

**BEHAVIOURAL AND NEUROBIOLOGICAL CORRELATES OF MATERNAL
SENSITIVITY IN HEALTHY NEW MOTHERS**

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SCHOOL OF MEDICINE

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LIST OF DEFINITIONS

Antagonist: A chemical that acts by reducing the physiological activity of another chemical substance

Antenatal: The period of gestation (refers to the infant)

Antepartum: The period of time before birth (refers to the mother)

Multigravida: A pregnant woman who had a previous pregnancy

Multiparous: A woman who has given birth more than once

Nulliparous: Has not given birth previously

Parity: The number of times that a woman has given birth to a fetus

Parturition: The process of giving birth

Perinatal: The period of time around an infant's birth

Postnatal: The period immediately after birth (refers to the infant)

Postpartum: The period of time following birth (refers to the mother)

Primigravida: A woman during her first pregnancy

Primiparous: A woman who has given birth once

LIST OF ABBREVIATIONS

AAI: Adult Attachment Interview

ANOVA: Analysis Of Variance

AVP: Vasopressin

BA: Brodmann's Area

BNST: Bed Nucleus of Stria Terminalis

BOLD: Blood Oxygenation Level

Dependence

CSD: Caesarean Section Delivery

CTQ: Child Trauma Questionnaire

DNA: Deoxyribonucleic acid

EPDS: Edinburgh Postnatal Depression
Scale

FDR: False Discovery Rate

fMRI: functional Magnetic Resonance
Imaging

FWE: Family Wise Error

HADS: Hospital Anxiety and Depression
Scale

HSMs: High Sensitivity Mothers

IBQ-R-v. short: Infant Behaviour
Questionnaire Revised very short form

LG-ABN: Licking and Grooming –Arched
Back Nursing (i.e. maternal care in animal)

LSMs: Low Sensitivity Mothers

MAAS: Maternal Antenatal Attachment
Scale

MACI: Manchester Assessment of
Caregiver-Infant Interaction

MBQS: Maternal Behaviour Q-sort

MFA: Maternal Fetal Attachment

MFAS: Maternal Fetal Attachment
Scale

MFR: Maternal Fetal Relationship

MII: Mother-infant interaction

MPOA: Medial preoptic area

NAcc: Nucleus Accumbens

NICHD: National Institute of Child
Health and Human Development

OT: Oxytocin

OTKO: Oxytocin knockout

OTR: Oxytocin Receptor

PAI: Prenatal Attachment Inventory

PBI: Parental Bonding Instrument

PVN: Paraventricular Nucleus

ROI: Region of Interest Analysis

SD: Standard Deviation

SES: Socioeconomic status

SON: Supraoptic nucleus

STAI-T: State Trait Anxiety
Inventory

VD: Vaginal Delivery

VTa: Ventral Tegmental Area

WTCRF: The Wellcome Trust
Clinical Research Facility

Behavioural and Neurobiological Correlates of Maternal Sensitivity in Healthy New Mothers

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ABSTRACT

Background: In spite of the importance of maternal sensitivity as a construct that fosters secure attachment and promotes a child's social and cognitive development, no routine clinical screening currently identifies mothers at risk of poor maternal sensitivity. This is partly because researchers have not identified all the factors that influence maternal sensitivity. As a result, parenting interventions to promote maternal sensitivity and optimise child outcomes tend to focus on clinical groups. Thus, more attention is needed to identify possible determinant factors. The neurobiological mechanisms underlying natural variation in maternal sensitivity (i.e. sensitive and less sensitive mothers) are poorly understood, especially the putative role of the hormone Oxytocin (OT). Literature has suggested that this variation in maternal sensitivity is an outcome of interaction between maternal OT, as well as social factors (e.g. perceived parenting) and this interaction charts the discrete profile of the maternal brain that is mediated by stress- and reward-related neural systems. To date no study examined for the neurobiological correlates of maternal sensitivity in a distinct group of mothers representing natural variations in maternal sensitivity. **Methods:** Out of 105 women recruited from community antenatal clinics during their pregnancy, to complete a set of self-reported questionnaires assessing their psychosocial characteristics, a total of 80 new (i.e. early postpartum) mothers and their infants were followed up and underwent evaluation of maternal sensitivity at 4-6 months postpartum. Using a stepwise regression, we examined for predictors of maternal sensitivity among the sample (Study I). Later, at 7-9 months postpartum, 30 mothers, representing extremes in maternal sensitivity, were selected from this sample of 80: 15 mothers with higher scores (high sensitivity mothers - HSMs), and 15 with lower scores for maternal sensitivity (low sensitivity mothers - LSMs), underwent functional Magnetic Resonance Imaging (fMRI) to examine their brain responses when viewing videos of their own and an unknown infant. Maternal plasma OT levels were also measured before and following an interactive play with their infant (Study II). **Results:** Mothers' self-reported experience of own parental care, and household income, independently predicted maternal sensitivity, accounting for 17% of the variance. Comparing mothers grouped by maternal sensitivity level, HSMs showed a drop in their plasma OT levels following the interaction with their infant. HSMs also showed significant brain activation in the right superior temporal gyrus in response to own infant (compared to unknown infant) when compared to LSMs. By contrast LSMs did not show any change in their plasma OT levels following interaction with their infant, and their brain responses to own infant did not show any significant brain activation when compared to HSMs. **Conclusions:** The findings may have implications for future novel approaches for early assessment of mothers at risk of low maternal sensitivity so they could be targeted by specialised assessments and consequently interventions to improve their parenting (Study I). Maternal sensitivity is accompanied by neural correlates that could act as a biomarker for future intervention studies that target vulnerable mothers (Study II).

DECLARATION

The author declares that no portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning

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DEDICATION

To the precious memory of my loving parents, whom I miss beyond words and whose words of encouragement ring in my ears.

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THE AUTHOR

Alya Elmadih graduated in 2002 from the Faculty of Medicine, University of Khartoum, Sudan. Following her graduation, she worked in a range of medical specialities before she moved to the UK in 2006, where she passed The Professional and Linguistic Assessments Board (PLAB) exam and obtained full registration with the General Medical Council. Through her university years and early career years, Alya found a special interest in academic work and decided to complete a PhD to combine her academic interest with her career. Given her passion about psychiatry, Alya has been secured a placement in the psychiatry speciality training programme and she is due to start her training in August 2013, hoping to pursue a career in child and adolescent psychiatry.

Chapter 1: **General introduction**

1.1. Background

Maternal sensitivity is generally considered within developmental psychology as a mother's "ability for perception, accurate interpretation of baby's signals, and appropriate responsiveness" (Ainsworth et al., 1978). The degree of appropriateness and responsiveness in fine-grained maternal behaviours during interaction with their infants, in quality as well as quantity, is distinct from parenting style or maternal caregiving, though the two are usually thought to be related (Mercer & Ferketich, 1995; Meins, 1997; Demers et al., 2010). A sensitive mother responds properly to her infant's displayed emotions by affirming positive emotions and reassuring in the context of negative ones (Sroufe, 2000). She also knows whether her behaviour is or is not adequate for her infant's needs (Kivijarvi et al., 2001) and modifies her responses accordingly in keeping with current circumstances and the child's developmental level (Pianta et al., 1989).

Such vigilance by the mother allows her to titrate responses appropriately, which gradually facilitates the child's exploratory interface with the novel world and allows the child time to adjust to and explore new situations (if appropriate) (Lohaus et al., 2004). Such flexibility of maternal sensitivity around the infant's needs does not affect the high face validity and moderate to high stability of the maternal sensitivity construct; indeed, these aspects allow it to be measured longitudinally and across different situations (De Wolff & Ijzendoorn, 1997; Lindhiem et al., 2011).

Evidence consistently supports the role of maternal sensitivity in fostering secure attachment (Ainsworth et al., 1978; Pederson et al., 1998) and in promoting the child's social, emotional and cognitive development (Kemppinen et al., 2006; Landry et al.,

2001; Lohaus et al., 2001; Mills-Koonce et al., 2007; Warren & Simmens, 2005). Low maternal sensitivity, however, may be associated with poorer infant outcomes (Alink et al., 2008; Downer & Pianta, 2006; Kochanska & Kim, 2012). Such outcomes might include behavioural problems (Alink et al., 2008; Kochanska & Kim, 2012) and poor school performance (Downer & Pianta, 2006). Low sensitivity may be associated with ‘harsh’ or even abusive parenting (Joosen et al., 2012; Lindhiem et al., 2011), which in its turn results in a range of mental disorders when children reach adulthood (see review by Norman et al., 2012).

This thesis aimed to provide better understanding for the natural variation in maternal sensitivity by examining healthy new (i.e. early postpartum) mothers. The thesis comprises two studies, Study I and Study II. The time frame for the data collection is presented in Figure 1.1.

1.1.1. Study I (Chapter 2-5 & Publication 1)

Natural variation in maternal sensitivity: What are the possible prenatal and postnatal predictors in healthy new (early postpartum) mothers?

Much research suggests that parenting interventions can be effective at improving maternal sensitivity (e.g. Bakermans-Kranenburg et al., 2003); however, their translation into service delivery has been very limited. This is in part due to two key reasons: First, no routine clinical screening currently identifies mothers at risk of poor maternal sensitivity. As a result, parenting interventions to promote maternal sensitivity and optimise child outcomes tend to focus on clinical groups (e.g. mothers with mental illness) (Murray et al., 2003; Forman et al., 2007; Barlow et al., 2008); or be promoted as a general population parenting measure such as the recent ‘CAN parent scheme’ (Parent scheme from Government, 2012). Second, to date, researchers have not identified all the factors that influence maternal sensitivity and study findings have been

somewhat inconsistent (Drake et al., 2007). This is possibly because of inconsistent measures used to examine maternal sensitivity that range from self-reporting (Shin et al., 2006; Drake et al., 2007) to observational measures (Downer & Pianta, 2006; Moore et al., 2009; Strathearn et al., 2012). In addition, some factors were examined more than others (Evans, 2008).

Previous studies suggested the following broad factors were related to maternal sensitivity: (1) social context (such as socioeconomic status (SES) and social support); (2) maternal prenatal mental state (such as anxiety, depression, and attachment to the fetus); (3) early care experiences of the mother in her family of origin; and (4) obstetric characteristics and infant temperament.

Firstly, evidence to date suggests that the most robust finding is a positive association between maternal sensitivity and SES (Evans, 2008), including maternal education (Pederson et al., 1990; Sacker et al., 2002) – with higher SES or education conferring a tendency to higher maternal sensitivity. Socioeconomic and educational variables may confer a range of advantages such that lower SES exposes the mother to a range of environmental risk factors and deprivations that challenge their sensitivity and emotional capacity (McAdoo, 2002; Evans, 2008). Social support, including partner support, may have a ‘buffering effect’ which prevents or alleviates the perception of parenting as a stressor (Andresen & Telleen, 1992). Social support has been positively associated with maternal sensitivity in studies of postnatal mothers (e.g. Pauli-Pott et al., 2003) and in a prenatal study which used self-rated measures of maternal sensitivity (Shin et al., 2006).

Secondly, a depressive mood and anxiety, even at non-clinical levels, impairs the communication of emotions between the mother and her infant (Blumberg, 1980, see Tronick & Reck, 2009). Studies have found a significant correlation between higher

postnatal maternal depression scores and lower maternal sensitivity in a community sample (Campbell et al. 2007; Mills-Koonce et al., 2008). Although a large body of research suggests that depression and anxiety impede maternal sensitivity (e.g. Campbell et al., 2007), the focus of much maternal depression research has been concerned with its impact on infant health and development without measuring maternal sensitivity (e.g. Kaplan et al., 2008). In addition, only a few focus on examining the impact of anxiety on maternal sensitivity (Nicol-Harper et al., 2007). Feelings of maternal ‘attachment’ towards the unborn child (Muller, 1996; Mercer & Ferketich, 1990) have also been associated with the quality of maternal interaction in community samples (Bloom, 1995; Siddiqui & Hagglof, 2000).

Thirdly, consistent with the ‘internal working model’ of attachment theory (Bowlby, 1969), early positive care experiences provide adults with the emotional and cognitive resources, and broader social learning, to provide sensitive caregiving themselves (Lindhiem et al., 2011). By contrast, experience of poor care, neglect and trauma in childhood confer later difficulties in parenting and maternal sensitivity to their own infants (Cicchetti et al., 2006). Fourthly, evidence relating obstetric variables (e.g. mode of delivery, feeding) to maternal sensitivity are inconsistent (Kuzela et al., 1990; Poindron, 2005) and need further exploration. Similarly, studies examining the role of difficult infant temperaments in low sensitive mothering have revealed mixed results (Crockenberg, 1981; Sroufe, 1985; Ghera et al., 2006). Therefore, while some suggest highly irritable infants make sensitive mothering more challenging (Crockenberg, 1981; Van den Boom, 1991; Van Ijzendoorn et al., 2007), others suggest the opposite (see review by Crockenberg, 1986).

Further exploration of the variables that could influence maternal sensitivity is important. We focused on the prenatal or early postnatal determinants of maternal

sensitivity in order to i) allow for early interventions to be targeted at those most in need; ii) modify maladaptive patterns of interaction before they become ‘ingrained’ and iii) optimise interaction during critical periods when the infant brain shows relative plasticity to positive change (see review by Kolb et al., 2011).

Study I of this thesis asks whether reliably and easily identifiable factors available prenatally or postnatally could predict future maternal sensitivity. The primary aim of Study I, therefore, was to provide evidence that would feed into future development of an easy screening of mothers at risk of low maternal sensitivity in clinical settings. This would enable us to refine assessments of risk for poor maternal sensitivity and facilitate early identification of at-risk women so they could be considered for a specialised assessment of maternal behaviour. A secondary aim was to provide detailed information of maternal psych-socio-demographic characteristics for Study II of this thesis that would investigate the neurobiological mechanism underlying natural variation of maternal sensitivity.

Using a sample of Caucasian UK mothers with no history of mental illness, we examined whether a range of psycho-socio-demographic factors (collected in the third trimester of pregnancy and at early postnatal period) could predict the level of maternal sensitivity assessed through play interaction at 4-6 months postpartum. Out of 148 women recruited from community antenatal clinics during their pregnancy, 105 women met the eligibility criteria and enrolled during their third trimester of pregnancy (mean = 33.90 antepartum weeks; SD = 3.19) ‘Time 1’. During a 35 minute interview, women completed a set of self-reported, validated questionnaires which assessed their perceived parenting experience in family of origin, mood (depression, anxiety), social support, their relationship (attachment) to their fetus, and childhood trauma (collated at a later stage). Demographic characteristics were also collected. When the infant was 4-6

months (mean = 19.36 postpartum weeks; SD = 2.46), 'Time 2', 80 mothers were visited at their homes for one hour to videotape a 6 minute interactive play between mothers and their infant. The interaction was later rated for maternal sensitivity. Within the same visit, mothers also reported their mood, the infant's temperamental behaviour, mode of delivery and feeding. Later, the predictive value of the assessed variables on maternal sensitivity was determined through a stepwise regression analysis.

In accordance with the rationale of the study (examining for predictors of maternal sensitivity in healthy women), we recruited from community antenatal clinics to avoid the high risk pregnancies associated with hospital antenatal clinics. Women were recruited prenatally because: First, we wanted to include a measure of maternal fetal attachment to see if it is related to maternal sensitivity later during postpartum. Second, response bias would also be minimised when 'potential participants' (i.e. women who fulfil the main inclusion criteria) were referred through their midwives rather than through advertisements. Third, we wanted to determine the clinical feasibility of collecting measures prenatally as this represents an ideal time for screening mothers. Chapter 2 includes the literature review, followed by methodology (Chapter 3), results (Chapter 4), and discussion (Chapter 5) for this study (i.e. Study I).

1.1.2. Study II (Chapter 6-10 & publication 2 & 3)

Neurobiological mechanisms underlying maternal behaviour in humans: Do the brain and endocrine responses to infant stimuli in less sensitive mothers differ from those in sensitive mothers?

Research in rodents and other mammals has highlighted the importance of the hormone oxytocin (OT) to facilitate the onset and maintenance of maternal behaviour (Insel, 1990; Rosenblatt et al., 1998; Champagne et al., 2001, 2003, 2007; Champagne, 2008). Greater levels of this hormone have been linked to greater maternal caregiving. For

example, among high ‘licking and grooming’ (i.e. high maternal caregiving) female dams, significantly higher levels of OT receptors were seen in brain regions implicated in the expression of maternal behaviour across species, during pregnancy, at parturition and when nursing pups (Champagne et al., 2001).

Recent evidence from human studies also suggests that higher levels of plasma OT are found in mothers who report higher maternal fetal attachment during pregnancy (Levine et al., 2007) and who show greater affectionate behaviours (such as gaze, vocalisations and positive affect) towards infant at postpartum (Feldman et al., 2007, 2010a; Gordon et al., 2010). Maternal synchrony (i.e. episodes when mother and infant coordinate their positive social engagement) was also reported to be positively correlated with the maternal plasma OT level, while maternal intrusiveness (i.e. inappropriate response from mother) was not (Atzil et al., 2011). OT levels have also been examined in relation to maternal own attachment experience (Strathearn et al., 2009). Higher levels of plasma OT were found among mothers who have secure attachment patterns with their own mothers compared to those with insecure attachment patterns (Strathearn et al., 2009). Even among non-parents, plasma OT levels have been positively correlated with self-reported parental care (Gordon et al., 2008; Feldman et al., 2012).

Recent evidence suggests a separate, but related, role for OT in the regulation of stress responses and this also appears to be related to previous experiences and difficulties in interpersonal relationships (Tabak et al., 2011). This includes difficulties in relationships with own mothers (Taylor et al., 2006; Feldman et al., 2011), own infant (i.e. interactive stress) (Feldman et al., 2011), or romantic partner (Marazziti et al., 2006; Taylor et al., 2010; Feldman et al., 2011). All these studies have reported higher levels of peripheral OT (i.e. plasma or urine) in relation to stress in these social

relationships. Thus, while OT appears to be an indicator of social affiliation, it might also be a 'signal' for the need to affiliate with others (Taylor et al., 2010).

Evidence linking OT to maternal behaviour in mothers requires further examination in mothers whose parenting behaviour has been rigorously defined considering the construct of maternal sensitivity which includes the quality of the interaction relationship with own infant. Furthermore, the link between OT and maternal behaviour should be examined in the light of early perceived parenting experience (Bartz et al., 2011; Strathearn et al., 2012). Feldman et al. (2011) is the only study examining maternal OT levels in relation to distress and poor mother-infant play relationships. However, maternal sensitivity was not rigorously defined, and OT elevation was only evidenced in urine.

Studies using functional magnetic resonance imaging (fMRI) in parenting research report a complex set of circuitry and neural networks in response to infant stimuli. While many studies examine maternal brain responses to infant stimuli (Lorberbaum 2002; Bartels & Zeki, 2004; Ranote et al., 2004; Noriuchi et al., 2008; Swain et al., 2008a, b; Strathearn et al., 2008; 2009), only a few recent studies have examined the neural correlates of observed maternal behaviour (Atzil et al., 2011; Musser et al., 2012). Only one study focuses on maternal sensitivity (Kim et al., 2011), yet not in distinct maternal sensitivity groups. Maternal behaviour is a composite of multiple behaviours, with discrete maternal brain activation in relation to each aspect of behaviour (Musser et al., 2012). This presents the possibility of identifying distinct pathways to sensitive mothering, and of using changes in brain activation in response to infant stimuli as potential biomarkers for the development and evaluation of new diagnostic and treatment strategies in at-risk mothers (Swain, 2008b).

Over the past decade, a number of clinical studies have demonstrated the positive effect of intranasal OT (exogenous OT) on emotion recognition (e.g. Guastella et al., 2010) and affiliative behaviour between individuals (see review by Striepen et al., 2011; Riem et al., 2011), including fathers (Weisman et al., 2012). These results provide evidence for possible future OT intervention studies in vulnerable mothers with poor sensitivity. If fMRI can discriminate different patterns of brain activation between mothers at opposite ends of a spectrum of high and low maternal sensitivity and if plasma OT responses to infants correlate with this, it prepares the way for future efficient hypothesis testing of the effects of novel interventions in small numbers of normal volunteers. In other words, a distinct neural profile of ‘higher’ sensitivity mothers means functional imaging can become a ‘biomarker’ for future interventions among mothers who receive intranasal OT to improve their parenting.

In summary, the literature suggests that natural variation in patterns of maternal sensitivity (i.e. high and low maternal sensitivity) results from ‘interaction’ between maternal oxytocin as well as early and current social experiences (Landgraf et al., 1991; Strathearn et al., 2011). Such interaction then charts discrete profiles of maternal (brain) responses to infants which is mediated by neural systems regulating both stress and reward processing (Swain et al., 2007; Atzil et al., 2011).

Study II aimed to shed the light on the interplay between hormonal and neurological pathways and to extend evidence for the neurobiological basis of human parenting (Feldman et al., 2007, 2010a, b; Strathearn et al., 2009; Atzil et al., 2011). In order to achieve this, we specifically examined differences between women representative of a general community sample, in whom maternal sensitivity has been rigorously ascertained as lying at opposite ends of the scale. Variation in normal maternal sensitivity among healthy mothers was documented as well as its relationship with

fMRI blood oxygenation level dependence (BOLD) activation to infant cues and plasma OT responses to infant challenge paradigms.

To our knowledge, this is the first study to examine simultaneously maternal brain responses and plasma OT responses in two groups of mothers rigorously defined by maternal sensitivity, while accounting for demographic differences between the groups. Plasma OT levels were also examined in relation to mothers' recall of their own perceived parenting experience.

Out of 80 women who were followed up and underwent evaluation of maternal sensitivity using videoed mother-infant interaction play at 4-6 months postpartum (mean = 19.38 weeks; SD = 2.47) (Study I), a total of 30 mothers, representing extremes in maternal sensitivity, were selected to comprise the final sample for Study II at 7-9 months postpartum (mean = 35.14 weeks). Fifteen women with a mean maternal sensitivity score of 4.47 (SD = 0.74) were rated as 'sensitive' mothers (scoring 4-7 on the sensitivity scale) and 15 women with a mean maternal sensitivity score of 2.13 (SD = 0.52) were rated as 'less sensitive' mothers (scoring 1-3 on the sensitivity scale). For descriptive purposes, women rated between 4-7 are referred to as 'high sensitivity mothers' (HSMs) and those rated between 1-3 are referred to as 'low sensitivity mothers' (LSMs). Presentation of the mean sensitivity scores for HSMs and LSMs (in relation to the normal distribution of maternal sensitivity among the whole sample (N = 80) are provided in Figure 8.1 (Chapter 8).

Mothers and their infants were invited to the Wellcome Trust Clinical Research Facility (WTCRF) at 7-9 months postpartum; plasma OT levels were measured before and after 10 minutes interactive play with the infant. Mothers also underwent neurological challenge using videos block of 'Neutral', 'Happy' and 'Sad' cues of 'own infant' and an 'unknown infant' while maternal brain responses were assessed through fMRI

scanning. Plasma OT responses and BOLD activation responses were compared between the two groups (HSMs/LSMs). We also examined for a coordinated association between maternal BOLD brain activation and the post interaction level of plasma OT among mothers.

The literature review for Study II is included in Chapters 6 & 7, followed by methodology (Chapter 8), results (Chapter 9), and discussion (Chapter 10). Chapter 11 provides a summary and conclusion of the whole thesis (Study I & Study II).

1.2. Rationale for Submitting the Thesis in an Alternative Format

This thesis is submitted in an alternative (publication) format. The thesis comprises 11 chapters and 3 research manuscripts written up in paper format, all first authored by the author of this thesis, and pending submission to international, peer-reviewed journals for publication. Several reasons determined the choice of an alternative format thesis. First, the study contained novel and important findings, which could have implications for future approaches to early assessment of mothers at risk of low maternal sensitivity. The findings might also aid the development of intervention, training and support for those vulnerable mothers. Second, planning of papers helped build the scope of the thesis structure at an earlier stage, which helped to provide a more focused and coherent thesis. Third, this format has provided the author with a great learning experience by taking her through the discipline of writing research papers; this provides extensive opportunities for review (including peer reviews when the papers are submitted) and feedback that strengthens the quality of the work.

Time	Study I		Study II							
	Time 1 (Pregnancy)	Time 2 (4-6 months)	Time 3 (7-9 months)							
	N = 105	N = 80	N = 30							
Data collected	Interview <ul style="list-style-type: none">• PBI• MFAS• Oslo 3-items• HADS• EPDS• Demographics	Mother-infant interaction <ul style="list-style-type: none">• Mother-infant free play (6 min)• CTQ• IBQ-R-v.short• HADS• EPDS• Obstetric variables	<div><div><div></div><div>Oxytocin</div></div><div><div></div><div>fMRI</div></div></div> <div>Plasma OT measurements<table><tr><td>10 min</td><td>10 min</td><td>5 min</td></tr><tr><td>Mother-infant separation</td><td>Mother-infant free play</td><td></td></tr></table><div><div>OT1</div><div>OT2</div><div>OT3</div></div><ul style="list-style-type: none">• HADS• EPDS</div>		10 min	10 min	5 min	Mother-infant separation	Mother-infant free play	
	10 min	10 min	5 min							
Mother-infant separation	Mother-infant free play									

Figure 1.1. Time chart for data collection times. **Note.** PBI: Parental Bonding Instrument, MFAS: Maternal Fetal Attachment Scale, Oslo3-items: social support scale, HADS: Hospital Anxiety and Depression Scale, EPDS: Edinburgh Postnatal Depression Scale, CTQ: Childhood Trauma Questionnaire, IBQ-R-v.short: Infant Behaviour Questionnaire revised-very short form, fMRI: functional Magnetic Resonance Imaging, OT: Plasma oxytocin sample. Maternal sensitivity rating was obtained from Time 2 video record of mother-infant interaction.

1.3. Publications

The three papers included in this thesis, aimed to achieve a better understanding of the mechanisms underlying natural variation in maternal sensitivity in healthy mothers. The author has made a major contribution to the papers including data collection, analysis of results and writing up. The initial drafts of all the papers included have been written by the author of this thesis and subsequent editing in response to co-authors has also been performed by the author. All research materials included in these papers were derived from the original research undertaken in this thesis.

Publication 1: Maternal sensitivity in healthy mothers: Can at-risk maternal sensitivity be predicted prenatally?

Alya Elmadih, Kathryn M Abel, Rebecca Elliott, and Ming Wai Wan

Abstract

In spite of the large research investment and accumulating evidence that parenting interventions which optimise infant developmental and mental health can improve maternal sensitivity, translation of such knowledge into service delivery has been extremely limited. Interventions are resource-intensive; selecting groups deemed at-risk (e.g. mothers with mental illness) may not best address the general population's mental health. An alternative approach would be to identify those mothers at risk of low maternal sensitivity in the prenatal period when all early postpartum mothers make contact with services in order to facilitate delivery of effective intervention early in the postpartum. **Objectives:** The primary aim of this study was to identify prenatally determined psycho-social and demographic factors, which might predict maternal sensitivity at 6 months postpartum. A secondary aim was to examine whether the number of psycho-social and demographic factors to which mothers were exposed predicted lower maternal sensitivity. **Design:** In the third trimester, 105 healthy, pregnant women were assessed on simple self-report measures. At 4-6 months postpartum, 6 minutes of unstructured mother-infant play was videotaped during a home visit and was blind rated for maternal sensitivity using the Manchester Assessment of Caregiver-Infant Interaction (MACI). **Results:** Several prenatally-measured factors (score of depressive symptoms, experience of own parental care, parental overprotection, history of trauma, household income, and educational attainment) were associated with maternal sensitivity at 4-6 months postpartum. Only two factors (mother's own reported experience of parental care, and household income) independently predicted maternal sensitivity, accounting for 17% of the variance. The number of psychosocial risk factors also predicted lower sensitivity: mothers exposed to 3+ psychosocial risk factors were more likely to show lower sensitivity to their infants. **Conclusion:** Relatively simple prenatal 'screening' of psycho-social and demographic risk factors in healthy mothers can identify those who are more likely to be at risk of low maternal sensitivity. However, asking mothers prenatally about their general social supports or how well they are bonding with their infants did not predict maternal sensitivity. Routine assessment of key maternal factors may be a relevant adjunct to other forms of antenatal health screening.

Publication 2: Does oxytocin modulate variation in maternal caregiving in healthy new mothers?

Alya Elmadih, Ming Wai Wan, Michael Numan, Rebecca Elliott, Darragh Downey, and
Kathryn M Abel

Abstract

Background: The extent to which a mother is sensitive to her infant's cues and developmental needs ('maternal sensitivity') contributes to the infant's social and cognitive development. Animal and recent human studies emphasise a major role for the neuropeptide Oxytocin (OT) in mediating sensitive caregiving behaviours. To date, no study has examined OT in relation to extreme variations in human maternal sensitivity.

Methods: : Out of 105 expectant mothers, 80 were followed up and underwent evaluation for maternal sensitivity at 4-6 months postpartum through 6 minute-free play interaction with their infants. Of these, 30 enrolled in the current study at 7-9 months postpartum: 15 'sensitive mothers' (henceforth high sensitivity mothers – HSMs) and 15 'less sensitive mothers' (henceforth low sensitivity mothers – LSMs) underwent plasma OT measurements before and after 10 minutes of play interactions with their infants. **Results:** Consistent with studies of plasma OT and stress in women, but not with studies of plasma OT and maternal behavior in women, baseline and post-interaction plasma OT levels were lower amongst HSMs. Only HSMs showed significant change in plasma OT; with reduction following the play-interaction.

Conclusion: Higher baseline OT levels in healthy LSMs may act as a biomarker for stress response owing to the demands of caring for an infant or for a gap in own parenting relationship. OT may be acting to reduce stress and anxiety. By contrast, play interaction with their infants may be associated with reduced stress (if any) in HSMs, as suggested by a significant reduction in plasma OT. Plasma OT might represent a useful biomarker of low maternal sensitivity. Considering mothers in well-defined sensitivity groups might 'tap' on an element of a stress or anxiety coping strategy and might foster better understanding of parental caregiving behaviour and its potential for modulation by OT.

Publication 3: Neural mechanisms underlying maternal behaviour in new mothers: Is natural variation in maternal sensitivity reflected in maternal brain responses to infant stimuli?

Alya Elmadih, Ming Wai Wan, Darragh Downey, Rebecca Elliott, and Kathryn M Abel

Abstract

Background: Animal and human evidence suggests that natural variation in maternal caregiving behaviour is related to variation in maternal Oxytocin (OT) levels. Discrete networks of maternal brain which mediate emotion processing, stress- and reward-related neural systems are thought key to healthy maternal responsiveness. Maternal behaviour is complex and a composite of multiple behaviours; recent evidence suggests that in responding appropriately to her infant, a mother's brain activation may reflect these maternal behaviours in discrete pathways. But to date, no study has examined distinct activation patterns related to the degree of sensitivity a mother shows in responding to her infant i.e. 'maternal sensitivity' (accurate and prompt responsiveness to infant signals). Such patterns may act as biomarkers for sensitive maternal brain and help in the development of future intervention studies to improve parenting. **Methods:** Out of 105 expectant mothers, 80 were blind rated for maternal sensitivity from videotaped free play interaction with their 4 to 6 month infant. At 7-9 months postpartum, 30 of these mothers (15 'higher sensitivity mothers' (henceforth high sensitivity mothers-HSMs) and 15 'lower sensitivity mothers' (henceforth low sensitivity mothers-LSMs)) underwent functional magnetic resonance imaging to examine brain responses to viewing 'own' versus 'unknown' infant videos, using a range of affects (neutral, happy, and sad). Maternal plasma OT measurements following play interactions with their infant were also performed. **Results:** Compared to LSMs, HSMs showed significantly greater blood oxygenation level dependent activation in the right superior temporal gyrus in response to own versus unknown neutral infant, and to own happy infant versus neutral control. Changes in brain activation were significantly 'negatively' correlated with plasma OT responses in those mothers. Conversely, compared to HSMs, LSMs showed no significant difference in brain activation in response to own infant separately or in contrast to unknown infant. **Conclusion:** Activation of superior temporal gyrus suggest the more attention given by HSMs to read their infant facial emotions; this was not shown by LSMs. Sensitive mothering may chart discrete brain responses which might act as biomarkers for future intervention studies to enhance the sensitivity of maternal care.

Study I: Natural variation in maternal sensitivity: What are the possible prenatal and postnatal predictors in healthy early postpartum mothers?

Chapter 2: **Study I Literature Review**

2.1. The Prenatal Development of Maternal Sensitivity

Observations of the intense grief shown by mothers whose infants have died during birth suggest the existence of a prenatal bond between a mother and her fetus (Kennell et al., 1970). Pregnancy not only includes the physical development of the fetus, but also the psychological adjustment of the expectant mother (Rosenblatt, 1998; DiPietro, 2010). This includes the development of a maternal identity, identity of her developing fetus and her relationship with the fetus (Cranley, 1981; Gloger-Tippelt, 1983). This combination of anxious preoccupations and pleasurable attachment towards the unborn infant prepares the mother for ‘motherhood’ (Leckman et al., 1999). This concept can be referred to as maternal-fetal attachment (MFA), defined as “the extent to which women engage in behaviours that represent an affiliation and interaction with their unborn child” (Cranley, 1981) and represents one aspect of the ‘transition to maternity’ that is thought to occur in primiparous women.

Transition to maternity is also evidenced in animals, though with some difference from humans (Ross et al., 2009). While virgin female rodents are aversive to pups, the extensive hormonal changes and the physiological events of pregnancy and puerperium (Moltz et al., 1970; Bridges, 1996) produce an ‘enriched environment’ that encourages mothers to interact with offspring in order to facilitate the development of maternal caregiving behaviour (e.g. nest building, pups retrieval) (Fleming et al., 1988). Animal research has provided increasing insight into the biological mechanisms underlying the

transition to maternity, with a special implication for the oestradiol and OT hormones (Poindron, 2005). Similarly, in humans, the early postpartum constitutes a period of tremendous hormonal changes that serve adaptive functions in preparation for caregiving (Workman et al., 2012). The particular implication of OT in the early development of maternal care behaviour has also been suggested by evidence from recent human studies, such as Levine et al. (2007) who reported a positive correlation between maternal-fetal attachment and the steady rise in plasma OT levels during pregnancy and the first postpartum month.

Following the infant's birth, the human mother-infant relationship continues to develop, with this caregiving now expressed as observable behaviours such as touch, 'motherese' vocalisation and affection (Feldman et al., 2007). Similarly in animals, pup-licking, grooming and arched-back nursing (LG-ABN) are seen (Champagne et al., 2001). However, in both humans and animals broad natural variations in these caregiving behaviours have been reported, ranging from high to mid to low levels of maternal care (Feldman et al., 2007; Gordon et al., 2008; Champagne et al., 2001).

2.2. What Is Maternal Sensitivity?

Mary Ainsworth's definition of maternal sensitivity has long been considered the 'gold standard' definition, that is: "the ability for perception and accurate interpretation of baby's signals, and appropriate responsiveness" (Ainsworth et al., 1978). Others have since focused on particular aspects of this definition, such as the *awareness* of the child's affective state (Crawley & Spiker, 1983) or the *behavioural response* to infant cries (Crockenberg, 1981; Egeland & Farber, 1984). The *appropriateness* of the mother's response is also highlighted as an important element of maternal sensitivity by some (e.g. Crittenden, 1981; Smith & Pederson, 1988), whereas others concentrate on

the *timing* of these maternal responses (e.g. Fish et al., 1991). Chibucos & Kail (1981) have talked about a physical component of maternal sensitivity in the form of *appropriate handling*. Crittenden (1981) and Crnic et al. (1984) believe that allowing the infant time to respond before further stimulation leads to *reciprocal interaction* which, according to Marfo (1992), results in the interaction being *mutually rewarding*. A sensitive mother, according to Skinner (1985), shows that her primary concern is for the child and not herself, in the concept of *particular attitude*. Nover et al. (1984) see sensitivity as the infant's free exploratory play with no interference, which introduces the idea of sensitivity being *non-intrusive* (Crawley & Spiker, 1983; Smith & Pederson, 1988). Others consider maternal sensitivity as the *emotional availability* of the mother to the child (Kivijarvi et al., 2001). Fonagy et al. (1994) and Meins (1997) raise the notion of *mind-mindedness*, which suggests maternal sensitivity to the infant's mental state, rather than to her/his physical state.

'Maternal sensitivity' is thus a relatively broad concept that includes a variety of interrelated affective and behavioural caregiving attributes (Thompson, 1997) in keeping with that defined by Ainsworth and her colleagues (Shin et al., 2008). A sensitive mother responds properly to her infant's displayed emotions by affirming the positive emotions or reassuring about the negative ones (Sroufe, 2000). A sensitive mother also modifies her responses according to the child's developmental level (Pianta et al., 1989), thus gradually allowing the child time to cope with and explore new situations (if appropriate) (Lohaus et al., 2004). In this beautiful 'reciprocal dance', a sensitive mother knows whether her behaviour is or is not adequate for her infant's needs (Kivijarvi et al., 2001).

2.3. Why Is Maternal Sensitivity Important?

2.3.1. Child outcomes

i. Attachment

Ainsworth et al. (1978) were the first researchers to examine the relationship between parental behaviours and attachment “the proximity seeking behaviour between the child and his main caregiver” Bowlby (1969; 1973; 1980) when they observed 26 middle-class mother-infant dyads from Baltimore. Mothers were visited at their homes for 4 hours every month during the first year of life. During these visits, a variety of maternal behaviours were assessed, namely sensitivity, acceptance, cooperation and accessibility. When they assessed attachment at 12 months, they found a strong correlation between security of attachment and sensitivity ($r = 0.78$). Accordingly, they suggested ‘sensitivity’ to be the crucial factor that fosters attachment. Nonetheless, this strong association between sensitivity and attachment has not been left without challenge as some subsequent studies found only moderate relationship between sensitivity and attachment security (e.g. Egeland & Farber, 1984; Smith & Pederson, 1988; Teti et al., 1995; Vondra et al., 1995; Seifer et al., 1996; Beckwith et al., 1999).

The less stronger association between maternal sensitivity and attachment found by some studies (as compared to Ainsworth’s strong association) may be attributed to: a) different measures used by studies to assess maternal sensitivity (e.g. Beckwith et al., 1999); b) different methodologies among different studies (i.e. context, assessment duration); c) lack of consensus on the conceptualisation of ‘maternal sensitivity’ (Meins et al., 2001); with some researchers using the term ‘maternal sensitivity’ interchangeably with the terms ‘maternal responsiveness’ (e.g. Blank et al., 1985; De Wolff & Van Ijzendoorn, 1997) and/or ‘maternal competency’ (e.g. Pianta et al., 1989; Zahr & Cole, 1991), which can be confusing; d) the crudeness of Ainsworth’s maternal

sensitivity scale (De Wolff & Ijzendoorn, 1997) such that some components of the measure are difficult to define as the child grows, e.g. 'promptly' (Lohaus et al., 2004). This diversity in studies' approaches is illustrated by the findings of two meta-analysts, Goldsmith & Alansky, (1987) and De Wolff & Ijzendoorn, (1997), who reported small to medium size effect sizes for the relationship between sensitivity and attachment ($r = 0.10$ to 0.30 and $r = 0.24$, respectively).

A main limitation of Goldsmith & Alansky (1987) is that they derived their effect size from only 12 studies in which a variety of measures (other than sensitivity) were examined in relation to attachment. Furthermore, although De Wolff & Ijzendoorn (1997) only include studies that used the 'Strange Situation' (Ainsworth & Bell, 1970), they were having a problem in dealing with: a) studies that have multiple outcomes (multiple variables to represent maternal sensitivity), and b) studies with multiple assessments at different time points. These manoeuvres are likely to have affected the size effect they reported when assessing the association between maternal sensitivity and security of attachment.

On the other hand, studies that adhered to Ainsworth's methodology (i.e. long, frequent visits) reported a strong positive relationship between maternal sensitivity and security of attachment (e.g. Isabella, 1993). A bigger relationship between maternal sensitivity and attachment was also reported by others who assessed sensitivity at a single visit, such as Pederson et al. (1998) who reported a strong correlation between the two concepts ($r = 0.51$). Recent studies, which assess maternal sensitivity longitudinally, have reported that maternal sensitivity at 4 months is a predictor for attachment security when the infant is 2 years old (Bigelow et al., 2010). Furthermore, interventions that were effective in enhancing parental sensitivity were also more effective in enhancing

attachment security, which supports the notion of a strong role of sensitivity in shaping attachment (Bakermans-Kranenburg et al., 2003).

ii. Infant social, emotional and cognitive development

The appropriate responsiveness accounted for by sensitive maternal care “instils an awareness of the caregiver’s availability and reliability, thus promoting a sense of security and trust” in the infant towards her/his caregiver (Lohaus et al., 2001). It is this trust which facilitates the social and emotional development of the infant (e.g. Landry et al., 2001; Kivijarvi et al., 2001). As part of the National Institute of Child Health and Human Development (NICHD) study, Belsky & Fearon (2002) report positive correlations between maternal sensitivity (observed at 24 months) and different dimensions of child development (i.e. social competence, expressive language, receptive language and school readiness).

Infant cognitive development which depends on materials and stimulation provided by the mother inside or outside the home to facilitate infant intellectual learning and development (Crosnoe et al., 2010) has also been shown to link to maternal sensitivity. For example, Downer & Pianta (2006) examined the relationship between maternal sensitivity and cognitive development in 832 infants who were followed from one month old until school grade 1 (about 4-5 years old). Children’s cognitive function was assessed both at school entry (54 months) and at the middle of grade 1 using mother’s and teachers’ reports. Maternal sensitivity was observed at 6, 15, 24, 36 and 54 months. They reported that children who had experienced more sensitive maternal care scored higher in maths and phoneme knowledge when assessed at grade 1. These findings suggested that early maternal sensitivity influences child cognitive development and, therefore, may also predict later academic performance. Although the study excludes

those with unfavourable conditions, e.g. young mothers, mothers who live in dangerous neighbourhoods, the strength of this study came from the large sample size.

In another large cohort study, Pearson et al. (2011) investigate the relationship between maternal responsiveness and infant mental development among 732 mother-infant dyads. Maternal responsiveness was observed at 12 months through book reading task (using the Thorpe Interaction Measure) and infant mental development assessed at both 18 months (using the Griffiths scales) and at 4 years (using the Wechsler Preschool and Primary Scale of Intelligence). They reported that maternal responsiveness was positively associated with infant mental development at 18 months. Although maternal responsiveness was not related to infant cognitive ability at 4 years, this could be related to the difference in the measures used at each time point.

iii. Child behaviour

Whereas sensitive maternal behaviours are positively associated with the infant's positive mood, as well as social and play behaviour (Kivijarvi et al., 2001; Kemppinen et al., 2006), a mother's inability to respond sensitively to her infant's cues may lead to negative emotional and behavioural outcomes (Denham & Moser, 1994). Several studies have suggested that maternal 'insensitivity' is a precursor of high levels of child aggression. For example, in a study investigating the relationship between maternal sensitivity, discipline (i.e. rules that set limits for the child) and child aggression among 117 mothers and their children, maternal sensitivity and child aggression were both observed at an average of 26 months (Alink et al., 2008). Their results showed that negative disciplines are related to child aggression only when mothers are insensitive. In another study, sensitive mothering during playing games and playful conversation was predictive of low levels of aggression at school age (Olson et al., 2000). It is possible that less maternal sensitivity means less support to help the children manage their

negative emotions independently, which results in an increase of negative behaviours (Alink et al., 2008). Interestingly, evidence also suggests that higher levels of maternal sensitivity in early childhood also contributed to later reductions in child anxiety and depressive symptoms in temperamentally-vulnerable children (Warren & Simmens, 2005).

2.3.2. Parenting quality

In addition to the influence of early maternal sensitivity on child developmental outcomes, maternal sensitivity in infancy also influences the quality of parenting in later years. Older studies have found a link between maternal intrusiveness (i.e. lack of respect for infant autonomy) –a concept that is linked to insensitive behaviour - and abusive parenting (e.g. Lyons-Ruth et al., 1987). Recently, Joosen et al. (2012) assessed maternal sensitivity among 73 mothers and their infants (using Ainsworth's sensitivity scale) at 3 and 6 months during bath and play interactions. Harsh parenting was then assessed through three home visits when the infant was 2 years old. Mothers were provided with an empty bag and some toys (on the floor) and instructed to ask the infant to clean the toys off the floor into the bag. Verbal harsh discipline (e.g. impatient, yelling) or physical (e.g. slapping, grabbing the child) harsh disciplines were then assessed. Low maternal sensitivity was found to be a predictor of harsh parenting or 'harsh discipline' during toddlerhood. The strength of this study is due to that their observational paradigm included non-distress and distressing interaction (through the Still Face Paradigm), which provides a comprehensive view of maternal sensitive responsiveness (Lindhiem et al., 2011).

2.4. How Is Maternal Sensitivity Measured?

There is great variation in the methods and procedures used to assess maternal sensitivity (De Wolf & Van Ijzendoorn, 1997), with rating methods ranging from maternal interviews to observations. A maternal interview reflects the mother's subjective perception of her relationship with her infant. Observational measures (in which a trained rater evaluates an episode of mother-infant interaction blind to other family information) are more objective and likely to be a more accurate representation of the quality of maternal caregiving behaviour. Therefore, observation remains the most frequently used measure. However, observational behavioural assessments may also vary in their setting, some taking place at home (e.g. Gordon et al., 2010) and others in a laboratory (e.g. Atzil et al., 2011). The context of the observed interaction between mother and infant also varies; while some studies examine the unstructured interaction between the mother and her infant (e.g. feeding and playing) (Gordon et al., 2010), others observe a challenging situation (e.g. infant frustration) (Atkinson et al., 2005). Furthermore, while some studies depend on long visits over a few months (e.g. Ainsworth et al., 1978; Downer & Pianta, 2006), others are based on a single interactive episode of a few minutes (e.g. Evans et al., 2007; Moore et al., 2009; Strathearn et al., 2012). Infant ages at sensitivity assessment time also vary widely (Lohaus et al., 2004), which might have an implication for the reliability of the assessment method (Lindhiem et al., 2011).

2.4.1. Validity of the short single interaction observation

The robust reports of detailed and frequent observations of mother-infant interaction do not necessarily imply limited reliability of short, single, time-point assessments (Mc Elwain & Booth, 2006). This is supported by the findings of Evans et al. (2007) who examined the validity of short videotaped, mother-infant laboratory observation against

the lengthy home assessment. Evans et al. observed 85 mother-infant dyads at home at 6, 12, and 24 months for 2-3 hours each. Maternal sensitivity was rated using MBQS (90 items). At 24 months, mother-infant dyads were observed again in the laboratory for 10 minutes and maternal sensitivity was rated using MBQS-Revised (81 items). Their results showed significant correlation in the maternal sensitivity rating from the short videotaped laboratory interaction with the lengthy home assessment ($r = 0.45$; $p < 0.01$). These findings support further the use of short observational assessments which are time efficient, thus more convenient for use by clinicians. It is possible that the lengthy duration of observation may increase the identification of positive (or negative) interactions, yet the use of short observation has also been proved to be a reliable indicator for these interactions. Currently, there is a range of short observational validated measures used in rating maternal sensitivity with no 'gold standard' (Lindhiem et al., 2011). Table 2.1 represents examples of the commonly used measures in rating maternal sensitivity through short observations.

In the current study, we rated maternal sensitivity through a short observation of the mother-infant play interaction, using the Manchester Assessment of Caregiver-Infant Interaction (MACI; Wan et al., 2012, 2013 online). This measure evaluates parent-infant interaction on seven 1-7 scales, including maternal sensitivity. MACI was adapted from the existing previously validated measures of mother-infant interaction, the Global Ratings Scales of Mother-Infant Interaction (Murray et al., 1996) and the CARE-Index (Crittenden, 1979-2004), both of which are suitable for use from 2 month infant age or younger, respectively. The MACI was developed in 2008 to meet the need for an assessment that is: (1) based on a normative developmental model (therefore with demonstrated validity in healthy samples, despite its use in at-risk infants); (2) relatively brief, and so suitable for quite large samples, as coding is resource intensive; (3) suitable for longitudinal measurement at about 6-15 months (in normative samples).

The MACI defines caregiver sensitivity as: “Contingent and appropriate behavioural responses to identified infant behaviours as is required and optimal to meet the infant’s immediate and developmental needs”. Thus, it is similar to the original definition by Ainsworth et al. (1978) - the mother’s ability to perceive infant signals and respond promptly and appropriately - and focuses on quality. This construct of sensitivity is the most commonly assessed in measures of maternal sensitivity (De Wolff & Van Ijzendoorn, 1997). The MACI has assessed maternal sensitivity in the home and lab, with pilot data showing high consistency of maternal sensitivity between contexts ($r = 0.68$; $p = 0.008$) (Green et al., 2013).

Table 2.1: Examples of commonly used measures for assessing maternal sensitivity through short mother-infant interaction observation

Measure	Author	Age	Setting	Situation	Length	Behaviour evaluated	Main advantage (s)	Main disadvantage (s)
Ainsworth's Maternal Sensitivity Scale	Ainsworth et al., 1978	Birth-12 months	Home	Distressed / Non-distressed	5 min	Bi-dimensional scale	Cost-effective and time-efficient	Needs long training; crude
The CARE-Index	Crittende, 1979–2004	Birth-30 months	Home, clinic, etc.	Non-distressed	3 min	7 scales	Applied by para-professionals	Needs extensive training; expensive
The Global Ratings Scale	Murray et al., 1996	2 months-6 months	Home, clinic, etc.	Non-distressed	5 min	13 mothers' behaviours, 7 infants' behaviours and 5 dyadic behaviours	Quick to rate, suitable for clinical and non-clinical groups	Small age ranges
The NICHD version of the ORCE	The NICHD Study, 1997	6, 15, 24 and 36 months	Home or child care centre	Distressed / Non-distressed	15 min	8 features of caregiver's interaction, and 5 features of child's behaviour	Developed as part of the largest, longest-term study of child care	Needs long training

2.5. Is Maternal Sensitivity a Stable Construct?

Despite the importance of maternal sensitivity as a concept, there are some inconsistencies in the literature related to its stability (i.e. continuity within the same mother) (Pianta et al., 1989; Lohaus et al., 2004). Many researchers assume the stability of maternal sensitivity across development (see De Wolff & Ijzendoorn, 1997); some researchers have tested this stability in longitudinal designs using a variety of assessment methods. Evidence from these studies showed high (Grossmann et al., 1985; Joosen et al., 2012), moderate (e.g. Vizziello et al., 2000; Kivijarvi et al., 2001) or even slight (Beckwith et al., 1999) stability for maternal sensitivity. When Grossmann et al. (1985) replicated Ainsworth's et al. (1978) study, they observed 49 mother-infant dyads of middle class families at 2, 6, 10 months (at home). Maternal sensitivity (assessed by Ainsworth's scale) was found to be highly stable across all assessments ($r = 0.61, 0.58$, and 0.50 ; all $p < 0.001$). In the aforementioned study, Joosen et al. (2012) also assessed maternal sensitivity, among 73 mothers and their second child both at 3 and 6 months (during bathing and play interaction for 5 and 15 minutes respectively). They reported a high stability in maternal sensitivity between the two assessments ($r = 0.58$; $p < 0.01$).

In contrast, a few researchers have reported only low stability in maternal sensitivity (e.g. Beckwith et al., 1999; Lohaus et al., 2004). In the study by Lohaus et al. (2004), 60 primiparous mothers and their infants were observed during free play interactions at home, both at 3 months and 12 months, for 1 hour at each time. Although, they found low stability for maternal sensitivity over time ($r = 0.19$), this could be attributed to their pure primiparous sample who lack experience with parenting and this could be reflected in their interaction behaviour. Perhaps the greater confidence and competency which was recorded by 12 months among these primiparous mothers (as reported by the

authors) was also interpreted as greater sensitivity as compared to their rating at 3 months postpartum. Consequently, a solely primiparous sample might affect the stability of their assessment.

Although Grossmann et al. (1985) examined a wider infant age range than that in Lohaus's study and also observed a mixture of situations (e.g. feeding, play, infant frustration) they found high to moderate stability for maternal sensitivity. This is possibly because Grossmann et al. provide a more comprehensive assessment for sensitivity by considering a range of interactions in their assessment, which is a representation of mother and infant daily routines.

Despite the notion that higher maternal sensitivity ratings are found in relation to infant distress compared to non-distress (McElwain & Booth-LaForce, 2006), this is actually reflecting the flexibility of sensitive mothering as a dynamic concept around the infant's needs, rather than instability in the construct itself. In other words, infants need change with the situation (or infant developmental stage). Therefore, it is to be expected that maternal sensitivity would also change in order to accommodate this in order to allow for 'appropriate responsiveness' (Ainsworth et al., 1978). Yet, this flexibility does not affect the high face validity and the moderate to high stability of the maternal sensitivity construct, allowing for it to be measured longitudinally and in different situations (Lindhiem et al., 2011).

2.6. Factors That Influence Maternal Sensitivity

In spite of the importance of maternal sensitivity, and although much research has been invested in this area, and has shown that parenting interventions can be effective in improving maternal sensitivity (e.g. Bakermans-Kranenburg et al., 2003), translation into service delivery has been very limited. This is due to two reasons. First, no routine

clinical screening currently identifies mothers at risk of poor maternal sensitivity. As a result, parenting interventions to promote maternal sensitivity and optimise child outcomes tend to focus on the clinical group, i.e. mothers with mental illness such as postnatal depression (e.g. Murray et al., 2003; Forman et al., 2007; Barlow et al., 2008). However, it is increasingly clear that far more children are exposed to poor parenting than such a restricted approach to risk identification is likely to access (Barlow et al., 2008). An alternative is to offer a more personalised approach focusing most efforts on those at-risk identifiable in the prenatal or early postnatal period. This is ideally when all early postpartum mothers make contact with health services, and when mother-infant dynamics may still be relatively malleable to interventions.

Second, to date researchers have not been able to identify all the factors that influenced maternal sensitivity and their findings were not always consistent. Much of the variance in maternal sensitivity remains unexplained (Drake et al., 2007). This is because a range of maternal behavioural outcomes were investigated, including maternal ‘competency’ and ‘responsiveness’, with no particular focus on maternal sensitivity (Bornstein et al., 2007) especially in healthy mothers. Two particular studies have identified multiple postnatal predictors of ‘self-rated’ maternal sensitivity using self-rating ‘mother’s identity with baby’ as a proxy measure for maternal sensitivity (Shin et al., 2006; Drake et al., 2007). Mothers’ reported sensitivity toward their 6-week-old infants strongly predicted by (retrospectively-reported) maternal-fetal attachment in a sample of 196 mothers (Shin et al., 2006). Employment status, social support and infant gestational age at birth were also significant predictors for maternal sensitivity. Comparatively, in the other study (N = 177), perceived life satisfaction, self-esteem and number of children (parity) independently predicted ‘maternal responsiveness’ at 2-4 months postpartum while maternal education, income and maternal age did not (Drake et al., 2007). However, in both studies the outcome measured was concerned more with

maternal affective experience (self-reported) rather than behavioural sensitivity observed in interaction.

Another reason for the lack of comprehensive evidence in what might predict maternal sensitivity is that some researchers focus on the early postpartum period (e.g. Shin et al. 2006), while some confine their study to a special group (adolescents) (e.g. Bloom, 1995). Studies also focus on maternal sensitivity as a predictor for infant behavioural and developmental outcomes rather than focusing on factors that influence sensitivity (Susman-Stillman, 1996; Bakermans-Kranenburg & Van Ijzendoorn, 2006).

Nonetheless, and among the limited evidence, the literature has highlighted three broad prenatal categories that might influence maternal sensitivity: a) mother's prenatal psychological characteristics, b) socio-demographic and support factors, c) early experience in family of origin, and two further categories that might be assessed postnatally: d) obstetric variables, and e) infant temperamental behaviour. Here, we review the evidence for these categories being associated with variation in maternal sensitivity. Figure 2.1 outlines a theoretical model for these categories in relation to maternal sensitivity.

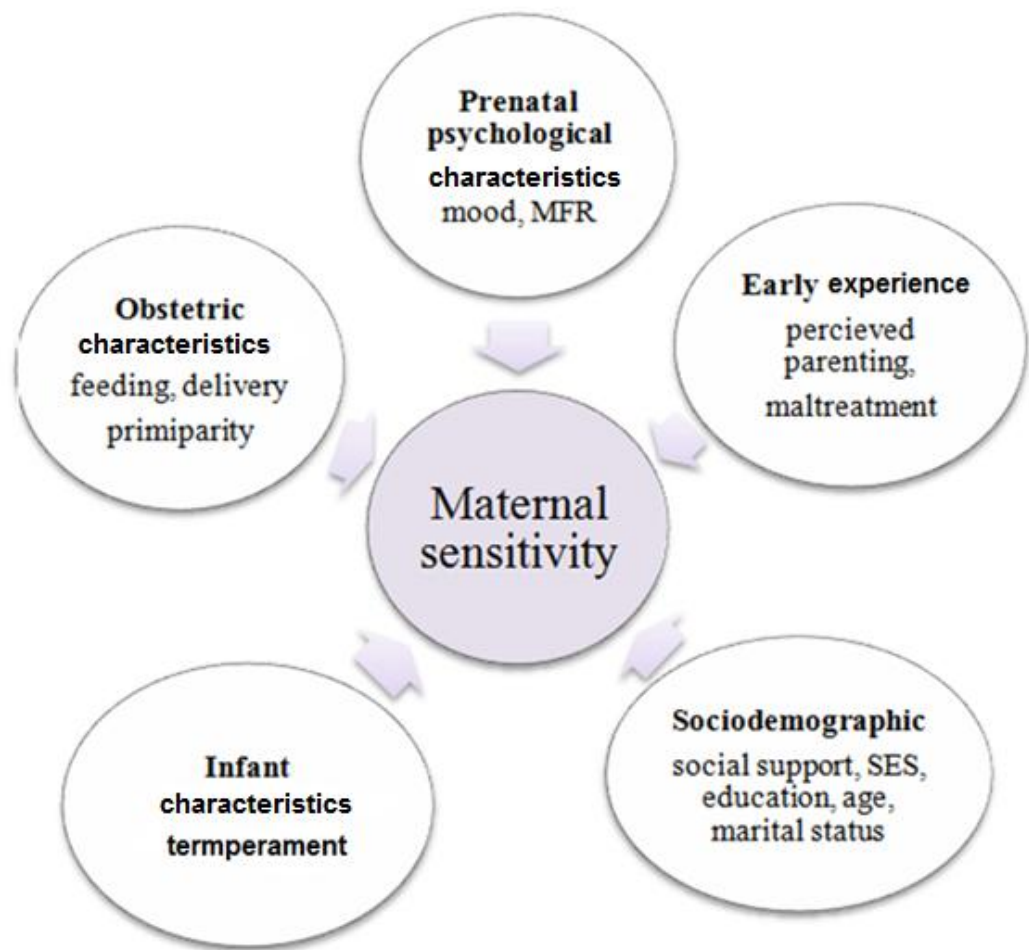


Figure 2.1 A theoratical model of factors that influence maternal sensitivity, based on current empirical evidence (model used to guide the literature review and data analyses). Note: MFR: Maternal-Fetal Relationship, SES: Socioeconomic status.

2.6.1. Mother prenatal psychological characteristics

i. Maternal mental state (depression and anxiety)

Depressive mood, even at non-clinical level, impairs the communication of emotions between the mother and her infant (Blumberg, 1980, see Tronick & Reck, 2009) and subsequently hinders maternal sensitivity (Sidor et al., 2011). This is because depression tends to make a mother less emotionally available to her infant; consequently, she may find it difficult to interpret and respond promptly to her infant's cues (Kemppinen et al., 2006; Tronick & Reck, 2009). Depressed mother might also lack the feeling of reward from social interaction, which makes sensitive responsiveness more challenging (Kemppinen et al., 2006). Most of the studies which examine the impact of depression on maternal sensitivity do so among clinically depressed samples (e.g. Murray et al., 1996) and only a few studies consider community (non-clinical) samples (e.g. Mills-Koonce et al., 2008; Sidor et al., 2011).

Studies have found significant correlation between postnatal higher maternal depression scores and lower maternal sensitivity in a community sample (Campbell et al., 2007; Mills-Koonce et al., 2008). Larger longitudinal studies, like the NICHD study (1999), were also able to demonstrate the impact of maternal depression on sensitivity. In that study, 1,215 women and their children were followed from birth to 36 months.

Depression was assessed by self-report questionnaire at 1, 6, 15, and 36 months and maternal sensitivity was observed through mother-infant play interaction at the same sessions. Mothers who reported chronic symptoms of depression (through 36 months) were found to score the least sensitivity rating when compared with those who had not experienced depression symptoms (NICHD, 1999).

Similar findings were reported by Campbell et al. (2007) who investigated the trajectories of maternal depressive symptoms among a community sample of mothers

and their 11 months to 7 years old children. They found that the rating for maternal sensitivity was generally high and increased when depressive symptoms were low and that maternal sensitivity was low or decreased when depressive symptoms were high. The mechanism underlying poor parenting in non-clinically depressed mothers is not clear; whether it is purely related to the effect of symptoms or to other unfavourable factors that co-exist with depressive mood (e.g. poverty, lack of social support and marital difficulties) remains to be examined (Tronick & Reck, 2009).

Among the few studies that were unable to demonstrate a relationship between depression and maternal sensitivity, some methodological issues were noticed. For example, a recent study by Sidor et al. (2011) examined maternal postpartum depressive symptoms among a non-clinical sample of 106 women (using the Edinburgh Postnatal Depression Scale-EPDS) while maternal sensitivity was observed (using the CARE-index). Although they did not find a correlation between maternal sensitivity and mood symptoms, the fact that their sample was chosen as a socially deprived sample (e.g. poverty, alcoholism, etc.) might conceal such relationship.

As with depression, only a few studies consider community sample when examining the impact of maternal anxiety on sensitive responsiveness. Among these, evidence suggests that anxiety decreases the mother's perceptual abilities and leads to less engagement when interacting with her infant (Blumberg, 1980), which might also decrease maternal sensitivity. Nicol-Harper et al. (2007) investigated the impact of maternal anxiety (using State Trait Anxiety Inventory-STAI-T) on mother-infant observed interaction in a community sample of 32 mothers with high anxiety (scored 40 or above in STAI-T) and 32 with low anxiety (scored 34 or less in STAI-T). High trait anxiety mothers showed lower sensitive responsiveness when compared to low anxiety trait mothers. The strength of this

study came from the fact that participants were screened for depression and excluded from the study if they showed depressive symptoms. This ensured that any group difference in mother-infant interaction would primarily be due to anxiety and not due to depression; given the comorbidity between the two (Pollack, 2005). In a study that examined self-regulation in toddlers, women who reported symptoms of anxiety scored less optimally than healthy controls on maternal sensitivity (Feldman & Klein, 2003).

ii. Maternal–fetal attachment

Some researchers argue that maternal prenatal attachment is not 'attachment' in the sense used in attachment theory (Bowlby, 1969), but is a multifaceted construct guided by the caregiving system, and is reciprocal to the attachment system. Therefore, some suggest that maternal-fetal attachment (MFA) or maternal fetal 'relationship' (MFR) is more concerned with the need to protect the infant, therefore having more in common with caregiving (Walsh, 2010). Cranley (1981) suggests that the Maternal Fetal Attachment Scale (MFAS) measures “the extent to which a woman engages in behaviours that represent an affiliation and interaction with her unborn child”. Muller (1996) emphasises that their measure, Prenatal Attachment Inventory (PAI), assesses the “unique, affectionate relationship that develops between a woman and her fetus”. Moreover, Condon & Corkindale (1997) suggest that their Maternal Antenatal Attachment Scale (MAAS) focuses mainly on “thoughts about the fetus”.

Research on the MFR has focused on factors that predict this early relationship (e.g. mood state, social support, demographic factors) (see Alhusen, 2008; den Bergh & Simons, 2009) rather than its relationship to postpartum mother-infant interaction or child outcomes. However, MFR has been positively related to a range of self-reported outcomes (as proxy for maternal sensitivity) such as self-reported separation anxiety at

1-2 months postpartum (Muller, 1996); ‘how a mother feels about her baby’ at 1 week and 8 months postpartum (Mercer & Ferketich, 1990); and identity with the baby at 1 to 6 weeks postpartum (Shin et al., 2006).

Accordingly, evidence for a relationship between MFR and an *observed* parent-infant relationship is very limited (e.g. Siddiqui & Hagglof, 2000; Fuller, 1990; Bloom, 1995). Bloom (1995), who assessed MFR among 47 pregnant teenage women using MFAS, found that the total MFAS score in the 3rd trimester (and not 1st or 2nd) was correlated with the number of affectionate behaviours in feeding in the first week postpartum ($r = 0.34$). Specifically, ‘attributing characteristics to the fetus’ subscale in the 3rd trimester was correlated with affectionate behaviours ($r = 0.32$) and caretaking behaviours ($r = 0.34$). However, these MFAS results have not been replicated in a wider demographic of mothers. In addition some researchers have raised concerns about the reliability of MFAS when used as ‘individual scales’ as opposing to an ‘overall measure’ (Galbally et al., 2011). Siddiqui & Hagglof (2000), who assessed prenatal attachment to the fetus among 100 pregnant women during the last trimester of their pregnancy, found that the PAI score was positively related to face-to-face interaction at 3 months postpartum, particularly in maternal stimulation behaviours using proximal behaviours, and negatively with maternal non-involvement.

In summary, investigating the unique relationship between the expectant mother and her unborn infant has provided some evidence to suggest that prenatal attachment is important for the postnatal relationship. However, findings are mixed, with a reliance on self-reported measures to assess mother-infant postpartum outcomes (e.g. Muller, 1996; Shin et al., 2006), and a focus on the MFR as an outcome in itself (Alhusen, 2008).

2.6.2. Socio-demographic and support factors

i. Socioeconomic characteristics (education/financial status)

Some studies suggest that maternal sensitivity correlates positively with maternal education, possibly because: a) educated mothers know that their infant uses them as the main source of information and learning (Walker et al., 1986); b) a better SES, since education grants mothers a higher job status, which is more likely to allow flexibility with child care to fit her parenting role (Pederson et al., 1990); or c) a combination of the two previous factors. However, some studies like the aforementioned study by Drake et al. (2007) fail to find such an association between education and maternal responsiveness. Perhaps at early postpartum (2-4 months after delivery) the influence of education on maternal behaviour may not be as powerful as other factors, such as hormones, in shaping maternal behaviours (Feldman et al., 2007). Thus, maternal education may become a more important influence at a later stage postpartum when the infant becomes more interactive.

One of the most robust findings, with respect to factors associated with maternal sensitivity, is SES. Low-income is associated with psychological stresses and diminished social support (Evans, 2008). Among 223 mothers assessed with their 13-year-old children at home, children in lower income families reported receiving low maternal responsiveness, and that their mothers were also highly stressed (Evans, 2008). Although this study depended on self-report measures (completed by children) to assess maternal responsiveness; their finding suggests that maternal psychological stress may act as a mediator in the relationship between poverty and maternal responsiveness. Others also report lower maternal sensitivity associated with lower SES mothers (e.g. Sacker et al., 2002; Bornstein et al., 2007). It is possible that, being of lower SES

exposes mothers to a range of environmental risk factors and deprivations that challenge their sensitivity to their infant and their emotional capacity (McAdoo, 2002; Evans, 2008). On the other hand, both higher social functioning and better social support exist among higher SES mothers and might explain better interactions with infants (Eccles & Harold, 1996). Although a study by Pederson et al. (1998) did not find an association between maternal sensitivity at 13 months (assessed by MBQS) and maternal income among the 60 mothers in their study, this is possibly due to their homogenous higher income sample (mean \$45,000/year) compared to the lower income sample in other studies (e.g. Evans, 2008).

ii. Social support

Social support refers to “the emotional, instrumental or financial aid that’s obtained from social relationship including partner’s contribution” (Bloom, 1994), has a positive role in improving parenting and, in particular, maternal sensitivity (Stiles, 2010). It has been suggested that the positive impact of social support on parenting works through preventing or alleviating the perception of parenting as a stressful duty (i.e. the buffering effect) (Andresen & Telleen, 1992). Emotional support also acts in a similar way by improving maternal self-esteem and raising the mother’s confidence in order to tackle the parenting role (Andresen & Telleen, 1992). Pauli-Pott and colleagues (2003) found that marital and emotional support positively correlated with maternal sensitivity. Similarly, Feldman & Klein (2003) reported a positive correlation between the father’s involvement at 3 months and the level of maternal sensitivity at 9 months. Even among mothers with mental illness, successful parenting is also related to stability within the family and having good financial and social support (Abel et al., 2005).

iii. Demographic factors (maternal age at infant birth/primigravidas)

Giardino et al. (2008) examined maternal responsiveness in 56 adolescent mothers (14-19 years) compared with 49 adult mothers (older than 19 years) at 6 weeks to 6 months postpartum, using self-report of alertness and sympathy, observation of mother-infant interaction, and measurement of physiological changes associated with responsiveness (e.g. maternal heart rate, corticosterone level). Their findings revealed that, while there was no difference between the two groups of mothers (adolescence/adult) in the self-reported measures which rated their maternal competency, the maternal sensitivity rating through observation showed less attentive responses to infants among the youngest mothers. In addition, the youngest mothers showed lower physiological responsiveness (i.e. assessed by maternal heart rate/corticosterone level) towards infants' cries compared with adult mothers. The authors relate the lower levels of maternal sensitivity among the younger group of mothers to their lower level of social support.

However, others like Demers et al. (2010) relate the low sensitivity among adolescent mothers to their lower levels of mind-mindedness (i.e. the capacity of the mother to comment appropriately on their infant's internal states) (Meins, 1997). Demers et al. (2010) examined mind-mindedness among 29 adult mothers (21 years or above) and 69 adolescent mothers (20 years or below) and maternal sensitivity was observed at 18 months postpartum (using MBQS for sensitivity). Maternal sensitivity, which was significantly higher among adult mothers compared to the younger mothers, was positively related to levels of mind-mindedness, which was also higher among this group compared to the younger group. Although in general, older mothers may be more likely to be rated as more sensitive than teenage mothers, the relationship between maternal age and maternal sensitivity is not consistently reported and may not be linear (Drake et al., 2007).

A limited literature has addressed the impact of ‘first time’ mothering on maternal sensitivity. In the aforementioned study by Drake et al. (2007), the number of children was a significant predictor of self-reported maternal responsiveness. It has also been suggested that mothers’ knowledge about parenting helps to structure more appropriate interaction with the infant (Benasich & Brooks-Gunn, 1996) and this could help them to score higher on measures of parenting skill (Damast et al., 1996). However, maternal sensitivity should be differentiated from competency to maternal role or maternal role achievement (Mercer & Ferketich, 1990).

2.6.3. Early experiences in family-of-origin

i. Perceived parenting

Consistent with attachment theory (Bowlby, 1969), early positive care experiences provide adults with the emotional and cognitive resources, and broader social learning, to provide sensitive caregiving (Belsky et al., 2002), while poor care, neglect and trauma in childhood confer later difficulties in parenting and sensitivity (Cicchetti et al., 2006; Bailey et al., 2012). This is supported by the finding of Lecuyer-Maus (2000) who examined 61 mothers and their 12 month-old infants and found a positive relationship between early perceived experience (assessed by the Parenting Bonding Instrument -PBI) and observed maternal sensitivity (assessed during play, feeding, teaching).

Furthermore, studies that used a discourse analysis procedure like the Adult Attachment Interview (AAI), also found a similar relationship between perceived parenting and maternal sensitivity (e.g. Pederson et al., 1998). In the study by Pederson et al. (1998), 60 mother-infant dyads were assessed for maternal sensitivity (using MBQS) at 13 months and for maternal attachment with own attachment figure (using AAI). Autonomous (secure) mothers were found to be more sensitive compared with non-

autonomous (ambivalence/avoidance) mothers. Even among teenage mothers ($N = 74$) higher levels of maternal sensitivity were found among secure mothers compared to ambivalence/avoidance mothers (Ward & Carlson, 1995). Although such experiences rely on adult retrospective report, there are no strong reasons to suspect that prenatal measurement would differ from postnatal or from earlier in adulthood (e.g. Talbot et al., 2009).

ii. Childhood maltreatment

Old literature suggest that early childhood adversity (maltreatment) has implications for future parenting (Belsky, 1984), and a range of self-reported maladaptive parenting was identified in relation to maltreatment. Among the studies that focus on maternal sensitivity as an outcome, high risk samples were considered (mothers with mental illness, substance abuse or mothers whose child is removed from the home) (Lindhiem et al., 2011) as part of interventions to improve their parenting skills (Cicchetti et al., 2006).

Of the available research that examined low risk samples, three studies rated maternal sensitivity in the observation setting. The first study (Moehler et al., 2007) assessed emotional availability (including sensitivity and non-intrusiveness) through 3 minutes of play interaction among 58 mothers with a history of abuse (scored above threshold in Child Trauma Questionnaire-CTQ) and 61 control mothers (scored below threshold in CTQ), both recruited through advertisement at 5 months postpartum. Results showed that mothers with a history of abuse scored significantly lower in non-intrusiveness ($p < 0.02$) and scored borderline significantly lower in sensitivity ($p < 0.08$). However, given that this is a low risk sample, their results, even at a trend, might still be considered interesting. The second study (Bailey et al., 2012), adopts a similar methodology to the first study, among 82 mothers of 4-6 year olds, but in order to increase the variability of

the sample participants had to have at least one social risk factor (i.e. young age at birth, low income, single) to be included in the study. Emotional availability (sensitivity, intrusiveness, hostility) was observed through play interaction, mother-directed clean up and shared snacks with the infant. Maternal maltreatment was reported using the History of Maltreatment and Trauma Form (CTQ was used to validate its use). The results partially supported the first study: the maternal self-reported history of childhood physical and emotional maltreatment was associated with hostility towards their own child, while experience of sexual abuse was associated with maternal self-concern regarding their parental competence.

Contrary to the previous two studies, the third study (Pereira et al., 2012) examined maternal sensitivity in the home setting among 291 mothers and their 16 month-old infants through 2 hours of observation for mother-infant daily routine (using MBQS). Parenting stress was assessed through self-reporting and through interaction observation (20 minutes toy deprivation task and 6 minutes when mother completed questionnaire during infant presence). Lower sensitivity was rated among those who reported maltreatment and those who experienced current parenting stress. They also reported that maternal distress was a significant mediator for the relationship between maternal sensitivity and maltreatment. This mediation through maternal distress is interesting and might also explain the borderline or the insignificant findings of the other two studies (Moehler et al., 2007; Bailey et al., 2012) with regard to the link between maltreatment and maternal sensitivity in particular. The three studies suggest the impact of childhood maltreatment on mother-child interaction and on maternal sensitivity, which is also detectable among the community sample (e.g. Pereira et al., 2012).

A maternal history of abuse not only impedes development of healthy maternal sensitivity but may also act as predictor of risk for child abuse. About 30% of mothers

who abuse their children were themselves abused (Knutson, 1995). The mechanisms underlying this relationship are not clear, but the high stress levels and poor quality of parenting (Hill et al., 2001; Pereira et al., 2012) associated with maltreatment are likely to play a role in this.

2.6.4. Obstetric characteristics

i. Mode of delivery

Animal studies have linked vaginal delivery (VD) to better quality maternal caregiving behaviour when compared with Caesarean section (CSD) (Poindron, 2005). Some have suggested this may be because of the vagino-cervical stimulation which occurs during vaginal delivery and which triggers the release of OT. In humans, however, no strong evidence connects vaginal delivery to better quality of maternal care or to higher level of OT. For example, most of the recent studies (albeit with rather small and limited samples) that examine maternal plasma OT levels, at baseline or following interaction with infant, do not find an association between OT and vaginal delivery (e.g. Feldman et al., 2007; Atzil et al., 2011).

However, indirect evidence from functional imaging (fMRI) does suggest that, in response to infants' cries at 2–4 weeks, mothers who delivered vaginally show more BOLD responses in brain areas related to maternal emotion, reward (amygdala) and motivations (cingulate cortex) compared to women who delivered by CSD (Swain et al., 2008a). It remains unclear whether mode of delivery would still influence maternal behaviour assessed at later stages during infant development.

ii. Mode of feeding

Breastfeeding represents a close physical contact between mother and infant and has been suggested to enhance the maternal infant bond (Feldman & Eidelman, 2003).

However, findings are inconsistent in this regard. Previously, some studies were unable

to support the relation between maternal sensitivity and breastfeeding. For example, Pridham et al. (2001) found no relationship between breastfeeding and maternal sensitivity observed through mother-infant interaction during feeding practice among 99 mothers and their infants at 1, 4, 8 and 12 months. Similarly, Drake et al. (2007) suggested that breastfeeding was not a significant predictor of maternal responsiveness. This might be attributed to the sample and measures of these studies, such as including premature and low birthweight infants in Pridham et al., and the use of self-report measures to rate sensitivity in the study by Drake et al.

On the other side, some studies links breastfeeding to greater maternal sensitivity. In a study that examines the relationship between breastfeeding, maternal sensitivity and attachment, Britton et al. (2006) recruited 152 women during pregnancy. Maternal sensitivity was observed during feeding (using the Nursing Child Assessment Satellite Training Feeding Scale) both at 3 and 6 months. They reported that mothers who breastfed showed greater sensitivity at 3 months compared to bottle feeding mothers and that the duration of breastfeeding correlated positively with the sensitivity rating. Similar findings were reported by Tharner et al. (2012) among 675 mothers. In that study, both mode of feeding and duration of breastfeeding were assessed at 2 to 6 months postpartum, while maternal sensitivity was observed at 14 months during free interaction for 13 minutes. The duration of breastfeeding was positively related to a higher maternal sensitivity rating. None of the two studies controlled for demographic factors related to breastfeeding, such as maternal age, education and SES, the thing which might have confounded their findings.

Recently, and as part of an fMRI study, Kim et al. (2011) assessed 9 breastfeeding mothers and 8 formula-feeding mothers for maternal sensitivity (using Coding Interactive Behaviour), observing this through mother-infant interactive play at home at

3–4 months postpartum. In this small sample, breastfeeding mothers showed higher sensitivity ratings ($p = 0.05$). However, with the exception of the study by Britton et al., none of these studies provides a strong evidence for the implication of breastfeeding or its duration in sensitive responsiveness, and thus further studies are needed to resolve inconsistency in this regard.

2.6.5. Infant temperamental behaviours

Researchers have focused on infant temperaments (i.e. individual personality differences in infants and young children) as a factor that could make sensitive mothering more challenging (Van Ijzendoorn et al., 2007). Studies examining infant temperament in relation to maternal behaviour have revealed mixed results. Thus, highly irritable infants may receive less sensitive care (as a result of their difficult temperaments) (Crockenberg, 1981; Van den Boom 1991). Van den Boom (1991) observed maternal sensitivity and infant temperament at monthly intervals over 6 months among 15 irritable and 15 non-irritable infants. Mothers of non-irritable infants were found to be more sensitive than those of irritable infants. This agrees with Thomas & Chess (1977), who suggest that infant temperament can make maternal responsiveness either highly challenging or less challenging. Whereas mothers of children with an ‘easy’ temperament can be more reassured about the adequacy of their parenting, those of ‘difficult’ temperament may be more likely to be distressed and unsure about their maternal care behaviour. The latter effect might hinder maternal self-efficacy (Bandura, 1977) and consequently maternal sensitivity.

Conversely, some mothers might interpret their infant’s temperament as a request for more care and accordingly show more responsive maternal care with irritable infants (see review by Crockenberg, 1986). According to Sroufe (1985), this is related to the

fact that parents attempt to be flexible around their infant's needs and hence give more attention to those who demand it. Ghera et al. (2006) examined 56 mothers and their 9 month-old infants (the latter were previously rated with negative reactivity through laboratory observation in another part of the study) for maternal sensitivity. Maternal sensitivity was observed during a 1 hour session that included feeding, free play, caregiving (using Ainsworth's scale). They used the Infant Behaviour questionnaire (IBQ) as a measure for maternal perception of the infant's 'soothability'. Their results showed that the relationship between infant negative temperament and maternal sensitivity is positive when the mother's perceive her infant as 'soothable' and negative when she perceived her/him as unsoothable. Therefore, the mothers of negatively reactive infants, who perceive their infants as not soothable or perceived herself as 'not capable' of soothing her/him, are at risk of providing low sensitivity care.

In contradiction to other studies that used maternal self-report measures (e.g. IBQ) to assess infant temperament, Ghera et al. used such measure as an index for how the mother perceived her child as soothable, rather than as an actual assessment for temperament. This clarifies some ambiguity in the literature in this matter. For instance, evidence suggests that studies that used observational measures to rate temperament (e.g. Crockenberg & Acredolo, 1983; Crockenberg, 1981; Van den Boom, 1994), tend to support a link between high irritability in infants and less sensitive maternal care. By contrast, only a few of those studies which rely on parent rating of infant temperament support this link (e.g. Campbell, 1979).

2.7. Summary

Natural variations in maternal sensitivity have been observed (Belsky et al., 2002).

Generally, insensitive mothering has been linked to poor infant emotional, social and

cognitive outcomes (Beckwith & Cohen, 1989; Kemppinen et al., 2006; Kivijarvi et al., 2001). The literature implies many individual factors which negatively influence maternal sensitivity. Maternal mood (depression/anxiety), even at non-clinical levels, has been suggested to have a negative impact on maternal sensitivity (Tronick & Reck, 2009). Prenatal maternal attachment to the unborn child appears to be important for the postnatal relationship, although there is no particular focus on maternal sensitivity (Alhusen, 2008). Social support (Andresen & Telleen, 1992), maternal education (Pederson et al., 1990) and financial stability (Evans, 2008) are all positively related to maternal sensitivity. The mother's experience in her family of origin has a significant influence on a mother's own future sensitivity with her children: better quality parental care provides a good 'model' to follow when caring for own children (Lindhiem et al., 2011). Conversely, maltreatment experiences (even in low risk samples) negatively affect a mother's sensitive responses (Pereira et al., 2012). Primiparity, mode of delivery and feeding show less robust association with subsequent maternal care behaviour and may be significantly confounded (e.g. Swain et al., 2008a). Similarly, mixed results are also seen in relation to difficult temperament of the infant (Ghera et al., 2006).

Targeted interventions are difficult when many of the variables that influence sensitivity are still unknown. This warrants further exploration for variables that could influence maternal sensitivity, especially those which could be determined prenatally so intervention could start in the early postpartum period before mother-infant patterns of interaction have become 'ingrained' and while the infant brain shows relative plasticity to positive change. We attempt to evaluate a more comprehensive set of factors thought to influence maternal sensitivity in order to answer this key question: In healthy mothers, can we identify prenatally or early postnatally which mothers are at risk of low maternal sensitivity at 4-6 months postpartum?

2.8. Study I Objectives

Using a sample of Caucasian UK mothers with no history of mental illness, the aim of the current study was to examine whether a range of psycho-social and demographic factors collated prenatally and postnatally could predict how sensitive mothers were toward their infants during observed play interaction in their home environment. We examined whether maternal sensitivity at 4-6 months is predicted by (1) the prenatally collated information regarding the mother's current mental state (depression, anxiety, maternal-fetal attachment), the mother's early experiences of being parented (care, overprotection) and maltreatment, socio-demographic characteristics (household income, educational level, maternal age) and social support; (2) the postnatally collated information regarding infant temperamental behaviour as perceived by mothers.

Chapter 3: **Study I Methodology**

3.1. Sample

Recruitment took place at 6 community antenatal clinics in Greater Manchester region in the North West of England between February 2011 and October 2011. For the purposes of inclusion, women must be Caucasian, of 18 to 40 years old, fluent English speakers, in the third trimester of pregnancy (28 weeks or more), with no current psychiatric illness and not on psychotropic medications. Women with any known abnormality or malformation in the current pregnancy, and who scored above threshold for depression (see below), were excluded. Although women were also excluded from follow-up if they scored above threshold for depression or their infants were diagnosed with medical, sensory or developmental disorders, none fell under either criterion. Following informed consent (see below), 105 women participated in the antenatal phase (Time 1) at a mean of 33.9 antepartum weeks ($SD = 3.19$) and all agreed to be contacted for follow-up postnatally.

Of 105 women included in Time 1, a total of 80 women and their infants were followed up at 4-6 months postpartum (mean = 19.36 weeks; $SD = 2.46$) (Time 2), with 25 women dropping out before Time 2 and therefore excluded from the analyses: 14 mothers were lost to follow-up, 9 discontinued participation and 2 were no longer eligible (1 infant was not living with the mother, 1 infant death). There was no difference in demographic characteristics between those who dropped ($N = 25$) and the final sample included in the analysis ($N = 80$) except in number of married women which was higher in the latter (Table 3.1). Also, no difference between the drop out and the follow up sample in regard to scores of measures completed at Time 1 (Appendix A).

Several reasons contribute to the selection of inclusion criteria. For example, since behaviours representing an affiliation with the infant are different across cultures (Alhusen, 2008), having a multi-cultural sample might demand a bigger sample to account for variability across cultures, which might not be feasible in the current study. Therefore, we confined our recruitment to white women. Furthermore, only fluent English speakers were included due to lack of validated translated versions from the questionnaires used in the study. We had to exclude women with current psychiatric illness to avoid being confounded by factors related to their own illnesses rather than to the actual parenting experience (Murray et al., 1996). Knowing about fetal malformation or abnormality might affect the mothers' responses towards the fetus and later after birth; these infants find difficulties in expressing their emotions in explicit ways (Van Ijzendoorn et al., 2007; Landry et al., 2001). Maternal sensitivity was assessed during 4-6 months rather than very early postpartum to ensure that mothers were more settled in their parenting role. Finally, mother infant play interaction was assessed at the women's own homes to maximise the reliability of this assessment by providing a naturalistic atmosphere during the interaction.

Table 3.1. Sample characteristics for women followed up postnatally (N = 80) and the drop-out (N = 25)

Characteristic	Women followed up in Time 2 (N = 80)	Drop-out after Time 1 (N = 25)	t (103)	Chi-square test	p-value
<i>Mean [SD]</i>					
Maternal age (years)	29.59 [5.53]	27.96 [6.62]	- 1.22		0.22
Gestational age (weeks)	34.10 [3.25]	33.28 [2.97]	- 1.12		0.77
Average maternal education (years)	14.06 [2.80]	14.15 [2.43]	- 1.87		0.43
Average annual household income (thousand pounds)	28.13 [4.26]	27.63 [4.64]	- 1.76		0.23
<i>Frequency (%)</i>					
Married/cohabiting	69 (86.3)	17 (68.0)		4.28	0.04
Primigravidas	41 (51.3)	13 (52.0)		0.01	0.95

3.2. Measures

3.2.1. The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987)

This 10-item self-report instrument is a commonly used effective screening tool for screening for depression in the postpartum period as well as during pregnancy (Murray & Cox, 1990). Women were asked to choose the response that provided a close representation of how they had felt during the last 7 days. An example of an item is “I have looked forward with enjoyment to things”. Items are rated on a 4-point Likert scale, and a cut-off score of 12 was used for screening positive.

3.2.2. The Hospital Anxiety and Depression (HADS) rating scale (Zigmond & Snaith, 1983)

This 14-item self-rating questionnaire is used to screen for anxiety and depression in clinical and community settings. Depression and anxiety are represented by 7 items each, rated on a 4-point (0-3) Likert scale ranging from ‘Not at all’ or ‘Definitely as much’ to ‘Most of the time’. Example of a depression item is “I still enjoy the things I used to enjoy”, and for anxiety “I get a sudden feeling of panic”. A score of 0-7 is normal, 8-10 ‘Borderline abnormal’, and a score > 11 is ‘Abnormal’. Severity ratings correlate highly with clinical psychiatric assessments ($r = 0.70$ depression and $r = 0.74$ anxiety) (Zigmond & Snaith, 1983). The measure has high internal consistency and high test-retest reliability (Crawford et al., 2001). Women were excluded from the study if scored both EPDS ≥ 12 and HADS > 11 .

3.2.3. Maternal-Fetal Attachment Scale (MFAS) Cranley (1981)

This 24-item scale measures the extent to which a pregnant woman engages in behaviours that represent an affiliation and interaction with their unborn child. Items are rated on a 5-point Likert scale ranging from ‘Definitely yes’ to ‘Definitely no’.

Examples of items were “I had pictured myself feeding the baby” and “I stroke my

tummy to quiet the baby when there is too much kicking”. In the current study, two modification were made: as most women would know the fetus’ gender by the time of recruitment (the third trimester), item 13 (“I have decided on a name for a baby boy”) was omitted and item 10 (“I have decided on a name for a girl baby”) was re-worded to include the word ‘boy’. Similar modification was done by Levine et al. (2007) to accommodate for their third trimester sample. The MFAS coefficient of reliability was reported as 0.85 (Cranley, 1981).

3.2.4. Parental Bonding Instrument (PBI) Parker et al. (1979)

This self-report measure examines an adult’s retrospective report of own parents’ caring behaviours (25 items for each parent) during the first 16 years of life, consisting of ‘care’ (12 items) and ‘overprotection’ (13 items) scales. Items are rated on a 4-point Likert scale ranging from ‘Very like’ to ‘Very unlike’. An example of a care item is “Spoke to me in a warm and friendly voice” and of overprotection is “Tried to control everything I did”. Participants were asked to score their parents as they remembered them in the first 16 years. The PBI possessed good internal consistency (Parker et al., 1979). Examination of test-retest reliability over 20 years supports the construct and convergent validity of the measure over an extended period of time which, was found to be independent of mood effects (Wilhelm et al., 2005).

3.2.5. Childhood Trauma Questionnaire (CTQ) Bernstein et al. (1997)

This 28-item retrospective self-report inventory screens for a history of childhood and adolescent abuse and neglect involving three subscales assessing abuse (Emotional, Physical, and Sexual) and two neglect subscales (Emotional and Physical) on a 5-point Likert scale (5 being the most negative response). The scale also includes three items to detect underreporting ‘denial/minimisation’ (items 10, 16 and 22). The measure is interpreted as an overall sum for all the scales. The reliability coefficient for the CTQ

scales ranged from satisfactory to excellent, with Test-retest reliability revealing high stability for the measure ranging between $r = 0.79$ and 0.86 for all scales (Bernstein et al., 1994).

3.2.6. The Oslo 3-items social support scale (Dalgard, 1996)

This 3-item scale covers different areas of social support. Participants reported the number of people close to them, ease of getting help from neighbours, and concern shown by others. Responses are rated in a 5-point Likert scale for items 1 and 3 and in 4-point Likert scale for item 2. Results are interpreted as a cumulative overall score which ranges from 3-14. One modification was made to item 1 in the current study: “How easily can you get help from neighbours if you should need it?” was modified to include ‘friends’ to emphasise the role of friends in social support as a more up-to-date indication of social support, particularly in urban areas, as early piloting found that women understood this mainly to mean immediate neighbourhood support.

3.2.7. The Manchester Assessment of Caregiver-Infant Interaction (MACI), Wan et al., 2012, 2013 online)

This observational measure of caregiver-infant interaction evaluates global features regarding the quality of interactions on a 7-point scale in 7 domains, including 2 caregiver scales (sensitive responsiveness and non-directiveness), 3 infant scales (attentiveness to caregiver, positive affect and liveliness), and 2 dyadic scales (mutuality and intensity of engagement). The measure is an adaptation of existing global scales of caregiver-infant interaction (Murray et al., 1996; Blazey et al., 2008) and the CARE-Index (Crittenden, 1979-2004) and has been validated for use in the 6-15 month-age range (Wan et al., 2012, 2013 online). In the current study, inter-rater reliability was tested for 30% of videotaped parent-infant interactions. Using absolute agreement inter-class correlation coefficients, moderate to high agreement was demonstrated as follows:

maternal sensitivity: $r = 0.70$, $p = 0.001$; maternal non-directiveness: $r = 0.55$, $p = 0.002$; infant attentiveness to parent: $r = 0.50$, $p = 0.004$; infant positive affect: $r = 0.62$, $p = 0.001$; infant liveliness: $r = 0.47$, $p = 0.001$; mutuality: $r = 0.72$, $p = 0.001$; and intensity of engagement: $r = 0.68$, $p = 0.001$. Any disagreements in the complete sample were resolved by both raters re-reviewing the clips to reach consensus.

The current study focused on one MACI domain: caregiver ‘sensitive responsiveness’, defined as the caregiver’s “contingent and appropriate behavioural responsiveness to identified infant behaviours as is required and optimal to meet the infant’s immediate and developmental needs. In this measure, responsiveness considers quality, and its broad definition includes an attentive attitude, and appropriate engagement, support and structuring in response to both infant behaviour and a lack of behaviour.” The rating of ‘sensitive responsiveness’ varies from (1) ‘minimally responsive/sensitive’ to (7) ‘very responsive/sensitive’ (Table 3.2; see Appendix B for full manual descriptions). This definition of ‘caregiver sensitive responsiveness’ is similar to the original definition of Ainsworth et al. (1978) of ‘maternal sensitivity’ (the mother’s ability to perceive infant signals and respond promptly and appropriately) and is the most commonly assessed construct of sensitivity in measures of maternal sensitivity (De Wolff & Van Ijzendoorn, 1997). Thus, to avoid confusion, this MACI domain is henceforth referred to as ‘maternal sensitivity’. MACI-rated maternal sensitivity has demonstrated moderately high stability between 7 to 14 months ($r = 0.48$; Wan et al., 2013 online). It is also independent of variables we do not expect to be related to interaction in normative populations, including infant non-verbal developmental level and infant gender (Wan et al., 2012).

Table 3.2. A brief description of rating definitions for maternal sensitivity on the MACI measure

Rating	Defining feature
1. Minimally responsive/sensitive	Little evidence: Generally does not respond, or responses are insensitive
2. Slightly responsive/sensitive	Occasional or very moderate sensitive responding
3. Fairly responsive/sensitive	Scattered evidence; ‘fair’ but misses opportunities, or takes over insensitively
4. Somewhat responsive/sensitive	A mixed picture: sometimes responsive or consistently mildly responsive
5. Generally responsive/sensitive	Clear examples offset by scattered or mildly insensitivity and/or responding
6. Responsive/sensitive	Clearly evident, substantially outweighing insensitivity/unresponsiveness
7. Very responsive/sensitive	Consistent pattern of moderate to highly sensitive responding throughout

3.2.8. Infant Behaviour Questionnaire Revised Very Short Form (IBQ-R-v. short) **(Gartstein & Rothbart, 2003)**

This revised version of the original Infant Behaviour Questionnaire (Rothbart, 1981) was developed in 2003 and refined in 2008 (<http://www.bowdoin.edu/~sputnam/rothbart-temperament-questionnaires>). The measure assesses the dimensions of temperament in infants of 3 to 12 months, as reported by parents. The IBQ-R-v. short measure consists of 37 items covering 3 “broad scales”: ‘surgency/extraversion’ (the degree to which a child is generally happy, active, seeking stimulation and enjoys vocalising) and ‘negative affect’ (the degree to which a child is not easily calmed), and ‘effortful control’ (the degree to which a child can focus attention, is not easily distracted) (Rothbart, 1981). Mothers rated the frequency of specific temperament-related behaviours observed over the past week on a 7-point Likert scale ranging from ‘Never’ to ‘Always’ and scored as 1 to 7 with 7 being the highest frequency for behaviour. An example of a Surgency item is “When tossed around playfully, how often did the baby laugh?” of a Negative affect item “When tired, how often did your baby show distress?”, and of Effortful Control “When singing or talking to your baby, how often did s/he soothe immediately?” Results are interpreted as an average for each scale separately.

All measures used in Study I are included in Appendix B.

3.3. Procedure

3.3.1. Time 1 (Pregnancy)

After completing the informed consent, women were interviewed in private at the antenatal clinic for 35 minutes, during which they completed the EPDS, HADS, MFAS,

PBI, and the Oslo 3-items social support scale. Detailed demographic information was also collected.

3.3.2. Time 2 (4-6 months postpartum)

After prior arrangement, eligible and contactable mothers (N = 80) were visited in their own homes at 4-6 months postpartum (mean = 19.36 weeks; SD = 2.46) at a time when the infant was healthy and likely to be alert. Mothers were instructed to play with their infant for 6 minutes on a floor mat as they would normally do, using toys (as supplied) or not as they wished, ignoring the researcher's presence. Mothers were asked not to have visitors or other members of the family present during the interaction recording. Interactions were stopped and later resumed if the infant got distressed, sick or upon the mother's request. Interactions were videotaped and later rated by an independent trained researcher blind to participant information using the MACI. Mothers were administered a structured interview which consisted of obtaining socio-demographic, obstetric and perinatal data, and were administered the EPDS, HADS, IBQ-R-v.short, in addition to CTQ which was delayed to this visit due to the sensitive nature of its questions. Informed consent was completed at the beginning of the visit. Table 3.3 summarises the measures used in Study I (Time 1 and Time 2).

Table 3.3. Summary of the measures used in Study I (Time 1 and Time 2)

Time of administration	Measure	Outcome of interest	Type of measure
Time 1	EPDS	Depression screening	Self-report
	HADS	<ul style="list-style-type: none"> • Depression screening • Depressive symptoms score • Anxiety symptoms score 	Self-report
	OSLO 3 items	Social support rating	Self-report
	MFAS	Maternal-fetal attachment rating	Self-report
	PBI	Women's own quality of parenting at family of origin rating <ul style="list-style-type: none"> • Parental care • Parental overprotection 	Self-report
Time 2	MACI	Maternal sensitivity rating	Observational measure
	EPDS	Depression screening	Self-report
	HADS	<ul style="list-style-type: none"> • Depression screening • Depressive symptoms score • Anxiety symptoms score 	Self-report
	IBQ-R-v.short	Infant temperamental behaviour score	Self-report
	CTQ	Mothers' childhood trauma score	Self-report

3.4. Statistical Analyses

3.4.1. Sample size

A priori power calculation was performed before recruitment to determine the sample size. The sample size of 80 is ample enough to detect relationships with up to 10 variables using regression analysis to detect a correlation of 0.21-0.25 (seen in the literature in the variables of interest, e.g. Tarkka, 2003; Shin et al., 2006) at a power of 0.81, a medium size effect (0.45) and an alpha level of 0.05. Taking into account dropouts and non responses over the two data collection times, a sample size of 105 women was selected at baseline (Time 1 of the study).

3.4.2. Data analyses

Sample descriptions were presented in frequency and descriptively, as appropriate. All variables were checked for their distribution, and logarithm or square root transformations were performed on variables that were skewed (showing less than - 0.8 or more than 0.8 skew). Pearson or Spearman correlations examined associations between key measure variables and in relation to maternal sensitivity. Assessments for covariates were performed and partial correlations were considered as appropriate. Because women were assessed for maternal sensitivity at different postpartum time (range: 16-26 weeks), infant age (at Time 2) was controlled for in all correlational analyses that included maternal sensitivity and also when maternal sensitivity was a dependent variable (regression analyses). Data were analysed using SPSS 19, and the level of significance for all analyses was set at 0.05.

3.5. Ethical Considerations

3.5.1. Ethics

Information about the study - including the aims of the study, what it involved in relation to participants, the nature of the questionnaires, as well as confidentiality issues - was explained to women verbally by the researcher and in written format through the information sheet. Women were given time to think about their participations and to ask freely should they have any query related to the study. Informed consent was obtained from each woman before each time they were involved in the study. Women were aware that their participation was entirely voluntary and they were free to withdraw at any time without giving a reason.

All personal data were kept anonymous, and all study data (paper, electronic, videotape) were stored in accordance with the Data Protection regulation at the University of Manchester, and Data Protection Act (1998). This study was approved by the North West 8 Research Ethics Committee-Greater Manchester East (Study Ref: 10/H1013/69).

3.5.2. Benefits to research participants

The women in the current study were very keen to participate and they enjoyed contributing to a study that might help to make a difference for some other mothers. One woman who sent a thank you letter wrote "...I hope the study helps women who have not been able to find that magical bond I have with my daughter". Nevertheless, as compensation for the time spent by women as a result of their participation, women were given a value of £3 pounds Johnson's baby starter pack at Time 1 and a value of £15 pounds Boots shopping vouchers at Time 2.

3.5.3. Safety considerations

Although the Time 2 visit was conducted at the mothers' home, a padded floor mat was provided and safety was assessed to ensure it was safe for the infant to play on the floor (e.g. no electrical sockets near the floor mat). The infant was always accompanied by the mother at all times. When the mother was busy completing the questionnaires, the infant had to be fastened in her/his seat to ensure her/his safety.

Chapter 4: **Study I Results**

The results are presented as follows: (1) Descriptive sample characteristics; (2) Characteristics for the mother-infant interaction; (3) Preliminary analysis of each measure (prenatal/postnatal) and its association with maternal sensitivity; (4) Main analyses to test the predictive value of assessed variables on maternal sensitivity (using stepwise regression).

4.1. Sample Characteristics

Within the final sample that followed up postnatally ($N = 80$ women) (Table 4.1), 61 (76.3%) had a natural delivery, 41 (51.2%) were primiparous, and 7 (8.8%) were less than 21 years at time of infant birth. All women had healthy singleton term babies, a mean birthweight of 3.45 kilograms ($SD = 0.45$), and 41 (51.3%) were female. More than half of infants ($n = 46$; 57.5%) were breastfed (exclusive or combined). At the time of follow-up (Time 2), the majority of mothers ($n = 68$, 85.0%) were on maternity leave, 9 (11.3%) were not employed, and 3 (2.9%) were back in work either as part time ($n = 2$) or full time ($n = 1$).

Table 4.1. Demographic characteristics for the sample (N = 80)

Demographic characteristic	Statistics (N = 80)
<i>Mean [SD]</i>	
Maternal age (years)	29.59 [5.53]
Gestational age at Time1 (weeks)	34.10 [3.25]
Infant age at Time 2 (weeks)	19.36 [2.46]
<i>Frequency (%)</i>	
Primiparity	41 (51.2)
Married/cohabiting	69 (86.3)
Household income/year:	
£15000 or less	19 (23.8)
£16000 -£25000	12 (15.0)
£26000 -£35000	17 (21.3)
£36000-£45000	11 (13.8)
£45000 and above	21 (26.3)
Highest educational level:	
Secondary (GCSE)	26 (32.4)
Post-secondary education (A-level or equivalent)	23 (28.8)
University degree and postgraduate	31 (38.8)

4.2. Characteristics of Mother-Infant Interaction (Manchester Assessment of Caregiver-Infant Interaction; MACI rating)

All the 7 domains (scales) within the MACI were normally distributed. After controlling for infant age, maternal sensitive responsiveness (maternal sensitivity) (mean = 3.31; SD = 1.31), correlated significantly with most other scales characterising mother-infant interaction (Appendix A). These were maternal non-directiveness (mean = 3.13; SD = 1.30) ($r = 0.50$; $p < 0.01$), mutuality (mean = 2.95; SD = 0.97) ($r = 0.72$; $p < 0.01$), intensity of engagement (mean = 4.06; SD = 0.88) ($r = 0.28$; $p < 0.01$), and infant attentiveness (mean = 3.40; SD = 0.96) ($r = 0.23$; $p < 0.05$), but not with infant positive affect (mean = 4.26; SD = 1.03) ($r = 0.07$; $p = 0.56$) or infant liveliness (mean = 3.18; SD = 0.97) ($r = 0.01$; $p = 0.99$). On the other hand, the other maternal domain of MACI (maternal non-directiveness) was only correlated with mutuality ($r = 0.38$; $p < 0.01$).

4.3. Preliminary Analyses (association of prenatal/postnatal factors with maternal sensitivity)

Variables were examined for correlation with maternal sensitivity to determine what would be examined as predictors in the main analysis.

4.3.1. Prenatal variables

i. Hospital Anxiety and Depression rating Scale (HADS) score

Depression score was based on HADS score and EPDS was only used as a screening tool. We limited our inclusion to women who scored below threshold in both EPDS and HADS depression (i.e. below 12 and 11, respectively). Mean EPDS for the included women was 6.40 (SD = 4.03). The sample produced relatively low anxiety (mean = 5.56; SD = 3.43) and depression scores (mean = 3.39; SD = 2.72). Most anxiety and

depression scores (the latter transformed as was positively skewed) were within the 'normal' range. However, five women scored in the abnormal range for anxiety (score = 11, 11, 14, 16 and 18). One participant scored in the abnormal range on the depression scale (score = 12) but had scored below the threshold on the EPDS (score = 11) and therefore fitted within our inclusion criteria. Although 16 women scored 'borderline abnormal' on anxiety, most of them ($n = 12$) were within the normal range in both anxiety and depression scales. Anxiety and depression scores showed a strong correlation ($r = 0.65$; $p < 0.01$). Accordingly their combined score was also examined. Maternal sensitivity was correlated with depression score ($r = -0.27$; $p = 0.02$) more significantly than with anxiety score ($r = -0.21$; $p = 0.07$) or the combined score ($r = -0.24$; $p = 0.04$). Accordingly, depression score was examined as a predictor variable in the main analysis presented later.

ii. Maternal-Fetal Attachment Scale (MFAS) score

The mean score for MFAS was 94.70 ($SD = 10.10$). Maternal sensitivity was not correlated with MFAS total score ($r = 0.06$; $p = 0.60$).

iii. Parental Bonding Instrument (PBI) scores

The PBI included 'care' scale and 'overprotection' scale for each own parent. Six women reported absence of their own father, and accordingly their PBI paternal reports were not completed. Maternal care (mean = 29.16; $SD = 8.70$) and paternal care (mean = 26.14; $SD = 9.76$) (both transformed as they were negatively skewed) were significantly correlated ($r = 0.39$; $p < 0.01$). Therefore, mean combined 'parental care' score (mean = 27.81; $SD = 7.50$) was analysed. Similarly, maternal overprotection (mean = 11.85; $SD = 6.26$) and paternal overprotection (mean = 11.47; $SD = 6.93$) were also highly correlated, and hence a mean combined 'parental overprotection' score (mean = 11.61; $SD = 5.64$) was analysed. Maternal sensitivity was correlated more

strongly with parental care score ($r = 0.31$; $p = 0.01$) than with parental overprotection score ($r = -0.24$; $p = 0.03$). Therefore, parental care was included in the final analysis.

iv. Childhood Trauma Questionnaire score

Considering the sensitive nature of the CTQ questionnaire, it was completed at Time 2. The overall CTQ score (mean = 32.25; SD = 14.14) was negatively correlated with maternal sensitivity ($r = -0.29$; $p = 0.01$) (after transformation), and therefore, was included as a candidate predictor in the main regression analysis. It is worth mentioning that our results showed 16 women (20.0%) with evidence of denial on the CTQ report (scored 3 on denial items). However, when we re-ran the analyses excluding those women, the results did not show significant change and therefore those women were not excluded from the analyses.

v. Socioeconomic status (SES)

Controlling for maternal age, maternal education and household income were strongly correlated with each other (Spearman's $r = 0.62$; $p < 0.01$) as well as with maternal sensitivity (Spearman's $r = 0.23$; $p = 0.04$, Spearman's $r = 0.27$; $p = 0.02$, respectively). Given the strong correlation related to the latter, household income was selected to represent SES in the final analysis.

vi. The Oslo 3-items social support scale score

We considered the overall sum of the 3 items (mean = 12.09; SD = 1.95). Controlling for parity, there was no significant correlation between the Oslo score (transformed as it was negatively skewed) (negative trend) and maternal sensitivity ($r = -0.20$; $p = 0.07$).

vii. Demographic characteristics related to parenting

Women who were less than 21 years, as expected at time of infant birth, ($n = 7$; 8.8%) showed a trend for lower maternal sensitivity (mean = 2.43; SD = 3.38) compared with

older mothers (mean = 3.38; SD = 1.31); [F (1, 77) = 3.42; p = 0.07]. Single marital status (n = 11; 13.7%) also showed a trend for lower maternal sensitivity (mean = 2.64; SD = 1.43) compared with married or cohabiting mothers (mean = 3.41; SD = 1.2); [F (1, 77) = 3.01; p = 0.09]. However given the small sample size for these two variables and the insignificant findings, no further analyses were performed.

A summary of the correlations between prenatal variables and maternal sensitivity is presented in Table 4.2.

Table 4.2. Correlations of prenatal variables with maternal sensitivity

Variable	Correlation with maternal sensitivity
HADS anxiety	- 0.21
HADS depression	- 0.26*
Maternal fetal attachment	0.06
Parental care	0.31*
Parental overprotection	- 0.24*
Overall CTQ score	- 0.29*
Oslo social support score	- 0.21
Household income¹	0.27*
Education¹	0.23*

*p < 0.05, 1: ordinal variable (Spearman's correlation coefficient).

4.3.2. Postnatal variables

i. Hospital Anxiety and Depression rating Scale score

HADS anxiety (mean = 4.91; SD = 2.98) and depression scores (2.91, SD = 2.26) generally remained low postnatally. Three participants scored above the threshold for 'abnormal' anxiety scores (score = 11, 13 and 19). None scored above the threshold on the depression scores. The majority of women were within the normal range in both scales (n = 65; 81.3%). Although a proportion of women (n = 10) scored borderline abnormal on anxiety, most of them (n = 8) were within the normal range for depression scale. Same as prenatally, postnatal anxiety and depression scores (the latter transformed as was positively skewed) were significantly correlated ($r = 0.50$; $p < 0.01$), and accordingly their combined score (mean = 0.44; SD = 3.43) was also examined. However, maternal sensitivity was not correlated with anxiety ($r = -0.08$; $p = 0.50$) or depression scores ($r = -0.04$; $p = 0.75$) separately or as a combined score ($r = 0.07$; $p = 0.54$). It is worth mentioning that prenatal and postnatal HADS depression scores were strongly correlated with each other ($r = 0.32$; $p = 0.01$), and the same for anxiety scores ($r = 0.60$; $p < 0.01$).

ii. Infant Behaviour Questionnaire Revised Very Short Form score

The three scales within IBQ-R-v.short, namely Surgency (mean = 3.80; SD = 0.82), Negative affect (mean = 3.03; SD = 1.01) and Effortful Control (mean = 5.33; SD = 0.64), were not correlated with maternal sensitivity ($r = 0.01$ to 0.13 ; $p = 0.25$ to 0.93).

4.4. Main Analysis: Predictors of maternal sensitivity (Stepwise regression)

Based on the preliminary analyses, no postnatal factor was significantly associated with maternal sensitivity; therefore, only prenatal factors were entered into a stepwise regression. Four prenatal variables which were significantly correlated with maternal

sensitivity were included in the regression analyses, namely: depression score, own parental care, childhood trauma, and household income in addition to infant age to account for its variability. The results are presented in Table 4.3. In the first model, infant age was entered, and then variables were added one at a time. In the second model, depression scores accounted for significant variance of maternal sensitivity but that was shared by parental care as evidence by cancellation of the depression effect when parental care was entered (model 3) (parental care correlated negatively with depression score, $r = -0.24$; $p = 0.02$). When childhood trauma was added in the fourth model, it cancelled the effect of parental care (parental care correlated negatively with childhood trauma, $r = -0.76$; $p < 0.01$). However, the childhood trauma score was not even significant and it did not add any improvement in the overall regression. Accordingly, childhood trauma was removed from the regression model. When household income was entered in the fifth model, it proved to be a significant predictor of maternal sensitivity, along with parental care. Therefore, about 17% of the variance in maternal sensitivity is predicted from prenatal variables, with parental care received by the mother and household income accounting for most of the variance.

Table 4.3. Stepwise regression examining prenatal predictors of maternal sensitivity (adjusted R^2) = 0.17

Model	Variable	Beta	P-value	Cumulative adjusted R2
1	Infant age	- 0.14	0.24	0.01
2	Infant age Depression score	- 0.13 - 0.23	0.27 0.05*	0.05
3	Infant age Depression score Parental care	- 0.16 - 0.17 0.29	0.16 0.15 0.01*	0.12
4	Infant age Depression score Parental care Childhood trauma	- 0.16 - 0.16 0.28 - 0.03	0.17 0.17 0.12 0.89	0.10
5	Infant age Depression score Parental care Household income	- 0.14 - 0.12 0.25 0.26	0.20 0.30 0.03* 0.03*	0.17

*p < 0.05

Chapter 5: Study I Discussion

5.1. Overview of the Findings

The present study (Study I) aimed to examine whether readily identifiable prenatal or postnatal factors could help determining mothers at risk of low maternal sensitivity at 4-6 months postpartum, in order to aid parenting interventions in the planning and targeting of scarce resources to parenting outcomes.

Six prenatal variables were significantly *correlated* with maternal sensitivity: maternal depression score, parental care, parental overprotection, household income, maternal education, childhood trauma score, and two of these were significant *predictors* for maternal sensitivity at 4-6 months postpartum (parental care, household income).

Conversely, maternal fetal attachment, maternal social support, young maternal age as expected at birth (< 21 years), and single marital status were not related to maternal sensitivity.

Although postnatal variables were measured at the same time as mother-infant interaction video data was collated (on which maternal sensitivity was evaluated), none of the postnatal variables were associated with maternal sensitivity, namely maternal postnatal mood scores (anxiety, depression), and maternal report of infant temperament. Accordingly, none of them was examined as a predictor. Our findings from the stepwise regression revealed that own parental care and household income were significant predictors of maternal sensitivity accounting for 17% of the variance in maternal sensitivity after controlling for infant age at time of sensitivity assessment.

The discussion includes sub-sections including discussion of the mother-infant interaction characteristics follow by our main findings from the regression model.

Interesting findings from the preliminary analysis, including the relationships between prenatal and postnatal variables with maternal sensitivity, were also discussed to inspire future hypotheses.

5.2. Mother-Infant Interaction

Our findings revealed that maternal sensitivity was correlated significantly with most other scales characterising parent-infant interaction, namely maternal scale (maternal non-directiveness), dyadic scales (mutuality, intensity of engagement) and an infant scale (infant attentiveness). Thus, maternal sensitivity ratings in this cohort appear to largely reflect the quality of overall interaction, and to a lesser extent the quality of infant behaviour. On the other hand, the other maternal domain (i.e. non-directiveness) correlated only with mutuality, signifying the unique contribution of maternal sensitivity in mother-infant interaction quality.

5.3. Predictors of Maternal Sensitivity

The first main finding, the mother's own reported level of parental care (maternal + paternal), as measured prenatally using the PBI, was found to be associated with her behavioural sensitivity to her own child. This is in line with attachment theory (Bowlby, 1969) as well as with other studies like Lecuyer-Maus (2000) and Pederson et al. (1998). This finding, suggests that a positive care experience serves as an internalised model for more sensitive ways of interacting with own infant (Ward & Carlson, 1995). Furthermore, this impact of maternal own parental experience on maternal sensitivity towards own children is consistent with the animal literature which reports a role for the early environment in shaping maternal caregiving behaviour towards own offspring (Francis, 1999, 2000; Champagne et al., 2007; Champagne, 2008). The concordance

between our findings and other studies that use a discourse analysis procedure (Pederson et al., 1998; Lindhiem et al., 2011) also support the reliability of self-report measures (i.e. PBI) in assessing own early parental care.

Another interesting finding related to parenting experience is also shown from the regression analysis. Although initial depression scores accounted for significant variance in maternal sensitivity, significant variance was shared with parental care. Therefore, the effect of maternal depressed mood prenatally on later sensitivity (if any) appears to be attributable to negative early care experiences, but not specifically to trauma. Other studies of healthy populations also showed increase in depression scores among those who showed low parental care or high parental overprotection (Hill et al., 2001; Avagianou & Zafiropoulou, 2008). Our results suggest that a mother's own experiences of less optimum/negative early care might place her at later risk of both a more depressed mood and lower behavioural sensitivity. Although one can expect that PBI is a self-report measure, and therefore the mother's own negative responses in this instrument may be the artefact of a depressed mood. The concordance between our findings and other studies that use a discourse analysis procedure (Pederson et al., 1998; Lindhiem et al., 2011) support the reliability of self-report measures in assessing previous parental care. Furthermore, studies like Hill et al. (2001) have assessed depressive mood through an adapted measure (Schedule for Affective Disorders and Schizophrenia), and they were also able to support the relationship between parental care and depression.

The second main finding from the regression analysis, in regard to household income (represents SES) as a significant predictor of maternal sensitivity, is also consistent with other studies (e.g. Pederson et al., 1990; Sacker et al., 2002; Evans, 2008). This relationship between SES and maternal sensitivity may be because higher SES mothers

have a more infant-centred approach to parenting than lower SES mothers (Ziv et al., 2000), and therefore are more capable in seeking resources to help their parenting skills (Bornstein & Bradley, 2003). The higher social functioning among higher SES mothers in general might also explain better interactions with infants (Eccles & Harold, 1996). This parental focus on infant fine-grained behaviours is exactly what is measured by the MACI (i.e. the sensitivity rating measure used in the current study). On the other hand, being of lower SES exposes mothers to a range of environmental risk factors and deprivations that challenge their sensitivity to their infant and their emotional capacity (McAdoo, 2002).

A previous study has reported SES as a significant predictor for *infant* responsiveness (Bornstein et al., 2007). Therefore, one can speculate that high SES not only works directly to enhance maternal sensitivity, but also through improving the reciprocal interaction between the mother and her infant through increasing infant responsiveness. Surprisingly, some researchers like Pederson et al. (1998) and Drake et al. (2007) did not find this relationship between SES and maternal sensitivity. However, this could be related to their methodological approaches as mentioned earlier. In comparison, in the current study women represent a wide range of social classes and maternal sensitivity was assessed through observation which allowed better chance to uncover this relationship.

The childhood trauma score was not a significant predictor of maternal sensitivity. Although previous studies among community samples reported negative associations between maltreatment and different aspect of maternal behaviours, including non-intrusiveness (Moehler et al., 2007) and hostility (Bailey et al., 2012), only one study was able to show maltreatment as a predictor of maternal sensitivity (Pereira et al., 2012). One might expect this is due to a low level of trauma in the community sample.

However, Bailey et al. (2012) increased the variability of their sample by only including women who have at least one social risk factor (i.e. young age at birth, low income, single), yet their findings revealed maltreatment to be related only to hostility towards the child and not to maternal sensitivity. Although Pereira et al. (2012) reported that maltreatment is a predictor of maternal sensitivity in a low-risk sample, yet they also reported that this relationship is only significant when mediated by maternal distress (observed and self-reported). The sample size of Pereira et al. was also much bigger compared with the current study, or the samples of Moehler et al. or Bailey et al. (N = 291 vs. 80, 58 and 82, respectively).

Although our stepwise regression model explains only 17% of the variance in maternal sensitivity, yet this is higher than some other studies like Drake et al. (2007) who examined the predictive capacity of multiple variables and could explain for 15% of variance in maternal sensitivity.

5.4. Associations between Maternal Sensitivity and Prenatal/Postnatal Variables

5.4.1. Prenatal variables

Aside from household income, our other proxy measure of SES (maternal education) was also positively associated with maternal sensitivity. This is possibly due to higher SES provided by education (Pederson et al., 1990), appreciation among educated mothers of their role in the infant's learning (Walker et al., 1986), or to more positive disciplinary techniques adopted by an educated mother and hence enabling more sensitive care (Augustine et al., 2009).

Unlike older studies such as Fuller (1990) and Siddiqui & Hagglof (2000), we did not find a relationship between maternal fetal attachment and maternal sensitivity. Several

explanations might account for this. First, we assessed maternal sensitivity much later (4-6 months) than Fuller or Siddiqui & Hagglof (first weeks postpartum). Therefore, maternal-fetal attachment may no longer be related to maternal interaction style at a later stage in postpartum and the interaction style by then is more related to other measures reflecting maternal and infant current characteristics rather than how the mother felt during pregnancy. Second, although Siddiqui & Hagglof (2000) reported that PAI score was positively related to face-to-face interaction at 3 months postpartum, particularly in maternal stimulation behaviours using proximal behaviours, and negatively with maternal non-involvement, PAI was unrelated to maternal responsiveness to infant behaviour. Therefore, MFR may be predictive of later maternal involvement and stimulation (rather than sensitive responsiveness), and thus highlight mothers at risk of withdrawal and neglect, rather than of low sensitive interaction per se.

Third, different measures have been used to measure MFR, for example while MFAS emphasises maternal behaviours (Cranley, 1981), the Prenatal Attachment Inventory (PAI) emphasises affiliation with regards to the prenatal relationship with the fetus (Muller, 1993). Although MFAS is the most widely used measure for studying the MFR (Beckwith et al., 1999), the subscales were theoretically rather than empirically derived, with high internal consistency only for 2 factors, while other measures (e.g. PAI, Maternal Antenatal Attachment Scale) have too few psychometrics published to date (Alhusen, 2008). Although there is some evidence to suggest that maternal fetal attachment might be related to future maternal responsive behaviour, better examination of this link should be considered (see review by DiPietro, 2010).

Continuity of affect states (depression and anxiety) from the prenatal period to postpartum period (at non-clinical levels) has been reported previously (Kaplan et al., 2008). Similarly, in the current study, both prenatal and postnatal HADS depression

scores were strongly correlated with each other (as were anxiety scores). However, depression scores in the prenatal period, but not at postpartum, significantly correlated with maternal sensitivity (negatively). One explanation is that, we found higher prenatal depressive symptoms compared to postnatal time (mean depression score 3.39 vs. 2.91 respectively, but statistically not significant). Thus the relationship between depressive symptoms and maternal sensitivity was only apparent prenatally especially with the relatively low depression scores among the sample in general.

Neither the prenatal nor the postnatal anxiety score correlated with maternal sensitivity, inconsistent with other studies (e.g. Nicol-Harper et al., 2007). However, this could be attributed to the relatively low anxiety scores in our sample. Interestingly, in spite of limiting our inclusion to mothers who scored below the threshold for depression screening, we were still able to show a relationship between depression scores and maternal sensitivity, indicating the high impact of depression (even at a non-clinical level) on parenting (Tronick & Reck, 2009).

Unlike other older studies (Goldstein et al., 1996; Barclay et al., 1997), we did not find an association between the level of maternal social support and maternal sensitivity. However, similar results were found by Han (2002) who did not find a difference in maternal sensitivity between those who received physical and psychological support and those who did not. Three reasons might contribute to our findings: First, some argue that it is the support from the spouse, rather than from other people, which is related to maternal responsiveness (Levitt et al., 1986; Crockenberg, 1988; Erel & Burman, 1995). Second, our measure focuses on quantitative nature of social support rather than qualitative one with the latter suggested by literature as being more relevant to maternal responsiveness (Crockenberg, 1988). The first reasoning is supported by our finding of a trend for lower maternal sensitivity among single mothers compared with married or

cohabiting mothers. Third, we assessed social support during pregnancy, yet the mother's demand for social support increases during the busy time following the infant's arrival (Andresen & Telleen, 1992) and, therefore, the mother's perception of her social support might have changed after delivery when maternal sensitivity was assessed.

5.4.2. Postnatal variables

None of the postnatal variables were significantly related to maternal sensitivity, namely postnatal mood scores (anxiety, depression) and maternal self-report of infant temperament. Maternal sensitivity was not related to dimensions of infant temperament as rated by mothers. However, comparing our results to Ghera et al. (2006) who found a positive correlation between IBQ score (as a measure of infant as being soothable) and maternal sensitivity, it is important to note that all the infants included in their study were previously rated as 'difficult temperamental' infants. Given that difficult temperament was only represented by about 10-15% of infants (Thomas & Chess, 1977), our sample (N = 80) might not be ample enough to show a big number of those infants.

In addition, some researchers argue that the relationship between maternal caregiving and infant temperament might depend on the mother's characteristics and beliefs, as well as the balance of stress and support in her life, e.g. mood state, social support, SES (Stifter & Wiggins, 2004). In other words, it is the presence of other favourable (or unfavourable) factors which lead a mother to perceive her infant's difficult temperament as either a request for more attention or as a strain (Sroufe, 1985; Mertesacker et al., 2004). This explains why many of those who used 'observational' measures to rate temperament supported the link between high irritability in infants and less sensitive care (e.g. Crockenberg & Acredolo, 1983; Crockenberg, 1981; Van den Boom, 1994),

whereas only a few of those who rely on parent rating of temperament support this link (e.g. Campbell, 1979). Ghera et al. (2006) also suggested that the relationship between an infant's difficult temperament and maternal sensitivity is positive if the mother perceives her infant as soothable and negative if she perceives her/him as unsoothable.

The strength and limitation of the study (Study I) as well as clinical implication and future directions are included in the conclusion chapter (Chapter 11).

Publication 1

**Maternal sensitivity in healthy mothers: Can
at-risk maternal sensitivity be predicted
prenatally?**

Maternal sensitivity in healthy mothers: Can at-risk maternal sensitivity be predicted prenatally?

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SYNOPSIS

In spite of the large research investment and accumulating evidence that parenting interventions which optimise infant developmental and mental health can improve maternal sensitivity, translation of such knowledge into service delivery has been extremely limited. Interventions are resource-intensive; selecting groups deemed at-risk (e.g. mothers with mental illness) may not best address the general population's mental health. An alternative approach would be to identify those mothers at risk of low maternal sensitivity in the prenatal period when all early postpartum mothers make contact with services in order to facilitate delivery of effective intervention early in the postpartum. **Objectives:** The primary aim of this study was to identify prenatally determined psycho-social and demographic factors, which might predict maternal sensitivity at 6 months postpartum. A secondary aim was to examine whether the number of psycho-social and demographic factors to which mothers were exposed predicted lower maternal sensitivity. **Design:** In the third trimester, 105 healthy, pregnant women were assessed on simple self-report measures. At 4-6 months postpartum, 6 minutes of unstructured mother-infant play was videotaped during a home visit and was blind rated for maternal sensitivity using the Manchester Assessment of Caregiver-Infant Interaction (MACI). **Results:** Several prenatally-measured factors (score of depressive symptoms, experience of own parental care, own parental overprotection, history of trauma, household income, and educational attainment) were associated with maternal sensitivity at 4-6 months postpartum. Only two factors (mother's own reported experience of parental care, and household income) independently predicted maternal sensitivity, accounting for 17% of the variance. The number of psychosocial risk factors also predicted lower sensitivity: mothers exposed to 3+ psychosocial risk factors were more likely to show lower sensitivity to their infants. **Conclusion:** Relatively simple prenatal 'screening' of psycho-social and demographic risk factors in healthy mothers can identify those who are more likely to be at risk of low maternal sensitivity. However, asking mothers prenatally about their general social supports or how well they are bonding with their infants did not predict maternal sensitivity. Routine assessment of key maternal factors may be a relevant adjunct to other forms of antenatal health screening.

INTRODUCTION

Early 'preventative' parenting interventions that take place in infancy aim to promote positive infant development and mental health by enhancing maternal sensitivity – the mother's accurate perception and prompt response to infant signals. The rationale for targeting maternal sensitivity is that evidence from developmental psychology supports its role in fostering secure attachment and in child social, emotional, and cognitive development (e.g. Landry et al., 2001; Lohaus et al., 2001; Warren & Simmens, 2005; Kemppinen et al., 2006; Mills-Koonce et al., 2008). Low maternal sensitivity is associated with later harshness or difficulties with parenting (e.g. Lindhiem et al., 2011; Joosen et al., 2012) and a range of poorer child outcomes, such as behavioural problems

(Downer & Pianta, 2006; Alink et al., 2008; Kochanska & Kim, 2012). Although much research has been invested and has shown that such parenting interventions can be effective in improving maternal sensitivity (e.g. Bakermans-Kranenberg et al., 2003), translation into service delivery has been very limited (Barlow et al., 2008) and has tended to focus on specific at-risk groups (Forman et al., 2007). Effective interventions are almost certainly too resource-intensive for a universal approach, yet those most in need are least likely to engage in services. An alternative is to offer a more personalised, tiered approach that focuses efforts on those identified to be at risk in the prenatal period when all new mothers make contact with health services and when mother-infant dynamics may still be relatively malleable. Whether factors identified prenatally could predict future maternal sensitivity is the focus of the current study.

No studies to our knowledge have examined the predictive value of multiple prenatally-measured factors on *observed* maternal sensitivity. Since continuity in maternal sensitivity is likely to be due largely to continuity of stable social contexts (Van Ryzin et al., 2011), it is possible that sensitivity can be predicted from associated socio-contextual factors already present before the infant's birth, assuming their continued stability. Two studies have identified multiple postnatal predictors of self-rated 'maternal sensitivity'. Among the data that could potentially be collated prenatally, mothers' reported sensitivity towards their 6-week-old infants strongly predicted (retrospectively-reported) maternal-fetal attachment in a Korean sample (Shin et al., 2006). Employment status and social support were also significant predictors. In a US study, perceived life satisfaction and self-esteem independently predicted 'maternal responsiveness' at 2-4 months postpartum (Drake et al., 2007). However, in both studies, the outcome measured was concerned more with maternal affective experience rather than behavioural sensitivity observed in interaction. One study identified prenatal predictors of (6-month) maternal sensitivity to distress, but the factors do not lend themselves to application in the health context (Leerkes, 2010).

As well as considering the independent predictive value of single risk factors, cumulative 'contextual' risk models have been widely conceptualised as developmental models (e.g. Sameroff & Seifer, 1983; Sameroff, 2006) that suggest that no single risk factor has a long-lasting effect on a child. Instead, it is the aggregate number of risk factors that alters developmental trajectories. Although cumulative risk models have predicted poor child and adolescent outcomes (e.g. Pasco Fearon & Belsky, 2011;

Watanabe et al., 2011), they have rarely examined maternal sensitivity as an outcome. In a study by Mertesacker et al. (2004) only a combination of risk factors at 4 months, rather than any single risk factor, predicted 4-8 month maternal sensitivity change, but the significant factors were either all infant-related (for instance, depression and anxiety scores with respect to their infants) or low social support was combined with at least one negative infant-related factor. The implication is that the mother's thoughts and feelings concerning her infant significantly contribute to maternal sensitivity, which cannot be measured until postpartum.

Studies that have focused on single factors that may be measurable prenatally and have been related to maternal sensitivity can be grouped into the following broad categories: (1) social context (such as socioeconomic status (SES) and social support); (2) maternal prenatal mental state (such as anxiety, depression, and attachment to the fetus); (3) early care experiences of the mother in her family of origin. Firstly, evidence to date suggests that the most robust finding is a positive association between maternal sensitivity and SES (Bornstein et al., 2007; Evans, 2008), including maternal education (Sacker et al., 2002) – with higher SES or education conferring higher sensitivity. Social support, which has a 'buffering effect' on parenting stress, has been positively associated with maternal sensitivity in postnatal studies (e.g. Pauli-Pott et al., 2003) and in a prenatal study, which has used self-rated measures of maternal sensitivity (Shin et al., 2006).

Secondly, some evidence suggests the effect of maternal prenatal mental states with respect to affect states (depression and anxiety) on maternal responsiveness (Grant et al., 2009) with continuity between the pre- and postnatal mental states reported by some (Kaplan et al., 2008). Furthermore, maternal-fetal attachment (MFA) towards the (unborn) child (Muller, 1996) has also been associated with maternal interaction quality in community samples (Siddiqui & Hagglof, 2000; Campbell et al. 2007; Mills-Koonce et al., 2008). Third, consistent with attachment theory (Bowlby, 1969), early positive care experiences provide adults with the emotional and cognitive resources, and broader social learning, to provide sensitive caregiving (Lindhiem et al., 2011), while poor care, neglect, and trauma in childhood confer later difficulties in parenting and sensitivity (Cicchetti et al., 2006; Bailey et al., 2012).

The aim of the current study was to examine, in a community sample, whether a range of psycho-socio-demographic factors collated prenatally could predict how sensitive mothers were towards their infants during observed play interaction in their home

environment. We examined whether (1) maternal sensitivity is predicted by the prenatally collated information regarding the mother's current mental state (depression, anxiety, maternal-fetal attachment), the mother's early experiences of being parented (care, overprotection) and maltreatment, socioeconomic status (household income, educational level), and social support; (2) low maternal sensitivity would be predicted by the *number* of psycho-socio-demographic risk factors present out of the following eight variables: young maternal age, single marital status, low social support, unemployment household, no education, low household income, own parental neglect.

METHODS

Participants

Participants were recruited from six community antenatal clinics in the northwest region of England (Greater Manchester). Of 148 Caucasian pregnant women, 105 met the eligibility criteria (18-40 years, 28 weeks or more, no current psychiatric illness, and scored less than the threshold for depression scores) and enrolled in 'Time1' (T1) of the current study.

At 4-6 months postpartum, 'Time 2' (T2), 14 women were lost to follow-up, 9 withdrew from the study, and 2 were no longer eligible (1 baby was not living with the mother and 1 baby death). No significant difference was seen in the demographic characteristics between the drop out sample (N = 25) and the follow-up sample (N = 80), except for number of married/cohabiting women which was higher in the follow-up sample. Among the remaining 80 women who were followed up at T2, 61 (76.3%) had a natural delivery, 41 (51.2%) were primiparous, and 7 (8.8%) were less than 21 years at time of infant birth. All women had healthy singleton term babies, mean birthweight was 3.45 kilograms (SD = 0.45), and 41 (51.3%) were girls. More than half of infants (n = 46; 57.5%) were breast fed (exclusive or combined). At T2 the majority of mothers (n = 68; 85.0%) were home on maternity leave, 9 (11.3%) were not employed and 3 (2.9%) were back to work. Table 1 shows the characteristics of the women at T1 and T2. The study was approved by the North West 8 Research Ethics Committee-Greater Manchester East (Ref: 10/H1013/69) and informed consent was obtained at each time of the study.

Table 1 about here ‘Demographic characteristics for the women enrolled in the study at T1 (N = 105) and T2 (N = 80)’.

Measures

The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987). This is a 10-item self-report instrument used to screen for depression in the postpartum and antenatal periods. Items are rated on a 4-point Likert scale. A cut-off score of 12 was used for screening positive.

The Hospital Anxiety and Depression (HADS) rating scale (Zigmond & Snaith, 1983). This is a 14-item self-rating questionnaire used to screen for anxiety and depression in normative and clinical samples. Items are rated on a 4-point Likert scale.

The Oslo 3-items social support scale (Dalgard, 1996). This is a 3-item scale covering different areas of social support (family, friends, and neighbourhood). It provides a cumulative overall score.

Maternal-Fetal Attachment Scale (MFAS) (Cranley, 1981). This 24-item self-report measure assesses women’s representation of affiliation towards their unborn child. Items are rated on a 5-point Likert scale, interpreted as an overall score. In the current study, item 13 (‘I have decided on a name for a baby boy’) was omitted and item 10 (‘I have decided on a name for a girl baby’) was re-worded to include the word ‘boy’.

Parental Bonding Instrument (PBI) (Parker et al., 1979). This self-report measure examines an adult’s retrospective report of her parents’ caring behaviours (25 items for each parent) during the first 16 years of life, consisting of ‘care’ (12 items) and ‘overprotection’ (13 items) scales. Items are rated on a 4-point Likert scale.

Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1994). This 28-item retrospective self-report inventory screens for a history of childhood and adolescent abuse (emotional, physical, and sexual) and neglect (emotional and physical) on a 5-point Likert scale.

The Manchester Assessment of Caregiver-Infant Interaction (MACI) (Wan et al., 2012, 2013 online). This observational measure of caregiver-infant interaction evaluates global features regarding the quality of interactions on a 7-point scale in 7 domains,

including 2 caregiver scales (sensitive responsiveness and non-directiveness), 3 infant scales (attentiveness to caregiver, positive affect, and liveliness), and 2 dyadic scales (mutuality and intensity of engagement). MACI was adapted by one of the authors (MWW; Wan et al., 2012) from the validated global scales of caregiver-infant interaction (Murray et al., 1996; Blazey et al., 2008) and the CARE-Index. MACI-rated maternal sensitivity has demonstrated high inter-rater reliability at 6-15 months of age ($r = .74$; $p < .001$) (Wan et al., 2013 online).

In the current study, 30% of videotaped parent-infant interactions were rated independently by a second trained coder blind to all participant information. Using absolute agreement inter-class correlation coefficients, moderate to high agreement was demonstrated in all scales ($r = .47$ to $.72$; all $ps < .004$), including maternal sensitivity ($r = .70$; $p < .001$). Any disagreements in the complete sample were resolved by both raters re-reviewing the clips to reach consensus.

The current study focused on one MACI domain: caregiver sensitive responsiveness (henceforth ‘maternal sensitivity’), defined as the caregiver’s ‘contingent and appropriate behavioural responsiveness to identified infant behaviours as is required and optimal to meet the infant’s immediate and developmental needs’. The rating of ‘sensitive responsiveness’ varies from (1) minimally responsive/sensitive’ to (7) very responsive/sensitive’ (see Appendix for sensitive responsiveness domain descriptions).

Procedure

In the third trimester of pregnancy (T1), the following measures were completed by mothers in the antenatal clinic: EPDS, HADS, MFAS, PBI, Oslo 3-item scale, and questions on demographic and participant characteristics. At 4-6 months postpartum (T2), a videotaped 6 minute mother-infant interaction episode of unstructured play was collated during a home visit. Mothers were instructed to play with their infants for 6 minutes on a floor mat as they normally would do, using toys or not, ignoring the researcher’s presence. Mothers also completed the CTQ (not completed in T1 due to the sensitive nature of the questions), EPDS, and HADS.

Data analysis

Examination for covariates was performed, covarying for particular characteristics as necessary, such as infant age. A preliminary analysis to examine correlation

relationships with maternal sensitivity was first performed. Next we ran two regression analyses to answer our questions about which prenatal characteristics could predict maternal sensitivity. First, a stepwise regression was performed to test for maternal sensitivity predictors from the variables assessed in the preliminary analyses above. Second, a binary logistic regression was undertaken to test whether low maternal sensitivity (MACI rating of 1-3) could be predicted by the *number* of risk factors present in mothers (as opposed to the presence of a particular factor).

RESULTS

Preliminary analysis

Mother-infant interaction characteristics. Maternal sensitivity ($M = 3.31$; $SD = 1.31$) correlated significantly with most other scales characterising parent-infant interaction, namely, maternal nondirectiveness (mean = 3.13; $SD = 1.30$) ($r = .50$; $p < .01$), mutuality (mean = 2.95; $SD = 0.97$) ($r = .72$; $p < .01$), intensity of engagement (mean = 4.06; $SD = 0.88$) ($r = .28$; $p < .01$), and infant attentiveness (mean = 3.40; $SD = 0.96$) ($r = .23$; $p < .05$).

Correlations of prenatal variables with maternal sensitivity. Variables were examined for correlation with maternal sensitivity to determine what would be examined as predictors in the main analysis. All correlations are shown in Table 2.

Maternal mental state. Given the exclusion of high EPDS scorers from the study (mean EPDS for included women = 6.40; $SD = 4.03$), HADS anxiety ($M = 5.56$; $SD = 3.43$) and HADS depression scores ($M = 3.39$; $SD = 2.72$), were generally low. HADS depression score (transformed), but not anxiety score, correlated with maternal sensitivity.

Maternal fetal attachment score. MFAS ($M = 94.70$; $SD = 10.10$) was not correlated with maternal sensitivity.

Maternal own parenting experience. PBI maternal care ($M = 29.16$; $SD = 8.70$) and paternal care ($M = 26.14$; $SD = 9.76$) (6 missing due to absence of own father) were significantly correlated, after transformation ($r = .39$; $p < .01$), so combined into a 'parental care' score. Similarly, PBI maternal overprotection ($M = 11.85$; $SD = 6.26$) and paternal overprotection ($M = 11.47$; $SD = 6.93$) were highly correlated ($r = .48$; $p < .01$).

.01), so combined into a ‘parental overprotection’ score. Maternal sensitivity was correlated with both parental care and parental overprotection.

Childhood maltreatment score. The 5 CTQ subscales were highly inter-correlated ($r = .47$ to $.62$; $p < .01$; all transformed) and their overall score ($M = 32.25$; $SD = 14.14$) was negatively correlated with maternal sensitivity.

Sociodemographic. Household income and maternal education were strongly correlated with each other (Spearman’s $r = .62$; $p < .01$) and with maternal sensitivity. Household income was chosen as a proxy indicator for socioeconomic status (SES) due to its stronger correlation.

Social support score ($M = 12.09$; $SD = 1.95$) was not correlated with maternal sensitivity. However, a trend of higher maternal sensitivity was found in married/cohabiting mothers ($M = 3.41$; $SD = 1.2$) compared with single mothers ($M = 2.4$; $SD = 1.43$) $F(1, 77) = 3.01$; $p = .09$.

Table 2 about here ‘Correlations of prenatal variables with maternal sensitivity’.

Presence of multiple social risk factors. Accumulation of multiple risk factors proposed by literature to impact upon early parent-child relationships were explored in the current study. These were: less than 21 years’ maternal age, single marital status, unemployment household, no educational attainment, poor social support (< 9 Oslo total score), low household income (\leq £15,000/year), neglectful maternal parenting (PBI maternal care score ≤ 27 + maternal overprotection score ≤ 27), neglectful paternal parenting (PBI paternal care score ≤ 24 + paternal overprotection score ≤ 24). Maternal sensitivity generally decreased with increase in number of social risk factors (Figure 1), and mothers who reported three or more social risk factors ($n = 14$; 17.5%) showed lower maternal sensitivity (mean = 2.36; $SD = 1.08$) compared with mothers who had two or fewer factors ($n = 66$) (mean = 3.50; $SD = 1.27$); $F(1, 77) = 9.15$, $p < .01$.

Figure 1 about here ‘Maternal sensitivity ratings across the sample ($n = 80$) by the number of psycho-socio-demographic risk factors present’.

Main analyses: Predictors of maternal sensitivity

Stepwise regression analysis. Four variables were entered, one at a time, into the regression model, in addition to infant age to adjust for its variability (Table 3).

Depression scores accounted for significant variance of maternal sensitivity after adjusting for infant age (Table 3, model 2), and this was shared by parental care (model 3). Parental care was significantly predictive of low maternal sensitivity, but CTQ score, added in model 4, cancelled the effect of parental care, possibly owing to the significant correlation between the two variables ($r = -.76$; $p < .01$). However, CTQ was not a significant predictor of low maternal sensitivity and it did not improve the regression model, and was therefore removed from the model. Household income (model 5) was a significant predictor of high maternal sensitivity along with parental care. Overall, 17% of the variance in maternal sensitivity was predicted from readily collected prenatal variables, with parental care received by the mother herself and household income accounting for most of the variance.

Table 3 about here ‘Stepwise regression examining prenatal predictors of maternal sensitivity among the sample ($N = 80$) (adjusted R^2) = .17’.

Logistic regression analysis. A binary logistic regression was performed to examine if the number of social deprivation factors significantly predict low maternal sensitivity (MACI 1-3; $n = 40$). Significant predictive capacity (Beta = $-.43$; $p = .02$; Nagelkerke $R^2 = .12$; $p = .03$) was found. When a more stringent definition of low maternal sensitivity was adopted (MACI rating of 1-2; $n = 27$) similar results emerged (Nagelkerke $R^2 = .13$; $p = .02$).

DISCUSSION

The present study examines whether variables collected prenatally could predict maternal sensitivity at 4-6 months postpartum. Our findings revealed that women’s own experiences as recipients of parental care, and household income, were significant independent predictors of maternal sensitivity, accounting for 17% of the variance, after controlling for infant age. Presence of multiple risk factors (young maternal age, single maternal status, poor social support, no educational attainment, low household income, unemployment household, own neglectful maternal parenting, and neglectful paternal parenting) were predictive of low maternal sensitivity and in this sample account for 12% of the variance.

The finding of an association between own parenting experience and later maternal sensitivity accords with attachment theory (Bowlby, 1969) and is consistent with other

studies which used recall measures like PBI (e.g. Lecuyer-Maus, 2000) or a discourse analysis procedure such as the Adult Attachment Interview (e.g. Lindhiem et al., 2011), and suggests that a positive care experience serves as an internalised model for more sensitive ways of interacting with own infant (Belsky et al., 2005). In our data, the association of maternal sensitivity and childhood maltreatment was precluded by a negative correlation between childhood maltreatment and parental care (the latter was a predictor in the model) which is in line with other studies (e.g. Hill et al., 2001).

Our finding that socioeconomic status (household income) was a significant predictor of postnatal maternal sensitivity is consistent with other more recent studies (e.g. Sacker et al., 2002; Evans, 2008). There are a range of possible social explanations for this. For example, higher SES mothers may have more support which in turn allows them greater capacity to provide a more infant-centred approach to parenting than lower SES mothers (Ziv et al., 2000). In addition, and perhaps as a result, they may be more interested in seeking materials which facilitate and support their own parenting skills (Eccles & Harold, 1996; Bornstein & Bradley, 2003). On the other hand, low socioeconomic status exposes mothers potentially to a range of deprivations that challenge their capacity to deliver sensitive maternal care (McAdoo, 2002), including their cognitive or affective deficits which would make mother predisposed to low maternal sensitivity. Where studies have not found a relationship between SES and maternal sensitivity, this is likely to reflect methodological issues such as the high income of the sample studied (e.g. Pederson et al., 1998) or the use of a self-assessment measure for maternal sensitivity (e.g. Drake et al., 2007).

Unlike Fuller (1990) and Siddiqui & Hagglof (2000), we did not report a relationship between maternal fetal attachment and maternal sensitivity. Siddiqui & Hagglof (2000) found that MFA (assessed at last trimester) was related to face-to-face interaction at 3 months postpartum, particularly in maternal stimulation behaviours using proximal behaviours, and negatively with maternal non-involvement. However, the MFA score was not unrelated to ‘maternal responsiveness’ – which may be most akin to sensitivity in their study. Therefore, MFA may be predictive of later maternal involvement and stimulation (rather than sensitive responsiveness), and thus highlight mothers at risk of withdrawal and neglect, rather than of low sensitive interaction per se. Other researchers who support this relationship either confined their mother-infant interaction assessment to the first few days postpartum (e.g. Fuller, 1990) or focused on a particular group (e.g.

adolescent) (Bloom, 1995) with results that have not been replicated in a wider demographic of mothers.

Unlike other older studies (Barclay et al., 1997; Goldstein et al., 1996) we did not find an association between level of maternal social support and maternal sensitivity. Some argue that it is the support from the spouse rather than from other people which is related to maternal responsiveness (Erel & Burman, 1995). This is further supported by our finding of lower maternal sensitivity among single mothers (significance at a trend), compared with married or cohabiting mothers.

Having more than one risk factor at the same time may present an overwhelming challenge to early postpartum mothers, resulting in a decline in the ability of the mother to pay attention to their infant and a decline in sensitive maternal behaviour (Mertesacker et al., 2004).

Strengths and Limitations

This study has some important strengths related to the relatively large, consecutive population sampling of a community group of expectant mothers. Given the known variation of maternal care in the population, we were particularly interested to look at maternal sensitivity predictors that would (1) be suitable to collect in routine antenatal care, (2) be easily collected by researchers and clinicians, and (3) would reflect a majority of women attending antenatal clinics rather than a smaller clinical risk sample. We also confined our recruitment to Caucasian women in order to minimise known cultural differences between maternal care behaviour in mothers (Alhusen et al., 2008), especially with the bigger number of variables we are already examining. In so doing, we acknowledge that this limits the generalisability of our findings to non-Caucasian mothers. However, our sample still has a mixed sociodemographic characteristic. Although the sample from which we derived the 80 mothers (in whom maternal sensitivity was assessed) was relatively large ($N = 105$), it was still quite small for uncovering all factors that might influence maternal sensitivity. Furthermore, we assessed early experiences using self-report measures (i.e. PBI, CTQ) which might be subjected to underreporting (Ballestrem et al., 2005). Nonetheless, good psychometric properties and good predictive validity have been reported for both PBI and CTQ (Wilhelm et al. 2005; Bernstein et al. 1994).

Clinical implication and future research

Our findings highlight the potential for early assessment of parental care. Positive parenting support to improve parenting sensitivity is a limited resource which needs careful identification of children at greatest risk of maladaptive care if we are to optimise children's future outcomes. Information that can readily be collected prenatally in routine clinical settings may provide both an invaluable and potentially highly cost-effective way in which to assess mothers most at risk, and thus the potential to intervene early in the mother-infant relationship. Targeting parenting interventions of mothers at risk of low maternal sensitivity may aid more appropriate distribution of resources and better planning of services. Future research needs to replicate these findings in a larger sample with wider ethnic diversity to assess the utility of these as predictor variables to other ethnic and minority groups and assess the cost effectiveness of implementing simple screening questionnaires as part of routine antenatal assessment.

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Table 1. Demographic characteristics for the women enrolled in the study at T1 (N = 105) and T2 (N = 80)

Demographic characteristic	Time 1 (N = 105)*	Time 2 (N = 80)
<i>Mean [SD]</i>		
Maternal age (years)	29.20 [5.82]	29.59 [5.53]
Gestational age (weeks)	33.90 [3.19]	34.10 [3.25]
<i>Frequency (%)</i>		
Primiparavity/primiparity	54 (51.4)	41 (51.2)
Married/cohabiting	86 (81.9)	69 (86.3)
Household income/year:		
£15,000 or less	30 (28.6)	19 (23.8)
£16,000–£34,000	38 (36.2)	29 (36.2)
£35,000 or more	37 (35.2)	32 (40.0)
Highest educational level:		
Secondary (GCSE)	38 (36.2)	26 (32.4)
Post-secondary education (A-level or equivalent)	32 (30.4)	23 (28.8)
University degree and postgraduate	35(33.4)	31 (38.8)

*Original (initial) sample.

Table 2. Correlations of prenatal variables with maternal sensitivity

Variables	Correlation with maternal sensitivity
HADS anxiety	- .21
HADS depression	- .26*
Maternal fetal attachment	.06
Parental care	.31*
Parental overprotection	- .24*
Overall CTQ score	- .29*
Oslo social support score	- .21
Household income ¹	.27*
Education ¹	.23*

*p < .05, **p < .01. Note.1: Ordinal variable (Spearman's)

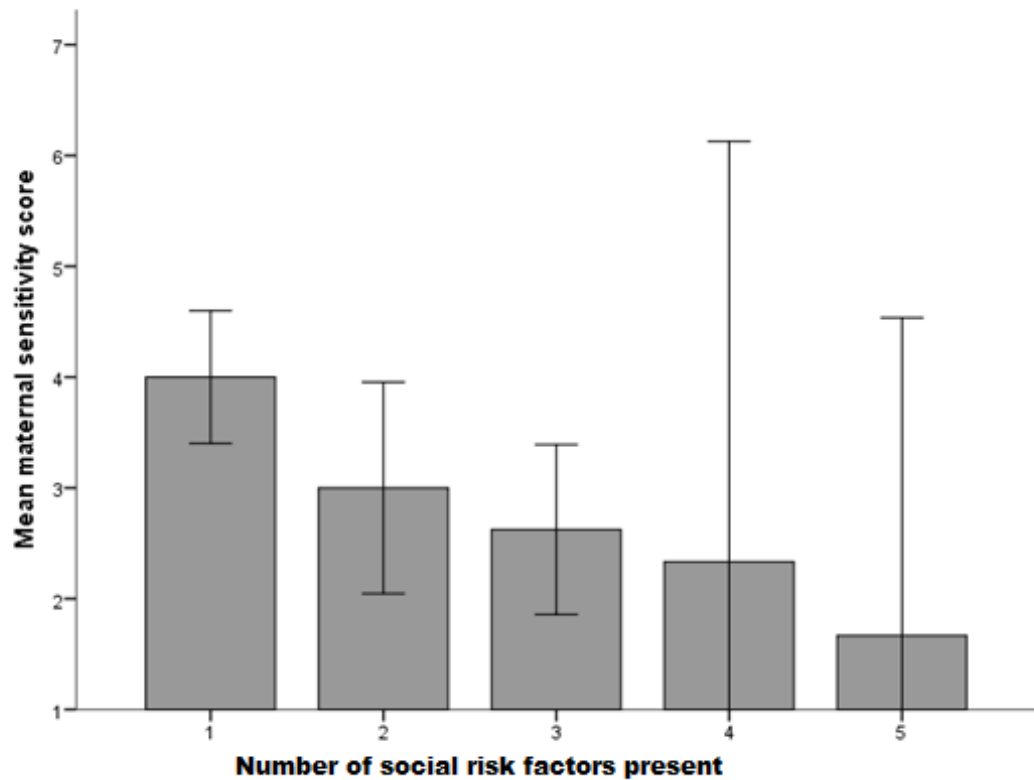


Figure 1. Maternal sensitivity ratings across the sample (N = 80) by the number of psycho-socio-demographic risk factors present

Table 3. Stepwise regression examining prenatal predictors of maternal sensitivity among the sample (N = 80) (adjusted R²) = .17

Model	Variable	Beta	P-value	Cumulative adjusted R2
1	Infant age	- .14	.24	.01
2	Infant age	- .13	.27	.05
	Depression score	- .23	.05*	
3	Infant age	- .16	.16	.12
	Depression score	- .17	.15	
	Parental care	.29	.01*	
4	Infant age	- .16	.17	.10
	depression score	- .16	.17	
	Parental care	.28	.12	
	CTQ	- .03	.89	
5	Infant age	-.14	.20	.17
	Depression score	-.12	.30	
	Parental care	.25	.03*	
	Household income	.26	.03*	

*p < .05

APPENDIX

A brief description of rating definitions for caregiver sensitivity on the MACI

Rating	Defining feature
1. Minimally responsive/sensitive	Little evidence: Generally does not respond, or responses are insensitive.
2. Slightly responsive/sensitive	Occasional or very moderate sensitive responding.
3. Fairly responsive/sensitive	Scattered evidence; ‘fair’ but misses opportunities, or takes over insensitively
4. Somewhat responsive/sensitive	A mixed picture: sometimes responsive or consistently mildly responsive.
5. Generally responsive/sensitive	Clear examples offset by scattered or mildly insensitivity and/or responding.
6. Responsive/sensitive	Clearly evident, substantially outweighing insensitivity/unresponsiveness.
7. Very responsive/sensitive	Consistent pattern of moderate to highly sensitive responding throughout.

Study II: The neurobiological mechanisms underlying maternal behaviour in humans:
Do less sensitive mothers' brain and endocrine responses to infant stimuli differ from sensitive mothers?

Chapter 6: Study II Literature Review (A)

6.1. Oxytocin (Background)

OT is a nonapeptide hormone synthesised mainly by the magnocellular neurons of the supraoptic (SON) and paraventricular (PVN) nuclei of the hypothalamus (Lee et al., 2009) and to a lesser extent from the spinal cord, bed nucleus of stria terminalis (BNST) (Carter & Murphy, 1989). Local synthesis in some peripheral tissues has also been reported, including the heart, thymus, gastrointestinal tract and testes (Gimpl & Fahrenholz, 2001). A range of brain regions receive OT projections, including the medial preoptic area (MPOA), nucleus accumbens (NAcc), amygdala, hippocampus, and ventral tegmental area (Ross & Young, 2009). This explains the wide distribution of this hormone in the body and brain (Feldman et al., 2011). Parturition, distension of the cervix, suckling, social recognition and pair bond might all act as stimuli for OT release (Lee et al., 2009). Depending on the stimulus, stored OT is released episodically from the posterior pituitary into the blood (peripheral effect) and the brain (central effect) (Gimpl & Fahrenholz, 2001).

6.1.1. Effects of Oxytocin

OT has well known 'peripheral effects' in humans and other mammals. These include its classical action in the *mammary tissues* to help with milk ejection, through the 'let-down' reflex (Gimpl & Fahrenholz, 2001), as well as on the *uterus* to facilitate myometrial contractility and parturition (Fuchs et al., 1995). OT is increasingly known

to have ‘central effects’ on behaviours related to social affiliation. In humans, such actions include enhancing *feelings of trust*, possibly by minimising amygdala activation to fear (Baumgartner et al., 2008; Meyer-Lindenberg, 2008). OT also increases *social memory* and *face recognition* (Lee et al., 2009), possibly through increased eye gaze to faces (Gimpl & Fahrenholz, 2001). OT works in a reciprocal way with the hypothalamic-pituitary-adrenal axis (HPA) which mediates stress responses (Dabrowska et al., 2011) and therefore exhibits an *anxiolytic effect* (anti-stress effect) by reducing the level of stress hormones in both humans (Legros, 2001) and rats (Stachowiak et al., 1995). This anti-stress effect also facilitates the initiation of breastfeeding (Uvnas-Moberg, 1998) and *affiliation* (social bonding) between individuals (Grippe et al., 2007).

The connection of OT with the dopaminergic reward system facilitates its role in romantic *pair bonding* (Williams et al., 1992) by the initiation of *sexual behaviour* and *sexual maturity* (Kow & Pfaf, 1998). Similarly, this connection with a reward system also helps the reinforcement of the infant’s value to its mother (Cardinal et al., 2002) and consequently mother-infant bonding (Galbally et al., 2011). The crucial role that OT plays in mediating *parental behaviour* in animals (e.g. Champagne et al., 2001, 2007, 2008) and humans in particular (Feldman et al., 2007; Gordon et al., 2010; Atzil et al., 2011; Galbally et al., 2011) is central to this thesis and therefore will be the focus of this chapter.

Because animal studies have *directly* examined the role of OT in the neurobiology of maternal bonding (Insel & Young, 2001), an outline of evidence from animal models is also provided in this chapter.

6.2. Animal Studies

OT is implicated in promoting positive maternal behaviour across a variety of animal species, including the licking and grooming of female rats (Landgraf et al., 1991), and the olfactory-based recognition of ewes by sheep (Levy et al., 1995; Meddle et al., 2007). The quality of maternal care that is received by an animal influences the future quality of care provided to its own offspring (cross-generational transmission of maternal behaviour) (Francis et al., 1999; Champagne, 2008), partially because animals adopt the same OT profile as their reared mothers (Champagne, 2008). Thus, the onset and maintenance of maternal behaviour have a hormonal and environmental basis (maternal care), in which OT plays a key role (Rosen et al., 2008).

6.2.1. Oxytocin and maternal behaviour in animal

Animal studies have directly examined the role of OT in maternal behaviour. In a pioneer study, Pedersen & Prange (1979) studied alloparental behaviour (i.e. nurturing behaviour that develops toward fostered pups) in virgin female rats after they were injected with OT, Vasopressin (AVP) or saline into the cerebral ventricles. Forty-two percent of the virgin females injected with OT displayed a full range of maternal behaviour (grooming, crouching over pups, licking pups, nest building and pup retrieval) towards foster pups within two hours. Conversely, none of the saline or AVP-treated virgin rats displayed these behaviours (Pedersen & Prange, 1979). In a follow up study, the effect of OT on maternal behaviour was reported to be dose-dependent, with higher doses of OT reported to elicit a greater range of maternal responses (Pedersen et al., 1982).

More recently, higher levels of OT receptor (OTR) density were found in the NAcc of virgin female prairie voles which displayed alloparental behaviour compared to those who ignored or attacked pups (Olazabal & Young, 2006). Within the same study,

administration of an OTR antagonist into the NAcc prevented expression of alloparental behaviours towards pups. In another study, the injection of OTR antagonist into the right lateral ventricle led to reduced postpartum maternal behaviour in rats (Van Leengoed et al., 1987). Although the antagonist did not interfere with parturition, a marked delay was observed in the onset of pup licking and grooming and other maternal behaviours among antagonist-treated mothers and, after one hour, two out of the six mothers had not yet picked up a single pup. On the other hand, the saline-injected controls started gathering the pups immediately following parturition, and showed all the elements of maternal behaviour within 10 minutes.

During pregnancy and when nursing, changes in the brain's OT levels and OTR have been reported to occur in the female rat brain (Lee et al., 2009), particularly in the ventral septum (Landgraf et al., 1991), SON, PVN and dorsal hippocampus (Landgraf et al., 1992). Significant increases in OTR expression are also seen during parturition throughout the brain in rats (Meddle et al., 2007). This increase in OTR expression facilitates the formation of a bond between mother and offspring (Leng et al., 2008). An increase in OTR expression is seen in the PVN and SON of postpartum female prairie voles (Wang et al., 2000), in the PVN, SON, and lateral hypothalamus of postpartum rabbits (Caba et al., 1996) and in the olfactory bulb of ewes at parturition (Levy et al., 1995).

Furthermore, high levels of OT immuno-reactive fibres were also found in brain areas implicated in maternal care in some animals (Rosen et al., 2008). Recent development of genetic 'knockout' experiments using mice with a deletion in either the OT or OTR gene have supported the previous findings in relation to the role of OT (Lee et al., 2009). OT knockout (OTKO) and OTR knockout (OTRKO) mice were able to mate and give birth without incident (Young et al., 1997; Takayangi et al., 2005) but were unable

to lactate (Nishimori et al., 1996); as a result, their pups were unable to survive. These mice were also reported to be more offensively aggressive, showing more infanticidal (i.e. kills pups) behaviour than controlled mice in the same environment (Ragnauth et al., 2005). These findings suggest that, at least in rodents, OT is essential for nursing and caregiving but not for parturition or reproductive behaviour.

6.2.2. Cross-generational transmission of maternal behaviour in animals

The quality of maternal behaviour in the early postpartum exhibits a measurable stable individual difference (Meaney, 2001; Champagne et al., 2003), which has an important impact on the physiology and behaviour of the offspring (see Champagne & Meaney, 2007). In a cross-fostering rat study by Francis et al. (1999), the biological female of 'low' licking and grooming arched-back nursing (LG-ABN) mothers reared by 'high' LG-ABN foster-mothers were reported to show similarly high levels of LG-ABN (seen by their foster-mothers) when they become adult themselves and handle their own pups. On the other hand, the biological offspring of high LG-ABN reared by 'low' LG-ABN foster-mothers were reported to show similarly low levels of LG-ABN (seen by their foster-mothers) when they handled their own pups. More recently, Champagne (2008) reported that 'high' licking and grooming mothers were also seen to show a high density of brain OTR similar to that of their high licking and grooming foster-mothers (Champagne, 2008). This suggests that maternal affiliative care induces non-genomic (epigenetic) changes in OTR expression in brain areas related to maternal motivation and behaviour such as the medial preoptic area, the lateral septum, and the bed nucleus of the stria terminalis in high LG-ABN lactating rats (Francis et al., 2000). Such changes in the offspring's gene are believed to be through Deoxyribonucleic acid (DNA)-methylation (Francis et al., 2002).

The quality of maternal care also has an epigenetic impact on stress reactivity/physiology and the behaviour of the offspring (see Champagne & Meaney, 2007). In rodents, for example, the offspring of high LG mothers showed an increase in the expression of glucocorticoid receptors in the hippocampus (Zhang & Meaney, 2010) and decreases in hypothalamus-pituitary-adrenal axis response to stress, which enhanced their learning and memory ability (Liu et al., 1997). This underscores the combined effect of maternal care and the OT system in shaping offspring reward and stress pathways (Feldman, 2011). It is worth noting that the expression and distribution of OT in the brain and its link to maternal behaviour show substantial variation between species (Ross et al., 2009). It is therefore important that the link between OT and social bonding/maternal caregiving behaviour is studied in humans, albeit considering the limitations and difficulties associated with such studies in humans.

6.3. Human Studies

6.3.1. Oxytocin and parental behaviour in humans

A number of recent studies have attempted to shed light on the role of OT in human parenting behaviour. Two studies examined OT in women during pregnancy and the early postpartum period. In the first study, Feldman et al. (2007) examined plasma OT levels in 62 women during the first trimester (T1), third trimester (T2) and the first postpartum month (T3). In this study, maternal behaviours (gaze, vocalisation, touch, and affect) were observed during unstructured play in the first postpartum month. Mothers were interviewed to assess levels of attachment representation towards their infants, preoccupation and infant checking behaviours. Plasma OT levels measured prenatally (T1) and postnatally (T3) were significantly correlated with maternal behaviour, attachment representation and infant checking behaviour. Furthermore, high

plasma OT at T1 predicted the amount of (postpartum) maternal behaviour, suggesting that OT plays a role in the quality and quantity of maternal behaviour in humans in the early postpartum period.

The second study examined the same cohort in a study of the relationship between maternal plasma OT levels during pregnancy and the mother's self-reported attachment to her fetus (using MFAS) in the third trimester (Levine et al., 2007). Interestingly, they reported that pregnant women showed five distinct patterns of plasma OT change: levels that decreased, that remained stable, that increased across pregnancy but dropped at postpartum, that dropped during pregnancy and increased at postpartum, and that steadily increased across all time points. While OT levels were not found to be correlated with MFAS score among the whole sample, significantly higher MFAS scores were found among women who showed a steady increase in plasma OT across all time points compared to women who showed other profiles. The variability in pattern of plasma OT in women during pregnancy is consistent with previous studies in pregnant women (De Geest et al., 1985; Dawood et al., 1978) and highlights the importance of taking multiple measurements when assessing plasma OT.

Both Feldman et al. (2007) and Levine et al. (2007) found high stability of plasma OT levels across assessments within each individual woman. This lends support to the validity of using plasma OT to assess OT in women. Neither study found any association between OT levels and demographic variables, including mode of feeding. Yet, they emphasised the association between plasma OT and the evolving mother-infant bond during pregnancy, at least for some women, as per the findings of Levine et al. (i.e. those who show a rise in plasma OT). The authors strengthened their design by keeping potential confounders 'constant' (by including only married or cohabiting

women). However, a wider approach to sampling women should be considered in future studies.

In the first study to examine plasma OT levels in both mothers and fathers, Gordon et al. (2010) studied 80 couples during the second and sixth postpartum months. At each visit, plasma OT was obtained from both parents and interactions between each of the parents and their infants were videotaped and coded for parental affectionate behaviours (i.e. infant-focused speech, vocalisation, and affectionate touch) and stimulatory behaviours (i.e. tactile stimulation and object presentation). An overall increase in plasma OT levels was observed throughout the study period, with the plasma OT levels of mothers and fathers being positively correlated at both assessments. Plasma OT was specifically positively correlated with the affectionate parenting behaviour among mothers and to stimulatory parenting behaviour among fathers, suggesting gender difference in relation to OT's role in parenting. The strength of this study came from the larger sample size and the naturalistic home setting in which observations of maternal behaviour were made. In addition this study was the first to link the mother's plasma OT profile to maternal behaviours later in the postpartum (2 and 6 months), and therefore add usefully and consistently to the findings in early postpartum (Feldman et al., 2007).

A similar design was undertaken by Feldman et al. (2010a) who, in addition to measuring plasma OT, also measured salivary OT among 112 mothers and fathers (not couples) when their infants were 4 to 6 months old. Parent and infant had play interaction (assessed for affectionate and stimulatory behaviour as earlier), after which plasma and saliva samples were measured. Plasma and salivary OT were positively correlated both within each parent, supporting the validity of both measures in assessing OT in humans (Hoffman et al., 2012). Consistently with Gordon et al. (2010), OT

measurements (plasma and salivary) were positively correlated with affectionate parenting behaviour in women and to stimulatory parenting behaviour in fathers. In another study which was a part of an fMRI study, Atzil et al. (2011) rated 23 mothers for their synchronous behaviour “episodes when mother and infant coordinate their positive social engagement” and intrusive behaviour “inappropriate responses from mother” with their 4-6 months infants (assessed through play interaction). Plasma OT levels were positively correlated with maternal-infant synchronous behaviour but not with intrusive behaviour. The micro-analytical assessments of maternal sensitive behaviour in this study are less crude compared with earlier studies (Feldman et al., 2010a, b) and also provide better insights into OT and maternal behaviour.

6.3.2. The cross-generational transmission of OT in humans

In an attempt to examine the epigenetic pattern of maternal behaviour (i.e. the effect of early caregiving experience) in humans, Feldman et al. (2010b) replicated their previous study (i.e. Feldman et al., 2010a), but this time with a smaller sample of 55 mothers and fathers (not couples) and their 4 to 6 month-old infants. Plasma OT was obtained from parents while salivary OT was taken from both parents and infants before and after the 15 minute-play interaction. Interaction was coded for parent behaviour (gaze, affect, vocalisation and touch) and infant behaviour (gaze, affect, vocalisation and touch), and rated as two composites: affect synchrony and infant social engagement. Similar findings to that of Feldman et al. (2010a), in regards to positive correlation between OT and parental behaviour, were also reported here. Interestingly, parent and infant OT levels were correlated positively with each other, providing evidence for the role of OT in mediating trans-generational behaviour in humans, equivalent to that reported in the rodent literature (Francis et al., 2000; Champagne et al., 2007).

6.3.3. Oxytocin and own perceived parenting experience

Examining the associations between OT and perceived bonding with own parents have been the focus of two OT studies among adults and one study among children. In the first study, Strathearn et al. (2009) assess the attachment representations of 61 pregnant women with their own mothers (using the AAI). Later at 7 months postpartum, plasma OT was examined before and following mother-infant play (physical and mirror-based) interaction in 15 women with secure attachment and 15 with insecure-avoidant attachment with own mother. Although baseline plasma OT did not differ between secure and insecure mothers, mothers with secure attachment showed higher post-interaction OT levels than mothers with insecure attachment (Strathearn et al., 2009). However, this difference disappeared when the interaction was mirror-based instead of physical, suggesting that the mother's own attachment experience and OT profile are apparent with parameters which relate to physical contact (e.g. touch), rather than to other modes of social interaction. This is consistent with earlier findings that link OT to maternal affectionate behaviour (rather than stimulatory behaviour) (Feldman et al., 2010a, b; Gordon et al., 2010). Within the same study, maternal fMRI responses to infant visual stimuli (pictures) at 11 months was related to increased activation in mesocorticolimbic rewards regions (areas implicated in OT and dopamine reward processing) among secure mothers compared to insecure-avoidant mothers (further details of this brain activation were discussed in Chapter 7). Although the authors speculate that OT might be a mechanism by which dopamine induces its effect in emotional reward behaviours, further evidence is needed when OT and brain activation are measured simultaneously (Galbally et al., 2011).

The second study examined the relationship between plasma OT and perceived own parenting experience in adults who have no children (non-parent). Gordon et al. (2008) measured the plasma OT of 45 women and men while their perceived bonding with

their own parents were assessed using the PBI. Plasma OT levels were positively correlated with PBI parental care scores (maternal and paternal care). Early experience of parenting may not only influence parenting behaviour towards own children (Strathearn et al., 2009), but also the physiological hormonal profile of individuals, including non-parents. This is also evidenced by the correlated OT levels between infants and their parent in the study by Feldman et al. (2010b).

In the third study, Fries et al. (2005) measured urinary OT in children (4.5 years old) who were raised by their own parents ($n = 21$) and children who were raised in orphanages ($n = 18$; adopted by the time of the study). Children interacted physically with both their mothers (foster or biological) and also with unfamiliar adults during video games while in the adult's lap for 30 minutes. This was performed in two occasions at 7 day intervals. Basal urinary OT levels were calculated as an average of the first urine of the day over four days. Although there was no difference in baseline OT measurement between the two groups (biological/adopted), children raised by their parents showed borderline significantly higher urinary OT ($p = 0.06$) following the interaction compared to those who were adopted. In spite of their statistically insignificant finding, it is interesting that the increase in children's urinary OT following the interaction was not related to whether the interacting adult was the mother or an unfamiliar adult. The authors did not include a measure to assess relationships between those children and their mothers in either of the groups.

6.3.4. Maternal behaviour and breastfeeding as a proxy measure for OT levels

In addition to research directly assessing plasma OT levels, two studies examine the relationship between maternal care and breastfeeding, where breastfeeding is used as a proxy for elevated plasma OT level. Feldman & Eidelman (2003) observed 86 mothers of premature infants for interaction prior to their hospital discharge. Mothers were

classified according to their milk production into ‘minimal’, ‘medium’, and ‘substantial’ amounts of milk. Infants in the three groups were matched for birthweight, gestational age, medical risk and family demographics. At 37 weeks, those who expressed substantial amounts of milk (more than 75% of infant nutrition) (as compared to the other two groups) exhibited more maternal postpartum affectionate touch. In the other study, an fMRI study, 9 breastfeeding mothers and 8 formula-feeding mothers were assessed for maternal sensitivity at 3 to 4 months, observed through interaction during feeding (Kim et al., 2011). Breastfeeding mothers showed higher sensitivity ratings compared to formula-feeding mothers. Similarly, their brain responses showed more activation in areas implicated in maternal behaviour, including striatum, amygdala and superior frontal gyrus (details of brain activation are discussed in Chapter 7).

Although the two studies provide interesting findings, neither provides direct evidence for the role of oxytocin in human maternal behaviour. In addition, the first study (Feldman & Eidelman, 2003) was among premature infants who interact less than their full term counterparts (Muller-Nix et al., 2004). In addition, mothers perceive premature infants as fragile, which lead to more overprotection (directiveness) that might challenge sensitive responsiveness (Singer et al., 1999). Many recent studies which reported differences in plasma OT responses between mothers did not find significant differences between mothers in relation to mode of feeding, including one study by the author of the first study (Feldman et al., 2007). This suggests the importance of including a direct measurement for OT in such studies.

6.3.5. Oxytocin and social relationships’ stress in mothers and women

In the first study to explore the relationship between OT and different human attachment relationships, Feldman et al. (2011) used self-report measures to assess attachment with own parents as well as with romantic partner among 71 mothers and 41

fathers. Relationship with own infant was also observed through interactive play at 4 to 6 months infant age. Plasma, salivary and urinary OT levels were assessed before and after 15 minutes play interaction with infants. Parents who were more synchronous with their infants in terms of affective expression showed higher plasma and salivary OT levels than 'low' synchrony parents, supporting previous findings that link OT to more positive parenting behaviour (Feldman et al., 2007; Gordon et al., 2010). However, among mothers, post-interaction urinary OT (which was not correlated with plasma or salivary OT) was positively correlated with anxiety in romantic attachment (i.e. relationship with partner), self-reported parenting stress, and interactive stress (i.e. proportion of time when the infant shows negative reactivity while the mother tries to re-engage her/him during 'observed' interactive play). Urinary OT levels were also reported to show a negative trend with own parenting care. In addition to the role of OT to indicate social affiliation, their findings suggest a role for OT in stress regulation similar to that reported by other studies in women (Turner et al., 2002; Marazziti et al., 2006; Taylor et al., 2006, 2010; Tabak et al., 2011).

Studies examining stress in women suggest that OT might also be a marker for social relationship stress, at least among women (Turner et al., 1999; 2002; Marazziti et al., 2006; Taylor et al., 2006, 2010; Tabak et al., 2011). This positive relationship between OT and stress may be related to the well known anti-anxiety and anti-stress effect of OT (Numan & Woodside, 2010). In other words, OT may be released in stressful situations in order to decrease or moderate stress responsiveness (Marazziti et al., 2006). In a study assessing stress in partnership among 85 adults in stable relationships (62% female and 38% male), plasma OT was positively significantly correlated with relationship distress in women (while plasma vasopressin correlated with relationship distress in men) (Taylor et al., 2010). In a further study by the same group, among 73 post menopausal women, plasma OT was negatively correlated in relationship to their

own mother, partner, and marginally significant in relation to their best friend (Taylor et al., 2006). Similarly, Tabak et al. (2011) reported positive correlation between plasma OT levels and post conflict (with partner, a relative or a friend) anxiety and decreased levels of forgiveness among 35 women.

Elevation of OT in response to stress in women might be confined to relationship distress and interpersonal difficulties rather than general stress. This is suggested by unsuccessful efforts to increase OT through laboratory stress induction using ‘Trier Social Stress Test’ (Ditzen et al., 2007). In addition, with the exception of the ‘anti-stress’ effect, most behavioural and physiological effects induced by OT can be blocked by administration of OT antagonist, suggesting a different receptor or mechanism (Uvnas-Moberg, 1998). Thus, the pathways by which OT mediates effects on stress and on social affiliation may be different (Taylor et al., 2010).

These findings suggest a dual role for OT in pro-social behaviours, so while OT increases as a result of affiliative contact it also increases as a ‘signal for demand to affiliate with others as the relationship is threatened’ (Taylor et al., 2010). It is therefore important to note that maternal sensitivity is a construct that requires a reciprocal interactive relationship between a mother and her infant, and similar to other relationships might also encounter some difficulties.

Table 6.1 outlines studies that have examined the role of OT in human parenting behaviour.

Table 6.1. Studies demonstrating the influence of oxytocin in the parent-infant bond

Study	Sample	Measures	Maternal behaviour measured/outcome variables	Time/method of OT assessment	Summary of findings
<i>OT among parents</i>					
Feldman et al. (2007) N = 62	Pregnant healthy females	YIPTA, Mother-infant play interaction	Plasma OT/Affectionate maternal behaviour	First, third trimester, and postpartum	Plasma OT at early pregnancy and postpartum are related to: maternal behaviour (gaze, vocalisation, touch, and affect)
Levine et al. (2007) N = 66	Pregnant healthy females	MFAS	Plasma OT/MFAS	First, third trimester, and postpartum	Significant correlation between OT and MFAS in women with rise in OT through pregnancy
Gordon et al. (2010) N = 160 couples	Healthy new mothers and fathers (couples)	Parent-infant play interaction	Affectionate/Stimulatory parenting behaviour/Plasma OT	At 2 months and 6 months	Parental OT is related to the parents' affectionate (mothers) or stimulatory contact (fathers) with infant
Feldman et al. (2010a)	Healthy mothers or fathers	BDI, STAI Interactive play	Affectionate/Stimulatory parenting behaviour/	At 4-6 months	OT level in plasma and saliva interrelated OT increased

Study	Sample	Measures	Maternal behaviour measured/outcome variables	Time/method of OT assessment	Summary of findings
N = 112 parents			Plasma & salivary OT (parents)	baby	only in mothers with high affectionate contact, and fathers with high stimulatory contact
Feldman et al. (2011) N = 112 (71 mothers)	Healthy mothers or fathers	Plasma, salivary, urinary OT (parent), interaction play. PSI, YIPTA, PBI, AAS	Affect synchrony/ Anxiety in romantic attachment/ Parenting stress/Interactive stress	4-6 months	Higher plasma and salivary OT levels in high affect synchrony parents. Urinary OT positively correlated with anxiety in romantic attachment, parenting stress, and interactive stress
<i>Cross-generational transmission of OT and parenting behaviour</i>					
Strathearn et al. (2009) N = 30	Healthy pregnant women	Third trimester = AAI, PDQ, BDI 7 months = BDI, PNAS + play session + plasma OT 11 months = fMRI 14 months = Bayley Scale	Adult attachment/ Plasma OT/Maternal brain responses	7 months	Secure mothers have higher plasma OT and more brain activity in reward areas in response to infant faces compared to insecure mothers

Study	Sample	Measures	Maternal behaviour measured/outcome variables	Time/method of OT assessment	Summary of findings
Feldman et al. (2010b) N = 55 parents	Healthy mothers or fathers	BDI, STAI, interaction play session. Plasma OT (parent), salivary OT (parent/infants)	Parent behaviour/Infant behaviour	4-6 months	Parent and infant OT levels were positively correlated, and both positively correlated with greater parent behaviour and affect synchronicity
Fries et al. (2005) N = 18 (fostered) N = 21 (biological)	Fostered and biological children	Urinary OT and vasopressin (children)	Children's urinary OT assessed following interaction during computer game with parent and other adult	4.5 years	Following interaction, OT was higher in children raised by biological parents compared with fostered children
Gordon et al. (2008) N = 45	Healthy males and females (non-parents)	PBI, plasma OT, Salivary cortisol STAI, BDI, AAS	Recall of perceived parenting 'adult attachment' /Plasma OT	24 years	Early perceived parenting correlated positively with salivary OT levels

Note. OT: Oxytocin, PRL: Prolactin. MFAS: Maternal Fetal Attachment Scale AAI: Adult Attachment Interview, PDQ: Personality Disorder Questionnaire, BDI: Beck Depression Inventory. AAS: Adult Attachment styles. PBI: Parental bonding instrument. PNAS: positive and negative affect schedule, fMRI: Functional Magnetic resonance imaging STAI: State trait anxiety inventory. YIPTA: Yale inventory of parental thoughts and actions. CSD: Caesarean section delivery, VD: Vaginal delivery, STAI: State trait anxiety inventory. ELISA: Enzyme Link Immunosorbent Assay, PSI: Parenting stress index.

6.4. Validity of Plasma OT in Reflecting True Levels of OT in Humans

While animal studies have focused on measuring centrally-produced OT, humans has been reliant on peripheral OT assessments (plasma, saliva, urine) as convenient indicators for centrally acting OT levels (Fries et al., 2005; Feldman et al., 2010 a, b; Bick & Dozier, 2010). This is because assessing brain OT, using cerebrospinal fluid (CSF) measurement, in humans is a technically difficult and stressful procedure and thus less likely to be feasible in healthy volunteers. In addition, being a stressful procedure might affect the reliability of the OT measurement. While this might be considered as a limitation of human studies in general (Modahl et al., 1998), recent studies provide some evidence that peripheral measures of OT are reliable indicators of the centrally acting OT, for example:

- a. Recent human studies were able to show modulation of peripheral OT in relation to social affiliation, including parental behaviours (Feldman et al., 2007; Gordon et al., 2010).
- b. fMRI studies show coordination of peripheral OT levels and BOLD activation in OT-rich brain areas (Strathearn et al., 2009; Atzil et al., 2011).
- c. The high individual stability of OT from early pregnancy to the postpartum period (Dawood et al., 1978; De Geest et al., 1985; Feldman et al., 2007; Levine et al., 2007) suggests that baseline OT levels are relatively stable, except during physiological processes such as breastfeeding (Feldman & Eidelman, 2003). Yet, these are controllable measures in any methodological design.
- d. Feldman et al. (2012) examined the link between plasma OT, variation in OTR gene and variation in CD38 gene (the latter is a multifunctional molecule that is implicated in axonal release of OT from hypothalamic neurons) in relation to

different parenting behaviours among 532 mothers, fathers and non-parents. They examined the presence of ‘risk alleles’ on the OTR (rs2254298/rs1042778 SNPs) and the risk alleles for the CD38 (rs3796863 SNP), all of which are known to be associated with increased risk of developmental disorders and social dysfunction (e.g. autism) (Lerer et al., 2010). They reported that individuals with higher risk alleles on OTR or CD38 had lower levels of plasma OT and the effects were similar across the whole group (mother, father, non-parents), suggesting some validity in measuring peripheral OT as a reflection of central neuropathology.

- e. Abnormalities in the hypothalamic production of OT might be reflected in the plasma level, as in a study of Modahl et al. (1998) where plasma OT was significantly lower in autistic children compared to unaffected children and these levels did not increase with age as they did with other children.
- f. Administration of intranasal OT to fathers (N = 35) increased the father’s salivary OT levels dramatically and induced more social behaviour (touches, engagement) with own infant during interactive play (Weisman et al., 2012). This supports further the validity of peripheral OT measurement.

6.5. Summary

Animal studies emphasise the importance of OT in mediating maternal caregiving behaviours (Pedersen & Prange, 1979; Van Leengoed et al., 1987; Olazabal & Young, 2006). There is growing evidence in humans to suggest that OT plays a key role in promoting high quality parenting (Feldman et al., 2007, 2010a; Atzil et al., 2011; for a review, see Galbally et al., 2011). Specifically, rising plasma OT from the first to third trimester of pregnancy appears to predict maternal bonding to the fetus (Levine et al., 2007). OT is also related to social behaviour among parents when they interact with their own infants (Feldman et al., 2010a; Gordon et al., 2010), and among infants when

they interact with their parents (Feldman et al., 2010b). OT has been positively correlated with attachment representation with own parents (Strathearn et al., 2009) and to memory about own parenting care (Gordon et al., 2008). However, evidence linking maternal sensitivity to breastfeeding as proxies for OT secretion was inconsistent (Feldman & Eidelman, 2003; Feldman et al., 2007; Kim et al., 2011) and merits further assessment, especially at the late stages during postpartum. Recent evidence suggests that OT might also be a marker for social relationship stress, in women (Turner et al., 1999; 2002; Marazziti et al., 2006; Taylor et al., 2006, 2010; Tabak et al., 2011) including mothers (Feldman et al., 2011)

In spite of promising evidence linking OT to maternal behaviour in humans, these data require further examination in a group of mothers whose maternal behaviour has been rigorously defined. Only one such study to date has considered grouping mothers according to their parenting style, i.e. ‘intrusiveness’ or ‘synchronous’ behaviour (Atzil et al., 2011). However, they did not consider sensitive responsiveness as a ‘comprehensive’ concept based on the reciprocal relationship between mother and infant, but rather as fine grained behaviours which are part of the sensitivity concept. This warrants further examination for the role of OT in maternal sensitive caregiving behaviour.

7.1. The Brain Basis of Maternal Sensitivity

The neurobiology of maternal caregiving behaviour has been investigated widely in animal (Insel & Young, 2001) and recently in humans using functional magnetic resonance imaging (fMRI) (Lorberbaum et al., 2002; Bartels & Zeki, 2004; Strathearn et al., 2008). However, evidence from animals of brain changes related to parenting is far in advance compared to the human literature (Champagne et al., 2001; Champagne, 2008). Given that aspects of basic maternal behaviour are likely to be shared across mammalian species (Lee et al., 2009), this chapter opens with an outline for the evidence from animal literature before reviewing the evidence from human studies.

7.2. Animal Studies

Animal studies have suggested that pregnancy hormones induce changes in female brains which prepare a new mother's brain for the transition to maternity. These changes follow the rise of progesterone and oestrogen during early pregnancy, which significantly alter the properties of neurons in specific brain regions such as the somatosensory cortex, the hippocampus, and the amygdala (Rasia-Filho et al., 2004). In addition, significant changes in the oxytocin system occur throughout pregnancy, parturition and lactation (Lee et al., 2009). Because animal behaviour in rodents involves a composite of motor activity such as arched back nursing, licking, grooming and nest building, different brain regions are activated as a result of this (Gammie, 2005). Three brain regions have been consistently implicated in animal maternal caregiving behaviour: (a) the dopaminergic reward system in the forebrain and midbrain which is crucial for motivation to caregiving in new mothers (Numan & Numan, 1997;

Strathearn et al., 2011); (b) the emotional regulation pathways in amygdala and septal regions (Slotnick & Nigrosh, 1975; Numan et al., 2010), and (c) the sensation-driven thalamocingulate region (Panksepp et al., 1994; Pereira & Morrell, 2011).

7.2.1. The dopaminergic reward system in forebrain and midbrain

The medial preoptic area (MPOA) is believed to have a central role in mammalian parenting (Numan & Stolzenberg, 2009). Lesions involving MPOA or the nearby ventral part of the bed nucleus of the stria terminalis (VBNST) cause disruption in maternal behaviour (Tsuneoka et al., 2010); and oestradiol injection into any of these areas enhances mammalian maternal behaviour (Numan & Insel, 2003). The neural projections from these two areas regulate maternal behaviours through interactions with dopamine containing neurons in the ventral tegmental area (VTA) and the substantia nigra (Numan & Stolzenberg, 2009). Disruption of this pathway may negatively affect maternal behaviour (Numan & Numan, 1997; Numan & Insel, 2003).

7.2.2. The emotional regulation pathways in amygdala and septal regions

Limbic circuits involving septal regions and the amygdala have been suggested to play a role in mammalian parenting. For instance, rodents with septal lesions are more likely to commit infanticide (Novakova et al., 1993). Such lesions also inhibit nest building, and pup retrieval (Numan & Insel, 2003). The amygdala appears to be involved both in facilitating and inhibiting parental behaviour. While lesions of the amygdala reverse the avoidance behaviour in nulliparous female rats (Numan et al., 1993) similar lesions have been found to inhibit maternal affiliation in animals (Oxley & Fleming, 2000; Numan et al., 2010). Recent studies suggested a more complex role for the amygdala in parenting that involves both detection of threat and processing of reward and biological valence that are required for social behaviour (Swain et al., 2007; Adolphs et al., 2010).

7.2.3. The sensation-driven thalamocingulate region

Anterior cingulate is rich in opiate receptors (Wise & Herkenham, 1982), which have been implicated in maternal retrieval of young (Panksepp et al., 1994). Research demonstrates cingulate activity in association with maternal behaviour in rats (Lonstein et al., 1998; Pereira & Morrell, 2011) and *partial* disruption of maternal behaviour (e.g. placing pup outside the nest while continue caregiving) following cingulate lesions in mice (Slotnick & Nigrosh, 1975) are inconsistent. Swain et al. (2007) argue that the cingulate might not be essential for parenting, but might be involved in the organisation of a range of complex behaviours, including parenting.

Compared to other mammals, human parenting is likely to be a more complex behaviour with many environmental and social influences (Kentner et al., 2010).

Humans do not generally exhibit a transition from avoidance of the new young infants to a maternal behaviour style, as is observed in rodent species (Novakova et al., 1993). Therefore, generalisation of results from animal studies to humans requires some caution (Bick & Dozier, 2010; Kentner et al., 2010).

7.3. Human Studies

The non-invasive and highly sensitive fMRI has added greatly to our knowledge about parenting, by mapping the changes in the brain's hemodynamic response (BOLD response) in relation to neuronal activity (Swain, 2010). Activation of neural cells in response to a stimulus leads to energy consumption within the brain (Raichle & Mintun, 2006); as a result, local changes in the relative concentrations of oxyhaemoglobin and deoxyhaemoglobin occur (Ogawa et al., 1993). The differences between oxygenated and deoxygenated haemoglobin provide a signal that is detected by the scanner. Brain activity during the scanning represents an integration of activity over blocks of several

seconds (Raichle & Mintun, 2006). Studies present varieties of stimuli to participants (e.g. parents) during these blocks, in order to generate maps related to specific thoughts or behaviour (e.g. Lorberbaum et al., 1999; Ranote et al., 2004; Strathearn et al., 2008). fMRI studies of parental responsiveness have employed a variety of infant stimuli with earlier researchers using infant auditory stimuli (the cry) (Lorberbaum et al., 1999), and later studies developing visual stimuli including still pictures (Strathearn et al., 2008, 2009), or more ecologically valid infant visual stimuli (video) (Ranote et al., 2004; Noriuchi et al. 2008; Atzil et al., 2011).

7.3.1. Parental brain responses to auditory stimuli

Own infant cries or an unknown infant cries: The use of infant cries in human studies of parental brain responses was first used by Lorberbaum et al. (1999). They recruited 7 mothers with a youngest child of less than 3.5 years to have fMRI scanning while they listened to blocks of 30 seconds of a recording of their own infant's cries and 30 seconds of control sounds (white noise). In this small preliminary study, Lorberbaum et al. report increased activity in the anterior cingulate and right medial prefrontal cortex with the infant cries compared to control sounds. Despite the small sample size that was considered in their final analyses ($N = 4$), and the long time since the subjects last gave birth, their findings were interesting and suggest the involvement of anterior cingulate in maternal empathy and urge to care in response to own infant cry (Liotti et al., 2000).

In a follow up study, Lorberbaum and colleagues replicated the previous study in 10 breastfeeding, first-time mothers with much younger children (4-8 weeks postpartum). Women listened to a recording of a standard infant cry (not from their own infants) as well as to control sounds. Activity in response to infant cries as compared to white noise was found in areas which are implicated in maternal behaviour in rats, including, the midbrain, hypothalamus, dorsal and ventral striatum, and the lateral septal region,

providing some evidence of consistency with animal findings. In addition Lorberbaum et al. also reported activation in regions responsible for planning of appropriate behaviour, including the right orbitofrontal cortex, and limbic areas of the anterior and posterior cingulate. Their findings implicated the involvement of mesocorticolimbic reward circuitry in human maternal behaviour; later studies using visual stimuli seemed to support this (e.g. Strathearn et al., 2009).

As a part of a study that investigated the effect of the parent's gender on brain responses, Seifritz et al. (2003) examined 20 mothers up to 3 years postpartum. Mothers were presented with an unknown child's laughs or cries. They reported greater responses to crying, in the amygdala which is associated with processing emotional salience which can be positive or negative, and accordingly involved in motivation as well as empathy (Breiter et al., 1996). However, contrary to the findings of Lorberbaum et al. (1999; 2002), Seifritz et al. reported decreased activity in the anterior cingulate to the infant stimuli. This inconsistency is not surprising given that the anterior cingulate has many subdivisions, each involved in a different social and emotional processing pathway (Bartels & Zeki, 2004). Swain (2008b) argues that this inconsistency might also be due to the use of an event-related design in the study by Seifritz et al., in which stimuli were presented for only 6 seconds as compared to 30 seconds blocks of stimulus presentation by Lorberbaum et al.

Comparing own infant cries and an unknown infant cries: Comparing the effect of own and unknown infant cries, Swain et al. (2003) conducted a longitudinal study including scans and interviews in a group of 9 new mothers at 2-4 weeks postpartum. Mothers listen to 30 seconds of their own infants' cries as well as to a standard unknown cries and control sounds. Their findings suggested that some brain regions were more active in response to own infant's cries compared to other cries. These include

mesocorticolimbic reward regions including the midbrain, basal ganglia, and cingulate cortex. These activation patterns in response to own infant stimuli may indicate involvement of a maternal motivational, reward pathway, as well as maternal learning in response to own infant cries. Swain et al. also reported activation in the amygdala and the insula, which are associated with emotional processing and empathy (the latter is also part of the mirroring neurons-see below) reflecting an increase in maternal arousal in response to own infant crying consistent with previous studies (Lorberbaum et al., 2002; Seifritz et al., 2003).

Swain et al. repeated the previous study in the same mothers at 3- 4 months postpartum (Swain et al., 2004a). Interestingly, while activation of mesocorticolimbic reward pathways (i.e. midbrain and cingulate cortex) was still found in response to own infant cries as compared to other infant cries, mothers did not show the same activation in the amygdala and insula. Instead, there was increased activation in areas related to the cognitive ability to read others' emotions (i.e. Theory of Mind), such as the medial prefrontal cortex and to areas involved in neurohormonal regulation, such as the hypothalamic regions. The changes in maternal brain activation reported by Swain's two studies might reflect the development of the parent-infant relationship (Swain, 2008b), which is accompanied by changes in maternal brain responses, parallel to that seen in animals (Pereira & Morrell, 2011). This might also explain for the different findings reported in the two studies by Lorberbaum et al. (1999, 2002).

Consistent with emerging data that OT regulates social bonding in parenting, Swain et al. (2008a) examine the effect of mode of delivery (as a proxy of OT levels) on maternal brain responses. They undertook fMRI at 2-4 weeks postpartum in 6 mothers who delivered vaginally (VD) and 6 mothers who had Caesarean deliveries (CSD). In this small preliminary study VD mothers' brains showed significantly greater BOLD

activation than CSD mothers' brains to own infant-cry in: limbic regions rich in OT receptors including the thalamus, and hypothalamus; motivational areas such as the caudate nucleus (striatum); emotional processing like the insula; areas for empathy like superior temporal gyrus and areas which involved in all the three function (motivation, emotion, and empathy) such as the amygdala. They also reported activation in areas for planning behaviour such as superior frontal gyrus. It is worth mentioning that the insula and superior temporal gyrus are part of 'mirroring neurons' (along with inferior frontal gyrus) (Iacoboni & Dapretto, 2006) and thus they facilitate reading others minds (Theory of Mind) (Gallagher & Frith, 2003). These findings in VD mothers may follow the release of oxytocin during parturition and vaginal delivery (Dawood et al., 1978; De Geest et al., 1985). However, at 2-4 weeks, maternal hormones (including OT) might be relatively high (see review by Feldman, 2012) and pain and stress in connection to the surgery (i.e. CSD) might still be evidenced. Further research is needed to examine whether the mode of delivery predicts differences in maternal brain activation to infant stimuli at later postpartum stages.

7.3.2. Parental brain responses to visual stimuli

Studies examining parental brain responses to infant visual stimuli compared to non-human control stimuli have generally, and not unexpectedly, found activation of the visual processing areas comprising the occipital and temporal cortices (Strathearn et al., 2008), and the fusiform face area (Sergent et al., 1992). Several studies have compared maternal responses to own infant versus unknown infants, using infant photographs (pictures) or infant-moving stimuli (video) with varying emotional valences. For example, in a small preliminary study, Nitschke et al. (2004) reported that primiparous mothers (N = 6), 2-4 months postpartum exhibited greater activation in bilateral orbitofrontal cortex when viewing smiling pictures of their own versus unfamiliar infants. Orbitofrontal cortex is associated with the perception of positive emotions

(Elliott et al., 2003) and also receives dopaminergic projections from the periaqueductal gray of the midbrain, which is rich in OTR (Lee et al., 2009) and therefore might represent reward value for mothers to their own infant's cues (Strathearn et al., 2011). Nitschke et al. also found that activation of orbitofrontal cortex correlated positively with pleasant maternal mood ratings, signifying a role for maternal mood in parental brain responsiveness (Swain et al., 2008b), and also suggesting mothers' empathy with their infant's emotional state.

Using a similar approach, Bartels & Zeki (2004) measured brain activity in 19 healthy mothers while viewing photographs of their own, familiar, and unknown children between the ages of 9 months and 3.5 years. In this larger study of a rather wide range of child ages, these authors reported that, compared to pictures of familiar or unknown children, pictures of own children were more likely to activate brain areas mediating the emotionally rewarding aspects of maternal care behaviour such as the anterior cingulate, the insula, and dopaminergic reward regions including the striatum of the basal ganglia, thalamus, and the periaqueductal grey of the midbrain. By contrast, they found deactivation in the prefrontal cortex, the posterior cingulate cortex, and the amygdala. Bartels & Zeki proposed that their results suggest that human parent-infant attachment has a "push-pull" mechanism with activation of reward pathways and deactivation of 'negative-avoidance circuits'. However, areas which were deactivated in that study (i.e. prefrontal cortex, the posterior cingulate cortex, and the amygdala) were not particularly a negative-avoidance circuit and activation of these areas were reported by others (Seifritz et al., 2003; Ranote et al., 2004; Swain et al., 2008a) in response to infant stimuli. This represents the inconsistency in the functions ascribed to each brain region by different studies, which lead to different interpretation, and consequently act as a limitation of the current literature. However, certain brain regions which have several roles such as the amygdala; which implicated in emotion regulation salience –

which can be either positive (Ranote et al., 2004), or negative as in arousal (Seifritz et al., 2003, Swain et al., 2003, 2008a), might also contribute to the mixed literature findings.

Leibenluft et al. (2004) use pictures of much older own and unknown children (i.e. 5-12 years), again in a relatively small sample of 7 mothers being asked to confirm the facial identity of the child in the picture. Using pictures of own children versus unknown children, they replicated the findings of Bartels & Zeki, but, unlike the latter, they reported activation of the amygdala, insula and posterior cingulate, supporting the role of these areas in emotional salience similar to other studies (e.g. Lorberbaum et al., 2002; Seifritz et al., 2003, Swain et al., 2003). Activation of amygdala in response to pictures of own infant versus other infant, was also reported among much younger children ages 2-4 months (N = 14) by Swain et al. (2004b). This later, and much larger study of Swain et al., also reported significant brain activation in reward areas such as the cingulate cortex, basal ganglia, visual processing areas in the occipital cortex, and in the brainstem; which was broadly consistent with others (Bartels & Zeki, 2004).

Different emotional affects: In an attempt to assess the effect of different infant emotional valence on maternal brain activation, Strathearn et al. (2008) conducted an fMRI study in a relatively large sample size (N = 28) of first time mothers at 5-10 months postpartum. Mothers were shown pictures of their own infant and unknown infants, all of which were displaying neutral, happy, or sad emotional expressions. Generally, viewing own infant's face as compared to unknown infants activated dopamine rich reward pathways reported by previous studies (Lorberbaum et al., 2002; Bartels & Zeki, 2004). In response to happy (but not sad) faces of own infant, greater activation was found in reward areas such as the substantia nigra and ventral tegmental area of the midbrain, motivation areas including the striatum of the basal ganglia,

anterior cingulate and areas for emotional processing and understanding others' emotion such as the insula (Singer et al., 2009).

In a follow-up study, Strathearn et al. (2009) attempted to link maternal brain responses to infant stimuli to mothers' own attachment representation (assessed by the AAI) among 30 first-time new mothers. In response to smiling cues of their own infant versus unknown infant, mothers who were rated as 'securely attached' (to their own mothers) ($n = 15$) were more likely to show activation in the mesocorticolimbic reward brain regions. These include the medial prefrontal cortex, ventral striatum, and ventral tegmental area. In addition, they also found activation in the hypothalamus and pituitary regions which was positively correlated with the rise in plasma OT (following their interaction with their infants) among those mothers, supporting the notion that implicates transgenerational transmission of maternal behaviour (see Chapter 6). Yet, the fact that plasma OT was measured 4 months before the fMRI scanning makes causal relationships less reliable. By contrast, 'insecurely attached' mothers ($n = 15$) showed more activation in the nigrostriatal pathways including dorsolateral prefrontal cortex, dorsal striatum and substantia nigra of the mid brain, which have also been reported by others in response to infant stimuli (e.g. Bartels & Zeki, 2004). Viewing their own infants' sad cues, securely attached mothers continued to show activation in mesocorticolimbic region while insecurely attached mothers show activation of the insula.

In spite of the overlap between the areas activated by the two groups, the authors proposed that activation of insula among insecure mothers might suggest avoidance or rejection of infant negative infant cues by those mothers. It is important to note that the insula is also involved in the experience of emotional affiliative responses between individuals (Leibenluft et al., 2004; Lenzi et al., 2009) including own infant (Strathearn

et al., 2008; Swain et al., 2008a). Therefore, its activation in insecure mothers might be a representation of a different variant of maternal responsiveness behaviour, especially with maternal interactive behaviour not assessed in that study. This study by Strathearn et al. provides the first evidence that link maternal brain correlates to plasma OT measurements in distinct group of mothers based on attachment representation with own parents.

Infant video stimuli: Still photographs provide reliable brain activations, but arguably, a more ecologically salient stimulus is the moving images (videos) of infants, which provide more naturalistic stimuli. For example, Ranote et al. (2004) compared maternal brain responsiveness to alternating blocks of own infant, unknown infants, and a neutral stimulus (moving traffic) among 10 healthy mothers at 4-8 months postpartum. In response to own infant, they found significantly greater activation in emotion processing areas such as the amygdala and in bilateral visual processing areas in the temporal pole and occipital cortex. Activation of main visual processing areas in the occipital cortex and temporal cortex in studies using video stimuli indicate the dynamic nature of the stimulus. In response to an unknown infant, Ranote et al. reported more activation in the orbitofrontal cortex and face processing areas indicating a lack of familiarity with the unknown infant. In spite of the limited sample size, their findings paved the way for later studies using a similar paradigm.

Using a similar paradigm of infant video stimuli, Noriuchi et al. (2008) extended the findings of Ranote et al. among 13 mothers who were shown video clips of their own and unknown infants at 16 months old. Viewing of own infant compared to unknown infants resulted in greater activation in areas rich in OT receptors such as the periaqueductal grey of midbrain, the dorsal and ventrolateral putamen, and areas associated with emotion processing including the anterior insula consistent with

previous findings (Lorberbaum et al. 2002; Bartels & Zeki, 2004; Swain et al., 2008a). They also reported activation of the dopaminergic reward pathways including the orbitofrontal cortex similar to Nitschke et al. (2004). The broader brain activation in response to own infant stimulus reported by Noriuchi et al. as compared to Ranote et al. might be related to the older infant stimuli used by the former, representing the development of mother infant bond and accordingly more complicated responses (Swain et al., 2007).

7.3.3. Maternal brain responses in relation to maternal behaviour

Recently some studies have focused on charting maternal brain correlates in relation to ‘observed’ maternal interactive behaviour with own infant. In the first study, Kim et al. (2011) examine 9 exclusively breastfeeding mothers (as a proxy representing higher OT secretion) in comparison to 8 exclusively formula-feeding mothers. Maternal BOLD activation patterns in response to own infant crying compared to an unknown infant’s cry at 3-4 weeks postpartum was examined. They reported that breastfeeding mothers showed greater activation in areas rich in OTR including striatum, areas implicated in emotional processing, motivation and empathy, such as the amygdala and insula, areas associated with planning of behaviour such as the superior frontal gyrus, and areas associated with reading others emotions like the superior temporal gyrus. In this small study, breastfeeding mothers were rated as showing significantly higher maternal sensitivity (observed at 3-4 months) compared to formula feeding mothers. Activation of the amygdala and superior frontal gyrus were also positively correlated with maternal sensitivity ratings among both groups of mothers (breast and formula feeding), suggesting that this brain pattern might be related to differences in maternal sensitivity rather than to the mode of feeding. Furthermore, Kim et al. did not measure maternal plasma oxytocin levels; limiting the inferences that can be made from this study about the role of maternal oxytocin in brain. However, these findings do complement more

recent evidence that variation in maternal behaviour in animals and humans is associated with variation in brain responses.

The second study examined the neural correlation of maternal behaviour in a distinct group of mothers (Atzil et al., 2011). In this study, the difference in brain responses among 23 mothers grouped according to their observed synchronous (N = 13) or intrusive (N = 10) caregiving behaviour with their 4-6 month-old infants examined by fMRI. Baseline plasma OT levels were also measured. Among all mothers, areas activated through the use of video in the case of own infant compared to an unknown infant were reported by previous studies (e.g. Bartels & Zeki, 2004) including limbic motivational pathways such as the right amygdala and left nucleus accumbens. Activation of these areas was positively correlated with 'proportion' of synchronous behaviour in mothers. Using a region of interest analysis they reported significant activation in the nucleus accumbens, amygdala, as well as areas implicated in reading others' mind, such as superior temporal gyrus, inferior frontal gyrus and the insula (Iacoboni & Dapretto, 2006), among synchronous mothers. As mentioned earlier, these areas are implicated in Theory of Mind, and their activation suggests that synchronous mothers have the ability to understand their infants' cues (Gallagher & Frith, 2003). On the other hand, intrusive mothers showed only activation in the right amygdala and left nucleus accumbens, with greater activation confined to the amygdala.

Atzil et al. used a paradigm for own and an unknown infant video, and, in addition, another video was shown of the mother playing with her own infant. This makes any comparison between their results with other studies more complicated. In addition, their grouping of mothers was not a priori but according to the proportion of synchronous and invasive behaviours showed by mothers in relation to other mothers included in the study (no distinct cut-off). This could explain for the big overlap in pattern of brain

activation reported by this study. This study provides general understanding about maternal behaviour rather than concentrate on a specific behavioural domain. For example, synchronous behaviour might overlaps with sensitivity and harmony each of which, according to Musser et al. (2012), represents distinct mode of behaviour and consequently activates different brain areas.

In the third study, Musser et al. (2012) examined brain response to own and unknown infant's cries among 22 first time mothers who were rated for, 'sensitivity', 'harmony' and 'intrusive' behaviour with their infant, through mother-infant play interaction (at 18 months). More sensitive behaviour was associated with greater activation in areas implicated in response inhibition at the frontal pole and areas for reading others mind such as inferior frontal gyrus in response to own infant as compared to unknown infant. Mothers who showed more harmony activated areas involved in recalling of memories such as left hippocampal regions. Mothers who showed more intrusive behaviours activated the temporal pole and areas suggest empathy with loved ones such as the left insula. Although their findings have previously been implicated in maternal brain responses, this study suggests the importance of considering discrete maternal behaviour when examining neural correlates.

Tables 7.1a, b, 7.2a, b, and 7.3 summarise the findings from studies reviewed in this chapter.

Table 7.1a. Maternal brain responses to own infant using auditory infant stimuli

Author (year)	Lorberbaum et al. (1999)	Lorberbaum et al. (2002)	Swain et al. (2003, 2004a)	
Number of participants	N = 4 mothers	N = 10 mothers	N = 9 mothers	
Age of infants at time of scan	3 weeks-3.5 years	4-8 weeks	2-4 weeks 3-4 months	
Study design	1.5T, 30s blocks, within-subjects	1.5T, 30s blocks, within-subjects	3T, 30s blocks, within-subjects	
Contrasts and infant stimuli used	Cry of own infant > control noise	Cry of unknown infant > control noise	Cry of own infant > unknown > Control noise	Cry of own infant > control noise
Septal regions (MPOA/VBNST/caudate head)		ACT	ACT	
Midbrain (including periaqueductal grey)		ACT	ACT	
Hypothalamus		ACT	ACT	
Thalamus		ACT		
Limbic structures:				
Amygdala		ACT (cry – rest)	ACT	
Anterior cingulate	ACT	ACT	ACT	ACT
Middle cingulate		ACT		
Posterior cingulate		ACT		
Anterior paracingulate			ACT	
Hippocampus				
Basal ganglia:		ACT	ACT	
Striatum/putamen/		ACT	ACT	

Author (year)	Lorberbaum et al. (1999)	Lorberbaum et al. (2002)	Swain et al. (2003, 2004a)	
nucleus accumbens				
Lentiform nucleus Globus pallidus		ACT	ACT	
Insula				
Frontal cortex:	ACT	ACT	ACT	ACT
Orbitofrontal/Inferior frontal gyri	ACT	ACT	DEACT	ACT
Medial frontal gyrus	ACT			ACT
Superior frontal gyrus				
Ventral prefrontal cortex				
Precentral gyrus				
Gyrus rectus				
Temporal/parietal cortex:		ACT	ACT	
Temporoparietal cortex		ACT	ACT	
Fusiform gyrus		ACT	ACT	
Temporal/auditory cortex			ACT	
Parahippocampal/limbic lobe	Not examined	Not examined	ACT	Not examined

ACT = activated, DEACT = deactivated.

Table 7.1b. Maternal brain responses to own infant using auditory infant stimuli

Author (year)	Swain et al. (2008a)	Seifritz et al. (2003)	Kim et al. (2011)	Musser et al. (2012)		
Number of participants	N = 12 mothers	N = 20 mothers	N = 17	N = 22		
Age of infants at time of scan	2-4weeks	< 3 years	2-4 weeks	18 months		
Study design	3T, 30s blocks	1.5T, 6s events, within-subjects	1.5T, 30s blocks, within-subjects	3T, blocks, within-subjects		
Contrasts and infant stimuli used	VD > CSD	Cry and laugh of unknown infant	Breastfeeding mothers>Formula feeding	Cry of own infant > unknown infant Sen. Har. Int.		
Septal regions (MPOA/VBNST/caudate head)						
Midbrain (including periaqueductal grey)						
Hypothalamus	ACT				ACT	
Thalamus	ACT				ACT	
Limbic structures:						
Amygdala	ACT	ACT (cries only)	ACT (correlated with sensitivity)		ACT	ACT (cries only)
Anterior cingulate		DEACT				DEACT
Middle cingulate		ACT				ACT
Posterior cingulate						
Anterior paracingulate						
Hippocampus						
Basal ganglia:	ACT		ACT		ACT	
Striatum/putamen/			ACT			

Author (year)	Swain et al. (2008a)	Seifritz et al. (2003)	Kim et al. (2011)	Musser et al. (2012)		
nucleus accumbens						
Lentiform nucleus Globus pallidus	ACT	ACT	ACT		ACT	ACT
Insula						
Frontal cortex:				ACT		
Orbitofrontal/Inferior frontal gyri				ACT		
Medial frontal gyrus		ACT		ACT		ACT
Superior frontal gyrus	ACT		ACT (correlated with sensitivity)	ACT	ACT	
Ventral prefrontal cortex	ACT				ACT	
Precentral gyrus						
Gyrus rectus						
Temporal/parietal cortex:	ACT	ACT			ACT	ACT
Temporoparietal cortex	ACT		ACT		ACT	
Fusiform gyrus	ACT		ACT		ACT	
Temporal/auditory cortex						
Parahippocampal/limbic lobe						

ACT = activated, DEACT = deactivated, Sen: sensitivity, Har: harmony, Int: intrusive.

Table 7.2a: Maternal brain responses to own infant using still pictures

Author (year)	Bartels & Zeki (2004)	Leibenluft et al. (2004)	Swain et al. (2004b)	
Number of participants	N = 19	N = 7	N = 9-14	
Age of infants at time of scan	9 months-3.5 years	5-12 years	Time 1: 2-4 weeks Time 2: 3-4 months	
Study design	2T, 15s blocks	1.5T, 1.5s events	3T, 30s blocks	
Contrasts and infant stimuli used	Photos of own children > photos of other known or unknown children	Photos of own child > photos of familiar child	Photos of own infant > control	Photos of unknown infant > control
Septal regions (MPOA/VBNST/caudate head)		.	ACT	
Midbrain (including periaqueductal grey)	ACT		ACT	ACT
Hypothalamus			ACT	
Thalamus	ACT	ACT	ACT	ACT
Limbic structures:				
Amygdala	DEACT	ACT		ACT
Anterior cingulate	ACT	ACT	ACT	ACT
Middle cingulate			ACT	ACT
Posterior cingulate	DEACT	ACT		
Anterior paracingulate		ACT		
Hippocampus				
Basal ganglia:				
Striatum/putamen/nucleus accumbens	ACT	ACT		ACT

Author (year)	Bartels & Zeki (2004)	Leibenluft et al. (2004)	Swain et al. (2004b)	
Lentiform nucleus Globus pallidus		ACT		ACT
Insula	ACT	ACT		
Frontal cortex:				
Orbitofrontal/Inferior frontal gyri	ACT	ACT	ACT	ACT
Medial frontal gyrus	DEACT	ACT	DEACT	ACT
Superior frontal gyrus		ACT		
Ventral prefrontal cortex	ACT			
Precentral gyrus		ACT		
Gyrus rectus		ACT		
Temporal/parietal cortex:				
Temporoparietal cortex	DEACT	ACT	ACT	ACT
Fusiform gyrus	ACT		ACT	ACT
Temporal/auditory cortex				
Parahippocampal/limbic lobe				ACT

ACT = activated, DEACT = deactivated

Table 7.2b: Maternal brain responses to own infant using still pictures

Author (year)	Nitschke et al. (2004)	Strathearn et al. (2008)	Strathearn et al. (2009)	
Number of participants	N = 6	N = 28	N = 30	
Age of infants at time of scan	2-4 months	5-10 months	7 months	
Study design	1.5T, 30s blocks	3T, 2s events	3T, 2s events	
Contrasts and infant stimuli used	Photos of own children > photos of unknown children	Photos of own > unknown infant in neutral, happy, and sad	Mothers with secure pictures of own vs. unknown child in neutral, happy, and sad	Photos of own children > photos of unknown children
Septal regions (MPOA/VBNST/caudate head)				
Midbrain (including periaqueductal grey)		ACT (more to happy)	ACT (periaqueductal)	
Hypothalamus		ACT	ACT	
Thalamus		ACT		
Limbic structures:				
Amygdala				
Anterior cingulate		ACT (more to happy)		
Middle cingulate		ACT		
Posterior cingulate				
Anterior paracingulate				
Hippocampus				
Basal ganglia:				
Striatum/putamen/		ACT (more to happy)	ACT (more to sad video)	

Author (year)	Nitschke et al. (2004)	Strathearn et al. (2008)	Strathearn et al. (2009)	
nucleus accumbens				
Lentiform nucleus Globus pallidus				
Insula		ACT (more to happy)	ACT	
Frontal cortex:				
Orbitofrontal/Inferior frontal gyri	ACT	ACT		ACT
Medial frontal gyrus			ACT	
Superior frontal gyrus		ACT (more to happy)	ACT	
Ventral prefrontal cortex				
Precentral gyrus		ACT		
Gyrus rectus				
Temporal/parietal cortex:				
Temporoparietal cortex		ACT		
Fusiform gyrus		ACT		
Temporal/auditory cortex	ACT			ACT
Parahippocampal/limbic lobe		ACT		

ACT = activated, DEACT = deactivated

Table 7.3: Maternal brain responses to own infant using video clips

Author (year)	Ranote et al. (2004)	Noriuchi et al. (2008)	Atzil et al. (2011)	
Number of participants	N = 10	N = 13	N = 23	
Age of infants at time of scan	4-8 months	16 months	4-6months	
Study design	1.5T, 20-40s blocks	1.5T, 32s blocks		
Contrasts and infant stimuli used	Silent video clips of own children > silent video clips of unknown children	Silent video clips of own children > silent video clips of unknown children	Synchronous mothers video of own vs. unknown child (N = 13)	Intrusive mothers video of own vs. unknown child (N = 10)
Septal regions (MPOA/ VBNST/caudate head)				
Midbrain (including periaqueductal grey)		ACT		
Hypothalamus		ACT		
Thalamus		ACT		
Limbic structures:				
Amygdala	ACT		ACT	++ ACT
Anterior cingulate		ACT	ACT	ACT
Middle cingulate				
Posterior cingulate		ACT		
Hippocampus	ACT			
Basal ganglia:				
Striatum/putamen/ nucleus accumbens		ACT	++ ACT	ACT

Author (year)	Ranote et al. (2004)	Noriuchi et al. (2008)	Atzil et al. (2011)	
Lentiform nucleus Globus pallidus				
Insula		ACT	ACT	
Frontal cortex:				
Orbitofrontal/Inferior frontal gyri	ACT	ACT	ACT	ACT
Medial frontal gyrus		ACT		
Ventral prefrontal cortex	ACT			
Dorsomedial prefrontal cortex		ACT		
Precentral gyrus		ACT	ACT	ACT
Temporal/parietal cortex:				
Temporoparietal cortex				
Fusiform gyrus	ACT			
Temporal/auditory cortex		ACT	ACT	
Parahippocampal/limbic lobe				
Occipital cortex	ACT		ACT	ACT
Cerebellum	ACT			

ACT = activated, ++ activation is more significant compare to the other group within the study.

7.4. Reasons for Inconsistency in Findings between Imaging Studies

Structures and pathways in a wide variety of maternal brain regions are activated by infant stimuli. Yet, some specific regions are more consistently implicated, than others. These include:

- 1) Thalamic and hypothalamic regions.
- 2) Frontal cortex, including orbitofrontal cortex.
- 3) Midbrain regions, including periaqueductal grey.
- 4) Limbic structures, especially cingulate cortex.
- 5) The basal ganglia, including striatum, putamen, nucleus accumbens.
- 6) Insular cortex.
- 7) Temporoparietal cortex, especially fusiform gyrus.
- 8) Occipital cortex.
- 9) The cerebellum.

Some of these areas are also implicated in studies of parental caregiving in animal, namely midbrain/basal forebrain, limbic and thalamocingulate structures, indicating consistency with the animal literature.

Overall, studies in humans using functional imaging provide some evidence of consistently activated maternal brain regions in response to infant's stimuli (Table 7.1a, b, 7.2 a, b, and 7.3). However, inconsistencies are also notable. For example, while some studies find amygdala activation (Seifritz et al., 2003; Swain et al., 2003, 2004, 2008a, Ranote et al., 2004; Lenzi, 2009), others report no such activation (Swain et al., 2004b) or deactivation (Bartels & Zeki, 2004). This lack of consistency could be explained by several reasons. First, many of the earlier studies are rather small (e.g. Lorberbaum et al., 1999; Nitschke et al., 2004). Second, age of infants varies considerably between studies (e.g. Lorberbaum et al., 2002;

Leibenluft et al., 2004) and brain activation may change as the mother and infant develop a relationship and as the infant gets older and more interactive with the mother. This may result in less activation in areas that support basic, reflexive caring in younger infants, such as nursing (mesolimbic) and areas that serve motivation and response to threat (mesocortical dopamine connections) in early postpartum (see review of Swain, 2010). This notion is supported by the extended findings of Lorberbaum et al. (2002); when they repeated their earlier study (Lorberbaum et al., 1999) in mothers at earlier postpartum time (4-8 weeks) and found more mesolimbic and mesocortical dopamine pathways activation in response to infant cries.

Third, maternal caregiving is a composite of multiple behaviours, each of which may have discrete neural correlates (Musser et al., 2012). Therefore, it is important to know about mothers' quality of 'mothering' (e.g. maternal sensitivity) in order to interpret maternal brain responses (Barrett & Fleming, 2011). Fourth, individual maternal experience with their own parents may influence the way women process their infant cues (Strathearn et al., 2009), and therefore must be considered when interpreting brain responses. The third and fourth points reflect the variability and complexity of human maternal behaviour and the capacity to parent (i.e. variation in maternal caregiving) (Swain et al., 2007).

Fifth, some brain regions subserve a range of different functions, e.g. the amygdala and insula, which could lead to mixed findings in different studies (Strathearn et al., 2009; Kim et al., 2011). Sixth, discrepant findings among studies may also be related to the use of different experimental and analytic paradigms (Barrett & Fleming, 2011); some studies used fixed effects analyses which do not consider inter-subject variability and therefore limit inference to the group studied.

Conversely, other studies use random effects analyses that account for inter-subject variability and permit generalisation of findings (Swain et al., 2007). Furthermore, some studies used block designs (Lorberbaum et al., 2002), while others used event related designs with relatively shorter stimuli (Seifritz et al., 2003). Finally, variation in the modality of the stimulus may affect the consistency of findings. While many studies used own infant stimuli, the use of control stimuli varied widely (e.g. unknown infants, familiar infant, or neutral scene). Moreover, some included different emotional valences (Strathearn et al., 2008, 2009) while others included more cognitively demanding tasks (Leibenluft et al., 2004).

7.5. Summary

While many studies examined maternal brain responses to infant stimuli, far fewer have examined the neural correlates in relation to maternal behaviour (Atzil et al., 2011; Musser et al., 2012), and only one study has attempted to focus on maternal sensitivity (Kim et al., 2011), yet due to design issues, firm conclusions from this study are limited. Maternal caregiving is a composite of multiple behaviours, and recent evidence suggests discrete maternal brain activation in relation to each of these maternal behaviours (Musser et al., 2012).

The aim of the present study was to examine maternal brain responses to own and unknown infant stimuli using videos in blocks of neutral, happy, and sad cues, comparing mothers from a community UK population. Mothers were chosen to represent healthy women in a population and therefore were recruited with no history of mental illness and to represent the natural variation in maternal sensitivity (i.e. high sensitivity and low sensitivity mothers). Also in these mothers, we examined the relationship between maternal BOLD brain activation to infant

stimuli, including OT rich brain areas, and levels of plasma OT following mother-infant interaction. This study was designed to address limitations from previous studies by including a larger sample ($N = 30$) of new mothers examined at a limited postpartum period (7-9 months) while measuring plasma OT and fMRI within the same session. Furthermore, mothers were assessed for obstetric and demographic influences which might represent potential confounders of any association and which might be relevant in mediating some of the differences we may find between the high and low sensitivity mothers.

To our knowledge, this study is the first to examine both brain and plasma OT responses to infant stimuli in healthy mothers rigorously defined by their maternal sensitivity rating. If BOLD activation in fMRI can discriminate between high and low maternal sensitivity mothers, it would give credence to the notion that functional imaging is a robust biomarker of ‘maternal sensitivity’. If we can show a significant relationship between plasma OT responses to infant challenge between high sensitivity mothers (HSMs) and low sensitivity mothers (LSMs), and, further make links to imaging patterns, it would imply that modulation of maternal behaviour by novel interventions could be studied in small numbers of normal volunteers.

7.6. Objectives of Study II (oxytocin & fMRI scanning)

In this study, we aimed to examine differences in plasma OT and brain correlates between women representing natural variation in human maternal sensitivity. We aimed to:

1. Examine whether plasma OT is distinct between HSMs and LSMs, both at baseline and following interaction challenge with their own infant, accounting for demographic differences between the two groups.
2. Extend previous finding by examining maternal plasma OT in relation to own perceived parenting experience (Gordon et al., 2008; Strathearn et al., 2009).
3. To confirm and extend previous findings in relation to activation of specific maternal motivational reward pathways in response to own infant compared to an unknown infant among all mothers.
4. To examine whether fMRI can discriminate between high and low maternal sensitivity and whether its modulation by OT can also be detected, more specifically:
 - i. To examine differences in maternal BOLD activation between HSMs and LSMs in response to own infant versus an unknown infant, regardless of the emotion displayed, as well as when emotion considered (i.e. neutral, happy and sad).
 - ii. To examine differences in maternal BOLD activation between HSMs and LSMs in response to own infant separately (without comparing it to unknown infant) for each emotional affect.
 - iii. To examine correlations between maternal BOLD activation in response to own infant and plasma OT responses following interaction with own infant.

7.7. Hypotheses of Study II

In regards to maternal plasma OT, we hypothesised that:

1. HSMs would show significantly higher plasma OT levels both at baseline and following infant play-interaction than LSMs.
2. Plasma OT levels in each group of mothers (HSMs/LSMs) will be positively correlated with positive rating of own parenting experience.

In regards to maternal brain responses, we hypothesised that:

- i. We would predict that our main effect comparing own infant with an unknown infant (among the whole sample) would show greater BOLD activation in areas previously reported by others (e.g. Ranote et al., 2004; Bartels & Zeki, 2004), specifically: reward areas in the prefrontal cortex, limbic areas at the anterior cingulate cortex and the amygdala.
- ii. Based on previous evidence that examined maternal neural correlations in relation to ‘maternal affiliative behaviour’ (Atzil et al., 2011; Musser et al., 2012), or to ‘proxies of maternal oxytocin responses’ (Swain et al., 2008a; Kim et al., 2011), we hypothesised that: maternal brain responses to the contrast of own infant versus an unknown infant video (all affects combined) would be significantly greater in the HSMs compared to LSMs, specifically in: areas implicated in OT secretion at the hypothalamus, areas associated with mirroring the emotions of others at the superior temporal gyrus, areas for emotional processing at the posterior cingulate gyrus, and areas for encoding emotional memories at the hippocampal formation.
- iii. Greater BOLD activation (in the same areas stated in (ii)) will be found in HSMs compared to LSMs in response to own infant facial affect (neutral, happy, and sad); when compared to an unknown infant of a similar affect

(or when compared to neutral control). However, given this is the first study to investigate differences in infant emotional affects between two distinct groups of mothers, sorting of areas in relation to each individual affect were left as exploratory.

- iv. BOLD activation in HSMs (in regions stated earlier in (ii) would correlate positively with their plasma OT levels following the interactive play with their infant.

Chapter 8: **Study II Methodology**

(Oxytocin & fMRI Scanning)

8.1. Sample

Study II was initiated at 7-9 months postpartum, with the cohort followed through from Study I. Exclusion criteria for this study were: (a) any contraindication to magnetic resonance imaging (MRI) (see MRI declaration form-Appendix B), (b) pregnancy, (c) left-handed mother, (d) a screen positive for depression (EPDS ≥ 12 and HADS > 11), and (e) mother not living with her infant. Out of 80 mothers who were followed up and who underwent evaluation of maternal sensitivity at 4-6 months postpartum (Study I-Time 2), 13 were not eligible for MRI (11 left-handed, 2 with contraindication to MRI), and 10 declined or were lost to follow up. Selection of the final sample was performed among the remaining 57 eligible mothers.

The final sample consisted of 30 eligible mothers representing opposite ends of maternal sensitivity distribution at a mean of 35.14 weeks postpartum (SD = 3.26): 15 classified as ‘sensitive’ mothers (blind rated 4-7 on the MACI sensitivity scale; mean = 4.47; SD = 0.74) and 15 women as ‘less sensitive’ mothers (blind rated 1-3 on the MACI sensitivity scale; mean = 2.13 (SD = 0.52). For description purposes, the two sub-groups respectively are referred to here as ‘high sensitivity mothers’ (HSMs) and ‘low sensitivity mothers’ (LSMs) (Figure 8.1). The selection of the HSMs and LSMs were initially determined by taking ratings of 1+ above the SD (ratings 5-7), and 1+ below the SD (ratings 1-2), respectively, from published

MACI data on a healthy sample of 47 mothers at 7 months postpartum (Wan et al., 2012). However, as this did not provide, in the current sample, the required number of $N = 15$ in each group (based on power calculation for the scanning study), the thresholds were increased, but with no overlap, such that HSM's included those rated 4-7 (equating to: general to high sensitive responsiveness) and LSM's included those rated 1-3 (equating to: minimal to moderate sensitive responsiveness (Figure 8.1).

Table 8.1 represents the demographic and obstetric characteristics for the high and low sensitivity mothers, and statistics comparing demographics between the two groups are presented with the results (Chapter 9).

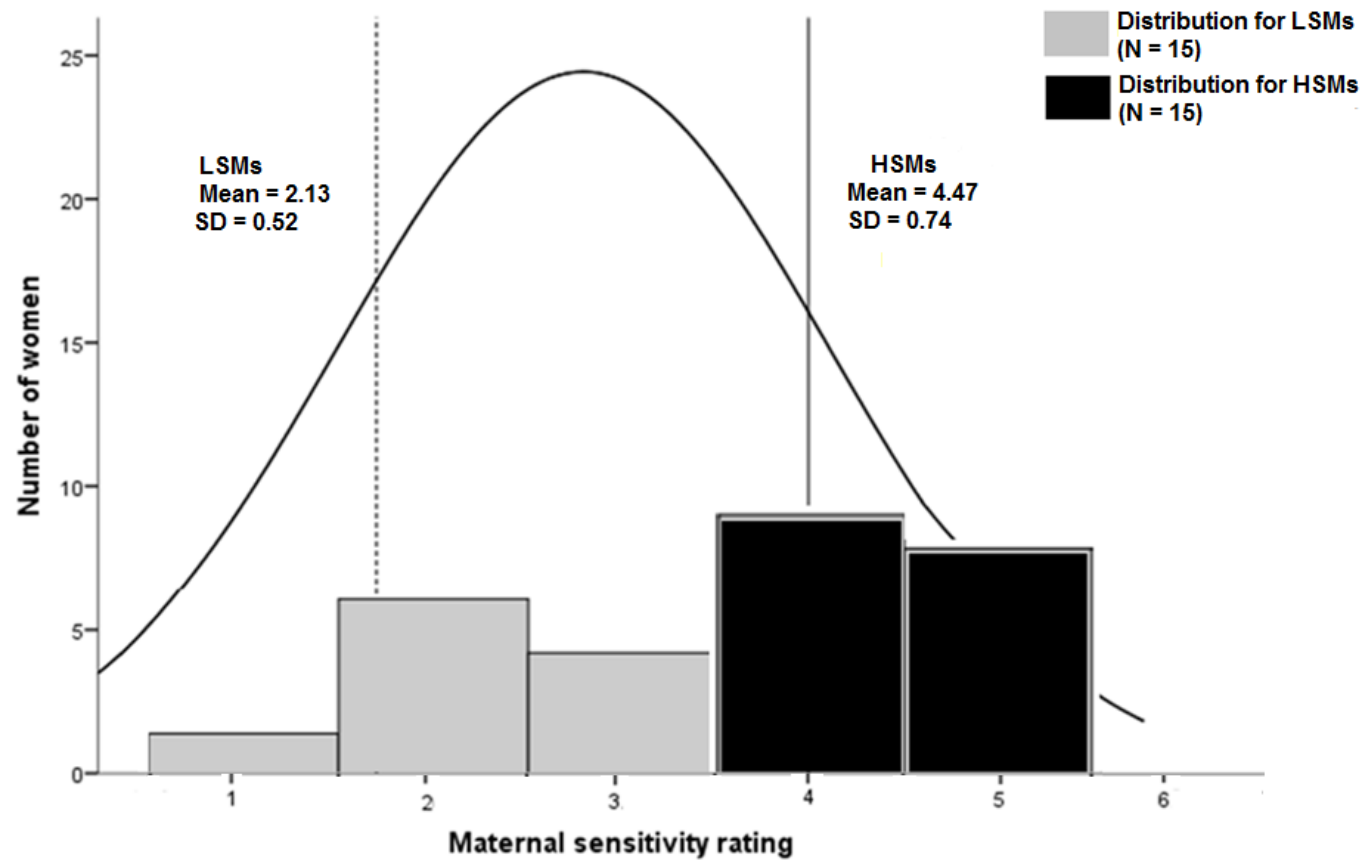


Figure 8.1. Distributions of high sensitivity mothers (HSMs, N = 15) and low sensitivity mothers (LSMs, N= 15) in relation to maternal sensitivity distribution for the whole sample (N = 80). **Key:** Means for high sensitivity mothers (vertical solid line) and low sensitivity mothers (vertical dashed line) in relation to the larger sample are also presented.

Table 8.1. The demographic and obstetric characteristics of the sample grouped by level of maternal sensitivity

Characteristic	High Sensitivity Mothers (N = 15)	Low Sensitivity Mothers (N = 15)
<i>Mean [SD]</i>		
Maternal age (years)	30.40 [5.37]	27.65 [4.76]
Postpartum stage (weeks)	35.93 [2.81]	34.29 [0.69]
Infant birthweight (kilograms)	3.44 [0.44]	3.23 [0.59]
<i>Frequency (%)</i>		
Married/cohabiting	13 (86.7)	11 (78.6)
Primiparity	6 (40.0)	9 (64.3)
Highest maternal education:		
Secondary (GCSE)	3 (20.0)	6 (40.0)
Post-secondary education (A-level or equivalent)	4 (26.7)	6 (40.0)
University degree and postgraduate	8 (53.3)	3 (20.0)
Household income/year:		
£15000 or less	1 (6.7)	5 (33.3)
£16000-£34000	5 (33.3)	6 (40.0)
£35000 or more	9 (60.0)	4 (26.7)
Infant gender (female)	10 (66.7)	7 (50.0)
Mode of delivery (vaginal)	10 (66.7)	11 (78.6)
Mode of feeding (breast)	11 (73.3)	7 (50.0)

8.2. Procedure

Potentially eligible mothers were contacted and if they showed interest in participation they were visited at their home to explain further about the study and to confirm their eligibility after mothers rated their mood using HADS and EPDS. Within this visit, following informed consent, a video of the infant's face was obtained to use as a stimulus during the fMRI. After prior arrangement mothers and infants attended the WTCRF in Manchester, for a two hour session when three samples of blood were collected and brain responses to infant stimuli were assessed through 35 minute-fMRI.

8.2.1. Oxytocin

i. Plasma Oxytocin samples

Mothers attended the session at the WTCRF either during menstruation or on their contraceptive pill free days (early follicular phase). Measurement of plasma OT was taken before and after mother-infant interactive play with their infants (instructions as per the earlier play interaction). Blood samples were taken from mothers at the same time in the early afternoon 1200 -1400 hours, and one hour after the last nursing feed (to control for the influence of diurnal and physiological changes, respectively). Mothers were asked to refrain from caffeine/smoking for at least two hours before the sampling. Three samples of blood (5 ml each) were taken from antecubital veins through an intravenous cannula. The first sample (OT1) was taken 10 minutes after the mothers were separated from their infants. Then the mother rejoined their infant and participated in interactive play for 10 minutes. Immediately after the interaction, the second sample was taken (OT2) followed by the third sample (OT3) 5 minutes after that. After each sampling, the cannula was flushed with 2 ml normal saline to maintain patency of the vein, and 3 ml of blood were discarded before each sample to ensure no dilution because of the saline. Refreshments were served after the blood sampling and before

scanning to overcome the influence of any possible anxiety provoked by the blood draw on the mother's brain.

ii. Sample processing & Assays

Each of the three samples (OT1, OT2 & OT3) was drawn into chilled vacutainer tubes containing lithium heparin injected with 200 ml of Trasylol (aprotinin) 500,000 KIU/ml blood. OT samples were kept ice-chilled and processed within 10 minutes. Samples were then centrifuged at 4° C at 3500rpm for 15 minutes, and 500ul supernatants were transferred to 2 microtubes (aliquot 1 & 2) and stored at - 80° C until transferred on dry ice, to the University of Manchester Laboratory for analysis. Optimisation to test the extraction method was performed through pilot samples before the actual analysis.

Determination of the OT was performed using the Max Binding Determination Competitive Assay protocol on Gen 5 software using a Biotek Plate reader. Samples were diluted 1 in 4 for assay and then results multiplied by 4 to compensate for dilution. Oxytocin analyses were performed by a laboratory scientist who was blind to the study setting and information.

8.2.2. fMRI scanning

i. fMRI paradigms

A series of alternating pre-recorded 20-second video clips was prepared consisting of 3 affect conditions (Neutral, Happy, and Sad) of each of two infants (the participant's 'own' infant, and an 'unknown' infant) for use in the fMRI scan. The unknown infant was matched on age, gender and ethnicity to the mother's own infant. To provide a measurement of BOLD signal change in active conditions compared to control condition, mothers were also presented with neutral control stimuli (i.e. video of slow moving traffic), which was a standard across subjects and used in a previous research study (Ranote et al., 2004). Active video blocks were interspersed with resting periods

(blank screen) for comparison with active (video) blocks BOLD responses. Videos lasting 16 minutes were presented in the following order: (Own neutral infant-neutral control-unknown neutral infant) x 4, REST, (Own happy infant-neutral control-unknown happy infant) x 4, REST, (Own sad infant- neutral control- unknown sad infant) x 4, REST (Figure 8.2). All stimuli were displayed from a computer controlled projector presented on a display screen and relayed to the participant via a mirror placed above the head while in the MRI scanner.

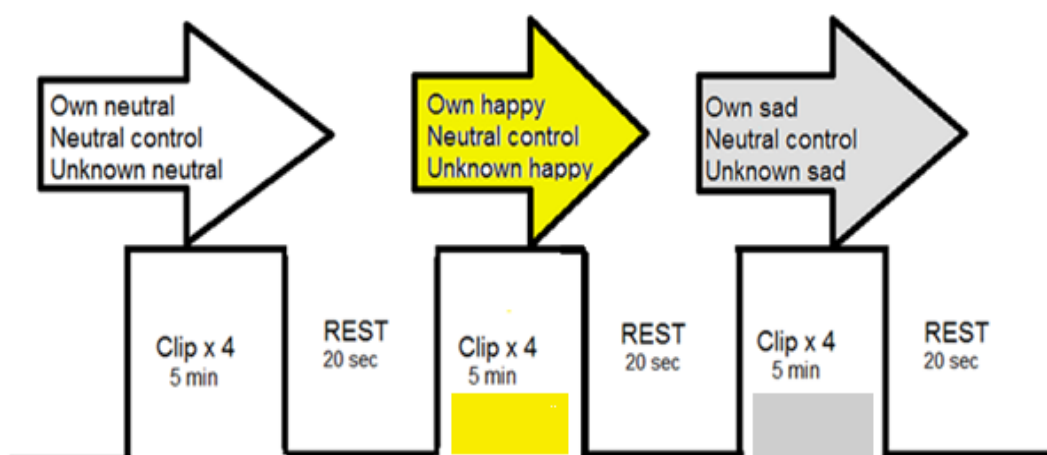


Figure 8.2. Model representing the order of video clips as viewed by mothers while in the scanner. Note: 20 sec ‘Neutral control’ was added to the first three blocks of each emotion.

For the video task we used the following contrasts to test our hypotheses (see Chapter 7):

- a. To examine the main effect, among all mothers: *all infant videos minus the neutral control*.

- b. Comparing high and low sensitivity groups: 1) *HSMs vs. LSMs (own infant minus unknown infant)* (all affects combined), 2) *HSMs vs. LSMs (own neutral minus unknown neutral infant, own happy minus unknown happy infant, and own sad minus unknown sad infant)*, 3) *HSMs vs. LSMs (own happy, own neutral, and own sad) subtracting neutral control*.
- c. The equivalent of (b) for LSMs vs. HSMs.

ii. fMRI Acquisition

Imaging was performed using a 1.5 Tesla Philips Intera MRI scanner running Explorer gradients (software version 11.1.4.4). High-resolution T1-weighted structural images were acquired to exclude any structural abnormality (none were found) and for coregistration with functional data. The structural scan using SENSE employed a 3D Contrast Turbo Field Echo Sequence with a temporal resolution (TR) of 9ms and an echo time (TE) of 4ms with an 8° flip angle producing 140 slices with a voxel size of 0.8 x 0.8 x 1.0 mm. Functional images were acquired using a multi-slice, single shot echo-planar imaging sequence, generating 29 ascending axial slices (TR = 2.5s, TE = 40ms, 4mm thickness with 0.5mm slice gap, in-plane resolution of 3.4 x 3.4mm). fMRI data were exported from the scanner as proprietary Philips PAR/REC files. These files were converted to IMG and HDR files using MRicro software (Rorden & Brett, 2000).

8.3. Statistical Analyses

8.3.1. Sample size

The sample size was recalculated for Study II to avoid overestimation or underestimation of the sample (Mumford & Nichols, 2008). The sample size of 30 mothers (15 in each group) is ample enough to produce a power of approximately 90% (Desmond & Glover, 2002).

8.3.2. Data analysis

Demographic and obstetric differences between high sensitivity and low sensitivity groups of mothers were assessed through independent sample t-test for interval variables and through Chi-square test for categorical variables.

i. Oxytocin analysis

Pearson correlations were used to explore correlations between plasma OT levels and other variables and stability of OT across the 3 assessments as well as correlations between OT and other behavioural measures. A repeated-measures analysis of variance (ANOVA) was employed to test for a significant change in plasma OT levels over time between groups (HSMs and LSMs). Analyses were performed using SPSS (version 19) and $p < 0.05$ (two-tailed) was considered statistically significant.

ii. fMRI analysis

Imaging data for each participant were pre-processed to reduce artefacts related to signal components, corrected for motion, and the individual data were spatially normalised for group analyses using Statistical Parametric Mapping (SPM8; <http://www.fil.ion.ucl.ac.uk>) and implemented in MATLAB (Math works Inc., Sherborn, MA, USA). All functional images were realigned using a least squares approach and a 6 parameter (rigid body) spatial translation (Friston et al., 1996). This was undertaken because in the scanner; participants, while in the head coil, may still undergo slight head movement. The first image was used as a reference scan and the following images were translated onto this, correcting for pitch, roll and yaw throughout the task. Translation and rotation corrections did not exceed 3.0 mm and 2.5° for any participant.

The realigned images were co-registered with the corresponding structural (T1 Weighted) scan and segmented into different tissue classes by matching grey matter to a grey matter reference template. Tissue classification registers the images with tissue probability maps (grey matter, white matter and cerebrospinal fluid) adapted from the International Consortium for Brain Mapping (ICBM) 452 T1-weighted scans. Following this, the scans were spatially (stereotactically) normalised onto standardised brain slices. This involves the warp of the images onto a standardised template. The standardised template conforms to the ICBM, NIH P-20 project and approximates the stereotactic atlas of Talairach & Tournoux (1988) (Ashburner & Friston, 1997; 1999). The standardized slices then underwent smoothing using an isotropic Gaussian kernel filter (10 mm full width half maximum [FWHM]) to increase the signal-to-noise ratio by use of the matched filter theorem (Friston et al., 2000). A parametric model was employed that enabled the modelling of linear hemodynamic responses. First level analyses were performed on each subject's data to generate a single mean image corresponding to canonical hemodynamic responses convolved with the block design compared to resting conditions. Second level group analyses were performed using a factorial ANOVA to contrast the conditions in each task.

8.4. Ethical Consideration

8.4.1. Ethics

Ethical regulations for Study I were also applied in Study II as appropriate; including detailed information about the study aims, what it involved in relation to participants (mothers), and ability of mothers to withdraw from the study at any time without giving any reasons. This was explained to mothers verbally and in written format through the information sheet. Eligibility for the fMRI was confirmed by completing the MRI

declaration form (ISBE; ethics Ref No. 02043, see Appendix B). Informed consents were obtained from each participant before their participation. Mothers also gave their permission so their GP would be informed if any abnormality was found in their structural brain image, and for their infant's videos to be shown to other participants in the study. Mothers were given a value of £30 pounds Boots shopping vouchers and a 'Thank You' card.

8.4.2. Safety considerations

Mothers' cannulation and blood withdrawal followed the Standard Operational Procedure (SOP) at the WTCRF, which is in accordance with the protocol followed in the Central Manchester University Hospitals, NHS Foundation Trust. Infants' safety measures while playing with mother was followed as in Study I (e.g. padded mat, no electrical sockets etc.). Mothers were given the option to visit the 'mock' MRI scanner at the University of Manchester prior to their actual scanning session to minimise possible discomfort or anxiety related to scanning.

Chapter 9: **Study II Results**

(Oxytocin & fMRI scanning)

9.1. Sample

Participants for this study (Study II) are 15 HSMs and 15 LSMs who completed Study I of this project at 4-6 months postpartum (see Chapter 8-Methods). Although household income and maternal education were both borderline higher among HSMs, the results were insignificant and therefore they were not controlled for to avoid over adjustment. In addition, the two groups of mothers did not differ significantly in: maternal age, marital status, parity (multiparous/primiparous), postpartum stage, infant birthweight, infant gender, mode of delivery (CSD/ VD), or mode of feeding (bottle/breast) (both at the 4-6 month visit or the current visit) (Table 9.1).

Table 9.1. Comparison of the demographic and obstetric characteristics of mothers grouped by level of maternal sensitivity (high sensitivity mothers, HSMs and low sensitivity mothers, LSMs)

Characteristic	HSMs (N = 15)	LSMs (N = 15)	t (28)	Chi-square test	p-value
<i>Mean [SD]</i>					
Maternal age (years)	30.40 [5.37]	27.65 [4.76]	- 1.38		0.18
Average maternal education (years)	15.06 [2.82]	12.80 [2.73]	- 1.87		0.07
Average annual household income (thousand pounds)	33.00 [4.61]	26.33 [4.24]	- 2.76		0.09
Infant birthweight (kilograms)	3.44 [0.44]	3.23 [0.59]	- 0.80		0.43
Postpartum stage (weeks)	35.93 [2.81]	34.29 [3.69]	- 1.37		0.18
<i>Frequency (%)</i>					
Married/cohabiting	13 (86.7)	11 (78.6)		0.56	0.65
Primiparous	6 (40.0)	9 (64.3)		1.71	0.19
Infant gender (female)	10 (66.7)	7 (50.0)		0.83	0.36
Mode of delivery (vaginal)	10 (66.7)	11 (78.6)		0.51	0.47
Mode of feeding (breast)					
<i>At 4-6 month visit</i>	11 (73.3)	7 (50.0)		1.68	0.19
<i>At 7-9 month visit</i>	3 (20.0)	3 (20.0)		0.55*	0.64

*Fisher exact test

9.2. Plasma Oxytocin Results

9.2.1. Preliminary analyses

Three samples of plasma oxytocin were collected from each woman before (OT1) and after (OT2 & OT3) interaction with their infant (see Chapter 8). Two participants did not have their OT3 assessed (due to technical difficulties) and hence their OT3 was assigned the same value as OT2. One outlier was excluded from this analysis (scored > 3 SD in all three assessments). The three plasma OT assessments (Table 9.2) were highly correlated with each other, both among HSMs ($r = 0.79-0.96$; $p < 0.01$) and among LSMs ($r = 0.92-0.99$; $p < 0.01$), indicating high levels of OT individual stability.

Table 9.2. Mean oxytocin levels (pg/ml) measured before and after play-interaction among mothers grouped by level of maternal sensitivity

Oxytocin sample	High Sensitivity Mothers (N = 15) mean [SD]	Low Sensitivity Mothers (N = 14) mean [SD]
OT1	235.09 [83.51]	301.87 [39.15]
OT2	223.67 [83.43]	303.27 [34.67]
OT3	210.01 [81.58]	301.56 [38.12]

Note: OT1: Oxytocin measured before mother-infant interaction, OT2 & OT3: Oxytocin measured after mother infant interaction.

After excluding the outlier, the two groups were re-examined for possible confounders. Household income was significantly higher in HSMs compared to LSMs and accordingly was controlled for in the subsequent analyses. The two groups remained matched and not significantly different with respect to other demographics including maternal age, marital status, maternal education, parity, infant birthweight, infant gender, mode of delivery, mode of feeding, and postpartum stage (Table 9.3).

Table 9.3. Comparing demographic and obstetric characteristics of mothers grouped by level of maternal sensitivity excluding the outlier

Characteristic	HSMs (N = 15)	LSMs (N = 14)	t (27)	Chi-square test	p-value
<i>Mean [SD]</i>					
Maternal age (years)	30.40 [5.37]	27.64 [4.77]	- 1.46		0.16
Average maternal education (years)	15.06 [2.82]	12.77 [2.76]	- 1.94		0.06
Average annual household income (thousand pounds)	33.00 [4.61]	25.12 [4.13]	- 2.11		0.04
Infant birthweight (kilograms)	3.44 [0.44]	3.20 [0.53]	- 1.10		0.28
Postpartum stage (weeks)	35.93 [2.81]	34.64 [3.22]	1.32		0.20
<i>Frequency (%)</i>					
Married/cohabiting	13 (86.7)	11 (78.6)		0.56	0.65
Primiparous	6 (40.0)	8 (57.1)		1.65	0.21
Infant gender (female)	10 (66.7)	7 (50.0)		0.83	0.36
Mode of delivery (vaginal)	10 (66.7)	11 (78.6)		0.51	0.47
Mode of feeding (breast)	3 (20.0)	3 (20.0)		0.55*	0.64

*Fisher exact test

9.2.2. Main analysis

Controlling for household income, a repeated measure ANOVA showed no overall change in the mean level of OT from baseline to post interaction (within subject effect) Greenhouse-Geisser [$F(1.37, 35.51) = 1.54; p = 0.23$]. Next, we examine between subject effect [$F(1, 26) = 8.42; p = 0.01$] and found significant difference in OT through the three assessment points when the two groups of sensitivity was compared with this change confined to HSMs (Figure 9.1). High variance on OT3 measurement among the HSMs is also evidenced from the graph (Figure 9.1).

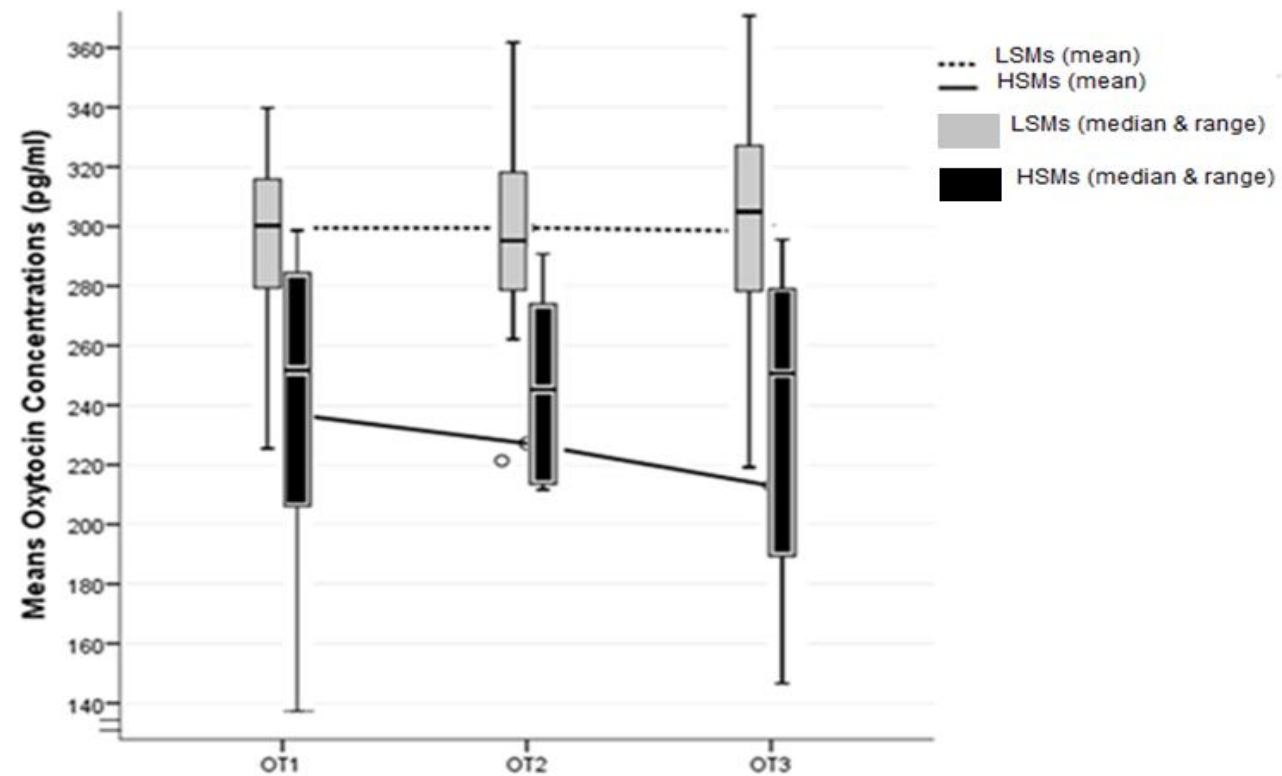


Figure 9.1. Box plots and means of plasma oxytocin measured before (OT1) and after mother-infant interaction (OT2 and OT3) among the high sensitivity mothers (HSMs, N = 15) and low sensitivity mothers (LSMs, N = 14), controlling for household income. **Key:** The **horizontal dashed line** represents the means of the three OT assessments among LSMs, and the **horizontal solid line** represents means of the three assessments among the HSMs.

9.2.3. Relationship between plasma OT and own perceived parenting experience

Controlling for household income, the two groups of mothers did not differ significantly in their prenatal self-reporting of own: maternal care (transformed) [$F(1, 26) = 0.01$; $p = 0.93$], paternal care (transformed) [$F(1, 26) = 0.41$; $p = 0.53$], maternal overprotection, [$F(1, 26) = 2.41$; $p = 0.13$], or paternal overprotection [$F(1, 26) = 0.52$; $p = 0.48$]. Next, we examined whether plasma OT was related to these self-reports of own parenting experience. To simplify interpretation, OT1 (OT_{pre}) and the mean of OT2 and OT3 (OT_{post}) were considered to test the correlations with perceived parenting experience. Maternal overprotection was positively correlated with both OT_{pre} and OT_{post} among LSMs but not among HSMs (Table 9.4; Figure 9.2). Maternal care, paternal overprotection and paternal care were not correlated with plasma OT (OT_{pre} or OT_{post}) in any of the groups. Furthermore, OT at all times was not correlated with mode of delivery or feeding.

Table 9.4. Correlations between plasma OT and self reported own parenting experience in mothers grouped by level of maternal sensitivity

	HSMs (N = 15)		LSMs (N = 14)	
	OT _{pre}	OT _{post}	OT _{pre}	OT _{post}
Maternal care¹	- 0.38	- 0.21	- 0.21	- 0.07
Maternal overprotection	0.28	0.07	0.62*	0.63*
Paternal care¹	- 0.34	- 0.34	- 0.09	0.18
Paternal overprotection	- 0.12	- 0.06	0.16	0.03

* $p < 0.05$. ¹: Transformed variable

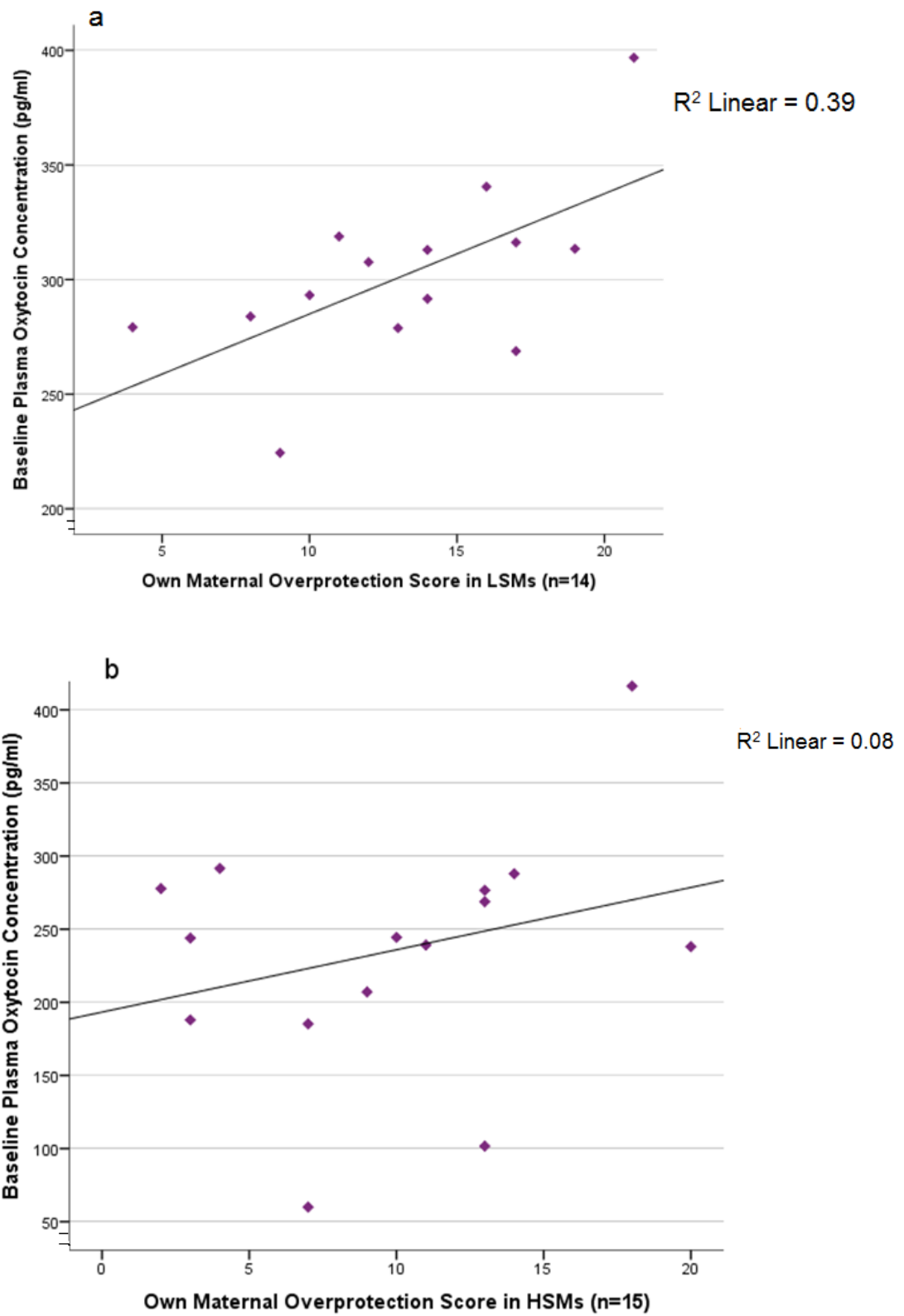


Figure 9.2. The relationship between baseline plasma oxytocin (OT_{pre}) and own maternal overprotection among: (a) low sensitivity ($N = 14$), and (b) high sensitivity mothers ($N = 15$) (similar relationships also shown with OT_{post}).

9.3. fMRI Results

9.3.1. Preliminary analysis

No participants were excluded from this analysis, and therefore the two groups represent the same characteristics presented at the beginning of this chapter (Table 9.1). Because one outlier was excluded from OT analyses ($> 3SD$), and therefore was also excluded when correlations between BOLD brain activation and plasma OT were examined.

9.3.2. Whole brain analyses of maternal brain responses

In order not to limit the extent of this exploratory analysis, we started by performing ‘whole brain analyses’ with a significant threshold specified as $p \leq 0.05$, Family Wise Error (FWE) corrected. Prior to testing the specific hypotheses, maternal responses to all infant stimuli (i.e. own + unknown) were compared with responses to neutral control stimuli (i.e. video of slow moving traffic). Thus, for analysis purposes, the first contrast analysed was ‘*All infants minus neutral control*’. This provided a measurement of BOLD signal change in active conditions compared to control conditions. Although no activation reached the threshold level, but subthreshold regions are shown in Table 9.5 for interest.

Next, the main effect was examined after combining all facial affects, to compare videos of own infant versus videos of an unknown infant ‘*own infant minus unknown infant*’. In response to own infant (compared to an unknown infant cues) enhanced BOLD activation was observed in the right inferior frontal gyrus (BA 47 & 9), and in a range of subcortical regions, including, left parahippocampal gyrus (BA 34), bilateral uncus (BA 28), and right anterior cingulate gyrus (BA, 24) (Table 9.5).

Table 9.5. Contrasts testing BOLD signals and ‘main effect’ in response to own and an unknown infant stimuli (combined all affects) among the whole sample (N = 30)

Contrast	Area	Sub-areas	BA	R/L	Talairach coordinates			Z score	FWE	FDR	KE
					x	y	z				
All infants minus neutral control	Parietal lobe	Postcentral gyrus	1	R	54	- 16	50	4.11	0.08	0.16	991
	Temporal lobe	Middle temporal gyrus		R	40	- 61	6	4.19	0.08	0.26	991
Own infant minus unknown infant	Frontal lobe	Inferior frontal gyrus	47	R	43	26	2	4.50	0.02	0.02	591
			9	R	47	11	27	4.08	0.01	0.04	591
	Limbic lobe	Parahippocampal gyrus	34	L	- 23	2	- 19	4.49	0.02	0.02	156
		Uncus	28	L	- 29	5	- 23	4.45	0.01	0.01	591
			28	R	33	2	- 23	4.55			
			28	R	30	5	- 19	3.85			
		Anterior cingulate gyrus	24		0	31	23	4.21	0.06	0.03	571

Note. All significant whole brain (Family Wise Error (FWE) ≤ 0.05) corrected for multiple comparison. BA: Brodmann’s area; L: Left, R: Right; FDR: False Discovery Rate, KE: Cluster size (provided for interest only and not as a significant reference).

9.3.3. Comparisons between high and low sensitivity mothers

Comparison of BOLD activation between HSMs and LSMs using whole brain analyses did not reveal significant results. Therefore, a ‘Region of Interest (ROI)’ with random effects analysis was set to test our main hypotheses regarding comparisons between the two sensitivity groups.

Region of Interest Analyses (ROI): Based on our hypothesis a single ROI composite was hypothesised to include: the right superior temporal gyrus, right posterior cingulate gyrus, left subthalamic nucleus and left hippocampal formation. We compared brain activation patterns between sensitivity groups using a two-factor random effects ANOVA model where ROI differences in BOLD activation were assessed using a threshold of $(FWE) \leq 0.05$, corrected for multiple comparisons. Activation was calculated between the two groups of mothers, HSMs (N = 15) and LSMs (N = 15) in a priori ROI. Activation between the two groups was compared using the t-test.

In post hoc analyses, we compared BOLD activation to own versus unknown infant video between the two sensitivity groups regardless of facial affect [*i.e. HSMs versus LSMs (own infant minus unknown infant)*]; similarly, we compared LSMs versus HSMs. No significant effects were found with these contrasts in any of the ROIs.

We also compared responses to own versus unknown infant video between the two sensitivity groups for each facial affect separately [*i.e. HSMs versus LSMs (own neutral infant minus unknown neutral infant), HSMs versus LSMs (own happy infant minus unknown happy infant)*], [*HSMs versus LSMs (own sad infant minus unknown sad infant)*], and similarly for LSMs versus HSMs. Compared to LSMs, HSMs showed greater BOLD activation in the right superior temporal gyrus (BA 41) in response to own neutral infant as compared to unknown neutral infant (Table 9.6, Figure 9.3);

whereas, compared with HSMs, LSMs did not show significant BOLD activation in any of the ROIs. Own infant happy or sad versus unknown happy or sad videos did not reveal significant differences in BOLD activation when the two groups were compared.

Finally, we compared BOLD responses to different facial affects between HSMs and LSMs using only own infant stimuli, [*i.e. HSMs versus LSMs (own neutral infant minus neutral control) HSMs versus LSMs (own happy infant minus neutral control), HSMs versus LSMs (own sad infant minus neutral control)*], and similarly for LSMs versus HSMs. Compared to LSMs, HSMs showed greater BOLD activation in the right superior temporal gyrus which was extending to the right insula (BA 13) in response to own happy infant (Table 9.6). By contrast, compared to HSMs, LSMs did not show significant BOLD activation in response to own happy infant video in any ROIs. Viewing own neutral or sad infant videos did not reveal significant differences in BOLD activation in the ROIs when the two groups were compared.

Table 9.6. Areas of significant BOLD activation within ROI, when comparing high sensitivity (N = 15) with low sensitivity (N = 15) mothers

Groups compared	Contrast	ROI	BA	Talairach coordinates			Z score	FWE	FDR	KE
				x	y	z				
High sensitivity mothers	Own neutral infant minus unknown neutral infant	Superior temporal gyrus	41	57	-25	13	3.39	0.05	0.22	25
	Own happy infant minus neutral control	Superior temporal gyrus	41	43	-32	5	3.92	0.01	0.15	118
Low sensitivity mothers			13	57	-32	18	3.38	0.05	0.16	118

Note. All significant ROI (Family Wise Error (FWE) ≤ 0.05) corrected for multiple comparison. BA: Brodmann's area; L: Left, R: Right; FDR: False Discovery Rate; KE: Cluster size (provided for interest only and not as a significant reference).

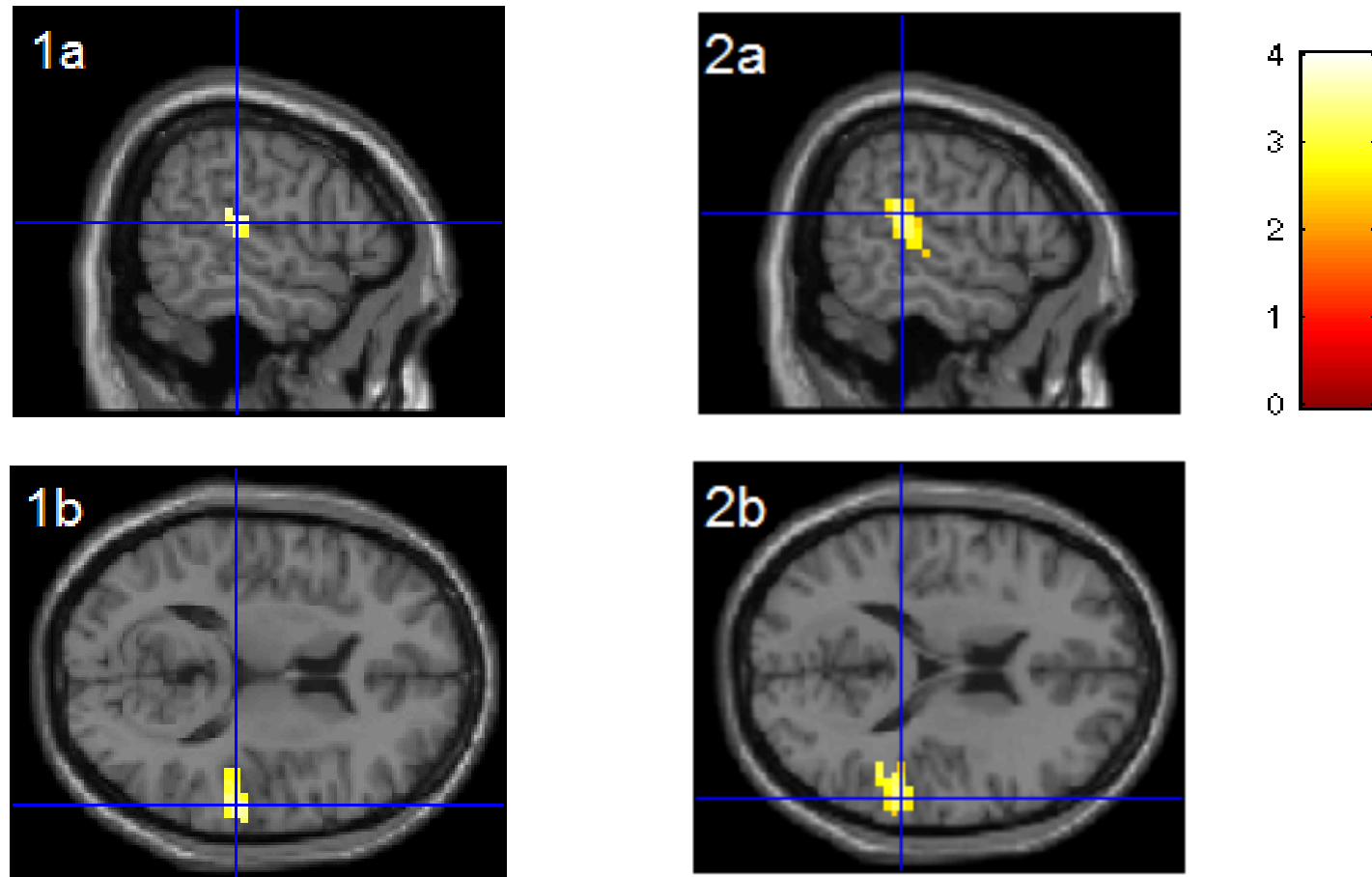


Figure 9.3. Maternal brain activation in response to infant stimuli: Compared with LSMs, HSMs show greater activation of the right superior temporal gyrus in response to: (1) own neutral infant versus unknown neutral infant video, and (2) own happy infant versus neutral control, at ROI-threshold of $FWE \leq 0.05$. Structural brain image created from average of all subjects.

9.3.4. Correlations of plasma oxytocin with ROI

Repeated measure ANOVA found a between-group correlation between BOLD activation of ROIs and plasma OT. The activation of the right superior temporal gyrus among HSMs (compared to LSMs) in response to *own happy infant minus neutral control* was negatively correlated with post-interaction plasma OT levels among those mothers (OT_{post}) ($r = -0.81$, $p < 0.01$). This implies that the greater the BOLD activation in the right superior temporal gyrus in HSMs when they viewed their infant happy cues (compared to neutral control), the lower their plasma OT levels following play interaction with their infant (Figure 9.4). No other significant correlations were found in other ROIs including, the left subthalamic nucleus.

On the other hand, in LSMs there was no significant correlation between the plasma OT_{post} and any of the a priori ROIs. Furthermore, no significant correlations were found between the a priori ROI activations and plasma OT levels when the entire sample was considered, and significant correlations between BOLD activation and OT_{post} emerged only when the HSMs group was examined separately, indicating that the origin of the correlations lies in the HSMs group.

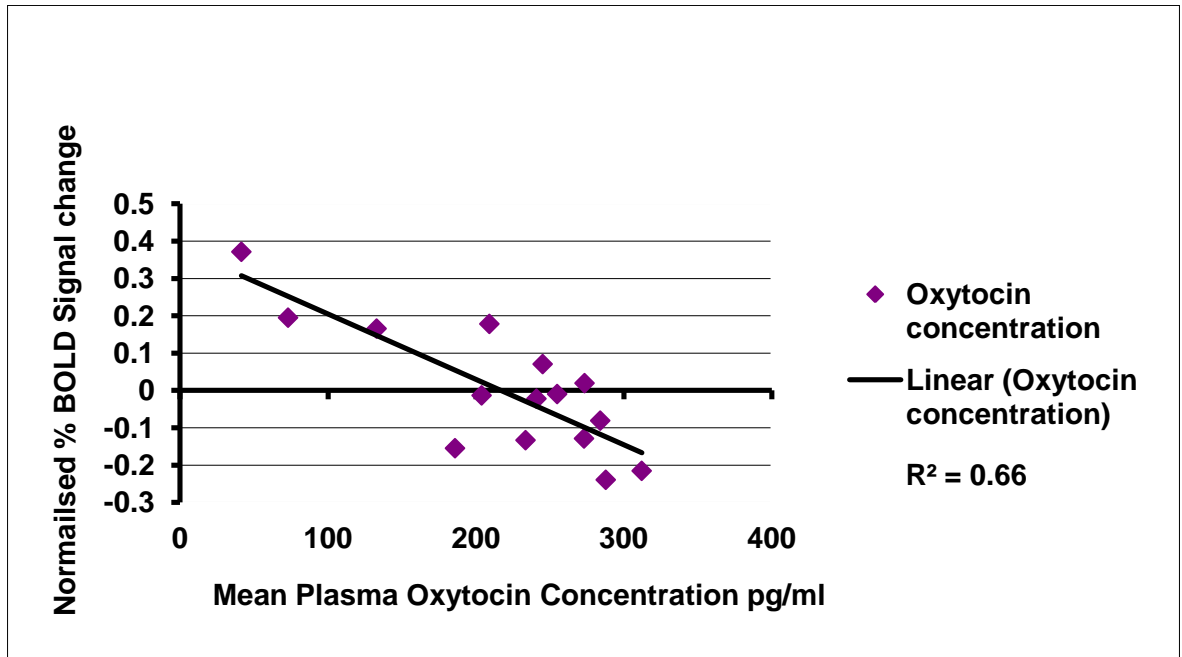


Figure 9.4. Correlation between BOLD activation in the right superior temporal gyrus (STG) and post interaction plasma oxytocin among high sensitivity mothers (N = 15)

Chapter 10: **Study II Discussion**

(Oxytocin & fMRI Scanning)

10.1. Plasma Oxytocin Discussion

10.1.1. Overview of the findings

We sought to examine further how natural differences in maternal sensitivity to infant cues are associated with maternal OT in a community sample of healthy mothers.

Contradictory to our main hypotheses, we report that: (1) HSMs have lower baseline plasma OT levels compared to LSMs, and (2) following a play-interaction with their infants, plasma OT levels significantly decrease in HSMs whereas no significant change was seen among LSMs. In accordance with our secondary hypothesis we report that, at least in LSMs, baseline and post interaction plasma OT levels were significantly correlated with own parenting experience. However, contradictory to our hypothesis (1) this correlation of OT, among LSMs, were positively correlated with *unfavourable* (not with favourable) own parenting experience, in particular; own maternal overprotection, whereas (2) both baseline and post interaction plasma OT levels among HSMs were not correlated with own parenting experience.

Recent parenting studies that examined correlation of OT to quality of affectionate behaviour among parents found a positive correlation between plasma OT levels and maternal affectionate (or paternal stimulatory) behaviour towards the infant (Feldman et al., 2007, 2010a; Gordon et al., 2010). However, a recent parenting study by the same group of authors (Feldman et al., 2011) reported higher urinary OT levels among mothers who experienced gaps in their positive social relationships, including their relationship with their own mother, romantic partner or own infant (Feldman et al.,

2011). This suggests an anti-stress role for OT similar to that reported by other studies among women (i.e. who were not necessarily mothers) (Taylor et al., 2010), which will be discussed further in this chapter.

In contrast to other parenting studies which examine correlation of OT with maternal or paternal behaviour, in the current sample, OT was assessed in two groups of women at opposite ends of the distributions of maternal sensitivity, selected from a larger community sample of 80 early postpartum mothers. This megagrouping implies women with distinct sets of affective and behavioural caregiving attributes (Thompson, 1997), and accordingly might ‘tap’ into an element of stress or anxiety coping strategy, which could be part of the sensitive responsiveness concept.

Similar to the aforementioned studies on parenting (Feldman et al., 2007; Gordon et al., 2010, Atzil et al., 2011) we did not find a relationship between baseline plasma OT levels and mode of delivery or feeding. This suggests no difference in OT between breastfeeding and formula feeding mothers when plasma OT was not sampled during feeding (Van der Post et al., 1997). It also suggested that when OT is measured later in postpartum (7-9 months), it is no longer necessarily reflecting birth history (e.g. VD/CSD) (Swain et al., 2008a), but rather is more likely to reflect parenting style (Feldman et al., 2010a). We infer that baseline plasma OT was not different between primiparous and multiparous women for similar reasons.

10.1.2. Why baseline OT was high in LSMs?

Elevated plasma OT levels have been reported in relation to gaps in positive social relationships. In a study assessing stress in partnership among 85 adults in stable relationships (62% women and 38% men), baseline plasma OT was positively correlated with ratings of distress in relationships in women (while plasma vasopressin correlated with relationship distress in men) (Taylor et al., 2010). In a further study,

among 73 post menopausal women, baseline plasma OT was negatively correlated with relationships with a woman's own mother, partner, and marginally significant (also negatively) with relationship with best friend (Taylor et al., 2006). Similarly, in a study that examined the relationship between romantic attachment and unstimulated plasma OT, 45 subjects (33 women and 12 men-not romantically attached to each other) reported their experience in romantic close relationships as well as their anxiety in these relationships (Marazziti et al., 2006). In that study, a significant positive correlation was found between plasma OT levels and anxiety in romantic relationship. The authors strengthened their findings by accounting for the pulsatile secretion of OT by considering the mean of three samples collected within one hour. However, their sample included individuals with and without a current romantic relationship; but they reported no difference in plasma OT levels with respect to this.

The implication of a role for OT in social relationships' development and difficulties was also reported among parenting studies. Although in the study by Feldman et al. (2011) plasma OT findings were inconsistent with our findings in that parents with high affective synchrony showed higher plasma OT, their urinary OT findings were consistent with our results. Urinary OT in that study was significantly and positively correlated with interactive stress, parenting stress and anxious romantic attachments. A correlation between plasma OT and urinary OT has been reported in other recent studies in humans (Hoffman et al., 2012) and animals (Polito et al., 2006). In addition, an increase in urinary OT was also reported following intravenous injection of exogenous OT, providing support for the reliability of using urinary OT to reflect systematic changes in plasma OT (Mitsui et al., 2011). Therefore, the absence of the correlation between plasma and urinary OT in the study by Feldman et al., is interesting and might suggest simultaneous multiple roles for the OT; in both reflecting and facilitating through an anxiolytic pathway, affiliative relationships.

In the current study, plasma OT levels in LSMs showed a positive correlation with own maternal overprotection-which was borderline higher in this group-which might explain the higher OT levels (at all three assessment times) among LSMs. Although in the current study there were no differences in marital status between HSMs and LSMs, we did not assess the quality of the 'relationship with partner' and so we cannot exclude distressed pair bond relationships as an explanation for the elevated plasma OT among the LSMs in our study.

Higher plasma OT was also reported in relation to more depressive symptoms. Taylor et al. (2010) found a positive correlation between plasma OT and depression scores in women who were not depressed. Similarly, Parker et al. (2010) measured OT hourly over a period of 16 hours among clinically depressed individuals and their control group, and found higher levels of OT among depressed individuals compared to the control group. Exploring a similar explanation among our sample (although not hypothesised) did not reveal differences in depression scores between the two groups of mothers. However, significantly higher mean depression scores were found among LSMs when sensitivity cut-off scores were applied to the larger sample ($N = 80$), $t(78) = 2.50$; $p = 0.01$. Had that difference been represented in our smaller sample ($N = 15$ in each group), it might have been reflected in an association with plasma OT as reported in previous studies in women (Taylor et al., 2010; Parker et al., 2010).

In summary, in women plasma OT might act as an anxiolytic or anti-stress hormone (Neumann et al., 2000, Numan & Woodside, 2010). Elevation among LSMs in the current study could be a reflection of their higher perceived maternal overprotection (as a representation for a difficult relationship with own mother), difficulties in pair bonding relationships or higher depressive symptoms, all of which are associated with

isolation or poor social networking (Grippe et al., 2007; Parker et al., 2010). Yet, only the first explanation was evidenced in the current study.

10.1.3. Why does OT drop in HSMs?

The significant reduction in plasma OT levels among HSMs following interaction with their infants is consistent with some previous reports e.g. Turner et al. (2002). These authors examine changes in plasma OT in response to laboratory-induced positive or negative emotions among 32 nulliparous women. Significant drop in plasma OT was reported after women viewed positive emotion (i.e. a comedy movie), whereas no change was found after women viewed negative emotions (sad movie). In another study, Bick & Dozier (2010) measured urinary OT levels in 26 healthy mothers following 25 minutes of physical interactions while playing computer games with their child aged 2.5-4.5 year old and again with an unfamiliar child of a similar age. Urinary OT was significantly higher following interaction with the unfamiliar child as compared with own child. They concluded that interaction with an unfamiliar child might constitute a (socially) stressful affiliative situation. Accordingly, they suggested that OT increased in order to modulate this stress and in order to ensure mothers exhibit pro-social behaviour with the unfamiliar child which would then compensate for the absence of a 'natural', biological bond. The authors did not measure pre-interaction urinary OT, and it is therefore possible that the lower OT levels (following interaction with own infant), represents a 'drop' in OT rather than an increase following interaction with unfamiliar child, which would be similar to our findings.

In a study that investigated the relationship between adult temperament (using the Adult Temperament Questionnaire) and plasma OT responses among mothers, Strathearn et al. (2012) examined plasma OT before and after mother infant interaction among 55 first time mothers and their 6-7 month-old infants. Effortful control (i.e. propensity to

focus on executing plans, performing tasks and maintaining focus and attention) was negatively correlated with the OT response (difference between baseline and post interaction levels). In other words, the more concentration and attention shown by the mother during the interaction with her infant, the less likely she experienced an increase in plasma OT following the interaction. Characteristics related to effortful control are actually important for sensitive mothering as mothers need focus and attention in order to respond ‘promptly’ and ‘appropriately’ to infant signals (Ainsworth et al., 1978).

We would therefore expect that the drop in plasma OT among HSMs following their interaction with their infant is part of the mechanism underlying their sensitive responsiveness. Thus, HSMs perceive their infant signals as a positive (affiliative) event and they give appropriate attention and focus to these signals; accordingly their plasma OT levels drop as a signal of the easy, focused, positive interaction with own infant. By contrast, LSMs (in our study) may not perceive interaction with their infant as a positive (affiliative) event and hence restrain/resist the alleviation effect of the socially affiliative interaction as compared to HSMs. They are also unable to give proper attention and focus to infant signals, possibly because they do not recognise such signals or attach appropriate emotional valence to them, and accordingly their plasma OT levels remain elevated as both a signal of a stressful, unfocused, negative (affiliative) interaction with own infant (Figure 10.1) and perhaps to enhance (affiliative) behaviours. This is consistent with Feldman et al. (2010a) who reported no difference in plasma OT levels among mothers rated as low in affectionate contact following interaction with their infants. Thus, by classifying mothers according to sensitivity behaviours, we may have ‘tapped’ into stress or anxiety coping, as well as pro-affiliative strategies, at least in part modulated by OT.

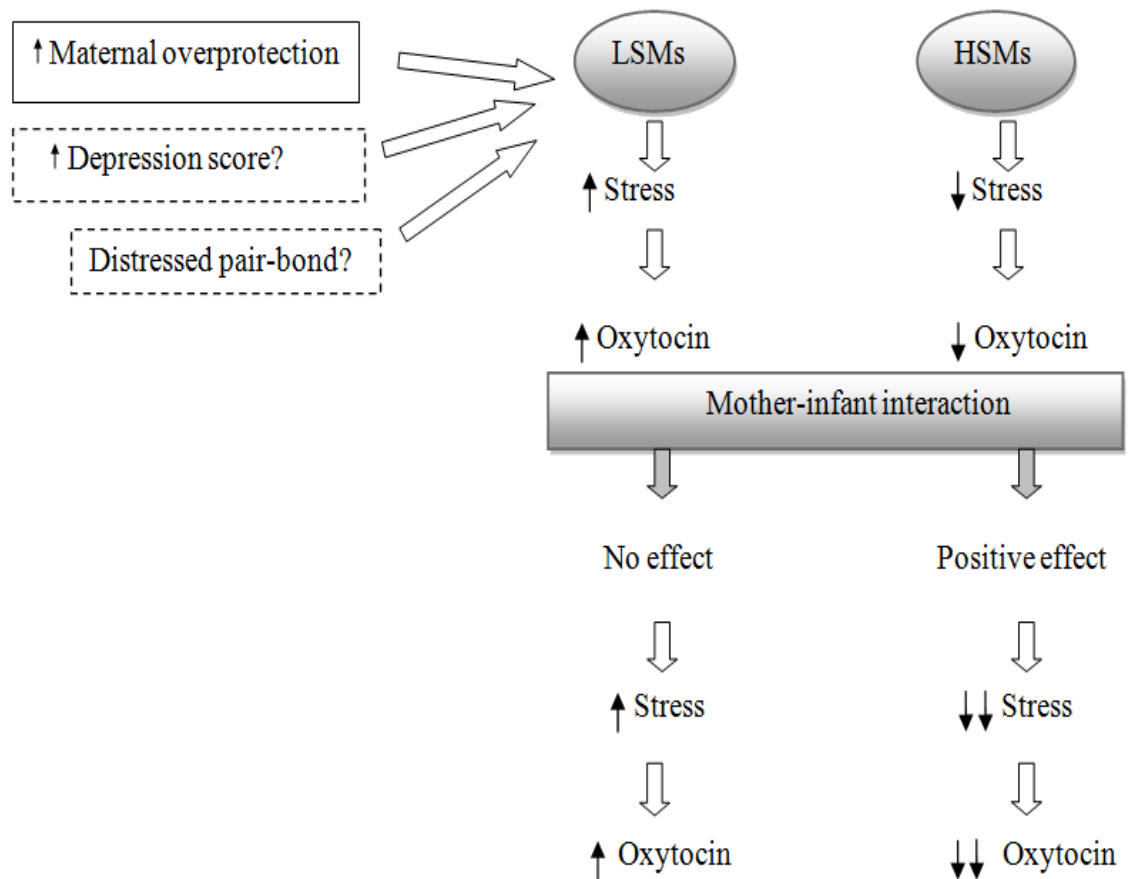


Figure 10.1. A model representing the possible role of oxytocin as an anxiolytic (anti-stress) (pro-affiliative) hormone in HSMs and LSMs: high levels of own maternal overprotection, and possibly high depression score or distressed pair-bonding have a stress-inducing effect in LSMs resulting in elevation of plasma OT levels. LSMs maintain the same stress level after interaction with their infant. HSMs experienced less stress in life and accordingly less plasma oxytocin levels with marked reduction in their OT levels following interact with their infants suggesting induction of positive emotions as a result of interaction. **Key: Solid Rectangle:** Possible factors with evidence from the current study, **Dashed Rectangle:** Proposed factors without evidence from the current study.

10.1.4. Does oxytocin has a dual action?

The animal literature (Numan & Woodside, 2010) makes it clear that OT serves a dual role in maternal behavior: It increases maternal motivation and it also decreases stress and anxiety (it has anxiolytic effects). The latter effect may aid the mother in coping with difficult circumstances related to infant care. With respect to the human literature, different methods, which include postpartum stage of the mother-infant dyad and the

ways in which mothers are classified, may differentially tap into one or the other of these two aspects of OT involvement in mother-infant interactions.

Accordingly, some recent studies suggest that, OT increases following affiliative interaction with own infant (Feldman et al., 2007; Gordon et al., 2010). Others studies, including the current study, suggest that at least in women, OT is triggered/released as a signal when there is a need to enhance or promote affiliation with others or when the social relationship is 'threatened' (including pair bonding or parental bonding) (Taylor et al., 2006, 2010; Bick & Dozier, 2010; Taylor et al., 2010; Feldman et al., 2011; Tabak et al., 2011). This putative role of OT as a biomarker for a distressed social relationship may occur primarily in women (Turner et al., 1999; Feldman et al., 2011). Women may use their close relationships with others in a different way to men: women may regulate their perception of and responses to stress through the development of close affiliative bonds (Marazziti et al., 2006). In this way, plasma OT may be secreted in some women particularly under what they perceive to be stressful situations in order specifically to prompt a desire for affiliation (Taylor et al., 2006). Interestingly, this dual action for OT, as a pro-social, pro-affiliative as well as an anxiolytic or anti-stress hormone might be represented simultaneously within the same individual, as suggested by Feldman et al. (2011).

Our findings support a role for OT in affiliative bond formation and in stress regulation. The pathways by which OT might mediate effects on stress and on social affiliation may be different. Taylor et al. (2010) suggest that, when OT increases as a result of social affiliation, it does not involve pathways implicated in anti-stress (e.g. dopamine pathways) (Neumann et al., 2000). Indeed, with the exception of the anti-stress (anxiolytic) effect, most behavioural and physiological effects induced by OT can be blocked by administration of OTR antagonist, suggests a different mechanism (Uvnas-

Moberg, 1998) when OT works as anxiolytic, yet further research into the role of OT in human social relationship is needed.

10.2. fMRI Scanning Discussion

10.2.1. Overview of the findings

Using whole brain analysis to examine brain activation to infant video stimuli among healthy early postpartum mothers at 7-9 months postpartum, we report the following main findings which were in accordance with our hypotheses: overall, when mothers viewed videos of their own infants compared to unknown infants (main effect), significant brain activation was elicited predominantly in 3 areas: i) the anterior cingulate gyrus, ii) the right inferior frontal gyrus, and iii) the left parahippocampal gyrus and bilateral uncus.

Using ROI analysis to compare brain responses between high sensitivity and low sensitivity group of mothers we report the following main findings: in accordance with our hypothesis, when compared to LSMs, HSMs showed greater BOLD activation in the right superior temporal gyrus in response to own neutral infant compared to an unknown infant video or in response to own happy infant compared to a neutral control stimulus. However, inconsistent with our hypotheses, this BOLD activation among HSMs was *negatively* (not positively) correlated with post interaction plasma OT concentration in those mothers. Also inconsistent with our hypotheses, HSMs did not show significant activation in other ROI, specifically the hypothalamus, posterior cingulate gyrus, or the hippocampal formation in response to own infant compared to an unknown infant video. Compared to HSMs, LSMs did not show significant activation in any ROI in response to their own infant, separately or when compared to an unknown infant.

10.2.2. Main effect

Previous studies have suggested a role for the anterior cingulate gyrus in emotional processing (see review by Barrett & Fleming, 2011). The inferior frontal gyrus is thought to have an important role in the decoding of facial expressions of emotions (Adolphs, 2002). Lesions in this region lead to an impaired ability to identify facial emotions in adults (Hornak et al., 1996). The inferior frontal gyrus has also been identified as one of the areas responsible of mirroring others' emotions (Theory of Mind) (Iacoboni & Dapretto, 2006). This suggests that a key to healthy maternal responsiveness is the capacity of mothers to recognise and respond to her infant's emotions; and in young, preverbal infants, this is perhaps especially through mirroring of emotional expressions and facial cues. Viewing of own infant also activated the parahippocampal gyrus and uncus; these regions are thought to encode emotional memories (Phelps et al., 2004; Swain et al., 2008b). Our findings in regards to all mothers, confirm the findings of previous studies (e.g. Ranote et al., 2004; Swain et al., 2008a).

10.2.3. Comparison of brain activation between HSMs and LSMs

Compared to LSMs, HSMs showed greater activation of the right superior temporal gyrus in response to own neutral infant compared to unknown neutral infant stimuli. This activation continued and extends towards the insula while HSMs viewed their own happy infant compared to neutral control video.

The superior temporal gyrus contains 'mirror neurons' (Iacoboni & Dapretto, 2006) which are activated in response to observing someone else experiencing an emotion; accordingly, the 'observer' mimics the emotion or action observed (Iacoboni et al., 1999; Iacoboni & Dapretto, 2006). This occurs in response to understanding and empathising with others 'Theory of Mind' (Blakemore & Decety, 2001; Gallagher &

Frith, 2003; Rizzolatti & Fabbri-Destro, 2008). However, one can argue that Theory of Mind suggests reading of thought, which is not necessarily accompanied by empathy with emotion. Yet, for early postpartum mothers to respond sensitively to their infant's needs, understanding infant emotion is a key aspect of sensitive mothering. Therefore we would anticipate that activation of an area rich in mirror neurons (the superior temporal gyrus) in HSMs might suggest that HSMs give more attention to read their infant facial emotion in order to react to this as a part of an internal maternal reflective function (Brunet et al., 2000; Lenzi et al., 2009), compared to LSMs. This notion is directly consistent with what attachment theorists have suggested about maternal sensitivity. Many considered maternal sensitivity as the response to the infant's mental state, rather than to her/his physical state (Fonagy et al., 1994; Meins, 1997), and thus a sensitive mother would expect to respond properly to her infant's displayed emotions by affirming the positive emotions or reassuring about the negative ones (Sroufe, 2000).

As mentioned in the literature review earlier (Chapter 7), a few studies considered examining maternal brain responses in relation to maternal interactive behaviour (Atzil et al., 2011; Kim et al., 2011; Musser et al., 2012). Yet, among these studies, only Kim et al. (2011) focus on maternal sensitivity, and they also reported activation of superior temporal gyrus in response to own infant's crying, among 9 exclusively breastfeeding mothers, at 3-4 weeks postpartum which was also positively correlated with maternal sensitivity ratings in those mothers at 3-4 months postpartum. Activation of the superior temporal gyrus was also reported in response to own infant crying at 2-4 weeks postpartum among 6 mothers who delivered vaginally as compared to 6 mothers who delivered by Caesarean section (Swain et al., 2008a). In another study, at a later postpartum time point (11 months), mothers who reported having had a secure attachment ($N = 15$) with their own parents also showed activation of the superior

temporal gyrus when viewing own versus an unknown infant, compared to those reporting an insecure attachment (Strathearn et al., 2009).

In contrast to our expectations, HSMs (as compared to LSMs) did not show activation in regions involved in hormonal regulation or in motivation such as the thalamus and the posterior cingulate gyrus respectively. Previous findings are equivocal, with some studies reported activation of the thalamus in response to infant's cry (Lorberbaum et al., 2002; Swain et al., 2008a), while others did not find this activation (Seifritz et al., 2003). Similarly in regards to the posterior cingulate cortex, while some studies reported activation of this region in response to infant's cry (Swain et al., 2003; 2004a), others did not report such activation in response to infant pictures (Bartels & Zeki et al., 2004). Yet in the current study lack of thalamic activation among HSMs, was in line with low plasma OT levels among those mothers (see OT results).

Interestingly the significant difference between HSMs and LSMs in response to infant stimuli was only in response to neutral emotion and not to happy or sad emotion. This is possibly because interpreting neutral cues demands more attention from the mother to decide on the nature of the expression, while happy and sad are ready to get interpreted.

10.2.4. Correlation between plasma oxytocin and brain activation

Previous studies suggest that OT has a dual role, both as 'affiliative' hormone and as 'anti-stress' hormone (Turner et al., 1999). Among LSMs its relative elevation may be indicative that they experience high stress levels overall (possibly associated with a lack of positive social relationships, including a poor relationship with own mother) (Marazziti et al., 2006; Feldman et al., 2011) (see OT discussion). On the other hand, it could be that HSMs experience relatively lower stress in their life (with associated reduced OT levels) and that they also experience significant reduction in plasma OT following interaction with their own children as a response to the positive reward and

calming effect infant interaction evokes for them. Our data support the notion that HSMs perceived their infant interaction as a more positive event than LSMs (Bick & Dozier, 2010), as evidenced by the drop in post interaction plasma OT levels among HSMs. A similar positive reaction towards their own infant is also consistent with their brain responses showing higher BOLD activation in the superior temporal gyrus which correlated with lower maternal plasma OT following interaction with their infant. This negative correlation between maternal brain responses and plasma OT levels provides further support for our explanation of why we found the lower plasma OT levels among our higher sensitivity mothers.

Even though, in our study, HSMs showed lower plasma OT levels at all time points compared to LSMs, their brain responses to own infant were similar to patterns of activation reported by other imaging studies using proxy measures of high OT levels i.e. mothers who delivered vaginally (Swain et al., 2008a) or who breastfeed (Kim et al., 2011). And also not far from brain activation reported after OT administration (e.g. Riem et al., 2011). This suggests that OT may act through different pathways in the mediation of affiliative responses compared to its role in modulating stress axis responsivity (Taylor et al., 2010) and also when administered (exogenous OT) and when naturally secreted (endogenous OT).

This is the first study to chart the difference in plasma OT response as well as the neurological response among a group of mothers representing distinct group of natural variation in maternal sensitivity. Our findings extend previous findings indicating a central role for OT in maternal caregiving behaviour and an ability of mothers' brain to chart their caregiving quality. Our findings suggest that mothers at the higher end of maternal sensitivity distribution activates brain regions that indicates their ability to understand their infant emotion and that their plasma OT show a remark change as a

result of their positive perception for these signals. Sensitive mothering requires recognising infant cues/signals, then paying attention and, responding to them appropriately and contingently (Ainsworth et al., 1978). This complex behaviour demands a mother to be flexible and able to switch attention appropriately when the situation requires. She must also be able to retain information about the infant and to manipulate the environment to make it suitable for the infant. In order to do this, mothers need a range of affective and cognitive capacities including the ability to pay attention selectively to some stimuli and ignore less salient stimuli; the ability to read an infant's emotions and intact working memory.

The study strength, limitation, clinical implication and directions for future research are included in the conclusion chapter (Chapter 11).

Publication 2

Does oxytocin modulate variation in maternal caregiving in healthy new mothers?

Does oxytocin modulate variation in maternal caregiving in healthy new mothers?

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Abstract

Background: The extent to which a mother is sensitive to her infant's cues and developmental needs ('maternal sensitivity') contributes to the infant's social and cognitive development. Animal and recent human studies emphasise a major role for the neuropeptide Oxytocin (OT) in mediating sensitive caregiving behaviours. To date, no study has examined OT in relation to extreme variations in human maternal sensitivity.

Methods: : Out of 105 expectant mothers, 80 were followed up and underwent evaluation for maternal sensitivity at 4-6 months postpartum through 6 minute-free play interaction with their infants. Of these, 30 enrolled in the current study at 7-9 months postpartum: 15 'sensitive mothers' (henceforth high sensitivity mothers – HSMs) and 15 'less sensitive mothers' (henceforth low sensitivity mothers – LSMs) underwent plasma OT measurements before and after 10 minutes of play interactions with their infants. **Results:** Consistent with studies of plasma OT and stress in women, but not with studies of plasma OT and maternal behavior in women, baseline and post-interaction plasma OT levels were lower amongst HSMs. Only HSMs showed significant change in plasma OT; with reduction following the play-interaction.

Conclusion: Higher baseline OT levels in healthy LSMs may act as a biomarker for stress response owing to the demands of caring for an infant or for a gap in own parenting relationship. OT may be acting to reduce stress and anxiety. By contrast, play interaction with their infants may be associated with reduced stress (if any) in HSMs, as suggested by a significant reduction in plasma OT. Plasma OT might represent a useful biomarker of low maternal sensitivity. Considering mothers in well-defined sensitivity groups might 'tap' on an element of a stress or anxiety coping strategy and might foster better understanding of parental caregiving behaviour and its potential for modulation by OT.

Keywords: Oxytocin, maternal sensitivity, stress regulation, mother-infant interaction.

Introduction

The infants of humans are one of the most immature creatures that depend on its caregiver for survival and soothing during stressful times (Feldman et al., 2007). The nonapeptide oxytocin (OT) has been implicated by animal (Francis et al., 2000; Champagne et al., 2001; Numan & Stolzenberg, 2009; Ross & Young, 2009) and recently by human studies as an important factor in enhancing social competence and initiating and promoting maternal caregiving behaviour (Lee et al., 2009; Gordon et al., 2010; Feldman et al. 2010a, b; Numan & Woodside, 2010). Among humans, mothers who showed a rising pattern of plasma OT reported higher maternal fetal attachment (Levine et al., 2007). Similarly, higher plasma OT levels during pregnancy and at the first postpartum month were correlated with higher levels of maternal postpartum behaviours, such as gaze, vocalisations, and positive affect in new mothers (Feldman et al., 2007). Maternal synchrony, which was defined as 'episodes when mother and infant coordinate their positive social engagement' (Atzil et al., 2011) was also found to be

correlated with maternal plasma OT levels while maternal intrusiveness ‘inappropriate response from mother’ was not.

OT was also examined in relation to maternal own attachment experience and higher levels of plasma OT were reported following mother-infant physical interaction among mothers with secured attachment (with own parents) compared with those with insecure attachment (Strathearn et al. 2009). Even among non-parents, plasma OT levels were positively correlated with self-reported recall of parental care (maternal and paternal care) (Gordon et al., 2008; Feldman et al., 2012). Similarly among children, urinary OT in children (4.5 years old) who were raised by their own parents showed a trend for higher levels compared with children who were raised in orphanages (Fries et al., 2005).

In contrast to the role of OT in affiliative behaviour, recent evidence from women studies suggests a role for OT in regulation of stress that is related to interpersonal relationship difficulties (Tabak et al., 2011). These studies reported higher levels of OT in relation to stress in social relationships, including relationships with romantic partners (Marazziti et al., 2006; Taylor et al., 2010; Feldman et al., 2011), own mother (Taylor et al., 2006), or best friend (Taylor et al., 2006). This positive relationship between OT and stress may be related to the well known anti-anxiety and anti-stress effect of OT (Numan & Woodside, 2010). In other words, OT may be released in stressful situations in order to decrease or moderate stress responsiveness (Marazziti et al. (2006).

In the first study to explore the relationship between OT and different human attachment relationships, Feldman et al. (2011) recruited 112 mothers and fathers (71 were mothers) and their 4-6-month-old infants. Plasma, salivary, and urinary OT levels of parents were assessed before and after play interaction with infants. Higher plasma and salivary OT levels were found amongst parents who showed ‘high’ affect synchrony towards infants as compared with ‘low’ synchrony parents, supporting previous findings that link OT to more affectionate parenting behaviour (Feldman et al., 2007; Gordon et al., 2010). However, among mothers only, post interaction urinary OT (which was not correlated with plasma or salivary OT) was positively correlated with anxiety in romantic attachments (i.e. relationships with a partner), with self-reported parenting stress, and with interactive stress (i.e. proportion of time when infant shows negative reactivity whilst mother tries to re-engage her/him during interactive play). Urinary OT levels were also reported to show a negative trend with own parenting care.

Their findings suggest a role for OT in stress regulation in mothers similar to that reported by other studies in women (Turner et al., 2002; Taylor et al., 2006, 2010). OT appears to be an indicator of social affiliation (Feldman et al., 2007, 2010a, b), but it might also be a 'signal' for the need to affiliate with others (Taylor et al., 2006, 2010; Tabak et al., 2011). Animal literature suggest that OT has an 'openness' to early social experience, with higher OT receptors density found in relation to enriched early perceived parenting environment (Champagne, 2008).

To date, parenting studies that focus on OT in relation to maternal affiliative behaviour have not included a rigorous examination of maternal sensitivity. Yet, maternal sensitivity is a concept that involves an interactive relationship with own infant (Ainsworth et al., 1978), as thus might encounter difficulties. In addition, only one study considered examining mothers' social relationships, including relationships with their own parents while also examining their affiliative bond with own infants (Feldman et al., 2011). In light of the above, the present study examined OT in relation to natural variations in maternal sensitivity in healthy early postpartum mothers, specifically examining differences between women representing opposite ends of rating in maternal sensitivity. Our study also explored the relationship between maternal OT and own parenting experience. Based on the studies which emphasize a positive relationship between OT and parenting, we hypothesised that: 1) HSMs will show significantly higher plasma OT levels at baseline and following interaction with their infants than LSMs; 2) post-interaction plasma OT in each group of mothers (HSMs/LSMs) will be positively related to favourable rating of own parenting quality.

Materials and methods

Participants

Women were recruited from community antenatal clinics across the northwest region of England (Greater Manchester), as part of a larger longitudinal study examining natural variation in maternal sensitivity. Initially, 105 women who were ethnically white British with no psychiatric illness, and scored below the threshold on depression screening (see below), were recruited during their last trimester of pregnancy (mean = 33.90 weeks; SD = 3.19). Following child birth, 80 women were then followed up and underwent evaluation of maternal sensitivity using videoed mother-infant interaction play at 4-6 months postpartum (mean = 19.38 weeks; SD = 2.47). Thirty mothers, representing extremes in maternal sensitivity, were selected from this sample of 80 and at a mean of

35.14 weeks postpartum (SD = 3.26) their OT levels were measured before and after a mother-infant interaction. Figure 1 outlines study recruitment stages. The study protocol was approved by the North West Research Ethics Committee: Ref: 10/H1013/69 and written consent was obtained from all women.

Figure 1 about here ‘Chart for data collection times’.

Measures

Manchester Assessment of Caregiver-Infant Interaction (MACI) (Wan et al., 2012, 2013 online)

This observational measure of caregiver-infant interaction evaluates global features of interaction from 6-mins unstructured play in 7 (2 caregiver, 3 infant, 2 dyadic) scales. The MACI was developed for research purposes to provide relatively brief rating scales suitable for a wide age range in infancy, and which would provide variance in the normal population and be sensitive in at-risk samples. Its scales were modified and refined from existing validated global scales of caregiver-infant interaction (Murray et al., 1996; Blazey et al., 2008). The MACI has demonstrated reliability, moderate 6-month stability and other psychometrics, and its scales are independent of socioeconomic status, infant gender and maternal age (Wan et al., 2012, 2013 online). The current study focused on the ‘caregiver sensitive responsiveness’ scale (henceforth ‘maternal sensitivity’), defined as the “the extent to which the infant’s moment-to-moment behaviour and developmental needs are responded to and supported by the caregiver, appropriately and contingently”. Sensitivity is rated on a scale from minimal (1) to high (7) after carefully reviewing the clip several times. In the current study, acceptable inter-rater agreement was demonstrated on maternal sensitivity (interclass correlation: $r = 0.70$; $p < 0.001$, absolute agreement) based on independent blind ratings of 30% of interaction clips in the complete sample. Disagreements were resolved by both raters re-reviewing the clips to reach consensus.

The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987)

This 10-item self-report instrument is widely used to screen for depression in the postpartum and antenatal periods. Items are rated on a 4-point Likert-type scale, and a cut-off score of 12 was used for screening positive.

The Hospital Anxiety and Depression (HADS) rating scale (Zigmond & Snaith, 1983)

This 14-item questionnaire is a self-rating instrument to screen for anxiety and depression (7 items each). Items are rated on a 4-point Likert scale. A score of 11 was used for screening positive. Women were excluded if they scored both: EPDS ≥ 12 and HADS-depression > 11 .

Parental Bonding Instrument (PBI) Parker et al. (1979)

This self-report measure examines an adult's retrospective report of parents' caring behaviours (25 items for each parent) during the first 16 years of life, consisting of 'care' (12 items) and 'overprotection' (13 items). Items are rated on a 4-point Likert scale.

Procedure

Time 1 & 2: Pregnancy & Mother-Infant Interaction

At the third trimester of their pregnancy (Time 1), women completed PBI, EPDS, and HADS. Mothers were excluded if they scored both EPDS ≥ 12 and HADS-depression > 11 at any time of the study. At 4-6 month postpartum (Time 2), mothers were visited at home and asked to play with their infant on a floor mat as they normally do, with or without toys (as supplied), as they wished. The interactions were videotaped for 6 minutes and later rated, using the MACI caregiver sensitivity scale, by a trained researcher who was blind to study information.

Time 3: Oxytocin measurement

Thirty mothers (15 HSMs and 15 LSMs) and their infants were invited to a clinical research facility for plasma OT measurement, which was conducted either during mothers' menstruation or on contraceptive pill free days. Blood samples were taken at the same time of day at 12:00–14:00 hours, an hour after the last nursing feed. Mothers were asked to refrain from caffeine and smoking for at least two hours beforehand. Three 5 ml samples of blood were taken from antecubital veins through an intravenous cannula. The first sample (OT1) was taken 10 minutes after mother-infant separation, followed by reunion and a 10-minute mother-infant play interaction (as described earlier). The second and third samples were taken immediately post-interaction (OT2) and 5 minutes later (OT3).

Oxytocin processing & assays

All samples were processed as follows: samples were drawn into chilled vacutainer tubes containing lithium heparin injected with 200 ml of Trasylol (aprotinin) 500,000

KIU/ml blood. OT samples were kept ice-chilled until processed within 10 minutes. Samples were then centrifuged at 4°C at 3500 rpm for 15 minutes. 500ul supernatants were transferred to 2 micro tubes (aliquot 1 & 2) and stored at -80° C until transferred on dry ice to the University lab for analysis. Determination of OT was performed using the Max Binding Determination Competitive Assay protocol on Gen 5 software using Biotek Plate reader. Oxytocin analyses were performed by a laboratory scientist who was blind to all study information.

Statistical analyses

Demographic differences between the two groups of mothers were assessed through independent sample t test or Chi square test. Pearson correlations were used to examine correlations between plasma OT levels at the three assessment points as well as correlations with own parental experience. A repeated-measures analysis of variance (ANOVA) was employed to test for a significant change in plasma OT levels over time between groups (HSMs and LSMs). Analyses were performed using SPSS (version 19).

Results

Among the 30 mothers included in the current study: 15 were classified as ‘sensitive’ mothers (blind rated 4-7 on the MACI sensitivity scale; mean = 4.47; SD = 0.74) and 15 mothers classified as ‘less sensitive’ mothers (blind rated 1-3 on the MACI sensitivity scale; mean = 2.13; SD = 0.52) (Figure 2). For description purposes, the two sub-groups respectively are referred to here as ‘high sensitivity mothers’ (HSMs) and ‘low sensitivity mothers’ (LSMs), respectively.

Figure 2 about here ‘Distributions of high sensitivity mothers (HSMs, N = 15) and low sensitivity mothers (LSMs, N = 15) in relation to maternal sensitivity distribution of the whole sample (N = 80)’.

Assessing for confounders

One outlier was excluded from analyses (scored > 3 SD in all OT assessments).

Household income was higher in HSMs compared with LSMs and accordingly was controlled for in the subsequent analysis. The two groups did not differ in maternal age, marital status, maternal education (in years), parity, infant birthweight, infant gender, mode of delivery, mode of feeding, or postpartum stage (Table 1).

Table 1 about here ‘Comparing demographic and obstetric characteristics of mothers grouped by level of maternal sensitivity’.

Plasma oxytocin

Three samples were collected from each participant (Table 2). A high level of OT individual stability was found in HSMs ($r = 0.79\text{--}0.96$; $p < 0.01$) and LSMs ($r = 0.92\text{--}0.99$; $p < 0.01$).

Table 2 about here ‘Mean plasma OT levels (pg/ml) among the high ($N = 15$) and low ($N = 14$) sensitivity group of mothers’

Repeated measure ANOVA showed no overall change in the mean level of OT from baseline to post interaction (within subject effect) Greenhouse-Geisser [$F(1.37, 35.51) = 1.54$; $p = 0.23$]. Next, we examined between subject effect [$F(1, 26) = 8.42$; $p = 0.01$], and found significant difference in OT through the three assessment points when the two groups of sensitivity were compared (between subject effects) with this change confined to HSMs (Figure 3). By looking at the graph, we can also see high variance on OT3 measurement among HSMs.

Figure 3 about here ‘Means and box plots for plasma oxytocin measured before (OT1) and after mother-infant interaction (OT2 and OT3) among the high sensitivity mothers (HSMs, $N = 15$) and low sensitivity mothers (LSMs, $N = 14$)’.

Relationship between plasma OT and mothers’ own parenting experience

Controlling for household income the two groups did not differ in: own maternal care (transformed) [$F(1, 26) = 0.01$; $p = 0.93$], own paternal care (transformed) [$F(1, 26) = 0.41$; $p = 0.53$], own maternal overprotection, [$F(1, 26) = 2.41$; $p = 0.13$], or own paternal overprotection [$F(1, 26) = 0.52$; $p = 0.48$].

OT1 (OT_{pre}) and the mean of OT2 and OT3 (OT_{post}) were considered to test the relation with own parenting experience. Own maternal overprotection was positively correlated with both OT_{pre} and OT_{post} among LSMs ($r = 0.62$; $p = 0.02$; and $r = 0.63$; $p = 0.02$, respectively) but not among HSMs ($r = 0.28$; $p = 0.31$; and $r = 0.07$; $p = 0.79$, respectively) (Figure 4). Own maternal care, own paternal care, or own paternal

overprotection were not correlated with plasma OT levels in any of the groups (all p s > 0.22).

Figure 4 about here ‘Relationship between baseline plasma oxytocin (OT_{pre}) and own maternal overprotection among: (a) low sensitivity (N= 14), and (b) high sensitivity mothers (N = 15).

Discussion

We sought to examine further how natural variation in maternal sensitivity to infant cues is associated with maternal plasma OT in a community sample of healthy mothers. Contrary to our main hypotheses, we report that: 1) HSMs have lower baseline plasma OT levels compared with LSMs, and 2) following a play-interaction with their infants, plasma OT levels significantly decreased in HSMs whereas no significant change was seen among LSMs. We also found that greater levels of baseline and post interaction plasma OT in LSMs were associated with unfavourable reports of their own experience of being parented (i.e. higher own maternal overprotection).

While these findings were contrary to most of the recent parenting studies which found positive correlations between plasma OT levels and maternal (or paternal) behaviour (Feldman et al., 2007; 2010a, b; Gordon et al., 2010; Atzil et al., 2011), it is in line with other studies that implicate OT in regulation of interpersonal stress in women (Taylor et al., 2006, 2010) including mothers (Feldman et al., 2011).

In this sample, OT was assessed in women at opposite ends of the distributions of maternal sensitivity which results in distinct affective and behavioural caregiving attributes (Thompson, 1997). By classifying mothers according to sensitivity behaviours, we have ‘tapped’ into stress or anxiety coping strategies, at least in part modulated by OT (see Numan & Woodside, 2010). As far as we are aware, this is the first study to find these results in healthy mothers who have been carefully selected for high and low maternal sensitivity from within the normal distribution.

The animal literature (Numan & Woodside, 2010) makes it clear that OT serves a dual role in maternal behavior: It increases maternal motivation and it also decreases stress and anxiety (it has anxiolytic-effects). The latter effect may aid the mother in coping with difficult circumstances related to infant care. With respect to the human literature, different methods, which include postpartum stage of the mother-infant dyad and the

ways in which mothers are classified, may differentially tap into one or the other of these two aspects of OT involvement in mother-infant interactions.

Explanations for elevated plasma OT in LSMs

Elevated plasma OT levels were reported in relation to social relationships' difficulties. In a study assessing stress in partnership among 85 adults in stable relationships (62% female and 38% male), plasma OT was significantly correlated with relationship distress in women (while plasma vasopressin correlated with relationship distress in men) (Taylor et al., 2010). In a further study by the same group, among 73 post menopausal women, plasma OT was negatively correlated with relationship with their own mother, or partner, and also marginally significant with relationship to best friend Taylor et al. (2006). Similarly, Marazziti et al. (2006) reported positive correlation between plasma OT levels and romantic relationship anxiety among 45 young subjects (12 men and 33 women). This suggests plasma OT increases as a 'signal to affiliate with others as the pair-bond relationship is threatened' and therefore OT might act as a biomarker for a distressed pair-bond relationship (Taylor et al. 2010).

The implication of OT in social relationships' difficulties was also reported among parenting studies. Although in the study by Feldman et al. (2011) plasma OT findings were inconsistent with our findings in that parents with high affective synchrony showed higher plasma OT, their urinary OT findings were consistent with our results; that is, urinary OT was positively correlated with interactive stress, parenting stress, and anxious romantic attachments. Previously, literature has support a significant correlation between plasma and urinary OT measurements in humans (Hoffman et al., 2012). Thus the contradictory findings reported by Feldman et al. are a representation of the dual role that OT plays in affiliation and regulation of stress. In the current study plasma OT among LSMs was positively correlated with negative recall of own maternal parenting experience, in particular higher maternal overprotection, which might suggest difficulties in relationships with their own mothers. We did not assess the quality of the 'relationship with partner' and so we cannot exclude distressed pair-bond relationships as another explanation for the elevated plasma OT among the LSMs in our study.

Explanations for plasma OT drops in HSMs

Our findings suggest that plasma OT levels are reduced in mothers after playing with their infants, but this is specific to mothers who display high sensitivity towards their infants. On the other hand, mothers who had previously shown low sensitivity towards

their infants during play showed no change in plasma OT level, which tended therefore to remain high. A previous study has also demonstrated a reduction in plasma OT in women ($n = 32$) after a laboratory-induced positive experience (viewing a comedy film), whereas no change was found after women viewed negative emotions (viewing a sad film) (Turner et al., 2002). Recently, a drop in maternal plasma OT was reported when mothers showed higher levels of ‘effortful control’ during interaction with own infants, which is a prerequisite of sensitive mothering (Strathearn et al., 2012). Moreover, urinary OT in mothers ($n = 26$) was significantly higher following interaction with the unfamiliar child (2.5–4.5 years) as compared with own child (Bick & Dozier, 2010). The authors concluded that interaction with an unfamiliar child might constitute a stressful situation that results in an OT increase in order to modulate this stress.

It is possible that OT in women, as in the current study, acts as an anti-stress modality against stressors related to own parenting experience, which explains for its elevation in LSMs. We would also expect that the drop in plasma OT among HSMs following their interaction with their infants is part of the mechanism underlying their sensitive responsiveness. HSMs perceive their infant signals as a positive event (Turner et al., 2002), give appropriate attention and focus to these signals (Strathearn et al., 2012), and their plasma OT levels accordingly drops. On the other hand, LSMs in our study may not perceive their interaction with their infant as a positive event, they do not give proper attention and focus to infant signals, and accordingly their OT levels remain elevated. This is consistent with Feldman et al. (2010a) who reported no difference in plasma OT levels among mothers rated as low in affectionate contact following interaction with their infants.

Although several studies implicate elevated OT levels in relational distress and poorer intimate relationships in women (Taylor et al., 2006, 2010; Marazziti et al., 2006; Tabak et al., 2011) this is the first study to suggest this in the context of mother-infant play. This is suggestive of a role for endogenous oxytocin as a biomarker for mothers at risk of low maternal sensitivity.

Strength and Limitations

As far as we are aware, this is the first study to chart the differences in plasma OT responses, between mothers selected to represent higher maternal sensitivity and lower maternal sensitivity. In spite of its strengths, this study has some important limitations. First, while the sample from which we derived the high and low sensitivity groups was

large enough to show a normal distribution of sensitivity and variability among HSMs and LSMs (N = 80), it was still relatively small to represent the diverse, natural variation in maternal sensitivity. Yet both the final (N = 30) and the original sample (N = 80) represent a set of well-matched demographics.

Second, although we classified mothers into two groups according to distinctly different ratings along a scale (LSMs = minimal to scattered sensitivity; HSMs = mixed to high sensitivity), we were unable to sample the extremes in the complete sample due to the overlap between phases of study and the interval needed to blind rate interactions.

Third, inferences about centrally functioning OT from plasma measurement must remain limited (Modahl et al., 1998) even if many previous studies do show modulation of peripheral plasma OT in relation to social affiliation (e.g. Gordon et al., 2008) or parenting brain responses (Strathearn et al., 2009). Fourth, the association we found between plasma OT and own maternal overprotection among HSMs does not imply a causal relationship, and there may be other, unidentified factors that could have accounted for this relationship. Finally, own parenting experience was assessed by a self-report measure, yet PBI has shown good psychometric properties and convergent validity over 20 years (Wilhelm et al., 2005).

These preliminary findings require replication in a larger population with additional dynamic measures of the relationship between OT and the stress response (Neumann et al., 2000). Plasma OT might usefully be employed in future studies exploring mechanisms of low sensitivity parenting and the effectiveness of interventions designed to improve parenting quality.

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Time	Time 1	Time 2	Time 3						
	Pregnancy	4-6 months	7-9 months						
	N = 105	N = 80	N = 30						
Data collected	<div>Interview<ul style="list-style-type: none">• PBI• HADS• EPDS• Demographics</div>	<div>Mother-infant interaction<ul style="list-style-type: none">• Mother-infant free play (6 min)• HADS• EPDS</div>	<div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div>HSMs (N = 15)</div><div>LSMs (N = 15)</div></div><div><div>Plasma oxytocin measurements</div><table><tr><td>10 min</td><td>10 min</td><td>5 min</td></tr><tr><td>Mother-infant separation</td><td>Mother-infant free play</td><td></td></tr></table><div><div>OT1</div><div>OT2</div><div>OT3</div></div><div><ul style="list-style-type: none">• HADS• EPDS</div></div></div>	10 min	10 min	5 min	Mother-infant separation	Mother-infant free play	
10 min	10 min	5 min							
Mother-infant separation	Mother-infant free play								

Figure 1. Chart for data collection times. **Note:** PBI: Parental Bonding Instrument, HADS: Hospital Anxiety and Depression Scale, EPDS: Edinburgh Postnatal Depression Scale, HSMs: high sensitivity mothers, LSMs: low sensitivity mothers, OT: plasma oxytocin sample. Maternal sensitivity (MACI score) was obtained from Time 2 video record of mother-infant interaction.

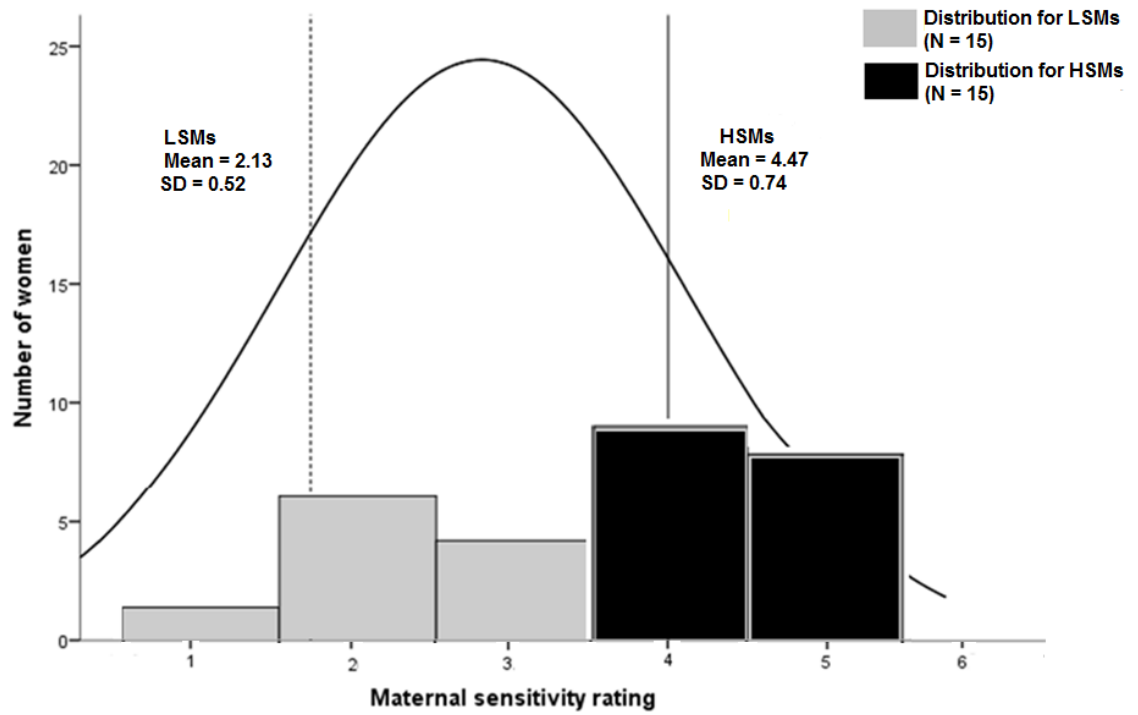


Figure 2. Distributions of high sensitivity mothers (HSMs, N = 15) and low sensitivity mothers (LSMs, N = 15) in relation to sensitivity distribution for the whole sample (N = 80). **Key:** Means for high sensitivity mothers (vertical solid line) and low sensitivity mothers (vertical dashed line) in relation to the larger sample are also shown.

Table 1. Comparing demographic and obstetric characteristics of mothers grouped by level of maternal sensitivity, excluding one outlier (high sensitivity mothers HSMs, N = 15 and low sensitivity mothers LSMs, N = 14)

Characteristic	HSMs (N = 15)	LSMs (N = 14)	t (27)	Chi-square test	p-value
<i>Mean [SD]</i>					
Maternal age (years)	30.40 [5.37]	27.64 [4.77]	- 1.46		0.16
Average maternal education (years)	15.06 [2.82]	12.77 [2.76]	- 1.94		0.06
Average annual household income (thousand pounds)	33.00 [4.61]	26.12 [4.13]	- 2.11		0.04
Infant birthweight (kilograms)	3.44 [0.44]	3.20 [0.53]	- 1.10		0.28
Postpartum stage (weeks)	35.93 [2.81]	34.64 [3.22]	1.32		0.20
<i>Frequency (%)</i>					
Married/cohabiting	13 (86.7)	11 (78.6)		0.56	0.65
Primiparous	6 (40.0)	8 (57.1)		1.65	0.21
Infant gender (female)	10 (66.7)	7 (50)		0.83	0.36
Mode of delivery (vaginal)	10 (66.7)	11 (78.6)		0.51	0.47
Mode of feeding (breast)	3 (20.0)	3 (20.0)		0.55*	0.64

*Fisher exact test

Table 2. Mean plasma OT levels (pg/ml) among the high (N = 15) and low (N = 14) sensitivity group of mothers'

Oxytocin sample	High Sensitivity Mothers (N = 15) mean [SD]	Low Sensitivity Mothers (N = 14) mean [SD]
OT1	235.09 [83.51]	301.87 [39.15]
OT2	223.67 [83.43]	303.27 [34.67]
OT3	210.01 [81.58]	301.56 [38.12]

Note: OT1: Oxytocin measured before mother-infant interaction, OT2 & OT3: Oxytocin measured after mother infant interaction.

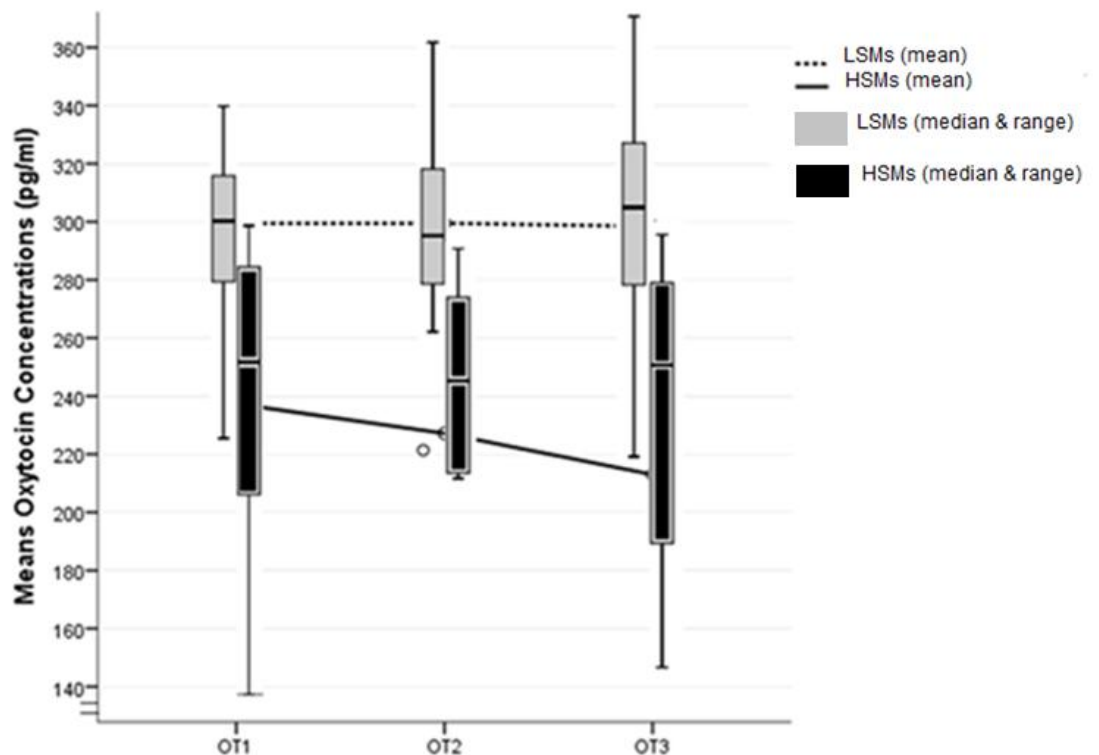


Figure 3. Means and box plots for plasma oxytocin measured before (OT1) and after mother-infant interaction (OT2 and OT3) among the high sensitivity mothers (HSMs, N = 15) and low sensitivity mothers (LSMs, N = 14), controlling for household income. **Key:** Dashed line represents the means of the three OT assessments among LSMs, and solid line represents means of the three assessments among the HSMs.

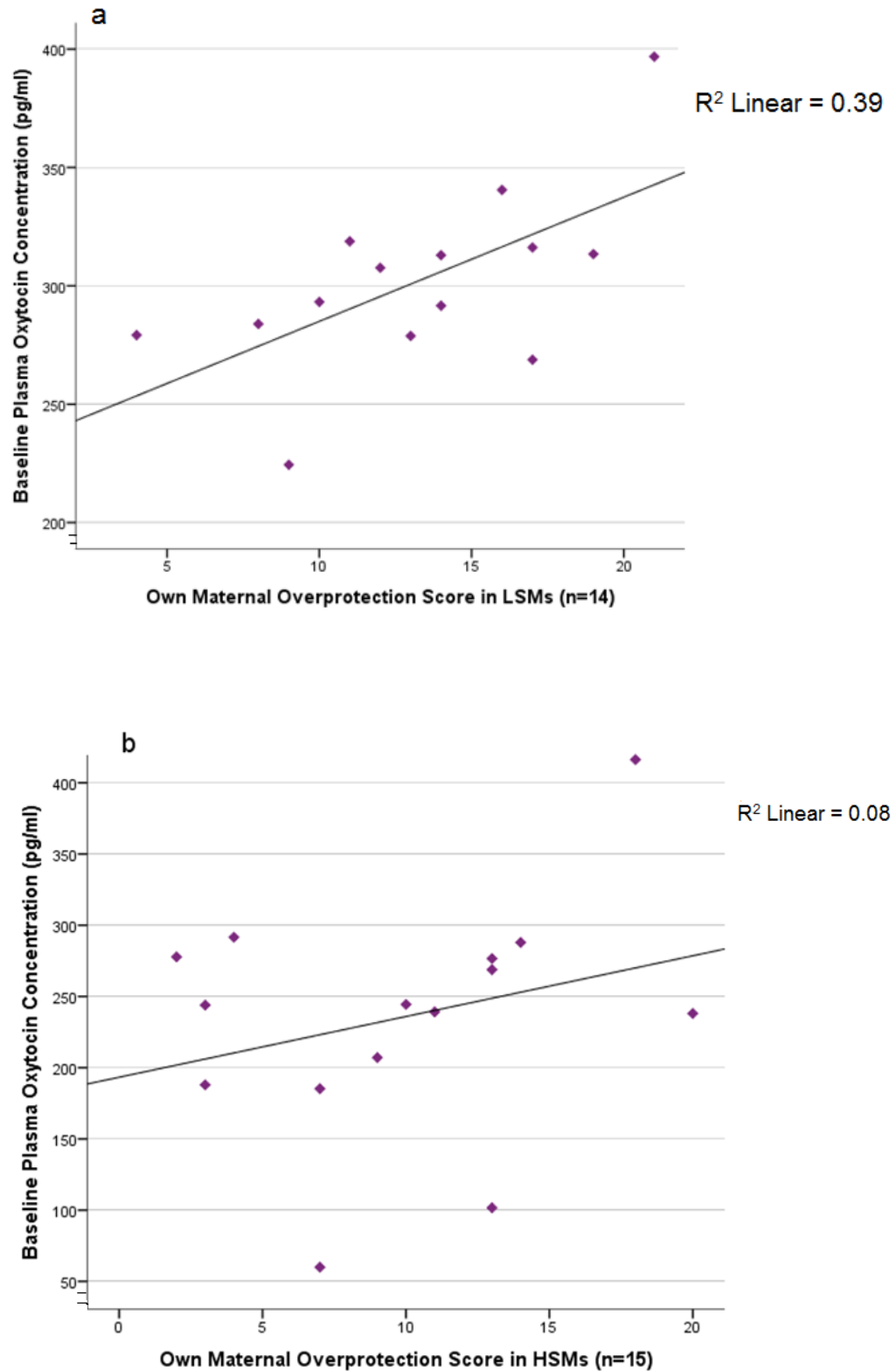


Figure 4. The relationship between baseline plasma oxytocin (OT_{pre}) and own maternal overprotection among: (a) low sensitivity ($N = 14$), and (b) high sensitivity mothers ($N = 15$).

Publication 3

**Neural mechanisms underlying maternal
behaviour in new mothers: Is natural variation
in maternal sensitivity reflected in maternal
brain responses to infant stimuli?**

Neural mechanisms underlying maternal behaviour in new mothers: Is natural variation in maternal sensitivity reflected in maternal brain responses to infant stimuli?

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ABSTRACT

Background: Animal and human evidence suggests that natural variation in maternal caregiving behaviour is related to variation in maternal Oxytocin (OT) levels. Discrete networks of maternal brain which mediate emotion processing, stress- and reward-related neural systems are thought key to healthy maternal responsiveness. Maternal behaviour is complex and a composite of multiple behaviours; recent evidence suggests that in responding appropriately to her infant, a mother's brain activation may reflect these maternal behaviours in discrete pathways. But to date, no study has examined distinct activation patterns related to the degree of sensitivity a mother shows in responding to her infant i.e. 'maternal sensitivity' (accurate and prompt responsiveness to infant signals). Such patterns may act as biomarkers for sensitive maternal brain and help in the development of future intervention studies to improve parenting. **Methods:** Out of 105 expectant mothers, 80 were blind rated for maternal sensitivity from 6 minute videotaped free play interaction with their 4 to 6 month infant. At 7-9 months postpartum, 30 of these mothers (15 'higher sensitivity mothers' (henceforth high sensitivity mothers-HSMs) and 15 'lower sensitivity mothers' (henceforth low sensitivity mothers-LSMs)) underwent functional magnetic resonance imaging to examine brain responses to viewing 'own' versus 'unknown' infant videos, using a range of affects (neutral, happy, and sad). Maternal plasma OT measurements following 10 minute play interactions with their infant were also performed. **Results:** Compared to LSMs, HSMs showed significantly greater blood oxygenation level dependent activation in the right superior temporal gyrus in response to own versus unknown neutral infant, and to own happy infant versus neutral control. Changes in brain activation were significantly 'negatively' correlated with plasma OT responses in those mothers. Conversely, compared to HSMs, LSMs showed no significant difference in brain activation in response to own infant separately or in contrast to unknown infant. **Conclusion:** Activation of superior temporal gyrus suggest the more attention given by HSMs to read their infant facial emotions; this was not shown by LSMs. Sensitive mothering may chart discrete brain responses which might act as biomarkers for future intervention studies to enhance the sensitivity of maternal care.

INTRODUCTION

Natural variation in maternal caregiving behaviour, ranging from neglect to optimum caregiving has been described in both animals (Champagne *et al.*, 2001) and humans

(Feldman *et al.*, 2012; Gordon *et al.*, 2010). Low levels of maternal sensitivity (i.e. the accurate interpretation of infant's signals and appropriate responsiveness) (Ainsworth *et al.*, 1978) in particular have been linked to poor infant social, emotional and cognitive outcomes (NICHD, 1999; Warren & Simmens, 2005). Understanding the neurobiology of maternal sensitivity is potentially of great importance in providing evidence of change following interventions that are designed to enhance parenting (e.g. Weisman *et al.*, 2012). Recent use of functional imaging (fMRI) (Raichle & Mintun, 2006) has added greatly to our knowledge about brain mechanisms associated with healthy parenting by mapping blood oxygenation level dependent (BOLD) brain responses to infant versus non-infant stimuli *in vivo*. The reported range of BOLD activation patterns in response to infant stimuli suggests that a complex network is involved in shaping maternal behaviour (Musser *et al.*, 2012). Such networks include motivational and reward pathways in the cingulate cortex and prefrontal cortex, areas for emotion processing such as the amygdala, areas for decoding emotional memories such as the hippocampus, and areas implicated in OT secretion such as the hypothalamus (Atzil *et al.*, 2011; Lenzi *et al.*, 2009; Lorberbaum *et al.*, 2002; Ranote *et al.*, 2004; Strathearn *et al.*, 2009; Swain *et al.*, 2008).

While many studies examined maternal brain responses to infant stimuli (Bartels & Zeki, 2004; Lenzi *et al.*, 2009; Lorberbaum *et al.*, 2002; Noriuchi *et al.*, 2008; Ranote *et al.*, 2004; Strathearn *et al.*, 2009; Swain *et al.*, 2008), far fewer have examined the neural correlates in relation to observed maternal behaviour (Atzil *et al.*, 2011; Musser *et al.*, 2012); and only one study has attempted to focus on maternal sensitivity (Kim *et al.*, 2011). Kim *et al.* (2011) compared the neural correlates of maternal sensitive responding between nine breastfeeding mothers and eight formula-feeding mothers following exposure, in an fMRI paradigm, to own and unknown infant cries at 3-4 weeks postpartum. They reported that breastfeeding mothers showed greater activation in areas involved in emotion processing and empathy, such as the amygdala and insula (the latter is also part of the mirroring neurons-see below); and in areas associated with planning behaviour, such as the superior frontal gyrus. Activation of the amygdala and superior frontal gyrus were positively correlated with observed maternal sensitivity ratings at 3-4 months. This is interesting especially with the amygdala has been previously implicated in multiple functions, all of which facilitate maternal behaviour, such as processing of emotional salience (positive or negative), motivation as well as empathy (Breiter *et al.*, 1996; Ranote *et al.*, 2004; Swain *et al.*, 2008). However, the

findings of Kim *et al.* have not been replicated in groups rigorously defined to represent variations in maternal sensitivity.

As far as we are aware, only one study has examined the neural correlates of maternal behaviour in mothers distinguished specifically on a measure of maternal sensitivity. Atzil *et al.* (2011) examined the difference in brain responses among 23 mothers grouped according to their observed ‘synchronous’ or ‘intrusive’ behaviour with their 4-6-month infants. In that study, both groups activated limbic motivational pathways, such as the right amygdala and the left nucleus accumbens. In addition, synchronous mothers showed significant BOLD activation in areas rich in ‘mirroring neurons’ (Iacoboni, 2009; Iacoboni & Dapretto, 2006), i.e. superior temporal gyrus, inferior frontal gyrus and the insula, suggesting the ability of synchronous mothers to read and understand their infant signals (Gallagher & Frith, 2003; Rizzolatti & Fabbri-Destro, 2008). Although synchrony constitutes part of ‘sensitive responsiveness’, it is important to note that maternal synchrony focuses on more fine-grained behavioural and affect attunement with the infant, which may be more closely related with brain processes. On the other hand, maternal sensitivity is probably more linked with many areas of development. Yet, sensitivity and synchrony are likely to be highly correlated. Mothers who respond promptly and appropriately to their infant’s behaviours (maternal sensitivity) are likely to show more coordination in affect, gaze, body movement etc. (synchrony).

Recently, Musser *et al.* (2012) examined brain responses to own and unknown infant cries among 22 first-time mothers who were rated for ‘sensitivity’, ‘harmony’ and ‘intrusive’ behaviour with their 18-month-old infant, through mother-infant play interaction. They reported that more sensitive behaviour was significantly associated with greater activation in areas implicated in reward and planning of behaviour in the frontal cortex, and areas for reading others’ minds, such as the inferior frontal gyrus (Adolphs, 2002). Mothers who showed more harmony also showed significantly greater activation in areas involved in recalling memories, such as the left hippocampal regions (Phelps *et al.*, 2004; Swain *et al.*, 2008); whereas, mothers who showed more intrusive behaviours activated the temporal pole and areas associated with empathy for loved ones, such as left insula (Atzil *et al.*, 2011). Although Musser *et al.* did not compare BOLD activation between distinct groups of sensitive and less sensitive mothers, and although brain activation was only examined in relation to proportions of maternal

behaviours, their findings support the importance of considering discrete maternal behaviour when examining neural correlates.

Maternal brain activation has also been linked with maternal oxytocin (OT) levels on the basis that the animal literature finds a good case for a central role of OT in mediating maternal care behaviour (Champagne, 2008). Mothers who delivered vaginally (Swain *et al.*, 2008) or who breastfeed their infants (Kim *et al.*, 2011) have both been used as a proxy measure for high maternal OT levels. Strathearn *et al.* (2009) reported that baseline maternal plasma OT levels were positively correlated with maternal BOLD activation in thalamocingulate regions (in response to own infant pictures) among mothers rated as securely attached to their own mothers, and as compared to mothers rated as insecurely attached to their own mothers. Similarly, Atzil *et al.* (2011) reported baseline plasma OT levels were positively correlated with BOLD activation in motivational brain areas such as the nucleus accumbens in ‘synchronous’ mothers and not in ‘intrusive’ mothers. To date, no study has examined the relationship between dynamic plasma OT responses to infant challenge and directly observed behavioural measures of maternal sensitivity.

In the current study, we attempt to extend previous findings by examining maternal BOLD activation (using fMRI) to own and unknown infant stimuli in a group of well-characterised mothers from a community UK sample. We compare responses and relationships between two groups of mothers representing natural variations of maternal sensitivity (sensitive and less sensitive mothers). We aimed to examine whether sensitive maternal responsiveness could chart discrete patterns of maternal brain activation, and whether such activation is correlated with dynamic responses in maternal plasma OT to infant challenge. We hypothesised that in response to own versus unknown infant video, mothers rated as demonstrating higher sensitivity would show significantly greater BOLD activation compared to less sensitive mothers, and this would be seen specifically in brain regions related to maternal behaviours, including: hypothalamus, cingulate cortex, hippocampal formation and superior temporal gyrus. We also hypothesised that maternal brain activation in response to own infant stimuli among mothers rated as higher sensitivity would be positively correlated with plasma OT responses following a play interaction with their infants.

MATERIALS AND METHODS

Participants

Women were recruited from six community antenatal clinics across the northwest region of England (Greater Manchester). One-hundred-and-five ethnically white British mothers were approached antenatally at a mean of 33.90 weeks (SD = 3.19) antepartum. Of these, 80 mothers with no psychiatric illness were recruited for evaluation of maternal sensitivity at 4-6 months postpartum (mean = 19.38 weeks; SD = 2.47). Thirty mothers, representing opposite ends of maternal sensitivity's distribution, were selected from this sample of 80 and at a mean of 35.14 weeks postpartum (SD = 3.26) they underwent fMRI scanning and their plasma OT levels were measured after a mother-infant interaction. Mothers were excluded if they (a) had any contraindication to magnetic resonance imaging, (b) were pregnant, (c) were left-handed, (d) scored positive for depression screening (see below), and (e) were not living with their infant.

The study protocol was approved by the North West Research Ethics Committee: Ref: 10/H1013/69, and written, informed consent was obtained from all participants.

Measures

Manchester Assessment of Caregiver-Infant Interaction (MACI) (Wan *et al.*, 2012, 2013 online)

This observational measure of caregiver-infant interaction evaluates global features of interaction from 6-minutes unstructured play in 7 (2 caregiver, 3 infant, 2 dyadic) scales. The MACI was developed for research purposes to provide relatively brief rating scales suitable for a wide age range in infancy, and which would provide variance in the normal population and be sensitive in at-risk samples. Its scales were modified and refined from existing validated global scales of caregiver-infant interaction (Murray *et al.*, 1996; Blazey *et al.*, 2008). The MACI has demonstrated reliability, moderate 6-month stability and other psychometrics, and its scales are independent of socioeconomic status, infant gender and maternal age (Wan *et al.*, 2012a, 2013 online). The current study focused on the 'caregiver sensitive responsiveness' scale (henceforth 'maternal sensitivity'), defined as the "the extent to which the infant's moment-to-moment behaviour and developmental needs are responded to and supported by the caregiver, appropriately and contingently". Sensitivity is rated on a scale from minimal (1) to high (7) after carefully reviewing the clip several times. In the current study, acceptable inter-rater agreement was demonstrated on maternal sensitivity (interclass correlation: $r = 0.70$; $p < 0.001$, absolute agreement) based on independent blind ratings

of 30% of interaction clips in the complete sample. Disagreements were resolved by both raters re-reviewing the clips to reach consensus.

The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987)

This 10-item self-report instrument is widely used to screen for depression in the postpartum and antenatal periods. Items are rated on a 4-point Likert-type scale, and a cut-off score of 12 was used for screening positive.

The Hospital Anxiety and Depression (HADS) rating scale (Zigmond & Snaith, 1983)

This 14-item questionnaire is a self-rating instrument to screen for anxiety and depression (seven items each). Items are rated on a 4-point Likert scale. Mothers were excluded if they scored: EPDS ≥ 12 and HADS-depression > 11 .

Procedure

Time 1: Mother-Infant Interaction

At 4-6 months postpartum, mothers were visited at home and asked-after a period of familiarisation -to play with their infant on a floor mat as they normally do, with or without toys, as they wished. The interactions were videotaped for six minutes and later rated, using the MACI caregiver sensitivity scale, by a trained researcher blind to study information. Mothers also completed EPDS, HADS, and obstetric information sheet. Mothers' demographic characteristics were collected previously in another part of the study.

Time 2: fMRI Scanning & Oxytocin Sampling

Video of the infant's face to be edited for use as fMRI stimuli were obtained during a preparatory home visit. Approximately two weeks later mothers and infants attended the Wellcome Trust Clinical Research Facility (WTCRF) where mothers were scanned using fMRI and their plasma OT samples were collected. During the 35 minute scanning session, mothers were instructed to view the video of their infant and an unknown infant as though they were watching TV. For plasma OT measurements, blood samples were taken from mothers at the same time in the early afternoon, 1200 -1400 hours, and one hour after the last nursing feed. Mothers were asked to refrain from caffeine and smoking for at least two hours before the sampling.

i. fMRI Paradigms

A series of alternating pre-recorded 20-second video clips consisting of three affect conditions (neutral, happy, and sad) of participant's 'own' infant and an 'unknown'

infant (matched on age and gender) in addition to a neutral control stimulus (moving traffic) was prepared for use in the fMRI scan. Videos lasting 16 minutes were presented in the following order: (Own neutral infant - neutral control - unknown neutral infant) x 4, REST (i.e. blank screen), (Own happy infant - neutral control - unknown happy infant) x 4, REST, (Own sad infant - neutral control - unknown sad infant) x 4, REST.

ii. fMRI Acquisition

Imaging was performed using a 1.5 Tesla Philips Intera MRI scanner running Explorer gradients (software version 11.1.4.4). High-resolution T1-weighted structural images were acquired to exclude any structural abnormality (none were found) and for co-registration with functional data. The structural scan using SENSE employed a 3D Contrast Turbo Field Echo Sequence with a temporal resolution (TR) of 9ms and an echo time (TE) of 4ms with an 8° flip angle producing 140 slices with a voxel size of 0.8 x 0.8 x 1.0 mm. Functional images were acquired using a multi-slice, single-shot echo-planar imaging sequence, generating 29 ascending axial slices (TR = 2.5s, TE = 40ms, 4mm thickness with 0.5mm slice gap, in-plane resolution of 3.4x3.4mm).

iii. fMRI Analysis

Imaging data were preprocessed, individual data corrected for motion, and the individual data were spatially normalised for group analyses using Statistical Parametric Mapping (SPM8) and implemented in MATLAB (Mathworks Inc, Sherborn, MA, USA). All functional images were realigned using a least squares approach and a six-parameter (rigid body) spatial translation (Friston *et al.*, 1996). The first image was used as a reference scan and the following images were translated onto this, correcting for pitch, roll and yaw throughout the task. Translation and rotation corrections did not exceed 3.0 mm and 2.5° for any participant.

The scans were spatially (stereotactically) normalised onto standardised brain slices. This involves the warp of the images onto a standardised template. The standardised template conforms to the ICBM, NIH P-20 project and approximates the stereotactic atlas of Talairach and Tournoux (1988). The standardised slices then underwent smoothing using an isotropic Gaussian kernel filter (10mm full width half maximum [FWHM]) to increase the signal-to-noise ratio by use of the matched filter theorem (Friston *et al.*, 2000). A parametric model was employed that enabled the modelling of linear hemodynamic responses. We compared brain activation patterns between our two

maternal sensitivity groups using a two-factor random effects ANOVA model, where differences in BOLD activation were assessed with a threshold of ≤ 0.05 Family Wise Error (FWE), corrected for multiple comparisons. Significance of differences in activation between the two groups was calculated using a Student's t-test.

iv. Oxytocin

Two sample of blood (5 ml each) were taken from antecubital veins through an intravenous cannula following a 10-minute interaction between the mother and her infant (as earlier). The first sample was taken immediately after the interaction and the second one 5 minutes after the first sample. The mean of the two samples was considered to account for the pulsatile secretion of OT. Samples were drawn into chilled vacutainer tubes containing lithium heparin injected with 200ml of Trasylol (aprotinin) 500,000 KIU/ml blood. OT samples were kept ice-chilled until processed within 10 minutes. Samples were then centrifuged at 4°C at 3500 rpm for 15 minutes. 500ul supernatants were transferred to two microtubes (aliquot 1 & 2) and stored at -80°C until transferred, on dry ice, to the University lab for analysis. Determination of OT was performed using the Max Binding Determination Competitive Assay protocol on Gen 5 software using a Biotek plate reader.

RESULTS

Among the 30 mothers included in the current study: 15 were classified as 'sensitive' mothers (blind rated 4-7 for maternal sensitivity; mean = 4.47; SD = 0.74) and 15 mothers classified as 'less sensitive' mothers (blind rated 1-3 for maternal sensitivity; mean = 2.13; SD = 0.52) (Figure 1). For description purposes, the two sub-groups respectively are referred to here as 'high sensitivity mothers' (HSMs) and 'low sensitivity mothers' (LSMs), respectively.

Figure 1 about here 'Distributions of high sensitivity mothers (HSMs, N = 15) and low sensitivity mothers (LSMs, N = 15) in relation to maternal sensitivity distribution of the whole sample (N = 80)'.

Assessing for Confounders

The two groups of mothers did not differ in: maternal age, marital status, parity (primiparous/multiparous), mode of delivery or feeding, postpartum stage, infant birthweight, or infant gender (Table 1). However, maternal education and household income were borderline significantly higher among HSMs, yet were not controlled for as they were insignificant.

Table 1 about here ‘The demographic and obstetric characteristics of mothers grouped by level of maternal sensitivity’

Whole Brain Analyses

Because one outlier was excluded from OT analyses ($> 3SD$), and therefore was also excluded when correlations between BOLD brain activation and plasma OT were examined.

In order not to limit the extent of these exploratory analyses, we initially examined the main effect using ‘whole brain analyses’ with a significant threshold specified as $p \leq 0.05$; FWE corrected in all mothers combined. Comparing own versus unknown infant videos, significantly enhanced BOLD activation was observed in the right inferior frontal gyrus (BA 47 & 9), and in a range of subcortical regions, including left parahippocampal gyrus (BA 34), bilateral uncus (BA 28), and anterior cingulate gyrus (BA, 24) (Table 2).

Table 2 about here ‘Significant BOLD signals for main effect in response to own versus unknown infant stimuli’

Comparisons between High and Low Sensitivity Mothers

To test our main hypotheses, we used a ‘Region of Interest (ROI)’ analysis with random effects comparing BOLD activations between the two groups of maternal sensitivity. Based on our hypothesis, a single ROI composite was hypothesised to include: right superior temporal gyrus, right posterior cingulate gyrus, left subthalamic nucleus and left hippocampal formation. Activation was compared between the two groups of mothers, HSMs ($N = 15$) and LSMs ($N = 15$) in the *a priori* ROI.

We compared responses to own versus unknown infant video between the two sensitivity groups for each facial affect separately [*i.e.* HSMs versus LSMs (own happy infant minus unknown happy infant)], HSMs versus LSMs (own neutral infant minus unknown neutral infant), HSMs versus LSMs (own sad infant minus unknown sad infant)], and similarly for LSMs versus HSMs. Compared to LSMs, HSMs showed greater BOLD activation in the right superior temporal gyrus (BA 41) in response to

own neutral infant as compared to unknown neutral infant (Table 3, Figure 2); whereas, compared with HSMs, LSMs did not show significant activation in response to own versus unknown infant contrasts in any of the ROIs. Comparing activation between HSMs and LSMs in own infant happy or sad versus unknown happy or sad videos did not reveal significant differences between the two groups.

Finally, we compared BOLD activation to different facial affects between HSMs and LSMs using only own infant stimuli versus neutral control, [*i.e. HSMs versus LSMs (own neutral infant minus neutral control), HSMs versus LSMs (own happy infant minus neutral control), HSMs versus LSMs (own sad infant minus neutral control)*], and similarly for LSMs versus HSMs. Compared to LSMs, HSMs showed greater BOLD activation in the right superior temporal gyrus extending to the right insula (BA 13) in response to own happy infant (Table 3, Figure 2). By contrast, compared to HSMs, LSMs did not show significant BOLD activation in response to own happy infant video in any ROIs. Viewing own neutral or sad infant videos did not reveal significant differences in BOLD activation in the ROIs when the two groups were compared.

Table 3 about here ‘Areas of significant BOLD activation within ROI in response to infant stimuli, when comparing high sensitivity (N = 15) and low sensitivity (N = 15) mothers’

Figure 2 about here ‘Maternal brain activation in response to infant stimuli: Compared with LSMs, HSMs show greater activation of the right superior temporal gyrus in response to: (a) own neutral infant versus unknown neutral infant videos, and (b) own happy infant versus neutral control, at ROI-threshold of $FWE \leq 0.05$. Structural brain image created from average of all subjects.’

Correlations of Plasma Oxytocin with ROI Activation

Post-interaction plasma OT was significantly lower among HSMs (mean = 210.01; SD = 81.58) compared to LSMs (mean = 301.56; SD = 38.12), $F(1, 26) = 9.7$; $p < 0.01$) (after controlling for household income which was lower in LSMs and after excluding the outlier). When considering the correlation between ROI activation and plasma OT, a between-group correlation was found. Activation of right superior temporal gyrus (in

response to own happy infant) was negatively correlated with plasma OT levels among higher sensitivity mothers ($r = -0.81$; $p < 0.01$) (Figure 3).

Figure 3 about here ‘Correlation between BOLD activation in the right superior temporal gyrus (STG) and post interaction plasma oxytocin among high sensitivity mothers ($n = 15$)’.

DISCUSSION

Overall, when early postpartum mothers viewed videos of their own infants compared to unknown infants, significant brain activation was elicited predominantly in three areas: i) the anterior cingulate gyrus, ii) the right inferior frontal gyrus, and iii) the left parahippocampal gyrus and bilateral uncus. This is consistent with previous findings (e.g. Kim *et al.*, 2011; Swain *et al.*, 2008). In accordance with our hypothesis, when compared to LSMs, HSMs showed greater BOLD activation in right superior temporal gyrus in response to own neutral infant compared to an unknown infant video or in response to own happy infant compared to neutral control stimulus. Inconsistent with our hypothesis, however: the BOLD activation among HSMs (in response to own happy infant) was negatively and not positively correlated with post-interaction plasma OT concentration in those mothers. Furthermore, and inconsistent with our hypothesis, HSMs did not show significantly greater BOLD activation in any other ROIs, specifically hypothalamus, posterior cingulate gyrus, or the hippocampal formation, in response to own versus unknown infant stimuli. When compared to HSMs, LSMs showed no significantly greater activation in any ROI in response to their own infants.

The superior temporal gyrus has been implicated in the perception of emotions in facial stimuli and were also understood to contains ‘mirror neurons’ (Iacoboni & Dapretto, 2006), and is thus implicated in understanding and empathising with others’ ‘Theory of Mind’ (Blakemore & Decety, 2001; Gallagher & Frith, 2003; Rizzolatti & Fabbri-Destro, 2008). For a postpartum mother to respond sensitively to her infant’s needs, recognising and understanding another’s emotions (i.e. her infant’s emotion) is a key aspect of sensitive mothering (Strathearn *et al.*, 2012). Therefore, our findings that HSMs show significantly greater activation in superior temporal gyrus suggests this is related to their behaviour. In other words, the findings suggest that HSMs give more

attention to read their infant facial emotions, whereas LSMs do not, possibly because of the superior maternal reflective function among the former (Brunet *et al.*, 2000; Lenzi *et al.*, 2009). Thus, a sensitive mother must have the capacity to recognise her infant's emotional and other cues/signals, pay attention to them and then respond to them by appropriately mirroring and affirming positive emotions or recognising and reassuring in relation to the negative ones (Ainsworth *et al.*, 1978; Sroufe, 2000).

Activation of superior temporal gyrus has also been reported in response to infant cry at 2-4 weeks postpartum among exclusively breastfeeding mothers ($n = 9$) when compared to formula-feeding mothers (Kim *et al.*, 2011), and in response to own infant cry at 2-4 weeks postpartum among mothers who delivered vaginally ($n = 6$) as compared to those who delivered by Caesarean section ($n = 6$) (Swain *et al.*, 2008). Both these groups were taken to represent more highly sensitive mothers with higher OT levels.

Contrary to our expectations, HSMs (as compared to LSMs) did not show significantly greater BOLD activation in regions involved in hormonal regulation, motivation, or encoding emotional memories such as thalamus, posterior cingulate gyrus, and hippocampal formation respectively. Previous findings are equivocal, with some studies reporting greater activation of these areas in response to infant cry (Kim *et al.*, 2011; Lorberbaum *et al.*, 2002; Swain *et al.*, 2004; Swain *et al.*, 2008), while others did not (Bartels & Zeki *et al.*, 2004; Seifritz *et al.*, 2003).

Our data support a role for OT in reducing or modifying social stress (Taylor *et al.*, 2010). Previously, Bick and Dozier (2010) measured urinary OT levels in 26 healthy mothers following 25 minutes of physical interactions while playing computer games with their own 2.5- 4.5-year-old children, and again with an unfamiliar child of a similar age. Urinary OT was significantly higher following interaction with the unfamiliar child as compared with own child. They concluded that interaction with an unfamiliar child might constitute a stressful situation and, accordingly, that OT increased in order to modulate this stress. Similarly, among 32 nulliparous women, a significant drop in plasma OT was reported after women viewed positively valenced stimuli (i.e. a comedy movie), whereas no change was found after women viewed negatively valenced stimuli (a sad movie) (Turner *et al.*, 2002).

Our findings suggest that, compared to LSMs, mothers at the higher end of the maternal sensitivity distribution (i.e. HSMs) perceived their infants and infant interaction as a less stressful, more positive event, as evidenced by their lower plasma OT levels

following interaction with their infant. They also activated brain regions that indicate a greater ability to recognise and understand their infant's emotional cues.

Strength and Limitations

As far as we are aware, this is the first study to chart the differences in neural responses, as well as plasma OT responses, in mothers who are highly sensitive in contrast to mothers with low maternal sensitivity. However, the study has some limitations. First, while the sample from which we derived the high and low sensitivity groups was large enough to show a normal distribution of sensitivity and variability among HSMs and LSMs ($N = 80$), it was still relatively small. Yet both the final ($N = 30$) and the original samples represent a set of well-matched demographics. Second, although we classified mothers into two groups according to distinctly different ratings along a scale (LSMs = minimal to scattered sensitivity; HSMs = mixed to high sensitivity), we were unable to sample the extremes in the complete sample due to the overlap between phases of study and the interval needed to blind rate interactions. Third, although a moderate to high degree of stability has been reported in maternal sensitivity (e.g. Joosen *et al.*, 2012), we rated maternal sensitivity at a mean of 11 weeks before the scanning and OT challenge visit. Previous reports do, however, suggest that MACI-rated maternal sensitivity has moderately high stability between seven and 14 months ($r = 0.48$) (Wan *et al.*, 2013 online). Finally, we confined our recruitment to white women (as a requirement for other parts of the study) which may limit the generalisability of our findings to early postpartum mothers of non-white-British ethnic origin.

CONCLUSION

Our findings extend previous reports and indicate an ability to chart the quality of maternal caregiving behaviour through BOLD activation responses to infant stimuli *in vivo*. Our findings also suggest that OT may particularly act to facilitate caregiving behaviour in lower sensitivity mothers. This prepares the way for using changes in brain activation in response to infant stimuli as potential biomarkers for development and evaluation of new diagnostic and treatment strategies in at-risk mothers (e.g. Riem *et al.*, 2011).

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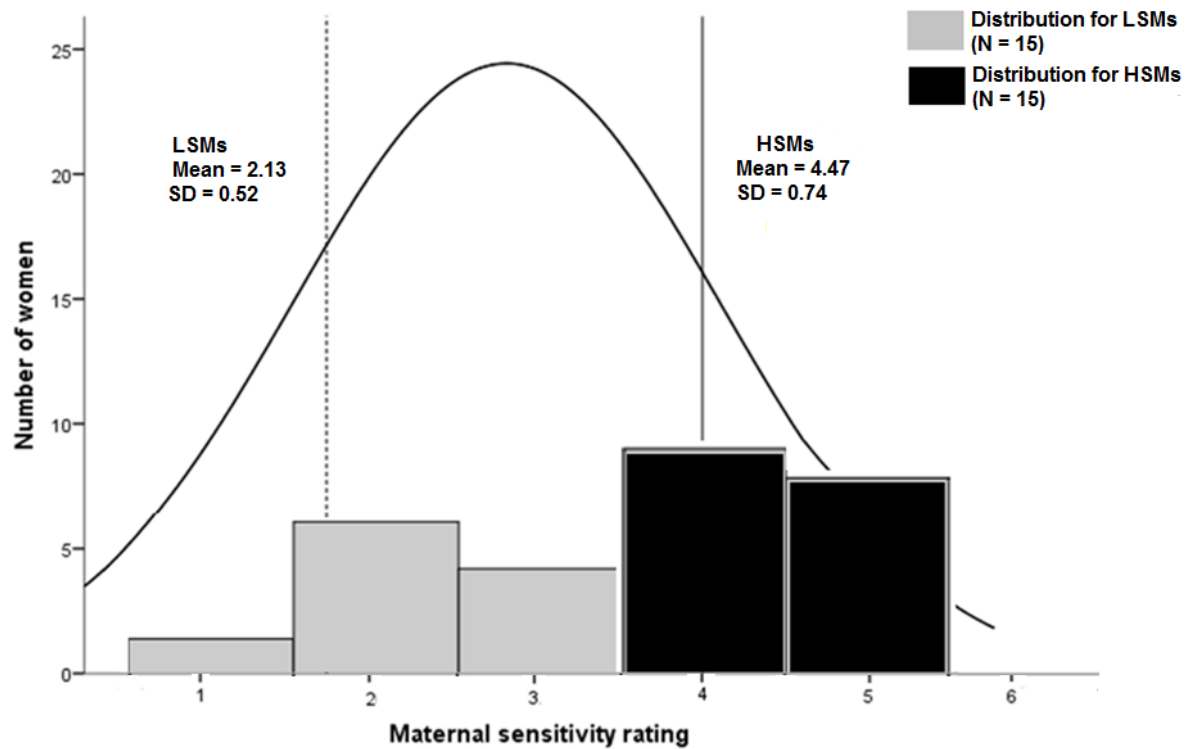


Figure 1. Distributions of high sensitivity mothers (HSMs, N = 15) and low sensitivity mothers (LSMs, N = 15) in relation to sensitivity distribution for the whole sample (N = 80). **Key:** Means for high sensitivity mothers (vertical solid line) and low sensitivity mothers (vertical dashed line) in relation to the larger sample are also presented.

Table 1. The demographic and obstetric characteristics of mothers grouped by level of maternal sensitivity (high sensitivity mothers - HSMs, and low sensitivity mothers - LSMs)

Characteristic	HSMs (N = 15)	LSMs (N = 15)	Statistics t (28)	Chi-square test	p-value
<i>Mean [SD]</i>					
Maternal age (years)	30.40 [5.37]	27.65 [4.76]	- 1.38		0.18
Average maternal education (years)	15.06 [2.82]	12.80 [2.73]	- 1.87		0.07
Average annual household income (thousand pounds)	33.00 [4.61]	25.33 [4.24]	- 2.76		0.09
Infant birthweight (kilograms)	3.44 [0.44]	3.23 [0.59]	- 0.80		0.43
Postpartum stage (weeks)	35.93 [2.81]	34.29 [3.69]	- 1.37		0.18
<i>Frequency (%)</i>					
Married/cohabiting	13 (86.7)	11 (78.6)		0.56	0.65
Primiparous	6 (40.0)	9 (64.3)		1.71	0.19
Infant gender (female)	10 (66.7)	7 (50.0)		0.83	0.36
Mode of delivery (vaginal)	10 (66.7)	11 (78.6)		0.51	0.47
Mode of feeding (breast)	3 (20.0)	3 (20.0)		0.55*	0.64

*Fisher exact test

Table 2. Significant BOLD signals for main affect in response to own versus unknown infant stimuli (combined all affects) among the whole sample (N = 30)

Contrast	Area	Sub-areas	BA	R/ L	Talairach coordinates			Z score	FWE
					x	y	z		
Own infant minus unknown infant	Frontal lobe	Inferior frontal gyrus	47	R	43	26	2	4.50	0.02
			9	R	47	11	27	4.08	0.01
	Limbic lobe	Parahippocampal gyrus	34	L	-23	2	-19	4.49	0.02
		Uncus	28	L	-29	5	-23	4.45	0.01
			28	R	33	2	-23	4.55	
			28	R	30	5	-19	3.85	
		Anterior cingulate gyrus	24		0	31	23	4.21	0.06

Note. All significant whole brain (Family Wise Error (FWE) ≤ 0.05) corrected for multiple comparison. BA: Brodmann's area; L: Left, R: Right.

Table 3. Areas of significant BOLD activation within ROI in response to infant stimuli, when comparing high sensitivity (N = 15) and low sensitivity (N = 15) mothers.

Groups compared	Contrast	ROI	BA	Talairach coordinates			Z score	FWE
				x	y	z		
High sensitivity mothers vs. Low sensitivity mothers	Own neutral infant minus unknown neutral infant	Superior temporal gyrus	41	57	-25	13	3.39	0.05
	Own happy infant minus neutral control	Superior temporal gyrus	41 13	43 57	-32 -32	5 18	3.92 3.38	0.01 0.05

Note. All significant ROI (Family Wise Error (FWE) ≤ 0.05) corrected for multiple comparison. BA: Brodmann's area; L: Left, R: Right.

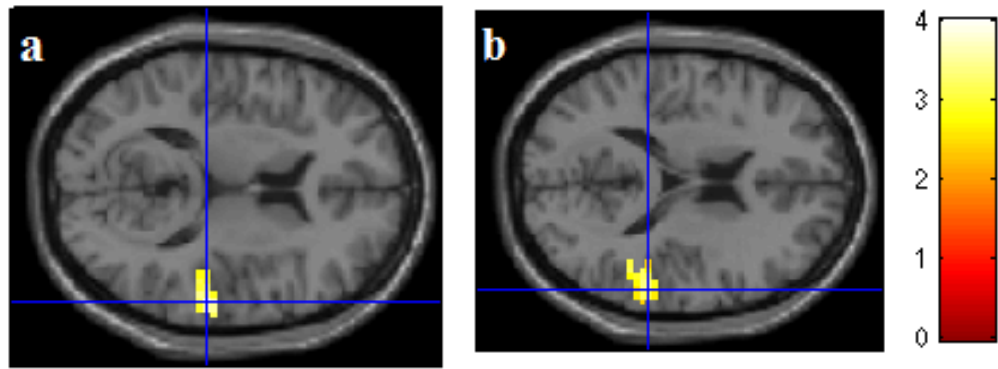


Figure 2. Maternal brain activation in response to infant stimuli: Compared with LSMs, HSMs show greater activation of the right superior temporal gyrus in response to: (a) own neutral infant versus unknown neutral infant videos, and (b) own happy infant versus neutral control, at ROI-threshold of $FWE \leq 0.05$. Structural brain image created from average of all subjects.

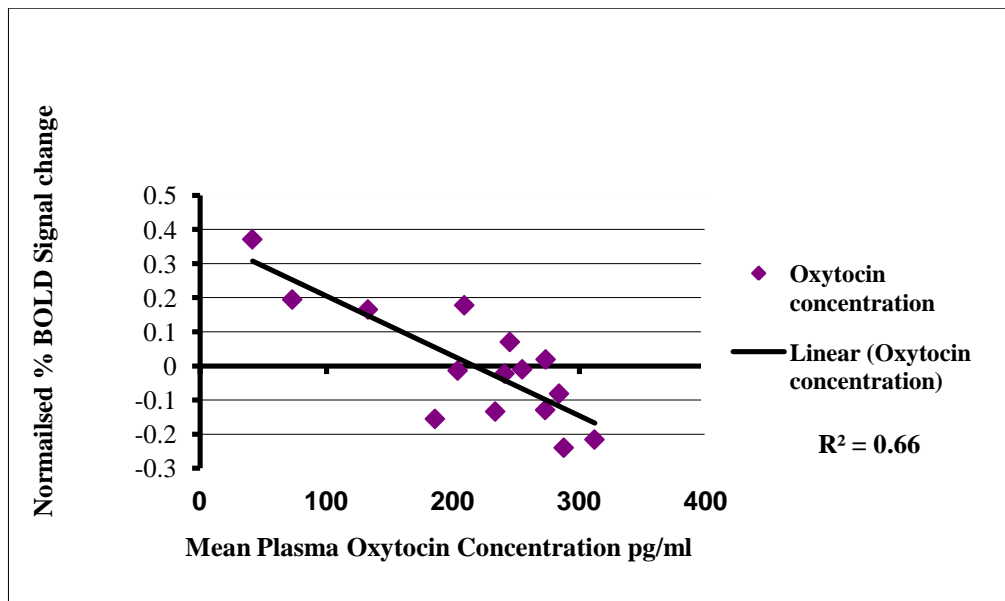


Figure 3. Correlation between BOLD activation in the right superior temporal gyrus (STG) and post-interaction plasma oxytocin among high sensitivity mothers (N = 15).

Chapter 11: **Summary and Conclusion**

1. The aims of the thesis
2. Summary of the findings
3. Clinical implications of the findings
4. Limitation of the thesis
5. Directions for future research
6. Conclusions

11.1. The Aims of the Thesis

The overall aim of the present thesis was to provide greater insight into the mechanisms underlying natural variation in maternal sensitivity in healthy mothers. Maternal sensitivity is a key predictor of child attachment and seems central to healthy child development. In order to identify mothers at risk of low maternal sensitivity, Study I of this thesis (Chapters 2, 3, 4 & 5) asked whether factors which could be reliably and easily identified and which were likely to be readily available pre-or postnatally could predict future maternal sensitivity. Such knowledge about predictors might help future ‘screening’ of mothers at risk of low maternal sensitivity so they could be targeted for more detailed postnatal assessment and consequently receive interventions aimed at improving their parenting capacities.

To achieve this, we approached 105 healthy women antenatally at around 30 weeks of gestation in community antenatal clinics across the North West of England. Using validated questionnaires, 80 pregnant women were assessed for possible predictors of

maternal sensitivity; maternal sensitivity was subsequently rated at 4-6 months at postpartum through using video observation of mother-infant play-interaction.

Study II (Chapters 6, 7, 8, 9 & 10) aimed to shed light on the interplay between hormonal and brain pathways underlying natural variation in maternal sensitivity (Feldman et al., 2007, 2010a, 2010b; Strathearn et al.; 2009; Atzil et al., 2011). Such knowledge about the distinct neurobiological profile of ‘higher’ sensitivity mothers might help prepare the way for future efficient hypothesis testing of the effects of novel interventions including the use of intranasal OT to improve parenting. Thus, Study II sought to answer these questions:

1. Can baseline and dynamic measures of plasma OT differentiate between sensitive and less sensitive mothers?
2. Does natural variation in maternal sensitivity result in discrete brain responses in response to own infant stimuli? Does this pattern of brain activation correlates with measures of plasma OT?

To achieve this, we examined differences between healthy (non-depressed) women who were ascertained from a representative general community sample (N = 105), but whose maternal sensitivity has been rigorously ascertained (N = 80). We compared women from this group whose sensitivity lay at opposite extremes of the sensitivity scale (N = 30; i.e. 15 in each extreme group).

11.2. Summary of the Findings

- Around a fifth of the variance in postnatal maternal sensitivity can be predicted from readily collected variables available prenatally. Parental care received by the mother herself and a measure of family SES via household income accounted for most of

the variance. This supports the idea that sensitive maternal care can be predicted, at least to some degree, and hence early intervention could be considered for those at risk (Chapter 4).

- Another 12% of the variance in maternal sensitivity was predicted by the presence of more than one social deprivation factor (i.e. young maternal age at birth, no education, single marital status, low income, unemployment household income, and early neglected parental care) and sensitivity decreased significantly as the number of these factors increased.
- Other prenatal measures, such as availability of social support, maternal attachment with the unborn infant, early experience of maltreatment, postnatal factors such as infant temperament, and postnatal mood scores did not predict postnatal maternal sensitivity. These results suggest the limited capability of these measures in predicting how sensitive a mother will be with her infant in a well population (Chapter 4).
- Contrary to our main hypothesis, we reported that: LSMs have higher baseline plasma OT levels compared to HSMs. We would suggest the high plasma OT levels in LSMs reflecting possible social stressors related to their relations with others, including own mothers. These findings support the role of OT as a biomarker for a distressed social relationship similar to what has previously been reported in studies in women (Marazziti et al., 2006; Taylor et al., 2006, 2010; Tabak et al., 2011; Feldman et al. 2011) (Chapter 9 & Chapter 10).
- The findings also suggest that OT does not have a unioversal pattern in relation to affiliative behaviour as it might decrease (not increase) in response to affiliative social interaction. This warns against using it as a universal biomarker to signal affiliative behaviour.

- Also contrary to our main hypothesis: following a play-interaction with their infants, plasma OT levels significantly decreased in HSMs, whereas no significant change was seen among LSMs. These results suggest that HSMs perceived their infant's signals as a positive event and their plasma OT levels drop accordingly in response to an easy, focused, positive interaction with their own infant (Taylor et al., 2002; Strathearn et al., 2012). LSMs may not perceive the interaction with their own infant as a positive event and hence restrain/resist the alleviating effect of the socially affiliative interaction as compared to HSMs; accordingly their plasma OT remains elevated (Chapter 9 & Chapter 10).
- In accordance with our secondary hypothesis, we found that plasma OT levels, at least among LSMs, were significantly correlated with mothers' own perceived parenting, supporting the role of early environment in shaping maternal hormonal profile (Champagne et al., 2007; Champagne, 2008; Strathearn et al., 2009). However, contrary to our hypothesis, the direction of this correlation was positive with self-reported unfavourable (not with favourable) own parenting experience, in particular, self-reported own maternal overprotection, as evidenced among LSMs. This finding supports a role for OT in regulating stress responsivity that is related to social relationships, including relationships with own parents (Marazziti et al., 2006; Taylor et al., 2010; Feldman et al., 2011) (Chapter 9 & 10).
- Overall, and in accordance with our hypotheses, when mothers viewed videos of their own infants compared to unknown infants, significantly greater brain activation was elicited predominantly in emotion processing areas (the right anterior cingulate gyrus), areas associated with encoding of facial expressions of emotions (right inferior frontal gyrus) and areas decoding emotional memories (the left parahippocampal gyrus and bilateral uncus). This provides support for previous findings and suggests that a key to healthy maternal parenting is the capacity of

mothers to recognise and respond to her infant's emotions; and in young, preverbal infants, this is perhaps especially through mirroring of emotional expressions and facial cues (Chapter 9).

- Also in accordance with our main hypothesis, we found that, compared to LSMs, HSMs showed significantly greater activation in brain areas associated with mirroring the emotions of others (the right superior temporal gyrus) in response to own infant compared to an unknown infant or compared to a neutral control. By contrast, when compared to HSMs, LSMs did not show any brain activation in response to their own infant stimuli. These results suggest that HSMs might give more attention to read their infant facial stimuli, compared to LSMs who do not give enhanced attention and focus to infant signals, possibly because the latter do not recognise these signals (as evidenced by the absence of brain activation) or do not attribute added salience to infant signals (Chapter 9).
- Contrary to hypothesis, HSMs did not show significantly greater activation in areas implicated in OT secretion, such as the hypothalamus, or in emotion processing areas, such as the posterior cingulate gyrus, or the hippocampal formation, in response to own infant compared to an unknown infant video. However, this may be consistent with our findings that suggest plasma OT's anxiolytic/anti-stress role (Numan & Woodside, 2010) rather than its socially affiliative role in HSMs who may not require OT to act in this way (Chapter 9).
- Inconsistence with our hypotheses the BOLD activation in the right superior temporal gyrus among HSMs was negatively (not positively) correlated with post interaction plasma OT concentration in those mothers. Again this is consistent with the plasma OT findings of those mothers and it supports the anti-stress role that OT might play in those mothers (Chapter 9, 10).

- We infer that differences between our present findings and those of other parenting studies which have assessed plasma OT in relation to maternal behaviour are because, in the present study, we assessed OT in two groups of women ascertained specifically to occupy opposite ends of the distributions of maternal sensitivity in the general population. The other studies, however, did not directly compare groups of mothers carefully ascertained for sensitivity, and in many cases used indirect proxies of sensitivity or OT, such as breastfeeding or mode of delivery (e.g. Kim et al., 2011). We think our findings could be ‘tapping’ into elements of stress or anxiety coping, which we suggest are an integral aspect of the concept of sensitive maternal responsiveness (Chapter 9, 10).

11.3. Clinical Implications of the Findings

- The current findings add significantly to current understanding of what underpins the natural variation in maternal sensitivity in a population of healthy women.
- It suggests this variation is related to a combination of behavioural, social and neurobiological differences.
- The results of these studies highlight the possibility of identifying predictors of lower sensitivity mothering.
- Evidence from the present studies and similar studies should facilitate future development of an ‘affordable’, ‘accessible’, and ‘easy’ tool, for health providers to screen women antenatally for at risk of low maternal sensitivity.
- Were such a tool readily available antenatally and acceptable to women, it would facilitate targetting of less widely available early interventions to improve their parenting.
- The empirical findings in these studies provide the basis for a new understanding of the multiple roles of OT in the modulation of maternal caregiving. They provide

further support for the notion that OT acts differentially depending on the ability of an individual to regulate emotion and cope with potentially stressful situations (Tabak et al., 2011). In the context of maternity, our results may imply that if the overwhelming experience of infant cues is stressful to a mother, OT may play a more prominent anxiolytic role than when a mother derives pleasure and reward from her infant's cues, or develops a 'positive emotion' as a result of interaction with her infant (Feldman et al., 2011).

- Thus, baseline and dynamic plasma OT responses may be a potentially useful biomarker of maternal sensitivity.
- The present studies provide further support for previous findings that maternal brain activation occurs in response to own infant stimuli in areas associated with emotion recognition and processing. It contributes additional evidence that suggests sensitive mothers have a greater capacity to recognise and understand their own infant emotions compared to less sensitive mothers.
- Sensitive maternal responsiveness appears to be accompanied by a discrete neural correlate. This provides a basis for neural activation patterns acting as a biomarker for monitoring future interventions that aim to improve parenting behaviour (e.g. Riem et al., 2011).
- The present findings also provide preliminary evidence for possible modulation of maternal brain responses by OT (i.e. as evidenced by the significant correlation between plasma OT and BOLD activation), although further studies are needed.

11.4. Limitations of the Thesis

The studies encountered a number of limitations which need to be considered:

- The original sample from which we derived the 80 mothers in whom maternal sensitivity was assessed was relatively large (N = 105). However, a larger sample is

more likely to uncover all the most important factors that influence maternal sensitivity in a population.

- Mothers' own parenting experience and early experience of maltreatment were assessed through self-report measures (PBI & CTQ). Both measures have shown good psychometric properties (Bernstein et al. 1994, Wilhelm et al., 2005) and the convergent validity for PBI was confirmed over 20 years (Wilhelm et al., 2005) but, given that this appears to be particularly relevant as a source of risk for lower maternal sensitivity, future research is needed to identify objective easy of measuring this variable.
- Although we classified mothers into two groups (Study II) according to distinctly different ratings along a scale for maternal sensitivity (LSMs = minimal to scattered sensitivity; HSMs = mixed to high sensitivity), we were unable to sample the extremes in the complete sample due to the overlap between phases of study and the interval needed to blind rate interactions.
- Inferences about centrally functioning OT from plasma measurement, although highly convenient, must remain limited (Modahl et al., 1998). However, many previous studies do show modulation of peripheral plasma OT in relation to social affiliation (e.g. Strathearn et al., 2012) and findings from fMRI studies also show coordinated peripheral OT levels and BOLD activation in OT rich brain areas (Strathearn et al., 2009; Atzil et al., 2011). Similarly, administration of intranasal OT has been shown both to increase peripheral OT (saliva) and to increase affiliative behaviours e.g. affectionate paternal behaviour (Weisman et al., 2012) (Chapter 6).
- We did not include a thorough assessment of mothers' social relationships or difficulties, including 'relationship with partner'. Therefore, we cannot exclude the

possibility that the presence of other distressed relationships is associated with the elevated plasma OT among the LSMs in our studies.

- The significant correlation we found between plasma OT and BOLD brain activation among HSMs does not imply a causal relationship. There might be other unidentified factors to account for this association.
- Because most of our measures are designed to measure behaviours representing bonding/affiliation (e.g. MFAS, MII), it was essential to consider different representation of these behaviours across cultures (Alhusen, 2008). Therefore, we confined our recruitment to white British women, in order to minimise the cultural differences between mothers. While this may be seen as a strength for the study design, it also limits the representativeness of the findings by not reflecting the ethnic diversity of the community in the sample.
- Maternal sensitivity was rated at a mean of 11 weeks prior to the OT measurements and the scanning assessment visit. We do not think this is likely to be of concern because several studies have reported moderate to high degree of stability in maternal sensitivity over this relatively short time period (e.g. Joosen et al., 2012). Moreover, previously the MACI-rated maternal sensitivity has also demonstrated moderately high stability between 7 to 14 months ($r = 0.48$; Wan et al., 2013 online).

11.5. Directions for Future Research

- Given the importance of identifying mothers most at risk of low maternal sensitivity, research must continue investigating key factors which indicate the future quality of maternal sensitivity, including maternal and infant characteristics (Chapter 2).

- Such complex interplay between maternal and child social, environmental, and psychological factors must be considered by future studies. How they might modulate the impact of risk of poor maternal sensitivity on the mother-infant relationship is a key question to be addressed (Mertesacker et al., 2004).
- Replication of these findings in a larger sample including wider ethnic and social diversity may find that the factors identified have a greater predictive value, especially if the current, less diverse sample may not have been sufficiently varied to capture such associations.
- Research in this area might also benefit from longitudinal designs that examine the continuity of these influences on the mother and child relationship at later stages of infant development (e.g. Beckwith et al., 1999).
- A great strength of the UK NHS system is that it provides many chances when broad representations of women are in regular contact with health services. This provides opportunities for the implementation of routine participation and the consideration of population-based screening. These and future studies should consider how best to exploit these opportunities. For example, health visitors have contact with all mothers following infant birth, and are uniquely placed for early detection of problems affecting the mother-infant relationship (Appleton et al., 2013).
- Expansion of the work of these studies might include enrolment of teenage mothers, to evaluate the effect of this young maternal age and its attendant difficulties and risks on maternal sensitivity. Particular attention should also be given to assess partner support in more detail and how it might affect maternal sensitivity, or create resilience or greater risk in the mother-infant relationship, or alter the risk set of the parenting environment in other ways.

- Although mother-infant interaction in the play context is a widely used and well-validated method with which to assess maternal sensitivity, it potentially lacks information about the mother's responsiveness to her infant in stressful situations (McElwain & Booth-LaForce, 2006). Therefore, more comprehensive assessment of variation in sensitivity (including under more stressful situations) should be considered by future research.
- Further studies replicating our design in a larger population, might be able to examine whether plasma oxytocin levels mediate the relationship between maternal overprotection and maternal sensitivity.
- Replication of Study II should consider the simultaneous assessment of maternal urinary or salivary OT along with plasma OT measures. This is especially pertinent given recent evidence from a parenting study which reported an elevation in urinary OT in mothers experiencing relationships difficulties (Feldman et al., 2011).
- Previous evidence suggests that elevation of plasma OT in relation to stress is only in the context of stimuli which are social stressors i.e. social relationship difficulties. However, future studies replicating the present design might usefully combine measurements of plasma OT with additional measures to evaluate the HPA or stress axis (e.g. cortisol) for more thorough evaluation of the OT role in stress regulation (Quirin et al., 2011).
- The present study found significantly greater activation in brain areas related to mothers' ability to read an infant's emotion (right superior temporal gyrus) in HSMs. Future studies are needed to examine further activation patterns using more detailed stimuli which probe specific aspects of affiliative and cognitive functions in relation to the complex demands of sensitive mothering.

11.6. Conclusions

- This set of studies is the first to chart the differences in both plasma OT responses as well as brain responses among mothers representing distinct ends of the spectrum of natural variation in maternal sensitivity. In addition, these are the first studies systematically to explore maternal characteristics that might contribute to this variation. Charting the profiles of maternal brain activation associated with sensitive parenting may be seen as a method of representing how a mother coordinates affective, social-behavioural and neural systems. A deeper understanding of such pathways is likely to prove useful in future studies of healthy and high risk mothers.

- Overall the findings answered our research questions as follows:
 1. Two readily identifiable factors available prenatally could facilitate prediction of future maternal sensitivity: parental care received by the mother and family SES (via household income).
 2. Plasma OT measures could differentiate between sensitive and less sensitive mothers.
 3. Discrete patterns of brain response to own infant stimuli could be evidenced by fMRI in sensitive early-postpartum mothers; and this pattern correlates with plasma OT responses of those mothers.

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Appendix A: Maternal sensitivity & prenatal variables

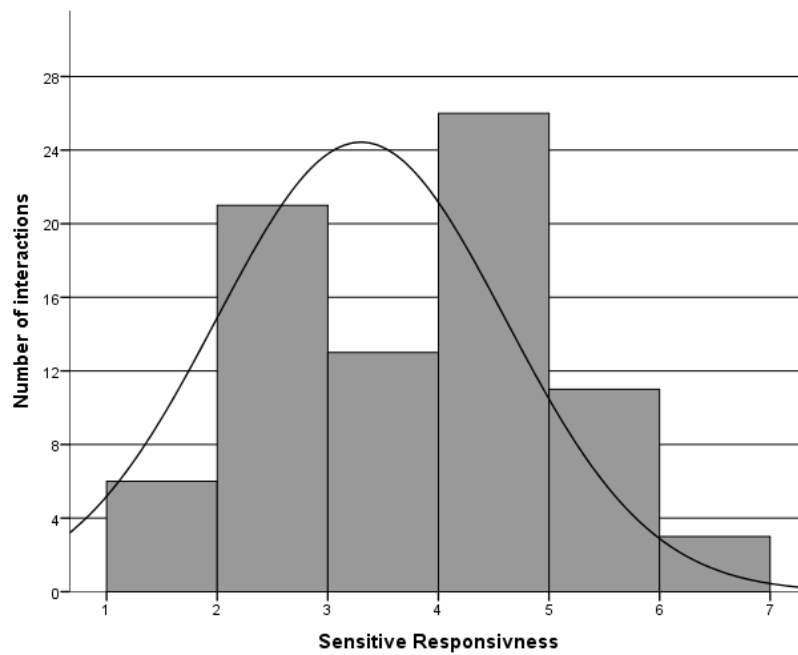


Figure 1. Distributions of the sensitive responsiveness (maternal sensitivity) domain of the MACI domains in the current sample (N = 80)

a

Table 1. Inter-correlation of the global aspect of MACI scales in the sample, controlling for infant age (N = 80)

	1	2	3	4	5	6
1. Maternal sensitivity	-					
2. Maternal non directiveness	0.48**	-				
3. Infant attentiveness	0.21*	- 0.03	-			
4. Infant positive affect	0.08	- 0.08	0.15	-		
5. Infant liveliness	- 0.01	0.10	0.21	- 0.01	-	
6. Mutuality	0.72**	0.38**	0.59**	0.27*	0.17	-
7. Intensity of engagement	0.28*	0.02	0.45**	0.47**	- 0.01	0.47**

*p < 0.05, **p < 0.01.

Table 2. Prenatal measures scores comparison between the followed-up sample (N = 80) and the drop-out (N = 25)

Characteristic	Women followed up postnatally (N= 80)	Drop-out after prenatal phase (N = 25)	Statistics t (103)	p-value
<i>Mean [SD]</i>				
EPDS score	6.40 (4.03)	7.00 (3.80)	0.66	0.51
HADS 1-anxiety	5.56 (3.43)	4.72 (2.67)	-1.13	0.26
HADS 1-depression*	3.39 (2.72)	3.04 (2.86)	-0.55	0.58
OSLO score*	12.14 (2.05)	12.04 (1.67)	-.22	0.83
MFAS score	94.70 (10.10)	91.56 (9.13)	-1.39	0.17
PBI maternal care*	29.16 (8.70)	29.16 (8.51)	-.01	1.00
PBI maternal overprotection	11.85 (6.26)	10.68 (6.60)	-0.81	0.42
PBI paternal care*	26.14; 6 missing (9.75)	23.80 (7.63)	-1.09	0.28
PBI paternal overprotection	11.47; 6 missing (6.93)	11.40 (6.33)	-.05	0.96

*t-test calculation performed for the transformed values (not shown).

Table 3. Comparing own perceived parenting between HSMs and LSMs, controlling for household income

Measure	HSMs (N = 15) Mean [SD]	LSMs (N = 14) Mean [SD]	F (1, 26)	p-value
Maternal care	1.43 [0.21]*	1.41 [0.19]*	0.01	0.93
Maternal overprotection	9.80 [5.51]	13.21 [4.62]	2.41	0.13
Paternal care	1.41 [0.16]*	1.27 [0.41]*	0.41	0.53
Paternal overprotection	10.40 [6.63]	13.93 [6.70]	0.52	0.48

*Value after transformation.

Appendix B: Measures used in the study

Hospital Anxiety and Depression Scale (HADS)

Patients are asked to choose one response from the four given for each interview. They should give an immediate response and be dissuaded from thinking too long about their answers. Instruct the patient to answer how it currently describes their feelings.

I feel tense or 'wound up':

Most of the time

A lot of the time

From time to time, occasionally

Not at all

I still enjoy the things I used to enjoy:

Definitely as much

Not quite so much

Only a little

Hardly at all

I can laugh and see the funny side of things:

As much as I always could

Not quite so much now

Definitely not so much now

Not at all

I get a sort of frightened feeling as if something awful is about to happen:

Very definitely and quite badly

Yes, but not too badly

A little, but it doesn't worry me

Not at all

Worrying thoughts go through my mind:

A great deal of the time

A lot of the time

From time to time, but not too often

Only occasionally

I feel cheerful:

Not at all

Not often

Sometimes

Most of the time

I feel as if I am slowed down:

Nearly all the time

Very often

Sometimes

Not at all

**I get a sort of frightened feeling like
'butterflies' in the stomach:**

Not at all

Occasionally

Quite Often

Very Often

I can sit at ease and feel relaxed:

Definitely

Usually

Not Often

Not at all

I have lost interest in my appearance:

Definitely

I don't take as much care as I should

I may not take quite as much care

I take just as much care as ever

**I look forward with enjoyment to
things:**

As much as I ever did

Rather less than I used to

Definitely less than I used to

Hardly at all

**I feel restless as I have to be on the
move:**

Very much indeed

Quite a lot

Not very much

Not at all

I get sudden feelings of panic:

Very often indeed

Quite often

Not very often

Not at all

**I can enjoy a good book or radio or TV
program:**

Often

Sometimes

Not often

Very seldom

Edinburgh Postnatal Depression Scale (EPDS)

In the past 7 days:

1. I have been able to laugh and see the funny side

of things

- ☐ As much as I always could
- ☐ Not quite so much now
- ☐ Definitely not so much now
- ☐ Not at all

2. I have looked forward with enjoyment to things

- ☐ As much as I ever did
- ☐ Rather less than I used to
- ☐ Definitely less than I used to
- ☐ Hardly at all

*3. I have blamed myself unnecessarily when things went wrong

- ☐ Yes, most of the time
- ☐ Yes, some of the time
- ☐ Not very often
- ☐ No, never

4. I have been anxious or worried for no good reason

- ☐ No, not at all
- ☐ Hardly ever
- ☐ Yes, sometimes
- ☐ Yes, very often

*5. I have felt scared or panicky for no very good reason

- ☐ Yes, quite a lot
- ☐ Yes, sometimes
- ☐ No, not much
- ☐ No, not at all

*6. Things have been getting on top of me:

- ☐ Yes, most of the time I haven't been able to cope at all
- ☐ Yes, sometimes I haven't been coping as well as usual
- ☐ No, most of the time I have coped quite well
- ☐ No, I have been coping as well as ever

*7. I have been so unhappy that I have had difficulty sleeping

- ☐ Yes, most of the time
- ☐ Yes, sometimes
- ☐ Not very often
- ☐ No, not at all

*8. I have felt sad or miserable

- ☐ Yes, most of the time
- ☐ Yes, quite often
- ☐ Not very often
- ☐ No, not at all

*9. I have been so unhappy that I have been crying

- ☐ Yes, most of the time
- ☐ Yes, quite often
- ☐ Only occasionally
- ☐ No, never

*10. The thought of harming myself has occurred to me

- ☐ Yes, quite often
- ☐ Sometimes
- ☐ Hardly ever

Infant Behaviour Questionnaire – Revised

Very Short Form

1	2	3	4	5	6	7	NA
Never	Very Rarely	Less Than Half the Time	About Half the Time	More Than Half the Time	Almost Always	Always	Does Not Apply

When being dressed or undressed during the last week, how often did the baby squirm and/or try to roll away?

1 2 3 4 5 6 7 NA

2. When tossed around playfully how often did the baby laugh?

1 2 3 4 5 6 7 NA

3. When tired, how often did your baby show distress?

1 2 3 4 5 6 7 NA

4. When introduced to an unfamiliar adult, how often did the baby cling to a parent?

1 2 3 4 5 6 7 NA

5. How often during the last week did the baby enjoy being read to?

1 2 3 4 5 6 7 NA

6. How often during the last week did the baby play with one toy or object for 5-10 minutes?

1 2 3 4 5 6 7 NA

7. How often during the week did your baby move quickly toward new objects?

1 2 3 4 5 6 7 NA

8. When put into the bath water, how often did the baby laugh?

1 2 3 4 5 6 7 NA

9. When it was time for bed or a nap and your baby did not want to go, how often did s/he whimper or sob?

1 2 3 4 5 6 7 NA

10. After sleeping, how often did the baby cry if someone doesn't come within a few minutes?

1 2 3 4 5 6 7 NA

11. In the last week, while being fed in your lap, how often did the baby seem eager to get away as soon as the feeding was over?

1 2 3 4 5 6 7 NA

12. When singing or talking to your baby, how often did s/he soothe immediately?

1 2 3 4 5 6 7 NA

13. When placed on his/her back, how often did the baby squirm and/or turn body?

1 2 3 4 5 6 7 NA

14. During a peekaboo game, how often did the baby laugh?

1 2 3 4 5 6 7 NA

15. How often does the infant look up from playing when the telephone rings?

1 2 3 4 5 6 7 NA

16. How often did the baby seem angry (crying and fussing) when you left her/him in the crib?

1 2 3 4 5 6 7 NA

17. How often during the last week did the baby startle at a sudden change in body position (e.g., when moved suddenly)?

1 2 3 4 5 6 7 NA

18. How often during the last week did the baby enjoy hearing the sound of words, as in nursery rhymes?

1 2 3 4 5 6 7 NA

19. How often during the last week did the baby look at pictures in books and/or magazines for 5 minutes or longer at a time?

1 2 3 4 5 6 7 NA

20. When visiting a new place, how often did your baby get excited about exploring new surroundings?

1 2 3 4 5 6 7 NA

21. How often during the last week did the baby smile or laugh when given a toy?

1 2 3 4 5 6 7 NA

22. At the end of an exciting day, how often did your baby become tearful?

1 2 3 4 5 6 7 NA

23. How often during the last week did the baby protest being placed in a confining place (infant seat, play pen, car seat, etc.)?

1 2 3 4 5 6 7 NA

24. When being held, in the last week, did your baby seem to enjoy him/herself?

1 2 3 4 5 6 7 NA

25. When showing the baby something to look at, how often did s/he soothe immediately?

1 2 3 4 5 6 7 NA

26. When hair was washed, how often did the baby vocalize?

1 2 3 4 5 6 7 NA

27. How often did your baby notice the sound of an airplane passing overhead?

1 2 3 4 5 6 7 NA

28. When introduced to an unfamiliar adult, how often did the baby refuse to go to the unfamiliar person?

1 2 3 4 5 6 7 NA

29. When you were busy with another activity, and your baby was not able to get your attention, how often did s/he cry?

1 2 3 4 5 6 7 NA

30. How often during the last week did the baby enjoy gentle rhythmic activities, such as rocking or swaying?

1 2 3 4 5 6 7 NA

31. How often during the last week did the baby stare at a mobile, crib bumper or picture for 5 minutes or longer?

1 2 3 4 5 6 7 NA

32. When the baby wanted something, how often did s/he become upset when s/he could not get what s/he wanted?

1 2 3 4 5 6 7 NA

33. When in the presence of several unfamiliar adults, how often did the baby cling to a parent?

1 2 3 4 5 6 7 NA

34. When rocked or hugged, in the last week, did your baby seem to enjoy him/herself?

1 2 3 4 5 6 7 NA

35. When patting or gently rubbing some part of the baby's body, how often did s/he soothe immediately?

1 2 3 4 5 6 7 NA

36. How often did your baby make talking sounds when riding in a car?

1 2 3 4 5 6 7 NA

37. When placed in an infant seat or car seat, how often did the baby squirm and turn body?

1 2 3 4 5 6 7 NA

Oslo 3-items social support scale

1. How easy can you get help from friends/neighbors if you should need it?

1. Very easy 2.Easy 3.Possible 4.Difficult 5.Very difficult

2. How many people are so close to you that you can count on them if you have serious problems?

0. None 1.1-2 2.3-5 3. 5+

3. How much concern do people show in what you are doing?

1. A lot 2.Some 3.Uncertain 4.Little 5.No concern.

Parent Bonding Instrument (PBI): MOTHER FORM *

As you remember your MOTHER in your first 16 years would you place a tick in the most appropriate box next to each question

	Likely	Moderately likely	Moderately unlikely	Very unlikely
Spoke to me in a warm and friendly voice				
Did not help me as much as I needed				
Let me do those things I liked doing				
Seemed emotionally cold to me				
Appeared to understand my problems and worries				
Was affectionate to me				
Liked me to make my own decisions				
Did not want me to grow up				
Tried to control everything I did				
Invaded my privacy				
Enjoyed talking things over with me				
Frequently smiled at me				
Tended to baby me				
Did not seem to understand what I needed or wanted				
Let me decide things for myself				
Made me feel I wasn't wanted				
Could make me feel better when I was upset				
Did not talk with me very much				
Tried to make me feel dependent on her/him				
Felt I could not look after myself unless she/he was around				
Gave me as much freedom as I wanted				
Let me go out as often as I wanted				
Was overprotective of me				
Did not praise me				
Let me dress in any way I pleased				

***Father form is typical**

Childhood Trauma Questionnaire

When I was growing up..	Never true	Rarely true	Sometimes true	Often true	Very often true
1.I didn't have enough to eat					
2. I knew that there was someone to take care of me and protect me					
3.People in my family called me things like stupid, lazy, or ugly					
4.My parents were too drunk or high to take care of the family					
5.There was someone in my family who helped me feel that I was important or special					
6.I had to wear dirty clothes					
7.I felt loved					
8.I thought that my parents wished I had never been born					
9.I got hit so hard by someone in my family that I had to see a doctor					
10.There was nothing I wanted to change about my family					
11.People in my family hit me so hard that it left me with bruises					
12.I was punished with a belt, a board or some other hard object					
13.People in my family looked out for each other					
14.People in my family said hurtful or insulting things to me					
15.I believe that I was physically abused					
16.I had a perfect childhood					
17.I got hit or beaten so badly that it was noticed by someone like, teacher or doctor					
18.I felt that someone in my family hated me					
19.People in my family felt close to each other					
20.Someone tried to touch me in a sexual way, or tried to make me touch them					
21.Someone threatened to hurt me or tell lies about me unless I did something sexual with them					
22.I had the best family in the world					
23.Someone tried to make me do sexual things or watch sexual things					
24.Someone molested me					
25.Ibelieve that I was emotionally abused					
26.There was someone to take me to doctor if I needed it					
27.I believe that I was sexually abused					
28.My family was source of strength and support					

Maternal –Fetal Attachment Scale

I think or do the following	Definitely yes	Yes	Uncertain	No	Definitely no
1.I talk to my unborn baby					
2.I feel all the trouble of being pregnant is worth it					
3.I enjoy watching my tummy jiggle as the baby kicks inside					
4.I pictures myself feeding the baby					
5.I'm really looking forward to seeing what the baby looks like					
6.I wonder if the baby feels cramped in there					
7.I refer to my baby by a nickname					
8.I imagine myself taking care of the baby					
9.I can almost guess what my baby's personality will be from the way s/he move around					
10.I have decided on a name for a girl baby					
11.I do things to try to stay healthy that I would not do if I were not pregnant					
12.I wonder if my baby can hear inside of me					
13.I have decided on a name for a boy baby					
14.I wonder if the baby thinks and feels things inside of me					
15.I eat meat and vegetables to be sure my baby gets a good diet					
16.It seems my baby kicks and move to tell me its eating time					
17.I poke my baby to get him/her to poke back					
18.I can hardly wait to hold the baby					
19.I try to picture what the baby will look like					
20.I stroke my tummy to quiet the baby when there is too much kicking					
21.I can tell that the baby has hiccups					
22.I feel my body is ugly					
23.I give up doing certain things because I want to help my baby					
24.I grasp my baby's foot through my tummy to move it around					

Brief description of the Manchester Assessment of Caregiver-Infant Interaction (MACI)

Domain	Description	Scale extremes
Caregiver		
Sensitive responsive-ness	The identification of, and behavioural response to, infant behaviour and signals that are contingent and appropriate to meet the infant's immediate and developmental needs. An attentive attitude, appropriate engagement, support and structuring in response to infant behaviour (and lack of behaviour).	1=Minimally sensitively responsive 7=Very sensitively responsive
Non-directiveness	A focus on the infant's experience and agenda as opposed to a caregiver-directed focus. High 'non-directiveness' includes accepting and encouraging non-intrusive behaviour, and positive comments reflecting the infant's experience. Low 'non-directiveness' includes demanding, intrusive, and negative behaviours and comments directed at the infant not at the service of promoting infant-initiated behaviour.	1=Highly directive 7=Highly non-directive
Infant		
Attentiveness to parent	The amount of visual contact with and amount and quality of interest in the parent directly (particularly in younger infants) and/or through mutual focus in a joint activity (particularly in older infants) as opposed to focus on other environmental stimuli or self-absorption. Considerations include infant body/face orientation toward the caregiver and interest in and acceptance of objects demonstrated by the parent, imitation and social referencing.	1=Inattentive 7=Very highly attentive
Positive affect	The amount and extent of positive mood, which includes positive expression and vocalisation, and enthusiasm, weighed against negative affect and behaviour, including negative expression, vocalisation and bodily gestures.	1=Highly negative affect 7=Highly positive affect
Liveliness	The level of physical activity, independent of the nature of the activity, weighting particularly behaviour initiated by the infant spontaneously over that which is in response to the mother's actions. Reflex movements and those controlled by the parent (e.g. by manipulating limbs) are not included.	1=Unlively 7=Extremely lively
Dyadic		
Mutuality	The degree of dyadic togetherness, 'tunefulness', and sharedness of the play experience, including shared attention, infant acceptance of maternal involvement, playing together, interactive flow, and shared body orientation.	1=Very low mutuality 7=Very high mutuality
Intensity of engagement	The intensity (not quantity) of mutual engagement at its most optimal point, either directly or through mutual focus on a third object. Intensity rates higher with level of interest and positivity, and includes smiles, vocalisations, deepening of interest, and peaks of infant excitement, with laughter or mirroring.	1=Almost no engagement 7=Very intense engagement

Participant declaration form

PATIENT DECLARATION – TO BE COMPLETED BEFORE EXAMINATION COMMENCES

Please answer the following confidential questions by circling YES or NO to each one. Some of the items mentioned (marked with *) may interfere with the quality of the pictures obtained during your scan and, in a few cases, can be hazardous to your safety.

If you do not understand any of the questions please ask a member of staff to help you.

- * 1 Do you have a pacemaker or artificial heart valve? YES/NO
- * 2a Do you have a hydrocephalus shunt? YES/NO
- * 2b If so, is it a programmable shunt? YES/NO
- 3 Have you had any operations on your head? YES/NO
- 4 Have you had any surgery to you head or body within the last two months? YES/NO
- 5 Do you have any joint replacements or metal implants? YES/NO
- * 6 Have you EVER had metal in your eyes or worked with metal at high speed, eg: in a machine shop? YES/NO
- 7 Do you have any shrapnel from a war injury? YES/NO
- 8 Do you wear a false limb, calliper or brace? YES/NO
- 9 Do you have dentures, a dental plate or a hearing aid? YES/NO
- 10 Have you suffered from epilepsy or blackouts? YES/NO
- 11 Do you have any ear implants, e.g. cochlear? YES/NO

TO BE ANSWERED BY WOMEN OF CHILD BEARING AGE

- a Do you have any intrauterine contraceptive device or coil? YES/NO
- * b Could you be pregnant? YES/NO

I confirm that I have read the above questions and that my answers are correct to the best of my knowledge and belief.

Signed: _____ Date: _____