Infant Regulatory Problems: Neurodevelopmental Vulnerability and Sensitive Parenting

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Declaration

Chapters one to six have been carried out entirely by myself. To the best of my knowledge it does not contain any materials previously published or written by another person except where due reference is made in the text. Contributions to the four research papers by others are as follows:

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- Dieter Wolke- planning, supervision of analysis, revisions
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Signature: Date:

Abstract

Infant regulatory problems (crying, sleeping, feeding) are a common concern for parents and practitioners. Although there is now good evidence of the long-term adverse influences of infant regulatory problems on mental health, in particular if they co-occur together (multiple regulatory problems), important gaps remain regarding the precursors of regulatory problems. In particular, it is unclear whether and how sensitive parenting and/or neurodevelopmental vulnerability are involved in the development of multiple regulatory problems. Furthermore, do regulatory problems impair the development of the infants' relationship to their mothers, i.e. attachment? This thesis explores neurodevelopmental vulnerability and sensitive parenting as precursors of multiple regulatory problems, and whether multiple regulatory problems increase the likelihood of insecure and/or disorganised attachment.

The thesis consists of four studies and uses preterm birth as a natural model to assess neurodevelopmental vulnerability due to the interruption caused by preterm birth on the key processes of brain development. Study 1, a meta-analysis, explored the relationship between neurodevelopmental vulnerability and maternal sensitivity by comparing maternal sensitivity in preterm and full-term infants. Findings indicate that having an infant with neurodevelopmental vulnerability does not alter mothers' sensitive parenting. In Study 2, using the Growth of at risk Infants (GAIN) study, the effect of neurodevelopmental vulnerability on regulatory problems across the first 18 months was investigated. Very preterm/very low birth weight infants experienced more multiple regulatory problems at term and 18 months compared to full-term infants. In Study 3, the longitudinal relationship between neurodevelopmental vulnerability, maternal sensitivity and multiple regulatory problems across infancy

was explored allowing for reciprocal associations between maternal sensitivity and multiple regulatory problems across infancy. Both maternal sensitivity and multiple regulatory problems were moderately persistent from term to 18 months. Consistent with our previous findings, it was revealed that neurodevelopmental vulnerability had an enduring impact on multiple regulatory problems. On the other hand, maternal sensitivity at term had only a short-term negative impact on multiple regulatory problems at 3 months. No evidence for a reciprocal influence of maternal sensitivity and multiple regulatory problems was found. Finally, Study 4 examined whether early multiple regulatory problems at 3 and 6 months increase the likelihood of insecure and/or disorganised attachment. Findings revealed that multiple regulatory problems as early as 3 months increased the risk of both insecure and in particular, disorganised attachment at 18 months.

In conclusion, neurodevelopmental vulnerability increases the risk of multiple regulatory problems, which are moderately persistent across the first 18 months of life. Furthermore, multiple regulatory problems do not impair maternal sensitivity but have adverse effects on the infants' relationship with their mothers by increasing the risk of insecure and disorganised attachment. Clinicians should be aware that multiple regulatory problems are a significant potential risk factor for poorer infant-mother relationship.

Structure of Thesis

Chapter 1 provides a general background on the development of regulatory behaviours and regulatory problems during infancy, detailing the outcomes of regulatory problems, and introducing the key explanations for the development of regulatory problems, including neurodevelopmental vulnerability, parenting and genetics.

Chapter 2 presents evidence for a neurodevelopmental explanation of the development of regulatory problems, introduces prematurity as a model to examine neurodevelopmental vulnerability and describes how prematurity is associated with regulatory problems.

Chapter 3 outlines how insensitive parenting may increase the odds of developing regulatory problems reviewing the relevant literature.

Chapter 4 provides a literature review about the development of attachment and reviews evidence on the association between early regulatory problems and attachment.

Chapter 5 outlines the research questions that guided the four studies included in this thesis.

Chapter 6 establishes the methodological processes underlying the research, outlining the relevant methods and measures used in each of the studies.

Chapters 7, 8, 9 and 10 consist of the four studies presented in this thesis, respectively.

Chapter 11 summarises the four studies, and provides an integrative discussion of the key findings. Strengths and limitations of the research are discussed, and implications and suggestions for future research and clinical practice are identified.

Chapter 1 Overview of Infant Regulatory (crying, sleeping, feeding) Problems

This chapter will present an overview of infant regulatory problems focusing on the definition and outcomes of infant regulatory problems. Finally, underlying mechanisms of infant regulatory problems will be briefly outlined; however, these will be described in more detail in the following chapters (chapter 2 and 3).

Normal Pattern of Regulatory Behaviours (crying, sleeping and feeding) during Infancy

Since birth, infants require adequate sleep and nutritional intake to reach optimal physical growth and cognitive/behavioural development (Dahl, 2007; St James-Roberts, 2012). Additionally, crying behaviour is the only mean of communication for infants to signal their needs (Brazelton, 1962). During the first few months of life, crying, sleeping, and feeding behaviours are subject to rapid change and development (St James-Roberts, 2012). It has been argued that these rapid changes are related to the maturation of infant's brain and central nervous system (Halpern, MacLean, & Baumeister, 1995; Kohyama, 1998).

Fussing and Crying

With respect to crying behaviour, it has been suggested that the majority of infants follow a similar crying pattern: they cry more during the first 3 months with a peak around 6 or 8 weeks of age (Barr, 1990), which decreases after 3 to 4 months (Brazelton, 1962; Lee, Barr, Catherine, & Wicks, 2007). Furthermore, the peak

crying usually occurs during the late afternoon and evening hours (St James-Roberts & Halil, 1991). This pattern of crying has been suggested to be similar in both Western cultures (Alvarez, 2004; Barr, 1990) and hunter-gatherer societies (Barr, Konner, Bakeman, & Adamson, 1991; St James-Roberts, Bowyer, Varghese, & Sawdon, 1994).

Sleeping

The normal development of infant sleep consists of two domains: the transition from fragmented to consolidated sleep, and a gradual decline in sleep needs (Sadeh, Raviv, & Gruber, 2000). A newborn infant spends two thirds of the day sleeping (Anders & Keener, 1985; Mindell, Owens, & Carskadon, 1999), which is distributed throughout the day and night with short durations (Davis, Parker, & Montgomery, 2004). At around 6 weeks to 3 months of age, circadian rhythm, which is more sleep during the day than night, will slowly emerge (Bramford et al., 1990; Davis, Parker, & Montgomery, 2004). During the first 3 months, few infants will sleep through the night. Therefore, it is very common for infants to wake up throughout the night; however, some infants are able to soothe themselves back to sleep without giving a signal to parents (Anders, Halpern, & Hua, 1992; St James-Roberts, 2012). Frequency of nocturnal awakenings may vary according to feeding type (breast-fed, formula-fed, mix-fed) and bed sharing (Hysing et al., 2014; Wolke, 1994). Infants who are breastfed have more frequent nocturnal awakenings in comparison to formula-fed infants or mix-fed infants (Kaley, Reid, & Flynn, 2012; Wolke, Meyer, Ohrt, & Riegel, 1995b).

Overall, infant sleep will gradually shift to more nocturnal sleep during the first year of life (Henderson, France, Owens, & Blampied, 2010; Iglowstein, Jenni, Molinari, & Largo, 2003) and nocturnal wakings will gradually decrease from 6 to 18 months

(Hysing et al., 2014; Palmstierna, Sepa, & Ludvigsson, 2008). Additionally, infancy is considered to be the period with the highest inter-individual variability of sleep duration (Bruni et al., 2014).

A recent systematic review (Galland, Taylor, Elder, & Herbison, 2012) analysed findings from 34 studies to examine the normal patterns of infant sleeping in terms of sleep duration and number of night wakings. Findings from this study revealed that infants sleep approximately 13 hours a day with night wakings ranging from 0 to 3.4 times per night. Furthermore, the largest individual variability in sleep duration was during the first few months. In another review study, the duration of longest sleep without awakening and the longest self-regulated sleep (being able to self-soothe back to sleep) during the first year of life was investigated (Henderson, France, & Blampied, 2011). Findings confirmed that the most important changes in sleep happen during the first two months of life. First, longest sleep duration without awakening ranged from 3 to 4.5 hours at one month of age, which increased to 6.2 hours at two months of age. Second, the longest self-regulated sleep duration ranged from 4.6 hours to 5.6 hours at one month of age but increased to 5.6 hours to 8.8 hours at two months of age. From 3 months onwards, changes in infants' sleep patterns become more gradual in comparison to changes during the first 2 months.

Feeding

Normal development of infant feeding first requires the coordination of infant oral-motor skills such as sucking, swallowing and breathing (Goldfield, Richardson, Lee, & Margetts, 2006), which develops throughout the first 6 months of age (Paul, Dittrichova, & Papousek, 1996). During this period, mothers are generally advised to exclusively breastfeed their infants and gradually introduce solid foods thereon (Kramer & Kakuma, 2002).

The frequency of infant feeding is dependent on the feeding method. To illustrate, breastfed infants are being fed more frequently in comparison to formula-fed or mixed fed infants since breast milk moves through the digestive system faster than formula and it is less easy to ascertain how much has been fed (Kaley et al., 2012; Wolke, Meyer, Ohrt, & Riegel, 1995a). Several studies support that breastfeeding is beneficial to healthy development of the infant and should be the preferred method of feeding (Anderson, Johnstone, & Remley, 1999; Ip et al., 2007).

Successful feeding experiences gradually become a social event, with opportunities to reinforce the mother-infant interaction and bonding (Morawska, Laws, Moretto, & Daniels, 2014). Approximately at 6 months of age, infants would be ready to initiate self-feeding gradually (Chatoor, Schaefer, Dickson, & Egan, 1984). By 15 to 18 months of age, the majority of infants will acquire self-feeding skills (Carruth, Ziegler, Gordon, & Hendricks, 2004), which develop rapidly during infancy based on neurological maturation and experiential learning (Reilly, Skuse, & Wolke, 2006; Stevenson & Allaire, 1991; Wolke, 1994).

Infant Regulatory (Crying, sleeping, feeding) Problems

Being able to self-regulate is a critical skill that infants develop, which allows them to self-soothe in response to changes in sensory stimuli, and regulate sleep states (Papoušek, 2011). Difficulties in self-regulation such as excessive crying, sleeping disturbances and feeding problems are often labelled as infant regulatory problems (Hemmi, Wolke, & Schneider, 2011; Popp et al., 2016). Approximately 20% of infants experience any one of these problems during the first year of life (Hemmi et al., 2011); a smaller percentage (4 to 10%) of infants experience two of these problems concurrently while 1 to 2% of infants experience all three problems at the same time (Schmid, Schreier, Meyer, & Wolke, 2010). Furthermore, regulatory

problems during infancy predict stable trajectories of behavioural dysregulation across childhood (Winsper & Wolke, 2014).

Despite the importance of regulatory problems, there has been no agreement yet regarding their definition, however, there are several suggestions (Popp et al., 2016). Inconsistencies in the definition have resulted in a large variability in prevalence estimates. In the following sections, differences in existing definitions of single and multiple regulatory problems will be discussed with a focus on studies that have provided empirical prevalence estimates.

Crying Problems

Infants with excessive crying beyond the age of 3 to 4 months have been considered as having a crying problem (St James-Roberts, 2012; Wolke, Gray, & Meyer, 1994). According to findings of a systematic review, researchers used 10 different criteria to assess infant crying problems (Reijneveld, Brugman, & Hirasing, 2001) with a focus mainly on the duration of crying and whether parents report it as a problem (Canivet, Hagander, Jakobsson, & Lanke, 1996; Estep & Kulczycki, 2000). Regarding the duration of crying, the most widely cited definition of crying problems are the Wessel's criteria (1954), which are commonly known as the rule of 3's: fussing or crying lasting for more than a total of three hours a day and occurring on more than three days for at least three weeks (Wessel, Cobb, Jackson, Harris, & Detwiler, 1954). Nevertheless, this definition has been revised more recently to focus on the cry duration during one week since it was suggested as not practical for clinicians to wait for 3 weeks to assess the problem (Lehtonen, Gormally, & Barr, 2000).

When assessed according to Wessel's criteria (1954), the prevalence of excessive crying was found to be 5.8% beyond 3 months of age and 2.5% beyond 6 months of

age (von Kries, Kalies, & Papousek, 2006). Based on the same measure, another study showed similar percentages, which was 4.6% at 3 months, and 2% at 6 months of age (Barr, Rotman, Yaremko, Leduc, & Francoeur, 1992).

When mothers were asked to report whether their infant's crying is a problem (Wake et al., 2006), the prevalence of crying problems was 12.8% at 4 months of age. Similarly by asking the mother whether compared to infants of the same age her infant cried more, the prevalence of crying problems were shown to be 11.9% at 3 months of age (Santos, Matijasevich, Capilheira, Anselmi, & Barros, 2015).

Schmid, Schreier, Meyer and Wolke (2011) measured crying problems at 5 months with a range of criteria: crying 120 minutes or more during the day, crying amount is above average, infant is difficult to soothe and/or consistently irritable. According to this large-scale study, the prevalence of crying problems at 5 months was 4.7%. In a similar study, Wolke et al. (1995a) assessed crying problems at 5 months with the same criteria, finding a prevalence of 20.1%.

In summary, the prevalence of infant crying problems varies according to the definition applied by researchers. Therefore, findings from each study have to be carefully evaluated based on the assessment criteria for a crying problem.

Sleeping Problems

During the early weeks, all infants wake up during the night for feeding (Lozoff, Wolf, & Davis, 1985) and the sleep-wake cycle is still in the process of establishment (Sidor, Fischer, Eickhorst, & Cierpka, 2013). However, after 3 months of age, the majority of infants acquire the skill to settle back into sleep themselves when they wake up during the night. The inability to achieve this skill has been suggested as the main explanation of the development of infant sleeping problems

(St James-Roberts, 2012). Since sleeping problems during early infancy might persist into later life and become chronic (Pollock, 1992; Simard, Nielsen, Tremblay, Boivin, & Montplaisir, 2008; Wolke et al., 1995b; Zuckerman, Stevenson, & Bailey, 1987), it remains crucial to identify the problems as early as possible. Armstrong, Quinn, and Dadds (1994) highlighted that parents reported sleeping problems even before 3 months of age. Although sleeping problems cannot be diagnosed before 3 to 6 months of age, early symptoms may still be markers for emerging sleeping problems.

Early definition of sleeping problems included the following symptoms: waking up 2 times or more during a night, waking for 20 minutes during a night, requiring parental presence to fall asleep or refusing to go to bed for more than 30 minutes, and mother reports severe sleep disruption (Richman, 1981; Zuckerman et al., 1987). More recently, Sadeh, Mindell and Rivera (2011) revealed that night wakings and sleep onset latency are the two core factors of a sleeping problem. Furthermore, it was confirmed by parents that they consider their infants' sleep as problematic if they have frequent night wakings and difficulties falling asleep (Bruni et al., 2014). However, Hiscock and Fisher (2015) argued that the most useful definition for sleeping problems would be the parental experiences, which is, if the parent thinks infant's sleep is problematic.

Teng, Bartle, Sadeh, and Mindell (2012) conducted a large-scale study in Australia and New Zealand to examine the patterns of sleep problems during infancy based on parental views of the problem. According to the findings of this study, 31.2% of parents viewed their infant as having a sleeping problem during the first 2 months. This percentage increased to 38.9% by 12 months and slightly reduced to 33.3% by 18 months. A similar study was conducted in the United States (Byars, Yolton,

Rausch, Lanphear, & Beebe, 2012) that examined the sleep problems prevalence based on parental report. This revealed that the prevalence of sleeping problems was approximately 10% at 6, 12, and 24 months. Furthermore, they reported that 21% to 35% of infants who had sleeping problems at one time point continued to have sleeping problems at later assessments. Finally, a large-scale binational study assessed the patterns of night waking, difficulties falling asleep and parental distress in Southern Finland and Southern Germany at 5, 20 and 56 months of age (Wolke, Sohne, Riegel, Ohrt, & Osterlund, 1998). The prevalence of night waking (≥ 2 per night) in very preterm infants was approximately 25% at 5 months, 22.5% at 20 months and 7% at 56 months of age in Southern Finland. In Southern Germany, the prevalence of night waking was approximately 14% at 5 months, 15% at 20 months and 12 % at 56 months in very preterm infants.

Schmid et al. (2011) measured the prevalence of sleeping problems with the definition of waking up two times or more and/or waking up for at least 15 minutes per night. When these criteria were used at 5 months of age, the prevalence of sleeping problems was 9.7%. Using a similar definition, von Kries et al. (2006) revealed that the prevalence of sleeping problems was 13% during the first year of life.

Overall, sleeping problems during infancy are quite common. The prevalence ranges from approximately 10% to 30% (Armstrong et al., 1994; Byars et al., 2012).

Feeding Problems

Feeding disorders have been recognised in diagnostic classification systems such as the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013); International Statistical Classification of Diseases

(ICD-10-CM; World Health Organisation, 1992) and Diagnostic Classification of Mental Health and Developmental Disorder of Infancy and Early Childhood (DC: 0-3R, ZERO TO THREE, 2005). Although generally focused on significant nutritional deficiency, these classification systems lack agreement (Kerzner et al., 2015).

Apart from the clinical diagnostic criteria of feeding disorders, numerous researchers have presented their own criteria and operational definitions for assessing feeding problems during infancy. Early on, Dahl and Sundelin (1986) defined feeding problems as refusal to eat, colic and vomiting. Similarly, another Swedish group of researchers (Bohlin, Hagekull, Lindberg, Thunstrom, & Engberg, 1995; Lindberg, Bohlin, & Hagekull, 1991) identified the most common feeding problems as early colic, refusal of solid food, poor appetite, and general refusal to eat based on parent and nurse ratings. More recently, feeding problems have been proposed to have the following core symptoms: limited appetite, little interest in feeding, selective food intake, or fear of feeding (Benjasuwantep, Chaithirayanon, & Eiamudomkan, 2013; Kerzner, 2009).

Apart from cross-sectional studies, infant feeding disorders have also been examined longitudinally using large samples. First, in a large UK cohort study, researchers investigated the prevalence of infant feeding problems such as oral-motor dysfunctions, poor appetite and avoidant eating at 6 weeks, 8 months and 12 months of age (Wright, Parkinson, & Drewett, 2006). Findings from this study revealed that at 6 weeks of age, 2.6% of infants had poor appetite and 5.3% of them had high oral-motor dysfunction. The percentage of infants who had poor appetite increased further from 8 months (9.3%) to 12 months (12.4%). Similarly, there was an increase in the percentage of infants with avoidant eating from 8 months (16.7%) to 12 months (19.8%). Another large cohort study from the UK (Motion, Northstone, Emond, &

The Alspac Study Team, 2001) assessed feeding problems as weak sucking and choking, and reported that the prevalence for feeding difficulties was 1% at 4 weeks of age, 3.4% at 6 months and 3.3% at 15 months. In addition, a large cohort study from Germany that focused on oral-motor difficulties, vomiting and not eating/drinking well, reported that the prevalence of feeding problems was 10.7% at 5 months, 8.9% at 20 months and 16.5% at 56 months of age (Schmid et al., 2010).

All in all, picky eating, food refusal, and oral-motor difficulties such as difficulties in sucking and/or vomiting, have been the major symptoms investigated by researchers (Art-Rodas & Benoit, 1998; Bryant-Waugh, Markham, Kreipe, & Walsh, 2010; Dahl & Sundelin, 1986; Wolke, Schmid, Schreier, & Meyer, 2009). These factors were additionally identified by parents of infants aged between 7 and 18 months as the main feeding problems (Lindberg et al., 1991). In addition to examining infant behaviours, other researchers focused on whether parents think their infant has a feeding problem or not (Davies et al., 2006).

Despite the inconsistency in the definition, feeding problems are a major concern during infancy and toddlerhood with a prevalence rate of approximately 20% to 30% in healthy infants (Benjasuwantep et al., 2013; Carruth, Ziegler, Gordon, & Barr, 2004; Wright, Parkinson, Shipton, & Drewett, 2007). The age of onset of these problems define the severity and duration of the consequent eating problems (Arts-Rodas & Benoit, 1998; Skuse, 1993); therefore, recognition of problems during infancy is crucial.

Infant Multiple Regulatory Problems

When infants experience regulatory problems in one area (crying, sleeping, or feeding) beyond three months of age, they are likely to have difficulties in another

area simultaneously (Schmid et al., 2010; St James-Roberts, 2012; von Kries et al., 2006; Wolke et al., 1995a). Having two or more regulatory problems at the same time has been defined as multiple regulatory problems (Hemmi et al., 2011). Nevertheless, the same concept has been referred to in different terms in the literature.

Infants who have multiple regulatory problems have been also referred as 'regulatory disordered' (Degangi, Dipietro, Greenspan, & Porges, 1991). Degangi, Breinbauer, Doussard-Roosevelt, Porges and Greenspan (2000) suggested infant regulatory disorders be defined as including the following: a) poor self-regulation (irritability, inconsolability, demandingness, and poor self-calming) and b) movement and/or tactile hypersensitivities. Furthermore, the severity of the disorder might increase if the following symptoms are also present: inattention, problems with visual processing, and poor emotional/behavioural control. However, this definition is too broad and not practical. Moreover, classification systems include infant regulatory problems in the category called as 'regulation disorders of sensory processing' (DC: 0-3R; ZERO to THREE, 2005). This diagnosis incorporates sleeping problems, feeding problems, sensory and sensomotoric problems as sub-categories. Although this classification has been suggested as useful in clinical practice, it still lacks support from empirical evidence (Degangi & Breinbauer,1997; Degangi et al., 2000; Postert, Averbeck-Holocher, Achtergarde, Muller, & Furniss, 2012). Additionally, it lacks crying problems as a separate sub-category, which has been considered as an important symptom in regulatory problems (Hofacker & Papoušek, 1998).

A clinically useful definition of regulatory disorders was suggested by the German Society of Child and Adolescent Psychiatry (2007), including a combination of the following three indicators: a) infant behavioural problems (excessive crying, sleeping

disorders, feeding disorders, reluctance/inability to play with chronic agitation, persistent and exaggerated shyness, excessive oppositional behaviour, aggressive behaviour, lack of interest), b) parent-infant interaction problems and c) parental stress. Nevertheless, practical examination of these guidelines yielded that it is feasible to use crying, sleeping and feeding problems as the core definition of regulatory disorder (Postert et al., 2012).

A large-scale study conducted in Germany revealed that 17% of infants had multiple regulatory problems at 3 months (Becker, Holtmann, Laucht, & Schmidt, 2004). Furthermore, following the suggestions of German Society of Child and Adolescent Psychiatry (2007), another large-scale study examined 4427 infants in regards to crying, sleeping, and feeding problems (Schmid et al., 2010) and revealed that the prevalence of multiple regulatory problems (two or more symptoms) was 4.4% at 5 months (Schmid et al 2010). In a clinical referral study, it was shown that 52% of crying problems, 48% of feeding problems and 46% of sleeping problems overlapped with problems in the other regulatory areas at 5 months of age (Wolke et al., 1995). Thus, a number of longitudinal studies have adapted a definition of multiple regulatory problems (having two or more of the following symptoms: excessive crying, difficulties in sleeping and problematic feeding).

Outcomes of Regulatory Problems (crying, sleeping, feeding)

There is increasing evidence that infant regulatory problems (crying, feeding and sleeping) are associated with childhood behaviour problems. In a meta-analysis study (Hemmi et al., 2011), 22 longitudinal studies were systematically analysed to understand the impact of early regulatory problems on behavioural outcomes. Results from this meta-analysis revealed that children with infant regulatory problems had more behavioural problems than controls and that the associations with dysregulation

problems such externalizing problems and ADHD were the strongest (Hiscock, Canterford, Ukoumunne, & Wake, 2007; Postert et al., 2012; Reid, Hong, & Wade, 2009). Furthermore, the risk of having behaviour problems increased if infants experienced persistent or multiple regulatory problems or had more family adversity.

Since the publication of the meta-analysis study in 2011, several longitudinal studies confirmed the finding that regulatory problems result in adverse negative impacts on behaviour in childhood and even adolescence (Choe, Sameroff, & McDonough, 2013; Hyde, O'Callaghan, Bor, Williams, & Najman, 2012; Price, Wake, Ukoumunne, & Hiscock, 2012; Sheridan et al., 2013; Sidor et al., 2013; Sivertsen et al., 2015). Santos et al. (2015) showed that infants who had excessive crying at 3 months had more internalizing and externalizing problems at 72 months. Infants who had multiple regulatory disorders during the first year had high scores on behavioural problems or disturbed sensory reactivity during early childhood (Dale et al., 2011a; Östberg & Hagelin, 2011; Rask, Ørnbøl, Olsen, Fink, & Skovgaard, 2013). Similar results were found in a study that followed infants clinically diagnosed with regulatory disorders from when they were 3 to 47 months old until 6.1 to 15.3 years of age indicating higher proportions of affective problems, anxiety problems, attention deficit/hyperactivity problems, oppositional defiant problems, and conduct problems when compared to a norm group (Bron, van Rijen, van Abeelen, & Lambregtse-van den Berg, 2012). Furthermore, Barnevik-Olsson, Carlsson, Westerlund, Gillberg, and Fernell (2013) linked early regulatory problems to the development of autism. Lastly, Quach, Hiscock, Canterford, and Wake (2009) revealed that four to five year-old infants with persistent sleeping problems had the poorest quality of life two years later.

Despite the fact that several studies examined the longitudinal impact of regulatory problems, so far only a limited number of them focused on their impact during infancy (18 months period). Early studies that examined the impact of excessive crying on mental and psychomotor development of the infant revealed somewhat conflicting findings (Sloman, Bellinger, & Krentzel, 1990; Stifter & Braungart, 1992). To illustrate, Sloman, Bellinger and Kretzel (1990) revealed that excessive crying resulted in negative mental and psychomotor development at 6 months with no impacts when assessed later on at 12, 18, and 24 months of age. On the other hand, Stifter and Braungart (1992) found that infants with and without colic had similar scores on mental development tests at both 5 and 10 months of age. In a more recent study (Sidor et al., 2013), a significant but low negative association was found between crying and sleeping problems during the first 6 months and social development at 12 months of age.

Other than their negative impact on child behaviour, infant regulatory problems have been related to negative outcomes in parents' behaviour and well-being. To illustrate, mothers who had an infant younger than 6 months had increased levels of frustration when being exposed to prolonged unsoothable crying (Barr et al. 2014). Similarly, sleeping problems in infants who were 3 to 6 months old resulted in poorer maternal mental and physical health in comparison to mothers of infants without a sleeping problem (Bayer, Hiscock, Hampton, & Wake, 2007). Additionally, mothers of infants with sleeping problems had moderate levels of fatigue, which in turn resulted in low parental efficacy and low parental warmth (Giallo, Rose, & Vittorino, 2011). Furthermore, increased levels of crying during early infancy, and mothers' inability to soothe their infant increased depressive symptoms in the mothers of both healthy infants (Radesky et al., 2013) and clinically referred infants (Maxted et al., 2005).

All in all, studies of regulatory problems during infancy have mainly focused on infants' mental and psychomotor development as well as maternal mental health. On the other hand, there is a lack of studies focused on the association between regulatory problems and attachment development during infancy. Since the negative influence of maternal mental health problems on attachment is underlined (Murray & Cooper, 1997), regulatory problems are also likely to be associated to attachment development. Moreover, it is crucial to focus more on the impact of regulatory problems on attachment patterns since their influence on cognitive development is small (Wolke et al., 2009).

Potential Underlying Mechanisms of Infant Regulatory Problems

Although several studies focused on the severity of the outcomes of infant regulatory problems, it remains unclear how regulatory problems develop. Three main possible mechanisms have been suggested to contribute to the development of infant regulatory problems: genetic vulnerability, neurodevelopmental vulnerability, and parenting.

Genetic vulnerability has been shown to be an important factor in the development of childhood psychopathology in general (Kaufman et al., 2006). Genetic vulnerability in interaction with insensitive parenting has been linked to an increase in behavioural problems such as externalizing problems (Bakermans-Kranenburg & van Ijzendoorn, 2006) and disorganized attachment (Bakermans-Kranenburg & van Ijzendoorn, 2007).

Conditions related to infant regulatory problems, such as ADHD, aggression and self-regulation, have been examined specifically in relation to dopamine receptor D4

genes (DRD4) (Berry, McCartney, Petrill, Deater-Deckard, & Blair, 2014; Faraone et al., 2005; Schmidt, Fox, Rubin, Hu, & Hamer, 2002). Nevertheless, only two studies examined infant regulatory problems directly in relation to genetics.

First, Becker et al. (2010) examined whether the DRD4 gene 7r allele moderates the risk of infants with regulatory problems for developing ADHD later in childhood. 300 infants were longitudinally assessed at 8 different time points from birth to 15 years of age. Findings from this study revealed that infants who both had regulatory problems and the DRD4 gene 7r allele had a greater risk of developing ADHD symptoms. Nevertheless, regulatory problems were not related to ADHD symptoms at 15 years of age if DRD4 7r allele was not present. Following the findings from this study, the interaction of infant regulatory problems, DRD4-7r allele, and maternal responsivity on the development of childhood dysregulation problems was examined (Poustka et al., 2015). When the infants were 3 months old, infant regulatory problems and maternal sensitivity were assessed. Findings from this study showed that the combination of regulatory problems, DRD4 gene 7r allele and low maternal responsivity predicted childhood dysregulation at 8 and 11 years of age. It was further highlighted that these variables do not have any main effects on childhood dysregulation when their interaction was not considered. Overall, these two studies suggest that infants who carry DRD4 gene 7r allele might have higher vulnerability to the negative impacts of insensitive parenting on behavioural/emotional development. However, the findings in this area are weak and still preliminary and there is a need for replication studies. Future approaches may need very large samples and whole genome wide association studies to determine whether infant regulatory problems, and outcomes such as ADHD, share the same genes. Therefore,

the study of the impact of genetics on infant regulatory problems will not be the focus of the current thesis.

Other than genetics, neurodevelopmental vulnerability and parenting factors have been the major focus in the study of infant regulatory problems. The impact of neurodevelopmental vulnerability has generally been assessed by using a sample with increased neurological risk. Specifically, longitudinal investigation of infants who were born before 32 weeks of gestational age, i.e. very preterm, has provided substantial information about the consequences of neurodevelopmental vulnerability since very preterm birth interrupts the development of brainstem functions (Darnall, Ariagno, & Kinney, 2006). In fact, very preterm birth has been found to be a significant predictor of both single and multiple regulatory problems at 5 months of age (Schmid et al., 2011). Thus, assessment of the differences between very preterm samples and their neurological risk, and full-term samples in relation to regulatory problems would provide a test of whether and how neurological vulnerability may associate with the development of regulatory problems, and also be of relevance for practitioners. Detailed information on this topic will be provided in the following chapter.

Another factor that researchers have suggested for the explanation of why infant regulatory problems develop is the quality of maternal parenting behaviours, specifically maternal sensitivity (Rautava, Helenius, & Lehtonen, 1993). Nevertheless, it remains unclear which factor (neurodevelopmental problems, often studied in preterm children, or parenting) makes the largest contribution or whether they interact in the development of infant regulatory problems. The evidence regarding these two factors will be discussed in detail in the following chapters (chapter 2 and 3).

Summary and Conclusions

Infants with regulatory problems exhibit excessive crying, sleeping difficulties and/or feeding problems. Regulatory problems might be present as single regulatory problems with problems only in one area (excessive crying, sleeping problems and feeding difficulties), or as multiple regulatory problems with problems in two or three areas. Multiple regulatory problems have been suggested as more strongly associated with later behaviour problems (Winsper & Wolke, 2014). Failure to consider the comorbidity of regulatory problems during infancy limits the interpretation of the majority of the findings in the literature (See Chapters 2 and 3). Furthermore, there is inconsistency in the definitions of single regulatory problems and multiple regulatory problems. This partly explains the variation in prevalence estimates of regulatory problems. Table 1 provides a summary of the core features of crying, sleeping, feeding and multiple regulatory problems, based on the criteria introduced by the most recently evaluated diagnostic interview for regulatory problems, the Baby-DIPS (Popp et al., 2016).

While there is now solid empirical evidence that infant regulatory problems are associated with future behavioural/emotional problems, little is still known about what factors increase the risk of, or maintain, multiple regulatory problems during infancy. There is currently only weak support for the role of genetics in the development of regulatory problems, infant neurodevelopmental vulnerability such as very preterm birth, and problems in sensitive parenting, have been the two major candidates for the explanation of how infant regulatory problems might develop or be maintained. Moreover, little is known about the association between multiple regulatory problems and attachment.

Table 1 Core features to define crying, sleeping, feeding problems used in the literature

Regulatory Problems	Variables	Definition Criteria	Age criteria
Crying Problems	Cry Duration	More than 3 hours per day for more than 3 days per week	3 months or older
	Inconsolable crying	Hard to soothe infant	
	Problematic Crying	Infant crying is problematic for the mother	
Sleeping Problems	Night waking frequency	At least 5 times per week (at least once per night)	
	Settling at bedtime problem	Child needs more than 30 minutes to fall asleep	Older than 6 months
	Sleep Duration	Less than 5 hours of sleep without waking up	
Feeding Problems*	Food refusal	Fighting against breast or bottle	Before 18 months
		Refusal to eat lumpy, pureed foods	At 18 months or older
	Picky eating	Eating a limited amount of food, restricting intake particularly of vegetables, being unwilling to try new foods, and having strong food preferences	At 18 months or older
	Oral-motor difficulties	Stopping after a few sucks, excessive dribbling/difficulty swallowing, gagging/choking, vomiting	

*The disturbance is not due to an associated gastrointestinal or other general medical condition. Please note that the table is adapted from Popp et al., 2016.

Chapter 2 Neurodevelopmental Explanation of Infant Regulatory Problems

This chapter will focus on the neurodevelopmental vulnerability explanations of the development of infant regulatory problems. Evidence from studies of infants with neurodevelopmental disorders will be briefly outlined. The review will focus on studies with prematurely born infants since they have been reported to be at increased risk of having neurodevelopmental disorders. Studying prematurely born infants in contrast to healthy full term born infants may provide a strategy to assess the neurodevelopmental vulnerability explanation of the development of regulatory problems during infancy.

Organic and Neurodevelopmental Explanation of the Development of Regulatory Problems during Infancy

A number of organic determinants have been proposed as an explanation for the development of regulatory problems during infancy (St James-Roberts, 2012). The first explanation suggested that organic disturbances such as low levels of gut microbiota (Pärtty, Kalliomäki, Endo, Salminen, & Isolauri, 2012) or cow's milk protein intolerance (Lindberg, 1999) might contribute to the development of regulatory problems. However, a literature review nearly two decades ago concluded that the prevalence of organic disturbances as the cause of infant excessive crying is low (Gormally & Barr, 1997). Thus, recent advances in studying biomarkers allow for more detailed study. A recent investigation indicated that infants who cry excessively had lower levels of gut microbiota in comparison to control infants (de Weerth, Fuentes, Puylaert, & de Vos, 2013). However, this may not indicate that this

is causally involved in the development or maintenance of excessive crying since a recent systematic review showed that treatments based on organic disturbances did not reduce the length of crying (Anabrees, Indrio, Paes, & AlFaleh, 2013). Similarly, findings from both a meta-analysis study (Sung et al., 2013) and a randomised control trial (Sung et al., 2014) revealed that probiotics had no strong influence on excessive crying. Based on the lack of strong support for allergy or gut related disturbances as determinant of infant regulatory problems, the explanation of the development of regulatory problems shifted towards neurodevelopmental disorders.

A neurodevelopmental vulnerability proposal for the development of infant regulatory problems has attracted growing attention from researchers. It has been repetitively documented that regulatory problems are more likely to be present in children with neurodevelopmental problems in comparison to healthy control groups (Barnevik-Olsson et al., 2013; Paavonen et al., 2008; Richdale & Prior, 1995). Specifically, parents reported more sleeping problems in children with Attention Deficit Hyperactivity Disorder (ADHD) in comparison to healthy controls (Mayes et al., 2009), as well as feeding problems such as severe selective eating during early childhood (Zucker et al., 2015). One specific sample which has increased risk for neurodevelopmental problems is prematurely born infants (Saigal & Doyle, 2008).

In infants born preterm, the normal processes of intrauterine brain development are altered or impaired during the second half of gestation (20 to 40 weeks) with the maturation of cerebral pathways, the formation of synapses, and brain growth being interrupted (Figure 1) (Chang, Chang, Yu, Ko, & Chen, 2000; Peterson et al., 2003). In particular, there are significant developmental changes in the brainstem functions from 33 to 38 weeks of gestation (Darnall et al., 2006). Therefore, there is an increased risk of altered brain development and superimposed brain abnormalities in

premature infants, such as cerebral white matter or grey matter injury, as well as reductions in whole brain volume and volumes of specific regions such as cerebellum or corpus callosum (Volpe, 2009). A recent meta-analysis (de Kieviet, Zoetebier, van Elburg, Vermeulen, & Oosterlaan, 2012) systematically reviewed studies that measured brain development in very preterm infants aged between 8 years and 18 years. Findings confirmed that total brain volume of very preterm/very low birth weight children is reduced on average 0.58 standard deviation compared to full-term born children. There were also reductions in white matter and grey matter volumes in comparison to full-term born infants. Furthermore, the three brain regions, which are cerebellum, hippocampus and the corpus callosum, had significantly lower volumes in very preterm/very low birth weight group.

Figure 1 Growth of the cerebellar surface from 24 to 40 gestational weeks Adapted from Volpe (2009).

Reductions in the volume of specific brain regions are associated with behavioural problems in children born very preterm, mainly hyperactivity/attention problems which are known to be related to infant regulatory problems (Bora, Pritchard, Chen, Inder, & Woodward, 2014; Hemmi et al., 2011; Rogers et al., 2012). To illustrate, Bora et al. (2014) measured the cerebral volume at term, and attention/hyperactivity problems longitudinally at 4, 6, and 9 years in very preterm and full-term infants. Findings of this study revealed that very preterm children with persistent attention/hyperactivity problems had the largest volumetric reductions in the proportion of total tissue within the sub regions of cerebral tissue volumes: ceredorsal prefrontal, orbitofrontal, premotor, sensorimotor and parieto-occipital. In

another study, these infants had smaller hippocampal volume, which was associated with increased hyperactivity at 5 years of age (Rogers et al., 2012).

The changes in brain volume in preterm children have also been found to be associated with widespread alterations in connectivity of the brain, and correlated to neurocognitive abilities into adulthood (Bauml et al., 2015; Meng et al., 2016).

To conclude, converging data indicate that preterm infants represent a sample who are vulnerable for altered brain development and abnormalities that are related to neurodevelopmental problems. Therefore, studying a very preterm sample is likely to provide an informative model to understand neurodevelopmental underpinnings of infant regulatory problems.

Premature Birth

Premature or preterm birth refers to birth before 37 completed weeks of gestation (WHO, 2012). Preterm birth is further subdivided into three categories based on gestational age (Figure 2): moderate to late preterm (MP; 32- <37 weeks); very preterm (VP; 28- <32 weeks) and extremely preterm (EP; <28 weeks) (Blencowe et al., 2012).

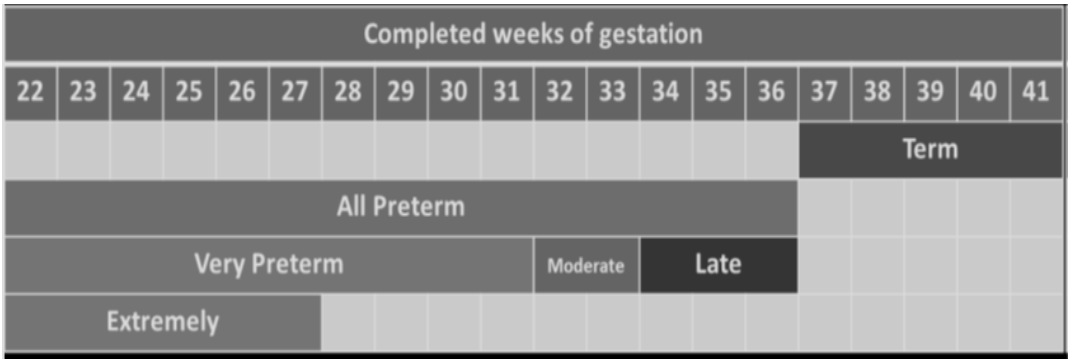

Figure 2 Prematurity: Definition of Terms

During the last twenty years, there has been an increase in the rate of preterm birth (Goldenberg, Culhane, Iams, & Romero, 2008). In a very recent report, it was shown that the preterm birth rate was 11.1% worldwide and 8.6% in developed countries (Blencowe et al., 2013). In the United Kingdom, the prevalence rate of preterm birth is approximately 7% (Macfarlane & Mugford, 2000).

Preterm birth is a major public health concern, which is related to high rates of neonatal mortality in both developed and developing countries (Berkowitz & Papiernik, 1993). In addition, preterm birth increases the risk of deaths due to other causes such as neonatal infections (Lawn, Cousens, & Zupan, 2005). Improvements in neonatal care such as the use of assisted ventilation in the 1970s, the introduction of advanced technology (Doyle et al., 1999; Saigal & Doyle, 2008) and changing attitudes towards intensive care (Soll, 1998) have resulted in marked increases in the survival rate of preterm infants (Spitzer, 1996).

Meta-analysis and systematic reviews of the development of preterm infants confirms the increased risk of difficulties in several areas such as language ability (Barre, Morgan, Doyle, & Anderson, 2011); decoding and reading comprehension (Kovachy, Adams, Tamaresis, & Feldman, 2015); academic achievement (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009; Aylward, 2014); attention (Aarnoudse-Moens et al., 2009; Arpi & Ferrari, 2013; Mulder, Pitchford, Hagger, & Marlow, 2009); and social competence (Ritchie, Bora, & Woodward, 2015) throughout childhood and school age. Moreover, preterm birth increases the risk of attention deficit hyperactivity disorder (ADHD) (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2016; Johnson & Marlow, 2011). Arpi and Ferrari (2013) systematically analysed the behavioural outcomes of preterm infants during infancy (0 to 2 years) and early childhood (3 to 5 years). Their findings

revealed that the most common problems were attention problems, poor behavioural and emotional self-regulation, poor interactional skills, and emotional difficulties, which remained fairly consistent from infancy to early childhood.

Among preterm born, very preterm infants are specifically at increased risk of impairments in multiple areas of development in comparison to full-term infants (Marlow, 2004). A recent review documented that the risk ratio of developing depressive disorder during young adulthood is 2.9 in very preterm infants, while it is 1.3 in moderate-to-late preterm infants (Johnson & Wolke, 2013). In a meta-analysis study (Aarnoudse-Moens et al., 2009), the developmental outcome of infants born very preterm or very low birth weight was systematically investigated in terms of academic achievement, executive function and behavioural problems such as internalizing, externalizing and attention problems. Fourteen studies on academic achievement, 12 studies on executive functioning and 9 studies on behavioural problems, published before 2008, were included in this meta-analysis. Findings of this meta-analysis confirmed that very preterm or very low birth weight children have significant academic underachievement, performed poorly in executive function tests and had significant behavioural problems. Results of this study further showed that different ages of assessment did not make any changes to the results, which suggests that the difficulties of very preterm/very low birth weight birth may remain stable from 5 to early adulthood.

The longitudinal deficits of very preterm birth have been confirmed so far; nevertheless, these deficits might already develop soon after birth. Studies that measured the outcomes of very preterm/very low birth weight birth during infancy mainly focused on cognitive and neurodevelopmental outcomes (Stoelhorst et al., 2003; Vanhaesebrouck et al., 2014; Wildin et al., 1995; Wolf et al., 2002). At 8

months very preterm infants performed poorly on executive functioning tasks in comparison to full-term infants (Sun, Mohay, & O'Callaghan, 2009). At 18 and 24 months corrected age, 40% of very preterm infants had delayed mental and psychomotor development (Stoelhorst et al., 2003).

Whilst neurodevelopmental disabilities are well documented in very preterm infants, few studies have examined the emotional development of very preterm born during infancy. In comparison to full-term infants, very preterm infants have been found to show less social referencing and more agitation at 6 months (Habersaat et al., 2013). On the other hand, a review study showed that preterm infants are not at a higher risk of insecure attachment compared to full-term infants (Korja, Latva, & Lehtonen, 2012). Nevertheless, growing evidence indicates that they might be at risk of developing disorganised attachment (van Ijzendoorn et al., 1999; Wolke, Eryigit-Madzwamuse, & Gutbrod, 2014).

Premature Birth and Regulatory Problems

As neurological immaturity and the hospital stay might impair the development of normal regulatory behaviours (crying, sleeping, feeding), premature infants have been suggested to be at risk of experiencing more crying, sleeping and feeding problems in comparison to full-term infants (Barr, Chen, Hopkins, & Westra, 1996; Holditch-Davis, Scher, Schwartz, & Hudson-Barr. 2004). Empirical studies revealed a strong link between preterm birth and feeding problems; on the other hand, findings remain contradictory in respect to differences between preterm and full-term infants in crying and sleeping problems (Bertoncelli, 2012; Schmid et al., 2011; Wolke et al., 1995b).

Consistently, it has been shown by several researchers that preterm infants are at risk of having feeding problems (Gewolb & Vice, 2006; Mathisen, Worrall, O'callaghan, Wall, & Shepherd, 2000; Samara, Johnson, Lamberts, Marlow, & Wolke, 2010a; Schädler, Süss-Burghart, Toschke, von Voss, & von Kries, 2007; Schmid et al., 2011; Wrotniak, Stettler, & Medoff-Cooper, 2009). At term equivalent age, preterm infants had longer and messier feeding in comparison to full-term infants (Törölä, Lehtihalmes, Yliherva, & Olsén, 2012). Moreover, in a large-scale study (Schmid et al., 2011), very preterm birth and neonatal seizures were found to be strong predictors of feeding problems at 5 months. At 18 months, 13% of preterm infants were reported to have feeding difficulties (Adams-Chapman, Bann, Vaucher, & Stoll, 2013), which increased to 23% at 24 months (Crapnell et al., 2013). Even at 6 years of age, eating problems were more common in preterm infants in comparison to full-term infants (Samara et al., 2010a). Preterm infants specifically had more oral-motor difficulties, hypersensitivity and behavioural problems around eating.

This consistent finding of feeding difficulties in preterm infants has been linked to the medical complications related to preterm birth, which could result in failure of achieving the essential skills needed for successful oral feeding such as rhythmical sucking or motor organization (Medoff-Cooper & Ratcliffe, 2005; Silberstein et al., 2009b). Medical complications related to preterm birth can further lead to delays in initiation and advancement of full oral feeds (Dodrill et al., 2004; Morris et al., 1999; Pridham, Limbo, Schroeder, Thoyre, & Van Riper, 1998). To illustrate, Medoff-Cooper, McGrath, and Shults (2002) examined the differences in sucking patterns between preterm and full-term infants at 40 weeks post-conceptional age. Preterm infants differed from full-term infants in many aspects of sucking patterns such as number of bursts, intersuck width, intersuck interval, sucks per burst, and suck width.

These delays could further result in stress among mothers, increasing problems in mother-infant relationships (Salvatori, Andrei, Neri, Chirico, & Trombini, 2015; Silberstein et al., 2009a). Furthermore, mothers of preterm infants were shown to perceive their infants as having more eating difficulties in comparison to parents of full-term infants (Jonsson, van Doorn, & van den Berg, 2013).

When measured during early infancy, some studies revealed that very preterm infants differ from full-term infants in crying and sleeping patterns (Korja et al., 2008; Manfredi, Bocchi, Orlandi, Spaccaterra, & Donzelli, 2009). Milidou, Sondergaard, Jensen, Olsen, and Henriksen (2014) examined the Danish National Birth Cohort to understand whether preterm birth is a risk factor for infantile colic. Findings from this large cohort study showed that as gestational age decreased, the risk for infantile colic at 6 months increased. Furthermore, there were differences in acoustic features of crying at 18 months between very preterm and full-term infants, and higher frequency of fussing bout in very preterm compared to full-term infants at 5 months of age, nevertheless, the duration of crying remained similar between the two groups (Maunu et al., 2006; Rautava et al., 2007).

With respect to sleeping problems in preterm infants, Huang, Paiva, Hsu, Kuo, and Guilleminault (2014) measured sleeping problems in preterm and full-term infants using a variety of measures such as parental questionnaire and diary, as well as objective measures such as polysomnography (PSG; recording sleep-system) and actigraphy monitor. Findings from this study showed that preterm infants have more problematic sleep in comparison to full-term infants, as well as more breathing problems during sleeping. In contrast, other studies revealed that preterm infants were comparable to full-term infants in sleep-wake state (Anders & Keener, 1985), sleeping problems (Hoppenbrouwers et al., 2005) and sleep structure (Curzi-

Dascalova, Peirano, & Morel-Kahn, 1988). This finding was also supported by a longitudinal study (Iglowstein, Latal Hajnal, Molinari, Largo, & Jenni, 2006), which showed no difference between preterm and full-term infants sleeping problems over 10 years.

On the other hand, a large scale epidemiological study conducted in Germany (Wolke et al., 1995b) assessed very preterm infants and full-term infants at 5, 20, and 56 months of age. The results of this study revealed no evidence for the argument that preterm infants have more sleeping problems than full-term infants. Indeed, they revealed that very preterm infants woke up less often and for shorter periods than full-term infants at 5 months. In another study, this data from German infants were compared to infants in Finland (Wolke et al., 1998), using the same methods. Very preterm infants from both countries woke up less often and for shorter durations at 5 months; however, they did not differ from full-term infants at 20 and 56 months. The most important predictor of night waking was breastfeeding, and preterm infants were less likely to be breastfed.

There is a scarcity of studies that have examined multiple regulatory problems in preterm infants. Schmid et al. (2011) investigated the predictors of multiple regulatory problems in a large sample with infants who were born prematurely or with neonatal complications. Findings from this study showed that very preterm birth increased the odds of having multiple regulatory problems 2 times at 5 months.

Summary and Conclusions

Examining prematurely born infants provides a natural model to study the link of impaired neurodevelopment to regulatory problems since premature birth may impair

healthy brain development, which increases the risk of neurodevelopmental deficiencies.

Empirical studies which focus on differences in crying and sleeping problems between preterm and full-term infants have yielded contradictory findings so far. While some studies showed that preterm infants have more crying or sleeping problems in comparison to full-term infants, others did not find any differences between the two groups. On the other hand, feeding problems are more likely to be prevalent among preterm infants as consistently found in a range of studies.

Multiple regulatory problems in preterm infants attracted the attention of only a small number of studies. Therefore, more research is required to identify whether multiple regulatory problems are more prevalent in prematurely born infants in comparison to full-term infants.

Chapter 3 Sensitive Parenting Explanation of the Development of Regulatory Problems

This chapter will focus on parenting, specifically sensitive parenting, and how it may be associated with regulatory problems. However, if one wants to study the effects of neurodevelopmental vulnerability and sensitive parenting simultaneously, it is important to determine whether sensitive parenting is confounded by neurodevelopmental vulnerability. Does neurodevelopmental vulnerability alter maternal sensitivity? Thus, first, evidence from studies with premature infants will be the focus to understand the link between neurodevelopmental vulnerability and parenting. Second, evidence on sensitive parenting and regulatory problems will be reviewed.

Sensitive Parenting and Premature Birth

Positive maternal parenting behaviour during the early months of life contributes to healthy development of the infant in areas such as social and emotional development (Landry & Smith, 2011; Landry, Smith, Swank, Assel, & Vellet, 2001). One important aspect of maternal parenting behaviour is maternal sensitivity, which has been defined as mother's ability to infer infant's signals and respond to them appropriately (Ainsworth, Bell, & Slayton, 1974). In full-term healthy children, sensitive and responsive parenting has been shown to increase cognitive, social and emotional outcomes (Bornstein & Tamis-Lemonda, 1997). On the other hand, insensitive parenting have been related to negative outcomes such as poor regulatory style in infancy (Calkins, 1994) and more psychological problems in young adulthood (Lyons-Ruth, Bureau, Holmes, Easterbrooks, & Brooks, 2013)

Premature birth has been considered as a unique experience which might put the mother-infant relationship at risk (Goldberg & DiVitto, 2002). After preterm birth, infants are likely to spend time in incubator care before being discharged from hospital (Phibbs & Schmitt, 2006; Ringborg, Berg, Norman, Westgren, & Jonsson, 2006). The duration of the incubator care depends on the infant's gestational age, birth weight and medical complications (Behrman & Butler, 2007). Some very preterm infants spend months in the hospital before they are discharged home (Behrman & Butler, 2007; Ringborg et al., 2006). This separation of the infant from the mother during the early days after birth might put sensitive parenting at risk (Bialoskurski, Cox, & Hayes, 1999; Cleveland, 2008).

Apart from the early separation, preterm delivery might impair the mother's perception about their ability to take care of their own infant (Beckwith & Rodning, 1996; Chapieski & Evankovich, 1997). Furthermore, being uncertain about infants' survival and developmental outcomes might increase the risk of depression in mothers (Meyer et al., 1995; Singer, Davillier, Bruening, Hawkins, & Yamashita, 1996) and lead to symptoms of posttraumatic stress disorder (PTSD) (Holditch-Davis et al., 2015). Nevertheless, the idea that preterm birth would increase maternal stress has been challenged by the findings of a recent study. Schappin, Wijnroks, Venema and Jongman (2013) systematically analysed 38 studies describing stress of parents of preterm infants. Their findings revealed that mothers of preterm infants described feeling only slightly more stress compared to mothers of term-born children, suggesting a high degree of resilience in many parents of those born preterm.

Interactions between mother-preterm infant dyads might be particularly challenging due to several factors. To start with, preterm infants might be less attentive in their communication with their mothers (Field, 1977); they might smile

less often (Segal et al., 1995) and they might be less responsive (Jaekel, Wolke, & Chernova, 2012; Zarling, Hirsch, & Landry, 1998). During dyadic interactions, preterm infants have been shown to be more passive and less alert in comparison to full-term infants at 3 months (Schmücker et al., 2005). Therefore, mothers of preterm infants might need to make more effort to initiate and maintain sensitive interactions with their infants (Singer et al., 2003).

Numerous empirical studies have examined parenting behaviour after preterm birth; however results of these studies remain contradictory (Korja, Latva, & Lehtonen, 2012). Some studies found that mothers of preterm infants were less sensitive in comparison to mothers of full-term infants during dyadic play interactions (Crnic, Greenberg, Ragozin, Robinson, & Basham, 1983; Müller-Nix et al., 2004). In contrast, other studies revealed no significant differences in sensitive parenting between mothers of preterm and full-term infants (Greenberg & Crnic, 1988; Korja et al., 2008; Montirosso, Borgatti, Trojan, Zanini, & Tronick, 2010; Schermann-Eizirik, Hagekull, Bohlin, Persson, & Sedin, 1997). Furthermore, there was even evidence suggesting that mothers of preterm infants are more sensitive (Crawford, 1982) than mothers of full-term infants. Thus, empirical research that examined if mothers of preterm infants are less sensitive than mothers of full-term infants has revealed substantially inconsistent findings so far.

Contradictory findings in the literature about the impact of premature birth on parenting could be explained by several factors. First of all, the degree of prematurity of the sample studied could explain the inconsistent results since the maternal behaviour could change according to the immaturity of the infant (Feldman & Eidelman, 2006). Therefore, sensitive parenting may be interfered with more in interaction with very preterm infants relative to moderate to late preterm infants.

Secondly, advances in the neonatal intensive care unit (NICU) such as increased parental access and more parental care in recent years, specifically in the new millennium, has decreased stress for parents and infants (Latva, Lehtonen, Salmelin, & Tamminen, 2004). Thirdly, the fact that infants were assessed at different time periods in different studies could account for the contradictory findings since the differences in maternal behaviour between preterm and full-term infants have been suggested to decrease after 6 months of age (Montirosso et al., 2010). Fourthly, a variety of concepts were used to assess maternal interactive behaviour, apart from sensitivity behaviours indicating "warmth" and "responsiveness". Finally, geographical variations in NICU care practices (Europe vs America) may account for some of the inconsistencies in the findings as neonatal care organisation and care practices might differ between continents. To illustrate, it has been shown that mother-infant dyads have better interaction quality at 24 months if they had positive interaction during their stay in the NICU (Gerstein, Poehlmann-Tynan, & Clark, 2015).

Overall, there is considerable uncertainty of whether parenting is impaired in mothers of preterm infants, who more likely suffer neurodevelopmental problems, compared to healthy term born.

Sensitive Parenting and Regulatory Problems

The transactional model of development (Sameroff & Chandler, 1975) postulates that the development of a problematic behaviour does not depend solely on the infant or the mother but is a product of ongoing interactions between the two. Likewise, according to many researchers, infant regulatory problems can be best understood in a relational context (Anders, Goodlin-Jones, & Sadeh, 2000; Bayer et al., 2007; Wake et al., 2006). To illustrate, feeding is a central activity for the development of

mother-infant relationship as it is one of the earliest recurrent communicative activities between the mother and the infant (Feldman, Keren, Gross-Rozval, & Tyano, 2004). Observation studies of mother-infant interaction during feeding have underlined that the feeding interaction represents the early form of affective and social dialogue (Papousek, 2007). Since these early interactions contribute to infants' self-development, mothers may act as an external guide to scaffold their infants' capacity to self-regulate (Fonagy, Gergely, Jurist, & Target, 2002). Similarly, it has been suggested that the normal progression of infant sleep patterns reflect the quality of mother-infant interaction (Anders, 1994) and mothers might act as external regulators of infants' biological rhythms and affect, influencing their self-regulation capacity (Grossmann & Grossmann, 1991). Furthermore, mother-infant interaction in response to infant crying signals the developing pattern of mother-infant relationship (Leavitt, 1998). If mothers are successful in terminating infant crying, are able to settle their infant to sleep and feed their infant, they could consequently have an improved relationship. In contrast, when there is a problem in maternal or infant interactive behaviour, this relationship is likely to be negatively influenced (Davies et al., 2006). Therefore, disturbances in maternal sensitive parenting have been suggested as significant risk factors for the development of childhood regulatory problems (Degangi, Porges, Sickel, & Greenspan, 1993; Schmid et al., 2011; Schmid & Wolke, 2014).

In recent years, there have been surprisingly few empirical studies on sensitive parenting and regulatory problems. Considering the few studies on sensitive parenting and regulatory problems, the presence of maternal depression could be used as an alternative to assess less sensitive parenting since maternal depression may adversely affect maternal sensitivity (Murray, Cooper, Wilson, & Romaniuk,

2003; Timmer et al., 2011). Nevertheless, using maternal depression does not necessarily provide an alternative measurement of maternal sensitivity since some studies showed that it is maternal sensitivity rather than depression that predicted poorer outcomes in children (Murray, Fiori-Cowley, Hooper, & Cooper, 1996). Furthermore, findings from studies that focused on the association between maternal depression and regulatory problems are inconclusive (Akman et al., 2006; Coulthard & Harris, 2003; Farrow & Blissett, 2006; Haycraft, Farrow, & Blissett, 2013; Lam, Hiscock, & Wake, 2003; Simard, Lara-Carrasco, Paquette, & Nielsen, 2011). Thus, studies need to use observational measures of maternal sensitivity rather than using a proxy measure of sensitivity to study the associations with regulatory problems.

Relative to the studies that examined the link between maternal depression, a potential proxy to actual maternal interaction, and infant regulatory problems, there are only a few longitudinal studies that examined the relationship between sensitive parenting and infant regulatory problems. In a recent study, Bordelau, Bernier and Carrier (2012) examined the association between maternal sensitivity during daytime at 12 months and the percentage of sleep at 3 to 4 years. Findings of this study showed that maternal sensitivity on its own did not predict the percentage of night-time sleep. In another study, there were no significant associations between maternal sensitivity and feeding problems at 10 months and 2 years of age (Hagekull, Bohlin, & Rydell, 1997). On the other hand, Hubbard and van Ijzendoorn (1991) conducted a study to investigate the impact of early maternal unresponsiveness on consequent infant crying duration. During the first 9 months, the participants were assessed at 3-week intervals 12 times. They defined maternal responsiveness as promptness of response to infant crying. Their findings provided strong evidence that infant crying decreased over time when mothers waited longer to respond. Thus being less

responsive in relation to crying may allow the infant to try self-soothing before actively responding. This is contrary to the assertion by attachment theorists that immediate responding should reduce crying (Bell & Ainsworth, 1972) and partly supportive of a behavioural control interpretation (Gewirtz & Boyd, 1977).

Evidence for a reciprocal relationship between maternal sensitivity and infant regulatory problems has been reported in studies that investigated infant sleep. In a recent study (Philbrook & Teti, 2016), the bidirectional association between infant sleep and night-time parenting was investigated across the first 6 months of life. At 1 month, 3 months and 6 months, video cameras were placed in families' homes for one night in order to capture maternal emotional availability (sensitivity, nonintrusiveness, structuring, nonhostility) during night-time as well as infant's night-time distress. Findings from this study provided support for a bidirectional relationship between infant night-time distress and emotional availability. When mothers were more emotionally available, infants slept for longer durations with little distress. On the other hand, when infants had more distressed sleep, mothers were less emotionally available. The reciprocal relationship between maternal sensitivity and sleeping problems was also shown in a parental report study (Bell & Belsky, 2008). In this study, parents reported on their children's sleeping problems when the child was 8 and 11 years old, and on maternal sensitivity when the child was 8 and 10 years old. Findings of this study revealed that decreased maternal sensitivity at 8 years increased sleeping problems in children at 10 years. Reciprocally, increased sleep problems at 8 years decreased maternal sensitivity at 11 years.

Apart from the above mentioned studies, a significant association between maternal sensitivity and infant regulatory problems has usually been investigated in cross-

sectional studies. For example, Priddis (2009) showed that mothers who had infants with poor sleeping had significantly lower scores for maternal sensitivity than mothers who had infants without sleeping problems at 2.5 years. Another cross-sectional study examined emotional availability (sensitivity, nonintrusiveness, structuring, nonhostility) at bedtime, and infant sleep quality when infants were between 1 and 24 months of age by using 7-day sleep diaries, questionnaires and video recordings for 1 night (Teti, Kim, Mayer, & Countermine, 2010). Results of the study showed that decreased maternal emotional availability increased problematic sleep in infants. In another study, infants below 18 months with and without food refusal and their mothers were observed during both play and feeding observations (Lindberg, Bohlin, Hagekull, & Palmérus, 1996). Results of this study showed that both during play observation and feeding observations, mothers of infants with food refusal were less sensitive, less cooperative and had more verbal control behaviour in comparison to mothers in the control group. Moreover, Becker et al. (2004) found that mothers of infants with multiple regulatory problems were less responsive, smiled less and vocalized less in comparison to mothers in a control group during diapering and playing at 3 months. Nevertheless, findings of the cross-sectional studies do not allow for causal explanations. The parents may just react with more controlling behaviour to an infant who is less well regulated and may need more external control.

In short, some studies showed one-directional associations between maternal sensitivity and child regulatory problems (Priddis, 2009; Teti, 2010), others have noted a bi-directional relationship between these variables (Bell & Belsky, 2008; Philbrook & Teti, 2016), and still others have revealed no significant link (Bates et al., 2002; Bordelau, 2012; Scher, 2001). Therefore, it is not possible to reach

conclusions about the presence or absence of an association between infant regulatory problems and maternal sensitivity, as well as the direction of this relationship.

Inconsistent results regarding the link between infant regulatory problems and maternal sensitivity could be due to diversity of methodology and the developmental period examined. Furthermore, the majority of the previous studies assessed single infant regulatory problems over two assessment points, but they did not consider multiple regulatory problems.

Summary and Limitations

Maternal parenting, specifically maternal sensitivity, has been reported to be a crucial element for the positive emotional development of the infant. Numerous studies have suggested that maternal parenting behaviour is highly dependent on infant related factors, two of which are an infant's neurodevelopmental vulnerability and regulatory problems.

Studies that compared mothers of preterm infants to mothers of full-term infants reported contradictory findings, either revealing a difference between the two groups or failing to find any difference between two groups. It remains crucial to determine whether or not mothers of preterm infants are as sensitive to their infants as mothers of full-term infants. This is important to investigate as a prerequisite for using preterm infants as a model to study the relationship of neurodevelopmental vulnerability and sensitive parenting to regulatory problems in a design that includes both preterm and term born infants.

There are several possible directions of the association between infant regulatory problems and maternal sensitivity: 1) early problems in maternal behaviours increase

infant regulatory problems; 2) early infant regulatory problems result in the impairment of maternal parenting behaviour; 3) the association between infant regulatory problems and maternal parenting is reciprocal; or 4) neither sensitive parenting or regulatory problems influence each other over time. Unfortunately, the limited number of longitudinal studies that have investigated the associations between maternal sensitivity and infant regulatory problems provide very limited evidence on the relationship of maternal sensitivity and regulatory problems across infancy. However, this knowledge may be important to prevent or treat infant regulatory problems. Therefore, longitudinal cross-lagged designs are needed to disentangle the currently unclear direction of influences between infant regulatory problems and maternal sensitivity.

Chapter 4 Attachment

Cascade models of development posit that the development of behavioural problems is best understood as a developmental trajectory across time of domain related and age-appropriate constructs, ultimately leading to impairment of the behaviour within the same domain (Masten & Cicchetti, 2010). Under the guidance of this model, it has been suggested that early regulatory problems can be the starting point of a dysregulation trajectory (Schmid & Wolke, 2014). Nevertheless, it has remained unclear whether early regulatory problems, and in particular multiple regulatory problems, are at all associated to other domain related constructs in infancy, such as infant attachment.

This chapter presents a brief overview of attachment theory and discusses its implications for child development incorporating findings from a series of meta-analyses. Moreover, this chapter will outline the factors related to the development of attachment patterns, along with studies that have investigated the association between regulatory problems and attachment patterns.

Attachment Theory and Its Implications on Child Development

Bowlby's (1969) attachment theory has made significant contributions to our understanding of how infants' early experiences with their caregiver is linked to consequent behavioural/emotional development. According to Bowlby (1969), infants will internalize the early disruptive experiences with their caregivers, which will endure throughout development, consequently influencing their psychosocial functioning. Resulting from this theory, Ainsworth, Blehar, Waters, and Wall (1978) identified three types of attachment patterns: secure, insecure-resistant, and insecure-

avoidant. Infants who are securely attached seek comfort from their caregivers, and, once comforted, they continue exploring the environment (Ainsworth et al., 1978). In contrast, infants who are insecurely attached either avoid their caregiver or are extremely focused on the caregiver but cannot be comforted. Main and Solomon (1990) further proposed that collectively, these three patterns of attachment employ an 'organised' system for managing stressful situations. They introduced a fourth category labelled as disorganised attachment (D) reflecting a disruption in the organisation of attachment behaviour and a breakdown of organised strategies (Main & Solomon, 1990; van Ijzendoorn, Schuengel, & Bakermans-Kranenburg, 1999).

Attachment patterns have been influential in understanding the individual variations of social/behavioural development across the life span. To illustrate, secure attachment during infancy has been linked to several positive outcomes across childhood and adulthood such as increased capacity for emotion regulation, social competence, better ability to deal with stress in romantic relationships, increased feelings of self-worth, and an increase in cognitive capacity (Jacobsen, Huss, Fendrich, Kruesi, & Ziegenhain, 1997; Sroufe, 2005; Weinfield, Sroufe, Egeland, & Carlson, 2008), as well as acting as a protective factor against negative impacts of parenting stress (Tharner et al., 2012b). The positive influence of secure attachment on infant development is specifically highlighted by an increased competence in social relationships with peers at school age (Bohlin, Hagekull, & Rydell, 2000). In a recent meta-analysis study (Groh et al., 2014), the association between attachment during infancy and social competence with peers up to 14 years of age was investigated drawing findings from eighty independent samples and 4441 participants. The systematic review indicated the significant positive influence of secure attachment on being socially competent in peer relationships, which remained

significant regardless of the age of assessment and socioeconomic risk of families. In contrast, formation of insecure attachment during infancy weakened social competence in peer relationships, and this was similar in all insecure attachment types including disorganised attachment.

In addition to associations with social relationships, the impact of insecure attachment has been proposed to be carried forward across childhood, adolescence and adulthood escalating in a range of mental health issues (Sroufe, 2005). When attachment pattern was measured during infancy, an increased risk for externalizing problems for infants with all insecure attachment types was found, with a specifically elevated risk for the infants with disorganised attachment across childhood and adolescence (Fearon, Bakermans-Kranenburg, van Ijzendoorn, Lapsley, & Roisman, 2010; Groh, Roisman, van Ijzendoorn, Bakermans-Kranenburg, & Fearon, 2012). Elevated vulnerability to develop externalizing problems remained similar among infants with disorganised attachment even after controlling for age of assessment and socioeconomic risk (Fearon et al., 2010; Groh et al., 2012).

Although meta-analytic examinations of the association between attachment and externalizing problems have highlighted the particular strong influence of disorganised attachment, it has remained unclear which specific attachment type makes the biggest contribution to the development of internalizing problems. There are conflicting findings from two recent meta-analyses. A meta-analysis of 42 samples revealed that insecure-avoidant attachment had only small associations with the development of internalizing problems, while insecure-resistant and disorganised attachment were not associated with the later development of internalizing problems (Groh et al., 2012). In contrast, another meta-analysis of 46 studies reported on significant and moderate associations between insecure-resistant attachment and

anxiety, and this relationship was even stronger during adolescence compared to early and middle childhood (Colonnesi et al., 2011). Furthermore, the contribution of insecure attachment types was similar in another meta-analytic investigation, revealing a two times increased likelihood of developing internalizing problems in insecurely attached in comparison to infants with secure attachment (Madigan et al., 2013). Likewise, a narrative review (Brumariu & Kerns, 2010) suggested that there is an overall significant link between insecure attachment and internalizing behaviour, nonetheless, the specific links of the two insecure attachment types have been challenging to evaluate and have yielded contradictory results.

When internalizing and externalizing symptoms were systematically investigated using the findings of attachment assessments during early childhood rather than infancy (Madigan, Brumariu, Villani, Atkinson & Lyons-Ruth, 2016), it was further confirmed that only disorganised attachment is associated with externalizing symptoms. However, all three insecure attachment types increased internalizing symptoms similarly, with a particular increase in depressive symptoms. This study concluded that when assessed in early childhood, insecure attachment is related to a 2.9 times increased risk of developing internalizing problems, and a 2.4 increased risk of developing externalizing problems.

Taken together, existing evidence highlights a differential significance of insecure attachment types for the development of internalizing and externalizing problems in which disorganised attachment was found to be strongly associated with subsequent externalizing problems. In contrast, the link of avoidant and resistant attachment style to internalizing problems is more tenuous and findings are mixed.

Factors that are Predictive of Attachment Development

Development of Secure versus Insecure Attachment

Attachment theory (Bowlby, 1969) proposes an environmental explanation, claiming that the individual variation in attachment patterns lies within the differences in caregivers' behaviour. Supporting this idea, a strong association was found between secure behaviour pattern and maternal sensitivity during extensive home observations (Ainsworth et al., 1978). Contrary to this robust finding, de Wolff and van Ijzendoorn's (1997) meta-analysis of 66 studies that investigated the association between maternal sensitivity and attachment revealed that the strength of the association was rather modest (0.24), irrespective of the duration of observation. However, maternal sensitivity has remained the major factor across studies associated with the formation of secure attachment strategies (Bakermans-Kranenburg, van Ijzendoorn, & Kroonenberg, 2004; van Ijzendoorn & Bakermans-Kranenburg, 2004). In addition to maternal sensitivity, it has been proposed that infants' secure attachment patterns reflect mothers' own childhood attachment representations (Main, Kaplan, & Cassidy, 1985) such that infants whose mothers have secure-autonomous attachment representations are more likely to be securely attached to their mothers (van Ijzendoorn, 1995; Verhage et al., 2016). Although maternal sensitivity has been suggested to mediate this association, a recent meta-analysis showed that sensitive parenting cannot solely explain how this intergenerational transmission of attachment happens (Verhage et al., 2016).

Alternatively, it was proposed that infant characteristics such as infant temperament, suggesting difficult temperament are involved in the development of insecure attachment (Vaughn & Bost, 1999). Nevertheless, this explanation was not

supported by empirical studies revealing weak and mixed findings (Ispa, Fine, & Thornburg, 2002; van IJzendoorn & Bakermans-Kranenburg, 2004). It has been documented that rather than a direct effect, the influence of difficult temperament on attachment is more likely to be indirect via its influence on maternal sensitivity (Mangelsdorf & Frosch, 1999; Planalp & Braungart-Rieker, 2013; Susman-Stillman, Kalkoske, Egeland, & Waldman, 1996). To illustrate, high levels of infant negative affect and low levels of infant soothability interrupt the formation of secure attachment due to their negative impact on maternal sensitivity (Mills-Koonce et al., 2007; Mills-Koonce, Propper, & Barnett, 2012). Thus, infant temperament on its own might not differentiate secure versus insecure infants (Ispa et al., 2002; Mangelsdorf & Frosch, 1999), but it is dependent of how the mother deals with the stress and how it affects her sensitivity in interaction. This is consistent with the "goodness of fit" model proposed by temperament researchers (Carey & McDevitt, 1995; Thomas & Chess, 1977). Other researchers proposed that infants' neurodevelopmental vulnerability such as preterm birth could relate to attachment insecurity. However, the majority of studies revealed that preterm infants had similar distributions of secure and insecure attachment compared to full-term infants (Brisch et al., 2005; Butcher, Kalverboer, Minderaa, van Doormaal, & ten Wolde, 1993; Wolke, Eryigit-Madzwamuse, & Gutbrod, 2014).

Other environmental factors such as marital conflict, income, family size, and young maternal age have also been revealed as influential on the development of attachment patterns through their proximal or distal influence on maternal sensitivity (Belsky, 1999; Cummings & Davies, 2002; Moss, Cyr, & Dubois-Comtois, 2004). To illustrate, in a recent study Lickenbrock and Braungart-Rieker (2015) explored the antecedents of infant attachment from an ecological systems perspective, integrating

parental sensitivity, marital functioning, and parental resources operationalized as parental age, education, occupation and income. Their findings revealed that infants who live in families with few resources together with mothers who show low sensitivity, are at the highest risk of developing insecure attachment. On the other hand, maternal sensitivity acts as a protective factor since in the cases where maternal sensitivity was high, living in families with low resources did not differentiate between attachment types.

All in all, explanations based on mothers' role in the formation of secure attachment have received more consistent support from empirical studies in comparison to infant-related factors. To illustrate, van Ijzendoorn, Goldberg, Kroonenberg, and Frenkel (1992) systematically investigated if the distribution of secure attachment of infants within samples where a mother-related clinical problem (e.g. depression) was present, differed from samples where a child-related clinical problem (e.g. prematurity) was present. Findings of this meta-analysis revealed that the distribution of secure versus insecure attachment classifications were in accordance with the distribution of normal samples when children had clinical problems; on the other hand, children of mothers with clinical problems were susceptible to develop insecure attachment patterns more often than found in normal samples. Hence, this meta-analysis concluded that mothers are often able to cope with child-related problems and assist their infants in forming secure attachment relationships. Additionally, when intervention studies on increasing maternal sensitivity and secure attachment were systematically analysed, it was shown that if an intervention is successful in increasing maternal sensitivity, it correspondingly increases secure attachment (Bakermans-Kranenburg, van Ijzendoorn, & Juffer, 2003). Drawing the

findings of these two meta-analyses together, there is support for a causal role of maternal sensitivity in the differentiation of secure versus insecure attachment.

Development of Disorganised Attachment

The precursors of disorganised attachment have been suggested to be different than those of insecure attachment, suggesting that insensitive parenting is not a sufficient reason for an infant to develop a disorganised attachment pattern (van Ijzendoorn et al., 1999). Instead, explanations for the development of disorganised attachment have been attributed to abusive parenting behaviours or maltreatment (Crittenden & Ainsworth, 1989), and parents' unresolved traumatic experiences (Main & Hesse, 1990). In one of the earliest studies, more than 80% of infants with disorganised attachment were reported to be maltreated (Beeghly & Cicchetti, 1994), this percentage was shown to be smaller in a meta-analysis (48%) while it nevertheless remained the strongest precursor identified (van Ijzendoorn et al., 1999). The meta-analysis further confirmed that maternal unresolved early loss or trauma was a precursor of disorganised attachment, as well as highlighting other predictors such as marital discord and the infant having a high risk for neurological impairment (van Ijzendoorn et al., 1999). In contrast, insensitive parenting, gender and temperament did not explain why some infants developed disorganised attachment.

Given the empirical suggestions, a theoretical model has been proposed that parents' unresolved traumatic experiences can relate to their atypical or frightening behaviour towards their infant, consequently leading the infant to develop disorganised attachment (Hesse & Main, 2000, 2006; Main & Hesse, 1990). This mediation model was explored in a recent meta-analysis (Madigan et al., 2006), revealing that both unresolved traumatic experiences and atypical parenting relate to disorganised attachment independently with modest effect sizes. Nevertheless, when the mediation

model was examined, atypical parenting behaviours explained only a very small part of the association (0.09) between unresolved traumatic experiences and disorganised attachment. Thus, despite the fact that unresolved traumatic experiences and atypical parenting partly independently explain the development of disorganised attachment, other factors must be involved in the development of disorganised attachment.

As an alternative to parent-related explanations, emerging evidence has underlined infant characteristics such as very preterm birth to understand how disorganised attachment develops (van Ijzendoorn et al., 1999; Wolke, Eryigit-Madzwamuse, & Gutbrod, 2014). Neurodevelopmental vulnerability of the infant could be a critical factor in shaping disorganised attachment since it was recently reported that infants who were admitted to NICU had 6 times increased odds to develop disorganised attachment in comparison to infants who were not admitted to NICU (Pennestri et al., 2015).

The role of genetics and gene-environment interaction have been further considered to distinguish organised versus disorganised attachment patterns, although findings are still preliminary and contradictory (Gervai, 2009). When the attachment patterns of monozygotic and dizygotic twins were compared, the evidence has been mixed regarding heritability of attachment patterns (Bokhorst et al., 2003; Finkel & Matheny, 2000; O'Connor & Croft, 2001). Moreover, the first investigation of a specific gene relating to attachment patterns highlighted that infants who carried the 7-repeat variant of the dopamine D4 receptor (DRD4) were at an increased risk for disorganised attachment (Lakatos et al., 2000), but this failed to be replicated by a another study using a larger sample (Bakermans-Kranenburg & van Ijzendoorn, 2004). Others proposed that the short polymorphism of the serotonin transporter gene (5HTT VNTR) increases disorganized attachment (Spangler, Johann, Ronai, &

Zimmermann, 2009), but again replications failed to show an association (Luijk et al., 2011; Pauli-Pott, Friedel, Hinney, & Hebebrand, 2009). Instead of focusing on the main impact of genes, a recent review highlighted that only when combined with environmental risk, genetics may explain the development of attachment patterns (Bakermans-Kranenburg & van Ijzendoorn, 2007).

Attachment and Infant Regulatory Problems

Infant regulatory problems, specifically multiple regulatory problems, might be related to attachment insecurity and/or disorganisation due to two reasons. First, multiple regulatory problems are a source of distress to parents (Hofacker & Papoušek, 1998; Sidor et al., 2013) and consequently may influence mothers' ability to be consistent in helping their infants to regulate their physiological states (Degangi, 1997). As a result, multiple regulatory problems could impair the developing secure infant-mother attachment patterns. Alternatively, multiple regulatory problems may be an indication of disorganisation in stressful situations, consequently relating to a disorganised strategy in infant-mother attachment relationship. Knowing that insecure and disorganised attachment are linked to behavioural problems (Fearon et al., 2010; Groh et al., 2012), attachment patterns may be important mediators between multiple regulatory problems and later behavioural outcomes. Nevertheless, it remains unknown whether a link between multiple regulatory problems and attachment exists at all.

Only a few existing studies explored the association between crying, sleeping and feeding problems, and attachment separately (Table 2). To illustrate, the association between crying problems and attachment has been examined by only two studies so far (Stifter & Bono, 1998; van IJzendoorn & Hubbard, 2000). In the first study, Stifter and Bono (1998) measured infantile colic when the infants were 3 to 5 weeks

of age and assessed attachment when they were 18 months old. Comparing 12 infants with colic to 88 infants without colic, this study revealed no significant differences between the two groups in their attachment patterns. In the second study, van Ijzendoorn and Hubbard (2000) conducted a detailed assessment of cry duration assessing the infants 12 times across the first 9 months of life. Similar to the findings from Stifter and Bono's (1998) study, there was no significant association between duration of crying and attachment types. Nevertheless, both of these studies were underpowered, which might have resulted in a failure to detect a statistically significant effect.

Table 2 Summary of Studies Exploring Regulatory Problems and Attachment

Author (Year)	Sample Size	Design	Assessment Points	Attachment Types Assessed	Key findings
			Crying Problems		
Stifter & Bono (1998)	100 (12 colic; 88 non-colic)	Longitudinal	Colic: 3 to 5 weeks Attachment: 18 Months	B vs A, C	No significant association between colic and attachment.
van Ijzendoorn & Hubbard (2000)	50	Longitudinal	Cry Duration: 12 times during the first 9 months Attachment: 15 Months	B vs A, C	No significant association between cry duration and attachment.
			Sleeping Problems		
Scher (2001)	94	Cross-sectional	12 months	B, C	No significant association between sleep patterns and attachment.
Morrell & Steele (2003)	100 (40 sleep problems; 60 controls)	Cross-sectional	14 to 16 months	B, A, C, D	Infants with higher sleeping problems had more often insecure-resistant attachment.
Higley & Dozier (2009)	44	Cross-sectional	12 months	B, A, C, D	No association between night-waking and attachment patterns.
McNamara (2003)	342	Longitudinal	Sleep Problems: 6 and 15 months Attachment: 15 months	A, C	Infants who experienced more sleeping problems both at 6 and 15 months of age had more often insecure-resistant attachment at 15 months.

Beijers, Jansen, Riksen-Walraven & de Weerth (2011)	177	Longitudinal	Night waking: 6 months (from week 1 to week 27, assessed 14 times with 2 weeks intervals) Attachment: 12 months	B, A, C, D	Infants who woke up more during the first 6 months had insecure resistant attachment at 12 months more often. Infants who woke up the least across the first 6 months had avoidant attachment at 12 months more often.
Zentall, Braungart-Rieker, Ekas, & Lickenbrock (2012)	46	Longitudinal	Night waking: 7 and 12 months Attachment: 12 months	B, A, C, D	No significant association between night waking and attachment at 7 months. At 12 months, infants with insecure-resistant attachment woke up more frequently compared to secure and disorganised attachment.
Pennestri et al., (2015)	134	Longitudinal	Sleep: 6, 12, 24, 36 months Attachment: 36 Months	B, A, C, D	Lower duration of nocturnal sleep, going to bed later, more night-wakings across the first 24 months, shorter periods of uninterrupted sleep (only at 12 months) and shorter periods of time in bed (only at 6 months) were associated to disorganised attachment at 36 months.
			Feeding Problems		
Valenzuela (1990)	84 (42 chronically underweight; 42 healthy)	Cross-sectional	17 to 21 months	B, A, C	More infants in the underweight group had insecure attachment compared to healthy infants.
Ward, Kessler, & Altman (1993)	54 (26 failure to thrive; 28 normal development)	Cross-sectional	12 to 15 months	B, A, C, D	Children with failure to thrive showed less secure and more often

					disorganised attachment compared to the normal group.
Lindberg (1996)	48 (24 food refusal; 24 healthy)	Cross-sectional	Below 18 months	B, A, C	No significant association between food refusal and attachment.
Chatoor, Ganiban, Colin, Plummer, & Harmon (1998)	101 (33 infantile anorexia; 34 picky eaters; 34 healthy eater)	Cross-sectional	12 to 37 months	B, A, C, D	Children in the infantile anorexia group showed more often insecure attachment compared to picky eaters and healthy eaters. There was no evidence for an increased rate of disorganised attachment within the infantile anorexia group.
Ward, Lee, & Lipper (2000)	218 (88 failure to thrive; 130 normal development)	Cross-sectional	11 to 32 months	B, A, C, D	Children with failure to thrive showed more often insecure and disorganised attachment compared to the normal group.

Please note that this table presents only the studies, which used the gold standard observational measure (strange situation procedure). Moreover, studies are not included if they used regulatory problems only as the outcome of attachment.

The association between sleeping problems and attachment patterns has been examined using both cross-sectional and longitudinal designs. When assessed with a cross-sectional design, studies on the association between sleeping problems and attachment have revealed contradictory findings. To illustrate, Scher (2001) investigated the concurrent association between sleeping patterns, such as the number of interrupted nights per week, number of awakenings per night, and the duration it takes infant to settle and resettle to sleep, and secure versus insecure-resistant attachment at 12 months. Findings of this study indicated no significant association between sleeping patterns and attachment. Similarly, another cross-sectional study demonstrated no influence of night-waking on attachment patterns at 12 months (Higley & Dozier, 2009). In contrast, Morrell and Steele (2003) found that infants with higher sleeping problems more often had insecure-resistant attachment when they were 14 to 16 months-old.

When assessed in a longitudinal design, the majority of studies revealed significant associations between early sleeping problems and attachment patterns. First, McNamara (2003) showed that infants with higher sleeping problems at 6 months had insecure-resistant attachment at 15 months. Similarly, Beijers, Jansen, Riksen-Walraven, and de Weerth (2011) revealed that infants who woke up consistently with the highest frequency across the first 6 months developed insecure-resistant attachment at 12 months. On the other hand, infants who had the lowest night-waking frequency over the first 6 months had insecure-avoidant attachment at 12 months. Moreover, Pennestri et al. (2015) revealed that infants who had lower duration of nocturnal sleep, more night-wakings and went to bed later at 6 to 24 months of age developed disorganised attachment more often by 36 months. On the other hand, another study revealed that night waking frequency at 7 months was not

associated with attachment patterns at 12 months (Zentall, Braungart-Rieker, Ekas, & Lickenbrock, 2012). However, infants with insecure-resistant attachment woke up with the highest frequency concurrently at 12 months.

With regards to feeding problems, existing literature has merely conducted cross-sectional studies in infants with clinically diagnosed feeding problems. To begin with, chronically underweight 17 to 21 month-old infants were found to have insecure attachment more often than healthy infants (Valenzuela, 1990). At 12 to 15 months, infants with failure to thrive showed less secure and more often disorganised attachment compared to healthy infants (Ward, Kessler, & Altman, 1993). Furthermore, Chatoor, Ganiban, Colin, Plummer, and Harmon (1998) compared the attachment pattern of infants in three groups of 12 to 37 month-old infants: infantile anorexia, picky eaters and healthy. Their findings revealed that the infantile anorexia group had more often insecure attachment compared to the other groups. In addition, using a relatively large sample, Ward, Lee, and Lipper (2000) found that children with failure to thrive more often had insecure attachment compared to healthy infants. On the other hand, one study revealed no significant associations between food refusal and attachment among infants who were under 18 months of age (Lindberg et al., 1996).

All in all, existing studies provide some support for an association between early regulatory problems and attachment. Although a good number of studies assessed sleeping in relation to attachment, there are only two and underpowered systematic investigations of the relationship between crying and attachment. Moreover, there were no studies investigating the association between feeding problems and attachment in a non-clinical sample. Lastly, no studies have examined the role of

multiple regulatory problems on attachment or controlled for the effect of co-morbid regulatory problems.

Summary and Conclusions

Attachment development is one of the major concepts in developmental psychology. While secure attachment appears to be associated with subsequent social competence in relationships, insecure attachment has been consistently found to increase the risk of mental health difficulties. Nevertheless, strongest associations to behavioural problems have been found with disorganised attachment.

Maternal sensitivity has so far been studied as the major precursor of the development of secure versus insecure attachment patterns, and abusive parenting has been a major factor in understanding the development of disorganised attachment. Apart from abusive parenting, neurodevelopmental vulnerability was shown as an important factor in the development of disorganised attachment. Moreover, early regulatory behaviours have been investigated in relation to attachment patterns; however, the existing evidence is based on few longitudinal studies and only a few were adequately powered. The majority of existing attachment studies have either only focused on one regulatory problem such as crying or sleeping in community samples, or used clinically referred groups of infants with feeding problems. None of the studies controlled for co-morbid regulatory problems and confounding can thus not be excluded. The relationship between multiple regulatory problems and attachment patterns has never been investigated as far as I am aware. Thus, it requires further exploration to understand whether or not early regulatory problems are predictive of attachment styles.

Chapter 5 Outstanding Issues and Research Questions

This chapter introduces the four studies that comprise this thesis, which are presented in Chapters 7 to 10. Following the previous overview of literature that identified current controversies or gaps in knowledge, a brief description of the rationale of each study is given, together with the key research questions.

In general, this thesis aimed to address two key research questions. The first research question explored in this thesis was the following: 'Which precursors are associated with multiple regulatory problems during infancy, neurodevelopmental vulnerability and/or sensitive parenting?' In order to address this question, preterm birth was used as a natural model for neurodevelopmental vulnerability (Volpe, 2009). Nevertheless, there may be a problem with using such a model since having an infant with neurodevelopmental vulnerability might impact maternal sensitivity (Korja, Latva, & Lehtonen, 2012). As a result, the influence of neurodevelopmental vulnerability and maternal sensitivity on multiple regulatory problems might be inter-related and confounded. Thus, first of all, Chapter 7 (Study 1) established the association between neurodevelopmental vulnerability and maternal sensitivity. Chapter 8 (Study 2) focused on the association between neurodevelopmental vulnerability and regulatory problems. In Chapter 9, study 3 investigates the influence of neurodevelopmental vulnerability, maternal sensitivity and multiple regulatory problems, considering the reciprocal associations between maternal sensitivity and multiple regulatory problems. The second research question explored in this thesis was as follows: 'Do multiple regulatory problems increase the risk of insecure and/or disorganised attachment?' Chapter 10 (Study 4) explored if multiple

regulatory problems at 3 and 6 months predict attachment insecurity or disorganisation at 18 months.

Study 1

As discussed in Chapter 3, an extensive amount of empirical research has been conducted to compare sensitivity in mothers of preterm children to full-term children; however, there are contradictory findings making it difficult to reach a clear conclusion whether sensitive parenting differs between term and preterm mother-child dyads (Korja et al., 2008; Montirosso et al., 2010; Rahkonen et al., 2014; Schmücker et al., 2005). This study is the first to systematically investigate whether or not maternal sensitivity is different between mother-infant dyads with preterm and full-term children. A range of potential moderators was considered such as degree of prematurity, the age of the infant, publication date of the study (to identify more recent advanced NICU treatment), type of parenting behaviour, and geographical setting of the studies.

Research Question:

- Is maternal sensitivity different in mothers of preterm infants in comparison to mothers of full-term infants?

Study 2

As reviewed in Chapter 2, while there is a suggestion that neurodevelopmental vulnerability may have an association with regulatory problems (St James-Roberts, 2012), the impact of preterm birth on regulatory problems across infancy has been rarely systematically investigated. Specifically, research on whether preterm infants have more crying or sleeping problems in comparison to full-term infants revealed inconsistent findings (Korja et al., 2014; Maunu et al., 2006; Schmid et al., 2011;

Wolke et al., 1998). Moreover, the majority of the studies reported only on single regulatory problems without reporting on comorbidity between crying, sleeping, and feeding problems (multiple regulatory problems) (Hemmi et al., 2011; Schmid et al., 2010).

Research Questions:

- Do very preterm/very low birth weight infants differ from full-term infants in single and multiple regulatory problems across infancy?
- How early can we predict regulatory problems at 18 months?
- Does the persistence of early regulatory problems enhance the prediction of regulatory problems at 18 months?

Study 3

Although maternal sensitivity and neurodevelopmental vulnerability have been suggested as the two main precursors contributing to the development of early regulatory problems, these have been mainly studied separately rather than within the same sample over time (Degangi et al., 1993; Schmid et al., 2011). Bringing together the associations between very preterm birth, maternal sensitivity and multiple regulatory problems, an explanation for the development of multiple regulatory problems during infancy can be suggested. In particular, maternal sensitivity and regulatory problems should be measured over time to consider the reciprocal nature of their relationship (Sameroff & Chandler, 1975).

Research Question:

- What is the prospective association between very preterm birth, multiple regulatory problems and maternal sensitivity?

Study 4

While early regulatory problems, defined as excessive crying, sleeping or feeding problems, have been related to childhood externalizing as well as internalizing problems (Hemmi et al., 2011), there is a paucity of research on how multiple regulatory problems are associated with later behavioural problems. One important mediator on the route to behaviour problems may be insecure or disorganised attachment. Nevertheless, the association between multiple regulatory problems and attachment has not previously been investigated.

Research Question:

- Do multiple regulatory problems increase the likelihood of insecure and/or disorganised attachment at 18 months?

Chapter 6 Methodology

The purpose of this chapter is to provide a broad overview of the Growth in At-risk Infants (GAIN) study, which is the data source used in study two, three and four. Key features of the GAIN study will be described, including the design, recruitment of participants, study sample, instruments and methods of data collection. Measures from the GAIN study, which are used in the current thesis, will be introduced. Infant regulatory problems will be described in full since they are the main focus of this thesis. Main outcome and predictor variables, including maternal sensitivity and attachment will be briefly described; more detailed information will be available in later chapters. Since Study 1 is a meta-analysis of research, the methods used will be discussed separately in Chapter 7.

Overview of GAIN (Growth of At risk Infants) Study

Growth in At-risk INfants (GAIN) is a longitudinal study, which focused on regulatory behaviours (crying, sleeping and feeding) across infancy and was conducted in 1998. The major aim of the study was to determine the impact of early regulatory problems on attachment and growth.

The GAIN study comprises of two samples: very preterm/very low birth weight (VP/VLBW) and full-term (FT) infants as well as their caretakers. After the first assessment of VP/VLBW infants during their stay in the Neonatal Intensive Care Unit (NICU), all participants were assessed at term, 3 months, 6 months and 18 months of age corrected for prematurity (Table 3). The assessment of two variables of interest (regulatory problems; parenting) at each of the time points allowed the analysis of direction of relationship between these variables. Furthermore, the GAIN study utilized both observational methods and face to face interviews.

Table 3 Overview of the GAIN Study Design

	Assessment Points Across Infancy				
VP/VLBW	Neonatal (Pre-Discharge)	Term*	3 Months*	6 Months*	18 Months*
FT		Term*	3 Months*	6 Months*	18 Months*
Assessment Type	Nurse Observation	Parental Report & Nurse Observation	Parental Report & Researcher Observation	Parental Report	Parental Report & Researcher Observation
Assessment Location	Hospital	Home	Home	Postal Questionnaire	University Observation Room

*Age corrected for prematurity; VP/VLBW= Very Preterm/Very Low Birth Weight, FT= Full-Term

Overview of the Procedure

Recruitment Procedure of the Sample

Identification of Neonatal Intensive Care Units (NICUs) and Ethical Approval

The Neonatal Intensive Care Units (NICUs) had to be within travelling distance from the University of Hertfordshire where the GAIN study was conducted. Therefore, the most suitable NICUs were identified as: Rosie Maternity (Addenbrookes Hospital, Cambridge); Queen Elizabeth II Hospital (Welwyn Garden City) and Luton and Dunstable Hospital (Luton). These three units were referral units for other smaller Special Care Baby Units in the area, which included the infants with the lowest gestation.

Ethical approval for the GAIN study was received from the Ethics Committee of the Psychology Department at the University of Hertfordshire, and NHS ethical approval at each of the Hospital Trusts.

Recruitment Procedure of VP/VLBW Infants

Infants who were born at or before 32 completed weeks of gestation, or weighing less than 1500g, at one of the three participating hospitals (Rosie Maternity-Addenbrooke's Hospital, Cambridge, Luton and Dunstable General Hospital; Queen Elisabeth II, Welwyn Garden City) in the East of England comprised the VP/VLBW group. Four exclusion criteria were applied: 1) If the infant was transferred into or out of the participating unit after birth and prior to discharge home since medical notes remain at hospital of origin, and would therefore not be available; 2) If the parental home was more than 2-hours drive from the hospital which would have been

impractical for follow-up assessments; 3) If the infant's mother had limited English which would have made the interviews difficult; 4) If the infant was being sent for fostering/adoption.

As depicted in Figure 3, among 560 VP/VLBW infants, 253 infants were potential participants to be included in the study. Unfortunately, 56 of these infants died within the first few weeks after birth. Due to limits of the number of children that could be scheduled for follow-up with available resources, a maximum of six infants per month could be recruited. Thus there were 112 infants eligible to be recruited into the GAIN study during the time frame, which was 18 months.

Once a target infant's condition had stabilised and he/she no longer required mechanical ventilation, the researcher introduced herself to the mother and explained the aims of the study and what participation would involve should she agree to the inclusion of her infant. An information sheet was also given to her at this time. A few days later, the mother was approached and asked whether she had had a chance to read the information sheet, had any questions about it, and was prepared to participate. If she agreed, written consent was obtained in the presence of an independent witness, and the infant and mother was thus recruited into the study.

The final consent rate for VP/VLBW infants was 86% (96 out of 112). Sixteen mothers declined to take part in the study due to the following reasons: cultural/religious objections to the research (N= 2); lack of willingness to put themselves or their infants through any more stress (N= 6); some of them felt that they could not afford the time due to demands of older children and/or work commitments (N= 4); and unwillingness to be involved in research due to

dissatisfaction with the hospital care (N= 3). Finally, one mother refused to participate because her infant was diagnosed with suspected serious brain damage.

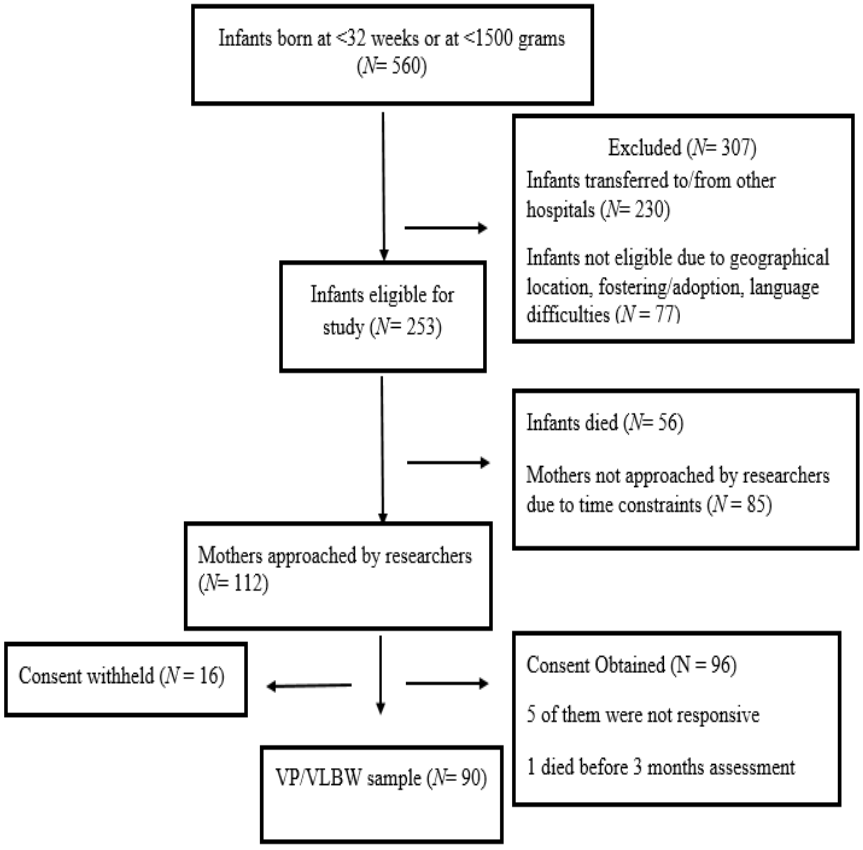

Figure 3 Recruitment Procedure of VP/VLBW Infants

Among the 96 infants recruited into the study, five were lost prior to the term assessment. In four cases they could not be contacted and/or repeatedly were not at home at arranged appointment times. In the fifth case the mother developed a psychiatric illness and the infant was temporarily fostered before the father became the primary caregiver. One infant was seriously ill at term and unfortunately died before the 3-month assessment. Thus, the final VP/VLBW sample of the GAIN study at the 3 months assessment comprised 90 infants.

Recruitment of FT Infants

Recruitment of full-term (FT) infants was conducted in the postnatal wards of the same hospitals within 48 hours of birth. One hundred and fifteen full-term infants (born between 37 and 42 weeks gestation) were recruited as potential participants of this study. There were five exclusion criteria for full-term infants: a) if they were born with a congenital malformation or admitted to a special care baby unit; b) if their parents had very limited English as interviews would have been difficult; c) if they were due to be given up for adoption after birth; d) if mothers were not medically fit to take part; and e) if mothers were not looked after by the Community Midwives' teams from the QEII, i.e., Welwyn Garden City, Hatfield, Waltham Cross/Cheshunt and Rural.

Mothers were selected based on screening of medical records and confirmation of selection criteria with a staff midwife for approach according to the criteria of maternal age, income, and multiple-birth, in order to match the FT sample with the VP/VLBW sample. Eight (6.9%) teenage mothers were also recruited for comparability.

One researcher approached the mother post-delivery on the postnatal ward following approval, and permission to approach, from the midwife. The researcher introduced herself to the mother, and the aim of the study and the procedures that would be involved were explained. An information sheet was also given to the parent at this point. Where appropriate, the mother was given time to enable her to discuss the study with her partner or relatives if she wished. One of the researchers approached her again within 24 hours, or telephoned her at home with her permission following her discharge home from the ward, to enable her to ask any questions she might have about the study. When consent was given on the ward, as in most cases, a consent form to confirm her participation in the study was signed in the presence of a midwife who countersigned to witness the mother's signature. All the data collection

was carried out by Tina Gutbrod, Libby Rust and Karin Edme with the support of the following student researchers: Laura Golders, Sue Philips, Stephanie Auge and Becky Segar.

The Sample of the Current Study

Participants of the current thesis include infants who completed the assessments at term, 3 months, 6 months and 18 months (N= 178). Detailed information about the demographical characteristics of the participants is provided in Chapters 8, 9, and 10.

Drop-outs

The number of participants who were lost to follow up at each assessment point is shown in Figure 4. Dropout analysis on participants who were lost across assessment points is provided in Study 2 (Chapter 8).

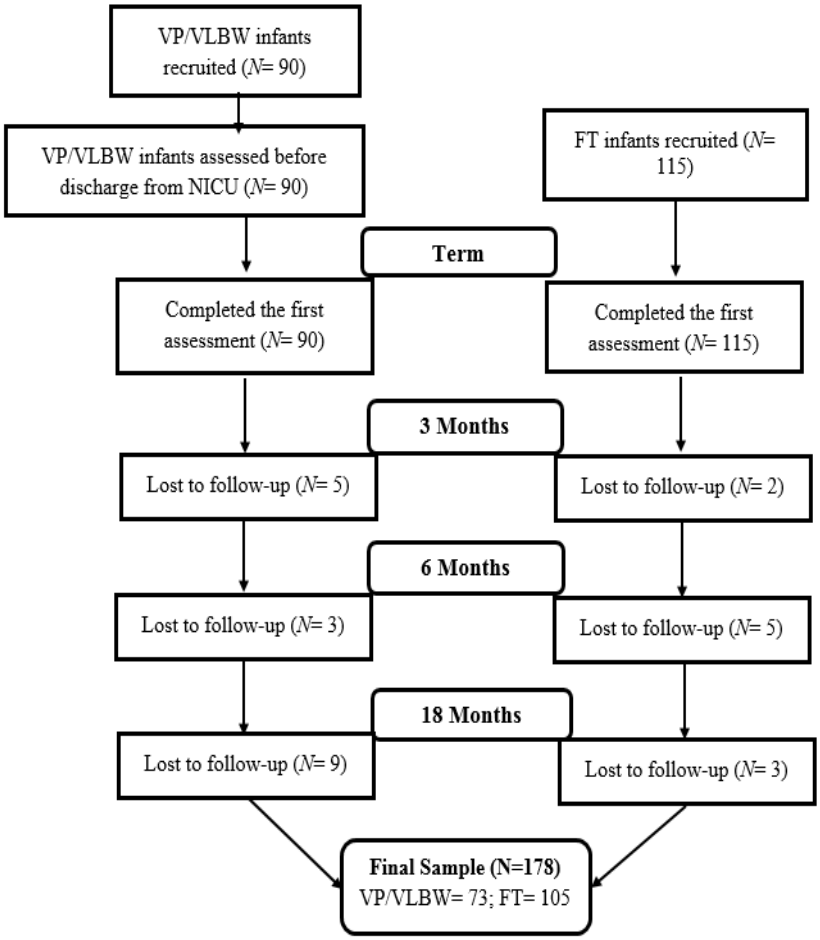

Figure 4 The Number of Dropouts across Assessment Points

Instruments of Predictor and Outcome Variables

Assessment instruments used in this study include parental questionnaires, nurse and researcher observations. The main measure of this study was the infant interview questionnaire on crying, sleeping and feeding, which was applied continuously at each assessment point and is outlined in detail below. Only at 6 months, it was posted to mothers as a questionnaire. Moreover, maternal sensitivity was observed with different instruments at term, 3 months and 18 months. The assessment procedures of these instruments are described in chronological order. Lastly, attachment was measured with the strange situation procedure at 18 months.

Infant Regulatory Problems

The major focus of the current study was infant regulatory problems (excessive crying, sleeping, and feeding difficulties), which was assessed with an interview on crying, sleeping and feeding at term, 3 months, 6 months and 18 months of age (Appendix A). The crying, sleeping, feeding interview provides detailed information about infants' crying, sleeping, and feeding patterns. The questions were administered as a structured interview at term, 3 and 18 months and sent as a postal questionnaire at 6 months, and were developed for the purposes of this study adapting items from the following measures: Infant Feeding Questionnaire (Skuse, 1987); Infant Feeding Interview (Ramsay & Gisel, 1996); Infant Sleep Habits Questionnaire (Seifer, 1992); Infant Sleep Questionnaire (Morrell, 1999); Crying Pattern Questionnaire (St James-Roberts & Halil, 1991). The questionnaire included 15 items assessing crying behaviour, 16 items assessing sleeping patterns, and 21 items assessing feeding behaviours. Items of the questionnaire included the following types: open-ended questions, 3-point-Likert scales, 5-point-Likert scales and dichotomous (yes/no) questions.

Guided by the findings of the previous literature, a selection of items from the maternal report on crying, sleeping, feeding interview across infancy was used to identify the infants who had regulatory problems. The rationale and the criteria for the determination of each single regulatory problem and multiple regulatory problems are described below.

Crying Problem

In order to measure crying behaviour until 18 months of age, mothers were asked to report how long their infant fusses/cries during an average day in minutes. Moreover, they reported on how easy or difficult it was to soothe their baby when it was crying (1= very easy; 5= very difficult). Lastly, they reported on whether their infants' crying/fussing was distressing or not (0= not at all, 1= a little, 2=very distressing). Based on these items, three criteria were determined to identify infants who have an excessive crying problem.

In general, the major criterion to determine a crying problem is based on the duration of crying. Infants who cry above a certain duration were considered as excessive criers using age specific criteria. To illustrate, excessive duration of crying was defined as crying for more than or equal to 180 minutes at term and 3 months based on adapted Wessel criteria (Wessel et al., 1954). At 6 months, it was defined as crying more than or equal to 120 minutes, and more than or equal to 60 minutes at 18 months, since fuss/cry average drops to approximately 60-70 minutes at 6 months and to below an hour at 18 months (Barr, Paterson, MacMartin, Lehtonen, & Young, 2005; Barr, St James-Roberts, & Keefe, 2001). In addition to excessive crying, mothers' experience of not being able to soothe their infant easily has been suggested as an influential variable to determine the crying problem (Wolke et al., 1995a). Mothers reported on how easy or difficult it was for them to soothe their baby on a 5-point scale (1= very easy; 5= very difficult), which was divided into two categories (0= easy to soothe, if scored ≤ 3; 1= difficult to soothe if scored ≥ 4). Lastly, mothers rated their perception of their infants' crying on a 3-point scale (0= not at all; 1= a little; 2= very distressing), which was divided into two categories: (0= not distressing, if scored ≤ 1; 1= very distressing, if scored 2). Based on their score on

the three items, infants were categorized into two groups= no crying problem (if the score was 0) and crying problem (if the score was ≥1).

Sleeping Problem

In order to measure sleeping problem until 18 months of age, mothers were asked to report on the following three open-ended questions: a) how many times their infant usually woke up at night, b) how long it took the mother to settle the infant to sleep in minutes and c) the longest sleep duration without waking up at night in minutes. Infants received a score of 1 according to the three criteria derived from the literature: a) if they woke up two times or more per night (0-5 am) on at least 5 nights during a week, b) if the duration of settling to sleep was longer than 30 minutes, and c) if the duration of sleeping without waking up was less than 5 hours. Afterwards, infants were divided into two categories according to their score: no sleeping problem (if the score was 0) and sleeping problem (if the score was ≥1).

Feeding Problem

In order to measure problem feeding behaviours until 6 months of age, mothers were asked to report whether or not their infant showed the following behaviours during most feeds: stopping after a few sucks, excessive dribbling/difficulty swallowing, gagging/choking during the feed, and fight against the breast/bottle. At 18 months, mothers were asked to rate the frequency (0= never, 1=occasionally, 2= often) of the following behaviours during meal time in the last month: drool when drinking, gagging/choking during the feed, problems swallowing, eats too little, leaves most of the food offered, poor appetite, picky eater, slow eater, refuses to eat lumpy food and refuses to eat puree.

Overall, feeding problems were grouped into two categories at each assessment point: oral/motor functioning difficulties and faddy eating/food refusal. Oral motor functioning included the following three items up to 6 months: stopping after a few sucks, excessive dribbling/difficulty swallowing, and gagging/choking during the feed. Furthermore, up to 6 months of age, faddy eating/food refusal was assessed with one item: fight against the breast/bottle. Existence of feeding problems up to 6 months was defined as infants who showed two or more problems in oral-motor functioning and/or showing faddy eating/food refusal.

At 18 months, oral-motor functioning category included the following items: drool when drinking, gagging/choking during the feed, and problems swallowing. Faddy eating/food refusal category included the following items: eats too little, leaves most of the food offered, poor appetite, picky eater, slow eater, refuses to eat lumpy food and refuses to eat puree. Infants were coded as having difficulties in oral-motor functioning if they often showed two or more of the oral-motor functioning variables. Furthermore, they were coded as having faddy eating/food refusal if they often showed five or more of the faddy eating/food refusal variables. If they had problems in oral-motor functioning and/or faddy eating/food refusal, infants were considered as having a feeding problem.

Multiple Regulatory Problems (Comorbidity of Regulatory Problems)

Participants' score on crying, sleeping and feeding problems were summed to create an overall regulatory problems score. They were further categorized into two groups indicating whether or not they had comorbidity of regulatory problems: no multiple regulatory problems (no regulatory problems or single regulatory problems) and multiple regulatory problems (two or three single regulatory problems). This score was computed at each assessment point.

Maternal Sensitivity

Maternal Sensitivity at Term

Maternal sensitivity at term was measured with the Boston City Hospital Assessment of Parental Sensitivity (BCHAPS; Zahr & Cole, 1991), which is a questionnaire completed by nursing staff to assess sensitive parenting in mothers of infants in Neonatal Intensive Care Units (NICU) (Appendix B). The BCHAPS measures how the mother cares for, interacts with and enjoys the relationship with her infant rated on thirteen items with 5-point Likert type scales (1=poor; 5=very competent). High concurrent and predictive validity of the questionnaire was established (Zahr & Cole, 1991).

The final weeks prior to hospital discharge seemed the most appropriate date for the first interview with the mother and for obtaining nursing staff ratings of sensitivity. At this point most infants were no longer in a critical condition and nursing staff had established contact with mothers for at least ten days. For FT infants, midwives visited the mother and baby at home several times during the first 10 days and completed the BCHAPS during home visits.

The 13 items in the BCHAPS (Appendix B) were summed to create a maternal sensitivity variable, in which higher scores indicated higher maternal sensitivity. Reliability of the scale was high (α_{total}= 0.95, $\alpha_{VP/VLBW}$= 0.96, α_{FT}= 0.85).

Maternal Sensitivity at 3 Months

Maternal sensitivity at 3 months was measured with the Mother-Infant Structured Play Assessment (MISPA). MISPA is an observational assessment tool, which includes an 8-minute, semi-structured face-to-face mother-infant play interaction

composed of 5 sessions (Table 4). Episodes 3 to 5 followed the Still Face interaction paradigm (Tronick, Als, Adamson, Wise, & Brazelton, 1978) to assess infant reaction the still face situation and repair of the interaction. Maternal behaviours (See Appendix C for a detailed description) were coded on 5-point scales according to a coding scheme adapted from the following established coding schemes: The Play Observation Scheme and Emotion Ratings: POSER (Wolke, 1986); The Emotional Availability Scales: EAS (Biringen, 1993); The Infant and Caregiver Engagement Phases: ICEP (Weinberg & Tronick, 1998). For the purposes of the current thesis, maternal behaviour ratings during the play situations (first 2 episodes) prior to the Still Face situation were utilised. The videotapes were coded by two observers blind to child characteristics and study aim with 5-point scales (Appendix C).

The 7 sub-scales assessing maternal behaviour were factor analysed using principal component analysis with varimax rotation. The analysis yielded 2 factors explaining a total of 42.4% of the variance for the entire set of variables. The first factor was labelled as 'maternal sensitivity' and includes the following subscales: sensitivity (1= highly insensitive; 5= highly sensitive), positive facial emotion expression (1= none; 5= very much), stimulation level (1=low; 5= high). All subscales had primary loadings of over 0.60. The scores of these three scales across the 3 episodes before the still-face paradigm were summed to yield the maternal sensitivity measure. The two researchers independently coded 20 videotaped interactions. The inter-rater reliability scores for each item were moderate to high ($\kappa_{\text{positive emotion}}$= 0.76, $\kappa_{\text{sensitivity}}$= 0.76, $\kappa_{\text{stimulation level}}$= 0.78) and the overall internal consistency of the maternal sensitivity factor was moderate ($\alpha_{\text{maternal sensitivity}}$= 0.73).

Table 4 Episodes and Durations of the MISPA

Episode	Task	Instructions	Duration
1	Structured toy play	"Please play with your baby using this toy in any way you want."	2 minutes
2	Unstructured Play	"Please play with your baby as you usually would if you had some free time. This time, please do not use toys."	2 minutes
3	Attention task	"Please get your baby to look at you and watch your face."	1 minute
4	Still Face: Perturbation	"Please make a "still face" (serious face; emotionless) – please do not touch or play with your baby."	1.5 minutes
5	Reunion (free play)	"Now please play with your baby again."	1.5 minutes

Maternal Sensitivity at 18 Months

Maternal sensitivity at 18 months was assessed with The Play Observation Scheme and Emotion Ratings (POSER; Wolke, 1986), which is a tool to measure mother-infant interaction in two play situations (unstructured and structured play), overall lasting for five minutes (Table 5). The unstructured play session included mother and infant playing with a shape-sorter toy in any way they like for 2.5 minutes.

Afterwards, in the structured play session, mothers were asked to play with their infant according to the structured instructions provided by the researcher.

The videotaped mother-infant play session was coded with The Play Observation Scheme and Emotion Ratings (POSER), which included items to measure maternal, infant and mother-infant joint behaviours (See Appendix D). After 3 months of training procedure, scales in both sessions were rated by two independent researchers who were blind to child characteristics. Each episode was viewed by the researchers three times, focusing firstly on maternal behaviours, followed by infant behaviours and mother-infant joint behaviours. Overall, the coding procedure took approximately half an hour.

Table 5 Episodes and Durations of POSER

Episode	Task	Instructions	Duration
1	Unstructured Toy Play	"Please play with your child using this toy in any way you want"	2.5 minutes
2	Structured Toy Play	"Please teach your child how to play with this toy"	2.5 minutes

Maternal behaviours were used for the purposes of this study, which were rated either on a 9-point scale or on a 5-point scale. The seven sub-scales relating to maternal behaviour were factor analysed using principal component analysis with varimax rotation. The analysis yielded 2 factors explaining a total of 64.1% of the variance for the entire set of variables. The first factor, which included amount of expressed positive emotion (1= none; 5= very much), sensitivity (1=highly

insensitive; 9= highly sensitive), and appropriateness of play (1= very inappropriate play; 9= very appropriate play), was labelled maternal sensitivity. All subscales had primary loadings of over 0.60. The inter-rater reliability of each maternal behaviour items ($\kappa_{\text{positive emotion}}$= 0.93, $\kappa_{\text{sensitivity}}$= 0.90, $\kappa_{\text{appropriateness of play}}$= 0.91) was high. The sum of these three subscales in in the unstructured and structured play situation generated the maternal sensitivity score, which had high overall internal consistency ($\alpha_{\text{maternal sensitivity}}$= 0.90).

The scales applied at 3 and 18 months were very similar to each other in structure (both play observations) and scales (adapted from similar measures); however, the measure at term was different. The reason to use a different measure neonatally was that a long period is needed to observe parent interaction in newborns who spend most of their time sleeping, thus making it very difficult to schedule observations at a time when parents are within the NICU environment or just discharged home. Therefore, after pilot work, observations conducted by nurses and midwives using a validated measure were implemented. Nevertheless, using a different measure could have had an impact on the association between maternal sensitivity measures over time. However, the high correlation between maternal sensitivity at term and maternal sensitivity at 3 months of 0.51 indicates that the same construct was assessed despite different data sources and measures. Moreover, another study (Halligan et al., 2013), which used the same observational measure to rate maternal sensitivity at 3 months and 15 to 18 months revealed a correlation of 0.29 between the two assessments. This correlation is comparable to the correlation between 3 months and 18 months maternal sensitivity measure (0.24) in our study. We are thus confident that the 3 sensitivity measures tapped the same construct.

Attachment

The gold standard for evaluating the quality of infant attachment to the caregiver at 18 months of age is a structured laboratory paradigm known as the strange situation procedure. During this procedure, infants experience separations and reunions with the attachment figure in order to elicit attachment behaviour (Ainsworth et al., 1978). The sequence, length and the procedure of the 8 episodes are outlined below in Table 6.

Table 6 Strange Situation Procedure

Episode	Description	Duration
1. Introduction	Observer introduces the mother and her infant to the room	30 seconds
2. Infant plays alone	The mother is nonparticipant while the infant explores the room.	3 minutes
	Play is stimulated after 2 minutes.	
3. Stranger enters the room	"Stranger" (Experimenter) enters and is silent	1 minute
	Talks to the mother	1 minute
	Approaches the infant	1 minute
4. First Separation	Mother leaves the room	
	Stranger's behaviour is geared toward the infant	3 minutes or less
5. First Reunion	Mother returns and stranger leaves.	3 minutes or more
	Mother leaves again	

6. Second Separation	Infant is alone	3 minutes or less
7. Stranger Returns	Stranger enters and interacts with infant	3 minutes or less
8. Second Reunion	Mother returns and stranger leaves	3 minutes or more

The mother and 18-month-old infant's behaviours during the 8 episodes were recorded by two video cameras in a child friendly laboratory room. The procedure was carried out by a PhD researcher who had been trained in the procedure and coding by Prof. Alan Sroufe's research group (Elizabeth Carlson) at the Child Development Lab at the University of Minnesota. In order to assess secure versus insecure-avoidant and insecure-resistant classifications, attachment behaviour was coded according to the scoring systems outlined in manuals of Ainsworth et al. (1978). Furthermore, the coding manual of Main and Solomon (1990) was used to determine attachment disorganisation. All tapes were sent for a coding of the attachment classifications at a Strange Situation accredited Laboratory at the Institute of Child Development, University of Minnesota, by Dr. Elizabeth Carlson who was blind to the research aim.

First, infants were classified as secure (B), insecure-avoidant (A) and insecure-resistant (C) based on their pattern of scores on four 7-point scales: proximity seeking behaviour, contact maintaining behaviour, avoidance of the caregiver, and resistance. Infants were classified as having a secure attachment if they showed moderately high proximity seeking and contact maintaining behaviours, along with low avoidance and resistance. Insecure-avoidant attachment was classified if they

showed low proximity seeking, contact maintaining and resistance, accompanied by high avoidance. Finally, infants were classified as having insecure-resistant attachment if they had high proximity seeking, contact maintaining, and resistance, together with low avoidance. The securely attached group (B) was coded as '1' and the rest of the participants were coded as '0' to compare secure vs. insecure attachment.

Attachment disorganisation scores were calculated according to Main and Solomon's (1990) continuous scale of attachment disorganisation on a 9-point scale, where '1' represented no signs of disorganisation and '9' represented definite signs of attachment disorganisation. Signs of disorganized attachment include contradictory behaviour such as avoidance and resistance at the same time or puzzling behaviour without an apparent function. In order to make the organised versus disorganised classification, those scoring ≥6 were classified as disorganised; those scoring 5 were given either a primary or a secondary disorganised classification depending on the particular case; and those scoring <5 were qualified as having organised attachment.

Overall, secure vs insecure (insecure-resistant, insecure-avoidant) and organised (secure, insecure-resistant and insecure-avoidant) vs disorganised categories were used for the purposes of this study as recommended standard practices. Insecure resistant (N= 8) and insecure-avoidant (N= 8) classifications were examined in one category since there was a lack of statistical power to conduct analysis on individual subgroups.

Background and Control Variables

A variety of individual and sociodemographic measures coded in the GAIN study were used as predictor or control variables throughout the analysis. Table 7 provides

a brief summary of each of these measures, including descriptions of each item, the instrument and the studies in which they were used.

Table 7 Descriptions of Variables used as Background or Control Measures

Variables	Items	Categories/Range	Definition	Assessment Type	Used in study
Sex	1	Male Female	Gender of the infant	Parent Interview	2, 3 & 4
Birth Weight	1		Weight at birth in grams	Medical Records	2, 3 & 4
Gestational Age	1		Calculated from the first day of the mother's last menstrual period and repeated ultrasound in pregnancy	Medical Records	2, 3 & 4
Small for Gestational Age (SGA)	1	Appropriate for Gestational Age (AGA) Small for Gestational Age (SGA)	Determined as below the 10^{th} percentile of birth weight according to gestation on standard growth charts (Norris et al., 2015)	Medical Records	2
Multiple Birth (Twins)	1	Twin Singleton	Twin status		2, 3 & 4
Respiratory Distress Syndrome (RDS)	1	Not present Mild Moderate Severe	X-ray evidence of insufficient development of the lungs: Small lung volume, air bronchograms or air in the airways of the lung, granular-looking areas on the lung and oxygen requirement of less than 28 days	Medical Records	2
Bronchopulmonary Dysplasia (BPD)	1	Not Present Present	The need for supplemental oxygen use for more than 28 days and X-ray evidence of lung changes such as the presence of hyperinflation, cystic changes on chest radiographs	Medical Records	2

Medical Risk	4		Composite of below 4 items	Medical Records	2, 3 & 4
a) Neurosensory Deficits		Not Present Mild/Moderate Severe	Clinically significant deficits in hearing, vision, muscle tone, or presence of hydrocephalus		
b) Rehospitalisation		Not readmitted One rehospitalisation only >1 rehospitalisation	Readmission to the hospital after discharge from the neonatal unit		
c) Surgical Procedures		No surgery Yes	Infant had surgery (e.g., for patent ductus arteriosus, nectorizing enterocolitis)		
d) Oxygen Dependency		No oxygen use Oxygen use at term but not at 3 months Oxygen use at 3 months	Oxygen use of more than 21%		
Central Nervous System (CNS) Defect	3	Not Present Present	Six brain ultrasound scans to measure haemorrhage, ventricular dilatation, and parenchymal cysts. All infants whose early scans were scored ≥1 had repeat scans at a later date. Based on the findings of the sixth scan, it was determined whether infants had a CNS defect or not.	Medical Records	2
a) Haemorrhage		None Subependymal/choroidal 1 side Intraventricular 1 side Parenchymal 1 side Subependymal/choroidal bilateral Intraventricular bilateral Parenchymal bilateral	Bleeding into the brain's ventricules		

b) Ventricular Dilatation		No Dilatation < 4mm 1 side > 4mm 1 side < 4mm bilateral > 4mm bilateral	Dilatation of lateral ventricles		
c) Parenchymal Cysts		None Porencephalic cyst 1 side Cystic leucomalacia 1 side Porencephalic cyst bilateral Cystic leucomalacia bilateral	White matter brain injury		
Breastfeeding	1	Not breastfeeding Breastfeeding	How mother feeds her infant	Parent Interview	2, 3 & 4
Income	1	£0–£25k £25k–£40k >£40k	Family income a year	Parent Interview	2, 3 & 4
Maternal Education	1	<10 years: No educational qualification 10 years: Basic educational qualification >10 years: Further educational qualification	Years of education	Parent Interview	2, 3 & 4
Maternal Depressive Symptoms	10	Ranging from 0 to 30	Maternal post-natal depressive symptoms measured with Edinburgh Depression Scale (Cox, Holden, & Sagovsky, 1987).	Parent Interview	3 & 4

Summary

Studies 2, 3, and 4 (Chapters 8-10) drew on data from the Growth of At Risk Infants (GAIN), a prospective study, comprising of 178 infants until 18 months of age and their caretakers recruited in the East of the UK. Infant regulatory problems were used as the primary measure throughout the research. In addition, a variety of individual, and sociodemographic characteristics were considered. Table 8 provides a summary overview of the measurement of main variables of the study, including the instrument and studies in which they were used.

Table 8 Main Variables Used from the GAIN study

Assessment Time	**Variable**	**Measures**	**Measurement Type**	**Used in**
NEONATAL* (VP/VLBW only)	Maternal Sensitivity	Boston City Hospital Assessment of Parental Sensitivity (BCHAPS)	Nurse Observation	Study 3 & 4
TERM (FT only)	Maternal Sensitivity	Boston City Hospital Assessment of Parental Sensitivity (BCHAPS)	Nurse Observation	Study 3 & 4
	RPs	Infant Crying, Sleeping, Feeding Interview	Parental Interview	Study 2 & 3
3 MONTHS	Maternal Sensitivity	Mother-Infant Structured Play Assessment (MISPA)	Researcher Observation	Study 3 & 4
	RPs	Infant Crying, Sleeping, Feeding Interview	Parental Interview	Study 2, 3 & 4
6 MONTHS	RPs	Infant Crying, Sleeping, Feeding Interview	Postal Questionnaire	Study 2, 3 & 4
18 MONTHS	Maternal Sensitivity	Play Observation Scheme and Emotion Rating (POSER)	Researcher Observation	Study 3
	RPs	Infant Crying, Sleeping, Feeding Interview	Parental Interview	Study 2 & 3
	Attachment	Strange Situation Task	Researcher Observation	Study 4

RPs= Infant Regulatory Problems. *VP/VLBW infants were assessed during neonatal period before discharge from the hospital when they reached term equivalent age.

Chapter 7 Maternal Sensitivity in Parenting Preterm Children: A Meta-Analysis

Context: Preterm birth is a significant stressor for parents and may adversely impact maternal parenting behaviour. However, findings have been inconsistent.

Objective: The objective of this meta-analysis was to determine whether mothers of preterm children behave differently (e.g. less responsive or sensitive) in their interactions with their children after discharge home than mothers of term children.

Data Sources: MEDLINE, PsychINFO, ERIC, PubMED, and Web of Science were searched from January 1980 through May 2014 with the following keywords: "premature", "preterm", "low birth weight" in conjunction with "maternal behavio*r", "mother-infant interaction", "maternal sensitivity", "parenting".

Study Selection: Both longitudinal and cross-sectional studies which used an observational measure of maternal parenting behaviour were eligible.

Data Extraction: Study results relating to parenting behaviours defined as sensitivity, facilitation and responsivity were extracted and mean estimates were combined with random effects meta-analysis.

Results: Thirty four studies were included in the meta-analysis. Mothers of preterm and full-term children did not differ significantly from each other in terms of their behaviour towards their children (Hedge's g= -0.07, 95 % CI: -0.22, 0.08; z= -0.94; *P*= 0.35). The heterogeneity between studies was significant and high (Q= 156.42; I^2= 78.9, *P*= 0.001) and not explained by degree of prematurity, publication date, geographical area, infant age or type of maternal behaviour.

Limitations: Heterogeneity of the studies was high.

Conclusions: Mothers of preterm children were not found to be less sensitive or responsive towards their children than mothers of full term children.

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Introduction

The survival rate of preterm infants has increased rapidly as a result of the improvements in medical and nursing care and technology in the last decades (Saigal, 2008). Infants born preterm often require care in Neonatal Intensive Care (NICU) or Special Care Baby Units (SCBU) for weeks and often months (Goldberg, 2002).

Being in close contact with the mother in the early days of life has been proposed to be crucial for the development of mother-infant bonding (Klaus & Kennell, 1976). Preterm birth and incubator care might influence the infant, the mother and their relationship. Preterm children experience more neurodevelopmental, cognitive and behavioural problems in infancy and childhood (Aarnoudse-Moens, 2009; Johnson, 2013) and may be less attentive in their communication with their mothers (Filed, 1977), smile less often (Segal, 1995), and be less responsive (Zarling, 1988; Jaekel et al., 2012). Furthermore, it might impair the mother's own perception about her ability to take care of the newborn (Beckwith & Rodning, 1996; Chapiesky, 1997). Apart from separation this is often a stressful time for parents due to uncertain outcomes for their infants. It has been reported to increase the risk of depression in mothers (Meyer et al., 1995; Singer et al., 1996), lead to symptoms of posttraumatic stress disorder (PTSD) (Pierrehumbert, Brisch, & Nicole, 2000) and may adversely affect the mother-infant relationship (Feldman, 2007; Wijnroks, 1999).

Maternal sensitivity has been defined as mother's ability to infer infant's signals and respond to them appropriately (Ainsworth et al., 1974). In full-term children, sensitive and responsive parenting has been shown to increase cognitive, social and emotional outcomes (Bornstein & Tamis-Lemonda, 1997; Landry, Smith, & Swank, 2006). On the other hand, insensitive parenting has been related to poor regulatory style in infancy (Calkins, 1994) and more psychological problems in young adulthood (Lyons-Ruth et al., 2013). Recent evidence indicates that sensitive parenting may be even more crucial for preterm children to achieve similar outcomes to full-term children (Jaekel, Pluess, Belsky, & Wolke, 2015). Thus, increasing maternal sensitivity and responsiveness with interventions has been reported to result in more developed communication skills, improved cognitive outcomes and more positive mood in preterm infants (Newnham, Milgrom, & Skouteris, 2009; Orton, Spittle, Doyle, Anderson, & Boyd, 2009; Ravn et al., 2012).

However, there is considerable inconsistency in findings, with several studies that reported mothers of preterm infants to be as responsive or sensitive (Korja et al., 2008; Montirosso et al., 2010; Rahkonen et al., 2014) or even more so than comparisons (Crawford, 1982). Concepts used in observation studies of parenting also differed; mainly referred to as "sensitivity" and "responsiveness". Other than these two terms, behaviours such as directiveness, suggestions and the frequency of smiling (Stern, Karraker, McIntosh, Moritzen, & Olexa, 2006) were also used by some studies. We use the term "facilitation" to generally refer to these behaviours.

These inconsistencies may be due to the children studied, i.e. whether they were born moderate to late preterm or very preterm. In addition, better parental access and more parental care in recent years (after 2000) have decreased stress for parents and infants (Latva, 2004). Infant age is also a critical factor as the differences in maternal

behaviour between preterm and full-term infants have been suggested to lessen after 6 months of age (Montirosso et al., 2010). Moreover, the difference in the measures used to evaluate type of parenting behaviour (sensitivity, responsivity, facilitation) could be a critical factor to consider in the explanation of findings. Finally, geographical variations in NICU care practices (Europe vs America) may account for some of the inconsistencies in the findings as care practices might differ between continents.

The aim of this meta-analysis was to systematically investigate whether observed maternal behaviour in interaction with their preterm infants or children differs systematically from that of mothers with their full term infants or children. Furthermore, we investigated whether the following would moderate the results: degree of prematurity (i.e., very preterm (<32 weeks gestation) vs moderate to late preterm birth (32-36 weeks gestation)), publication date before 2000 versus after (indicator of recent modern NICU care and open visiting patterns), type of parenting behaviour and finally, infant age, and geographical setting of the studies (Europe, America).

Methods

The current meta-analysis was conducted in line with MOOSE (Meta-Analysis of Observational Studies in Epidemiology) Guidelines (Stroup et al., 2000).

Search Strategy

A literature search was conducted for cross-sectional and longitudinal studies of maternal behaviour in preterm infant-mother dyads, published between January 1980 and May 2014. The article search was finalized on 30 June 2014. The following electronic databases were searched: MEDLINE, PsychINFO, ERIC, PubMED, and

Web of Science. The keywords used were as follows: “premature”, “preterm”, “low birth weight” in conjunction with “maternal behavio*r”, “mother-infant interaction”, “maternal sensitivity”, “parenting”.

MEDLINE search yielded 3 articles, PsychINFO yielded 336 articles, ERIC yielded 11 articles, PubMED yielded 70 articles and Web of Science yielded 111 articles. Overall, 531 articles were included in the literature search. 43 duplicates were removed from the search. Overall, the final literature search included 488 articles Figure 5.

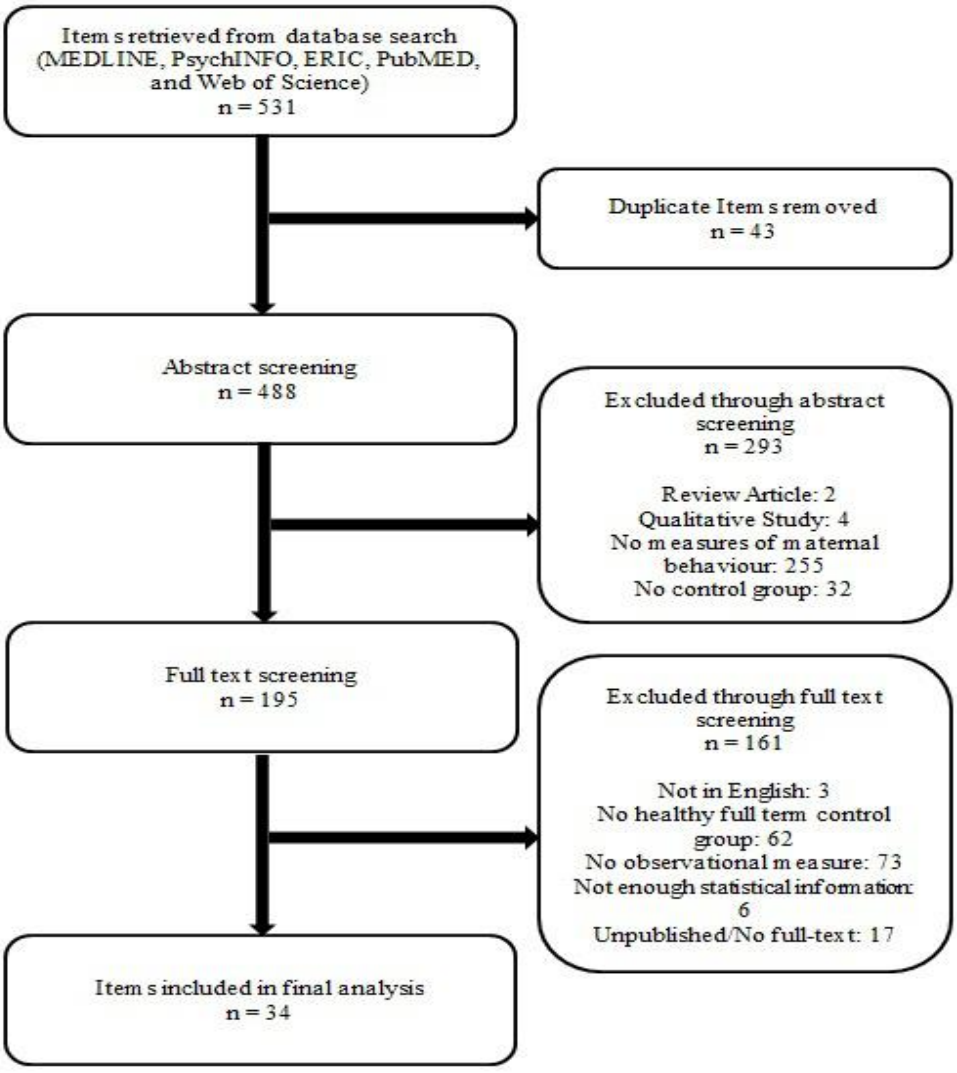

Figure 5 Flow Diagram Showing Study Eligibility

Study Inclusion and Exclusion Criteria

Studies were included in the analysis according to five criteria. First, articles should report on the following maternal parenting behaviour constructs: maternal sensitivity which is defined as mother's ability to perceive and infer the meaning behind her infant's behavioural signals, and to respond to them promptly and appropriately (Ainsworth et al., 1974); "maternal responsiveness" (Barratt, 1992; Stevenson, Roach, ver Hoeve, & Leavitt, 1990) such as providing stimulation to the infant; or "maternal facilitation" (Barnard, Bee, & Hammond, 1984; Schmucker et al., 2005) such as positive regard and respect for the child's autonomy (Potharst, 2012). Since these terms tapped into similar constructs, our review used maternal parenting behavior as an umbrella term to refer to maternal sensitivity, maternal responsiveness and maternal facilitation. Second, studies had to use an observational instrument to measure maternal parenting behaviour. Third, studies had to include a full-term comparison group. Fourth, enough statistical information (correlations, means and standard deviations, sample size, p or t values) should be reported in the articles or provided by authors after contacting them to enable computing effect sizes. Last, the articles had to be in English language. Studies not fulfilling these criteria were excluded (Figure 5).

The titles and abstracts of 488 articles were reviewed and 293 excluded based on abstract only. We reviewed the full text of the remaining 195 articles according to the inclusion criteria and 155 articles were excluded. Furthermore, 6 studies had no information to compute effect sizes. Contact information of one of the authors (Gerner, 1999) could not be found. The other authors of these studies were contacted, however, three of the authors did not reply (Crnic, Ragozin, Greenberg, Robinson, & Basham, 1983; Crnic et al., 1983; Landry, 2001) and two could not provide the

information (Feldman, 2007; Stern, 2006). Thirty-four studies were included in the meta-analysis (Table 9). The selection process of articles was performed by two researchers independently. The overall agreement in selection of articles according to the predefined criteria was Cohen's kappa 0.86 at the abstract selection stage and 0.83 at the full-text retrieval stage. The discrepancies in 10 articles were discussed and mutually resolved by the coders.

Quality Assessment

The Newcastle Ottawa Scale (NOS; Wells et al., 1999) was used to assess the quality of studies referring to selection, comparability, and outcome or exposure, for case control and cohort studies. Scores in this scale could range from 0 to 9 with higher scores indicating higher quality. Studies were rated by two independent coders and the agreement for overall rating for each study was found to be high (Kappa= 0.82). The overall ratings of the studies ranged from 7 to 9 (M= 8.08, SD=0.79) indicating overall high quality.

Data Extraction

Eligible studies were reviewed in order to extract the observed maternal behavior data. When available, information about the comparison of preterm and full-term group was extracted directly from the article. Different studies provided the data in different formats; sample size with means and standard deviations, p-value or t-value. When any of this information was unavailable, it was requested from the authors. In the cases where the researchers reported the statistical information for each observed maternal behavior separately, a mean score and a pooled standard deviation score were computed. Furthermore, categorical information regarding the degree of prematurity, being published before/after 2000, geographical setting, type

of parenting and infant age were extracted from the articles (Table 9). Furthermore, type of parenting behavior was coded as maternal sensitivity or responsivity in accordance with what was reported in the results section. Facilitation was coded where maternal behaviors were reported separately without being referred to as sensitivity or responsiveness. One exception was Barnard et al. (1984), which was coded as facilitation even though responsivity was also reported in the study since facilitation was reported at all measurement times. The categorization of these variables was completed by the first author under the supervision of the second author.

Table 9 Summary of the Studies Included in the Analysis

Study	N	Age	Birth Weight (grams) Mean (SD)	GA (weeks) Mean (SD)	Gender (M/F)	Design	Duration of Observation	Instrument	Result	Moderators: Type of Parenting Behaviour	Degree of Prematurity	Publication Date	Geographical Setting	Infant Age
Agostini, Neri, Dellabartola, Biasini, & Monti (2014)	P: 69, F: 60	3M	P: 1040.71 (127.49), F: 3410.24 (462.76)	P: 28.53 (1.7), F: 39.86 (1.13)	P: 45/24; F = 42/38	CS	5 mins	Global Rating Scales(Murray, Stanley, Hooper, King, & Fiori-Cowley, 1996): 5-point scale to rate sensitivity, intrusiveness, remoteness, signs of depression	NS	Maternal Sensitivity	VPT	After 2000	Europe	<= 6m
Barnard, Bee, & Hammond (1984)	P: 88, F: 166	4M, 8 M, and 24 M	No information	P: ≤34, 31.1 (1.45); F: 39.4 (1.1)	P: 40/48; F: 83/83	LN	1-to-2 hrs	4-point scale to rate maternal responsiveness to infant's distress or satiation cues	S/S/S	Maternal Facilitation	VPT	Before 2000	America	>6m
Barratt, Roach, & Leavitt, (1992)	P: 24, F: 24	4 M	P: 1460 to 2420 (M= 2099); F: 2849 to 4408 (M = 3493)	P: 31 to 36 (M= 34); F: 37 to 42 (M= 40)	No information	CS	1 hr 10 mins	Initiations of the following behaviours were coded: mother vocalizations, touches and smiles.	S	Maternal Responsiveness	M/LPT	Before 2000	America	<= 6m

Barratt, Roach, & Leavitt (1996)	P: 21, F: 21	12M and 20M	P: 1460-2420 (M=2125), F: 2892-4253 (M= 3505)	P: 31 to 36 (M= 34), F: 38 to 43 (M=40)	P: 8/13; F: /13	LN	90 mins	Coded behaviours: Manual directives, Manual assistance, Intrusion in the toddler's play, demonstration of object properties, object exchanges, smiles, looking	NS/S	Maternal Responsiveness	M/LPT	Before 2000	America	>6m
Bendersky, & Lewis (1986)	P: 31, F: 28	3 M	P: 1615.3 (709 to 2180), F: 3587.9 (2608 to 4564)	P: 32.2 (26 to 37), F: 40.14 (39 to 42)	No information	CS	15 mins	A checklist developed to measure responsiveness (Lewis, 1974). Responsiveness was conceptualized as the amount of behaviour, which involves response to the infant.	NS	Maternal Responsiveness	M/LPT	Before 2000	America	<= 6m
Coppola, Cassibba, & Costantini (2007)	P: 20, F: 20	3 M	P: 1201.25 (166.2), F: 3368 (445.5)	P: 29.9 (2.6), F: 38.9 (0.8)	18/22	CS	10 mins	Parental sensitivity items from Emotional Availability Scale (Biringen, Robinson, & Emde, 2000)	NS	Maternal Sensitivity	VPT	After 2000	Europe	<= 6m
Crawford (1982)	P: 16 F: 17	6, 8, 10, 14 M	P: 1287 (660-1850), F: 3242 (2610-3740)	P: 29.6 (24-33), F: 39.6 (38-42)	No information	LN	10 mins	The frequency of the following behaviours: Holding the infant, attending to the needs of the infant, affectionate kissing or hugging, talking to infant.	S/S/S /NS	Maternal Facilitation	VPT	Before 2000	America	>6m

Davis, & Thoman (1988)	P: 10 F: 29	2,3,4,5 weeks	P: 1520 (1260 to 2100), F: 3536 (2750 to 4395)	P: 31 (28 to 35), F: 40 (37 to 42)	P: 5/5; F: 17/12	LN	7 hrs	Frequency of the following behaviours: move, rock, pat, caress, talk, look, vis-a-vis, hold/carry, smile/laugh, suck/stimulate.	S	Maternal Facilitation	M/LPT	Before 2000	America	<= 6m
DeWitt et al. (1997)	P: 115 F: 105	6 M, 12 M	P: 1072.5, F: 3111	P: 29.2, F: 39.7	P: 51/64; F: 52/53	LN	70 mins	5-point rating scale based on (Ainsworth, 1978) and (Crockenberg, 1987)	S	Maternal Sensitivity	VPT	Before 2000	America	>6m
Feldman, & Eidelman (2007)	P: 56 F: 52	Term, 3 M	P: 1278.1 (234.1), F: 3321 (457.1)	P: 30.38 (2.5), F: 38.82 (2.98)	P: 30/26; F: 29/23	LN	15 mins at term, 90 mins at 3 months	At term coded by Mother-Newborn Coding System of the Coding Interaction Behavior Manual(Feldman, 1998); at 3 months HOME(Caldwell, 1984) and a microanalytic computerized coding system.	S/NS	Maternal Facilitation	VPT	After 2000	Europe	<= 6m
Forcada-Guex, Pierrehumbert, Borghini, Moessinger, & Muller-Nix (2006) [a]	P: 47 F: 25	6 M and 18 M	No information	P: <34, 31 (2); F: ≥37, 40 (1)	P: 22/25; F: 10/15	LN	10 mins	Third revision of Care Index(Crittenden, 1988) assesses 3 scales: sensitivity, control and unresponsiveness.	S	Maternal Sensitivity	M/LPT	After 2000	Europe	<= 6m
Greenberg, & Crnic	P: 30	24 M	P: 1407 (840-1800), F:	P: 31	P: 17/13; F: 17/23	CS	10 mins	Ratings were on the following behaviours: gratification from the	NS	Maternal Facilitation	M/LPT	Before 2000	America	>6m

(1988)	F: 40		3521 (2860-4520)	(27-36), F: 40 (39-42)				interaction, general affective tone, sensitivity to infant cues.							
Greene, Fox, & Lewis (1983)	P: 30 F: 32	3 M	P: 1642 (303), F: 3518.5 (588.5)	P: 32.8 (2.4), F: 40 (1.2)	P: 15/15; F: 16/16	CS	15 mins	Checklist sheet (Lewis, 1974). Frequency of the following Maternal behaviours was rated: (1) touch; (2) hold; (3) vocalization to infant (vocalization to other category omitted); (4) look; (5) smile/laugh; (6) play with infant; (7) change diaper/bathe (wash his/her hands, face); (8) feed (includes breast, bottle, spoon); (9) rocks subject; (10) read; (11) kiss; and (12) give toy/pacifier.	S	Maternal Facilitation	M/LPT	Before 2000	America	<= 6m
Halpern, & McLean (1997)	P: 20 F: 20	4 M	P: 1673.3, F: 3421.3	P: 32.8 (28 to 36), F: 40 (38 to 43)	No information	CS	15 mins	12 item rating scale (Egeland, 1975) which rated supportiveness, patience, expression of positive and negative feelings, responsivity, behavioural repertoire.	NS	Maternal Facilitation	VPT	Before 2000	America	<= 6m
Jaekel,	P:	6 Y	P: 1296 (308),	P: 30.4 (2.3),	P: 143/124;	LN	12 mins	A standardised coding system,	S/S	Maternal Sensitivity	VPT	After 2000	Europe	>6m	

Wolke, & Chernova (2012)	2673 M, F: 8 Y 2985 M	F: 3388 (450)	F: 39.6 (1.2)	F: 152/146			"Assessment of Mother-Child Interaction with the Etch A Sketch"(Schneider et al., 2009)						
Jean, & Stack (2012)	P: 5 M 40 F: 40	P: 1092 (237), F: 3476 (395)	P: 28.5 (2.3), F: 39.74 (1.08)	P: 18/22; F: 20/20	CS	6 mins	Sensitivity scale of Emotional Availability Scale(Biringen et al., 2000)	S	Maternal Sensitivity	VPT	After 2000	America	<= 6m
Korja et al. (2008)	P: 6M and 32 F: 12 M 36	P: 1008 (289), F: 3589 (406)	P: 28 (3), F: 40 (1)	P: 19/13; F: 19/17	LN	5 mins	Parent Child Early Relational Assessment(Clark, 1985), 5-point Likert Scale	NS/NS	Maternal Facilitation	VPT	After 2000	Europe	>6m
Landry, Chapieski, Richardson, Palmer, & Hall (1990)	P: 36 M 48 F: 21	P: 1258.5 (283), F: 3200 (760)	P: 30.4 (2.11), F: 41 (2.1)	P: 25/23; F: 12/9	CS	20 mins	Frequency of the following behaviours: Directives, Suggestions, Restrictions, Praise	S	Maternal Facilitation	VPT	Before 2000	America	>6m
Laucht, Esser, & Schmidt (2001)	P: 3 M 119 F: 228	P: 1625.5 (229.5), F: 3274 (419)	P: 33 (2.3), F: 39.4 (1.7)	171/176	CS	10 mins	Mannheim Rating System(Esser, 1989)	NS	Maternal Sensitivity	VPT	After 2000	Europe	<= 6m
Levy-Shiff, & Mogilner (1989)	P: 2, 3, and 4 weeks 38 F: 38	P: 1254 (375), F: 3510 (450)	P: 30 (3.2), F: 41 (0.8)	P: 19/19; F: 19/19	LN	30 mins	Behaviours coded: caregiving, talking, playing and stimulating, expressing positive affection, holding, looking.	S	Maternal Facilitation	M/LPT	Before 2000	Europe	<= 6m

Miljkovitch et al. (2013)	P: 48 F: 23	6M, 18 M	No information	P: <33, F:>37	No information	LN	5 mins	Ainsworth Maternal sensitivity scale(Ainsworth, 1978) and the Care-Index(Crittenden, 1988) which codes the following behaviors: sensitivity, controlling, unresponsive	S/NS	Maternal Sensitivity	VPT	After 2000	Europe	>6m
Minde, Perrotta, & Marton (1985)	P: 20 F: 20	1, 2, and 3 M	P: 1124 (173), F: 3196 (326)	P: 26-32	P: 10/10 F: 8/12	LN	10 mins	Frequency and duration of the following behaviours: Look, verbalize, touch, hold, nipple in mouth.	S/S/S	Maternal Facilitation	VPT	Before 2000	America	<= 6m
Montirosso, Borgatti, Trojan, Zanini, & Tronick (2010)	P: 25 F: 25	9 M	P: 1516 (483), 845-2450, F: 3293 (382), 2540-3840	P: 32.1 (2.8), 26-36, F: 39.9 (1.2), 37-41	P: 14/11; F: 13/12	CS	6 mins	Infant and Caregiver Engagement Phases(Weinberg, 1998)	NS	Maternal Facilitation	M/LPT	After 2000	Europe	>6m
Muller-Nix, Forcada-Guex, Pierrehumbert, Jaunin, Borghini, & Ansermet (2004)[b]	P: 47 F: 25	6M and 18 M	No information	P: 31 (2), F: 40 (1)	P: 22/25; F: 10/15	LN	10 mins	Third Revision of Care Index(Crittenden, 1988) assesses 3 scales: sensitivity, control and unresponsiveness	S/S	Maternal Sensitivity	M/LPT	After 2000	Europe	>6m
Potharst et al. (2012)	P: 94 F:	5 Y	P: <1000, F: >2500	P:<30, F: >37	No information	CS	15 mins	The NICHD (2003) Early Child Care Research Network coding	S	Maternal Facilitation	VPT	After 2000	Europe	>6m

	84						system(Network., 2003) which measure mother's supportive presence and respect for the child's autonomy.						
Rahkonen et al. (2014)	P: 48 F: 16	2 Y	P: 876 (194), F: 3613 (354)	P: 26.3 (1.2), F: 40.2 (0.9)	P: 31/17; F: 11/5	CS	15 mins	Mutually Responsive Orientation(Aksan, Kochanska, & Ortmann, 2006) and Quality of Relationship(Egeland, 1990)	NS	Maternal Sensitivity	VPT	After 2000	Europe	>6m
Schermann-Ezirik, Hagekull, Bohlin, Persson, & Sedin (1997)	P: 142 F: 70	2M, 4M, 6 M	P: 1829.5 (440), F: 3558 (409)	P: 31.4 (1.7), F: 39.7 (1.1)	P: 58/84; F: 29/41	LN	5 mins	Behaviours rated on a 5-point scale were: Sensitivity, Intrusiveness, and Involvement.	NS/NS /NS	Maternal Sensitivity	VPT	Before 2000	Europe	<= 6m
Schmucker et al. (2005)	P: 79 F: 35	3 M	P: 938.3 (288.4), F: 3333 (400.3)	P: 27.5 (2.7), F: 39 (1.2)	P: 36/43; F: 12/22	CS	10 mins	Microanalytic coding system of mother-infant interaction(Jorg, 1994)	S	Maternal Responsiveness	VPT	After 2000	Europe	<= 6m
Singer, Fulton, Davillier, Koshy, Salvator, & Baley (2003)	P: 171 F: 117	8M, 12 M	P: 1111 (205.5), F: 3463 (520)	P: 28.8 (2), F: 39.8 (1)	P: 79/92; F: 58/50	LN	No information	The Nursing Child Assessment Feeding Scale(Summer, 1994)	NS/NS	Maternal Sensitivity	VPT	After 2000	America	>6m
Stevenson, Roach, Ver Hoeve, & Leavitt (1990)	P: 17 F: 17	8 M	P: 2140 (216), F: 3509 (464)	P: 34.1 (1.3), F: 39.9 (1.6)	P: 8/9; F: 8/9	CS	10 mins	Onset and offset of the following behaviours were recorded: Proffer food, Vocalize, Look	S	Maternal Facilitation	M/LPT	Before 2000	America	>6m

							toward, Touch Infant, Smile, Present objects						
Watt, & Strongman (1985)	P: 14 F: 10	2M and 3 M	No information	P: 33.1, 31 to 35	No information	LN	P: 32.4 mins (21.8 to 43), F: 34.7 mins (19.8 to 47.6)	Frequency of the following behaviours were recorded: Vocalise, Look, Smile, Kiss, Hug, Rock, Tickle, Affectionate Touch, Play	NS/S	Maternal Facilitation	M/LPT	Before 2000	Europe	<= 6m
Wille (1991)	P: 36 F: 18	6 M	P: 1929.5 (353), F: 3495 (218)	P: 34 (1.5), F: 40 (1)	P: 19/17; F: 9/9	CS	15 mins	Second-by-second monadic phase system(Tronick, 1980)	S	Maternal Facilitation	M/LPT	Before 2000	America	<= 6m
Wolke, Eryigit-Madzwamuse, & Gutbrod (2013)	P: 90 F: 115	Term, 3M	P: 1245, 521 to 2158, F: 3170, 1820 to 4380	P: 30, 24 to 33, F: 39, 37 to 42	P: 51/39; F: 63/52	LN	3 mins	Mother Infant Structured Play Instrument, 5-point scale of maternal positive emotional expression, sensitivity, stimulation level adapted from Emotional Availability Scales(Biringen, 1990a) and Infant and Caregiver Engagement Phases(Weinberg & Tronick, 1996)	S/NS	Maternal Sensitivity	VPT	After 2000	Europe	<= 6m
Zarling, Hirsch,	P: 34	6 M	P: 1243 (218),	P: 30 (2),	P: 51/39; F: 63/52	CS	5 mins	5-point scale, which measures the reciprocity,	S	Maternal Sensitivity	VPT	Before 2000	America	<= 6m

& Landry (1988)	F: 30	F: >2500	F: 30 to 40	intrusiveness, responsiveness, affect, successfulness with infant, appropriateness of verbal and nonverbal techniques.

[1]Mean, SD, and range values are reported if available. CS, cross-sectional; F, full-term; HOME, Home Observation for Measurement of the Environment; LN, longitudinal; M/LPT, moderate to late preterm; P, preterm; NICHD, Eunice Kennedy Shriver National Institute of Child Health and Human Development; NS, no significant difference; S, significant difference; VPT, very preterm. GA, gestational age.

[a]These 2 studies reported findings from the same sample. We used the 18-month data from the Muller-Nix et al study and the 6-month data from the Forcada-Guex et al study.

Data Analysis

Analysis was conducted with Comprehensive Meta-Analysis version 2 software (Borenstein, Hedges, Higgins, & Rothstein, 2005). All studies provided continuous measures of observed maternal parenting behaviour, comparing preterm and full-term control sample. Mean effect sizes were calculated with CMA software when studies reported group differences at different time points. A random effects model was used to generate the combined estimate of the effects (Hedges G). Random effects model takes into account that effect sizes will differ from one study to another since they are sampled from an unknown distribution (Borenstein, Hedges, Higgins, & Rothstein, 2009). Heterogeneity of studies was assessed with Cochran's Q and Higgins I^2. Moderator analyses were conducted with five variables: degree of prematurity, being published before/after 2000, geographical setting, infant age and type of parenting behaviour. Sensitivity analysis was undertaken with outlier.

Publication bias analysis was assessed as follows: 1. Rosenthal's failsafe number (Rosenthal, 1979; 1991) to address the file drawer problem. Rosenthal's fail safe number test produces the number of unpublished studies needed to bring the combined effect size to statistically non-significant level. Publication bias does not exist if Rosenthal's fail safe number exceeds 5k+10, where "k" is the number of studies used in meta-analysis. 2. The trim and fill procedure (Duval & Tweedie, 2000) was used to examine the symmetry of effect sizes plotted by the inverse of the standard error. Ideally, the effect sizes should mirror on either side of the mean. 3. Begg and Mazumdar rank correlation test (Begg & Mazumdar, 1994) was used to examine the likelihood of bias in favour of small sample size studies. Non-significance of correlation indicates no publication bias. 4. The Egger's test (Egger,

Davey, Schneider, & Minder, 1997) examined whether publication bias related to the direction of study findings. The intercept value provided by this test shows the level of funnel plot asymmetry from the standard precision.

Results

The 34 studies included a total of 3905 participants, 1981 preterm and 1924 full-term comparison children. Thirteen of the studies investigated moderate to late preterm (32-36 weeks gestation) and 21 studies very preterm children (<32 weeks gestation). The mean birth weight was 1374 grams (SD= 234) for the preterm participants, and 3450 grams (SD=545) for the full-term participants. The mean gestational age of the preterm children was 30.4 weeks (SD= 2.2) compared to 39.8 weeks (SD= 1.1) in full-term comparisons. Fifty percent (N=17) of the studies were longitudinal (i.e. had more than one assessment point). Four of the studies reported on observed maternal responsivity (12%), 14 on observed maternal sensitivity (41%), and the rest described observed mother behaviour as maternal facilitation (47%). Overall sample size of the studies ranged from 33 to 565 (Median= 71). The mean age of the participants included in the studies was 13.9 months (Mode= 3 months, Median= 6 months). Twenty-one of the studies included participants younger than 12 months with a mean age of 4 months, range: 2 weeks to 9 months. The other 13 studies included participants aged 12 months or older (M= 28.07 months, range: 12 months to 8 years 5 months).

The combined mean effect size of observed maternal parenting behaviour was Hedge's g= -0.07 (95 % CI: -0.22, 0.08; z= -0.94; *P*= 0.35) indicating no difference in the parenting behaviour of mothers of preterm and full-term comparison children. Heterogeneity analysis indicated significant and high variation in effects between studies (Q= 156.42; I^2= 78.9, *P*= 0.001) (Figure 6).

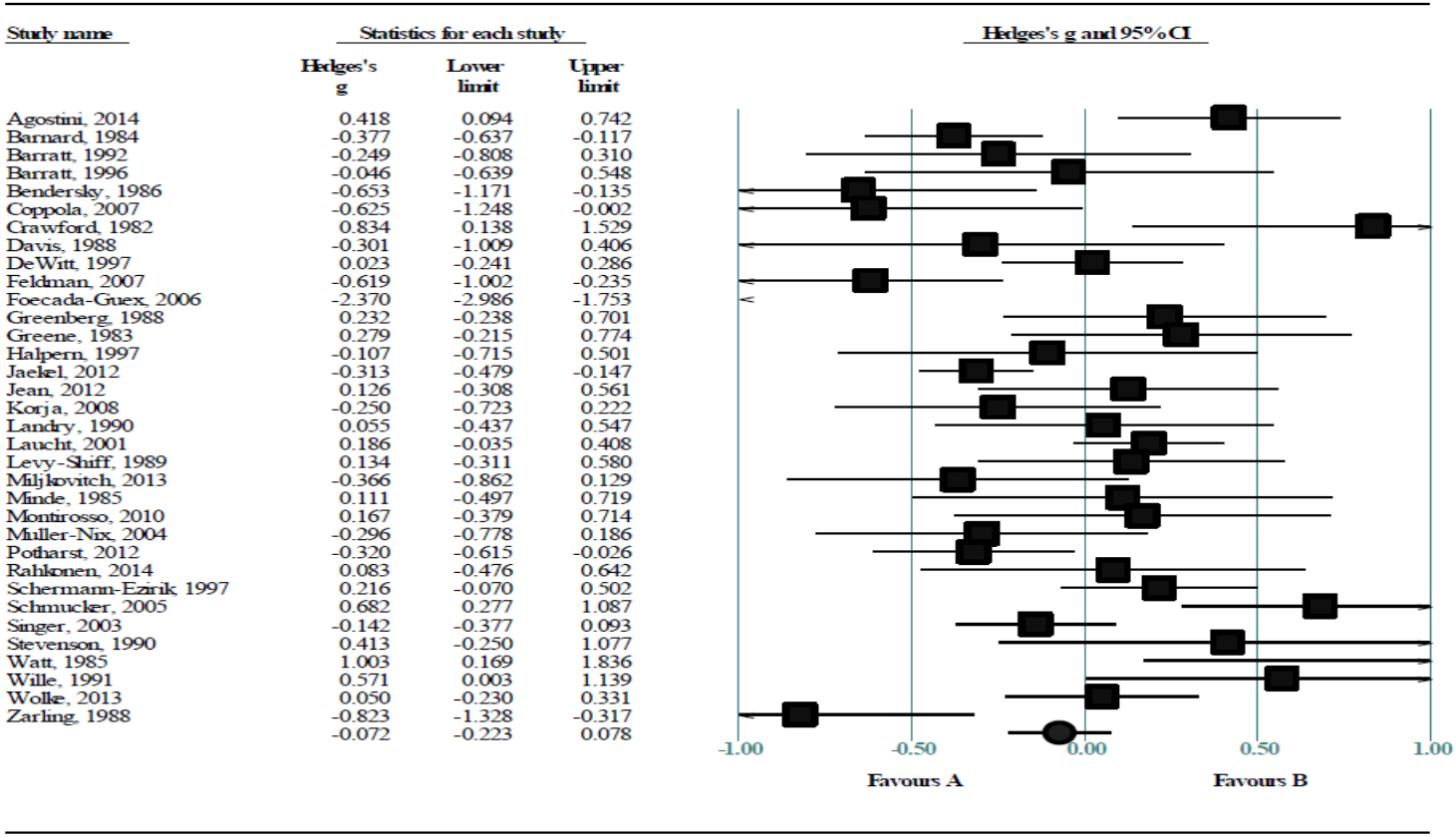

Figure 6 Difference between Preterm and Full-Term Mother Infant Dyads

CI, confidence interval. Favours A, Favours full-term infants; Favours B, favours preterm infants

Moderator Analysis

Planned moderator analysis found that degree of prematurity was not a significant moderator ($Q_{=}$ 0.02, *P*=0.88) (See Appendix E.1). Being published before or after 2000 was also not a significant moderator for the main analysis ($Q_{=}$ 1.47, *P*=0.23) (See Appendix E.2) nor was whether the studies were carried out in North America or Europe ($Q_{=}$ 0.77, *P*=0.38) (See Appendix E.3). Similarly, infant age ($Q_{=}$ 0.01, *P*=0.92) (See Appendix E.4) and the type of observed maternal parenting behaviour did not moderate the findings ($Q_{=}$ 2.76, *P*=0.25) (See Appendix E.5).

Outliers and Sensitivity Analysis

Outliers are defined as studies that had significantly different effect sizes from the other studies (Borenstein et al., 2009). One study (Forcada-Guex, Pierrehumbert, Borghini, Moessinger, & Muller-Nix, 2006) was identified as an outlier since it had substantially higher effect sizes than the other studies. As suggested by Borenstein et al. (2009), we repeated the meta-analysis excluding the outlier to check whether this altered the combined effect size and reduced heterogeneity. Results remained non-significant when the outlier was removed from the analysis (Hedge's g= -0.02, *P*= 0.76) (Figure 7) and the level of heterogeneity decreased (Q= 103.07; I^2= 68.95, *P*= 0.001).

Publication Bias

The Fail-Safe N addresses the concern that the observed differences may be false and was not relevant in the current study since the combined result did not indicate group differences. Under the random effects model the point estimate and 95% confidence interval for the combined studies is -0.097 (-0.33, 0.13). Using Trim and Fill these values remained unchanged indicating no publication bias. Furthermore, the Begg

and Mazumdar rank correlation was not significant and Egger's test was statistically not significant indicating no evidence for publication bias.

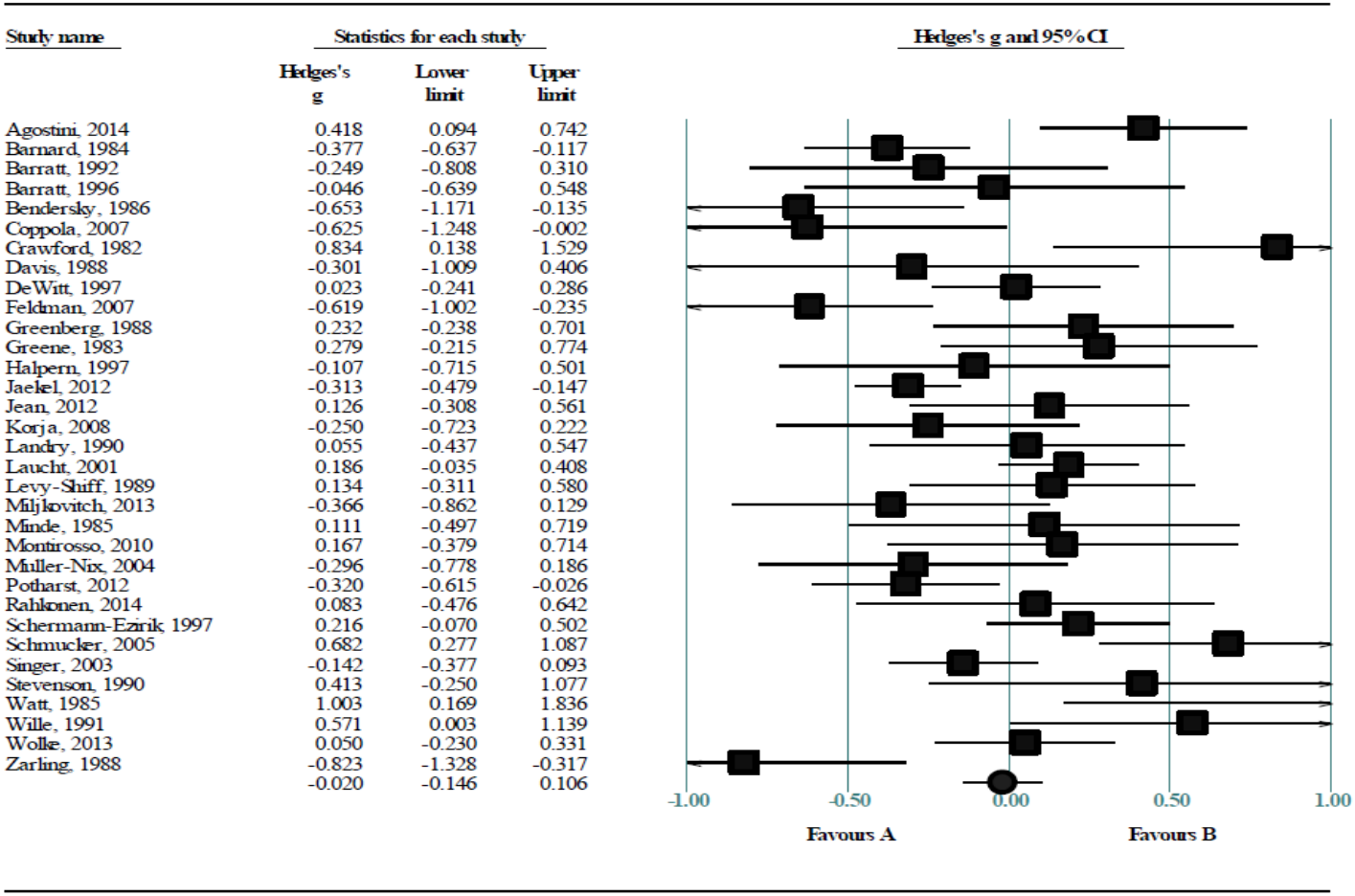

Figure 7 Differences between Preterm and Full-Term Mother Infant Dyads- Without Outlier

CI, confidence interval. Favours A, Favours full-term infants; Favours B, favours preterm infant

Discussion

This meta-analysis found no evidence for differences of mothers observed parenting behaviour with their preterm infants or children compared to mothers of full term children. The findings did not alter significantly when moderators such as degree of prematurity, geographical location, infant age, type of parenting behaviour or time of neonatal care (before or after the Millennium) were considered. Furthermore, excluding the outlier did not alter the findings and the results cannot be accounted for by publication bias.

Repeatedly, mothers of preterm children have been described as at risk of being less sensitive in their interaction with their infants (Korja et al., 2012). It has been proposed that mothers' ability to respond to their preterm infants' needs appropriately might be negatively affected by long term incubator care (Klaus, Kennell, Plumb, & Zuehlke, 1970; Klaus, Jerauld, Kreger, McAlpine, Steffa, & Kennell, 1972; Klaus & Kennell, 1976) or by mothers' high levels of stress (Müller-Nix et al., 2004). Nevertheless, the results from our meta-analysis indicate that mothers of preterm children provide, on average, similar observed sensitive and responsive parenting for their preterm offspring as mothers who had a full term infant. This finding provides support to the studies, which reported similar levels of observed maternal behaviour in preterm and full-terms during the first year of life (Korja et al., 2008; Montirosso et al., 2010).

Maternal sensitivity has been previously reported to be a predictor of the development of secure infant to mother attachment (De Wolff & van Ijzendoorn, 1997). In preterm infants, maternal sensitivity has been linked to positive developmental outcomes (Magill-Evans & Harrison, 2001), whereas, insensitivity

has been found to increase impairments in self-regulation (Clark, Woodward, Horwood, & Moor, 2008). Similar outcomes in preterm infants were also observed when maternal responsivity and facilitation has been measured (Landry & Smith, 2011). We have carefully distinguished between the different maternal parenting behaviours: sensitivity; responsivity, facilitation. This allowed us to examine the impact of all parenting behaviour as well as the moderating role of using different constructs in analysis. Nevertheless, type of parenting did not make a difference in the outcome, which suggests that our findings are generalizable across these different maternal parenting behaviours.

Increased levels of maternal stimulation and intrusiveness have been associated with negative outcomes (Feldman, 2006). However, Wijnroks (1998) showed that intrusive parenting did not lead to negative outcomes in preterm children. On the contrary, preterm children were found to have better cognitive outcomes and better ability to sustain attention at the age of two. Similarly, Jaekel, Pluess et al. (2015) and Wolke et al., (2014) reported that differences in parenting behaviour disappeared once controlled for intellectual abilities of the infants/children. Thus children who were delayed and had lower IQ may need more framing and directive parenting which may be considered as intrusive in normally developing children. Knowing that preterm children are more likely to have developmental delay, our finding of no differences in observed parenting is even more remarkable.

Evidence from some recent studies suggests that differences between preterm and full-term infants in observed maternal behaviour may decrease after the first 6 months (Korja et al., 2008; Montirosso et al., 2010). In this meta-analysis, 19 studies included infants aged 6 months or younger; 15 studies children 7 months or older. No

impact of infant age on maternal observed behaviour was found in moderator analysis.

Previous research considered the length of stay in hospital and the degree of neonatal illness as important predictors of the socio emotional development of preterm infants (Plunkett, Meisels, Stiefel, Pasick, & Roloff, 1986). Increased neonatal morbidity and prolonged hospital stay may adversely shape the quality of the relationship between the mother and infant (Minde, Whitelaw, Brown, & Fitzhardinge, 1983). Very preterm infants experience, on average, more neonatal complications, interventions and longer hospital stay than moderate to late preterm infants (Goldenberg et al., 2008). However, no difference in observed parenting behaviour of mothers of very vs moderate to late preterm infants was found in the current meta-analysis. This provides no evidence for the suggestion that lower gestational age, often associated with longer hospitalisation, adversely affects observed maternal parenting. This finding is in line with studies that directly studied the impact of severity of neonatal illness (Landry et al., 2001) or birth weight on maternal parenting behaviour (Laucht, Esser, & Schmidt, 2001).

Alleviating maternal stress by early intervention has been shown to increase the amount of sensitivity of mothers of preterm infants at 12 months (Ravn et al., 2012). Recent improvements in neonatal support have been proposed to have led to more involved care and improved interaction during initial hospitalisation (Korja et al., 2008). Practices in NICU care regarding parent involvement started changing in the 1990s but this has varied widely between units within and between countries. We used 2000 as an “approximation” cut-off point to distinguish between less and more family centred care. European NICUs, in particular, the UK implemented parental 24 hour visiting routinely in the 1980/90s while this appears to have been later in many

North American NICUs. However, our moderator analyses did not show a significant effect of being conducted before or after 2000, or of being conducted in Europe or America.

The finding that preterm and full-term mothers do not differ in their observed parenting behaviour is highly reassuring for health professionals and parents. The stress of having a preterm child has been often considered to adversely affect parenting behaviour and long term development (Singer et al., 2010). Nevertheless, our findings indicate considerable resiliency in observed parenting behaviour. New longitudinal research indicates that preterm children may need even more sensitive and facilitative parenting to scaffold their behaviour to deal with tasks and emotional regulation (Jaekel, Pluess et al., 2015). This may include more guided and directive behaviour (Greene, Fox, & Lewis, 1983; Agostini et al., 2014; Feldman, 2007). Furthermore, the finding that preterm infants are more influenced by low or high sensitive parenting suggests more susceptibility to parenting (Jaekel, Pluess et al., 2015). Thus, we speculate that mothers of preterm children may need to be even more responsive and facilitative than mothers of full term children to reach the same potential.

Strengths and Limitations

Strengths are that we only included studies that had direct observations of maternal parenting behaviour with usually high inter-observer reliability. We excluded studies that used self-report questionnaires of maternal parenting behaviour. Direct observations provide only a short window into maternal parenting behaviour while maternal reports of behaviour refer to longer periods but may often be influenced by maternal factors such as depression (Gartstein, Bridgett, Dishion, & Kaufman, 2009). Furthermore, expert observations checked for inter-observer agreement are less

likely to be biased by previous experiences and mental state than maternal reports of parenting.

A limitation is that the current meta-analysis included only articles published in English. We cannot be certain whether this may have introduced bias. However, for the studies analysed here and published in English language, no indication of publication bias was found. Furthermore, heterogeneity was high indicating considerable variation among studies. This heterogeneity might arise from incorporating studies, which have various designs and sample sizes. To address this, we used random effects model in the analysis and conducted moderator analysis with potential variables. However, the predefined moderator variables could not explain the heterogeneity between studies and further moderators may be considered in future research. The major heterogeneity may arise by the use of a wide range of observation methods. However, we could not test this as measures differed from one study to another. Moreover, we used 2000 as an artificial cut-off point, a convenient approximation of changed NICU care (visiting patterns), and this might not represent the exact time for the improvements in NICU's included in the meta-analysis. Finally, we computed mean scores if the study reported observations of mother behaviour over several time points. Therefore, longitudinal changes were not addressed in the current analysis but may be of interest in future. The influence of specific medical complications on any potential differences between mothers of preterm and full-term infants could not be addressed. Very few studies provided information on medical complications and thus it could not considered as a moderator. However, it is critical for future studies to consider the level of medical complications in preterm infants when studying mothers' behaviour.

Conclusion

In conclusion, despite being born preterm and often spending weeks or months in neonatal care, observed maternal parenting behaviour in interaction with their preterm children was not found to be less sensitive, facilitative or responsive than that of mothers of full-term children. The findings provide reason for optimism that most mothers, despite their initial shock and stress and the challenges of dealing with a preterm infant, show comparable sensitive and responsive behaviour as mothers of full term children. However, whether these similar levels of observed maternal behaviour are sufficient or appropriate to foster optimal development of preterm children requires further longitudinal investigation (Jaekel, Pluess et al., 2015).

Chapter 8 Regulatory Problems in Very Preterm and Full-Term Infants over the First 18 Months

Objectives: This study is an investigation of differences in regulatory problems (RP; crying, sleeping, feeding) expressed by infants born very preterm (VP; <32 weeks gestation) or with very low birth weight (VLBW; <1500 grams) and infants born at full term (FT) during the first 18 months of life. It investigates the prevalence of single and multiple RPs, their persistence and how early in infancy RPs still found at 18 months of age can be predicted.

Method: This prospective longitudinal study of 73 VP/VLBW and 105 FT infants utilized a standard interview of mothers to assess regulatory problems among the infants at term, 3, 6, and 18 months of age.

Results: Few differences were found between VP/VLBW and FT infants in the first 6 months. At 18 months, VP/VLBW infants had more single sleeping (RR=2.2, CI=1.3 to 3.7), feeding (RR= 1.4, CI= 1.03 to 1.8), and multiple RPs (RR=1.7, CI=1.02 to 2.8) than FT infants. In VP/VLBW infants, RPs as early as 3 months and in FT infants RPs as early as 6 months predicted RPs at 18 months. Those infants who had persistent RPs in the first 6 months of life were more likely to still have RPs at 18 months.

Conclusions: VP/VLBW children are at slightly increased risk for RPs at term and in the second year of life. Clinicians should be aware that RPs that persist across the first 6 months point to increased risk of continuing RPs into toddlerhood in both VP/VLBW and FT infants.

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Introduction

Approximately 20% of full-term healthy infants experience regulatory problems (RPs) defined as excessive crying, sleeping, or feeding problems during the first year of life (von Kries et al., 2006; Wake et al., 2006). These are transient in the majority of cases (Schmid et al., 2010). Early RPs may be associated with trajectories of dysregulation into childhood (Winsper & Wolke, 2014) and subsequent cognitive, behaviour and attention problems (Wolke, 2002; 2009; Degangi, 1993; DeSantis, 2004; Rautava, 1995; Forsyth, 1991; Hemmi, 2011), especially if crying or feeding problems persist beyond the age of 3 to 4 months (Hyde et al., 2012; Papoušek & von Hofacker, 1995; Schmid et al., 2010; St. James-Roberts, Conroy, & Wilsher, 1998; von Kries et al., 2006; Wake et al., 2006; Wolke et al., 2009). In addition, multiple RPs, i.e. having two or three single RPs at the same time, increases the likelihood of later behaviour problems (Hemmi et al., 2011; Hyde et al., 2012).

There is some suggestion that preterm birth is associated with more RPs in early infancy (Ferrari, Grosoli, Fontana, & Cavazzuti, 1983; Korja et al., 2014; Korja et al., 2008; Schmid et al., 2011). Others have not found an association between preterm birth and increased crying or sleeping problems (Maunu, 2006; Barr, 1996; Wolke, 1998). Feeding problems, on the other hand, have been consistently found to be more frequent after preterm birth (Bertoncelli, 2012; Cerro, Zeunert, Simmer, & Daniels, 2002; Gewolb & Vice, 2006; Mathisen et al., 2000; Samara et al., 2010a; Schädler et al., 2007; Schmid et al., 2011; Wrotniak et al., 2009). Previous studies of

preterm populations were usually of small sample size or they just looked at single RPs (Anders & Keener, 1985; Barr et al., 1996; Lau, Sheena, Shulman, & Schanler, 1997; Lau, Smith, & Schanler, 2003). None, as far as we are aware, examined whether VP/VLBW and FT infants differ in early crying, sleeping and feeding or have multiple RPs more often beyond 6 months of age.

The aims of the current study were: 1) to examine if there is a difference in prevalence of single and multiple RPs among VP/VLBW and FT infants at term, 3 months, 6 months and 18 months of age; 2) to determine whether RPs at 18 months can be predicted by early RPs and whether prediction is enhanced if RPs persist across the first 6 months.

Methods

Participants

Caretakers of 112 infants who were born VP/VLBW (<32 weeks of gestation or <1500 gr) in three neonatal units were approached during an 18 months period. Seventy six caretakers of 90 VP/VLBW infants participated at the first assessment point at term. Recruitment of full-term children was conducted in the postnatal wards of the same hospitals within 48 hours of birth. One hundred and fifteen FT infants (37- 42 weeks gestation), matched for socio-economic status, sex and multiple birth and their caretakers (N=98) were also recruited from the same units (see Wolke, Jaekel, Hall, & Baumann (2013) for a detailed description).

Participants were assessed at term, 3 months, 6 months and 18 months of age corrected for prematurity. Seventeen VP/VLBW and 10 FT infants did not complete the study up until 18 months of age. VP/VLBW participants who did not complete the study (N= 17) differed from participants who remained in the study in that they

had significantly higher medical risk neonatally (F (1, 88) = 4.5, P< .05) and had parents with lower income (X^2(1,105) = 10.6, P= .005) (Table 10). Otherwise, those who dropped out did not differ from those who remained in the study on birth weight, rates of SGA and gestational age or maternal education.

The final sample with complete longitudinal data comprised of 73 VP/VLBW (63 caretakers) and 105 FT infants (89 caretakers). VP/VLBW sample included 69 (94.5%) infants below 32 weeks of gestational age and 4 (5.5%) infants above or equal to 32 weeks of gestational age but with birth weight below 1500g. VP/VLBW and FT samples did not differ in terms of gender, multiple births, maternal age, income, and maternal education. VP/VLBW infants were significantly less likely to be breastfed at term (X^2(1,178) = 9.81, P= .002) than FT infants. However, there were no differences in feeding type at 3 months (X^2(1,177) = 3.31, P= .07) and 6 months (X^2(1,167) = .027, P= .87) (See Table 10).

Table 10 Infant and Maternal Characteristics of the Participants

	VP/VLBW (N=73)	FT (N=105)
Gender: N (Male/Female)	41 (56.2%)/32 (43.8%)	60 (57.1)/45 (42.9)
Birth weight (g) (M/Range)	1285.8 (521-2158)	3205.1 (1820-4380)
Gestational Age (weeks) (M/Range)	29.4 (25-33)	38.9 (37-42)
SGA (N/%)	17 (23.3%)	NA
Multiple births: twins (N/%)	21/ 28.8%	32/ 30.5%
Medical Risk (M/SD)[1]	.64 (.73)	NA
RDS (Respiratory Distress Syndrome) (N/%)		NA
Mild	44/ 60.3%	
Moderate	1/ 1.4%	
Severe	2/ 2.7%	
BPD (Bronchopulmonary Dysplasia) (N/%)	22/ 30.1%	NA
CNS (Central Nervous System) damage (N/%)[2]	5/ 6.9%	NA
Breastfeeding (N/%)*		
Term*	21/ 28.7%	55/ 52.3%
3 Months	13/ 17.9%	31/ 29.5%
6 Months	10/ 13.7%	13/ 12.4%
Maternal Age (years) (M/SD)	30.5 (5.7)	30.7 (5.9)
Income (GBP): N (%)		
£0- £25k	30 (41.1%)	38 (36.2%)
£25k- £40k	18 (24.7%)	25 (23.8%)
>£40k	18 (24.7%)	41 (39%)
Maternal Education (years): N (%)		
<10 years[a]	2 (2.7%)	3 (2.9%)
10 years[b]	43 (58.9%)	60 (57.1%)
>10 years[c]	23 (31.5%)	34 (32.4%)

[1]Composite score of neurosensory deficits, rehospitalisation, surgical procedures, and prolonged oxygen dependency, measured at 3 months. [2]Brain scans were performed for haemorrhage, ventricular dilatation, parenchymal cysts. [a]No educational qualification, [b]Basic educational qualification (O-levels), [c]Further education (A-levels) or college education. *Statistically significant difference between very preterm and full-term group at p<0.5 level.

Measures

Background Measures

Medical risk was a composite of the following variables: Neurosensory deficits, rehospitalisation, surgical procedures, and prolonged oxygen dependency assessed from medical notes and interviews at 3 months. Neurosensory deficits were defined as clinically significant deficits in hearing, vision, muscle tone or presence of hydrocephalus. Re-hospitalization was defined as whether the infant was readmitted to the hospital after discharge from the neonatal unit or not. Surgical procedures were defined as whether the infant had any surgery (e.g. for Patent Ductus Arteriosus, Nectorizing Enterocolitis) or not. Lastly, oxygen dependency was defined as oxygen use of more than 21% (1: never, 2: oxygen dependency still at term, 3: oxygen dependency still at 3 months). Additionally, Respiratory Distress Syndrome (RDS) and Bronchopulmonary Dysplasia (BPD) were recorded. RDS was recorded based on X-ray evidence at three levels: mild, moderate and severe (Northway, Rosan, & Porter, 1967). BPD was defined as the need for supplemental oxygen use for more than 28 days (Ehrenkranz et al., 2005; Northway et al., 1967) in addition to chest X-rays of lung changes and coded as a dichotomous variable. Income was divided into 3 groups based on gross family income per annum: 1) 0- £25000, 2) £25000-£40000, 3) >£40000. Maternal education was divided into 3 groups based on years of education: 1) <10 years (not completed), 2) 10 years (basic), and 3) > 10 years (further education).

Regulatory Problems (RPs)

A standard structured interview about crying, sleeping and feeding problems was conducted at term, 3, 6 and 18 months. Definition of crying, sleeping and feeding problems were derived from the literature (Table 11).

Table 11 Regulatory Problems Definition

	Definition at Term and 3 Months	Definition at 6 Months	Definition at 18 Months
Crying			
1) Duration of Crying AND/OR (Schmid et al., 2010; St. James-Roberts et al., 1998)	More than or equal to 180 mins	More than or equal to 2 hours	More than or equal to an hour
2) Easy or difficult to soothe AND/OR (Wolke, 1995)	Infant is difficult or very difficult to soothe	Infant is difficult or very difficult to soothe	Infant is difficult or very difficult to soothe
3) Mother thinks the crying is distressing (Wolke, 1995)	Mother thinks the crying is very distressing	Mother thinks the crying is very distressing	Mother thinks the crying is very distressing
Sleeping			
1) The duration it takes for mother to settle the infant for sleep AND/OR (Degangi, 2000)	Longer than 30 minutes	Longer than 30 minutes	Longer than 30 minutes
2) The frequency of infant waking up AND/OR (Winsper & Wolke, 2014)	2 times or higher	2 times or higher	2 times or higher
3) The longest period of sleep which infant has had without waking	Less than 5 hours	Less than 5 hours	Less than 5 hours

Feeding			
1) Problems in Oral-Motor Functioning AND/OR (Samara, Johnson, Lamberts, Marlow, & Wolke, 2010b)	Two or more: stopping after a few sucks, excessive dribbling/difficulty swallowing, gagging/choking during the feed	Two or more: stopping after a few sucks, excessive dribbling/difficulty swallowing, gagging/choking during the feed	Two or more: drools when drinking, gagging/choking during the feed, problems swallowing
2) Faddy Eating/ Food Refusal (Dahl & Sundelin, 1986)	Fighting against breast/bottle	Fighting against breast/bottle	Five or more: Eats too little, leaves most of the food offered, poor appetite, picky eater, slow eater, refuses to eat lumpy food, refuses to eat puree

A crying problem was defined by the presence of at least one of three criteria (excessive duration of crying, difficult to soothe, mother's perception of crying as very distressing) (Barr et al., 1996; Degangi et al., 1993; St. James-Roberts et al., 1998; Wolke et al., 1995a; Wolke, Rizzo, & Woods, 2002).

Sleeping problems were measured with 3 items at all measurement points. Participants were considered as having sleeping problems when at least one of the following criteria was present: a) woke up more than one time per night, b) took longer than 30 minutes to settle infant to sleep, c) the longest duration without waking up was less than 5 hours.

Feeding problems were measured with 2 summary items at term, 3, 6 and 18 months. Problems in oral-motor functioning were measured with the following three items: a) stopping after a few sucks, b) excessive dribbling/difficulty swallowing, c) gagging/choking during the feed. Participants were dichotomized into two groups: no oral-motor functioning problems (0 or 1 problem present) and oral-motor functioning problems (2 or 3 problems present). Faddy eating/food refusal was measured with one item (fighting against the bottle/breast) at term, 3 and 6 months. At 18 months, a faddy eating/food refusal scale was created including the following variables: Eats too little, leaves most of the food offered, poor appetite, picky eater, slow eater, refuses to eat lumpy food, or refuses to eat puree even selectively. Internal consistency of this scale was high; .81 for the VP/VLBW and .74 for FT. Participants were categorized as having faddy eating/food refusal problems if they had 5 or more problems.

Participants were categorized as having multiple RPs if they had two or three single RPs.

Control Variables

Breastfeeding has previously been found to be related to more frequent sleeping problems and decreased feeding problems in infancy (Thunstrom, 1999; Schmid 2011; Wolke, 1998). In preterm infants, breastfeeding has been reported to increase the duration of crying (Thomas, 2000). Based on these findings, mothers were asked about how they fed their infant at term, 3 months and 6 months. They were divided into two categories: breastfed and not breastfed. The breastfed category included infants who were only partially breastfed. Furthermore, CNS (Central Nervous System) problems have been suggested as influential factors in preterm infants' sleeping pattern (Doussard-Rossevelt, Porges, & Mcclenny, 1996). In order to control for possible impact of CNS problems in preterm infants, brain ultrasound scans were used to measure haemorrhage, ventricular dilatation and parenchymal cysts at term. The type of haemorrhage was coded as following: 0) none, 1) subependymal/choroidal one side, 2) intraventricular one side, 3) parenchymal one side, 4) subependymal/choroidal bilateral, 5) intraventricular bilateral, 6) parenchymal bilateral. Ventricular dilatation was coded as following: 0) no dilation, 1) less than 4mm one side, 2) more than 4mm one side, 3) less than 4mm bilateral, 4) more than 4mm bilateral. Parenchymal cysts were coded as: 0) none, 1) porencephalic cyst one side, 2) cystic leucomalacia one side, 3) porencephalic cyst bilateral, 4) cystic leucomalacia bilateral. All those infants whose early scans were scored ≥1 had repeat scans at a later date. According to the results of final scan (6^{th} scan), infants were divided into two categories: CNS problem present (score ≥1) and not present (score= 0).

Statistical Analysis

Data were analysed with SPSS (IBM, version 21.0). One-way ANOVA and chi-square test (X^2) were used to compare the dropouts and non-dropouts. Chi-square test was also used to compare the RPs of VP/VLBW and full-term groups at each time point. Contingency coefficients were computed as indices of the associations of RPs across measurement points. Binominal logistic regression was used to estimate the odds ratio of having RPs at 18 months. All analyses, except for differences in frequencies at 18 months were adjusted for breastfeeding. Furthermore, analyses for VP/VLBW infants were adjusted for CNS problems. Statistical significance was defined as $P<.05$.

In the data analysis regulatory problems were considered as transient if they were present only at one measurement point (term, 3 months, or 6 months) in the first 6 months. If regulatory problems were present at two or three measurement points during the first 6 months, they were considered as persistent regulatory problems. VP/VLBW infants were assessed at term, 3, 6 and 18 months corrected for prematurity and controls at chronological age.

Results

Differences between very preterm and full-term infants at term, 3 months, 6 months, and 18 months

Frequencies of single and multiple RPs are shown in Table 12.

There were little differences in RPs between VP/VLBW and FT infants. At term, VP/VLBW had slightly higher risk ratios of having crying, feeding or multiple regulatory problems than FT. At 3 months and 6 months, there were no significant

differences between groups. At 18 months, VP/VLBW had more often single sleeping, feeding, and multiple RPs (See Table 12).

The impact of having lung disease (RDS, BPD) on RPs was further investigated in VP/VBW infants. Chi-square analysis revealed no significant differences between those who suffered from lung disease and who did not in RPs at all measurement points. Additionally, the impact of being SGA (Small for Gestational Age) was investigated. Results revealed no differences at any measurement point between those who were SGA and those who were AGA (Appropriate for Gestational Age). Furthermore, VP/VLBW infants who were SGA did not differ from full-term infants.

Table 12 Comparison of Regulatory Problems in Very Preterm and Full-term Infants

	Term N (%)			3 Months N (%)			6 Months N (%)			18 Months N (%)		
	VP/VLBW (N=73)	FT (N=105)	RR (95% CI)	VP/VLBW (N=73)	FT (N=105)	RR (95% CI)	VP/VLBW (N=73)	FT (N=105)	RR (95% CI)	VP/VLBW (N=73)	FT (N=105)	RR (95% CI)
None	7 (9.6)	9 (8.6)		37 (50.7)	52 (49.5)		31 (42.4)	52 (49.5)		16 (21.9)	32 (30.5)	
1 RP	21 (28.8)	47 (44.8)		27 (37)	40 (38.1)		30 (41.1)	32 (30.5)		29 (39.7)	45 (42.9)	
Multiple RPs	45 (61.6)	49 (46.7)	**1.3 (1.01 to 1.7)**	9 (12.3)	13 (12.4)	.99 (.5 to 2.2)	12 (16.5)	21 (20)	.8 (.44 to 1.5)	28 (38.4)	28 (26.6)	**1.7 (1.02 to 2.8)**
Type of Problem												
Crying*	36 (49.3)	33 (31.4)	**1.7 (1.2 to 2.5)**	14 (19.2)	18 (17.1)	1.1 (.6 to 2.1)	15 (20.5)	20 (19)	1.1 (.6 to 1.9)	16 (21.9)	27 (25.7)	.9 (.5 to 1.5)
Sleeping*	53 (72.6)	83 (79)	.92 (.8 to 1.1)	19 (26)	21 (20)	1.3 (.74 to 2.2)	21 (28.8)	35 (33.3)	.9 (.6 to 1.4)	25 (34.2)	17 (16.2)	**2.2 (1.3 to 3.7)**
Feeding*	37 (50.7)	36 (34.3)	**1.5 (1.1 to 2.1)**	15 (20.5)	31 (29.5)	.71 (.4 to 1.2)	19 (26)	20 (19)	1.4 (.8 to 2.3)	42 (57.5)	45 (42.9)	**1.4 (1.03 to 1.8)**

VP/VLBW: Very Preterm, FT: Full-term, RR: Relative Risk; RP: Regulatory Problem. *Frequencies and percentages of crying, sleeping, feeding problems represent overall number. Boldface type indicates significant associations.

How Early Can We Predict Crying, Sleeping, and Feeding Problems at 18 Months?

Figure 8 illustrates the contingency coefficients between the 3 early measurement points and 18 months outcome for crying, sleeping and feeding RP in VP/VLBW and FT.

For FT infants, the contingency coefficient between early RPs and 18 months sleeping, feeding, and multiple RPs increased with age (i.e. 6 months had the highest correlation). This pattern was not evident for VP/VLBW infants for crying, sleeping and multiple RPs, where the highest correlation with 18 months was already found at 3 months. Only for feeding RPs, VP/VLBW infants followed the same association pattern as FT infants.

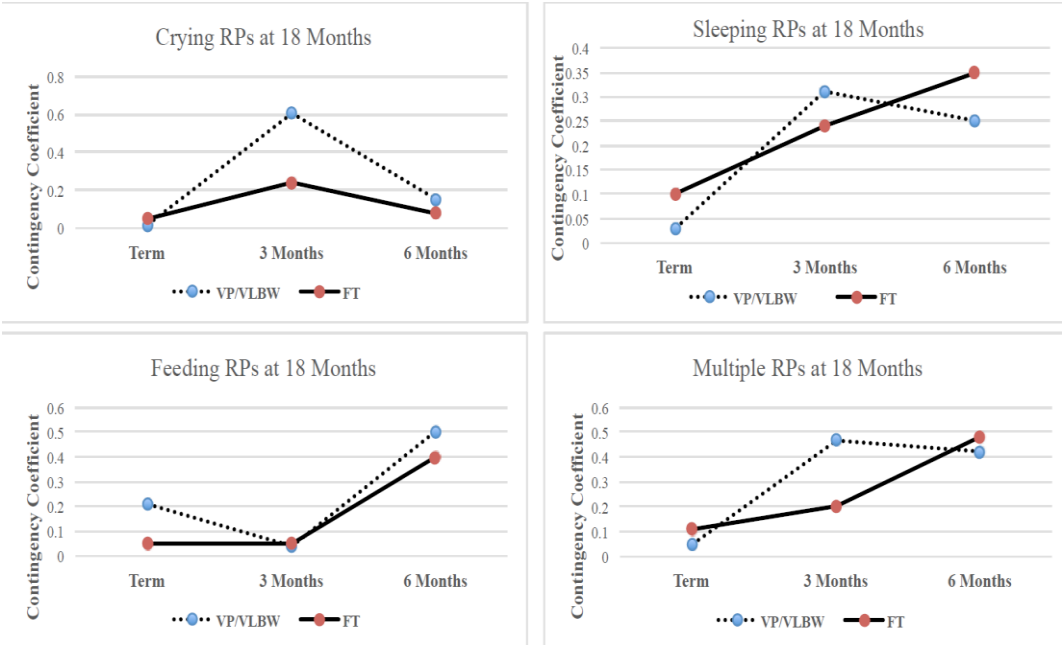


Figure 8 Associations between Regulatory Problems (RPs) at Early Months (term, 3, 6 months) and 18 Months

Associations between Persistence of RPs until 6 Months and RPs at 18 Months

In VP/VLBW infants, having either transient (i.e. at one measurement point) (OR= 3.3, CI= 1.2 to 5.8) or persistent RP (OR=4.2, CI= 1.4 to 12.9) in the first 6 months was associated with sleeping RP at 18 months. Furthermore, having persistent RPs at 3 measurement points (OR= 3.9, CI= 1.3 to 6.1) was significantly related to multiple RPs at 18 months in VP/VLBW infants.

In FT infants, having persistent RPs during the first 6 months of life (OR= 3.4, CI= 1.2 to 3.9) was also associated with sleeping RP at 18 months (Table 13). Moreover, having persistent RP (OR= 3.5, CI= 1.2 to 5.9) was associated with multiple RPs at 18 months.

Table 13 Persistence of any RPs at Measurement Points until 6 months and 18 Months Outcomes in Very Preterm/Very Low Birthweight and Full-Term Infants

		VP/VLBW					FT			
		Crying	Sleeping	Feeding	Multiple RPs		Crying	Sleeping	Feeding	Multiple RPs
	N	0R (95% CI)	0R (95% CI)	0R (95% CI)	0R (95% CI)	N	0R (95% CI)	0R (95% CI)	0R (95% CI)	0R (95% CI)
Never	2					6				
At one measurement point	20	1.21 (.32 to 4.6)	**3.3 (1.2 to 5.8)**	1.2 (.4 to 3.7)	2.8 (.7 to 10.5)	23	2.8 (.75 to 10.2)	2.3 (.8 to 5.9)	2.1 (.8 to 5.5)	2.9 (.8 to 10.7)
At two measurement points	29	3.5 (.89 to 14.1)	**3.7 (1.6 to 5.2)**	2.1 (.8 to 5.8)	2.7 (.88 to 8.3)	49	2.71 (.85 to 8.6)	**3.3 (1.1 to 5.5)**	2.1 (.84 to 5.23)	2.1 (.71 to 6.1)
At three measurement points	22	3.03 (.93 to 9.88)	**4.2 (1.4 to 12.9)**	1.9 (.6 to 5.8)	**3.9 (1.3 to 6.1)**	27	2.11 (.82 to 5.44)	**3.4 (1.2 to 3.9)**	1.72 (.71 to 4.24)	**3.5 (1.2 to 5.9)**

Note. Odds Ratios (OR) and Confidence Intervals (CI) in bold are significant at the p<.05 level.

Discussion

This study investigated early regulatory problems (crying, sleeping, and feeding) in VP/VLBW infants in comparison to FT infants during the first 18 months. Our findings indicate few differences between VP/VLBW and FT infants in the first 6 months of life but emerging differences in sleeping, feeding or multiple RPs at 18 months. For predicting 18 months RPs, associations were emerging slightly earlier (i.e. at 3 months) in VP/VLBW infants for crying, sleeping and multiple RPs than full term children. Moreover, persistence of any RP across the first 6 months increased the odds of having multiple RPs or sleeping RPs in both VP/VLBW and FT infants.

The prevalence of single and multiple RPs was similar to previous reports during the first 18 months of life (Forsyth & Canny, 1991; Richman, 1981; Wolke et al., 1995b). However, crying RPs in FT infants at 3 months (17.1%) was found to be lower than in one previous study (29%) (St James-Roberts, 1991). Furthermore, in VP/VLBW infants, the prevalence of sleeping RPs at 18 months was 34%, which was somewhat higher than the rates reported in previous studies (approximately 15%) (Wolke, 1995; 1998).

There were few differences between VP/VLBW and FT infants in sleeping, feeding or multiple RPs in the first 6 months but they emerged at 18 months. This is consistent with previous findings of no differences in crying patterns and durations between preterm and full-term infants before 3 months (Barr et al., 1996; Maunu et al., 2006; Shinya, Kawai, Niwa, & Myowa-Yamakoshi, 2014). Some differences were found in feeding skills between VP/VLBW and FT infants both early at term when sucking coordination is important (Lau & Smith, 2011; Lau et al., 2003;

Wrotniak et al., 2009) and after 6 months of age when processing of solids is required (Migraine et al., 2013; Pridham, Steward, Thoyre, Brown, & Brown, 2007; Samara et al., 2010a). Consistent with previous research, no differences in sleeping patterns between very preterm and full-term infants during the first 6 months of life was found (Anders & Keener, 1985; Mirmiran, Baldwin, & Ariagno, 2003; Shimada et al., 1999). However, our finding that very preterm infants had increased odds of sleeping problems at 18 months contradicts findings of other studies (Iglowstein et al., 2006; Wolke et al., 1998). Higher sleeping problems in VL/VLBW infants might reflect insecure or disorganised attachment which has been shown to increase sleeping problems in full-term infants (McNamara, 2003) and has been found to be more frequent in VP/VLBW toddlers (Wolke et al., 2014).

Having any RP that persisted from term to 6 months increased the odds of having sleeping RPs or multiple RPs in both VP/VLBW and FT infants. This result was apparent despite the fact that the analysis had less statistical power to detect sleeping and multiple RPs rather than feeding RPs, which were more frequent. Persistence of RPs has been repeatedly found to predict later behaviour problems (Papousek & von Hofacker, 1998; Papoušek & von Hofacker, 1995; Schmid et al., 2010; Winsper & Wolke, 2014; Wolke et al., 2002). Our findings support the significance of persistence of RPs for predicting sleeping and multiple RPs in both VP/VLBW and FT infants in the toddler years. However, there were also some differences between full term and VP/VLBW infants in predicting 18 months RPs. In FT infants, regulatory problems at 18 months were mainly related to persistent regulatory problems at two or three measurement points in the first 6 months. Previous research showed that single or transient regulatory problems are less likely to lead to later adverse behaviour indicating early behaviour adaptation in the first 6 months of life

(Scher, Zukerman, & Epstein, 2005; St. James-Roberts et al., 1998; Stifter & Braungart, 1992). In contrast, persistent or multiple problems experienced in the first 6 months have been consistently reported to increase the risk of later RPs or adverse outcomes in infants (Hyde et al., 2012; Rao, Brenner, Schisterman, Vik, & Mills, 2004; Schmid et al., 2010; von Kries et al., 2006; Wolke et al., 2002). This study suggests that VP/VLBW infants may be more susceptible to develop long term multiple problems and this is predicted at an earlier age. Single or multiple regulatory problems at term and 3 months already predicted 18 months sleeping and multiple regulatory problems in VP/VLBW but less so in FT infants. Similar findings have been recently reported in a longitudinal study of crying problems of preterm infants in Finland (Korja et al., 2014).

In contrast, single crying or feeding RPs at 18 months were not predicted by early persistent RPs in both groups. Thus crying and feeding RPs were poorly predicted by early child behaviour. Mother-infant interaction problems, maternal stress and maternal anxiety have been suggested as critical factors in developing crying and feeding problems (Fujiwara, Barr, Brant, & Barr, 2011; Lester et al., 1995; Maxted et al., 2005; McDonough, Rosenblum, Devoe, Gahagan, & Sameroff, 1998; Miller-Loncar, Bigsby, High, Wallach, & Lester, 2004; Sidor et al., 2013; Wurmser et al., 2006). Future research may take into account the impact of maternal mental health and/or mother-infant interaction in alleviating or leading to crying and feeding problems.

Strengths and Limitations

The strength of this study is the detailed definition of crying, sleeping and feeding problems. Most previous studies either used one or two indicators of the problems.

Furthermore, to our knowledge this is the first study to measure all three regulatory problems (crying, sleeping and feeding) in both very preterm and full-term infants during the first 18 months of life. Moreover, this study controlled for the impact of breastfeeding and CNS problems on regulatory problems. In addition, this study had a matched sample on the number of twins to control for parenting effects in VP/VLBW infants and controls equally.

There are also limitations. Regulatory problems were assessed with a standard interview using mothers as data source. Using diaries or observational methods would have provided more objective information than parental interviews; however, they are prone to lower and selective participation rates (Barr, Kramer, Boisjoly, McVey-White, & Pless, 1988). Furthermore, our sample included 4 infants with equal to or above 32 weeks of gestational age but with a very low birth weight. We included these infants in our study for two reasons: a) exclusion did not change our findings and b) other studies report on very preterm and very low birth weight (VP/VLBW) sample combined (Aarnoudse-Moens et al., 2009; Gedolf et al., 2014; Reijneveld et al., 2006).

Conclusions

VP/VLBW infants are only at slightly increased risk for experiencing more regulatory problems at term and in the second year of life than healthy full term children. In particular, persistent regulatory problems in the first 6 months forebode increased sleeping and multiple RPs at 18 months in both VP/VLBW and full term children. Clinicians should be aware that persistency of crying, sleeping or feeding problems in the first 6 months, and their co-occurrence, increases the risk of long-lasting problems, which might still have an impact on parents a year later.

Chapter 9 Development of Multiple Crying, Sleeping, Feeding Problems across Infancy: Neurodevelopmental Vulnerability and Parenting

Background: Regulatory problems (excessive crying, feeding, and sleeping difficulties), specifically their comorbidity, are early warning signs of future problems. Insensitive parenting and neurodevelopmental vulnerabilities have been suggested as factors explaining development or maintenance of regulatory problems. Nevertheless, none of the previous studies investigated these factors within the same sample across infancy, taking into account the reciprocal influences between maternal sensitivity and regulatory problems.

Aim: To investigate the prospective association between very preterm birth, comorbid regulatory problems and maternal sensitivity.

Subjects: 178 participants including 73 very preterm/very low birth weight and 105 full-term infants and their caretakers.

Study Design: A prospective study from birth to 18 months.

Measures: Regulatory problems were measured at term, 3 months and 18 months with a structured parental interview. Maternal sensitivity was measured with a nurse observation at term, and a researcher observation of play tasks at 3 months and at 18 months.

Results: Very preterm birth was associated with regulatory problems at term (β=0.19, SE= 0.10, p< 0.05) and at 18 months (β=0.21, SE= 0.10, p< 0.05), while it had no association to maternal sensitivity across infancy. There were no cross-lagged

reciprocal effects between maternal sensitivity and regulatory problems across infancy. Maternal sensitivity at term had a negative association to regulatory problems at 3 months (β=-0.26, SE= 0.12, p< 0.05)**,** nonetheless this association disappeared afterwards.

Conclusions: Neurodevelopmental vulnerabilities provided more consistent prediction of regulatory problems in comparison to sensitive parenting.

Introduction

Regulatory problems (crying, sleeping, and feeding) during infancy affect approximately 20% of infants in the first year (Hemmi et al., 2011). They have been shown to be relatively stable across the early years (Schmid et al., 2010) and can lead to stable trajectories of dysregulation across childhood (Winsper & Wolke, 2014).

There is increasing evidence that infant regulatory problems are associated with increased childhood behaviour problems such as externalizing problems and ADHD, as supported by the results of a meta-analysis of 22 longitudinal studies (Hemmi et al., 2011). Since 2011, several longitudinal studies have further supported the finding that regulatory problems have an adverse impact on behaviour in childhood and even adolescence (Choe et al., 2013; Hyde et al., 2012; Price et al., 2012; Sheridan et al., 2013; Sidor et al., 2013; Sivertsen et al., 2015). Moreover, there is evidence that especially the co-occurrence of more than one regulatory problem has a stronger negative long term adverse impact than a single regulatory problem occurring in isolation (Hemmi et al., 2011; Wake et al., 2006; Wolke et al., 1995a).

Yet despite the growing evidence about multiple infant regulatory problems as precursors of later behaviour problems, there is a scarcity of research which is focused on how these problems develop during infancy. Two major explanations

have been suggested to understand how regulatory problems develop: a) neurodevelopmental vulnerabilities of the infant and b) maladaptive parenting (Degangi et al., 1993; Schmid et al., 2011; Schmid & Wolke, 2014). The development of regulatory functions is dependent upon the maturation of the brain stem, which undergoes substantial changes after 33 weeks of gestation (Darnall et al., 2006). Converging evidence reveals that very preterm infants who are born before 32 weeks of gestation are at risk of disruptions in brain stem development (Chang et al., 2000; Peterson et al., 2003). The early warning signs of this disturbance include excessive crying, sleeping and feeding difficulties (Geva & Feldman, 2008). Hence, studying the effects of very preterm birth provides a human model to understand the neurodevelopmental underpinnings of infant regulatory problems.

Alternatively, infant regulatory problems may be best understood within a relational context (Anders et al., 2000; Bayer et al., 2007; Wake et al., 2006). Surprisingly few longitudinal studies have examined the relationship between sensitive parenting, referring to mothers' ability to respond appropriately to infant cues (Ainsworth et al., 1974), and infant regulatory problems. Some that focussed on single regulatory problems such as sleeping or crying, showed one-directional associations between maternal sensitivity and child regulatory problems (Priddis, 2009; Teti et al., 2010), others noted a bi-directional relationship between these variables (Bell & Belsky, 2008; Philbrook & Teti, 2016), and still others revealed no significant link (Bordeleau et al., 2012; Hagekull et al., 1997; Scher, 2001b). Thus, the verdict is still out on whether lower maternal sensitivity increases regulatory problems or vice versa or whether parenting has little influence on the development of regulatory problems. Consequently, in order to disentangle the currently unclear direction of influences

between infant regulatory problems and maternal sensitivity, longitudinal cross-lagged designs are needed.

Overall, the purpose of the present study was to investigate the prospective association between very preterm birth, comorbid regulatory problems and maternal sensitivity across the first 18 months of life. We hypothesized that regulatory problems and maternal sensitivity will have a reciprocal relationships across infancy. Furthermore, very preterm birth will increase regulatory problems, on the other hand preterm birth will not influence maternal sensitivity based on the findings from a recent meta-analysis (Bilgin & Wolke, 2015).

Methods

Participants

Participants of this study comprised 178 infants and their caretakers. Seventy-three of the infants were very preterm/very low birth weight (VP/VLBW) and 105 of them were full-term (FT) born. The sample included 101 males and 77 females with a mean of 35 (4.9) weeks of gestational age and 2409 (1062) grams of birth weight. Mothers had a mean age of 30.6 years (5.8) and a majority had > 10 years of education (62.4%). Demographics for VP/VLBW and FT samples are shown in Table 14.

Table 14 Characteristics of the Infants and Mothers

	VP/VLBW (N=73)	FT (N=105)
Gender: N (Male/Female)	41 (56.2%)/32 (43.8%)	60 (57.1%)/45 (42.9%)
Birth weight (g) (M/Range)	1285.8 (521-2158)	3205.1 (1820-4380)
Gestational Age (weeks) (M/Range)	29.4 (25-33)	38.9 (37-42)
Multiple births: Twins (N/%)	21/ 28.8%	32/ 30.5%
Maternal Age (years) (M/SD)	30.5 (5.7)	30.7 (5.9)
Medical Risk: (M/SD)	0.64 (0.73)	NA
1. Neurosensory Deficits		
None (N/%)	57 (79.2%)	NA
Mild (N/%)	15 (20.8%)	NA
2. Rehospitalisation		
Not admitted (N/%)	57 (79.2%)	NA
One readmission (N/%)	12 (16.7%)	NA
>1 readmission (N/%)	3 (4.2%)	NA
3. Surgical Procedures		
No (N/%)	65 (90.3%)	NA
Yes (N/%)	7 (9.7%)	NA
4. Oxygen Dependency		
Never (N/%)	63 (87.5%)	NA
Oxygen only at term (N/%)	5 (6.6%)	NA
Oxygen at 3 months (N/%)	4 (5.6%)	NA
Income (GBP): N (%)		
£0- £25k	30 (41.1%)	38 (36.2%)
£25k- £40k	18 (24.7%)	25 (23.8%)

>£40k	18 (24.7%)	41 (39%)
Maternal Education: N (%)		
<10 years[a]	2 (2.7%)	3 (2.9%)
10 years[b]	43 (58.9%)	60 (57.1%)
>10 years[c]	23 (31.5%)	34 (32.4%)
Maternal Depression (M/SD)*	8.1 (5.7)	6.3 (4.4)
Maternal Sensitivity (N/SD)		
Term	4.52 (0.65)	4.41 (0.54)
3 Months	3.98 (0.56)	3.87 (0.56)
18 Months	5.71 (1.4)	6.13 (1.4)
Multiple Regulatory Problems (N%)		
Term*	45 (61.6%)	49 (46.7%)
3 Months	9 (12.3%)	13 (12.4%)
18 Months *	28 (38.4%)	28 (26.6%)

VP/VLBW: Very Preterm/Very Low Birth Weight, FT: Full-Term; Medical Risk: Composite score of neurosensory deficits, rehospitalization, surgical procedures, and prolonged oxygen dependency (oxygen use of more than 21%); [a]No educational qualification, [b]Basic educational qualification (O-levels), [c]Further education (A-levels) or college education. *$p<0.05$.

Procedure

VP/VLBW infants were recruited from three neonatal units in the East of England during an 18 months period. Written consent was obtained from the mother in the presence of an independent witness. Ethics approval was given by the NHS ethical review boards of the participating hospitals. Recruitment of FT infants was conducted in the postnatal wards of the same hospitals within 48 hours of birth. FT infants (37- 42 weeks gestation) were frequency-matched with VP/VLBW infants on socio-economic status, sex and twin birth. The reason for matching both groups on

twin birth was that it has been identified as a major factor influencing caretaking and early development (Thorpe, Rutter, & Greenwood, 2003).

Measures

Very Preterm Birth

Very preterm birth was coded as a dichotomous variable based on the gestational weeks of birth: 0) full-term (FT) infants, who were born after 36 weeks of gestation; 1) very preterm/very low birth weight (VP/VLBW) infants, who were born at 28 to <32 weeks of gestation. Additionally, in the VP/VLBW group there were 4 (5.5%) infants who were born at 32 weeks of gestational age but with a birth weight <1500 grams.

Maternal Sensitivity

Maternal sensitivity was observed at term, 3 months and 18 months of age. Before discharge neonatal care nurses rated maternal sensitivity of mothers of preterm infants based on their observations in the last week on the Boston City Hospital Assessment of Parental Sensitivity (BCHAPS; (Zahr & Cole, 1991)). For full-term infants, midwives completed the BCHAPS during home visits in the first 10 days of infant's life. The BCHAPS measures how the mother cares for, interacts with and enjoys the relationship with her infant rated on thirteen items with 5-point Likert type scales (1=poor; 5=very competent). Internal consistency of the scale was high (α= 0.95).

Maternal sensitivity at 3 months was measured with a structured play observation: Mother-Infant Structured Play Assessment (MISPA). The play observation consisted of 2 minutes of play with a toy and 2 minutes of free play. Maternal behaviour included 5-point-Likert scales measuring verbal involvement, physical contact,

positive emotion expression, negative emotion expression, stimulation, and sensitivity. These scales were adapted from three interaction coding schemes: The Emotional Availability Scales (Biringen, 1990b); The Infant and Caregiver Engagement Phases (Weinberg & Tronick, 1998); and The Play Observation Scheme and Emotion Ratings (Wolke, 1986). The videotaped maternal behaviour was coded by two independent researchers (Wolke et al., 2014). Factor analysis yielded that maternal positive emotion expression (factor loading= 0.87), sensitivity (0.85) and stimulation (0.84) loaded onto one maternal sensitivity factor. The inter-rater reliability scores for each rating item were moderate to high ($\kappa_{\text{positive emotion}}$= 0.76, $\kappa_{\text{sensitivity}}$= 0.76, $\kappa_{\text{stimulation level}}$= 0.78) and the overall reliability of maternal sensitivity factor was moderate ($\alpha_{\text{maternal sensitivity}}$=0.73).

Maternal sensitivity at 18 months was measured with POSER which is an observational measure to rate behavioural and affective characteristics of maternal and infant behaviours (Wolke, 1986). During POSER, mothers were asked to interact with their children firstly using a shape sorter (2.5 minutes) and afterwards using a little people trailer (2.5 minutes) (Wolke, Skuse, & Mathisen, 1990). Maternal scales were based on validated measures such as the Assessment of Mother-Child Interaction with Etch-a-Sketch (Jaekel, Eryigit-Madzwamuse, & Wolke, 2015; Jaekel et al., 2012), which were rated on a 9-point Likert scale (1= highly insensitive; 9= highly sensitive). Exploratory factor analysis revealed that maternal positive emotion expression (0.64), sensitivity (0.74) and appropriateness of play (0.84) loaded on a maternal sensitivity factor. Inter-rater reliability of each item was high ($\kappa_{\text{positive emotion}}$= 0.93, $\kappa_{\text{sensitivity}}$=0 .90, $\kappa_{\text{appropriateness of play}}$= 0.91) and the internal consistency reliability of the maternal sensitivity factor was high ($\alpha_{\text{maternal sensitivity}}$=0.90). In

addition, the maternal sensitivity factor was validated by another study (Hipwell, Goossens, Melhuish, & Kumar, 2000).

Multiple Regulatory Problems

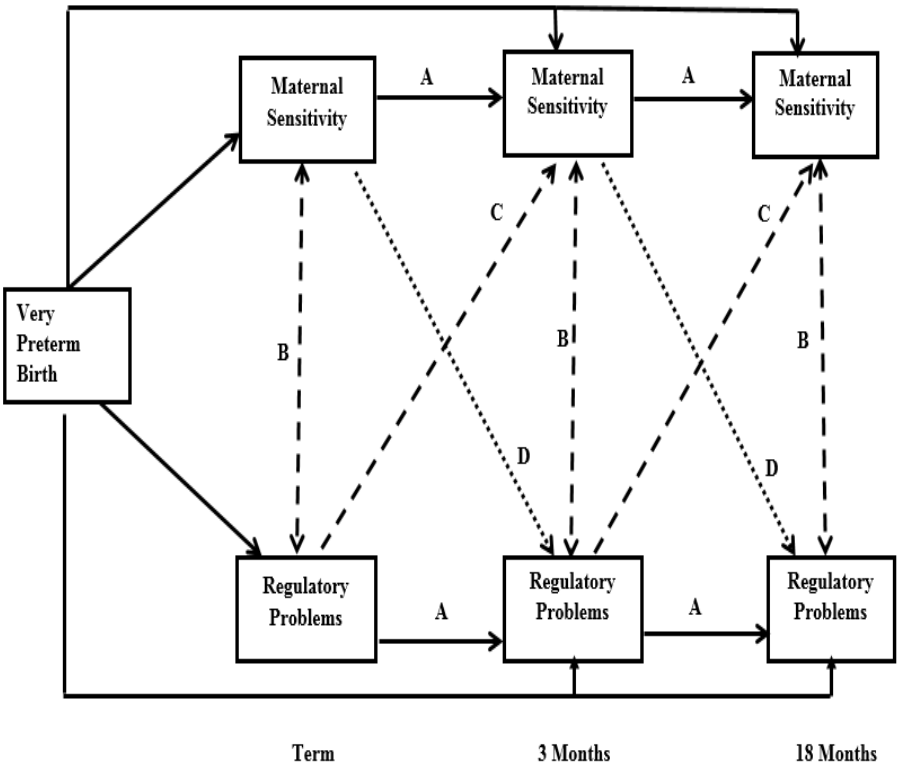
Regulatory problems were assessed via a standard structured interview about crying, sleeping and feeding problems at term, 3 and 18 months. Definitions of crying, sleeping and feeding problems were derived from the literature (Bilgin & Wolke, 2016; Dahl & Sundelin, 1986; St. James-Roberts et al., 1998) and are shown in Table 11 (Chapter 8). The focus of this study was on the multiple occurrences of crying, sleeping and feeding problems. Participants were categorized as having multiple regulatory problems if they had two or three single regulatory problems based on the scores from the crying, sleeping, and feeding interview. The reliability of the scale was high at each time point (α_{Term}=0.71, $\alpha_{3Months}$=0.73, $\alpha_{18Months}$ =0.75).

Control Variables

Medical risk, breastfeeding, maternal depressive symptoms, twin status, maternal education and age, and sex of the infant were included as control variables due to their possible impact on the association between maternal sensitivity and regulatory problems (Musser, Ablow, & Measelle, 2012; Thunstrom, 1999; Wolke et al., 1998). Medical risk was assessed as neurosensory deficits, rehospitalisation, surgical procedures and prolonged oxygen dependency (Table 14). Maternal depressive symptoms were assessed at 6 months using the Edinburgh Depression Scale (Cox et al., 1987), a 10-item screening tool to assess postnatal depressive symptoms with 4-point scales. Individual scores were summed up to create a continuous depression score, which can range from 0 to 30.

Statistical Analysis

Cross-lagged panel model (Bollen & Curran, 2004) was used to assess the reciprocal relationship between multiple regulatory problems and maternal sensitivity, in which the bidirectional associations between the two can be examined with controlling for factors (preterm birth, medical risk, sex) before the first assessment. Analysis was conducted with MPlus (Version 7, Los Angeles, CA) (Muthén & Muthén, 1998-2015) using a maximum-likelihood estimator with robust standard errors (MLR) to account for any nonnormality of the study variables. MLR is an extension of maximum likelihood; hence, all missing data were assumed missing at random and accurately handled. Four models (Figure 9) were assessed: 1) an autoregressive baseline model with only autoregressive effects and concurrent correlations between maternal sensitivity and multiple regulatory problems but no prospective associations from one construct to the other at a later time point; 2) maternal sensitivity unidirectional model with autoregressive effects and cross-lagged paths from early maternal sensitivity to subsequent multiple regulatory problems; 3) multiple regulatory problems unidirectional model with autoregressive effects and cross-lagged paths from early multiple regulatory problems to later maternal sensitivity; 4) reciprocal model with the autoregressive effects and reciprocal paths from both multiple regulatory problems and maternal sensitivity. Analysis was adjusted for the control variables.



Model 1: No cross-lagged associations; paths "C" and "D" are dropped. **Model 2**: Maternal sensitivity predicts regulatory problems; dashed path "C" is dropped. **Model 3**: Regulatory problems predict maternal sensitivity; dotted path "D" is dropped. **Model 4:** Reciprocal model with all paths are included. Regulatory problems refer to infants who have multiple crying, sleeping, and feeding problems.

Figure 9 Cross-Lagged Path Model of Maternal Sensitivity and Multiple Regulatory Problems

In order to evaluate the goodness-of-fit, χ^2 tests and the goodness-of-fit indices were considered. Among the various fit indices, incremental fit indices such as Comparative Fit Index (CFI) and Root Mean Square Error of Approximation (RMSEA) (Bentler, 1990) were used as they are less sensitive to the impact of sample size. For the CFI, values greater than .90 show an acceptable fit and values greater than 0.95 indicate a good fit (Hu & Bentler, 1999). For the RMSEA, values less than .05 indicate a good fit and values less than 0.08 an acceptable fit.

Results

Table 15 shows the results of the model fitting for the cross-lagged relationships between maternal sensitivity and multiple regulatory problems. The unidirectional model, indicating that decrease in early maternal sensitivity increases regulatory problems, was accepted as the best fit with the data (CFI= 0.95, RMSEA= 0.05).

Table 15 Model Fit Indices for Model Testing between Maternal Sensitivity and Multiple Regulatory Problems

	Chi-Square			
Model	X^2	p	CFI	RMSEA
1) Autoregressive Model, No Cross-Lags	14.19	0.11	0.89	0.06
2) Maternal Sensitivity ⟶ Multiple Regulatory Problems	10.29	0.17	0.95	0.05
3) Multiple Regulatory Problems ⟶ Maternal Sensitivity	13.71	0.06	0.86	0.07
4) Reciprocal Model	10.02	0.12	0.92	0.06

Maternal sensitivity at term predicted maternal sensitivity at 3 months (β=0.51, SE= 0.05, p<0.001), which predicted maternal sensitivity at 18 months (β=0.24, SE= 0.08, p< 0.05). Similarly multiple regulatory problems at term predicted multiple regulatory problems at 3 months (β=0.39, SE= 0.18, p< 0.01), which also predicted multiple regulatory problems at 18 months (β=0.35, SE= 0.16, p<0.01).

Maternal sensitivity at term had a direct effect on multiple regulatory problems at 3 months (β=-0.26, SE= 0.12, p< 0.05), with higher maternal sensitivity at term predicting lower multiple regulatory problems at 3 months. Except for this

association, maternal sensitivity and multiple regulatory problems followed independent paths over the next 15 months. VP/VLBW birth did not influence maternal sensitivity at any time point, however VP/VLBW birth was related to increased regulatory problems at term (β=0.19, SE= 0.10, p< 0.05) and 18 months (β=0.21, SE= 0.10, p< 0.05) (Figure 10).

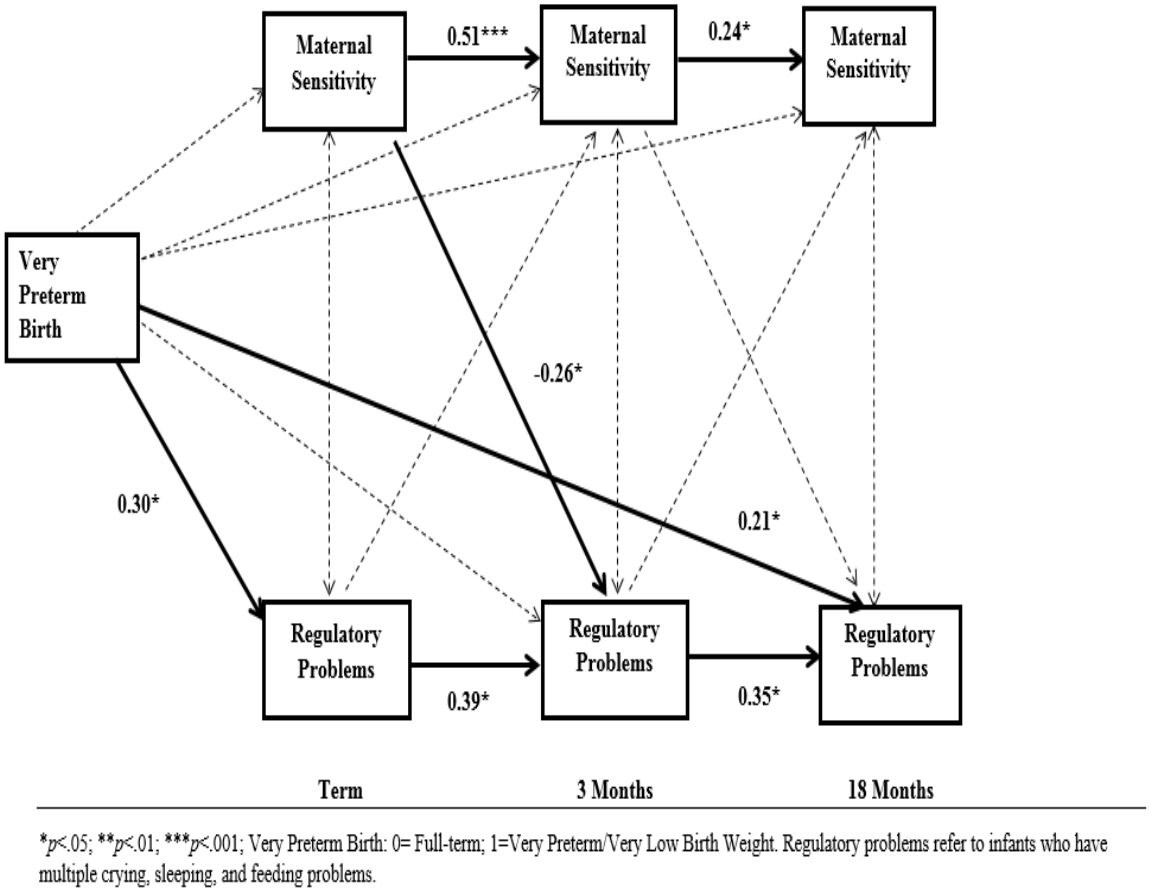


Figure 10 Longitudinal significant Associations between Very Preterm Birth, Maternal Sensitivity and Multiple Regulatory Problems

Discussion

This prospective study indicates that very preterm birth was related to the comorbidity of regulatory problems at term and at 18 months. Furthermore, the relationship between maternal sensitivity and comorbid regulatory problems was unidirectional. Decreased maternal sensitivity at term increased comorbid regulatory problems at 3 months of age; nonetheless, this association disappeared after 3 months. Hence, our findings provide stronger support for a neurodevelopmental

vulnerability explanation in the development of regulatory problems than explaining regulatory problems with sensitive parenting.

Our design has the advantage that it assessed both maternal sensitivity and comorbid regulatory problems over time, which surprisingly revealed that there was no reciprocal relationship between the two variables. Sensitive maternal behaviours early on are helpful to settle infants' regulatory problems at 3 months, whereas early regulatory problems did not influence maternal sensitivity at the following assessment points. This is consistent with previous research that found no association of early excessive crying with subsequent maternal sensitivity during the first year of life (St James-Roberts, Conroy, & Wilsher, 1998; Stifter & Braungart, 1992). Moreover, consistent with our findings, several previous studies revealed the significant impact of maternal sensitivity on regulatory problems in the first few months of life (Fish, Stifter, & Belsky, 1991; Jahromi & Stifter, 2007) but no lasting impact of early maternal sensitivity on infant regulatory problems at 18 months (Owens, Shaw, & Vondra, 1998; Scher, 2001b). This appears at odds with the limited intervention research that showed that changes in parenting behaviour can reduce at least excessive crying (van den Boom, 2001; Wolke et al., 1994). However, the positive effect of changing parent management for a specific regulatory problem such as excessive crying in clinical groups does not allow the conclusion that it was a cause.

Findings of our study revealed that very preterm birth increases comorbid regulatory problems at term and at 18 months of age; nevertheless, it had no significant impact at 3 months of age. This finding corresponds to the bio-behavioural shift in the development from birth to 3 months during which infants go through substantial

changes in biological, cognitive and behavioural domains (Emde, 1998). Therefore, changes in regulatory problems at 3 months might be independent from the impacts of very preterm birth.

Strengths and Limitations

The current study has several strengths. To our knowledge this is the first study to measure comorbid regulatory problems and maternal sensitivity longitudinally at the same time intervals during infancy. Furthermore, this study is the first to consider both very preterm birth and maternal sensitivity to explain the development of regulatory problems. Moreover, using observations at all measurement points to measure maternal sensitivity yielded a reliable assessment. There are also limitations. To begin with, regulatory problems were assessed with a standard interview using mothers as data source. However, interview reports despite probing may be less objective than direct observation or diary recordings (St James-Roberts, Hurry, & Bowyer, 1993; St. James-Roberts & Wolke, 1988). In addition, maternal sensitivity was assessed with different observation measures at each time point, which might influence our results. However, using the same measure was not possible due to the need to have age appropriate measures. Moreover, maternal sensitivity assessment at term was conducted in different settings for VP/VLBW (during hospital stay) and FT (at home) infants. The raters knew the parents of VP/VLBW infants for longer in the special care unit while midwives visited the families of FT infants several times during the first 10 days. Furthermore, it needs to be highlighted that sleeping disorders should not be diagnosed before 6 months of age (Zuckerman et al., 1987). However, our measurements at term and 3 months reflect sleeping adaptation rather than a sleeping problem diagnosis, based on the importance of assessing sleep adaptation in early infancy for prediction of child and parent wellbeing (Crichton &

Symon, 2016; Williams & Sciberras, 2016). Lastly, the suggestions that genetics might contribute to the development of regulatory problems (Becker et al., 2010; Poustka et al., 2015; Räikkönen et al., 2015) could not be assessed in this study but warrants exploration in large population studies. Future studies are needed to address whether early multiple regulatory problems are a starting point of other facets of regulation problems such as hyperactivity/inattention and emotion dysregulation, leading to childhood behaviour problems.

Conclusions

In conclusion, maternal sensitivity had little influence on the development of comorbid regulatory problems across infancy once controlled for very preterm birth. Our study highlights that the early effects that prematurity has on brain development may manifest themselves as increased comorbid regulatory problems. Interventions may target especially those infants with comorbid regulatory problems during infancy (Douglas & Hill, 2013). Moreover, crying, sleeping and feeding behaviours of infants who were born prematurely should be monitored to identify those at risk of future problems as early as possible.

Chapter 10 Early Regulatory Problems Predict Attachment Insecurity and Disorganisation

Background: Regulatory problems (excessive crying, sleeping and feeding difficulties) are a common concern for parents and practitioners and are associated with an increased risk of behaviour problems. Although regulatory problems are highly stressful for parents, the literature on the relationship between regulatory problems and attachment is sparse. This longitudinal study examined the association between early regulatory problems and attachment insecurity and disorganisation.

Methods: 178 infants were assessed for regulatory problems at 3 months and 6 months with a structured parental questionnaire. Both single and multiple regulatory problems (two or more) were assessed. Maternal sensitivity in interaction was assessed at term and 3 months of age. Attachment was measured at 18 months using the strange situation procedure.

Results: Controlling for maternal sensitivity and several other potential confounders, attachment insecurity at 18 months was predicted by early multiple regulatory problems at 3 months (OR= 2.3, CI: 1.14- 4.41) and 6 months (OR= 2.5, CI: 1.86- 4.88), whilst none of the single regulatory problems were associated with attachment insecurity. In contrast, disorganised attachment at 18 months was predicted by sleeping problems (OR= 3.2, CI: 1.32- 4.63) at 6 months. The strongest associations were found between multiple regulatory problems at both 3 months (OR= 3.8, CI: 1.32- 5.22) and 6 months (OR= 4.2, CI: 2.80- 5.56) and disorganised attachment at 18 months.

Conclusions: Early infant multiple regulatory problems are an indicator of risk for impaired attachment development of infants to their mother.

Introduction

Early regulatory problems refer to infants' difficulty in adjusting to their environment, and can manifest as excessive crying, and difficulties in sleeping and feeding (Hemmi et al., 2011). The majority of infants (20%) experience only one regulatory problem (i. e., crying, sleeping or feeding problems) (Hemmi et al., 2011), whilst a smaller group of infants (4 to10%) experience more than one regulatory problem at the same time, i.e. multiple regulatory problems (MRP) (von Kries et al., 2006). Infant regulatory problems can predict stable dysregulation trajectories across childhood (Winsper & Wolke, 2014) and behavioural or emotional problems, specifically externalizing problems and ADHD (Hemmi et al., 2011). Multiple regulatory problems appear to have the strongest associations with future problems (Schmid et al., 2010; Winsper & Wolke, 2014). Nevertheless, it is still unclear whether multiple regulatory problems signify an early risk factor or maybe an early phenotype of under-regulation problems.

Given that multiple regulatory problems reflect an inability to self-regulate and return to an initial consolidated state in more than one domain (e.g., unable to stop crying, settle back into sleep and accept food) (St James-Roberts, 2012), one may speculate that multiple regulatory problems are an early phenotype of behavioural under-regulation. Starting with physiological regulation during early infancy, self-regulation abilities precede the regulation of emotion, attention and behavioural domains (Calkins, 2009), thereby impacting future behavioural adjustment and emotional development (Calkins & Fox, 2002). In this regard, multiple regulatory problems may be likely to influence infant-mother attachment, since infants develop their ability to self-regulate in relation to mothers' consistent response to their alert states (Kopp, 1982). However, taking care of infants who have multiple regulatory

problems could challenge mothers' ability to provide consistent responses to their infants' distress (Degangi, 2000). Internalization of inconsistent patterns in maternal behaviour may consequently increase the risk of insecure attachment (Cassidy, 1994), or particularly disorganised attachment since regulatory problems may indicate an inability to find organised strategies in social situations (Hofacker & Papoušek, 1998).

Attachment, known as the emotional and enduring bond of the infant to their caregiver (Bowlby, 1969), reflects an infant's ability to use their caregiver as a secure base to return to when subjected to stressful situations. Insecure attachment can increase both externalizing and internalizing problems in childhood and adolescence, whilst disorganised attachment seems to be particularly associated with externalizing problems (Fearon et al., 2010; Madigan et al., 2013).

The development of both insecure and disorganised attachment has been mainly explained with problems in the parenting context (Ainsworth, Blehar, Waters, & Wall, 1978; van Ijzendoorn, Schuengel, & Bakermans-Kranenburg, 1999) and maternal depressive symptoms (Atkinson et al., 2000; van Ijzendoorn et al., 1999). Disorganised attachment has further been predicted by neurodevelopmental problems, specifically very preterm birth (Brisch, Bechinger, Betzler, & Heinemann, 2003; Siegel, 1999; Wolke, Eryigit-Madzwamuse, & Gutbrod, 2014). Thus, regulatory problems may indicate early neurodevelopmental disorganisation and be related to disorganised attachment in particular.

Only a few studies have examined crying, sleeping, or feeding problems in relation to attachment patterns. Two studies that investigated infant crying revealed no association with subsequent attachment security (Stifter & Bono, 1998; van IJzendoorn & Hubbard, 2000), whereas the majority of studies that studied infant

feeding problems found higher levels of insecure or disorganised attachment in infants with clinically diagnosed feeding problems (Chatoor et al., 1998; Ward et al., 2000). In contrast, studies on infant sleeping problems reported inconsistent findings (Beijers et al., 2011; Pennestri et al., 2015; Scher, 2001a). Importantly, the majority of these studies only assessed the occurrence of one regulatory problem but did not take into account other regulatory problems. However, regulatory problems often co-occur during infancy and may indicate general dysregulation (Winsper & Wolke, 2014). Thus, from the existing studies it is difficult to conclude whether a specific regulatory problem such as feeding or sleeping may be associated with attachment or whether any associations may be accounted for by multiple regulatory problems. As far as we are aware, there has been no prospective investigation of the association between multiple regulatory problems in infancy and the development of attachment insecurity and disorganisation into toddlerhood.

The main purpose of the present study was to investigate the link between early multiple regulatory problems in the first 6 months of life and attachment insecurity and disorganisation at 18 months of age. We further investigated the association between single regulatory problems and attachment insecurity and disorganisation, controlling for the presence of other regulatory problems in infancy. We hypothesized that early multiple regulatory problems may increase the risk of insecure attachment and particularly increase the risk of disorganised attachment.

Methods

Participants and Design

Participants of this study were recruited from three hospitals in East England and assessed longitudinally at birth, 3, 6 and 18 months of age. The sample comprised of 73 Very Preterm/Very Low Birth Weight (VP/VLBW) and 105 Full-Term (FT) infants and their caretakers. A design including both preterm and full term infants and their mothers was chosen to investigate both potential precursors and consequences of crying, sleeping and feeding problems in infancy as reported here (Bilgin & Wolke, 2016). Infant and mother characteristics of the study sample are shown in Table 16. The overall sample included 101 males and 77 females with a mean of 35 (4.9) weeks of gestational age and 2409 (1062) grams of birth weight. Mothers had a mean age of 30.6 years (5.8) and a majority had at least 10 years of education (62.4%).

Table 16 Descriptive characteristics of infants and mothers

	Total Sample (N= 178)
Gender: N (%) (Male/Female)	101 (56.7%)/77 (43.3%)
Birth weight (g) (M/Range)	2409 (521-4380)
Gestational Age (weeks): (M/Range)	35.03 (25-42)
Very Preterm/Very Low Birth Weight (N/%)	73 (41%)
Multiple births: twins (N/%)	53 (29.8%)
Medical risk: M (SD)	0.64 (0.73)
Maternal Age (years): M (SD)	30.6 (5.8)
Income (GBP): N (%)	
£0- £25k	68 (40%)
£25k- £40k	43 (23.3%)
>£40k	59 (34.7%)
Maternal Education: N (%)	
<10 years	5 (3%)
10 years	103 (62.4%)
>10 years	57 (34.5%)
Breastfeeding: N (%)	
Term	76 (42.7%)
3 Months	44 (24.9%)
6 Months	23 (13.8%)
Maternal Depression: M (SD)	7.1 (5.1)
Maternal Sensitivity: N (SD)	
Term	4.47 (0.60)
3 Months	3.91 (0.56)
Regulatory Problems: N (%)	
No Regulatory Problems	

3 Months	89 (50%)
6 Months	83 (46.6%)
Single Regulatory Problems	
3 Months	67 (37.6%)
6 Months	62 (34.8%)
*Crying Problems**	
3 Months	32 (18%)
6 Months	35 (21.7%)
*Sleeping Problems**	
3 Months	40 (23.3%)
6 Months	56 (35.7%)
*Feeding Problems**	
3 Months	46 (26%)
6 Months	39 (23.6%)
Multiple Regulatory Problems	
3 Months	22 (12.4%)
6 Months	33 (18.5%)

*Please note that percentages of crying, sleeping, and feeding problems represent overall numbers.

Measures

Early Regulatory Problems

Mothers were asked to report on infants' crying, sleeping, and feeding problems at 3 and 6 months via a standard structured interview. Definition of crying, sleeping and feeding problems were derived from the literature (Bilgin & Wolke, 2016; Dahl & Sundelin, 1986; St James-Roberts, 1998) and are shown in Table 11. Based on the

specific criteria for each regulatory problem, three categorical variables were created: 1) crying problem: 0= no crying problem, 1= crying problem; 2) sleeping problem: 0= no sleeping problem, 1= sleeping problem; 3) feeding problem: 0= no feeding problem, 1= feeding problem. Furthermore, infants were considered as having multiple regulatory problems if they had two or three single regulatory problems.

Attachment Insecurity and Disorganisation

Attachment insecurity and disorganisation were assessed at 18 months with the strange situation procedure (SSP), a widely used and well-validated laboratory procedure to measure the quality of attachment (Ainsworth et al., 1978). During SSP, infants experience separations and reunions with the attachment figure in order to elicit attachment behaviour. The experimenters were trained by Dr. Elizabeth Carlson and all tapes were sent to and coded at the Institute of Child Development, University of Minnesota. The coders were blind to child and family characteristics and regulatory problems. 38% of VP/VLBW and 32% of FT tapes were randomly selected for inter-rater reliability assessment, which was acceptable for both the VP/VLBW (κ=0.74) and FT sub-samples (κ=0.76).

First, infants were classified as secure (B), insecure-avoidant (A) or insecure-resistant (C) based on the pattern of scores on four 7-point scales: proximity seeking behaviour, contact maintaining behaviour, avoidance of the caregiver, and resistance, using the scoring systems outlined in the manuals of Ainsworth et al. (1978). Afterwards, a categorical variable was created to measure attachment insecurity: 0=secure versus 1=insecure (insecure-avoidant and insecure-resistant).

Attachment disorganisation scores were coded according to Main and Solomon's (1990) continuous scale of attachment disorganisation on a 9-point scale (1= no signs

of disorganisation, 5= border, 9= high levels of disorganisation). In order to make the organised versus disorganised classification, those scoring ≥6 were considered as disorganised; those scoring 5 were given either a primary or a secondary disorganised classification depending on the particular case; and those scoring <5 were classified as having organised attachment. Signs of disorganized attachment include contradictory behaviour such as avoidance and resistance at the same time or puzzling behaviour without an apparent function. For current analysis, a categorical variable was created: 0= organised versus 1= disorganised.

Control Variables

Very Preterm Birth

Although preterm birth has not been found to affect maternal sensitivity (Bilgin & Wolke, 2015) or secure versus insecure attachment classification, there is evidence that it is related to disorganised attachment (Wolke, Eryigit-Madzwamuse, & Gutbrod, 2014). Thus, the impact of very preterm birth was controlled in this study. Very preterm birth was coded as a dichotomous variable based on the gestational age and birth weight of the infant: 0) full-term (FT) infants, 1) very preterm/very low birth weight (VP/VLBW) infants.

Maternal Sensitivity

Maternal sensitivity was observed at term and 3 months of age. At term, nursing staff rated maternal sensitivity using the Boston City Hospital Assessment of Parental Sensitivity Scale (BCHAPS; Zahr & Cole, 1991) based on their observation in the last week of hospital stay for the VP/VLBW sample and midwives rated it during repeated home visits in the first 10 days of the infant's life for the FT sample. The BCHAPS measures how the mother cares for, interacts with and enjoys the

relationship with her infant rated on thirteen items with 5-point Likert type scales (1=poor; 5=very competent). An example item is 'mother changes behaviour in response to baby's cues'. Internal consistency of the scale was high (α= 0.95). Maternal sensitivity at 3 months was measured with a structured play observation: Mother-Infant Structured Play Assessment (MISPA). The play observation consisted of 2 minutes of play with a toy and 2 minutes of free play. Video recordings of maternal behaviour were rated on 5-point-Likert scales from videotapes measuring verbal involvement, physical contact, positive emotion expression, negative emotion expression, stimulation, and sensitivity. These scales were adapted from three interaction coding schemes: The Emotional Availability Scales (EAS; Biringen, Robinson, & Emde, 1990, 1993); The Infant and Caregiver Engagement Phases (ICEP; Weinberg & Tronick, 1998); and The Play Observation Scheme and Emotion Ratings (POSER; Wolke, 1986). The videotaped maternal behaviour was coded by two independent raters (Wolke, Eryigit-Madzwamuse, & Gutbrod, 2014). Factor analysis yielded that the three scales maternal positive emotion expression (0.87), sensitivity (0.85) and stimulation (0.84) loaded onto a maternal sensitivity factor. The inter-rater reliability scores for each item were moderate to high ($\kappa_{\text{positive emotion}}$= 0.76, $\kappa_{\text{sensitivity}}$= 0.76, $\kappa_{\text{stimulation level}}$= 0.78) and the overall reliability of the maternal sensitivity factor was moderate ($\alpha_{\text{maternal sensitivity}}$= 0.73).

Maternal Depressive Symptoms

At 6 months, mothers completed the Edinburgh Depression Scale (Cox et al., 1987), which is a widely used 10-item screening tool to assess postnatal depression on 4-point scales. Individual scores were summed up to create a continuous depression score.

Additional Control Variables

Income, maternal education, maternal age, multiple birth (twins), medical risk and breast-feeding were other control variables. Medical risk was extracted from medical records at 3 months with a composite score of neurosensory deficits, rehospitalisation, surgical procedures and prolonged oxygen dependency, which has been outlined in detail elsewhere (Bilgin & Wolke, 2016). Breastfeeding has been shown to relate to both regulatory problems and attachment classifications (Tharner et al., 2012a; Thunstrom, 1999; Wolke et al., 1998). Based on maternal report about how they fed their infant, a categorical variable was used to differentiate between infants who were breastfed and who were bottle-fed or mixed-fed at term, 3 months and 6 months.

Statistical Analysis

All statistical analyses were conducted using SPSS version 23.0. Hierarchical binary logistic regression analyses were carried out to investigate the association between early regulatory problems and insecure and disorganised attachment, separately. In step one, maternal sensitivity at term and 3 months were entered, based on theoretical associations with attachment. In step two, very preterm birth, control variables (breastfeeding, income, maternal education, maternal age, multiple birth, medical risk and maternal depressive symptoms) and each single regulatory problem and multiple regulatory problems were entered. The reference group was no regulatory problems at 3 months and 6 months.

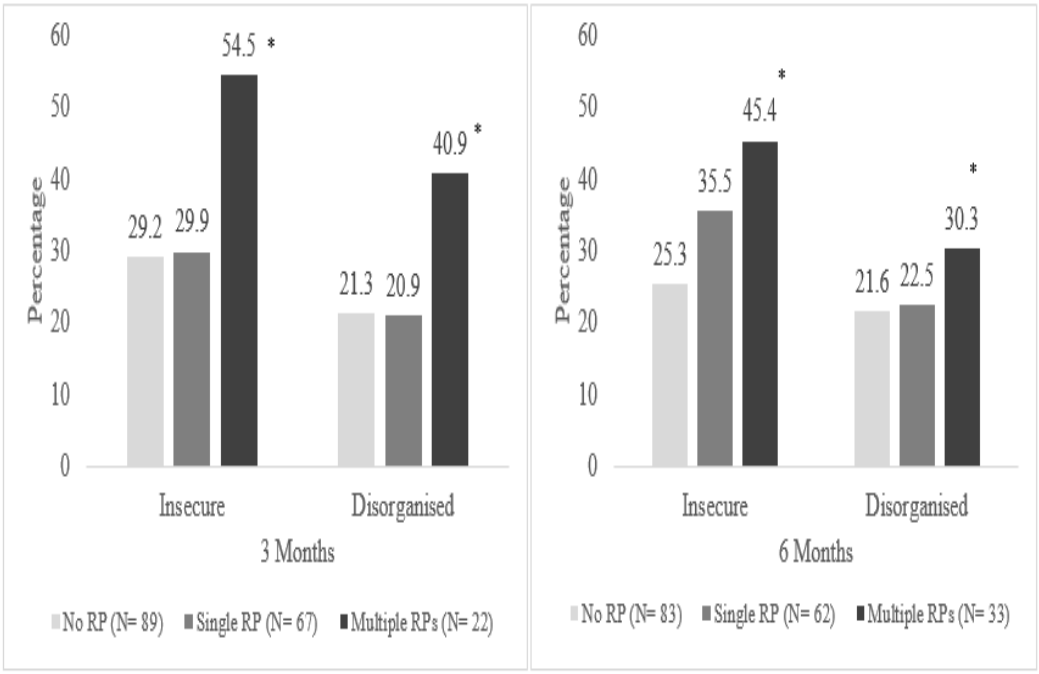
The continuous variables maternal sensitivity and depressive symptoms were centered (i.e. the mean was set to zero) and standardized (the variance was set to 1) prior to conducting the analyses since using centered predictor variables increases the

interpretability of the results (Aiken & West, 1991). Nevertheless, centering a variable is complex when multiple groups are included in a study (Enders & Tofighi, 2007). In such cases, grand mean centering would result in the loss of group comparisons. Thus, within-group centering was applied in the current study, which includes two groups of infants (VP/VLBW and FT).

Results

Descriptive Analyses

Of the 178 infants, 120 (67.4%) were classified as securely attached, 8 (4.5%) as insecure-avoidant, 8 (4.5%) as insecure-resistant and 42 (23.6%) as disorganised. The percentages of no regulatory problems, single regulatory problems and multiple regulatory problems at 3 and 6 months in infants who had insecure and/or disorganised attachment at 18 months are shown in Figure 11 (Please see Appendix F for further information).



RP= Regulatory Problem. *p<0.05

Figure 11 Percentages of regulatory problems at 3 and 6 months in infants who had insecure or disorganised attachment at 18 months

Associations between Early Regulatory Problems and Attachment Insecurity

No associations were found between early (3 and 6 months) crying, sleeping, and feeding problems and insecure attachment at 18 months. In contrast, multiple regulatory problems both at 3 months (OR= 2.3, CI: 1.14- 4.41) and 6 months (OR= 2.5, CI: 1.86- 4.88) were associated with increased rates of insecure attachment, after adjusting for control variables. The other predictor of attachment insecurity was maternal sensitivity assessed at term (OR= 0.21, CI: 0.07- 0.56) and 3 months (OR= 0.23, CI: 0.10- 0.42); however, this effect disappeared after controlling for multiple regulatory problems, very preterm birth, maternal depressive symptoms and other control variables (Table 17).

Associations between Early Regulatory Problems and Attachment Disorganisation

No associations were found between crying and feeding problems at both 3 and 6 months and disorganised attachment. In contrast, sleeping problems at 6 months (OR= 3.2, CI: 1.32- 4.63) was associated with a higher risk of attachment disorganisation. Moreover, multiple regulatory problems both at 3 months (OR= 3.8, CI: 1.32- 5.22) and 6 months (OR= 4.2, CI: 2.80- 5.56) were associated with significantly higher odds of disorganised attachment.

Table 17 Associations between Regulatory Problems and Attachment Insecurity and Disorganisation

	Insecure Attachment		Disorganised Attachment	
	Step1	Step2	Step1	Step2
	OR (95%)	OR (95%)	OR (95%)	OR (95%)
Maternal sensitivity at term*	**0.21 (0.07-0.56)**	0.12 (0.02-1.32)	0.33 (0.02-1.71)	0.20 (0.04-1.76)
Maternal sensitivity at 3 months*	**0.23 (0.10-0.42)**	0.11 (0.01-1.46)	0.39 (0.10-1.48)	0.27 (0.02-1.27)
Crying Problems at 3 Months		1.55 (0.23-2.31)		1.62 (0.70-1.33)
Crying Problems at 6 Months		1.67 (0.65-4.30)		1.27 (0.47- 3.44)
Sleeping Problems at 3 Months		1.43 (0.25-2.01)		1.02 (0.41- 2.50)
Sleeping Problems at 6 Months		1.16 (0.53-2.69)		**3.15 (1.32- 4.63)**
Feeding Problems at 3 Months		2.11 (0.99-4.97)		1.18 (0.55- 2.58)
Feeding Problems at 6 Months		1.48 (0.61-2.20)		1.23 (0.85- 1.76)
Multiple Regulatory Problems at 3 Months		**2.3 (1.14-4.41)**		**3.78 (1.32-5.22)**
Multiple Regulatory Problems at 6 Months		**2.5 (1.86-4.88)**		**4.10 (2.80-5.56)**

Step1: maternal sensitivity at term, at 3 months; Step2: control variables and regulatory problems.

Please note that for better readability significant results are printed in bold.

Maternal sensitivity was not a significant predictor of insecure attachment after control variables and regulatory problems were included in the analysis.

* When we centre the independent variable, the interpretation of OR remains the same.

Discussion

The major finding of this study is that multiple regulatory problems increase the odds of developing both insecure attachment and, in particular, disorganised attachment. On the other hand, single regulatory problems were not related to attachment security, however, sleeping problems at 6 months increased the odds of disorganised attachment. Moreover, insecure attachment was predicted by maternal sensitivity, however, this association disappeared once regulatory problems and other control factors were taken into consideration.

Our findings highlight that infant sleeping at 6 months and multiple regulatory problems as early as 3 months are related to disorganised attachment in a stressful separation and reunion situation. A plausible explanation for the role of early MRPs on disorganised attachment can be made under the guidance of the cascade model of development (Masten & Cicchetti, 2010), which postulates that dysfunction in one domain can progress into another domain along the development of psychopathology. Both multiple regulatory problems and disorganised attachment represent an inability of self-regulation, the former being at physiological level and the latter at relationship level. Thus, early multiple regulatory problems may lead to documented negative behavioural outcomes in childhood and adolescence (Hyde et al., 2012) by predisposing infants to disorganisation in mother-infant attachment relationship which in turn may increase the risk of developing behaviour problems. This would suggest a mediation model or cascade of events leading to behaviour problems. Two separate meta-analytic investigations have indicated that both multiple regulatory problems (Hemmi et al., 2011) and disorganised attachment (Fearon et al., 2010) pose infants at great risk of externalizing problems.

Alternatively, early regulatory problems may impact both on early attachment of the infant to the mother and set the infant on a trajectory of behavioural dysregulation (Winsper & Wolke, 2014), increasing the odds of developing behaviour problems. Future research including assessments of multiple regulatory problems, infant attachment and childhood behaviour problems may clarify whether multiple regulatory problems affect both attachment and behaviour or the relationship between multiple regulatory problems and behaviour problems is mediated by the early infant-parent attachment relationship.

Sleeping problems during the first 6 months were not associated with insecure attachment but were associated with disorganised attachment at 18 months. This is consistent with a recent study which found more problematic sleeping patterns in toddlers with disorganised attachment in comparison to secure and/or resistant toddlers (Pennestri et al., 2015). However, our findings are in contrast to the findings of a previous study, which measured night wakings repeatedly over the first 6 months and reported that infants who later developed insecure-resistant attachment were the ones with the highest frequency of night-waking across the first 6 months (Beijers et al., 2011). Nonetheless, the focus of the Beijers et al (2011) study was only on night-wakings, whereas the present study additionally asked about settling difficulties and uninterrupted sleep duration which are also important indicators of a sleep problem (Byars et al., 2012). However, as feeding and crying problems were not assessed, we cannot be certain that those who had sleep and other problems were those who more often had insecure attachment, a finding that would tally with our results showing an association between multiple regulatory problems and insecure attachment. Nonetheless, our findings indicate that sleeping problems as early as 6 months may flag up later disorganised attachment relationship problems.

In addition to disorganised attachment, multiple regulatory problems predicted attachment insecurity over and above maternal sensitivity. From the perspective of attachment theory, the development of insecure attachment patterns are predominantly explained by mothers' ability to be sensitive to their infants' cues (Ainsworth et al., 1978; Bowlby, 1969). However, the development of insecure attachment in infants with multiple regulatory problems might be more linked to infant-related characteristics. To benefit from maternal sensitivity, infants with multiple regulatory problems might need a higher level of maternal sensitivity compared to infants without problems (Belsky, 2005).

Strengths and Limitations

The strengths of this study are the measurement of important covariates and detailed information regarding crying, sleeping and feeding problems during early infancy. Furthermore, this study assessed attachment using a large sample of infants and attachment was classified by independent experts blind to child characteristics and study hypotheses. Nevertheless, there are also limitations. First, the assessment of regulatory problems with maternal reports might produce less objective findings than observation or diary recordings (St. James-Roberts & Wolke, 1988). Nevertheless, there is a high likelihood of dropout in observation or diary studies (Barr et al., 1988). Second, the assessment of maternal sensitivity at term was conducted in different settings for VP/VLBW (hospital) and FT (home) sample, and VP/VLBW infants were observed for a longer time than FT infants. In addition, a diagnosis of sleeping problems should not be made before 6 months of age (Zuckerman et al., 1987), hence our assessments at 3 months reflect sleeping adaptation rather than a sleeping problem diagnosis. Moreover, we were unable to investigate the role of genetics (Bakermans-Kranenburg & van Ijzendoorn, 2007) and harsh parenting (van

Ijzendoorn et al., 1999) in explaining individual differences in attachment patterns. Furthermore, we were unable to analyse the differences between insecure-resistant and insecure-avoidant attachment categories due to the small sample size in these categories. Since sleeping problems might be more apparent in infants with insecure-resistant attachment than those with insecure-avoidant attachment (McNamara, 2003; Morrell & Steele, 2003), it is important for future studies to focus on the differences between the insecure categories.

Conclusions

This longitudinal study found that early multiple regulatory problems are important predictors of insecure and, in particular, disorganised attachment. Findings of the current study indicate that early multiple regulatory problems alter the social relationship to their mother independent of maternal sensitivity in interaction. Future research may determine whether attachment is an important mediator between multiple regulatory problems and behaviour problems in childhood and beyond (Schmid & Wolke, 2014; Winsper & Wolke, 2014). Clinicians should be aware that multiple occurrences of crying, sleeping and feeding problems as early as 3 months of age put infants at an increased risk of attachment problems. Thus, infants' multiple regulatory problems may indicate emerging relationship problems of the infant to their caretakers despite sensitive parenting and may warrant early intervention. Future research should explore if the association between early multiple regulatory problems and disorganised attachment links to externalising problems and ADHD.

Chapter 11 Overall Discussion

This chapter provides a summary of the major findings related to the overall aim from the four studies undertaken, followed by a discussion integrating the findings with the literature. Furthermore, the strength and limitations of the research will be discussed. Lastly, implications of the findings and suggestions for future research will be presented.

This thesis set out to determine the predictive role of neurodevelopmental vulnerability and sensitive parenting on multiple regulatory problems. Moreover, it investigated the association between multiple regulatory problems and infant-mother attachment.

Summary of Results

To investigate the independent or conjoint effect of neurodevelopmental vulnerability on regulatory problems across the first 18 months of age, it was important to first determine whether it was possible to use a naturalistic experimental design. In particular, using a mixed sample of infants born with neurodevelopmental vulnerability (i.e. born preterm or full-term) to determine the effect of neurodevelopmental vulnerability without a confounding effect on maternal sensitivity. For this purpose, a meta-analysis was conducted to determine whether the stress associated with preterm birth may alter maternal sensitivity of caretakers of preterm children. The meta-analytic investigation (study 1) indicated that neurodevelopmental vulnerability, i.e. preterm birth did not alter maternal sensitivity of mothers compared to mothers of full-term born infants. Thus, it was justified to

use a sample comprising both preterm and full-term infants to investigate the effects of neurodevelopmental vulnerability and maternal sensitivity on the development of regulatory problems and infant attachment. Study 2 investigated whether VP/VLBW infants experienced higher levels of single and multiple regulatory problems compared to FT infants across the first 18 months. It was found that neurodevelopmental vulnerability was associated with an increased rate of multiple regulatory problems at term and 18 months. Study 3 explored the longitudinal association between initial neurodevelopmental vulnerability, and interplay of maternal sensitivity and multiple regulatory problems over the first 18 months of life. Applying a cross-lagged model of multiple regulatory problems and maternal sensitivity over 3 time points, it was found that neurodevelopmental vulnerability had a continuing effect on multiple regulatory problems at term and 18 months. Maternal sensitivity at term was associated with multiple regulatory problems at 3 months but maternal sensitivity at term or 3 months did not have an impact on regulatory problems at 18 months nor did the empirical results indicate any cross influences of multiple regulatory problems on maternal sensitivity. Finally it was tested in study 4 if multiple regulatory problems are predictors of later insecure or disorganised attachment. Study 4 found that once controlled for maternal sensitivity and other confounders, multiple regulatory problems as early as 3 months were associated with both security of attachment and even more strongly with disorganised attachment to the mother.

Integrated Discussion

Neurodevelopmental vulnerability operationalized by preterm birth was found to have no adverse impact on maternal sensitivity compared to maternal sensitivity in parenting full term born children. Despite the fact that some studies in the parenting

literature have suggested that prematurity adversely impacts parenting (Forcada-Guex et al., 2006; Korja et al., 2012; Schermann-Eizirik et al., 1997), the current meta-analysis revealed no evidence for an influence of preterm birth on maternal sensitivity. Regardless of the stressful experiences during NICU stay after preterm birth (Goldberg & DiVitto, 2002), mothers of preterm children engage with their infants in a similar sensitive manner as those of full term children. This finding is in correspondence with the results of another meta-analysis study, which revealed maternal sensitivity as similar in samples with and without autism spectrum disorders (van Ijzendoorn et al., 2007). The findings indicate considerable resilience of mothers who are able to show similar sensitive caretaking despite early infant-related stressful experiences. Mothers of preterm children show considerable adjustment in their behaviour despite increased stress experience (Savage-McGlynn et al., 2015).

Although neurodevelopmental vulnerability did not relate to maternal sensitivity, it contributed to the development and maintenance of multiple regulatory problems. This is consistent with a previous study that reported that very preterm birth was a strong predictor of multiple regulatory problems at 5 months (Schmid et al., 2011). Moreover, other studies highlighted that more neurological immaturity (Papoušek & von Hofacker, 1995) and elevated levels of respiratory sinus arrhythmia (Dale, O'Hara, Keen, & Porges, 2011b) in infants were associated with multiple regulatory problems compared to those not affected by regulatory problems. Furthermore, both neurodevelopmental vulnerability and regulatory problems are associated with the same behavioural outcome in the long-term, namely ADHD (Hemmi et al., 2011; Johnson & Marlow, 2011; Lindstrom, Lindblad, & Hjern, 2011). Thus, children's under-regulation behaviour is likely to be preceded by neurodevelopmental vulnerability. Nonetheless, using only a preterm sample has restricted the application

of this finding to other samples at risk for neurodevelopmental problems (Papoušek & von Hofacker, 1995). Since feeding problems have been consistently more frequent in preterm samples, it may be that the combinations including feeding regulatory problems might be more strongly associated to neurodevelopmental vulnerability compared to combined crying and sleeping problems. However, our sample size was too small to investigate the various permutations of multiple regulatory problems.

Maternal sensitivity had some but only short-term impact on multiple regulatory problems during infancy, which is consistent with previous literature regarding the development of childhood behavioural problems (Ciciolla, Gerstein, & Crnic, 2014; Hartz & Williford, 2015). The absence of bidirectional associations between general maternal sensitivity and multiple regulatory problems across infancy contradicts the transactional model of development which puts a strong emphasis on the impact of bidirectional influences between mother and child on the development of problematic behaviours (Sameroff, 2009). A plausible explanation is that the strength of bidirectional associations between maternal and child behaviour could vary with respect to the developmental period during which the analysis is conducted. The bidirectional association between mother and child behaviour has usually been documented in studies with older children (Eisenberg, Taylor, Widaman, & Spinrad, 2015; Serbin, Kingdon, Ruttle, & Stack, 2015). In particular, the influence of child on maternal behaviour may become more apparent with advancing age (Burke, Pardini, & Loeber, 2008) since children become more independent as they get older. Our findings suggest that multiple regulatory problems are moderately persistent despite sensitive parenting from 3 months onwards.

While interpreting our findings regarding maternal sensitivity, it should be acknowledged that the current thesis evaluated general maternal sensitivity as observed in play situations. Hence, our findings might not be applicable to sensitive parenting in other settings, which are closely linked to regulatory problems such as while feeding a regular meal, during soothing, or night-time sleep practices (Lindberg et al., 1996; Philbrook & Teti, 2016). However, there is evidence that maternal sensitivity is consistent across different settings such as bathing and free play in infants without regulatory problems (Joosen, Mesman, Bakermans-Kranenburg, & van Ijzendoorn, 2012), and during feeding and free play in children with feeding problems (Atzaba-Poria et al., 2010). Nevertheless, it was important for the purpose of the current thesis to measure maternal sensitivity in a play situation. If maternal sensitivity was observed during regulatory problem related situations such as during crying, then maternal behaviour might be a reaction to high stress demand in regulating the behaviour under consideration (regulatory problems) and the measure of maternal sensitivity, partly measured as reaction of the infant to maternal behaviour, would result in confounding the measurement of infant behaviour. Thus, while in clinical settings mothers may present with inappropriate ways to deal with infant crying or sleep problems, this may be a reaction rather than a cause of the multiple regulatory problem according to the findings here. Thus, if observed outside dealing with the behaviour of interest (regulatory problem) such as in a play situation, this is more likely to be a representation of maternal sensitivity in general or maternal potential for sensitivity.

Multiple regulatory problems are relatively stable over time, consistent with the reports from other longitudinal studies (Schmid et al., 2010; Wake et al., 2006; Winsper & Wolke, 2014). A new finding is that multiple regulatory problems were

as stable as maternal sensitivity over time. During the first few months, infant behaviour undergoes rapid changes (Lamb, Bornstein, & Teti, 2002) and usually there is very limited stability in areas such as cognitive development (Bremner & Fogel, 2004). On the other hand, maternal behaviours tend to be more stable even during infancy (Behrens, Hart, & Parker, 2012). Hence, this finding is quite remarkable and an indication that regulatory abilities at the extreme (multiple regulatory problems) are moderately enduring characteristics of the infant. Likewise, numerous studies in the field of "difficult" temperament research revealed that temperamental characteristics are relatively stable from infancy to childhood (Hayes, McCoy, Fukumizu, Wellman, & DiPietro, 2011; Komsi et al., 2006; Pedlow, Sanson, Prior, & Oberklaid, 1993).

A further novel finding is that multiple regulatory problems were found to be associated with both insecure attachment over and above maternal sensitivity, and highly associated with disorganised attachment. This finding highlights that although having multiple regulatory problems did not impact on maternal sensitivity it impaired the infants' attachment behaviour towards their mother. Accordingly, infant characteristics that indicate behaviour organisation are shown to be crucial for the developing relationship of infant to the mother even when mothers are sensitive. Due to the lack of previous empirical studies that examined the relationship between multiple regulatory problems and attachment, one can only speculate whether attachment style may be a mediator or moderator of the relationships between early regulatory problems and the development of externalizing and internalizing problems. It has been established by meta-analysis studies that both regulatory problems (Hemmi et al., 2011) and disorganised attachment (Fearon et al., 2010) are risk factors for the development of externalizing problems in childhood and beyond.

Moreover, both regulatory problems (Hemmi et al., 2011) and insecure attachment (Madigan et al., 2013) increase the likelihood of internalizing problems. The cascade model of development proposes that the emergence of a problematic behaviour is more likely to be explained by sequential changes in age-appropriate domain-related factors, rather than evolving from a single precursor (Masten & Cicchetti, 2010). Therefore, the separate relationships between disorganised attachment and externalizing problems, and insecure attachment and internalizing problems may imply two possible behavioural dysregulation trajectories beginning with multiple regulatory problems. Overall, this finding adds to the growing evidence that regulatory problems may start a cascade of effects including the infant's social relationship to the mother, setting toddlers on a trajectory leading to further behavioural under-regulation in childhood (Schmid & Wolke, 2014; Winsper & Wolke, 2014). Future research needs to determine whether attachment style is an important factor in the cascade from infant regulatory problems to mental health problems.

Longitudinal research starting in infancy provides invaluable information regarding the processes of normal and abnormal development due to the temporal ordering of variables in the development of abnormal behaviour, and the identification of risk and protective factors of disorders (Cicchetti & Cohen, 2016; Masten & Cicchetti, 2010). Consequently, using a developmentally oriented research framework has important implications for the development of effective interventions (Cicchetti & Toth, 1992). In clinical child samples, maternal characteristics and maladaptive parenting behaviours often make a contribution (Crandall, Deater-Deckard, & Riley, 2015; Goodman & Gotlib, 1999; Reck, Nonnenmacher, & Zietlow, 2016), however, this does not allow the conclusion that parenting style was responsible for the child's

problems in the first place as has been shown here. The findings indicate that multiple regulatory problems are a moderately enduring individual characteristic. This information is helpful to relieve parents' feelings of guilt and responsibility for their infants' problem. Nonetheless, it does not imply that changing parents' behaviour to manage regulatory problems might not be helpful (Bradley & Corwyn, 2008; Pluess & Belsky, 2010). Indeed, an intervention study targeting mothers of irritable 6-month old infants (van den Boom, 1994) revealed that an increase in maternal sensitivity resulted in an increase in infants' ability to self-soothe and increased the likelihood of secure attachment 3 months later. Increasing maternal sensitive behaviours via interventions has been specifically important for infants with problematic behaviours since those with greater problems appear to be more susceptible to the influence of environment (Belsky, 2005). Whether those with multiple regulatory problems are differentially susceptible to environmental factors such as parenting requires future investigation (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2011).

Bringing these findings together, it is clear that infants with multiple regulatory problems have problems adapting to the postnatal environment since their problems are moderately persistent and little influenced by sensitive parenting. Multiple regulatory problems are an indicator of under-regulation even shown in infants' attachment behaviour, and can occur even within sensitive parenting. Irrespective of the multiple regulatory problems, mothers are able to continue being generally sensitive towards their infants in situations that are outside of dealing with their infants crying, sleeping or feeding. However, regulatory problems may in the long term alter parents' perceptions of their infant, such as perceiving their infant as

difficult and alter situations they expose their infant to, such as to other adults or children (Lehtonen, 2001).

Strengths and Limitations of the Research

My work has a number of strengths. First, this thesis includes the first meta-analysis comparing maternal sensitivity in parenting preterm and full-term children. Findings of this meta-analysis provide important guidance for clinical practitioners and mothers of preterm infants. Moreover, this thesis has benefitted from the design of the GAIN study, which assessed regulatory behaviours and parenting behaviours across infancy at several time points, allowing us to apply a cross-lagged panel model to the analysis. Hence, it allows for the interpretation of the time ordered direction of associations between maternal sensitivity and regulatory problems. Cross-lagged panel analysis decreases parameter bias and allows time for factors to have their effects (Cole & Maxwell, 2003). Furthermore, the GAIN study incorporated several covariates as well as detailed information about the neurological risks within the VP/VLBW sample, combining medical records, ultrasound scans and parent reports.

Another strength of the current thesis is the measurement of maternal sensitivity during play interactions at 3 months and 18 months. This provides a better measure of mothers' capacity to be sensitive in comparison to measuring it during feeding, or nocturnal sleep, the situations used to define infant's regulatory problems (Joosen et al., 2013). Accordingly, it would have been challenging to differentiate whether mothers' behaviour reflected their capacity for sensitivity compared to the regulatory problems of the infant. Hence, it is crucial to measure mothers' behaviour during a neutral task, which does not relate to infants' regulatory problems (the behaviour of interest) to gain a measure of the mothers' capacity for sensitive parenting.

There are also limitations. Firstly, the data of the GAIN study have been collected during the period 1998-2001. NICU practices have changed in several ways over the last one and a half decade. Survival of extremely preterm infants has increased (Zeitlin et al., 2013) but there is so far little evidence that neurodevelopmental outcome has improved (Moore et al., 2013). Furthermore, there are large variations in terms of practices between neonatal units. For this purpose the GAIN study recruited from 3 different NICU's including one Regional Centre and two county level hospitals to account for treatment variations. The regional centre (Addenbrooke's Hospital) had an outreach nurse service to help mothers with breast feeding not available in the other two NICUs. However, the breastfeeding rates of the mothers in the Gain study did not differ and were similar in all NICUs. Thus maternal and infant experiences may be different during NICU stay than nearly two decades ago (Berrington & Ward Platt, 2016). To determine whether this has influenced the effect of neurodevelopmental risk and parenting on regulatory problems does require replication in the future.

Secondly, the sample of the GAIN study might not be representative of the UK population. However, requirement of a representative sample is dependent on the research aim. To illustrate, Rothman, Gallacher and Hatch (2013) suggested that using a representative sample is not a requirement for longitudinal studies, which aim to investigate the association between predictors and outcomes. Indeed, simulations have shown that predictions are little influenced by samples not being representative (Wolke et al., 2009). Representativeness is required in prevalence studies to increase the accuracy of the estimates but this was not the aim of the GAIN study.

Thirdly, consistent with the majority of research in this area, variables used to assess regulatory problems were treated as categorical variables, which allowed for

identification of multiple regulatory problems. This was applied since there was no continuous measure of regulatory problems at the time when the study was conducted. Dichotomization of continuous measures may lead to loss of information about individual differences in the level of regulatory problems and statistical power. Although categorizing the data might reduce the variability and it might result in a loss of information (Altman & Royston, 2006), it is a common practice to identify infants with regulatory problems (Becker et al., 2004; Popp et al., 2016). An advantage is that it makes the results easier to interpret and communicate to clinicians/practitioners (Altman & Royston, 2006). Furthermore, the categorization of variables in the current thesis was guided by a priori definition informed by previous literature. The rationale for categorization and the specific chosen boundaries are reported (Turner, Dobson, & Pocock, 2010).

Fourthly, there are limitations to the cross-lagged panel analysis reported in Study 3. To illustrate, the cross-lagged model assumes that the assessments are ordered in time, nonetheless it does not account for the length of interval between assessments (Cole & Maxwell, 2003). Furthermore, including more than 3 assessment points is more likely to produce explanations for reciprocal interactions between variables (Collins & Graham, 2002) than using just two or three. Thus, the analysis in this study could have been improved with incorporating an assessment at 6 months, which was not possible due to the unavailability of maternal sensitivity assessment at that time point. The reason was to balance the number of observational assessments in the university lab and avoid selective dropout, which is a general problem of observational longitudinal studies (Farrington, 1991; Mann, 2003). In addition, there were limited resources and it was deemed too high a burden on the parents who lived often many miles away to return to the lab at 6 months.

Fifthly, as mentioned in discussions of previous chapters, the assessment of maternal sensitivity at term generated three concerns. First, the assessment setting was different for VP/VLBW infants and FT infants, being the hospital and the infants' home respectively. Second, the assessment of maternal sensitivity was conducted by several nursing staff, which may have endangered inter-rater reliability. Third, the nursing staff knew mothers of preterm infants for a longer time than mothers of full-term infants. However, there were two advantages. The first advantage was that the assessments by nurses or midwives were conducted by those with a lot of experience with mothers and infants. The second advantage was that the assessment was conducted over a prolonged period of time using a previously validated instrument, the BCHAPS. This resulted in a more accurate assessment of maternal sensitivity in mothers of preterm infants, which was still not different from the mothers of full-term infants. Moreover, maternal sensitivity was assessed with different measures at each time point. However, using different measures was necessary to make the assessment applicable to the infant's age.

Sixthly, although a good range of covariates were controlled throughout the analysis, there is always the possibility that the findings are attributable to remaining confounding variables not included in the analysis. To illustrate, maternal eating disorders have been shown to be linked to infants' feeding problems (Cooper, Whelan, Woolgar, Morrell, & Murray, 2004; Reba-Harreleson et al., 2010). Furthermore, mothers' prenatal exposure to substances such as nicotine has been linked to an increase in child sleeping problems (Stone et al., 2010). Moreover, maternal life stress, anxiety or depression during pregnancy have been shown to be associated to adverse behavioural outcomes such as crying/fussing (Wurmser et al., 2006) and sleeping problems during infancy (O'Connor et al., 2007). The current

study started at birth and the prenatal factors could not be assessed prospectively. A study starting prenatally would be ideal to account for the impact of prenatal factors. However, such a study would have to include a very large sample to have a group with neurodevelopmental vulnerability (e.g. prematurity), which would not allow for a detailed assessment of maternal sensitivity (Winsper & Wolke, 2014). Thus, both types of studies are required. In the current thesis, the focus was to conduct detailed observations of maternal sensitivity.

Seventhly, although our findings revealed that the likelihood of single regulatory problems were also high within infants with neurodevelopmental vulnerability at term and 18 months, further analyses within the current thesis was on multiple regulatory problems owing to the strong associations to later behavioural problems (Hyde et al., 2012). Specifically, feeding problems were related to neurodevelopmental vulnerability at both term and 18 months. Therefore, future research may examine how maternal sensitivity and neurodevelopmental vulnerability interact to explain the development of feeding problems.

Eighthly, using a combined insecure attachment category might have resulted in the loss of the differences between insecure-avoidant and insecure-resistant categories. Specifically, infants with insecure-avoidant attachment might signal night wakings less frequently to inhibit contact with their caregivers, whereas infants with insecure-resistant attachment might signal more night wakings and it might take them longer to fall asleep (McNamara, 2003). Accordingly, multiple regulatory problems during infancy might be more apparent in infants with insecure-resistant attachment compared to those with insecure-avoidant attachment.

Finally, no assessment of candidate genes or genes across the genome (susceptibility genes) was possible (Ellis et al., 2011). Although still preliminary, there is evidence

that infants who carry the DRD4 exon 3 VNTR 7r allele (Becker et al., 2010; Poustka et al., 2015) are at increased risk of developing regulatory problems. Future research with very large samples (Visscher, Brown, McCarthy, & Yang, 2012) is necessary to determine whether genes are related to multiple regulatory problems or whether a range of susceptibility genes associated with a multiple regulatory phenotype may interact with parenting. This research is missing so far.

Future Directions and Implications

The current thesis contributes to the knowledge base of multiple regulatory problems with important implications for practitioners and researchers. Our findings highlight that there is continuity in multiple regulatory problems even from term to 3 months and the presence of multiple regulatory problems beyond 3 months of age is more likely to be explained by factors within infants rather than problems of maternal sensitive parenting. In other words, multiple regulatory problems are able to develop despite sensitive parenting.

Maternal sensitivity was moderately stable from term to 18 months. This finding suggests that maternal sensitivity might be a moderately stable personality trait such as agreeableness and contentiousness (Smith et al., 2007). However, there is still a large amount of variation in maternal sensitivity that is not stable. Indeed, intervention studies have shown that maternal sensitivity can be modified in parent-child interaction with irritable infants (van den Boom, 1994). Nevertheless, future interventions, which aim to increase maternal sensitivity, may include an assessment to measure the personality traits of the mother.

Practitioners should be aware of the importance of multiple regulatory problems during infancy and provide psychoeducation to parents. Nonetheless, in a

randomised control trial to prevent multiple regulatory problems, Hiscock et al. (2014) showed no influence of educational intervention on decreasing the regulatory problems. Nevertheless, parents reported that they trusted their parenting abilities more after the treatment and maternal depression rates were also decreased. Therefore, although it might be hard to change infants' behaviour, parents could benefit from receiving psychoeducation as early as possible.

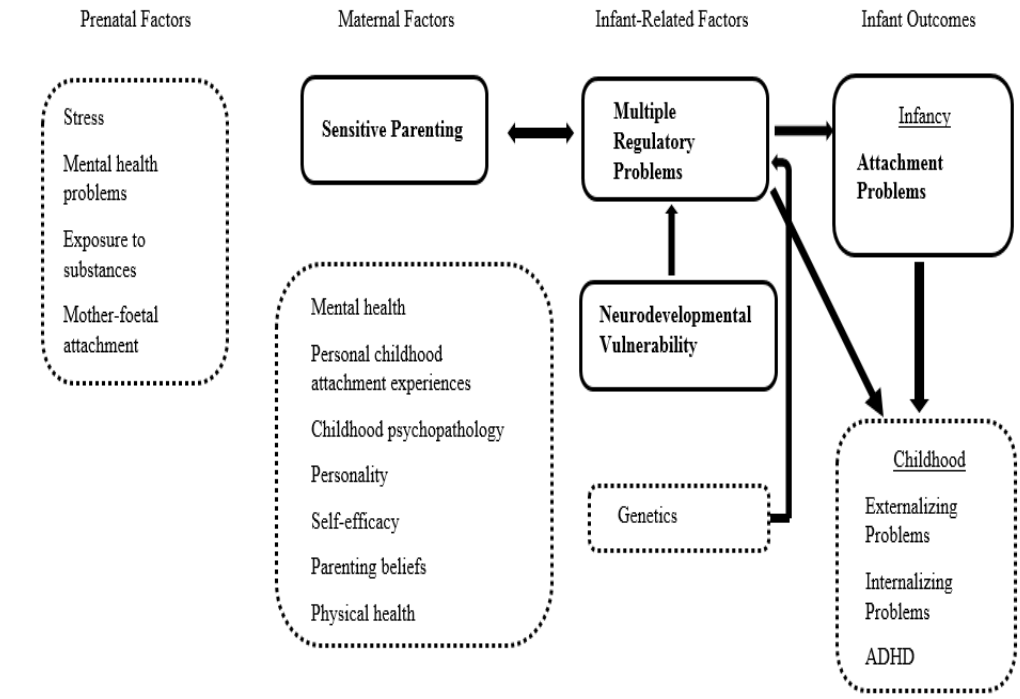
The factors that could play a role in the development of multiple regulatory problems are depicted in Figure 12 (Page 191). Apart from the factors addressed in the current thesis, other factors need to be explored in future studies regarding mothers' contribution to the development of infant multiple regulatory problems. First, knowing that mothers' negative experiences such as anxiety or depression prior to and during pregnancy increase regulatory problems during infancy (Petzoldt, Wittchen, Einsle, & Martini, 2016), there is a need to assess if multiple regulatory problems relate to mothers' mental health difficulties during pregnancy beyond neurodevelopmental vulnerability and their potential interaction. Consequently, a detailed psychological assessment during pregnancy can be used to identify mothers at risk as early as possible. Furthermore, little is known about how maternal-foetal attachment is linked to the development of regulatory problems (Branjerdporn, Meredith, Strong, & Garcia, 2016). Knowing that maternal depressive rumination and perseverative thinking during pregnancy are related to impairments in maternal-foetal attachment (Schmidt, Seehagen, Vocks, Schneider, & Teismann, 2016), which in return might impair maternal sensitivity (Maas, de Cock, Vreeswijk, Vingerhoets, & van Bakel, 2016) and infant-mother attachment relationship (Alhusen, Hayat, & Gross, 2013), future longitudinal studies should explore the association between maternal-foetal attachment and infant regulatory problems.

In addition to these maternal factors, studies investigating the development of regulatory problems from a family systems perspective have so far excluded the role of fathers on infant regulatory problems (Tikotzky, Sadeh, & Glickman-Gavrieli, 2011). Parents influence each other through their own personal resources as well as the quality of their relationship (Cabrera, Fagan, Wight, & Schadler, 2011). Therefore, fathers could have both direct and indirect impacts on infant regulatory problems via influencing maternal sensitivity (Lamb, 1980; Lucassen et al., 2011). Future studies assessing fathers' direct and indirect role via its influence on maternal sensitivity might give an insight into how the inter-relations within the family explain the development of regulatory problems. Moreover, further investigation of the development of regulatory problems in single-parent families would be helpful to understand the importance of inter-relations within family (Rosenkrantz Aronson & Huston, 2004).

Above all, the most crucial question that has arisen from the current thesis is to address the two possible mediation links, first between early multiple regulatory problems and disorganised attachment on consequent ADHD or externalizing problems, second between early multiple regulatory problems and insecure attachment on internalizing problems. For example, if multiple regulatory problems are mediated by disorganised attachment, then early multiple regulatory problems can be considered as the starting point of a dysregulation trajectory as suggested before in large-scale studies (Schmid & Wolke, 2014; Winsper & Wolke, 2014). Examination of the mediation links is crucial to advance the understanding of the sequential process associated with behavioural dysregulation problems, resulting in the identification of the most suitable developmental period for most effectively targeting risk factors. Knowing that multiple regulatory problems persist across

childhood (Winsper & Wolke, 2014), it is crucial to not underestimate the signs during early infancy.

Notwithstanding the importance of multiple regulatory problems, they have only been recently considered as a factor in developmental and clinical psychology literature. The evidence of the ill effect on infant-mother attachment and long-term mental health problems warrants further investigation on understanding the mechanisms as well as more effort in treating these problems in the first two years of life.



Please note that many factors in this graph were adapted from Papousek and von Hofacker's (1995) model of the development of parent-infant communication based on crying and revised according to evidence from literature. Factors to be addressed in future studies were represented in dashed boxes. The factors addressed in the current thesis are presented in bold boxes.

Figure 12 The links assessed in the current thesis regarding the development of multiple regulatory problems (MRPs) and factors to be assessed in the future studies

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Appendices

Appendix A- Infant Crying, Sleeping, Feeding Interview

GAIN-STUDY

FEEDING

Now I would like to ask you some questions about your baby's feeding.

1) First, I would like to ask you whether your baby was ever fed with...

feeding type **yes? (a)**	**start (b)**	**stop(c) (if continued 999999)**
7) tube - expressed breast milk ☐	wks _____	wks: _____
8) tube - formula ☐	wks: _____	wks**:** _____
9) breast ☐	wks:_____ _____	wks:_____ ____
10) bottle -expressed breastmilk ☐	wks:_____ _____	wks:_____ ____
11) bottle - formula ☐	wks:_____ _____	wks:_____ ____
12) solids ☐	wks:_____	wks:_____

2. On <u>what</u> milk is your baby fed at present?

_____

1	2	3	4	5
solely breast milk	mainly breast	both 50/50	mainly formula	formula milk

3. You said you were breastfeeding, did you ever exclusively breastfeed?

☐ yes, still do (go to Q18)

☐ yes, stopped (go on),

☐ no *(*go to Q15*)*

4a-h. If you stopped exclusively breast feeding, what were the reason(s) for this?

☐ didn't have enough milk for baby
☐ feeding difficulties
☐ on the advice of doctor/nurse/health visitor
☐ baby unsettled on breastmilk
☐ baby seems to gain weight poorly on breast milk
☐ inconvenience/hassle
☐ going back to work
☐ other reason, please specify: .....

FORMULA ☐ not applicable

5. If partly/fully bottle feeding, which formula are you currently using?

☐ Cow & Gate: Premium
☐ Cow & Gate: Plus
☐ Cow & Gate: Infasoy
☐ Milupa: Aptamil
☐ Milupa: Milumil
☐ Farley: 1st milk
☐ Farley: 2nd milk
☐ Farley: Soya
☐ SMA: Gold Cap
☐ SMA: White Cap
☐ SMA: Wysoy
☐ still using preterm formula - specify_____
☐ Other:

_____

6. Did your baby get a preterm formula, if yes, which one did you use?

☐ not applicable - (*go to question 18)*
☐ Cow & Gate: Nutriprem
☐ Cow & Gate: Nutriprem 2
☐ Farley: Premcare
☐ Farley: Osterprem 2

☐ Milupa: Prematil

☐ SMA: Low Birthweight Formula

☐ Other - specify

_____

7. At what age/weight did you change to a standard formula?

☐ not applicable (still special formula)

age: ☐☐ weeks ☐☐ days

weight: ☐☐.☐ kg

SOLIDS ☐ not applicable, never tried

8. How many times each day do you give your baby solids of these food types?

Baby cereal ☐ times

Pureed fruit/veg ☐ times

Tin/jar/packet ☐ times

Other - specify _____ ☐ times

9. Have you experienced any of the following difficulties in introducing solids?

☐ Gagging/choking

☐ Falling asleep before feed is finished

☐ Excessive dribbling

☐ Regurgitation/possiting

☐ Sickness/vomiting

☐ Poor appetite

☐ Wriggling

☐ Frequent food refusal/Faddy eating

☐ Very irritable during feeding

☐ Other - please specify

_____

☐ not applicable

GENERAL FEEDING

10. When you first start to feed your baby, how does he/she react to the breast/bottle?

1	2	3	4	5
always eager	usually eager	eager half / reluctant half	usually reluctant	always reluctant

10b. (If 3, 4 or 5) If **he/she is reluctant what do you do then?** .....

11. How long does your baby usually go from the beginning of one feed to the beginning of the next feed?

☐☐ hrs ☐☐ mins

12. a) How long did the last feed take? ☐☐ mins

Was this a breastfeed? ☐
bottlefeed? ☐
tubefeed? ☐
solid ? _____ ☐
b) if bottle/tube: quantity taken in ☐☐☐☐ ounces

13. a) How many milk feeds does your baby usually have in 24 hours?
Day: (6am - 10pm) ☐☐
Night: (10pm - 6am) ☐☐
Total: ☐☐

if on solids
b) How many solid feeds does your baby usually have in 24 hours?

Total:☐☐ n/a ☐

14. Does your baby do any of the following during most feeds? *(tick as many as apply):*

☐ fight against the breast or bottle ☐ cry/fuss
☐ have difficulty latching on

☐ stop after a few sucks
☐ dribble a lot of milk
☐ suck weakly
☐ wriggle about
☐ gag/choke
☐ vomiting/posseting
☐ fall asleep before the feed is finished
☐ colicky pains/wind
☐ other _____

☐ not applicable

15. Is your baby fed:

1	2	3	4	5
totally on demand	mainly on demand	half and half	mainly by schedule	totally by schedule

16. Do you ever worry that your baby is not growing fast enough?

1	2	3	4	5
never	rarely	half the time	often	always

17. Do you think your baby has a feeding problem?

☐ no

☐ yes, mild problem

☐ yes, serious problem

18. Have you sought advice regarding your baby's weight gain/feeding?

☐ no

☐ yes

If yes, was it from:

☐ a relative
☐ friend
☐ community paediatric nurse
☐ dietician
☐ doctor (GP or hospital)
☐ health visitor

☐ SCBU staff

☐ other specify _____

_____

19. Does your baby have problems with diarrhoea?

☐ no ☐ yes, ☐☐ times a month ***or*** ☐ times a week

20. Does your baby have problems with constipation?

☐ no ☐ yes, ☐☐ times a month ***or*** ☐ times a week

21. So, in general, how would you describe your baby's feeding since you have been home from SCBU?

_____

1	2	3	4	5
very poor	poor	average	good	very good

22. Do you talk to your baby while feeding him/her?

_____

1	2	3	4	5
never	rarely	sometimes	often	always

SLEEPING

Now I would like to ask you some questions about your baby's sleeping.

23. When do you usually put your baby down to sleep for the night?

☐☐☐☐ hrs

24. How does your baby usually fall asleep? (tick all)

☐ being cuddled/held

☐ being fed

☐ in crib/cot

☐ in parental bed

☐ other _____

25. Where does your baby <u>usually</u> sleep most of the night?

☐ in own cot/room

☐ in own cot/shared parent(s) room

☐ in own cot/shared room with siblings or others

☐ sleeps in parent(s) bed

☐ sleeps in bed with others

☐ other - specify _____

26. How often does your baby sleep in your bed at night?

☐ never

☐ once a month or less

☐ 1-4 times a month

☐ 2-3 times per week

☐ 4 times a week or more

27. How long does it usually take you to settle your baby for his or her night time sleep once you have started the process?

☐☐ mins

28. Do you usually stay with your baby until he/she is asleep?

☐ yes

☐ no

29. On average, how many hours does your baby sleep in 24 hrs?

hours per day (6am -10pm) ☐☐.☐

hours per night (10pm - 6am) ☐☐.☐

total ☐☐.☐

30. How many times does your baby usually wake him/herself up at night?

☐☐ times

31. How do you usually settle your baby back to sleep?

☐ feed

☐ other

32. How long is the longest period of sleep which your baby has had without waking (last two weeks)?

☐☐.☐ hours

33. Do you <u>now</u> ever wake your baby for feeds: ☐ no ☐ yes

a) during the day (6am-10pm)? ☐☐ times

b) during the night? (10pm-6am) ☐☐ times

If yes to either a) or b) above, is this because of:

☐ medical advice

☐ concern that baby not feeding enough

☐ concern that baby not gaining enough weight

☐ other - specify _____

34. If your baby wakes at night, is this distressing for you?

_____

1	2	3
not at all	a little distressing	very distressing

35. Do you think your baby has a sleeping problem?

☐ no

☐ yes, mild problem

☐ yes, serious problem

36. Have you sought advice regarding your baby's sleeping?

☐ no

☐ yes

If yes, was it from:

- ☐ relative
- ☐ friend
- ☐ community paediatric nurse
- ☐ doctor (GP or hospital)
- ☐ health visitor
- ☐ SCBU staff
- ☐ other specify _____

CRYING

Now I would like to ask you a few questions about your baby's fussing and crying.

37. Overall how irritable is your baby?

_____

-3 -2 -1 0 +1 +2 +3

very irritable very calm

38. For how long does your baby fuss or cry during an average day (e.g. yesterday)?

a) ...during the morning (6am - noon) .....hrs .....mins

b) ...during the afternoon (noon - 6pm) .....hrs .....mins

c) ...during the evenings (6pm-midnight) .....hrs .....mins

d) ...during the night (midnight - 6am) .....hrs .....mins

39. How many separate bouts of fussing and crying are there typically in an average day (e.g. remember yesterday)? (If there is no crying at all, please record "0"). *(A "bout" is defined as a period of time in which you could not put your baby down without him/her starting to cry or fuss again).*

number of bouts

a) ...during the morning (6am - noon) ☐

b) ...during the afternoon (noon - 6pm) ☐

c) ...during the evenings (6pm-midnight) ☐

d) ...during the night (midnight - 6am) ☐

40. How much does the amount of fussing and crying vary from day to day?

1	2	3	4	5
not at all	a little	somewhat	much	very much

41. Does your baby cry more or less than you had expected?

1	2	3	4	5
much less	less	about the same	more	much more

42. Is your baby's crying and fussing distressing for you?

1	2	3
not at all	a little	very distressing

43. Since the last interview, has the amount of crying.....

1	2	3	4	5
decreased a lot	decreased	about the same	increased	increased a lot

44. During the last week or so, how long have you usually waited before responding to your baby's crying?

☐ hrs ☐☐ mins

45. Have you ever tried leaving your baby to "cry it out"?

1	2	3	4
no	yes, once	yes, a few times	yes, often

46. How easy or difficult is it for you to calm or soothe your baby when s/he is upset?

1	2	3	4	5
very easy		about average		very difficult

47. Do you think your baby has a crying problem?

☐ no

☐ yes, mild problem

☐ yes, serious problem

48. Have you sought advice regarding your baby's crying?

☐ no

☐ yes

If yes, was it from:

☐ a relative
☐ friend
☐ community paediatric nurse
☐ doctor (GP or hospital)
☐ health visitor
☐ SCBU staff
☐ other specify _____

49. How long is your baby typically carried/cuddled during a 24h period? (including during feeding)

☐☐ hrs ☐☐ mins

50. When my baby cries or fusses, it is easy to tell what s/he wants.

(Please indicate on the line by making a cross how much the statement applies to your baby) (For example, a cross to the far left indicates that it applies "not at all", to the far right that it applies "very much/often", in the middle if it applies moderately (or sometimes does, sometimes does not)

|_____|

1 not at all easy 5 very easy

51. When my baby fusses or cries, his/her crying usually sounds...

(Please indicate on the line by making a cross how much the statement applies to your baby.)

not at all/never very much/always

Frantic |_____|

High pitched |_____|

Loud |_____|

Angry |_____|

Pained |_____|

Spoilt |_____|

Earpiercing |_____|

Aggressive |_____|

Worried |_____|

Whimper |_____|

Unpleasant |_____|

Desperate |_____|

Sad |_____|

Heartbreaking |_____|

Whiney |_____|

Appendix B- Boston City Hospital Assessment of Parental Sensitivity (BCHAPS)

GAIN

Please indicate how well the mother understands, cares for, interacts with and enjoys her preterm infant by circling the appropriate number.

For office use

	Not observed	Poor		Average		Very Competent	
1. Mother changes behaviour in response to baby's cues	0	1	2	3	4	5	BCHM1 ☐
2. Mother changes behaviour in response to nurse's instructions	0	1	2	3	4	5	BCHM2 ☐
3. Mother talks to baby	0	1	2	3	4	5	BCHM3 ☐
4. Mother touches/holds baby	0	1	2	3	4	5	BCHM4 ☐
5. Mother appropriately tries to bring baby to an alert state	0	1	2	3	4	5	BCHM5 ☐
6. Mother effectively soothes baby	0	1	2	3	4	5	BCHM6 ☐
7. Mother is attentive to baby	0	1	2	3	4	5	BCHM7 ☐
8. Mother takes delight in baby	0	1	2	3	4	5	BCHM8 ☐
9. Mother appears comfortable with							
a) touching	0	1	2	3	4	5	BCHM9a ☐
b) holding	0	1	2	3	4	5	BCHM9b ☐
c) feeding	0	1	2	3	4	5	BCHM9c ☐
d) bathing	0	1	2	3	4	5	BCHM9d ☐
10. Mother enquires about progress of baby	0	1	2	3	4	5	BCHM10 ☐

Appendix C- Coding Scheme of Maternal Behaviours in Mother-Infant Structured Play Assessment (MISPA)

	Definition	Coding Range
Sensitivity	Consider: • Does mother use baby's feedback, taking up baby's initiatives • Mother's enjoyment of interaction vs. boredom or helplessness, does mother seem at ease with child? • Gives opportunity for turn-taking • Appropriateness of pacing • Correctness of mother's interpretations (running comments) • Appropriateness of language (slow enough, repetitive, breaks for the child to take its turn, adapted to the child's capacity) • Intrusiveness • Emotion expression Links to other maternal scales • If Intrusiveness >2 then Sensitivity not >3. • If geared at own vs. baby's wishes, moods then score not >3 • If Negative Emotion Expression >2, Sensitivity not >3 • **General coding rules**	**1 Highly insensitive:** • Mother either ignores or overrides or does not understand infant or she withdraws from interaction • Geared almost exclusively to her own wishes • Initiations are prompted mainly by signal within herself • She does not seem to see or understand the baby's communication, the meaning of baby behaviour is distorted or ignored. • Only if baby's signals are prolonged and intense, mother may respond to them. • Mother may show marked affective negativity (harshness, disinterest or depression). • Mother appears inflexible to adjust to infant's needs. • Interaction is painful to observe. **2 Insensitive:** • Mother does not respond to baby's signals appropriately (half-hearted, impatiently etc.) and/or not promptly (marked delay in responding) or finishes transaction before baby is satisfied. • Again she does not seem to see or understand what her baby communicates. • Mother is not consistently insensitive and is not ill-meaning.

	• As a <u>general rule</u>: No 5 cannot be given if: Appropriateness <4, Positive emotion expression <4, Negative emotion expression >1, Intrusiveness >1 or Undercontrol >2. • **If in doubt mark down.**	• When baby is demanding attention intensively, the mother will modify her behaviour • She acknowledges some of infant behaviour, but her response is mostly inappropriate • Mother's affect may be negative/flat, depressed, passive or irritable **<u>3 Inconsistently sensitive or neither sensitive nor particularly insensitive (bland)</u>:** • Mother may seem somewhat helpless or bored without really being overly insensitive **or** • Mother is quite sensitive on occasion, but there are periods when she is not. She may misinterpret some but not all communications. • Sometimes she responds promptly and appropriately but sometimes delayed and insensitive • She sometimes overrides or ignores infant activity. • Mother may change mood or style in the middle of the interaction, from joyful and creative to flat or helpless. • Mother may want her Infant to perform well. • Interactions may seem all right as long as baby is cheerful and happy but insensitive and difficult when baby is moody. **<u>4 Sensitive</u>:** • This mother is generally sensitive but may not be overly creative or is shortly absent minded or misses out the meaning or a few minimal infant signals but never clear signals. • She does not override nor ignore her infant. • The mother clearly enjoys her baby **<u>5 Highly sensitive</u>:** • No real criticism possible

		• Positive, appropriate interaction • Genuine, authentic and congruent interest in infant • Facial expressions and tone of voice are pleasant • Mother reads all infant's signals accurately and reacts appropriately and promptly • Mother is flexible to adapt to infant's needs • She imitates and expands on her baby's actions frequently. A special, smooth interaction, in which mother gives her baby the chance to contribute to the interaction
Positive Facial Emotion Expression	Vocal and facial expression: praise, smile, laugh, play-face - not touching! Consider congruency of voice, face and body language, quality and quantity. **<u>General coding rules:</u>** Note inappropriateness if: frozen smile, overpraising, exaggerated and performance-like, not genuine or in general wrong timing (e.g. smile when baby cries). **If in doubt between 4 and 5 code 5. Otherwise if in doubt mark down.**	1 None 2 Seldom (up to 25%) 3 Moderate (around half the time) 4 Mostly smiling, joyful, play-face (may be frozen: inappropriate) 5 Very much, joyful and smiling all the time, very expressive
Negative Facial Emotion Expression	Sharpness, disappointed face, anger, irritation, helplessness, stern face, rejections, criticism, boredom, strained look. Consider verbal and facial expression. Also code negative comments like "you don't want to look at Mummy", "he just does not care" if with disappointed or sharp or only mock laughter undertone. **If in doubt mark up.**	1 None 2 Mild and short 3 More conspicuous helplessness, boredom, strained; but no anger, being disappointed, sternness, rejection 4 Very clear helplessness or boredom; slight anger, being disappointed, sternness, or rejection 5 Very clear negative emotion expression

Verbal Involvement	Percentage of the episode that mother talks to infant. A second yes/no scale refers to inappropriateness (flat or sharp tone, continuous talk without a break). Coding rule: Mothers who talk continuously without leaving a chance for the infant to respond should receive a 5 but it should be rated as "inappropriate" and get a higher rating on Intrusiveness. **If in doubt mark down.**	1 None, mother never or very seldom talks to infant (< 5 % of time). 2 Very little, mother seldom talks to infant (5-25% of time). 3 Moderate, mother talks to infant 25-50% of time. 4 Much, mother frequently talks to infant, but at least 2 silent periods of 5 sec. and not more than a total 75% of time. 5 Very much, mother talks to infant throughout most of the session. Inappropriate: yes/no 1 appropriate, 2 inappropriate: continuous talking without chance for turn-taking, no gaps, 3 inappropriate: flat or sharp
Under-control (Stimulation Level)	Passivity, watching unengagedly, not structuring, not providing stimuli. **General coding rules:** Do not consider purposeful sensitive step back when child needs break. If in doubt mark up.	1. No undercontrol 2. Brief undercontrol or very slightly so: Not as engaged in activity as 1, but usually tries to get infant's attention (effectively). 3. Brief but clear or mild but longer undercontrol: A marked hesitation, withdrawal, in the rest of the episode mother is engaged. 4. Marked undercontrol: Mother initiates or structures sometimes, but otherwise shows withdrawal, hesitation, watching neutral for more than a few seconds. 5. marked and persistent undercontrol: Mother constantly withdraws from interaction, she does not organise baby's attention in providing stimuli, mother seems hesitant or at loss. She passively watches her baby, talks little and shows a neutral face (>50%).

Physical Involvement	Refers to the amount of time/frequency of **direct** physical contact (includes all sorts of touching: gestures of affection, attention getting, stimulation, touching in games, but also intrusive physical involvement, but **not** touching infant with **toy**). Inappropriate yes/no (refers to perceived intrusiveness). **General coding rules:** **If in doubt mark up.**	1. Mother never touches infant. 2. Mother seldom touches infant (<10%), and contacts are of brief duration. 3. There are contacts of moderate duration or several brief contacts (<25% of time). 4. Frequent or longer contact (< 50% of time). 5. Very frequent, most of the session spent in physical contact (>50% of time).
Intrusiveness	Mother moves baby's body or head to face her **or** Mother speaks in a loud and abrupt voice **or** Mother makes movements or noises too close to baby's face **or** Mother's actions are too quick/change to often so that baby has difficulty to follow **or** She interrupts or ignores infant activity **or** She continuously touches baby (not if only rest hand on tummy or leg, but constant fondling of the baby is inappropriate) **General coding rules:** **Try not to consider infant reaction. If in doubt mark up.**	1 Not intrusive at all: Always gently approaches infant, Lets infant lead but gives guidance where necessary. 2 Mostly unintrusive: May show a few minimal intrusive actions. 3 A little intrusive: One or two short but markedly intrusive actions **or** Borderline intrusiveness or overstimulation throughout the episode. 4 Intrusive: Clear intrusiveness or overstimulation or interference with child activity, but not continuous. 5. Very intrusive: The mother constantly interferes with baby's activity, Often and markedly is either too close to baby's face or is too loud or moves baby's body around. It seems she leaves no space for the infant to respond. Observer feels the need to hold the mother back and tell her to be less active.

Appendix D- Coding Scheme of Maternal Behaviours in POSER

1. Amount/frequency of verbal involvement

This scale is primarily concerned with how much the mother talks to the infant throughout the play session. What proportion of the play session is the mother (M) talking to the infant (I)? This could be initiated conversation or in response to the infant.

1. **None:** M never talks to I.
2. **Between 1 and 3**
3. **Very little**: M seldom talks to I.
4. **Between 3 and 5**.
5. **Moderate**: M occasionally talks to I, primarily in response to I, makes some spontaneous comments.
6. **Between 5 and 7**
7. **Much**: M frequently talks to I, but there may be lapses when she is silent.
8. **Between 7 and 9**.
9. **Very much**: M talks to I throughout most of the session.

2. Verbal Control Behaviour

This scale is primarily concerned with the extent to which M interacts in a directive controlling manner. Controlling verbalisations are those that try to channel the infant's behaviour in a certain specific direction, inhibiting some tendencies and initiating others. Autonomy orientated verbalisations are those that provide the child with information or feedback about his behaviour.

1. **Very high**: M almost always uses directive and/or prohibitive statements. M continually attempts to control I. The directive statements are very forceful and compelling.
2. **Between 1 and 3**
3. **High**: M uses directing and/or prohibiting statements frequently, most of the statements are forceful, M uses attention getting or specific/general information statements less than half the time.
4. **Between 3 and 5**.
5. **Moderate:** M uses directive/prohibitive statements sometimes, she uses attention getting, specific or general information statements about half the time, directing statements are of mixed intensity.
6. **Between 5 and 7**.
7. **Low**: M seldom directs and or prohibits the directing statements are mostly passive and low key, M uses mainly attention getting and feedback encouraging statements.
8. **Between 7 and 9**.

9. **Very low**: M hardly ever uses directing statements, and they are extremely passive. M nearly always uses attention getting, specific and general feedback statements.

3. Control and teaching behaviour

This scale is primarily concerned with the extent to which M is trying to control the outcome of the play session. The controlling mothers *demonstrates the toy, teaches and *tutors frequently. Demonstration and other controlling behaviour are not always mutually exclusive. M can be either demonstrative, controlling or both. On the other end of the continuum is the mother who allows the infants autonomy. She is only occasionally attention directing and mainly assists the infant by material selection or supervises by sitting attentively and enters into the play when invited by the infant.

1. **Very often**: M is continually attempting to control I's play behaviour, she exhibits demonstrating and modelling behaviour to the task, very directive teaching takes place: constant teaching and drilling.
2. **Between 1 and 3**.
3. **Often**: M frequently demonstrates toy, tends to be controlling and tutors but also uses less directive strategies occasionally.
4. **Between 3 and 5**.
5. **Moderate**: M uses toy demonstration and teaching about half the time, demonstration of task id partly used to get the session going and to get the I's attention, less directive behaviour is also used the other half of the time.
6. **Between 5 and 7**
7. **Seldom**: M rarely uses demonstration/tutoring; most of the time she is either trying to get the infant's attention or is supervising.
8. **Between 7 and 9**.
9. **Never**: M is almost never demonstrating the toy or tutoring, she's attentive and supervising and only enters the play if invited or to direct the infant's attention; she may also engage in imaginative, non-task related play.

***Demonstrating: mother completes the task herself**
***Tutoring: mother completes the task with some infant involvement**

4. Physical involvement

This scale refers to how much the mother touches and has physical contact with her infant. Consider frequency and duration. Score in terms of how much of the play session is characterised by physical contact or touching. Do not code negative punishing behaviour, such as hitting, smacking, pulling, shaking, etc.

1. **None**: M never touches, holds or places the infant on her lap or in physical contact.
2. **Between 1 and 3**
3. **Little**: M seldom touches, holds of places the I on her lap or in physical contact. Contacts are brief and most of the session is without physical contact.
4. **Between 3 and 5**.
5. **Moderate**: M occasionally touches her I. There is moderately frequent physical contact, or few contacts of moderate duration.

6. **Between 5 and 7**
7. **Much:** M frequently touched I.
8. **Between 7 and 9**.
9. **Very much**: M constantly touches I or has I on lap or in close bodily contact for most of the session.

5. Sensitivity

The extent to which M is exhibiting sensitive behaviour toward her infant. Insensitive mothers (those below a rating of 5) miss and override their infant's cues seem more geared to their own needs. Mothers who receive a score of 5 are often inconsistent or robotic in their sensitivity, where as a sensitive mother (those with rating above 5) is good at reading and interpreting their infant's communications and at mood setting.

1. **Highly insensitive**: the extremely insensitive mothers seems geared almost exclusively to her own wishes, moods and activity. That is, the mother's interventions and initiations of interaction are prompted or shaped largely by signals within herself. If they mesh with the baby's signals it is no more than a coincidence. This is not to say that the mother never responds to the I's signals; sometimes she does if the signals are intense enough, prolonged or even repeated enough. Furthermore, since there is usually a disparity between mother's own wishes and activity and baby's signals, mothers who are geared to her own signals routinely ignore or distort the meaning of the I behaviour. Thus, when the mother responds to the I's signals, her response is in appropriate in king, or fragmented and incomplete.
2. **Between 1 and 3**.
3. **Insensitive**: this mother frequently fails to respond to the I 's communications appropriately and/or promptly, although she may on some occasions show the capacity for sensitivity in her responses to and interactions with her I. Her insensitivity seems linked to inability to see things from the I's point of view. She may be too frequently preoccupied with other things and therefore inaccessible to his signals and communications, or she may misperceive his signals and interpret them inaccurately because of her own wishes or defences, or she may know well enough what I is communicating but be disinclined to give him what he wants – because it is inconvenient or she is not in the mood for it, or because she is determined not to spoil him. She may delay an otherwise inappropriate response to such an extent that it is no longer contingent upon his signal, and indeed perhaps is no longer appropriate to his state, mood or activity. Or she may respond with seeming appropriateness to the I's communications but break off the transactions before the baby is satisfied, so that their interactions seem fragmented and incomplete or her responses perfunctory, half-hearted or impatient. Despite such clear evidence of insensitivity, however, this mother is not as consistently or pervasively insensitive as mothers with even lower ratings. Therefore, when the I's own wishes, moods, and when the baby is truly in distress or otherwise very forceful and compelling in his communication, this mother can modify her own behaviour and goals at this time and can show sensitivity in her handling of the child.
4. **Between 3 and 5**.

5. **Inconsistently insensitive**: although this mother can be quite sensitive on occasions, there are some periods in which she is insensitive to the I's communications. Mother's inconsistent sensitivity may occur for any one of several reasons, but the outcome is that she seems to have lacunae in regard to her sensitive dealings with the I – being sensitive to some aspects of his experience, but not in others. Her awareness of the I may be intermittent – often fairly keen, but sometimes impervious. Or her perceptions of the I behaviour may be distorted in regard to one or two aspects although it is accurate in other important aspects. She may be prompt and appropriate in response to his communications at some times and in most respects, but either inappropriate or slow at other times and in other responses. On the whole, however, she is more frequently sensitive than insensitive. What is striking is that a mother who can be as sensitive as she is on so many occasions can also be so insensitive on other occasions.
6. **Between 5 and 7**.
7. **Sensitive**: this mother also interprets the I's communications accurately and responds to them promptly and appropriately – but with less sensitivity than mothers with higher ratings. She may be less attuned to the I's more subtle behaviours than the highly sensitive mother. Or, perhaps because she is less skilful in dividing her attention between the I and competing demands, she may sometimes 'miss her cue'. The I's clear and definite signals are, however, neither missed nor misinterpreted. This mother emphasises with the I and sees things from her point of view; her perceptions of his behaviour are not distorted. Perhaps because her perception is less sensitive than of mothers with higher ratings, her responses are not as consistently prompt or as finely appropriate – but although there may be occasional little 'mismatches', the M interventions and interactions are never out of tune with the I's tempo, state and communications.
8. **Between 7 and 9**.
9. **Highly sensitive**: this mother is exquisitely attuned to I's signals, and responds to them promptly and appropriately. She is able to see things from the I's point of view; her perceptions of his signals and communications are not distorted by her own needs and defences. She reads the I's signals and communications skilfully, and knows the meaning of even his subtle, minimal and understated cues. She nearly always gives her I what he indicates, although perhaps not invariably so. When she feels that it is best not to comply with his demands – for example, when he is too excited, over-imperious, or want something he should not have – she is tactful in acknowledging his communication and in offering an acceptable alternative. She has 'well rounded' interactions with I, so that the transaction is smoothly completely and both M and I feel satisfied. Finally, she makes her responses temporally contingent upon I's signals and communications.

6. Appropriateness of play interaction

In general, the criterion is that play is appropriate if it gives pleasure to both infant and mother. Pushing the distinction further, play is appropriate if it gives the infant pleasure, and play is appropriate if it is undertaken wholly and chiefly at the whim of the adult and without regard to the I's mood and state.

Appropriate play is geared both to the state and mood of the baby and to his developmental level. What may delight a baby at one time will be inappropriate at another time. Thus, for example, a baby may sometimes enjoy being pulled repetitively from a supine to a sitting position, but not if he is drowsy, or hungry and expecting to be fed. At one age a baby may enjoy being sailed up in the air and held there in a face-to-face confrontation, but at a younger age he may feel very insecure when this is done to him. An imaginative and spontaneous parent will, on occasion make errors, transgressing on mood, state or developmental level but, if sensitive, will desist as soon as he discovers that the baby does not like it.

Play is inappropriate if it does not give the I pleasure, or if it is so intense or prolonged that the excitement generated passes from the range of pleasure into the range of pain and distress. Play can be dominating, controlling or even tormenting. The adult may have fun forcing a response from the I by playing on his automatic response patterns despite the fact that the I does not enjoy it. The adult may have a desire to show off the I or he may be trying to train him in sensorimotor competence, or teach him to tolerate insecurity beyond his present level of tolerance. These efforts may or may not be appropriate; they are inappropriate if they do not give pleasure to the I.

Ideally, play gives pleasure to both child and adult. Play cannot be really appropriate if the adult himself des not enjoy it and is merely trying to entertain the I by going through the motions without any real delight or spontaneity. Spontaneous and flexible play, which gives delight to both parties, can grow out of an activity, perhaps apart of a routine or by the mother picking up cues from the I's behaviour and improvising a game around it. In an atmosphere of playful relaxation even a young I may improvise play. Familiar play patterns can also be enjoyable to infants, although play becomes increasingly less pleasurable if the adult is playing mechanically without enjoying it.

Note: If there is no play the rating of 'Appropriateness of play interaction' should not be undertaken.

1. **Very inappropriate play:** M's play with I is inappropriate because it is either:
    a) Controlling, teasing or even tormenting
    b) Grossly over-stimulating.
    c) Very badly geared to I's developmental level, being either mechanical, simple, and boring or far beyond I's capacities for response
    d) Obviously for M's own gratification rather than for I's pleasure.
2. **Between 1 and 3**
3. **Inappropriate play:** M's play with I is inappropriate because it is either:
    a) Mechanical and unspontaneous
    b) An attempt to distract or instruct I rather than to give him enjoyment
    c) Has some features of being over-stimulating, controlling, teasing or overextending without warranting a lower rating.
4. **Between 3 and 5**.

5. **Moderately appropriate play:** M sometimes plays with I fairly spontaneously and sometime mechanically. But she either lacks the capacity for delighted interaction that is implied by higher ratings, or she occasionally intersperses inappropriate play that is characteristic of lower ratings, or a combination of both.
6. **Between 5 and 7**
7. **Appropriate play:** When M plays with I she seems to have I's enjoyment as her chief purpose, and a the same time enjoys herself. She has some spontaneity and flexibility. She has considerable ability to adapt her play to I's mood and level of development. She may occasionally over-stimulate, but she usually knows when it is time to stop play or at least to reduce its level of intensity.
8. **Between 7 and 9**.
9. **Very appropriate play:** M plays with I spontaneously and delightedly. Her play is sensitively appropriate to his mood and level of development. She constantly gears her play actions to cues given by I's behaviour and play is so interwoven with her routine care and other interactions that it can scarcely be distinguished from them.

7. Amount/frequency of expressed positive emotion – verbal and non-verbal (praise, hugs, kisses, etc.)

This scale refers to how much the mother expresses positive emotion. Expressed positive emotion verbally expressed statements as well as explicit non-verbal expressions, such as hugs or kisses and any other expression of endearment. Less weight should be given to smiles and laughs by itself. If the mother makes one positive comment she usually receives a score of '2' since this item occurs relatively infrequently.

1. **None**: M never expresses such emotion
2. **Very Little**: M seldom expresses such emotion.
3. **Moderate**: M occasionally/sometimes expresses positive emotion.
4. **Much**: M often expresses positive emotion.
5. **Very much:** M expresses such emotion frequently

8. Amount/frequency of negative emotion, verbal and non-verbal (criticism, threats, hits, pushes, irritability, sharpness)

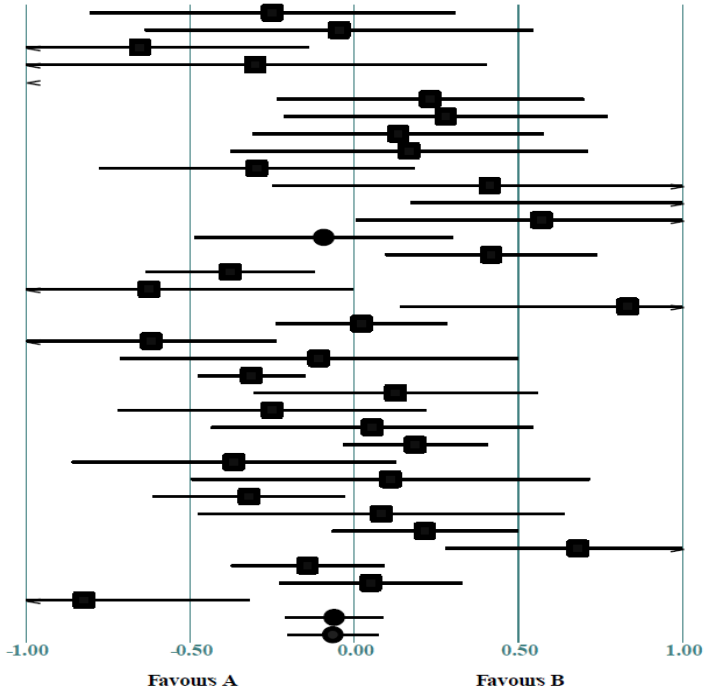
This scale refers to how much the mother expresses negative emotion. Negative emotions include negative verbal statements and non-verbal cues (i.e. tone of mothers' voice and sharpness).

1. **Very much**: M expresses negative emotion frequently
2. **Much**: M often expresses such emotion
3. **Moderate**: M sometimes expresses negative emotion
4. **Very little:** M seldom expresses negative emotion.
5. **None**: M never expresses negative emotion

Appendix E- Moderator Analysis of Maternal Sensitivity in Preterm Children

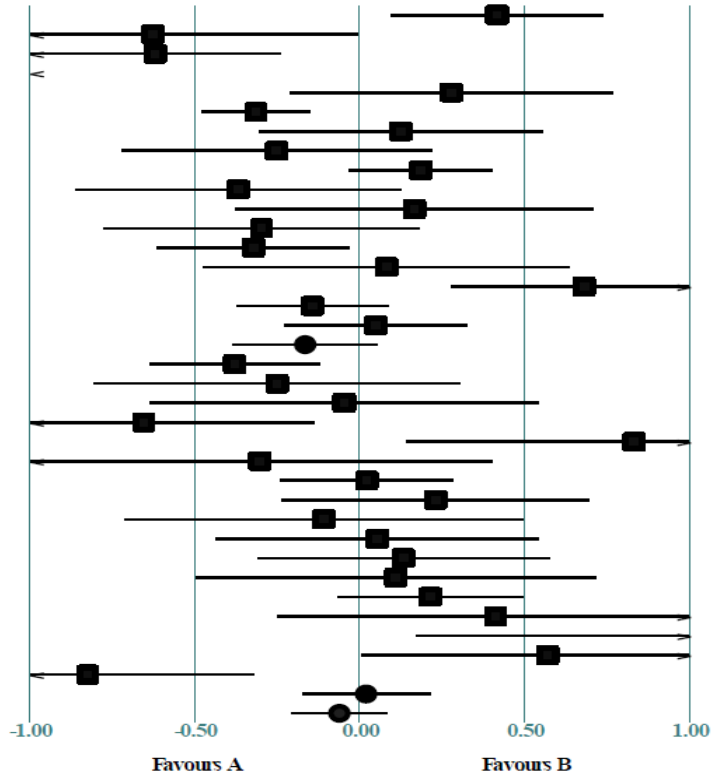
E. 1 Degree of Prematurity as Moderator

Group by degree of prematurity	Study name	Hedges's g	Lower limit	Upper limit
moderate to late	Barratt, 1992	-0.249	-0.808	0.310
moderate to late	Barratt, 1996	-0.046	-0.639	0.548
moderate to late	Bendersky, 1986	-0.653	-1.171	-0.135
moderate to late	Davis, 1988	-0.301	-1.009	0.406
moderate to late	Foecada-Guex, 2006	-2.370	-2.986	-1.753
moderate to late	Greenberg, 1988	0.232	-0.238	0.701
moderate to late	Greene, 1983	0.279	-0.215	0.774
moderate to late	Levy-Shiff, 1989	0.134	-0.311	0.580
moderate to late	Montirosso, 2010	0.167	-0.379	0.714
moderate to late	Muller-Nix, 2004	-0.296	-0.778	0.186
moderate to late	Stevenson, 1990	0.413	-0.250	1.077
moderate to late	Watt, 1985	1.003	0.169	1.836
moderate to late	Wille, 1991	0.571	0.003	1.139
moderate to late		-0.093	-0.489	0.303
very	Agostini, 2014	0.418	0.094	0.742
very	Barnard, 1984	-0.377	-0.637	-0.117
very	Coppola, 2007	-0.625	-1.248	-0.002
very	Crawford, 1982	0.834	0.138	1.529
very	DeWitt, 1997	0.023	-0.241	0.286
very	Feldman, 2007	-0.619	-1.002	-0.235
very	Halpern, 1997	-0.107	-0.715	0.501
very	Jaekel, 2012	-0.313	-0.479	-0.147
very	Jean, 2012	0.126	-0.308	0.561
very	Korja, 2008	-0.250	-0.723	0.222
very	Landry, 1990	0.055	-0.437	0.547
very	Laucht, 2001	0.186	-0.035	0.408
very	Miljkovitch, 2013	-0.366	-0.862	0.129
very	Minde, 1985	0.111	-0.497	0.719
very	Potharst, 2012	-0.320	-0.615	-0.026
very	Rahkonen, 2014	0.083	-0.476	0.642
very	Schermann-Ezirik, 1997	0.216	-0.070	0.502
very	Schmucker, 2005	0.682	0.277	1.087
very	Singer, 2003	-0.142	-0.377	0.093
very	Wolke, 2013	0.050	-0.230	0.331
very	Zarling, 1988	-0.823	-1.328	-0.317
very		-0.061	-0.212	0.091
Overall		-0.065	-0.206	0.077



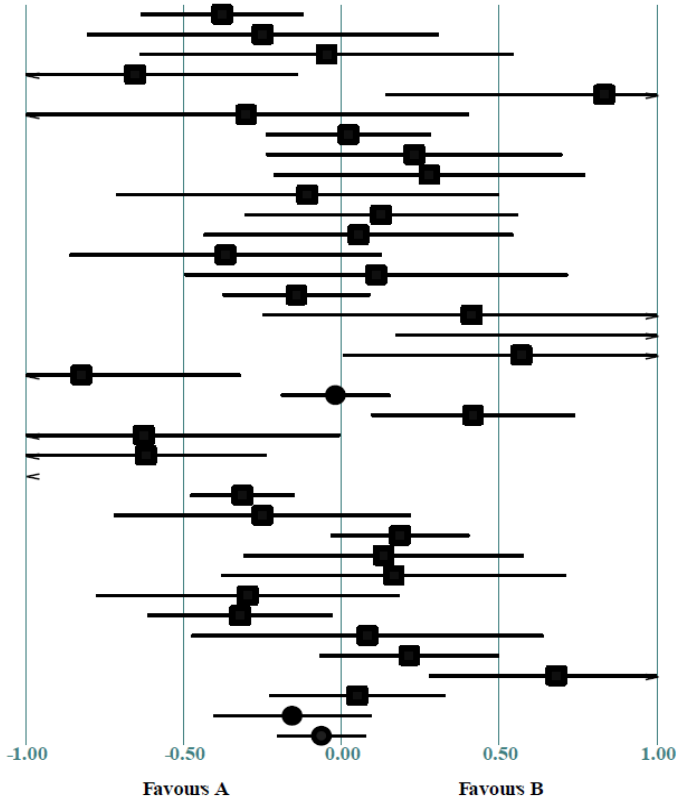
E.2 Publication Date as Moderator

Group by publication date	Study name	Hedges's g	Lower limit	Upper limit
after 2000	Agostini, 2014	0.418	0.094	0.742
after 2000	Coppola, 2007	-0.625	-1.248	-0.002
after 2000	Feldman, 2007	-0.619	-1.002	-0.235
after 2000	Foecada-Guex, 2006	-2.370	-2.986	-1.753
after 2000	Greene, 1983	0.279	-0.215	0.774
after 2000	Jaekel, 2012	-0.313	-0.479	-0.147
after 2000	Jean, 2012	0.126	-0.308	0.561
after 2000	Korja, 2008	-0.250	-0.723	0.222
after 2000	Laucht, 2001	0.186	-0.035	0.408
after 2000	Miljkovitch, 2013	-0.366	-0.862	0.129
after 2000	Montirosso, 2010	0.167	-0.379	0.714
after 2000	Muller-Nix, 2004	-0.296	-0.778	0.186
after 2000	Potharst, 2012	-0.320	-0.615	-0.026
after 2000	Rahkonen, 2014	0.083	-0.476	0.642
after 2000	Schmucker, 2005	0.682	0.277	1.087
after 2000	Singer, 2003	-0.142	-0.377	0.093
after 2000	Wolke, 2013	0.050	-0.230	0.331
after 2000		-0.164	-0.387	0.059
before 2000	Barnard, 1984	-0.377	-0.637	-0.117
before 2000	Barratt, 1992	-0.249	-0.808	0.310
before 2000	Barratt, 1996	-0.046	-0.639	0.548
before 2000	Bendersky, 1986	-0.653	-1.171	-0.135
before 2000	Crawford, 1982	0.834	0.138	1.529
before 2000	Davis, 1988	-0.301	-1.009	0.406
before 2000	DeWitt, 1997	0.023	-0.241	0.286
before 2000	Greenberg, 1988	0.232	-0.238	0.701
before 2000	Halpern, 1997	-0.107	-0.715	0.501
before 2000	Landry, 1990	0.055	-0.437	0.547
before 2000	Levy-Shiff, 1989	0.134	-0.311	0.580
before 2000	Minde, 1985	0.111	-0.497	0.719
before 2000	Schermann-Ezirik, 1997	0.216	-0.070	0.502
before 2000	Stevenson, 1990	0.413	-0.250	1.077
before 2000	Watt, 1985	1.003	0.169	1.836
before 2000	Wille, 1991	0.571	0.003	1.139
before 2000	Zarling, 1988	-0.823	-1.328	-0.317
before 2000		0.021	-0.177	0.218
Overall		-0.060	-0.208	0.088



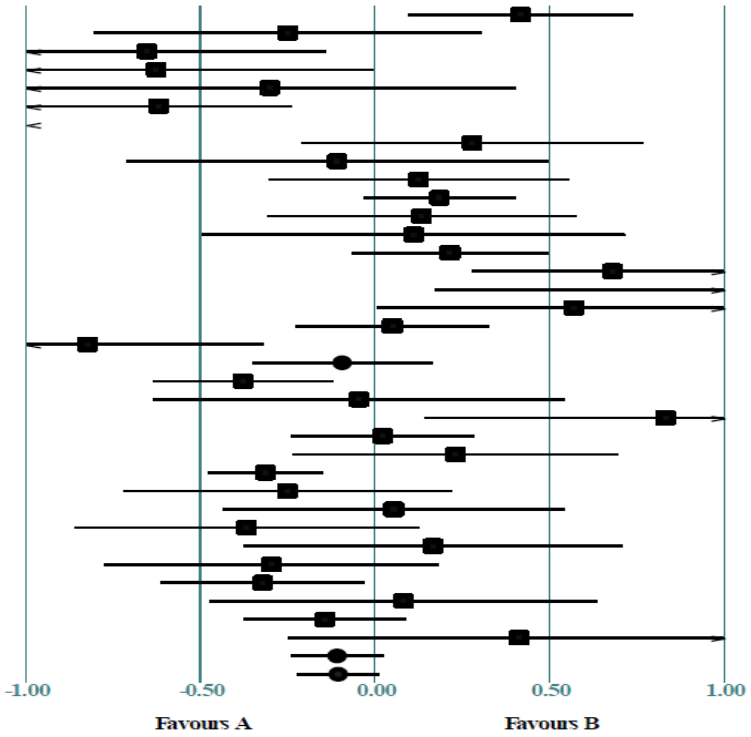
E. 3 Geographical Setting as Moderator

Group by geographical setting	Study name	Hedges's g	Lower limit	Upper limit
America	Barnard, 1984	-0.377	-0.637	-0.117
America	Barratt, 1992	-0.249	-0.808	0.310
America	Barratt, 1996	-0.046	-0.639	0.548
America	Bendersky, 1986	-0.653	-1.171	-0.135
America	Crawford, 1982	0.834	0.138	1.529
America	Davis, 1988	-0.301	-1.009	0.406
America	DeWitt, 1997	0.023	-0.241	0.286
America	Greenberg, 1988	0.232	-0.238	0.701
America	Greene, 1983	0.279	-0.215	0.774
America	Halpern, 1997	-0.107	-0.715	0.501
America	Jean, 2012	0.126	-0.308	0.561
America	Landry, 1990	0.055	-0.437	0.547
America	Miljkovitch, 2013	-0.366	-0.862	0.129
America	Minde, 1985	0.111	-0.497	0.719
America	Singer, 2003	-0.142	-0.377	0.093
America	Stevenson, 1990	0.413	-0.250	1.077
America	Watt, 1985	1.003	0.169	1.836
America	Wille, 1991	0.571	0.003	1.139
America	Zarling, 1988	-0.823	-1.328	-0.317
America		-0.018	-0.192	0.156
Europe	Agostini, 2014	0.418	0.094	0.742
Europe	Coppola, 2007	-0.625	-1.248	-0.002
Europe	Feldman, 2007	-0.619	-1.002	-0.235
Europe	Foecada-Guex, 2006	-2.370	-2.986	-1.753
Europe	Jaekel, 2012	-0.313	-0.479	-0.147
Europe	Korja, 2008	-0.250	-0.723	0.222
Europe	Laucht, 2001	0.186	-0.035	0.408
Europe	Levy-Shiff, 1989	0.134	-0.311	0.580
Europe	Montirosso, 2010	0.167	-0.379	0.714
Europe	Muller-Nix, 2004	-0.296	-0.778	0.186
Europe	Potharst, 2012	-0.320	-0.615	-0.026
Europe	Rahkonen, 2014	0.083	-0.476	0.642
Europe	Schermann-Ezirik, 1997	0.216	-0.070	0.502
Europe	Schmucker, 2005	0.682	0.277	1.087
Europe	Wolke, 2013	0.050	-0.230	0.331
Europe		-0.155	-0.407	0.096
Overall		-0.063	-0.206	0.081



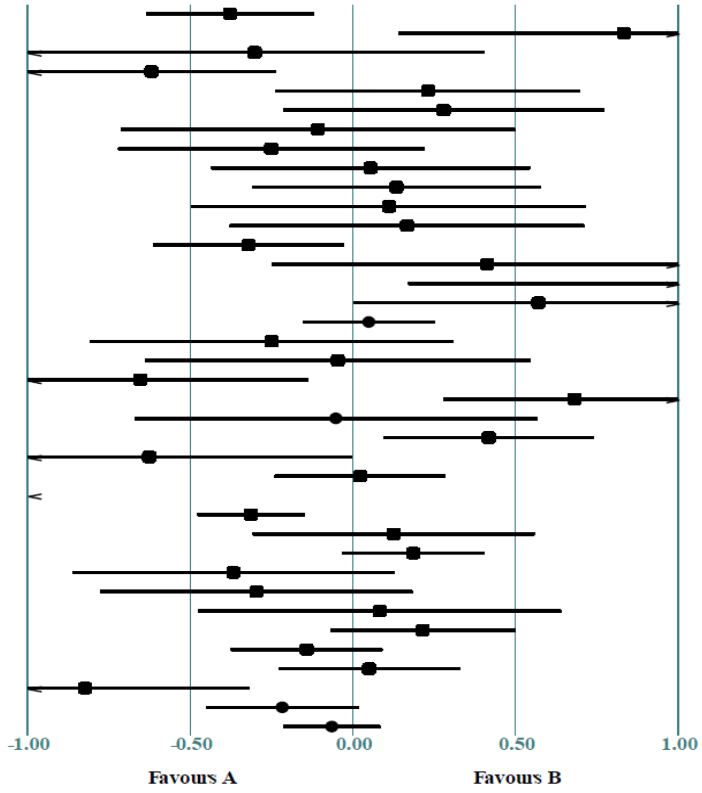
E.4 Infant Age as Moderator

Group by age	Study name	Hedges's g	Lower limit	Upper limit
<= 6m	Agostini, 2014	0.418	0.094	0.742
<= 6m	Barratt, 1992	-0.249	-0.808	0.310
<= 6m	Bendersky, 1986	-0.653	-1.171	-0.135
<= 6m	Coppola, 2007	-0.625	-1.248	-0.002
<= 6m	Davis, 1988	-0.301	-1.009	0.406
<= 6m	Feldman, 2007	-0.619	-1.002	-0.235
<= 6m	Foecada-Guex, 2006	-2.370	-2.986	-1.753
<= 6m	Greene, 1983	0.279	-0.215	0.774
<= 6m	Halpern, 1997	-0.107	-0.715	0.501
<= 6m	Jean, 2012	0.126	-0.308	0.561
<= 6m	Laucht, 2001	0.186	-0.035	0.408
<= 6m	Levy-Shiff, 1989	0.134	-0.311	0.580
<= 6m	Minde, 1985	0.111	-0.497	0.719
<= 6m	Schermann-Ezirik, 1997	0.216	-0.070	0.502
<= 6m	Schmucker, 2005	0.682	0.277	1.087
<= 6m	Watt, 1985	1.003	0.169	1.836
<= 6m	Wille, 1991	0.571	0.003	1.139
<= 6m	Wolke, 2013	0.050	-0.230	0.331
<= 6m	Zarling, 1988	-0.823	-1.328	-0.317
<= 6m		-0.093	-0.354	0.167
> 6m	Barnard, 1984	-0.377	-0.637	-0.117
> 6m	Barratt, 1996	-0.046	-0.639	0.548
> 6m	Crawford, 1982	0.834	0.138	1.529
> 6m	DeWitt, 1997	0.023	-0.241	0.286
> 6m	Greenberg, 1988	0.232	-0.238	0.701
> 6m	Jaekel, 2012	-0.313	-0.479	-0.147
> 6m	Korja, 2008	-0.250	-0.723	0.222
> 6m	Landry, 1990	0.055	-0.437	0.547
> 6m	Miljkovitch, 2013	-0.366	-0.862	0.129
> 6m	Montirosso, 2010	0.167	-0.379	0.714
> 6m	Muller-Nix, 2004	-0.296	-0.778	0.186
> 6m	Potharst, 2012	-0.320	-0.615	-0.026
> 6m	Rahkonen, 2014	0.083	-0.476	0.642
> 6m	Singer, 2003	-0.142	-0.377	0.093
> 6m	Stevenson, 1990	0.413	-0.250	1.077
> 6m		-0.108	-0.243	0.028
Overall		-0.105	-0.225	0.015



E.5 Type of Parenting Behaviour as Moderator

Group by type of parenting behavior	Study name	Hedges's g	Lower limit	Upper limit
maternal facilitation	Barnard, 1984	-0.377	-0.637	-0.117
maternal facilitation	Crawford, 1982	0.834	0.138	1.529
maternal facilitation	Davis, 1988	-0.301	-1.009	0.406
maternal facilitation	Feldman, 2007	-0.619	-1.002	-0.235
maternal facilitation	Greenberg, 1988	0.232	-0.238	0.701
maternal facilitation	Greene, 1983	0.279	-0.215	0.774
maternal facilitation	Halpern, 1997	-0.107	-0.715	0.501
maternal facilitation	Korja, 2008	-0.250	-0.723	0.222
maternal facilitation	Landry, 1990	0.055	-0.437	0.547
maternal facilitation	Levy-Shiff, 1989	0.134	-0.311	0.580
maternal facilitation	Minde, 1985	0.111	-0.497	0.719
maternal facilitation	Montirosso, 2010	0.167	-0.379	0.714
maternal facilitation	Potharst, 2012	-0.320	-0.615	-0.026
maternal facilitation	Stevenson, 1990	0.413	-0.250	1.077
maternal facilitation	Watt, 1985	1.003	0.169	1.836
maternal facilitation	Wille, 1991	0.571	0.003	1.139
maternal facilitation		0.050	-0.156	0.255
maternal responsiveness	Barratt, 1992	-0.249	-0.808	0.310
maternal responsiveness	Barratt, 1996	-0.046	-0.639	0.548
maternal responsiveness	Bendersky, 1986	-0.653	-1.171	-0.135
maternal responsiveness	Schmucker, 2005	0.682	0.277	1.087
maternal responsiveness		-0.052	-0.673	0.569
maternal sensitivity	Agostini, 2014	0.418	0.094	0.742
maternal sensitivity	Coppola, 2007	-0.625	-1.248	-0.002
maternal sensitivity	DeWitt, 1997	0.023	-0.241	0.286
maternal sensitivity	Foecada-Guex, 2006	-2.370	-2.986	-1.753
maternal sensitivity	Jaekel, 2012	-0.313	-0.479	-0.147
maternal sensitivity	Jean, 2012	0.126	-0.308	0.561
maternal sensitivity	Laucht, 2001	0.186	-0.035	0.408
maternal sensitivity	Miljkovitch, 2013	-0.366	-0.862	0.129
maternal sensitivity	Muller-Nix, 2004	-0.296	-0.778	0.186
maternal sensitivity	Rahkonen, 2014	0.083	-0.476	0.642
maternal sensitivity	Schermann-Ezirik, 1997	0.216	-0.070	0.502
maternal sensitivity	Singer, 2003	-0.142	-0.377	0.093
maternal sensitivity	Wolke, 2013	0.050	-0.230	0.331
maternal sensitivity	Zarling, 1988	-0.823	-1.328	-0.317
maternal sensitivity		-0.216	-0.453	0.021
Overall		-0.064	-0.215	0.087



Appendix F- Frequencies of Regulatory Problems at 3 and 6 months with regard to Attachment Patterns

	Secure N (%)	Insecure N (%)	Organised N (%)	Disorganised N (%)	Total N (%)
3 Months					
No Regulatory Problems	63 (70.8%)	26 (29.2%)	70 (78.7%)	19 (21.3%)	89
Single Regulatory Problems	47 (70.1%)	20 (29.9%)	53 (79.1%)	14 (20.9%)	67
Multiple Regulatory Problems	10 (45.5%)	12 (54.5%)	13 (59.1%)	9 (40.9%)	22
6 Months					
No Regulatory Problems	62 (74.7%)	21 (25.3%)	65 (78.4%)	18 (21.6%)	83
Single Regulatory Problems	40 (64.5%)	22 (35.5%)	48 (77.5%)	14 (22.5%)	62
Multiple Regulatory Problems	18 (54.6%)	15 (45.4%)	23 (69.7%)	10 (30.3%)	33
Total	120	58	136	42	178
3 Months					
*Crying**	18 (56.3%)	14 (43.8%)	22 (68.8%)	10 (31.3%)	32
*Sleeping**	23 (57.5%)	17 (42.5%)	26 (65%)	14 (53%)	40
*Feeding**	27 (58.7%)	19 (41.3%)	34 (73.9%)	12 (26.1%)	46
6 Months					
*Crying**	27 (77.1%)	8 (22.9%)	28 (80%)	7 (20%)	35
*Sleeping**	39 (69.6%)	17 (30.4%)	44 (78.6%)	12 (21.4%)	56
*Feeding**	29 (74.4%)	10 (25.6%)	34 (87.2%)	5 (12.8%)	39

Please note that this table shows the percentages without adjusting for control variables. *Frequencies of crying, sleeping, feeding problems represent the overall numbers.