to the one without BB (24% vs. 3% respectively). In addition, we saw a positive relationship between EPDS shortly after childbirth and the BB severity (MBQ score) within the first postpartum week, which is not surprising given that the leading symptom of BB is negative changes in mood. Also, the EPDS levels during the first 12 weeks remained higher in the BB group at all observational time points paralleled by increased levels of stress. The BB group also showed a tendency toward poorer adaptation to postpartum stress. While the stress levels of those without BB decreased with time, the stress levels in the BB group remained elevated throughout the entire 12-week period. The differences in EPDS and stress levels during the follow-up are likely to be explained by the higher number of AD and PPD cases in the BB group. Both conditions, PPD and AD, were previously shown to be associated with higher EPDS levels and worse adaptation to postpartum stress (Hahn et al., 2021; Stickel et al., 2021).

Reward processing is thought to be disturbed in mood disorders (Su and Si, 2022). In the MID task, across all study participants, the GA vs. LA comparison resulted in a robust activation in the striatum, the thalamus, the DLPFC and the bilateral SMA/SFG, regions known to be strongly linked to monetary reward processing (Diekhof et al., 2012; Wilson et al., 2018). In addition, major differences between the BB and No BB groups were observed during the anticipation trials. During both types of anticipation trials (GA and LA), a stronger activation in the pg/sgACC was seen in subjects not affected by BB. Anticipation being associated with a feeling of excitement about something that is due in the near future, it represents a critical phase of incentive processing. Both reward and loss anticipation robustly engage key nodes of the salience network including the anterior insula and the ACC (Wilson et al., 2018). The orbitofrontal prefrontal regions were seen to be recruited particularly during the reward outcome, likely representing the value of the reward received (Oldham et al., 2018), supporting the notion that the orbitofrontal prefrontal ACC is a central part of the reward network. Thus, lower levels of pg/sg ACC activation in women affected by BB likely suggest lower engagement of the reward processing networks in women experiencing BB. As regards the effect of pregnancy on emotion processing and stress regulation, the sgACC (in addition to

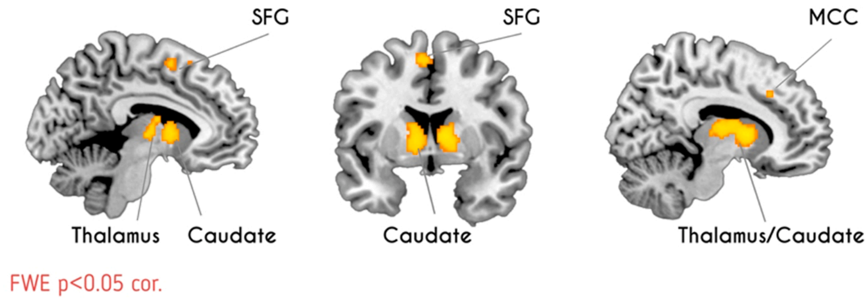

Fig. 3. Brain regions activated during gain anticipation (GA) > loss anticipation (LA) across all study participants. SFG: Superior frontal gyrus; MCC: Mid-cingulate cortex.

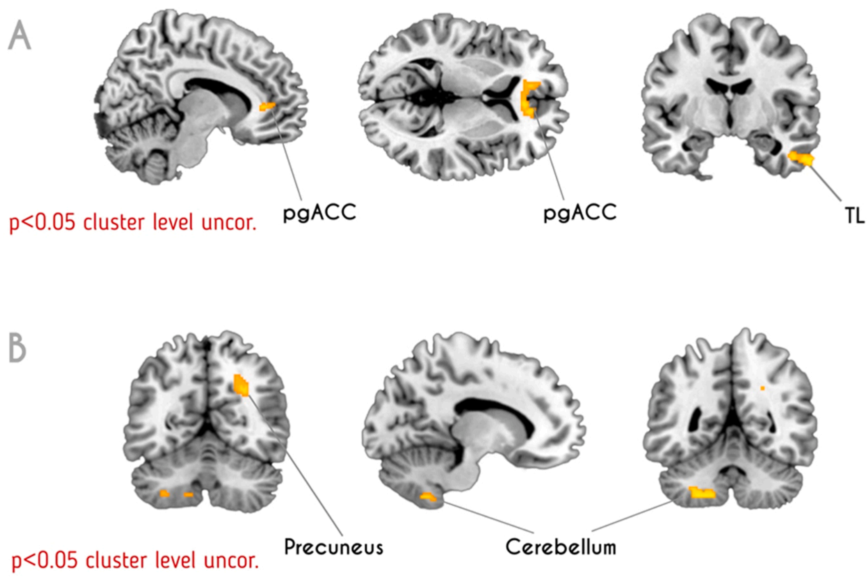

Fig. 4. Brain regions activated during gain anticipation and loss anticipation (GA + LA), contrasted for women with no baby blues (No BB) compared to women with baby blues (BB).

the amygdala and the hippocampus) is related to the regulation of emotions and stress (Bludau et al., 2016). In line with that, a recent study by our group found postpartum women with higher cumulative hair cortisol concentration in the last trimester of pregnancy to have lower activation in the sgACC during emotional interference involving anxious emotions shortly after childbirth (Stickel et al., 2019). SgACC activity has also been found to distinguish depressed from non-depressed individuals during the exposure to emotional faces (Gotlib et al., 2005), and it has also been postulated to play a central role in the neurobiology of depression and affective disorders (Davidson et al., 2003). During the winning trials (GW and LW), in the BB group we observed a stronger activation in the left STG/MTG, the right insula/IFG and the left midbrain, regions known to be involved more strongly during monetary gain versus monetary loss (Votinov et al., 2015). In the same group, the loosing trials were found to be associated with stronger activation in the right midbrain, the right cerebellum/fusiform gyrus, the left precuneus, the left temporal lobe/MTG and the right IFG. As reward processing is suggested to be deeply affected in depression (Su and Si, 2022), our results indicate that BB, which also cause negative changes in mood and is a risk factor for depression, can be at least temporarily linked to a lower activation of the reward processing networks, primarily the subgenual part of the ACC.

In terms of behavioral responses, no differences were found between the two types of anticipation trials. Notably, no differences had been observed even when the performances of depressed and never-depressed participants were compared during incentive processing (Knutson et al., 2008). Contrary to our expectation, we did not find any differences in the striatum, either. However, these negative results are in line with previous studies. For instance, in the MID task, depressed and never-depressed participants did not differ in affective or behavioral responses during gain anticipation, and there were no differences in terms of striatal response. The never-depressed participants did, however, exhibit increased ACC activation during anticipation of increasing loss (Knutson et al., 2008).

One limitation of the study is its retrospective assessment of BB, for which prospective daily symptom assessments are recommended. In our cohort, the MBQ was only administered three weeks after delivery. However, a particular strength of the study is that it included euthymic women, i.e., only those who did not have prenatal depression and did not present with clinically significant depressive symptoms at the time of delivery. Thus, we can assume that the neuronal activity observed during the MID task had been triggered by the BB and not by any pre-existing depression.

Finally, neural activation during BB had not been previously investigated. According to our previous results, there are no differences in functional connectivity, brain structure or cortical thickness between women affected by BB and those who are not (Chechko et al., 2021a; Schnakenberg et al., 2021a). As BB represent a very brief and temporary condition, fMRI tasks are likely to help assess the changes in activity associated with the timing of this condition. Here, we show, for the first time, that the timeframe associated with BB can overlap with an alteration of brain networks linked to incentive processing. The crucial

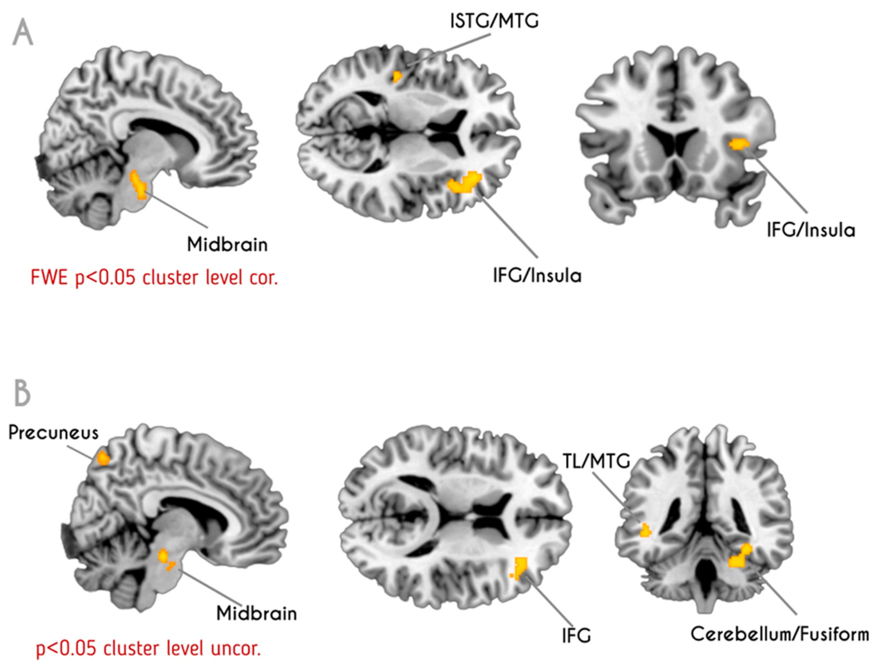

Fig. 5. A) Brain regions activated in women with baby blues (BB) compared to women without baby blues (No BB) during A) all win trials (GW and LW) and B) all loss trials (WL and LL).

differences were found to occur during anticipation, with the No BB participants showing less activation in the sgACC.

In sum, our results suggest that BB, which is an important risk factor for, or often an indicator of, PPD, has functional correlates in areas related to the development of depression (Davidson et al., 2003). Therefore, the identification of women at a higher risk of PPD while they experience the symptoms of baby blues may contribute to an early recognition of PPD. Interventions starting upon the very onset of baby blues, particularly in those with severe symptoms of the condition, can potentially prevent the development of PPD.

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Ethics statement

The study protocol conformed to the Declaration of Helsinki and was approved by the ethics committee at the medical faculty of RWTH Aachen (reference number EK 208-15).

Declaration of interest

The authors have no conflicts of interest to declare.

Data Availability

The data that support the findings of this study are not publicly available due to privacy or ethical restrictions, but are available on request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2022.105991.

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