OUTCOMES IN REGULATORY DISTURBED CHILDREN

FULL TITLE
Associations between problems with crying, sleeping, and/ or feeding in Infancy and long-term Behavioural Outcomes in Childhood – A Meta-Analysis

SHORT TITLE
Outcomes in Regulatory Disturbed Children

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KEYWORDS
Infant regulatory problems, excessive crying, feeding problems, sleeping problems, childhood behaviour problems.

ABBREVIATIONS
RP=regulatory problems; BP=behaviour problems; ADHD=attention deficit/hyperactivity problems; ES=weighted mean effect size d; FSN=Fail-Safe N
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ABSTRACT

Objective: Infant excessive crying, sleeping, or feeding problems, often referred to as infant regulatory problems, are found in approximately 20% of infants. Uncertain is whether regulatory problems are predictors for behaviour problems. We conducted a quantitative meta-analysis of 22 studies testing the association between regulatory problems and internalizing, externalizing, and ADHD problems.

Methods: All longitudinal studies from 1987 to 2006 that tested the association between infant regulatory problems and childhood behaviour problems statistically were included in the meta-analysis. A total of 16’848 children (1’935 with regulatory problems) were tested. We used Cohen’s d to express the association between regulatory problems and behaviour problems. Heterogeneity of the effect sizes was assessed using the I-squared statistics and meta-ANOVAs and meta-regressions were conducted to assess the influence of moderators. Rosenthal’s classic fail-safe N and correlation of sample sizes to effect sizes were used to assess publication bias.

Results: The weighted mean effect size (ES) for the main regulatory problems – behaviour problems association was .41 (95%CI=.28 to .54) indicating that children with former regulatory problems show more behaviour problems in childhood than controls. Externalizing and ADHD problems were the strongest outcome of any regulatory problem indicated by the highest fail-safe-N and lowest correlation of sample size to effect size. Meta-ANOVA’s revealed no significant moderating influences of regulatory problem co-morbidity ($I^2=44.0; p>.05$), type ($I^2=41.8; p>.05$), or duration ($I^2=44.0; p>.05$). However, cumulative problems and clinical referral increased the risk of behaviour problems.

Conclusions: The meta-analyses suggest that children with former regulatory problems show more behaviour problems in childhood than controls, particularly in multi-problem families.
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There is a need of further studies to assess behavioural outcomes of former sleep, feeding, or multiple disturbed children.
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INTRODUCTION

Approximately 20% of all infants show symptoms of excessive crying, sleeping difficulties, and/or feeding problems, often referred to as regulatory problems (RP), in the first year of life.(1-4) RP are a common concern of parents resulting in frequent help seeking, family disruption, and considerable costs for the health services.(5, 6) Within clinical classification systems,(7) infants with RP have difficulties with self-regulation of fussiness, irritability, or coping with change i.e. they cry longer, need longer despite assistance to settle back to sleep once awoken or have problems to overcome neophobia to new foods.

Although RP are transient in the majority of infants they are stable across the preschool years for a considerable minority of children.(8) Question arise whether RP are associated with adverse child behaviour. Transient RP, most notably excessive crying within the first three months, has been reported to show an overall good prognosis without any negative long-term consequences in the behaviour (9-11) whereas persistent and / or multiple RP have been reported to affect the child’s behaviour long term. (4, 12-15) Some etiological models suggest that the hyper sensitivity to stimuli,(12) ineffective regulatory competences,(16) or early deficit in executive control,(13, 15) may be early precursors pointing to less effective regulation of behaviour later in childhood.

The aim of this meta-analysis was first, to identify the nature and strength of associations between RP in early infancy and behaviour problems (BP) in childhood. Secondly, the analysis of moderator variables was conducted in order to aid explanation of relationships between early RP and BP in childhood.
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METHODS

Selection of studies:

A computer based literature search for studies presenting quantitative data on the association between RP in infancy and BP in childhood was performed using PubMed, PsychInfo and Google Scholar database, with the following keywords: colic, excessive / persistent crying, sleeping / feeding problem, infant sleep, night waking, infant feeding / refusal to eat, choosy, picky, psychopathology, behaviour problem, behavioural outcome, preschool, childhood, attention, ADHD, hyperactivity, hyperkinetic, characteristic, follow-up, longitudinal study, prospective. In addition, the bibliography of all relevant studies was reviewed and authors were contacted for further unpublished manuscripts. These steps produced a study pool of 72 studies (reported in 70 articles) published during the period 1987 to 2006. Twenty-two studies met the inclusion criteria.

Inclusion criteria:

1. RP was confined to crying, sleeping and/or feeding problems within the first year of life occurring as an isolated problem or in combination with each other. 2. Studies had to include a measure of internalizing, externalizing, ADHD, or general BP of the target infant in childhood and the association between infant RP and childhood BP was tested statistically. 3. Only prospective studies including at least one follow-up assessment were included.

Studies reporting on child characteristics not related to RP such as difficult temperament, cognitive functioning, or developmental status were excluded.

Study set:

Of the final 22 studies, 10 studies reported on consequences of excessive crying, 4 on sleeping problems, 3 on feeding problems, and 5 studies on multiple RP (table 1). The mean age of children at the baseline measurement of RP was 5.2 months (±4.8 SD), 2.6 (±0.98 SD)
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for excessive crying; 5.8 (±3.8 SD) months for sleeping disturbance; 8.1 (±7.5 SD) months for feeding problems, and 8.8 (±7.1 SD) months for multiple RP. The mean age of children with a crying problem was later than the typical peak crying period in community studies (17, 18) suggesting that the crying problem had persisted in these infants. The participants’ age at follow-up assessments ranged from 1.3 years to 10 years (mean age 4.5 years ±2.3 SD). A total of 16’848 children (1’935 with RP) participated in the studies. Sufficient information on socio-demographic characteristics of the study sample was only available for 10 studies (table 1). Most of the children were Caucasian (85%), the majority of the mothers were married or lived in a stable relationship (96%) and 77% of the families were classified as “middle” or “high” socioeconomic status. Finally, 59% of the studies referred to community-based samples and 41% to clinically referred samples.

Regulatory problems:

Identification of RP constituted a major challenge to our meta-analysis since no consistent diagnostic criteria exist to date. (19) All studies where RP was considered as a serious problem by the caregiver or a clinician were included (table 1). Excessive crying was defined as crying with intense, unsoothable cry bouts without any apparent reasons in the first three months of life. (20) Sleeping problems were categorized as either difficulties in settling at bedtime, or failure to sleep through the night without interruptions. (3, 21) Feeding problems comprised vomiting, food refusal, little appetite, or swallowing problems. (1, 22) Persistent RP was referred to excessive crying exceeding the third month of life and sleeping and feeding problems that occurred at initial assessment and follow-up. Isolated RP referred to one of these three RP types, whereas multiple RP was a combination of either two or three of them. Studies used combinations of parent interviews (60%), questionnaires (41%), infant diaries (32%), or observations (18%) to assess RP. The majority of informants were parents; experts
(e.g. paediatricians, child health nurse) gave additional information in some studies. Co-
morbidity was reported in 9 studies, however only 5 studies analyzed multiple RP (table 1).

Behaviour problems:
Childhood BP were divided into four categories: internalizing, externalizing, ADHD, and
general BP (table 2).(37) Internalizing behaviour comprised anxiety, depression, or
withdrawal. Externalizing problems referred to aggressive, destructive, conduct problems, or
temper tantrums. ADHD symptoms included hyperactivity, whole ADHD diagnosis,
inattention, and concentration problems. General BP referred to any BP that was reported in
the studies (i.e. internalizing, externalizing, ADHD, or total scores of BP) (table 2). The
informants of BP were the caregiver; child, teacher or clinicians gave additional information
in some studies. Fifteen studies reported externalizing BP, eleven studies internalizing BP, 13
studies ADHD problems, and 16 studies reported multiple BP outcomes.

Number of risk factors:
A variable “number of risk factors” was constructed to assess the impact of cumulative initial
family risk factors and RP characteristics on the RP–BP associations. Number of risk factors
comprised adding characteristics of RP (isolated/multiple, transient/persistent) and family risk
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factors (table 1) measured at baseline together. A score of 1 refers to isolated or transient RP without any family risk factors prevailing, whereas a maximum score of 6 refers to multiple persistent RP and negative parent-infant interaction, social adversities, a depressed or stressed mother, and a negative family environment.

Coding of the studies:

The first author and a research trainee coded the extracted information from the selected studies independently. To assess inter-coder agreement, regular meetings were held to discuss any differences regarding the data extraction. Inter-coder agreement was high (range: .89 to 1.00) after discussion to resolve disagreement. (38)

Meta-analytic method

We used Cohens’ d to express the standardized mean difference for the occurrence of BP between children with former RP and children without RP. (39) The standardized mean difference is a measure of overlap between distributions, i.e. when different studies use diverse instruments to assess BP, which was the case in this meta-analysis. The effect size reflects the difference between the distributions in the two groups. (40) The random-effects model was used for all calculated weighted mean effect sizes d (ESs) because of the heterogeneity of the study set. Each ES was weighted by the inverse of its variance(40) and was interpreted as followed: 0.2, 0.5, and 0.8 indicate a small, medium and large effect, respectively.(39) Positive ESs imply that former RP children show more BP than non-RP children. Additionally, the z statistic (test of the null) was two-tailed and the p value set at p<.05. To ensure independence of observations, each study contributed only one ES to the analysis by averaging across all RP and BP comparisons contained within each study. When research groups reported multiple follow-ups of the same study sample, one measurement point was randomly selected to avoid a selective bias of ES overestimation for a specific child
age (table 1). Heterogeneity of the ESs was assessed using the I-squared statistic, a measure that assesses the proportion of the observed variance, which reflects real differences in ES. An I-squared near 0 indicates that almost all of the observed variance is spurious, whereas high values indicate that the variation may not be due to sampling error and that moderators may explain the variability.(40). Analyses were carried out in two steps: Primary analyses included testing the main RP-BP association (i.e. any RP–general BP) and all individual RP (crying, feeding, sleeping, and multiple problems) and BP (general, internalizing, externalizing, and ADHD) combinations. In a second step subgroup analyses using meta-ANOVAs and meta-regressions were conducted with RP characteristics (RP type, transient/persistent RP, isolated/multiple RP), methodological (RP measurement instrument, RP/BP informant, and sample characteristics), number of risk factors, and the child’s age at follow-up for the main and individual RP-BP associations. No attempt for Bonferroni correction was made since the procedure is too conservative and therefore not appropriate for explorative research.(41) However, Rosenthal’s classic fail-safe N(42) and correlation of sample size to ES(43) was used to assess publication bias for each association. A negative correlation between sample size and ES is an indicator for a bias against publishing findings that are not statistically significant indicating overestimated ES. (43) For all meta-analytic computations, Comprehensive Meta-Analysis Version 2 was used.(44)

**RESULTS**

The weighted mean ES for the main RP-BP association was .41 (95%CI=.28 to .54) indicating a medium effect size (table 3). Children with former RP had more BP in childhood than controls. The homogeneity analyses for the main association ($I^2=44.02$; p<.05) as well as for externalizing ($I^2=65.6$; p<.001) and ADHD ($I^2=73.0$; p<.001) problems were high and significant indicating that moderating variables were likely to exist. Significant medium ES was found for externalizing (d=.51) and low-to-medium ESs for internalizing (d=.34) and
ADHD problems (d=.36) for any RP. Crying problems led to the highest ESs: general BP (d=.51), externalizing (d=.56), internalizing (d=.50), and ADHD (d=.42), respectively. Multiple RP and feeding difficulties were only associated to general BP (multiple: d=.45; feeding=.21). Sleeping problems showed inconsistent ESs ranging from small to high: internalizing (d=.24), general BP (d=.42) and ADHD (d=1.30), respectively.*

FSN and negative correlations of sample size and ES indicated possible publication bias in studies for feeding, sleeping, and multiple RP, and where internalizing outcomes were examined (table 3).

Moderator Analysis

RP characteristics

Neither co-morbidity (isolated vs. multiple; $I^2=44.0; p>.05$) nor type of RP (crying, feeding, or sleeping problems; $I^2=41.8; p>.05$), or duration (transient vs. persistent; $I^2=44.0; p>.05$) was a moderator for the main and all individual associations.

Method Factors

BP informant was a moderator for the main RP–BP comparison. Post-hoc analysis revealed that the ES was larger if expert reported BP rather than caregiver ($ES_{\text{expert}}=1.10$ vs. $ES_{\text{caregiver}}=.35; I^2=45.5; p<.05$; table 4). There was a trend for RP assessment method to moderate any RP–externalizing problems ($I^2=60.83; p=.07$). Post hoc analysis revealed that questionnaires and interviews differed significantly in their ES ($ES_{\text{questionnaire}}=.22$ vs. $ES_{\text{interview}}=.89; I^2=53.41; p<.01$) but not in respect to infant diaries. The association between

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The findings remained similar if samples with sleeping problems reported below 6 months were excluded.
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any RP and general BP (ES_{clinical}=.61 vs. ES_{community}=.30; \( I^2=44.02; p<.05 \)) was higher and stronger in samples recruited from referred populations than from community-based samples (table 4).

--- table 4 ---

Number of risk factors:

Former sleep and multiple RP children who experienced numerous adverse regulatory and family risk factors as infants showed more BP than children with a small number of risk factors in univariate meta-regressions: any RP–externalizing problems (\( \beta=0.15; \ SE=0.08; \ p=.08 \)), sleeping–general BP (\( \beta=0.35; \ SE=0.17; \ p<.05 \)), sleeping–externalizing (\( \beta=0.39; \ SE=0.21; \ p=.06 \)), and multiple–ADHD problems (\( \beta=0.23; \ SE=0.09; \ p<.05 \)).

Age at follow-up:

Results of univariate meta-regression analyses indicated that the difference between the child age at follow-up and initial assessment was a predictor for the main RP–BP association (\( \beta=0.04; \ SE=0.02; \ p=.05 \)), whereby larger ESs were observed in middle than early childhood. This effect remained stable for the following individual associations: crying–general BP (\( \beta=0.06; \ SE=0.03; \ p<.05 \)), crying–ADHD (\( \beta=0.07; \ SE=0.03; \ p<.05 \)), and sleeping–general BP (\( \beta=0.22; \ SE=0.12; \ p=.06 \)).

DISCUSSION

Children with RP in infancy were more likely to experience BP in childhood than children without former excessive crying or sleeping problems. The associations between any RP and
internalizing, externalizing, and ADHD problems were found to be particularly strong. The associations for externalizing and ADHD problems were moderate and fairly solid considering that it would take 276 and 106 studies, respectively to falsify the effects found. Stronger associations of RP with BP were found for referred samples and where RP was assessed with more rigorous methods including interviews and behavioural outcome assessed by experts, or when multiple risk factors were present. Moreover, persistent crying mainly accounted for the ES as the mean age of the infants at initial assessment was later than the cry peak reported in community samples. (17, 18).

This meta-analysis highlights the need for a better understanding of the early development of child mental disorders. To explain the association between RP and BP, it has been suggested that initial deficits in regulatory competences and stimuli control may be early markers for similar processes of inadequate or under controlled behaviour in toddler- and childhood.(12, 16, 45) For example, a certain gene polymorphism of the dopaminergic system has been found to be associated with both, ADHD and externalizing problems in childhood(46) and multiple RP in infancy. (47) Others have proposed that early caregiving relationships, infant temperament, and cognitive functioning may affect infant self-regulation and the development of subsequent BP. (16, 48)

Concerns about their baby’s crying, sleeping, or feeding problems are a major reason for many parents seeking professional help. (6) Clinically referred children often came from families with a range of risk factors (e.g. obstetric, interactional, or psychosocial problems) in addition to multiple RP. (2). The accumulation of child symptoms and negative family characteristics was thus more predictive for BP than any particular combination of them. (49, 50)

This meta-analysis suggests the need for early prevention and intervention of RP. A reduction of RP symptoms after altering parenting behaviour was repeatedly reported. (51-54) Behavioural intervention programs of regulatory disturbed children may not only promote a
positive parent-child relationship but may also influence the behavioural development positively.

Limitations

First, our study set was highly heterogeneous and hence comparability of these studies was restricted. We tried to address this issue by conducting moderator analyses with relevant influencing variables and used the random effects model. Second, the CBCL was the predominant instrument used for the assessment of BP although the validity of the anxiety/depression scale has been criticized. Additionally, non-reported or lack of assessment of co-morbidity of RP may have led to biased conclusions regarding the effects of single RP. Several studies could show that crying, feeding, and sleeping problems do coexist in infancy, however, the majority of the studies only focused on a single RP without controlling for another. Finally, the study set was characterized by uneven reporting practices, which hindered the identification of all potential moderators and limited power.

Conclusion

RP in infancy can increase the likelihood of developing behaviour problems in childhood. Children of multi-problem families face the worst outcomes in terms of externalizing and ADHD problems, in particular if they had sleep or multiple problems in infancy. Our findings highlight the need for prospective follow-up studies of regulatory disturbed infants and require reliable assessments of crying, sleeping, or feeding problems. The evidence from this systematic review suggests that those with persisting regulatory problems in families with other problems may require early interventions to minimize or prevent the long-term consequences of infant RP.
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ACKNOWLEDGMENT

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COMPETING INTERESTS

None.

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Key Points

What is already known on this topic

- Infant excessive crying, sleeping, or feeding problems, often referred to as infant regulatory problems (RP), are found in approximately 20% of all infants.
- Early regulatory problems can have any adverse effect on behaviour or cognitive development. However, findings have been inconsistent.
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What this study adds

- Regulatory problems in infancy increase the risk of developing behaviour problems in childhood
- The risk is highest in those with multiple regulatory problems in infancy in multiple risk families
- Future studies should include reliable measures of multiple infant regulatory problems and outcome assessments by experts in addition to parent reports.
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### TABLE 1 Study characteristics: Samples and Definition of Regulatory Problems (RP) at baseline of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Age</th>
<th>Sample</th>
<th>Type RP</th>
<th>RP Duration</th>
<th>M-tech1**</th>
<th>Informant RP</th>
<th>RP diagnosis criteria</th>
<th>SOC</th>
<th>Family1**</th>
<th>Number of risk factors</th>
</tr>
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<tbody>
<tr>
<td>Canivet et al. (2000)(23)</td>
<td>50</td>
<td>102</td>
<td>3</td>
<td>Comm</td>
<td>Crying</td>
<td>Transient</td>
<td>D/I</td>
<td>Wessel (1954)</td>
<td>No</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>DeSantis et al. (2004)(12)</td>
<td>14 persistent RP</td>
<td>14 transient RP</td>
<td>2</td>
<td>Clin</td>
<td>Crying</td>
<td>Persistent</td>
<td>D/I</td>
<td>Number of hours of crying and/or fussing</td>
<td>No</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Elliot et al., (1997)(24)</td>
<td>10 RP</td>
<td>72</td>
<td>1.8</td>
<td>Comm</td>
<td>Crying</td>
<td>Transient</td>
<td>Q</td>
<td>Wessel (1954)</td>
<td>No</td>
<td>Parent-infant interaction</td>
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<tr>
<td>Neu &amp; Robinson (2003)(25)</td>
<td>20</td>
<td>20</td>
<td>2.5</td>
<td>Comm</td>
<td>Crying</td>
<td>Transient</td>
<td>I/Q</td>
<td>Minimum 2.8h/day crying for at least 3 days with 1 month</td>
<td>Yes</td>
<td>Psychosocial situation, maternal psychopathology, family functioning, parent-infant interaction</td>
<td>5</td>
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<tr>
<td>Papousek et al. (2001)(26)</td>
<td>60</td>
<td>45</td>
<td>4.1</td>
<td>Clin</td>
<td>Crying</td>
<td>Persistent</td>
<td>D</td>
<td>Wessel (1954)</td>
<td>No</td>
<td>-</td>
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<tr>
<td>Rao et al. (2004)(27)</td>
<td>9</td>
<td>165</td>
<td>2.4</td>
<td>Comm</td>
<td>Crying</td>
<td>Persistent</td>
<td>I/Q</td>
<td>Daily uncontrolled crying without any apparent reason for at least 2 weeks</td>
<td>No</td>
<td>-</td>
<td>2</td>
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<tr>
<td>Rautava et al. (1995)(28)</td>
<td>338</td>
<td>527</td>
<td>3</td>
<td>Comm</td>
<td>Crying</td>
<td>Transient</td>
<td>Q</td>
<td>Colic questionnaire, Scores 1-3 (no colic); 4 (moderate colic); 5 (severe colic)</td>
<td>Yes</td>
<td>-</td>
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<td>Wolke et al. (2002)(13)</td>
<td>64</td>
<td>64</td>
<td>4</td>
<td>Clin</td>
<td>Crying</td>
<td>Persistent</td>
<td>D</td>
<td>Modified Wessel (1954)</td>
<td>Yes</td>
<td>-</td>
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<tr>
<td>Lam et al. (2003)(30)</td>
<td>36</td>
<td>78</td>
<td>9</td>
<td>Comm</td>
<td>Sleeping</td>
<td>Transient</td>
<td>Q</td>
<td>Caregiver considers baby’s sleep as problematic</td>
<td>Yes</td>
<td>Maternal psychopathology</td>
<td>2</td>
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<td>Scher et al. (2005)(14)</td>
<td>13 poor sleepers</td>
<td>12 good sleepers</td>
<td>3</td>
<td>Comm</td>
<td>Sleeping</td>
<td>Persistent</td>
<td>Q</td>
<td>Caregiver considers baby’s sleep as problematic</td>
<td>No</td>
<td>-</td>
<td>2</td>
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<td>Thunstrom (2002)(31)</td>
<td>25</td>
<td>25</td>
<td>8.5</td>
<td>Comm</td>
<td>Sleeping</td>
<td>Transient</td>
<td>I/D</td>
<td>More than two night wakings/night; baby needs more than 15 min to fall asleep</td>
<td>No</td>
<td>Psycosocial situation, parent-infant interaction</td>
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<td>Zuckerman et al. (1987)(32)</td>
<td>23</td>
<td>33 transient RP</td>
<td>8</td>
<td>Comm</td>
<td>Sleeping</td>
<td>Persistent</td>
<td>I</td>
<td>More than 3 night wakings/night; baby needs</td>
<td>Yes</td>
<td>Psychosocial situation, maternal</td>
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</table>
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<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Mean Age</th>
<th>Study Type</th>
<th>Feeding</th>
<th>RP Duration</th>
<th>Measurement Technology</th>
<th>Informant</th>
<th>Family Risks Assessed</th>
<th>Parents-Infant Interaction</th>
<th>Psychosocial Situation</th>
<th>Parent-Infant Interaction</th>
<th>Psychosocial Interaction</th>
<th>Parent-Infant Interaction</th>
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<td>Dahl (1987) (22)*</td>
<td>25</td>
<td>7.8</td>
<td>Clinical</td>
<td>Transient I/O M/E</td>
<td>more than 1h to fall asleep (after night waking) or any problem causing severe disruption to the mother’s sleep</td>
<td>No</td>
<td>Parent-infant interaction</td>
<td>Psychosocial interaction</td>
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<td>Lindberg (2000) (33)</td>
<td>10</td>
<td>21</td>
<td>Clinical</td>
<td>Persistent I/O M/E</td>
<td>Minimum 1 month RTE</td>
<td>No</td>
<td>Parent-infant interaction</td>
<td>Psychosocial situation</td>
<td>5</td>
<td></td>
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<tr>
<td>Motion et al. (2001) (34)</td>
<td>373</td>
<td>10669</td>
<td>Community</td>
<td>Transient Q M</td>
<td>Feeding difficulties with 4 weeks 1 SD above mean of one factor = isolated RP; 1 SD above mean at irritable and somatic functioning = multiple RP</td>
<td>No</td>
<td>Parent-infant interaction</td>
<td>Psychosocial situation</td>
<td>4</td>
<td></td>
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<td>1</td>
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<tr>
<td>DeGangi et al. (1993) (15)</td>
<td>9</td>
<td>13</td>
<td>Clinical</td>
<td>Transient I/O M/E</td>
<td>Crying: Difficulties with self-consoling, hypersensitive to new stimulations; baby needs more than 20 min to fall asleep, frequent night wakings (&gt;2/night); baby shows distress at feeding time</td>
<td>Yes</td>
<td>Parent-infant interaction</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeGangi et al. (2000) (4)</td>
<td>22</td>
<td>38</td>
<td>Clinical</td>
<td>Transient I/Q M</td>
<td>Crying: Difficulties with self-consoling, hypersensitive to new stimulations; baby needs more than 20 min to fall asleep, frequent night wakings (&gt;2/night); baby shows distress at feeding time</td>
<td>Yes</td>
<td>Parent-infant interaction</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forsyth &amp; Canny (1991) (1)</td>
<td>115</td>
<td>205</td>
<td>Community</td>
<td>Transient I M</td>
<td>Caregiver considers baby’s crying and feeding as a problem</td>
<td>Yes</td>
<td>Parent-infant interaction</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wake et al. (2006) (36)</td>
<td>84 (sleep problems) 55 (cry/fuss problems) 313</td>
<td>2 (crying) 8 (sleeping)</td>
<td>Community</td>
<td>Transient Q/D M</td>
<td>Caregiver considers baby’s crying and sleeping as a problem</td>
<td>Yes</td>
<td>Parent-infant interaction</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Participants (at follow-up) note that N_{RP} and N_{CC} may be different from total participants at follow-up due to subgroup analyses in some studies, N_{RP}=number of RP infants, N_{CC}=number of control children; Age1=mean age at baseline (months); Sample, Clin=Clinically referred sample; Comm=Community-based sample; RP Type, Crying=Crying problems, Sleeping=Sleeping problems, Feeding=Feeding problems; RP Duration, T=Transient, P=Persistent; Measurement technology1 (M-tech1), D=Diary, I=Interview, Q=Questionnaire, O=Observation; Informant1=Informant at baseline, M=Mother, E=Expert; SOC=Sociodemographic information available; Y=Yes, N=No; Family1=Family risks assessed at baseline; *=Duplicated data, one assessment point randomly selected; **=details on specific RP or family risk factors assessment instruments available from the first author on request.
## OUTCOMES IN REGULATORY DISTURBED CHILDREN

### Table 2: Assessment of Behavioral outcomes in childhood of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Age2</th>
<th>Type BP</th>
<th>M-tech 2**</th>
<th>Informant BP</th>
<th>ES (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canivet et al. (2000)(23)</td>
<td>50</td>
<td>102</td>
<td>4</td>
<td>E/I/ADHD</td>
<td>Rutter Preschool Questionnaire</td>
<td>M</td>
</tr>
<tr>
<td>Elliot et al., (1997)(24)</td>
<td>10 RP</td>
<td>72</td>
<td>3</td>
<td>G</td>
<td>Behavior Style Questionnaire (BSQ), ADHD Checklist of the Diagnostic Interview for Children and Adolescents, Revised, CBCL</td>
<td>M</td>
</tr>
<tr>
<td>Neu &amp; Robinson (2003)(25)</td>
<td>20</td>
<td>20</td>
<td>7</td>
<td>E/I/ADHD</td>
<td>Infant Characteristics Questionnaire (ICQ), CBCL</td>
<td>M/E</td>
</tr>
<tr>
<td>Papousek et al. (2001)(26)</td>
<td>60</td>
<td>45</td>
<td>2.5</td>
<td>E/I</td>
<td>CBCL, Denver Development Screening Test (DDST)</td>
<td>M</td>
</tr>
<tr>
<td>Rao et al. (2004)(27)</td>
<td>9</td>
<td>165</td>
<td>5</td>
<td>ADHD</td>
<td>Personality Inventory for Children (PIC)</td>
<td>E</td>
</tr>
<tr>
<td>Rautava et al. (1995)(28)</td>
<td>338</td>
<td>527</td>
<td>3</td>
<td>E</td>
<td>CBCL, Denver Development Screening Test (DDST)</td>
<td>M</td>
</tr>
<tr>
<td>Savino et al. (2005)(29)</td>
<td>67 persistent RP (referred to colic)</td>
<td>38 evening criers</td>
<td>1.3</td>
<td>E/ADHD/G</td>
<td>Behavior Screening Questionnaire (BSQ)</td>
<td>M/E</td>
</tr>
<tr>
<td>St.James-Roberts et al. (1998)(11)</td>
<td>64</td>
<td>64</td>
<td>9.7</td>
<td>E/I/ADHD/G</td>
<td>Bayley Scales of Infant Development &amp; Infant Behavior Record (IBR)</td>
<td>M/E</td>
</tr>
<tr>
<td>Wolke et al. (2002)(13)</td>
<td>36</td>
<td>78</td>
<td>3.6</td>
<td>E/I</td>
<td>CBCL</td>
<td>M</td>
</tr>
<tr>
<td>Lam et al. (2003)(30)</td>
<td>13 poor sleepers</td>
<td>12 good sleepers</td>
<td>3.5</td>
<td>G</td>
<td>CBCL</td>
<td>M</td>
</tr>
<tr>
<td>Scher et al. (2005)(14)</td>
<td>25</td>
<td>25</td>
<td>5.5</td>
<td>ADHD</td>
<td>Psychomotor Questionnaire (PPQ), Preschool Questionnaire (PSQ), Griffiths’ Developmental Scale II, Scandinavian motor-perceptual scale (MPU), Standardized interview schedule for criteria for ADHD</td>
<td>M/E</td>
</tr>
<tr>
<td>Zuckerman et al. (1987)(32)</td>
<td>23</td>
<td>33 transient RP</td>
<td>3</td>
<td>E/I/ADHD</td>
<td>BSQ</td>
<td>M</td>
</tr>
<tr>
<td>Lindberg (2000)(33)</td>
<td>10</td>
<td>21</td>
<td>7.5</td>
<td>I/G</td>
<td>Rutter Child Questionnaire</td>
<td>M/T</td>
</tr>
<tr>
<td>Motion et al. (2001)(34)</td>
<td>373</td>
<td>10669</td>
<td>3.9</td>
<td>E/ADHD</td>
<td>Emotionality, Activity, Sociability (EAS) SDQ</td>
<td>M</td>
</tr>
<tr>
<td>Becker et al. (2004)(35)*</td>
<td>55</td>
<td>264</td>
<td>6.4</td>
<td>ADHD/G</td>
<td>Mannheim Parent Interview</td>
<td>M/C/E</td>
</tr>
<tr>
<td>DeGangi et al. (1993)(15)</td>
<td>9</td>
<td>13</td>
<td>4</td>
<td>ADHD/G</td>
<td>Sensorimotor History Questionnaire</td>
<td>E</td>
</tr>
<tr>
<td>DeGangi et al. (2000)(4)</td>
<td>22</td>
<td>38</td>
<td>3</td>
<td>E/I</td>
<td>CBCL</td>
<td>M</td>
</tr>
<tr>
<td>Forsyth &amp; Canny (1991)(1)</td>
<td>115</td>
<td>205</td>
<td>3.5</td>
<td>ADHD/G</td>
<td>Richman Behavior Checklist (BCL)</td>
<td>M</td>
</tr>
</tbody>
</table>
OUTCOMES IN REGULATORY DISTURBED CHILDREN

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Age at Follow-up</th>
<th>Type of BP</th>
<th>Measurement Technology</th>
<th>Informant</th>
<th>Age2</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wake et al. (2006)</td>
<td>84 RP (sleep problems) 313</td>
<td>2 E/I/G CBCL</td>
<td>M</td>
<td>.20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>55 RP (cry/fuss problems)</td>
<td></td>
<td></td>
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</tbody>
</table>

Participants (at follow-up) note that nRP and nCC may be different from total participants at follow-up due to subgroup analyses in some studies, RP=number of RP infants, CC=Control children; Age2=mean age at follow-up (years); Type of BP, E=externalizing, I=internalizing, ADHD, G=general; Measurement technology2 (M-tech2); Informant2=Informant at follow-up, M=Mother, E=Expert, C=Child, T=Teacher; ES (d)=weighted mean effect size d; *=Duplicated data, one assessment point randomly selected; **=References of the BP assessment instruments available from the first author on request.
## OUTCOMES IN REGULATORY DISTURBED CHILDREN

**Table 3** Significant (p<.05) ESs of the main and individual associations

<table>
<thead>
<tr>
<th>Associations</th>
<th>K</th>
<th>ES</th>
<th>Variance</th>
<th>95% Confidence Interval</th>
<th>(I^2)</th>
<th>FSN</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any Regulatory Problem</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General BP</td>
<td>22</td>
<td>0.412</td>
<td>0.004</td>
<td>LL 0.281 - 0.544</td>
<td>44.0*</td>
<td>433</td>
<td>-0.382</td>
</tr>
<tr>
<td>Externalizing</td>
<td>15</td>
<td>0.507</td>
<td>0.009</td>
<td>LL 0.318 - 0.697</td>
<td>65.6***</td>
<td>276</td>
<td>-0.361</td>
</tr>
<tr>
<td>Internalizing</td>
<td>11</td>
<td>0.345</td>
<td>0.005</td>
<td>LL 0.203 - 0.488</td>
<td>0.000</td>
<td>46</td>
<td>0.437</td>
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<tr>
<td>ADHD</td>
<td>13</td>
<td>0.363</td>
<td>0.014</td>
<td>LL 0.130 - 0.596</td>
<td>73.0***</td>
<td>106</td>
<td>-0.435</td>
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<tr>
<td><strong>Crying Problems</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General BP</td>
<td>10</td>
<td>0.506</td>
<td>0.010</td>
<td>LL 0.308 - 0.704</td>
<td>33.465</td>
<td>94</td>
<td>0.248</td>
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<tr>
<td>Externalizing</td>
<td>9</td>
<td>0.562</td>
<td>0.017</td>
<td>LL 0.309 - 0.815</td>
<td>56.428*</td>
<td>93</td>
<td>0.100</td>
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<tr>
<td>Internalizing</td>
<td>5</td>
<td>0.498</td>
<td>0.014</td>
<td>LL 0.270 - 0.726</td>
<td>0.000</td>
<td>17</td>
<td>0.600</td>
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<tr>
<td>ADHD</td>
<td>6</td>
<td>0.417</td>
<td>0.033</td>
<td>LL 0.059 - 0.774</td>
<td>64.442**</td>
<td>20</td>
<td>0.600</td>
</tr>
<tr>
<td><strong>Feeding Problems</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>General BP</td>
<td>3</td>
<td>0.211</td>
<td>0.003</td>
<td>LL 0.102 - 0.319</td>
<td>0.000</td>
<td>6</td>
<td>0.500</td>
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<tr>
<td><strong>Sleeping Problems</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>General BP</td>
<td>5</td>
<td>0.423</td>
<td>0.028</td>
<td>LL 0.094 - 0.752</td>
<td>35.637</td>
<td>15</td>
<td>-0.700</td>
</tr>
<tr>
<td>Internalizing</td>
<td>3</td>
<td>0.239</td>
<td>0.011</td>
<td>LL 0.035 - 0.443</td>
<td>0.000</td>
<td>1</td>
<td>-1.000***</td>
</tr>
<tr>
<td>ADHD</td>
<td>2</td>
<td>1.303</td>
<td>0.318</td>
<td>LL 0.198 - 2.408</td>
<td>0.000</td>
<td>0</td>
<td>-1.000***</td>
</tr>
<tr>
<td><strong>Multiple Regulatory Problems</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>General BP</td>
<td>4</td>
<td>0.445</td>
<td>0.045</td>
<td>LL 0.031 - 0.859</td>
<td>54.361*</td>
<td>12</td>
<td>-1.000***</td>
</tr>
</tbody>
</table>

*\(p<0.05; \**p<0.01; ***p<0.001*

Positive effect sizes indicate higher rating of behavioural problems for RP children.

K=number of studies; ES=weighted effect size (d); \(I^2\)=ratio of true heterogeneity to total variation in observed effects; FSN=Rosenthal’s Fail-Safe N; r=correlation of sample sizes to ES (negative correlations indicate that ES may be overestimated (43)).

Note: No effect was found for feeding–externalizing (z=1.07; p>.05), feeding–internalizing (z=-0.11; p>.05), feeding–ADHD (z=1.05; p>.05), sleeping–externalizing (z=1.667; p>.05), multiple–ADHD outcomes (z=0.550; p>.05), and multiple–internalizing and externalizing outcomes (referred to only 1 study).
### Table 4 Meta-ANOVA of moderator variables

<table>
<thead>
<tr>
<th>Domain</th>
<th>Association</th>
<th>Moderator</th>
<th>$\hat{I}^2$</th>
<th>p-value</th>
<th>K</th>
<th>ES</th>
<th>Variance</th>
<th>95% Confidence Interval</th>
<th>FSN</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rating at follow-up</strong></td>
<td>Any RP – general BP</td>
<td>Expert</td>
<td>45.5</td>
<td>0.02</td>
<td>2</td>
<td>1.09</td>
<td>0.10</td>
<td>0.46</td>
<td>1.72</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mother</td>
<td></td>
<td></td>
<td>14</td>
<td>0.34</td>
<td>0.01</td>
<td>0.21</td>
<td>0.49</td>
<td>-1.00***</td>
</tr>
<tr>
<td><strong>RP assessment method</strong></td>
<td>Any RP - externalizing</td>
<td>Questionnaire</td>
<td>53.41</td>
<td>0.00</td>
<td>3</td>
<td>0.22</td>
<td>0.00</td>
<td>0.12</td>
<td>0.32</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interview</td>
<td></td>
<td></td>
<td>4</td>
<td>0.89</td>
<td>0.05</td>
<td>0.45</td>
<td>1.32</td>
<td>15</td>
</tr>
<tr>
<td><strong>Sample characteristics</strong></td>
<td>Any RP – general BP</td>
<td>Clinically referred</td>
<td>44.02</td>
<td>0.05</td>
<td>9</td>
<td>0.61</td>
<td>0.02</td>
<td>0.31</td>
<td>0.91</td>
<td>70</td>
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<tr>
<td></td>
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<td>Community based</td>
<td></td>
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<td>0.00</td>
<td>0.18</td>
<td>0.42</td>
<td>143</td>
</tr>
</tbody>
</table>

*p< 0.05; **p<0.01; ***p<0.001

$I^2$ = ratio of true heterogeneity to total variation in observed effects; K = number of studies; Mean ES = weighted ES (d); FSN=Rosenthal’s Fail-Safe N; r=correlation of sample sizes to ES (negative correlations indicate that ES may be overestimated (43)).