

The association between prenatal maternal anxiety disorders and postpartum perceived and observed mother-infant relationship quality

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ABSTRACT

Introduction: Prenatal maternal anxiety disorders have been associated with adverse outcomes in offspring including emotional, behavioral and cognitive problems. There is limited understanding of the mechanisms underpinning these associations, although one possible candidate is an impaired mother-infant relationship. The authors investigated whether prenatal anxiety disorders were associated with poorer postpartum mother-infant relationship quality, measured by maternal self-reported bonding and observed mother-infant interactions.

Methods: A cohort of 454 pregnant women recruited from an inner-city maternity service in London (UK) were assessed for mental disorders using the Structured Clinical Interview for DSM-IV and followed up at mid-pregnancy and 3-months postpartum. Depressive symptoms were assessed at baseline and mid-pregnancy (using the Edinburgh Postnatal Depression Scale). At three months postpartum, women were assessed for self-reported bonding difficulties (using the Postpartum Bonding Questionnaire) and a subsample ($n = 204$) participated in video-recorded mother-infant interaction, coded using the Child-Adult Relationship Experimental Index by an independent rater.

Results: Prenatal anxiety disorders were associated with higher perceived bonding impairment, but not associated with observed poor mother-infant interaction quality. Higher levels of depressive symptoms were associated with lower maternal sensitivity.

Conclusions: Interventions for anxiety disorders in the perinatal period could be tailored to address anxieties about mother-infant relationship and co-morbid depressive symptoms.

1. Introduction

Anxiety disorders are common during pregnancy and the postpartum period (Dennis, Falah-Hassani, & Shiri, 2017), with a higher prevalence than depression in some studies (Howard et al., 2018; Matthey, Barnett, Howie, & Kavanagh, 2003). Children of mothers with anxiety disorders are at increased risk of adverse outcomes during childhood, including difficult temperament, emotional and behavioral problems, cognitive difficulties (Glover, 2014; Newman, Judd, & Komiti, 2017; Stein et al., 2014) and of developing anxiety disorders and other psychopathology during later life (Eley et al., 2015; Telman,

van Steensel, Maric, & Bögels, 2018). Currently, there is limited understanding of the mechanisms that underpin these associations, although it has been suggested that a modifiable pathway of risk is through parenting behaviors in early mother-infant interactions (Eley et al., 2015; Stein et al., 2014).

Core aspects of mother-infant interactions include maternal sensitivity (a mother's capacity to notice and respond appropriately to her infant's emotional and behavioral cues) and disrupted interactions are characterized by maternal unresponsiveness and intrusiveness (Crittenden, 2010). As well as the actual behaviors of parents that can be observed, parents' perceptions and experiences of their interactions

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are important for both parent and child. This is because parents' perceptions (cognitions) have the potential to influence parenting behaviors and interactions with their infants (Muzik et al., 2013). However, the role of anxiety for perception and behavior is unclear. Understanding how anxiety is related to parents' perceptions of bonding and behavior during interactions may provide targets for interventions during the perinatal period, a time when women are in regular contact with healthcare professionals, thus providing an ideal opportunity for early implementation of interventions and potential prevention of adverse outcomes (Fontein-Kuipers, Nieuwenhuijze, Ausems, Budé, & Vries, 2014; Howard, Megnin-Viggars, Symington, & Pilling, 2014).

The influence of anxiety on parenting perceptions and behaviors is likely to be a complex process involving internal worries as well as differences in behavior (Kaitz & Maytal, 2005). Increased levels of awareness and vigilance are a normal part of parenting a young infant, especially for first-time mothers. Yet for some mothers, their levels of anxiety can disrupt their everyday functioning and impair their ability to parent. Negative cognitions and perceptions, commonly associated with anxiety disorders, may also have the potential to distort a mother's interpretation of her infant's signals, which in turn could influence the mothers behavioral response to the infant (Kaitz & Maytal, 2005).

Studies investigating maternal perceptions of bonding using the Postpartum Bonding Questionnaire (PBQ, a self-reported questionnaire designed to measure mother's perception of emotional bonding with their infant) reported that higher self-reported anxiety symptoms during pregnancy (Dubber, Reck, Müller, & Gawlik, 2015; Farré-Sender et al., 2018) and postnatal anxiety disorders (Tietz, Zietlow, & Reck, 2014) were associated with perceived impaired bonding. Higher levels of maternal anxiety symptoms have also been associated with increased parenting stress and lower perceived parenting competence, measured using the Parenting Stress Index (Abidin, 1995; Huizink et al., 2017; Misri et al., 2010). Although, these studies give insight into the association between maternal anxiety and mothers' perception of bonding, it is important to investigate maternal perceptions of bonding alongside observational measures of mother-infant interactions, as the two aspects are linked (Muzik et al., 2013), but not the same construct. It is also important to investigate the influence of clinical levels of anxiety (i.e. anxiety disorders).

Previous studies investigating the association between maternal anxiety disorder (using diagnostic interviews) and observed mother-infant interactions within the first postpartum year have mostly been small, usually cross-sectional, and report inconsistent findings. A few studies report no evidence for differences in maternal sensitivity between mothers with anxiety disorders compared to mothers without anxiety disorders, especially after accounting for depression (Challacombe et al., 2016; Grant, McMahon, Reilly, & Austin, 2010; Reck, Tietz, Müller, Seibold, & Tronick, 2018; Weinberg, Beeghly, Olson, & Tronick, 2008). However, some studies have found evidence of associations. For example, an early study by Weinberg and Tronick (1998) described a group of 30 mothers diagnosed with a combination of Panic Disorder (PD), Obsessive Compulsive Disorder (OCD) and Major Depressive Disorder (MDD) as disengaged and unresponsive towards their 3-month-old infants compared to control mothers with no diagnosed disorder ($n = 30$). Similarly, Warren et al. (2003) observed reduced sensitivity in mothers with anxiety ($n = 25$) compared to control mothers ($n = 24$) during mother-infant interactions at 4–8 months postnatal. Another study found that compared mothers with no anxiety disorder ($n = 59$), mothers with anxiety disorders ($n = 19$) were less sensitive and more intrusive during interactions with their infants at 9 months postpartum (Feldman et al., 2009). A larger study, by Murray, Cooper, Creswell, Schofield, and Sack (2007) (social phobia $n = 96$; controls $n = 94$) found that although mothers with social phobia were more anxious and disengaged during interactions with their 2-month-old infants, sensitivity scores were not significantly different to healthy control mothers. Similarly, Kaitz, Maytal, Devor, Bergman, and Mankuta (2010) reported no significant differences in

sensitivity between mothers with a current anxiety disorder ($n = 36$) and healthy controls with no diagnosis ($n = 59$) when interacting with their 6-month-old infants, but observed anxious mothers to react in a more exaggerated manner towards their infants (eye gaze, speech and expression of positive affect) compared to non-anxious mothers, which was contrary to previous findings that that anxious mothers are more disengaged (Murray et al., 2007).

One explanation for these inconsistent findings could be the nature of different observational tasks used in previous studies. For example, structured parent-child tasks may elicit anxiety-related parenting behaviors in both anxious and non-anxious mothers (Ginsburg, Grover, Cord, & Ialongo, 2006; Murray et al., 2007, 2012). Therefore, to tap into the nature of potential associations between maternal anxiety and mother-infant interactions, observations during free-play tasks (with a reduced potential to provide task-related anxiety) may be a more ecologically valid method of assessing a more natural interaction between a mother and baby. Another plausible explanation could be that depression might be having a greater influence than anxiety on mother-infant interactions and therefore it is important to consider the role of depression and comorbid depression and anxiety. Also, inconsistencies could be due to sampling variance in previous studies, as associations derived from small samples could differ from each other.

1.1. Current study

To our knowledge, this is the first study to prospectively investigate the influence of maternal antenatal anxiety disorder (measured using a validated diagnostic instrument) and postpartum maternal perceptions of bonding with her infant and observed mother-infant interactions during a free-play session. The primary aims of the study were: 1) To investigate the association between maternal anxiety disorders during pregnancy on maternal self-reported postpartum bonding difficulties as measured using the Postpartum Bonding Questionnaire, and 2) To investigate the association between maternal anxiety disorders during pregnancy and postpartum video-recorded mother-infant interactions. The secondary aim of the study was to examine the association between maternal comorbid anxiety and depressive disorders during pregnancy and postpartum mother-infant relationship quality (self-reported postpartum bonding difficulties and observational mother-infant interactions). We also aimed to investigate the correlation between maternal self-reported bonding and observed mother-infant interactions.

We hypothesized that, compared to mothers without an anxiety disorder during pregnancy, mothers who met diagnostic criteria for a DSM-IV anxiety disorder would have poorer scores on the bonding questionnaire (indicating self-perceived bonding difficulties) and exhibit a poorer quality of mother-infant interaction (lower sensitivity and higher unresponsiveness).

2. Methods

2.1. Participants and procedures

The sample (mother-infant dyads) comprised of participants drawn from two linked datasets that were recruited for a program of research examining the Effectiveness of Services for Mothers with Mental Illness (Howard et al., 2018; Trevillion et al., 2016) <https://www.kcl.ac.uk/ioppn/depts/hspr/research/ceph/wmh/projects/a-z/esmi.aspx>. Ethical approval was obtained by the National Research Ethics Service, London Committee - Camberwell St Giles (ref no 14/LO/0075). All participants provided written informed consent after receiving a complete description of the study and opportunity to ask questions. Language interpreters were used where required.

Recruitment and data collection were conducted between November 2014 and June 2017, in South-East London, a socio-economically and ethnically diverse population. Exclusion criteria included women aged under 16-years-old, those who had a termination or

miscarriage prior to the study baseline interview or lacked capacity to provide informed consent. Eligible pregnant women were recruited into the study at approximately 10–12 weeks' gestation and took part in the baseline interview within 3 weeks from the first prenatal booking appointment ($n = 556$, mean pregnancy gestation: 14 weeks). The baseline interviews were conducted by trained postgraduate researchers and research midwives, and consisted of a diagnostic interview, questions about mothers' depressive symptoms, sociodemographic and obstetric history. Researchers received training on the administration and scoring of the semi-structured diagnostic interview for 3 months prior to the recruitment of participants and attended weekly supervision with L.M.H during the study period to achieve consensus on anxiety and depression diagnosis.

Women were followed up at mid-pregnancy ($n = 508$, 91% follow-up rate, mean pregnancy gestation: 29 weeks) and approximately 3-months postpartum ($n = 484$, 87% follow-up rate). At both follow-up interviews, women completed questionnaires. Midway during the 3-month-postpartum data collection period, we obtained additional funding to approach a subsample of women ($n = 264$) to participate in a home visit to collect observational mother-infant interaction data (78% agreed, $n = 206$). See Fig. 1 for a flow-chart of participants through the study.

2.2. Measures

2.2.1. Exposures during pregnancy: Antenatal anxiety and depressive disorder

The Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders* (4th ed; DSM-IV) Axis I Disorders was administered (SCID, research version) (First, Spitzer, Gibbon, & Williams, 2002) and used to establish diagnostic groups of women with “anxiety disorders” and “depression”. The SCID is a semi-structured diagnostic interview, consisting of standardized diagnostic questions arranged in modules corresponding to each DSM-IV Axis I disorder. For the current analysis, the “anxiety disorders” group included women who met diagnosis for one or more current anxiety disorder [including Generalized Anxiety Disorder (GAD), Panic Disorder (PD), social phobia, agoraphobia, Obsessive Compulsive Disorder (OCD) and Post-Traumatic Stress Disorder (PTSD)]. Women who met diagnostic criteria for a “specific phobia” were not included as phenomenologically, phobias are reactions to specific stimuli (such as blood, animals, environments or situations) and therefore may not be expected to be associated with disruptions in the mother-infant relationship (Kaitz, Maytal, Devor, Bergman, & Mankuta, 2010). Although DSM-5 no longer formally classifies PTSD and OCD as anxiety disorders (American Psychiatric Association, 2013), there is some evidence to suggest PTSD and OCD maybe be associated with problems in mother-infant interactions (Challacombe et al., 2016; Ionio & Di Blasio, 2014; Kaitz et al., 2010), and as we used the SCID for DSM-IV they were included within the anxiety disorder group. There were minor changes to the diagnostic criteria for GAD, PD, social phobia and agoraphobia between DSM-IV and DSM-5, but these are unlikely to influence any potential associations between maternal anxiety disorder and outcome mother-infant relationships. The depression group for the current analysis consisted of those who met criteria for current “major depressive episode” and/or “major depressive disorder”.

2.2.2. Maternal mental health

2.2.2.1. Depressive symptoms during pregnancy. The Edinburgh Postnatal Depression Scale (EPDS) is a ten-item self-complete questionnaire that measures perinatal depressive symptoms and includes one item that assesses thoughts of self-harm (Cox, Holden, & Sagovsky, 1987). Each item consists of a statement which is scored on a four-point Likert scale ranging from a score of 0 (no symptom) to 3 (severe symptoms). Items 1, 2 and 4 are scored as marked and items 3 and 5–10 are reverse scored. The scores are then summed to create a continuous score of

depressive symptoms ranging from 0 to 30, with higher scores indicating higher depressive symptoms. The EPDS has been validated in 20 languages and different socioeconomic groups (Cox, 2019; Gelaye, Rondon, Araya, & Williams, 2016; Hanusa, Scholle, Haskett, Spadaro, & Wisner, 2008). Using Cronbach's α coefficient the internal consistency of the scale was 0.89 at baseline interview and 0.87 at the mid-pregnancy follow-up interview. The mean score of baseline and mid-pregnancy EPDS symptoms was used to create a variable to indicate women's depressive symptoms during pregnancy.

2.2.2.2. Borderline personality disorder. The Structured Clinical Interview DSM-IV Axis II Borderline Personality Disorders sub-section module for borderline personality disorders (SCID-II) was used for the diagnoses of DSM-IV Axis II borderline personality disorders (Zanarini, Frankenburg, Sickel, & Yong, 1996).

2.2.2.3. Eating disorder. The Structured Clinical Interview DSM-IV Axis I Eating Disorders module (SCID-I) was used for the diagnoses of DSM-IV Axis I eating disorders, including anorexia nervosa, bulimia nervosa and binge eating disorder (First et al., 2002).

2.2.3. Outcome at 3-months postpartum: mother-infant relationship

2.2.3.1. Mothers perception of bonding (self-report). The Postpartum Bonding Questionnaire (PBQ) is a 25-item self-report measure, designed to provide early indications of bonding disorders by using the assessment of a mother's feelings and attitudes towards her infant (Brockington et al., 2001; Brockington, Fraser, & Wilson, 2006). The measure consists of statements rated on a six-point Likert scale scored as 0 (always), 1 (very often), 2 (quite often), 3 (sometimes), 4 (rarely) and 5 (never). Positive statements, such as “I enjoy playing with my baby” are scored as marked. Where statements reflect a negative emotion/attitude such as “I am afraid of my baby”, the scoring is reversed. Total scores are generated by summing the 25 items (scores range between 0–125). Higher scores indicate more impaired bonding. Using a community sample of British mothers ($n = 96$), the psychometric properties of the total scale reported good internal reliability (Cronbach's α : 0.76) and reasonable validity (Spearman's rho correlations with other validated scales ranging between 0.30 – 0.46, $p < 0.01$) (Wittkowski, Wieck, & Mann, 2007; Wittkowski, Williams, & Wieck, 2010). For the total PBQ scale in the current analysis, Cronbach's α coefficient was 0.85, indicating good internal consistency.

2.2.3.2. Mother-infant interactions (observation). The Child-Adult Relationship Experimental Index (CARE-Index) was used to code mother-infant interactions from recordings of a 5-minute free-play session (Crittenden, 2010). The CARE-Index assesses three patterns of a mother's interactive behavior with her infant (sensitive, controlling and unresponsive) and four patterns of infant interactive behavior with the mother (cooperative, difficult, compulsive and passive). All patterns are rated on a scale of 0–14, with higher scores indicating a higher rating of the specific pattern. This is a reliable and valid coding system for infants aged between 0 and 15 months and validated across different social class and ethnic backgrounds (Crittenden, 2010; Leventhal, Jacobsen, Miller, & Quintana, 2004). The one coder was highly experienced and certified with Level II + research level coding reliability. To obtain this level of reliability, the coder was required to reach the bivariate correlation coefficients against a standard set of test videotaped interactions. This included 0.80 (or higher) on 3 or more of the scales (including both sensitivity and cooperativeness), a mean of 0.70 (or higher) and no scale below 0.50 (Crittenden, 2010). The coder was also independent to the study team and blind to the specific aims of the study and women's mental health status. The interaction patterns of interest for the current analysis included maternal sensitivity and unresponsive maternal patterns based on previous mixed findings (Feldman et al., 2009; Kaitz et al., 2010;

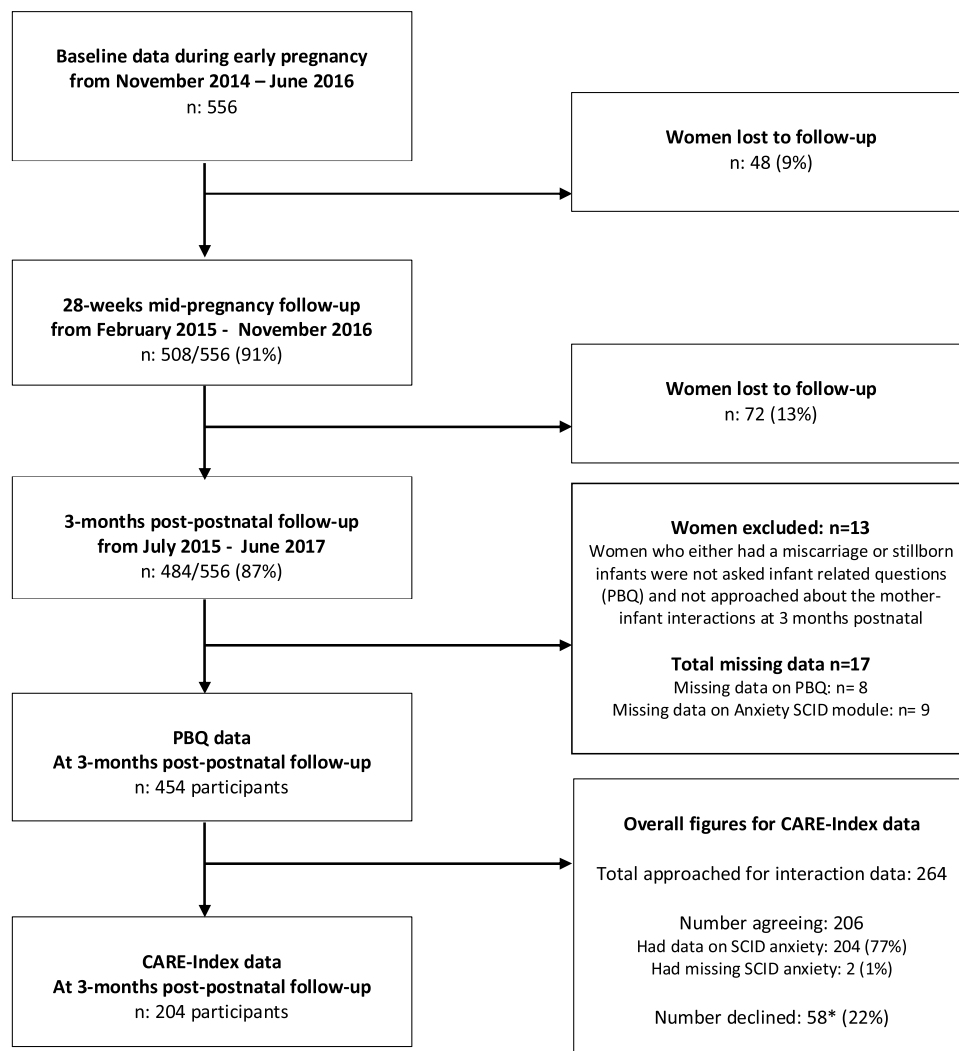


Fig. 1. Flow chart of participants through the study time points and subsample with mother-infant interaction data.

*Reasons for declining mother-infant interactions:

- 32 (55%) Uncomfortable with being recorded/videotaped.
- 3 (5%) Declined home visit or any form of face-to-face visit.
- 3 (5%) Baby father did not want baby to be recorded/videotaped.
- 4 (7%) Baby asleep during home visit and mother did not want another home visit.
- 1 (2%) Other children upset at home visit.
- 2 (3%) Mother or baby not well during home visit and did not want another home visit.
- 1 (2%) Technical problem.
- 12 (21%) Other e.g. woman did not want interpreter.

Murray et al., 2007; Warren et al., 2003; Weinberg & Tronick, 1998), as well as cooperative and passive infant patterns (description of patterns are in eTable 1 in the Supplement).

2.2.4. Sociodemographic characteristics

Information about maternal age and education were obtained at the baseline interview. Age in years was treated as a continuous variable and education was divided into three categories (none/school level, College/Diploma/Higher Certificate/training and degree level/post-graduate qualification). Information regarding infant date of birth (to calculate gestational age at birth) was collected during the 3-month home visit.

2.3. Missing data

Nine participants had missing data on the SCID anxiety module and eight participants had missing data on the PBQ questionnaire.

Therefore, 454 had complete data on the PBQ and SCID anxiety module. There was missing data on one infant date of birth. The EPDS also had some missing data at baseline (11 had 1–3 items missing and 5 had all items missing) and mid-pregnancy (5 had 1–3 items missing and 1 had all items missing). Consistent with our previous method of dealing with missing EPDS data (Howard et al., 2018), predictive mean matching option in Stata (v15.0) was used to impute missing EPDS data where women had 1–3 items (10–30%) missing. Of the participants that provided mother-infant interaction data, 2 had missing data on the SCID anxiety module. There were no other missing data for the variables of interest used in the analysis. We used a complete case analysis for multivariable models.

2.4. Statistical analysis plan

Data management and analyze were conducted using Stata v.15. Representativeness of the sample was checked by comparing basic

Table 1
Characteristics of mothers and infants in the sample with PBQ data (n = 454) and of the sub-sample with additional mother-infant interaction CARE-Index data (n = 204); by mother with and without anxiety disorders.

	PBQ data (N = 454)				CARE-Index data (Sub-sample, n = 204)									
	No anxiety disorder N = 356		Anxiety disorder N = 98	t/X ² (df)	p	Overall (total) N = 454		No anxiety disorder N = 140		Anxiety disorder N = 64	t/X ² (df)	p	Overall (total) N = 204	
Maternal mental health														
Depressive symptoms across pregnancy EPDS														
Mean	6.77	12.30	-9.90(452)	< 0.001	7.97	7.54	12.59	-6.63(202)	< 0.001	9.12				
SD	4.71	5.50			5.39	5.01	5.12			5.55				
Range	0 - 23	1 - 28			0 - 28	0 - 22	1 - 28			0 - 28				
Median	6	12			7	7	12			9				
IQR	7	8			8	6	7.5			8				
Borderline personality disorder (SCID)														
No	N	N			N	N	N			N	%		N	%
Yes	350	94	2.05(1)	0.152	444	98%	137	98%	61	95%	0.99(1)	0.318	198	97%
	6	4			10	4%	3	2%	3	5%			6	3%
Eating disorder (SCID) ^a														
No	350	92	3.87(1)	0.049	442	98%	138	99%	60	94%	3.58(1)	0.059	198	97%
Yes	6	5			11	2%	2	1%	4	6%			6	3%
Depressive disorder (SCID) ^b														
No	295	39	73.30(1)	< 0.001	334	74%	99	71%	23	36%	22.10(1)	< 0.001	112	60%
Yes	61	59			120	59%	44	29%	41	64%			82	40%
Maternal characteristics														
Age (years)														
Mean	33.05	32.17	1.45(452)	0.148	32.86	32.85	31.90	1.20(202)	0.232	32.55				
SD	5.05	6.27			5.35	4.62	6.39			5.24				
Range	18 - 46	19 - 48			18 - 48	22 - 43	19 - 45			19 - 45				
Median	33.45	33.32			33.40	32.94	32.98			32.94				
IQR	7.00	8.25			7.31	6.63	8.51			7.13				
Education														
None/school qualifications	N	N			N	N	N			N	%		N	%
College/Diploma/Higher/Certificate/training	31	16	4.92(2)	0.086	47	10%	11	8%	12	19%	5.22(2)	0.074	23	11%
Degree level/ Postgraduate qualifications	128	34			162	36%	53	38%	21	33%			74	36%
Translator required	197	48			245	54%	76	54%	31	48%			107	52%
Employment status ^c														
No	334	89	1.08(1)	0.296	423	93%	130	93%	60	94%	0.05(1)	0.815	190	93%
Yes	22	9			31	7%	10	7%	4	6%			14	7%
Employment status ^c														
Employed	238	64	5.74(4)	0.245	302	67%	96	69%	42	67%	5.50(4)	0.212	138	68%
Student	17	2			19	4%	3	2%	2	3%			5	3%
Unemployed	37	12			49	11%	13	9%	8	13%			21	10%
Homemaker	45	9			54	12%	22	16%	5	8%			27	13%
Not working due to illness/Other	18	10			28	6%	5	4%	6	9%			11	6%
Income ^d														
< £15000	34	20	10.77(4)	0.041	54	15%	18	16%	12	24%	5.28(4)	0.260	30	18%
£15,000-£30,999	47	13			60	17%	18	16%	7	14%			25	15%
£31,000-£45,999	45	10			55	15%	14	12%	9	18%			23	14%
£46,000-£60,999	45	11			56	16%	15	13%	8	16%			23	14%
£61,000 or more	111	21			132	37%	50	43%	13	27%			63	38%
Relationship status														
In a relationship/marriage/cohabiting	321	83	2.35(1)	0.125	404	89%	125	89%	55	86%	0.47(1)	0.491	180	88%
Single/separated/divorced/widowed	35	15			50	11%	15	11%	9	14%			24	12%
Have older children														
No	173	50	0.18(1)	0.671	223	49%	62	44%	35	55%	1.91(1)	0.167	97	48%
Yes	183	48			231	51%	78	56%	29	45%			107	52%
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Table 1 (continued)

	PBQ data (N = 454)				CARE-Index data (Sub-sample, n = 204)			
	No anxiety disorder N = 356	Anxiety disorder N = 98	$t/X^2(df)$	p	Overall (total) N = 454	No anxiety disorder N = 140	Anxiety disorder N = 64	Overall (total) N = 204
Infant characteristics								
Gestational age at birth (weeks) ^e								
Mean	39.26	38.84	1.77(451)	0.077	39.17	39.44	38.89	39.27
SD	1.90	2.61			2.08	1.47	2.52	1.88
Range	24 - 42	25 - 42			24 - 42	33 - 42	25 - 42	25 - 42
Median	40	39			40	40	39	40
IQR	1	2			1	2	2	1
Birth weight (grams) ^f								
Mean	3335	3295	0.62(448)	0.539	3327.23	3385	3266	3347.59
SD	537.02	699.75			575.38	468.69	614.97	520.32
Range	490 - 4620	360 - 4720			360 - 4720	1596 - 4504	778 - 4205	778 - 4504
Median	3395	4360			3360	3420	3270	3375
IQR	590	770			630	580	710	630
Infant age (weeks) ^e								
Mean	15.30	15.73	-0.54(451)	0.123	15.39	15.71	16.07	15.82
SD	2.38	2.55			2.42	2.52	2.78	2.60
Range	11 - 24	11 - 23			11 - 24	11.57 - 23.14	11.14 - 23.14	11.14 - 23.14
Median	15	15			15	15	16	12
IQR	3	3			3	3	4	3.5
Infant gender ^g								
Female	N 178	N 49	% 50%	0.980	N 227	N 74	N 36	N 110
Male	177	49	50%	0.00(1)	226	66	28	94

^aEating disorders grouping included women that met SCID criteria for current anorexia nervosa, atypical anorexia nervosa, bulimia, binge eating disorder, purging disorder and/or other specified feeding or eating disorder.

^bDepressive disorder grouping included women that met SCID criteria for current major depressive episode and/or major depressive disorder.

^cTwo participants had missing data on employment.

^d97 participants had missing data on income (for those that had PBQ data) and 40 participants had missing data on income (for those that had CARE-Index data).

^eOne participant had missing data on infant date of birth so infant gestational age at birth and age in weeks could not be calculated.

^fThere was missing birthweight data on 4 infants.

^gOne participant had missing infant gender data.

demographics of women in the base population (women booking at the maternity site during the study recruitment period) with samples used in the analysis of outcomes PBQ and mother-infant interaction. Sociodemographic characteristics of women with antenatal anxiety disorders vs women without anxiety were compared using independent samples *t* test for continuous variables, and chi-square tests (or Fisher's exact-test for cells $n < 5$) for categorical variables. Outcome variables PBQ score and CARE-Index patterns (maternal sensitivity, maternal unresponsiveness, infant cooperativeness and infant passivity) were initially checked by tabulating means and standard deviations. Pearson correlations were used to check inter-correlations between the PBQ and CARE-Index.

Unadjusted linear regression was run to investigate the association between maternal antenatal anxiety disorders and maternal self-reports of bonding with infants (PBQ score) (model 1). Potential confounding variables were chosen *a priori* and based on previous literature (Stein et al., 2014). On this basis, the multivariable regression analysis (model 2) adjusted for maternal age, education and infant gestational age at birth. In a final step, we investigated whether any associations were also independent of continuous maternal depressive symptoms during pregnancy using the EPDS measure (model 3). Using the subsample with complete SCID anxiety disorder and mother-infant interaction data (CARE-Index scores, $n = 204$), regression models (models 1, 2 and 3) were repeated for mother-infant interaction patterns as outcomes (maternal sensitivity, maternal unresponsiveness, infant cooperativeness, and infant passivity).

To investigate the potential association between comorbid anxiety and depressive disorder during pregnancy and mother-infant relationship quality, regression models were repeated with the exposure of comorbid anxiety and depressive disorder and outcomes self-reported bonding problems (model 4) and observational maternal sensitivity (model 5). The exposure variable consisted of 4 groups according to SCID diagnosis of any anxiety disorder or depressive disorder; i.e. no anxiety/no depression, anxiety only/no depression, no anxiety/only depression, or comorbid anxiety and depression.

Prior to analysis, outcome data were checked for accuracy, missing data, outliers and normality. All outcome variables were skewed. Therefore, a sensitivity analysis was conducted on models 2–5 using log transformations for outcome measures that were significantly associated with maternal anxiety disorder. The transformed outcome replicated the main findings, thus untransformed results are presented to facilitate interpretability of the findings.

3. Results

3.1. Sample representativeness

Comparison of key demographics on age, ethnicity and number of children between the base population ($n = 9963$), study baseline sample ($n = 556$), sample with PBQ data ($n = 454$) and those with mother-infant interaction ($n = 204$) data are presented in eTable 2 in the Supplement. The baseline sample demographics were broadly similar to those in the base population. Samples used in the analyses with the outcomes PBQ data were slightly older and more were from white ethnic background, compared to the baseline sample that were not included in the PBQ data analysis. Whereas, there were no significant differences between those with mother-infant interaction data and those who were in the baseline sample but not included in the mother-infant interaction analysis.

3.2. Descriptive statistics

Of the women with complete SCID anxiety module and PBQ data ($n = 454$), 98 (22%) met criteria for an anxiety disorder (GAD $n = 48$, PD $n = 3$, social phobia $n = 14$, agoraphobia $n = 1$, OCD $n = 11$, PTSD

$n = 8$, two or more comorbid anxiety disorder $n = 13$) and 356 (78%) did not. On examination of comorbidity with depressive disorder (SCID), 39 women (9%) met criterion for an only anxiety disorder and no depressive disorder, 61 (13%) had only depressive disorder, 59 (13%) had comorbid anxiety and depressive disorder, and 295 (65%) had no anxiety or depressive disorder. Women with anxiety disorders were more likely to have a lower income, depressive disorder (SCID), higher depressive symptoms during pregnancy (EPDS continuous score) and marginally more likely to have an eating disorder (SCID) compared to women without anxiety disorder (see Table 1 for report of maternal mental health, sociodemographic and infant characteristics comparing mothers with and without anxiety disorders). There were no other differences in sociodemographic characteristics (see Table 1).

Of the 204 dyads who provided mother-infant interaction data, 64 women (31%) met criteria for anxiety disorders (GAD $n = 35$, PD $n = 3$, social phobia $n = 7$, agoraphobia $n = 1$, OCD $n = 5$, PTSD $n = 7$, two or more comorbid anxiety disorder $n = 6$) and 140 (69%) did not. On examining comorbidity with depressive disorders (SCID), 23 women (11%) met criterion for only anxiety disorder and no depressive disorder, 41 (20%) for only depressive disorder, 41 (20%) for comorbid anxiety and depressive disorder, and 99 (49%) had no anxiety and no depressive disorder. As shown in Table 1, there were no significant differences in this sub-sample between mothers with and without an anxiety disorder on any of the sociodemographic factors considered or infant characteristics, but mothers with anxiety disorder had higher depressive symptoms (EPDS continuous score) and depressive disorder (SCID) compared to mothers without anxiety disorder (see Table 1).

Table 2 presents descriptive statistics for the outcome variables PBQ and mother-infant interaction CARE-Index patterns. Correlations between PBQ scores and mother-infant interaction CARE-Index patterns are presented in eTable 3 in the Supplement. There were no significant associations between maternal perceptions of bonding (PBQ scores) and mother-infant interactions (CARE-Index patterns). As expected, there were high correlations between maternal sensitivity and infant cooperation and also between maternal unresponsiveness and infant passivity.

3.3. Unadjusted univariate analysis

In the unadjusted linear regression analysis, anxiety disorders during pregnancy were associated with self-reports of higher bonding problems but were not associated with any observed mother-infant interaction patterns (Table 3, model 1).

3.4. Multivariable regression analysis

After adjusting for maternal sociodemographic factors (age and education) and infant gestational age at birth, maternal anxiety disorder continued to be associated with higher self-reports of bonding problems (Table 3, model 2). However, after further adjusting for maternal EPDS depressive symptoms during pregnancy (Table 3, model 3), there was no longer evidence for an independent association between maternal anxiety disorder and impaired bonding. See eTable 4 in the Supplement for presentation of all variables in model 3. Higher EPDS depressive symptoms and higher education level both remained significantly associated with perceived bonding problems. The overall model's adjusted R^2 fit was 6%. With regards to the observational data, maternal anxiety disorders were not associated with maternal sensitivity, although higher levels of depressive symptoms and younger age were associated with lower maternal sensitivity in the final adjusted model (see eTable 4 in the Supplement). In order to investigate the association between GAD and mother-infant relationship, we conducted a post hoc analysis which repeated models 1, 2 and 3 with maternal antenatal GAD as the exposure and outcomes maternal self-reports of

Table 2

Descriptive of PBQ and mother-infant interaction CARE-Index patterns (outcomes) of those with and without anxiety disorders.

Outcome	No anxiety disorder	Anxiety disorder	t/X ² (df)	p	Overall (total)
Mother's perception of bonding (PBQ score)					
N	356	98			454
Mean	7.15	9.30	-2.49(452)	0.013	7.62
SD	7.32	8.45			7.62
Range	0 – 55	0 – 43			0 – 55
Median	5	7			5
IQR	8	8			9
Mother-Infant interaction patterns					
N	140	64			204
Maternal sensitivity					
Mean	4.29	3.81	1.10(202)	0.271	4.14
SD	3.00	2.61			2.88
Range	0 – 13	0 – 13			0 – 13
Median	4	4			4
IQR	4	3			4
Maternal unresponsiveness					
Mean	5.92	6.45	-1.00(202)	0.321	6.09
SD	3.49	3.65			3.54
Range	0 – 14	0 – 13			0 – 14
Median	6	6			6
IQR	6	5			6
Infant cooperation					
Mean	3.23	2.61	1.40(202)	0.163	3.04
SD	3.20	2.64			2.97
Range	0 – 13	0 – 12			0 – 13
Median	3	2			2
IQR	3	4			3
Infant passive					
Mean	3.57	4.45	2.38(202)	0.162	3.85
SD	3.99	4.55			4.18
Range	0 – 14	0 – 14			0 – 14
Median	3	4			3
IQR	7	9			7

bonding (PBQ score) and observational mother-infant interaction (CARE-Index scores). Findings for all regression models (1, 2 & 3) were similar to the main findings of exposure anxiety disorder on mother-infant relationships (see eTable 5 in the Supplement).

Table 3

Associations between maternal anxiety disorder and mother-infant bonding (maternal self-report PBQ and mother-infant interaction CARE-Index patterns) (continuous outcomes).

Outcomes	Model 1 Unadjusted			Model 2 Adjusting for confounding maternal and infant factors ^a			Model 3 Adjusting for confounding maternal and infant factors, and pregnancy depressive symptoms ^b		
	Coefficient	95%CI	p	Coefficient	95%CI	p	Coefficient	95%CI	p
PBQ (self-report) (n = 454)	2.15	0.45 – 3.84	0.013	2.42	0.71 – 4.13	0.006	0.92	-0.93 – 2.76	0.329
Mother-infant patterns (n = 204)									
Mother patterns									
Sensitive	-0.48	-1.34 – 0.38	0.271	-0.32	-1.17 – 0.53	0.460	0.07	-0.86 – 1.00	0.878
Unresponsiveness	0.53	-0.52 – 1.59	0.321	0.53	-0.52 – 1.58	0.320	0.64	-0.51 – 1.97	0.274
Infant patterns									
Cooperative	-0.63	-1.51 – 0.26	0.163	-0.46	-1.33 – 0.42	0.306	-0.10	-1.05 – 0.86	0.843
Passive	0.88	-0.36 – 2.12	0.163	0.94	-0.29 – 2.17	0.133	1.06	-0.30 – 2.41	0.125

^a Adjusting for maternal age (continuous in years), infant gestational age at birth (continuous in weeks) and maternal education.

^b Adjusting further for mean depressive symptoms during pregnancy.

3.4.1. Comorbidities analysis

The unadjusted and adjusted regression models (adjusting for maternal age, education and infant gestational age at birth) showed that compared to women with no anxiety or depressive disorder, women with comorbid anxiety and depressive disorder and those with only depressive disorder but no anxiety reported higher bonding problems (see Table 4, model 4). Women with anxiety but no depressive disorder did not report significantly different bonding scores compared to women with no anxiety or depressive disorder. The overall model's adjusted R² fit was 5%. No associations were found between comorbid anxiety and depressive disorder and maternal sensitivity (see Table 4, model 5). The overall model's adjusted R² fit was 4%.

3.4.2. Sensitivity analysis

The sensitivity analysis replicated all of the main findings by re-running regression analysis with log transformed outcomes PBQ and maternal sensitivity. For PBQ outcome in model 2 (transformed Coef: 0.27, 95%CI: 0.10 – 0.44, p = 0.002) and model 3 (transformed Coef: 0.15, 95%CI: -0.04 – 0.33, p = 0.117), the overall models adjusted R² fit were 6%. For maternal sensitivity in model 2 (transformed Coef: -0.03, 95%CI: -0.15 – 0.09, p = 0.651) and model 3 (transformed Coef: 0.03, 95%CI: -0.10 – 0.16, p = 0.673), the overall models adjusted R² fit were 8%. Also comorbid anxiety and depression were significantly associated with log transformed PBQ outcome (model 4 - transformed Coef: 0.45, 95%CI: 0.21 – 0.63, p < 0.001, R² fit = 5%), but not associated with log transformed outcome maternal sensitivity (model 5 - transformed Coef: -0.01, 95%CI: -0.16 – 0.13, p = 0.852, R² fit = 7%).

4. Discussion

Using a prospective cohort study design, we found that mothers with anxiety disorders perceived themselves as having more bonding problems with their infants compared to mothers without anxiety disorder. After accounting for depressive symptoms during pregnancy, maternal anxiety disorders were no longer associated with mothers' perceptions of bonding problems, but depressive symptoms were. We also found that comorbid anxiety and depressive disorder was significantly associated with lower perceived bonding. Thus, depressive symptoms during pregnancy was an important driver of perceived bonding difficulties, replicating findings from previous studies conducted during the postnatal period using the same measures as the current study (EPDS and PBQ) (Edhborg, Matthiesen, Lundh, & Widström, 2005; Kerstis et al., 2016; Moehler, Brunner, Wiebel, Reck, &

Table 4

Associations between maternal comorbid anxiety and depressive disorder (SCID) and mother-infant bonding (maternal self-report PBQ and maternal sensitivity) (continuous outcomes).

Predictors	PBQ (n = 454)				Maternal sensitivity (n = 204)			
	Unadjusted		Adjusted (model 4)		Unadjusted		Adjusted (model 5)	
	Coefficient (95%CI)	p	Coefficient (95%CI)	p	Coefficient (95%CI)	p	Coefficient (95%CI)	p
Maternal comorbid anxiety & depression	Reference		Reference		Reference		Reference	
No anxiety or depression								
Anxiety only / no depression	0.81 (−0.70 – 3.33)	0.526	1.14 (−1.37 – 3.65)	0.374	−0.85 (−2.17 – 0.47)	0.205	−0.46 (−1.78 – 0.86)	0.490
No anxiety / only depression	2.50 (0.42 – 4.58)	0.018	2.74 (0.67 – 4.81)	0.010	−0.28 (−1.34 – 0.78)	0.608	0.06 (−1.00 – 1.11)	0.914
Comorbid anxiety and depression	3.74 (1.64 – 5.86)	0.001	4.06 (1.95 – 6.18)	< 0.001	−0.40 (−1.46 – 0.66)	0.460	−0.22 (−1.26 – 0.82)	0.679
Maternal Age (years)	0.06 (−0.07 – 0.19)	0.359	0.01 (−0.13 – 0.14)	0.909	0.11 (0.04 – 0.19)	0.003	0.09 (0.01 – 0.17)	0.025
Infant gestational age at birth (weeks)	−0.13 (−0.47 – 0.21)	0.463	−0.13 (−0.46 – 0.21)	0.459	0.08 (−0.14 – 0.29)	0.485	0.05 (−0.16 – 0.27)	0.619
Maternal Highest Education level								
None/school qualifications	Reference		Reference		Reference		Reference	
College/Diploma/Higher /Certificate/training	1.37 (−1.09 – 3.83)	0.135	1.74 (−0.72 – 4.20)	0.166	0.26 (−1.07 – 1.60)	0.697	−0.14 (−1.52 – 1.23)	0.839
Degree level/ Postgraduate qualifications	3.04 (0.68 – 5.41)	0.012	3.45 (1.02 – 5.89)	0.005	1.42 (0.13 – 2.70)	0.031	0.84 (−0.52 – 2.20)	0.223

Resch, 2006; Muzik et al., 2013; Tikotzky, 2016).

With regards to observational mother-infant interactions, we found anxiety disorders were not significantly associated with lower maternal sensitivity or unresponsiveness observed during mother-infant interactions, replicating some of the previously existing literature (Challacombe et al., 2016; Grant et al., 2010; Reck et al., 2018; Weinberg et al., 2008). Although the direction of effect was as expected (i.e. mothers with anxiety had lower sensitivity and higher unresponsiveness mean scores compared to non-anxious mothers). Depressive symptoms during pregnancy were associated with lower maternal sensitivity, also replicating previous findings (Murray, Halligan, & Cooper, 2010; Stein et al., 2014). We did not find comorbid anxiety and depressive disorder to be associated with lower maternal sensitivity. Thus, it appears from this study that previous associations reported between maternal anxiety disorders and adverse child outcomes (Eley et al., 2015; Glover, 2014; Newman et al., 2017; Stein et al., 2014; Telman et al., 2018), may not be mediated by poor quality of observational mother-infant interactions. Indeed, the overall model fit statistics (R^2) were low, suggesting that there are many other factors influencing mother-infant relationships which were not accounted for by our model.

One potential factor that warrants further investigation in relation to mother-infant interaction quality is maternal negative cognitions (Stein, Lehtonen, Harvey, Nicol-Harper, & Craske, 2009). Recurrent negative thought processes (referred to as worrying or rumination) are key characteristics of anxiety disorders, but differ in specific content and style (McEvoy, Watson, Watkins, & Nathan, 2013). A study where mothers with generalized anxiety disorder (GAD) were randomly allocated to a worry/rumination or neutral task prior to being observed playing with their infants, found that mothers in the post-rumination group to be less responsive (Stein et al., 2012). This suggests that when mothers with GAD have characteristic negative thinking patterns activated, interactions with their infants may be less optimal. Furthermore, there is also evidence to suggest associations between mothers' repetitive negative thinking patterns and lower self-reported bonding (Schmidt et al., 2017). Cognitions in other anxiety disorders may be activated by different tasks or situations. Therefore, when asked to take part in a free-play session with their infant without activation of their specific negative thoughts (such as in the current study), the mothers' attention may be focused on the infant. Thus, women with anxiety disorders may have negative thought processes that could lead them to perceive an overall negative impact on of their bonding with their infants, but when particular negative cognitions are not active, their interactions with their infants may be similar to non-anxious mothers. This theory would require testing in future research. Other factors that

might also influence mother-infant interactions include (but are not limited to) prenatal fetal attachment (Foley & Hughes, 2018) and child temperament (Stein et al., 2014) which should be included in future research.

4.1. Strengths & limitations

Strengths of this study include the prospective nature of the study design, which allow us to make inferences regarding the direction of associations, a validated diagnostic measure for anxiety disorders and an observational mother-infant interaction measure rated by a coder who was unaware of the study hypothesis and maternal mental health status. The sample with mother-infant interaction data were broadly representative of the base population and language interpreters were used to include non-English speaking women. Our sample size of mother-infant interactions ($n = 204$) was high in comparison to the typically small sample sizes of previous observational studies and we used a well-validated coding system which is culturally sensitive (Crittenden, 2010; Leventhal et al., 2004). The study has ecological validity as recordings of mother-infant interactions were conducted in the mothers' homes and mothers were free to choose the play activity. We also accounted for maternal education, infant gestational age at birth and maternal depressive symptoms in our analysis.

Limitations include differences between the women who self-reported on the PBQ and the base population. Women who reported on the PBQ were more likely to be older and of white ethnic background, compared to those that took part in the baseline sample who were broadly representative of the base population study site from which the women were recruited. There was a smaller subsample participating in the observed mother-infant interactions than the perceived bonding (self-reported PBQ) component, due to funding limitations. Although this may have limited statistical power, as the direction of effect for the association between antenatal anxiety disorder and observed mother-infant interactions was nevertheless as expected, our sample of mother-infant interactions ($n = 204$) is larger than most previously published studies that collected data on mother-infant interactions (Challacombe et al., 2016; Grant et al., 2010; Kaitz et al., 2010; Reck et al., 2018; Warren et al., 2003). In order to investigate the potential influence of specific anxiety disorders, we were able to conduct analysis using GAD, but were unable to conduct analysis by the other types of anxiety disorders (PD, social phobia, agoraphobia, OCD, and PTSD) as we did not have adequately large sample sizes of these anxiety disorders. The influences of anxiety disorders on mother-infant interaction could be disorder specific with different anxiety symptoms being exhibited depending on the anxiety disorder type (Murray et al., 2012). For

example, OCD might be associated with preoccupation when triggered by intrusions (Challacombe et al., 2016), whereas social phobia may only be relevant in the context of social situations around strangers (Murray et al., 2007, 2012). This is something that could be investigated in future research with larger sample sizes of mothers with specific anxiety disorders. Finally, we were unable to carry out repeated SCID assessments during the postnatal period.

4.2. Conclusions and clinical implications

In summary, our study found that mothers with anxiety disorders during pregnancy interacted with their infants as sensitively as mothers without anxiety disorders, but had negative perceptions of bonding with their infants which were accounted for by their symptoms of depression during pregnancy. Furthermore, comorbid anxiety and depression, but not anxiety alone was associated with negative perceptions of bonding. This suggests that mothers with anxiety disorders during pregnancy who later perceive their bonding to be impaired when it is not, may lack self-confidence with their infants which is influenced by their depressive symptoms. Left untreated, this may have negative implications for the parent-child relationship over time because the perceptions can influence confidence and behaviors which may eventually get picked up as the infant becomes more aware and verbal. If replicated, our findings suggest that interventions targeted at mothers with anxiety disorders during pregnancy should focus on mothers' negative perceptions of bonding and depressive symptoms in the context of preparing for motherhood. This could be delivered in an intervention tailored for mothers with antenatal anxiety disorder and if needed video-feedback during the postnatal period (Newman et al., 2017; Trevillion et al., 2016).

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Declaration of Competing Interest

None.

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Appendix A. Supplementary data

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