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## Abstract

**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 ( $\beta=0.19$ ,  $SE=0.10$ ,  $p<0.05$ ) and at 18 months ( $\beta=0.21$ ,  $SE=0.10$ ,  $p<0.05$ ), 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 ( $\beta=-0.26$ ,  $SE=0.12$ ,  $p<0.05$ ), but not from 3 to 18 months.

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

**Keywords:** regulatory problems, crying, sleeping, feeding, maternal sensitivity

## Introduction

Regulatory problems (crying, sleeping, and feeding) during infancy affect approximately 20% of infants in the first year [1]. They have been shown to be relatively stable across the early years [2] and can lead to stable trajectories of dysregulation across childhood [3].

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 [1]. Since 2011, several longitudinal studies further supported the finding that regulatory problems have adverse impact on behaviour in childhood and even adolescence [4]. 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 [1, 5].

Yet despite the growing evidence about multiple infant regulatory problems as precursors of later behaviour problems, there is a scarcity of research which 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 [6]. The development of regulatory functions is dependent upon the maturation of the brain stem, which undergoes substantial changes after 33 weeks of gestation [7]. Specifically, the maturation of sleep-wake cycle and cardiac vagal tone are dependent on the development of the brain stem which has been found to predict later sleeping and crying patterns [8]. Converging evidence revealed that very preterm infants who are born before 32 weeks of gestation are at risk of disruptions in brain stem development [9]. The early warning signs of this disturbance include excessive crying, sleeping and feeding difficulties [10]. 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 [5]. Surprisingly few longitudinal studies examined the relationship between sensitive parenting referring to mothers' ability to respond appropriately to infant cues [11] 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 [12], others noted a bi-directional relationship between these variables [13], and still others revealed no significant link [14, 15]. Thus, the verdict is still out 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. We hypothesized that regulatory problems and maternal sensitivity will have reciprocal relationships across infancy. Furthermore, we hypothesized that very preterm birth as a proximate of neurodevelopmental vulnerability would be related to regulatory problems. In contrast, we hypothesized that preterm birth would be unrelated to maternal sensitivity in accordance with findings of a recent meta-analysis [16].

## **Method**

### **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 1.

### **Procedure**

VP/VLBW infants were recruited from three neonatal units in East of England during an 18 months period. Written consent was obtained from the mother in the presence of an independent witness (See Appendix A for a full description). 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.

### **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[17]). For full-term infants, midwives completed the BCHAPS during home visits in the first 10 days of infant's life. Both nurses and midwives were given structured instruction on how to complete the BCHAPS by the researchers. 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 ( $\alpha = 0.95$ ).

Maternal sensitivity at 3 months was measured with a structured play observation: the Mother-Infant Structured Play Assessment (MISPA). The play observation consisted of 5 episodes (structured toy play, unstructured toy play, attention task, still-face and reunion), lasting 8 minutes overall. It comprised global rating scales of maternal behaviour, infant behaviour and mother-infant joint behaviour which were adapted from three established interaction coding schemes: The Emotional Availability Scales [18]; The Infant and Caregiver Engagement Phases [19]; The Play Observation Scheme and Emotion Ratings [20]. For the purposes of this study, maternal behaviour rating scales during the first two play episodes, 2 minutes of play with a toy (rattle) and 2 minutes of free play, were used. Maternal behaviour included 5-point-Likert scales measuring verbal involvement, physical contact, positive emotion expression, negative emotion expression, stimulation, and sensitivity. The videotaped maternal behaviour was coded by two independent researchers who were trained during a 4-month period. 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 the Play Observation Scheme of Emotion Rating (POSER) which is a validated measure [21] to rate behavioural and affective characteristics of maternal and infant behaviours [20]. 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). Videotaped mother-infant interaction was coded by two independent researchers who were trained over a period of 2 months. Maternal rating scales (verbal involvement, verbal control, control and teaching behaviour, physical involvement, sensitivity, appropriateness of play interaction, expressed positive emotion, and expressed negative emotion) were based on validated measures such as the Assessment of Mother-Child Interaction with Etch-a-Sketch [22], 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 ( $\alpha_{\text{maternal sensitivity}} = 0.90$ ).

### **Comorbid Regulatory Problems**

Regulatory problems were assessed via a standard structured interview about crying, sleeping and feeding problems at term, 3 and 18 months. Definition of crying, sleeping and feeding problems were derived from the literature [23] and are shown in Table 2. 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. The focus of this study was the comorbidity of crying, sleeping and feeding problems. Participants were categorized as having comorbid (multiple) regulatory problems if they had two or three single regulatory problems based on the scores from crying, sleeping, feeding interview. The reliability of the scale was high at each time point ( $\alpha_{\text{Term}}=0.71$ ,  $\alpha_{3\text{Months}}=0.73$ ,  $\alpha_{18\text{Months}}=0.75$ ).

### **Control Variables**

Medical risk and sex of the infant were included as control variables. Medical risk was assessed as neurosensory deficits, rehospitalisation, surgical procedures and oxygen dependency (Table 1). Oxygen dependency was defined as oxygen use of more than 21%.

### **Statistical Analysis**

Cross-lagged panel model [24] 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)[25] 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 (Fig. 1) 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 medical risk and sex.

In order to evaluate the goodness-of-fit,  $\chi^2$  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) [26] 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.[27] For the RMSEA, values less than .05 indicate a good fit and values less than 0.08 an acceptable fit.

## Results

Table 3 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, had the best fit with the data (CFI= 0.95, RMSEA= 0.05).

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

Maternal sensitivity at term had a direct effect on multiple regulatory problems at 3 months ( $\beta=-0.26$ , 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. Prematurity did not influence maternal sensitivity at any time point, however VP/VLBW birth was related to increased regulatory problems at term ( $\beta=0.19$ , SE= 0.10,  $p<$

0.05) and 18 months ( $\beta=0.21$ ,  $SE= 0.10$ ,  $p< 0.05$ ) (Fig. 2). Medical risk and infant sex are not shown in the model since they did not have a significant impact.

## 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 for insensitive 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 on subsequent maternal sensitivity during the first year of life [28]. 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 [29] but no lasting impact of early maternal sensitivity on infant regulatory problems at 18 months [15]. This appears at odds with the limited intervention research that showed that changes in parenting behaviour can reduce at least excessive crying [30]. 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 [31]. Therefore, changes in regulatory problems at 3 months might be independent from the impacts of very preterm birth.

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 [32]. 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, this study did not include parental stress or depression which could have been important covariates considering their possible impact on maternal sensitivity [33], which should be addressed in future research. In addition, it needs to be highlighted that sleeping disorders should not be diagnosed before 6 months of age [34]. 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 [35]. Lastly, the suggestions that genetics might contribute to the development of regulatory problems [36] 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.

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 [37]. Moreover, clinicians should reassure mothers of infants with regulatory problems that regulatory problems might occur despite sensitive parenting. Finally, 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.

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**Conflict of Interest:** None declared.

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## Figure Legends

**Fig. 1.** Cross-lagged path model of maternal sensitivity and comorbid regulatory problems.

**Fig. 2.** Longitudinal significant associations between very preterm birth, maternal sensitivity and comorbid regulatory problems.