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FULL TITLE

Associations between problems with crying, sleeping, and / or feeding in Infancy and longterm 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

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.

There is a need of further studies to assess behavioural outcomes of former sleep, feeding, or multiple disturbed children.

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.

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)

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 (table1). 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. Comorbidity was reported in 9 studies, however only 5 studies analyzed multiple RP (table 1).

-- 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.

-- table 2 --

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

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 standaradized 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 metaregressions 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).

-- 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_{expert}=1.10 vs. ES_{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_{questionnaire}=.22 vs. ES_{interview}=.89; I^2 =53.41; p<.01) but not in respect to infant diaries. The association between

* The findings remained similar if samples with sleeping problems reported below 6 months were excluded.

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 (β =0.15; SE=0.08; p=.08), sleeping-general BP (β =0.35; SE=0.17; p<.05), sleeping-externalizing (β =0.39; SE=0.21; p=.06), and multiple-ADHD problems (β =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 (β =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 (β =0.06; SE=0.03; p<.05), crying–ADHD (β =0.07; SE=0.03; p<.05), and sleeping–general BP (β =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.(55) 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,(3, 56) 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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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.

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.

REFERENCES

- 1 Forsyth BW, Canny PF. Perceptions of vulnerability 3 1/2 years after problems of feeding and crying behavior in early infancy. *Pediatrics*. 1991;88:757-763.
- Von Hofacker N, Papousek M. Disorders of excessive crying, feeding, and sleeping: The Munich interdisciplinary research and intervention program. *Infant Ment Health J*. 1998;19:180-201.
- 3. Wolke D, Meyer R, Orth B, et al. Co-morbidity of crying and feeding problems with sleeping problems in infancy: concurrent and predictive associations. *Infant Child Dev*. 1995;4:191-207.
- DeGangi GA, Breinbauer C, Roosevelt JD, et al. Prediction of childhood problems at three years in children experiencing disorders of regulation during infancy. *Infant Ment Health J.* 2000;21:156-175.
- Forsyth BW, Leventhal JM, McCarthy PL. Mothers' perceptions of problems of feeding and crying behaviors. *American Journal of Diseases in Childhood*. 1985;139:269-272.
- 6 St James-Roberts I. Infant crying and sleeping: helping parents to prevent and manage problems. *Prim Care*. 2008;35:547-567.
- 7 ZERO-TO-THREE. Diagnostic classification of mental health and developmental disorders of infancy and early childhood revised edition. Washington: Zero to Three Press; 2005.

- Schmid G, Schreier A, Meyer R, et al. A prospective study on the persistence of infant crying, sleeping and feeding problems and preschool behavior. *Acta Paediatr*. 2010;99:286-290.
- 9 Stifter C, Braungart J. Infant colic: a transient condition with no apparent effects. *J Appl Dev Psychol.* 1992;13:447-462.
- 10 Sloman J, Bellinger DC, Krentzel CP. Infantile colic and transient developmental lag in the first year of life. *Child Psychiatry Hum Dev.* 1990;21:25-36.
- 11 St James-Roberts I, Conroy S, Wilsher C. Stability and outcome of persistent infant crying. *Infant Behav Dev.* 1998;21:411-435.
- DeSantis A, Coster W, Bigsby R, et al. Colic and fussing in infancy, and sensory processing at 3 to 8 years of age. *Infant Ment Health J.* 2004;25:522-539.
- Wolke D, Rizzo P, Woods S. Persistent infant crying and hyperactivity problems in middle childhood. *Pediatrics*. 2002;109:1054-1060.
- Scher A, Zuckerman S, Epstein R. Persistent night waking and settling difficulties across the first year: early precursors of later behavioural problems? *J Reprod Infant Psychol*. 2005;23:77-88.
- DeGangi GA, Porges SW, Sickel RZ, et al. Four-year follow-up of a sample of regulatory disordered infants. *Infant Ment Health J.* 1993;14:330-343.

- Olson SL, Bates JE, Sandy JM, et al. Early developmental precursors of impulsive and inattentive behavior: from infancy to middle childhood. *J Child Psychol Psychiatry*. 2002;43:435-447.
- 17 Barr RG. The normal crying curve: what do we really know? *Dev Med Child Neurol*. 1990;32:356-362.
- St James-Roberts I, Halil T. Infant crying patterns in the first year: normal community and clinical findings. *J Child Psychol Psychiatry*. 1991;32:951-968.
- 19 Postert C, Averbeck-Holocher M, Beyer T, et al. Five systems of psychiatric classification for preschool children: do differences in validity, usefulness and reliability make for competitive or complimentary constellations? *Child Psychiatry Hum Dev*. 2009;40:25-41.
- Wessel MA, Cobb JC, Jackson EB, et al. Paroxysmal fussing in infancy, sometimes called colic. *Pediatrics*. 1954;14:421-435.
- 21 Richman N. A community survey of characteristics of one- to two- year-olds with sleep disruptions. *J Am Acad Child Psychiatry*. 1981;20:281-291.
- Dahl M. Early feeding problems in an affluent society. III. Follow-up at two years: natural course, health, behaviour and development. *Acta Paediatr Scand*. 1987;76:872-880.
- Canivet C, Jakobsson I, Hagander B. Infantile colic. Follow-up at four years of age: still more "emotional". *Acta Paediatr*. 2000;89:13-17.

- Elliot MR, Pedersen EL, Mogan J. Early infant crying: child and family follow-up at three years. *Can J Nurs Res.* 1997;29:47-67.
- Neu M, Robinson J. Infants with colic: their childhood characteristics. *J Pediatr Nurs*. 2003;18:12-20.
- Papousek M, Wurmser H, von Hofacker N. Clinical perspectives on unexplained early crying: challenges and risks for infant mental health and parent-infant relationships. In: Barr RG, St James-Roberts I, Keefe MR. eds. *New evidence on unexplained early infant crying: it origins, nature and management.* New Jersey: Skillman; 2001.
- 27 Rao MR, Brenner RA, Schisterman EF, et al. Long term cognitive development in children with prolonged crying. *Arch Dis Child*. 2004;89:989-992.
- Rautava P, Lehtonen L, Helenius H, et al. Infantile colic: child and family three years later. *Pediatrics*. 1995;96:43-47.
- Savino F, Castagno E, Bretto R, et al. A prospective 10-year study on children who had severe infantile colic. *Acta Paediatr Suppl.* 2005;94:129-132.
- Lam P, Hiscock H, Wake M. Outcomes of infant sleep problems: a longitudinal study of sleep, behavior, and maternal well-being. *Pediatrics*. 2003;111:203-207.
- Thunstrom M. Severe sleep problems in infancy associated with subsequent development of attention-deficit/hyperactivity disorder at 5.5 years of age. *Acta Paediatr*. 2002;91:584-592.

- Zuckerman B, Stevenson J, Bailey V. Sleep problems in early childhood: continuities, predictive factors, and behavioral correlates. *Pediatrics*. 1987;80:664-671.
- Lindberg L. Long-term outcomes of early feeding problems related to infant behaviours, attachment, and maternal behaviours. *Paper presented at the 7th Congress of the World Association for Infant Mental Health*. 2000.
- Motion S, Northstone K, Emond A, et al. Persistent early feeding difficulties and subsequent growth and developmental outcomes. *Child Care Health Dev.* 2001;7:231-237.
- Becker K, Holtmann M, Laucht M, et al. Are regulatory problems in infancy precursors of later hyperkinetic symptoms? *Acta Paediatr*. 2004;93:1463-1469.
- Wake M, Morton-Allen E, Poulakis Z, et al. Prevalence, stability, and outcomes of cry-fuss and sleep problems in the first 2 years of life: prospective community-based study. *Pediatrics*. 2006;117:836-842.
- Achenbach TM, Edelbrock C, Howell CT. Empirically based assessment of the behavioral/emotional problems of 2- and 3- year-old children. *J Abnorm Child Psychol*. 1987;15:629-650.
- 38 Fleiss JR. *Statistical methods for rates and proportions*. 2nd ed. New York: John Wiley; 1981.
- 39 Cohen J. *Statistical power analysis for the behavioural sciences*. 2nd ed. Hillsdale NJ: Erlbaum; 1988.

- 40 Borenstein M, Hedges LV, Higgins JPT, et al. *Introduction to Meta-Analysis*: John Wiley & Sons, Ltd.; 2009.
- 41 Moran MD. Arguments for rejecting the sequential Bonferroni in ecological studies. *OIKOS*. 2003;100:403-405.
- 42 Rosenthal R. The file drawer problem and tolerance for null results. *Psychol Bull*. 1979;86:638-641.
- Levine R, Asada, K. Sample sizes and effect sizes are negatively correlated in metaanalyses: evidence and implications of a publication bias against nonsignificant findings. *Annual meeting of the international communication association*; 2007; San Francisco.
- Borenstein M, Hedges LV, Higgins JPT, et al. *Comprehensive meta-analysis Version*2. Englewood NJ: Biostat; 2005.
- Barkley RA. Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. *Psychol Bull*. 1997;121:65-94.
- El-Faddagh M, Laucht M, Maras A, et al. Association of dopamine D4 receptor (DRD4) gene with attention-deficit/hyperactivity disorder (ADHD) in a high-risk community sample: a longitudinal study from birth to 11 years of age. *J Neural Transm.* 2004;111:883-889.
- 47 Becker K, El-Faddagh M, Schmidt MH, et al. [Dopaminergic polymorphisms and regulatory problems in infancy]. *Z Kinder Jugendpsychiatr Psychother*. 2007;35:145-151.

- Raiha H, Lehtonen L, Huhtala V, et al. Excessively crying infant in the family: mother-infant, father-infant and mother-father interaction. *Child Care Health Dev*. 2002;28:419-29.
- 49 Rutter M, Quinton D. Psychiatric disorder: ecological factors and concepts of causation. In: McGurk M, ed. *Ecological factors in human development*. Amsterdam: Noord-Holland; 1977.
- Green JG, McLaughlin KA, Berglund PA, et al. Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: associations with first onset of DSM-IV disorders. *Arch Gen Psychiatry*. 2010;67:113-123.
- Taubman B. Clinical trial of the treatment of colic by modification of parent-infant interaction. *Pediatrics*. 1984;74:998-1003.
- Wolke D, Gray P, Meyer R. Excessive infant crying: a controlled study of mothers helping mothers. *Pediatrics*. 1994;94:322-332.
- Ramchandani P, Wiggs L, Webb V, et al. A systematic review of treatments for settling problems and night waking in young children. *BMJ* 2000;320:209-213.
- Kerwin ME. Empirically supported treatments in pediatric psychology: severe feeding problems. *J Pediatr Psychol*. 1999;24:193-214.
- Ferdinand RF. Validity of the CBCL/YSR DSM-IV scales Anxiety Problems and Affective Problems. *J Anxiety Disord*. 2008;22:126-134.

von Kries R, Kalies H, Papousek M. Excessive crying beyond 3 months may herald other features of multiple regulatory problems. *Arch Pediatr Adolesc Med.* 2006;160:508-511.

TABLE 1 Study characteristics: Samples and Definition of Regulatory Problems (RP) at baseline of included studies

Study	Partic	ipants	Age1	Sample	Type RP	RP Duration	M- tech1**	Informant RP	RP diagnosis criteria	SOC	Family1**	Number of risk factors	
	N _{RP}	N _{Control}										2401015	
Canivet et al. (2000)(23)	50	102	3	Comm	Crying	Transient	D/I	M	Wessel (1954)	No	-	1	
DeSantis et al., (2004)(12)	14 persistent RP	14 transient RP	2	Clin	Crying	Persistent	D/I	M	Number of hours of crying and/or fussing	No	-	2	
Elliot et al., (1997)(24)	10 RP	72	1.8	Comm	Crying	Transient	Q	M	Wessel (1954)	No	-	1	
Neu & Robinson (2003)(25)	20	20	2.5	Comm	Crying	Transient	I/Q	M	Minimum 2.8h/day crying for at least 3 days with 1 month	Yes	Parent-infant interaction	1	
Papousek et al. (2001)(26)	60	45	4.1	Clin	Crying	Persistent	D	M	Wessel (1954)	No	Psychosocial situation, maternal psychopathology, family functioning, parent-infant interaction	5	
Rao et al. (2004)(27)	9	165	2.4	Comm	Crying	Persistent	I/Q	M/E	Daily uncontrolled crying without any apparent reason for at least 2 weeks	No	-	2	
Rautava et al. (1995)(28)	338	527	3	Comm	Crying	Transient	Q	M/E	Colic questionnaire, Scores 1-3 (no colic); 4 (moderate colic); 5 (severe colic)	Yes	-	1	
Savino et al. (2005)(29)	48	48	2	Clin	Crying	Transient	-	-	Wessel (1954)	No	-	2	
St.James-Roberts et al. (1998)(11)	67 persistent RP (referred to colic)	38 evening criers 55 moderate criers	1	Comm	Crying	Transient	I/D	M	Modified Wessel (1954)	Yes	Parent-infant interaction, maternal psychopathology, family functioning	3	
Wolke et al. (2002)(13)	64	64	4	Clin	Crying	Persistent	D	M	Modified Wessel (1954)	Yes	-	2	
Lam et al. (2003)(30)	36	78	9	Comm	Sleeping	Transient	Q	M	Caregiver considers baby's sleep as problematic	Yes	Maternal psychopathology	2	
Scher et al. (2005)(14)	13 poor sleepers	12 good sleepers	3	Comm	Sleeping	Persistent	Q	M	Caregiver considers baby's sleep as problematic	No	-	2	
Thunstrom (2002)(31)	25	25	8.5	Comm	Sleeping	Transient	I/D	M	More than two night wakings/night; baby needs more than 15 min to fall asleep	No	Psychosocial situation, parent-infant interaction	4	
Zuckerman et al. (1987)(32)	23	33 transient RP	8	Comm	Sleeping	Persistent	I	M	More than 3 night wakings/night; baby needs	Yes	Psychosocial situation, maternal	3	

TABLES

									more than 1h to fall asleep (after night waking) or any problem causing severe disruption to the mother's sleep		psychopathology	
Dahl (1987)(22)*	25	25	7.8	Clin	Feeding	Transient	I/O	M/E	Refusal to eat (RTE) for at least 1 month without medical reason	No	Parent-infant interaction, psychosocial situation	1
Lindberg (2000)(33)	10	21	10.5	Clin	Feeding	Persistent	I/O	M/E	Minimum 1 month RTE	No	Psychosocial situation, parent-infant interaction	5
Motion et al. (2001)(34)	373	10669	1	Comm	Feeding	Transient	Q	M	Feeding difficulties with 4 weeks	No	-	1
Becker et al. (2004)(35)*	55	264	3	Clin	Crying / Sleeping / Feeding	Transient	I/O	M/E	1 SD above mean of one factor = isolated RP; 1 SD above mean at irritable and somatic functioning = multiple RP	Yes	Psychosocial situation, parent-infant interaction	4
DeGangi et al. (1993)(15)	9	13	9.5	Clin	Crying / Sleeping / Feeding	Transient	I/O	M/E	Crying: Difficulties with self- consoling, hypersensitive to new stimulations; baby needs more than 20 min to fall asleep, frequent night wakings (>2/night); baby shows distress at feeding time	No	-	2
DeGangi et al. (2000)(4)	22	38	18.5	Clin	Crying / Sleeping / Feeding	Transient	I/Q	M	Crying: Difficulties with self- consoling, hypersensitive to new stimulations; baby needs more than 20 min to fall asleep, frequent night wakings (>2/night); baby shows distress at feeding time	Yes	Parent-infant interaction	2
Forsyth & Canny (1991)(1)	115	205	4	Comm	Crying / Feeding	Transient	I	M	Caregiver considers baby's crying and feeding as a problem	Yes	-	2
Wake et al. (2006)(36)	84 RP (sleep problems) 55 RP (cry/fuss problems)	313	2 (crying) 8 (sleeping)	Comm	Crying / Sleeping	Transient	Q/D	M	Caregiver considers baby's crying and sleeping as a problem	Yes	-	1
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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.

 TABLE 2: Assessment of Behavioral outcomes in childhood of included studies

Study	Parti	cipants	Age2	Type BP	M-tech 2**	Informant BP	ES (d)	
•	N _{RP}	N _{Control}		• •			- (-)	
Canivet et al. (2000)(23)	50	102	4	E/I/ADHD	Rutter Preschool Questionnaire	M	.47	
DeSantis et al., (2004)(12)	14 persistent RP	14 transient RP	5.6	E/I/ADHD/G	Sensory Profile, Child Behavior Checklist (CBCL) & TRF (Teacher Report Form)	M/T	04	
Elliot et al., (1997)(24)	10 RP	72	3	G	CBCL	M	.21	
Neu & Robinson (2003)(25)	20	20	7	E/I/ADHD	Behavior Style Questionnaire (BSQ), ADHD Checklist of the Diagnostic Interview for Children and Adolescents, Revised, CBCL	M/E	.56	
Papousek et al. (2001)(26)	60	45	2.5	E/I	Infant Characteristics Questionnaire (ICQ), CBCL		.76	
Rao et al. (2004)(27)	9	165	5	ADHD	Personality Inventory for Children (PIC)	E	.97	
Rautava et al. (1995)(28)	338	527	3	Е	CBCL, Denver Development Screening Test (DDST)	M	.26	
Savino et al. (2005)(29)	48	48	10	E	-	M	1.31	
St.James-Roberts et al. (1998)(11)	67 persistent RP (referred to colic)	38 evening criers 55 moderate criers			M/E	.46		
Wolke et al. (2002)(13)	64	64	9.7	E/I/ADHD/G	Strength and difficulties questionnaire (SDQ)	M/C/T	.64	
Lam et al. (2003)(30)	36	78	3.6	E/I	CBCL	M	.34	
Scher et al. (2005)(14)	13 poor sleepers	12 good sleepers	3.5	G	CBCL	M	.88	
Thunstrom (2002)(31)	25	25	5.5	ADHD	Psychomotor Questionnaire (PPQ), Preschool Questionnaire (PSQ), Griffiths' Developmental Scale II, Scandinavian motor-perceptual scale (MPU), Standardized interview schedule for criteria for ADHD	M/E	1.67	
Zuckerman et al. (1987)(32)	23	33 transient RP	3	E/I/ADHD	BSQ	M	.98	
Dahl (1987)(22)*	25	25	2	E/I/ADHD	Preformulated list: Sleeping problems, shyness/fears, whining, hyperactive and restless, tempers	M	1.07	
Lindberg (2000)(33)	10	21	7.5	I/G	Rutter Child Questionnaire Emotionality, Activity, Sociability (EAS)	M/T	.09	
Motion et al. (2001)(34)	373	10669	3.9	E/ADHD	SDQ	M	.21	
Becker et al. (2004)(35)*	55	264	6.4	ADHD/G	Mannheim Parent Interview	M/C/E	.34	
DeGangi et al. (1993)(15)	9	13	4	ADHD/G	Sensorimotor History Questionnaire	Е	1.82	
DeGangi et al. (2000)(4)	22	38	3	E/I	CBCL	M	.96	
Forsyth & Canny (1991)(1)	115	205	3.5	ADHD/G	Richman Behavior Checklist (BCL)	M	.08	

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, 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.

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

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

^{*}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); I²=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

Domain	Association	Moderator	I^2	p-value	K	ES	Variance	95% Conf	idence Interval	FSN	r
								LL	UL		
Rating at follow-up	Any RP – general BP		45.5	0.02							
		Expert			2	1.09	0.10	0.46	1.72	0	-1.00***
		Mother			14	0.34	0.01	0.21	0.49	156	-0.28
RP assessment method	Any RP - externalizing		53.41	0.00							
		Questionnaire			3	0.22	0.00	0.12	0.32	12	-0.76
		Interview			4	0.89	0.05	0.45	1.32	15	0.74
Sample characteristics	Any RP – general BP		44.02	0.05							
		Clinically referred			9	0.61	0.02	0.31	0.91	70	-0.23
		Community based			13	0.30	0.00	0.18	0.42	143	-0.28

^{*}p<0.05; **p<0.01; ***p<0.001 f' = 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)).