

ORIGINAL ARTICLE

Follow-up of infants with colic into childhood: Do they develop behavioural problems?

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Aim: To assess whether infants with colic (IC) demonstrate persisting developmental dysregulation into childhood, manifested as behavioural problems, and to determine if these behavioural problems are associated with parenting factors.

Methods: Preschool children with a history of IC at the age of 0–3 months, as defined by the Wessel criteria, were invited to participate in an observational follow-up study, in which their caregivers completed the Child Behaviour Checklist (CBCL). Raw scores and clinical-range scores on the internalising, externalising and total behavioural problems scales were compared with a Dutch normative sample using independent *t*-tests and Chi-square tests. For the clinical-range scores, multivariable logistic regressions (odds ratios [99% confidence interval, CI]) were used to adjust for confounders and to identify variables associated with behavioural problems.

Results: Two hundred and fifty-eight children with a history of IC (median age 5.1 (interquartile range, IQR 4.6–5.5) years, 51.9% boys) were included. The cases had a significantly higher adjusted risk (adjusted odds ratios (aORs) [99% CI]) of scoring in the clinical range of the emotionally reactive, internalising and total problems scale (2.96 [1.24–7.06]; 2.50 [1.35–4.62]; 2.98 [1.46–6.07], respectively). Internalising ($P < 0.001$), externalising ($P < 0.001$) and total ($P < 0.001$) behavioural problems in children with a history of IC were associated with higher parenting stress scores.

Conclusions: Children with a history of IC demonstrated significantly more internalising behavioural problems at preschool age compared to the norm sample. Specific advice and support need to be available for parents to understand and regulate the behaviour of their child, from infancy to childhood.

Key words: excessive crying; infancy; internalising behaviour; parenting stress.

What is already known on this topic

- 1 Infant colic (IC) has been shown to be linked to adverse development of the child and family functioning on the short term, including maternal postnatal depression, or in the long term, including behavioural problems.
- 2 Results, however, must be interpreted with caution because most studies are of retrospective nature, with a high risk of recall bias.

What this paper adds

- 1 A significantly higher percentage of preschool children with a history of IC have emotionally reactive, internalising and total behaviour problems compared to the norm group.
- 2 Internalising, externalising and total behavioural problems in children with a history of IC were associated with higher parenting stress scores.

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Excessive, inconsolable crying, often described as infant colic (IC), is a common concern for parents and health care providers. It causes 10% of all paediatrician or healthy baby clinic visits of infants aged 2 weeks to 3 months.^{1–3} Prevalence rates of infant colic range from 17 to 25%.⁴ Infant colic resolves spontaneously after 4–5 months of age in the majority of infants.⁵ Accordingly, some studies demonstrate an overall good prognosis without any long-term behavioural consequences in children who cried excessively in the first 3 months of life followed until the age of 4 years.^{6,7} However, other studies link infant colic to adverse development of the child and family functioning. In the short term, infant colic has been associated with increased maternal postnatal depression,⁸ decreased breastfeeding duration,⁹ and child abuse or shaken baby syndrome.^{10,11} In the long term, behavioural problems have been attributed to IC.^{12–14} A meta-analysis found that children with a history of excessive crying were more likely to experience general behavioural problems, internalising behavioural problems (i.e. anxiety, depression or withdrawal), externalising behavioural problems (i.e. aggressive or destructive behaviour) or ADHD.¹⁵ In addition, it was demonstrated that negative family characteristics increased these behavioural problems.¹⁵ Based on these results, it was questioned whether IC in isolation is only a small risk for childhood behavioural problems, compared to the relatively large influence of a negative family environment, such as parental stress or maternal mental health, on these behavioural problems.^{2,12,15} Results of the meta-analysis, however, must be interpreted with caution because most studies were of retrospective nature, with a high risk of recall bias.

In the present study, we conducted a structured observational prospective follow-up study of children with a history of IC who participated in a large randomised controlled trial (RCT) between 2001 and 2003, studying the effect of swaddling.¹⁶ It was our aim to assess whether parents reported more clinically relevant behavioural problems in their 3- to 5-year-old children with a history of IC compared to a Dutch norm sample. Furthermore, we assessed if behavioural problems in children with a history of infant colic were associated with maternal mental health during infancy or parental stress during childhood.

Methods

Study population and procedure

We conducted a prospective observational follow-up study between April and December 2006. Data were obtained from an RCT which was conducted between February 2001 and March 2003 at the Wilhelmina Children's Hospital in Utrecht, The Netherlands. Participants included in the original RCT were invited to participate in this prospective observational follow-up study. The original RCT assessed the effect of a standardised approach of regularity and stimulus reduction compared to the same approach supplemented with swaddling in excessively crying infants up to 12 weeks of age.¹⁶ The primary outcome focused on amount of crying in minutes per 24 h. Healthy infants with a maximum age of 12 weeks and 6 days born after a minimal gestational age of 32 weeks were included.¹⁶ All recruited infants fulfilled the modified Wessel criteria for excessive crying (i.e. crying for more than 3 h/24 h for at least 3 days in the

previous 3 weeks).¹⁷ Exclusion criteria were an increased risk of developmental dysplasia of the hip, and positive clinical response to a hypoallergenic diet. The design and all results of this RCT have been described in detail elsewhere.¹⁶

This follow-up study was exempt from the Medical Research Involving Human Subject Act according to the institutional review board of the University Medical Centre Utrecht. Between April and December 2006, all families of the 382 infants who completed at least 4 weeks of intervention of the original RCT and gave informed consent for follow-up, were approached for participation by mail. Parents were asked to complete two pen-and-paper questionnaires regarding behaviour of the child and parental stress.

Questionnaires

Socio-demographics

During the original RCT, a questionnaire was filled out regarding socio-demographics including date of birth, sex, the highest level of education achieved by both parents and parental country of birth. The educational level of the mothers was categorised as low, middle or high.¹⁸

Child Behaviour Checklist

At time of follow-up, parents completed the preschool forms for children aged 1.5–5 years of the Child Behaviour Checklist (CBCL 1.5–5) to assess behavioural and emotional problems.¹⁹ Additional detailed information on this questionnaire is shown in Data S1.

Normative sample

Data S2 demonstrates explicit information on the Dutch normative sample of the CBCL, which was used as comparison data for the CBCL results of the preschool children with a history of

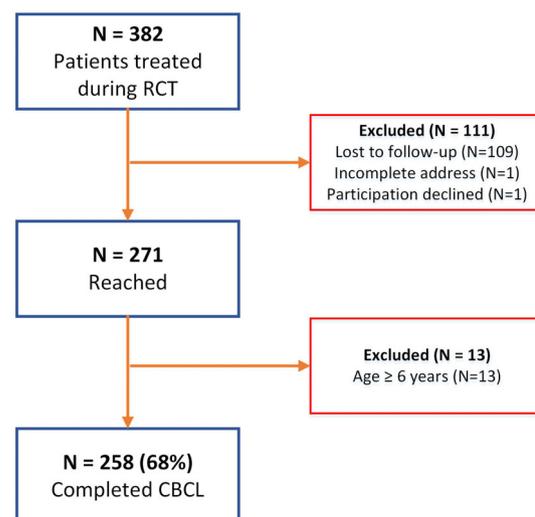


Fig. 1 Flow diagram of participating children with a history of infant colic.

IC. In total, 421 children of the Dutch normative sample were included.

Associated factors

Factors associated with behavioural problems were also assessed. Parental stress during childhood was measured at time of the follow-up study by use of the Nijmeegse Ouderlijke Stress Index-Kort (NOSI-K).²⁰ Maternal mental health during infancy was measured at the time of the original RCT by using the General Health Questionnaire-28 (GHQ-28).²¹ Data S1 depicts the detailed description of the two questionnaires.

Statistical analyses

First, baseline characteristics were compared between participants of this follow-up study and non-participants, that is, the

families who did participate in the original RCT, but were non-responders for this follow-up study. This was done using the Chi-square or Fisher's exact test. Second, differences in demographics between children with a history of IC (cases), and the CBCL Dutch norm sample (controls) were analysed using the Mann-Whitney *U*-test and Chi-square test. Differences on CBCL raw scale scores were analysed for better understanding of the severity of behavioural problems using independent *t*-tests and Cohen's *d* effect sizes were calculated based on means, SD's and sample sizes of the two groups. Effect sizes of 0.2, 0.5 and 0.8 were considered small, moderate and large, respectively.²² To evaluate clinically relevant behavioural problems, the percentage of children who scored in the clinical range of the CBCL scales was compared between the case group and the normative sample using the Chi-square test. Statistical significance was set at $P \leq 0.01$ to correct for multiple testing. In a univariable logistic regression model, the association between a history of IC and

Table 1 Baseline characteristics of the participants versus non-participants

	Participants (n = 258)	Non-participants (n = 124)	<i>p</i> Value
<i>Child factors</i>			
Gender (n,%)			0.595†
Boy	134 (51.9%)	68 (54.8%)	
Girl	124 (48.1%)	56 (45.2%)	
Gestational age (weeks)			0.012‡
<37	8 (3.1%)	12 (9.7%)	
≥37	250 (96.9%)	112 (90.3%)	
Birthweight (g)			0.012‡
<2500	8 (3.1%)	12 (9.7%)	
≥2500	250 (96.9%)	111 (89.5%)	
Missing	n/a	1 (0.8%)	
Apgar score			0.706‡
<8	5 (1.9%)	3 (2.4%)	
≥8	233 (90.3%)	103 (83.1%)	
Missing	20 (7.8%)	18 (14.5%)	
<i>Family factors</i>			
Mother age at child birth (years)			0.329†
<20	0 (0%)	1 (0.8%)	
20–40	255 (98.8%)	121 (97.6%)	
>40	3 (1.2%)	2 (1.6%)	
Education mother (n,%)			<0.001†
Low§	2 (0.8%)	9 (7.3%)	
Middle¶	139 (53.9%)	81 (65.3%)	
High††	117 (45.3%)	34 (27.4%)	
Ethnicity parents (n,%)			0.011†
Dutch‡‡	216 (83.7%)	89 (71.8%)	
Non-Dutch	41 (15.9%)	33 (26.6%)	
Missing	1 (0.4%)	2 (1.6%)	
Parity			0.909‡
First born	141 (54.7%)	67 (54.0%)	
Parents living together at child's birth			0.007†
Yes	250 (96.9%)	113 (91.1%)	
No	6 (2.3%)	11 (8.9%)	
Missing	2 (0.8%)	n/a	

† Chi-square test. ‡ Fisher's exact test. § Low = no education/primary school. ¶ Middle = pre-vocational secondary education/secondary vocational education/senior general secondary education/pre-university secondary education. †† High = higher professional education/university. ‡‡ Defined as: both parents are born in the Netherlands.

behavioural problems on all problem scales of the CBCL was analysed. In a multivariable model, this association was adjusted for the following variables: age, gender, education of the mother and ethnicity of the parents. Each potential confounder was added to the model individually (model 1), and retained if the regression coefficient of the central determinant (case or Dutch norm sample) changed at least 10% (model 2). Finally, a second logistic regression model was used to assess which factors were associated with behavioural problems on all problem scales of the CBCL in children with a history of infant colic. First, univariable logistic regression was performed on possible associated factors. Factors with a significance level of $P < 0.05$ were then included in the multivariable logistic regression model. Statistical significance for the outcomes of the multivariable logistic regression models was set at $P \leq 0.01$ to correct for multiple testing. Odds ratios (ORs) and their corresponding 99% confidence intervals (CIs) were calculated.

All analyses were performed using IBM SPSS Statistics 25 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Response rate

Figure 1 depicts the flow diagram of the study. Of the 382 infants who completed at least 4 weeks of intervention during the RCT, 1 family address was not complete and 1 family refused to participate in a future follow-up study. Of the 380 eligible families, 271 (71%) responded. Of the 271 responders, 13 were excluded as they exceeded the age limit for the CBCL. In total, 258 children

with a history of IC were included, with a mean (SD) follow-up of 4.89 (0.55) years after treatment. Table 1 demonstrates baseline characteristics of participants ($n = 258$) versus non-participants, that is, non-responders ($n = 124$). Participants had significantly higher educated mothers compared to the non-participants ($P < 0.001$). Furthermore, more parents of the participants lived together at the child's birth ($P = 0.007$).

Children with a history of IC compared with CBCL norm group (N = 679)

Demographics

Study participants had a significantly higher median age than the normative sample (5.1 years (interquartile range, IQR 4.6–5.5) vs. 4.5 (IQR 3.7–5.3), $P < 0.001$) (Table S1). Educational level of the mothers of the study group was significantly higher compared to the norm group ($P = 0.001$). In addition, significantly more parents of children with a history of IC were both born in the Netherlands, compared to the norm group (84% vs. 77%, $P = 0.030$). In the study group, mothers completed the CBCL in 81% of the cases, and in the normative sample, the mother was the informant in 98% of the cases.

CBCL raw scale scores

Children with a history of IC had higher levels of internalising behavioural problems compared to the norm group, reflected by statistically significant higher mean scores on the anxious/depressed and withdrawn syndrome scales ($P = 0.009$ and $P < 0.001$, respectively) (Table S2). Effect sizes on these two scales were small ($d = 0.22$ and $d = 0.31$, respectively). No

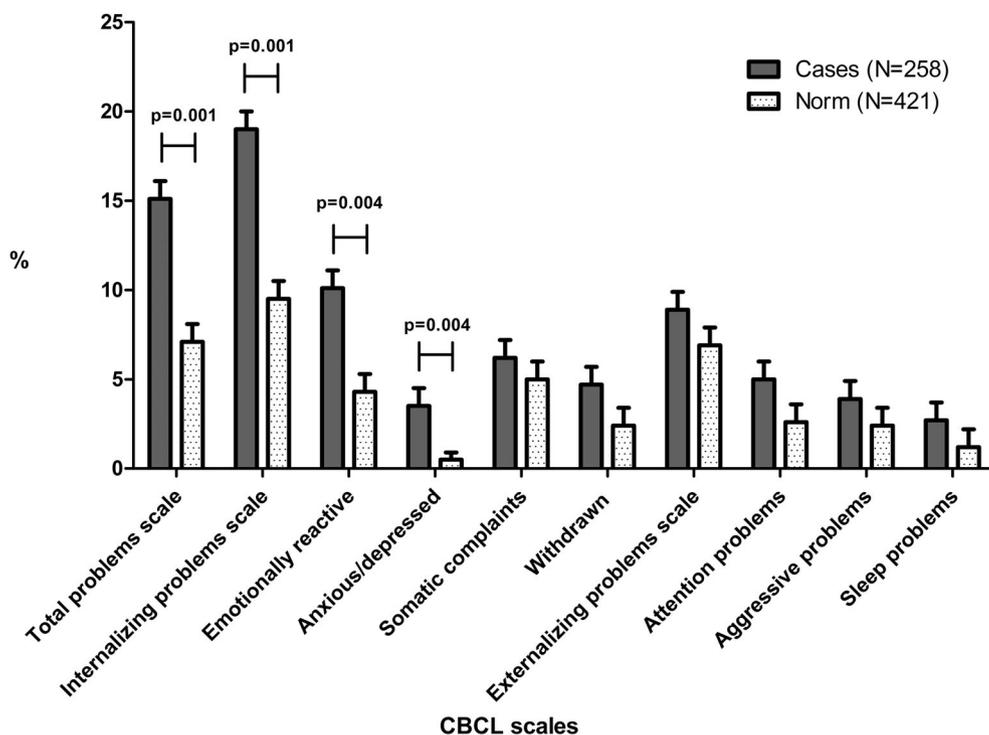


Fig. 2 Percentages of cases compared to the norm group scoring in the clinical range of the Child Behaviour Checklist (CBCL) scales.

significant differences between the two groups were found for externalising or total behavioural problems.

CBCL clinical scores

The percentage of children scoring in the clinical ranges of the CBCL scales is shown in Figure 2. Children with a history of IC scored significantly more often in the clinical range of the emotionally reactive, anxious/depressed, internalising problems and total problems scale (10.1% vs. 4.3%, $P = 0.004$; 3.5% vs. 0.5%, $P = 0.004$; 19.0% vs. 9.5%, $P = 0.001$; and 15.1% vs. 7.1%, $P = 0.001$, respectively) compared to the Dutch norm sample.

Association between a history of IC and behavioural problems

In a multivariable logistic regression model, the confounders age, gender, education of the mother and ethnicity of the parents were added separately to adjust the association between a history of IC and the aforementioned behavioural problems. For the emotionally reactive, internalising problems and total problems scale, maternal education was the only confounder that changed the regression coefficient for a history of IC by more than 10% (Table 2). After adjusting for this confounder, the risk (adjusted odds ratios (aORs) [99% CI]) for the cases of scoring in the clinical range of the emotionally reactive, internalising problems and total problems scale remained significant (2.96 [1.24–7.06]; 2.50 [1.35–4.62]; 2.98 [1.46–6.07]).

Children with a history of IC ($N = 258$)

Association between behavioural problems and other variables in children with a history of IC

The NOSI-K total score (parental stress) during follow-up was significantly associated with the emotionally reactive ($P < 0.001$), anxious/depressed ($P < 0.001$), withdrawn ($P = 0.001$), attention problems ($P < 0.001$), aggressive behaviour ($P < 0.001$), internalising ($P < 0.001$), externalising ($P < 0.001$) and total problems ($P < 0.001$) scales (Table S3). In addition, parents who were non-Dutch perceived more sleep problems in their children compared to parents who were Dutch ($P = 0.006$).

Discussion

In this study, we found that preschool children with a history of infant colic had significantly higher mean scores on the anxious/depressed and withdrawn syndrome scales of the CBCL as perceived by the parents, compared to a Dutch norm sample. In addition, more children with a history of infant colic had emotionally reactive, internalising and total behaviour problems compared to the children of the norm group, even after adjusting for confounding factors. Moreover, these problems were associated with higher parental stress scores.

Our finding of a possible association between IC and emotionally reactive internalising behavioural problems during childhood is in line with previous studies.^{2,12,15} Contradictory to this, two other studies showed an overall good prognosis without any long-term behaviour consequences in children who cried excessively in the first 3 months of life followed till the age of 4 years.^{6,7} However, both studies had small sample sizes. Furthermore, the study by St. James-Roberts *et al.*⁶ assessed behavioural

problems at a younger age of 15 months, which might explain the difference in results.

We can only speculate about the explanations for the association between IC and parent-reported childhood internalising behavioural problems, in our study mainly reflected by higher emotional reactivity. It might be neurodevelopmental, as initial deficits in regulatory abilities and stimuli control, resulting in excessive crying, have been suggested to be early markers of inadequate or under-controlled behaviour in childhood.^{15,23} Indeed, infant colic has been linked to emotional dysregulation.²⁴ In turn, emotional dysregulation has been linked to internalising behavioural problems.^{25–27} This supports the hypothesis that neurodevelopmental vulnerability may underlie both IC as well as internalising behavioural problems later in life. Another explanation might be psychosocial, as excessive crying during infancy may complicate the bonding between infant and parents, potentially causing behavioural problems at later age,^{28,29} as has been demonstrated before.¹⁵

Our study showed that parent-reported internalising and total behavioural problems were related to higher parenting stress. This finding is in line with the study by Scholten *et al.*, who found that higher parental stress was significantly related to higher parental-reported CBCL scores in chronically ill children.³⁰ It might be hypothesised that parenting stress indirectly affects parental perception and thus reporting of problems of their child. However, the reverse might also hold true, as behavioural problems might influence parenting stress as well. To better objectify causality of behavioural problems during childhood, the use of the Caregiver-Teacher Report Form of the CBCL,³¹ or objective video behaviour assessment is recommended.

In the group of children with a history of IC, we did not find a relation between maternal mental health during infancy and parent-reported behavioural problems during childhood. Other studies have shown contradictory results, which may have been caused by different study designs.^{2,32–35} An impaired mother-child relationship has been suggested as the underlying mechanism for the association between maternal mental health problems and childhood behavioural problems.³⁶ However, due to the lack of follow-up of a control group in our study, it is difficult to draw firm conclusions on the association between maternal mental health during infancy and childhood behavioural problems in the specific group of children with a history of IC.

One of the strengths of this follow-up study is the relatively large number of participants. Furthermore, the presence of IC was assessed during the original study,¹⁶ thereby avoiding recall bias. Next, the response rate was 64%, which is in line with other follow-up studies in children with a history of IC with reported response rates ranging from 41 to 74%.^{12,37} Moreover, our response rate is significant after 3–5 years of follow-up, especially when compared to commonly reported response rates of 5–25% in large follow-up studies.³⁸ On the other hand, our response rate of 64% still indicates the need to take attrition bias and recruitment bias into account. Indeed, our drop-out analyses demonstrated that mothers of children who participated in our study were significantly higher educated compared to mothers of non-participating mothers, which has limited the conclusions following our study results.

A limitation of our study is the lack of a control group of healthy children, without a history of infant colic. Therefore, we

Table 2 Logistic regression model of behavioral problems predicted by a history of infant colic

CBCL scales		Total	Internalizing	Emotionally reactive	Anxious/depressed	Somatic complaints	Withdrawn	Externalizing	Attention	Aggressive	Sleep
<i>Univariable analysis</i>											
N = 679	OR (99% CI)										
Case versus norm group	2.32**	2.23**	2.51*	7.57*	1.26	2.01	1.32	1.98	1.66	2.32	
Cases (history of IC)	(1.20–4.50)	(1.24–4.04)	(1.12–5.69)	(1.00–57.32)	(0.52–3.04)	(0.65–6.16)	(0.63–2.80)	(0.68–5.80)	(0.51–5.34)	(0.51–10.63)	
<i>Multivariable analysis – Model 1</i>											
N = 679	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)
Case versus norm group	2.32	2.23	2.50	7.60	1.26	1.99	1.31	1.97	1.64	2.35	
Cases (history of IC)	(1.19–4.51)	(1.23–4.03)	(1.10–5.68)	(1.00–57.57)	(0.52–3.04)	(0.64–6.14)	(0.62–2.80)	(0.67–5.78)	(0.51–5.32)	(0.51–10.78)	
Adjusted for:	2.35	2.04	2.46	5.89†	1.45†	1.66†	1.46	2.27†	3.21†	3.10†	
Sex	(1.15–4.79)	(1.09–3.82)	(1.03–5.90)	(0.75–46.39)	(0.56–3.80)	(0.52–5.31)	(0.65–3.30)	(0.70–7.43)	(0.77–13.41)	(0.55–17.54)	
Female	2.98†	2.50†	2.96†	6.78	1.39†	2.30†	1.50†	2.57†	2.15†	3.41†	
Age in months	(1.46–6.07)	(1.35–4.62)	(1.24–7.06)	(0.89–51.59)	(0.56–3.42)	(0.72–7.39)	(0.69–3.26)	(0.81–8.08)	(0.62–7.43)	(0.66–17.66)	
Education mother	2.45	2.40	2.70	6.98	1.32	2.24	1.34	1.96	1.54	3.01†	
High	(1.23–4.82)	(1.32–4.38)	(1.17–6.22)	(0.92–52.96)	(0.55–3.21)	(0.70–7.13)	(0.62–2.88)	(0.67–5.76)	(0.50–5.14)	(0.63–14.31)	
<i>Multivariable analysis – Model 2</i>											
N = 679	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)	aOR (99% CI)
Case versus norm group	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Cases (history of IC)	N.A.	N.A.	N.A.	5.89 (0.75–46.39)	1.62 (0.60–4.34)	1.90 (0.57–6.34)	N.A.	N.A.	3.09 (0.86–11.06)	4.41 (0.95–20.43)	7.90 (0.93–66.98)
Adjusted for:	2.98**	2.50**	2.96*	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Sex	(1.46–6.07)	(1.35–4.62)	(1.24–7.06)	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Female	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Age in months	2.98**	2.50**	2.96*	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Education mother	(1.46–6.07)	(1.35–4.62)	(1.24–7.06)	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
High	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Ethnicity parents	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Non-Dutch	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.

† Changed the regression coefficient of central determinant (case or control group) > 10%. * P < 0.01. ** P < 0.001. Model 1: all confounders were added to the univariable logistic regression model individually. Model 2: confounders of model 1 that changed the regression coefficient of the central determinant (case or control group) > 10%. aOR, adjusted odds ratio; CBCL, child behavior checklist; IC, infant colic; OR, odds ratio.

used the data of a Dutch norm sample of healthy, non-clinical children aged 3–5 years to compare the scores on the CBCL of the children with a history of IC.³⁹ However, the normative group differed significantly from the cases on several baseline characteristics, which hampers strong conclusions based on our findings. At the same time, we controlled for these differences by adjusting for these factors in our analyses. In addition, parental reporting of infant's crying and children's behaviour is susceptible for reporting bias. It has been demonstrated that maternal-reported dysregulation at 6 months was associated with maternal-reported behaviour problems at later age, but not with youth's self-reported problems.² In our study, the children were too young for self-reports and unfortunately we were not able to get assessments by daycare professionals, teachers or other informants. Therefore, our outcome only relies on the parental reports, mostly of the mothers, and could have been influenced by maternal psychological well-being and social factors. Furthermore, it could have been influenced by a persistent distortion of the early mother-child relationship. However, despite these limitations, our results demonstrate that the parents, and therefore their children, have higher levels of stress and mental health symptoms, and they therefore warrant more parental support.

Conclusion

In summary, we found that children with a history of IC had a significant higher risk for parent-reported emotionally reactive, internalising and total behavioural problems at preschool age compared to the norm sample. Furthermore, these problems were associated with higher parental stress. Despite the fact that our results should be interpreted cautiously due to selection and information bias, our findings suggest that parents of infants with colic need specific advice and support to regulate their infants behaviour. This might be given in the form of a training to address the principles of positive parenting, infant development, facing challenges as a parent and partner support.⁴⁰

References

- Akhnikh S, Engelberts AC, van Sleuwen BE *et al.* The excessively crying infant: Etiology and treatment. *Pediatr. Ann.* 2014; **43**: e69–75.
- Hyde R, O'Callaghan MJ, Bor W *et al.* Long-term outcomes of infant behavioral dysregulation. *Pediatrics* 2012; **130**: e1243–51.
- Benninga MA, Faure C, Hyman PE *et al.* Childhood functional gastrointestinal disorders: neonate/toddler. *Gastroenterology* 2016; **150**: 1443–1455.e2.
- Wolke D, Bilgin A, Samara M. Systematic review and meta-analysis: fussing and crying durations and prevalence of colic in infants. *J. Pediatr.* 2017; **185**: 55–61.e4.
- Barr RG, St. James-Roberts I, Keefe MR. *New Evidence on Unexplained Early Infant Crying: Its Origins, Nature and Management*. Skillman, NJ: Johnson & Johnson Pediatric Round Table Series; 2001.
- St. James-Roberts I, Conroy S, Wilsher C. Stability and outcome of persistent infant crying. *Infant Behav. Dev.* 1998; **21**: 411–35.
- Elliott MR, Pedersen EL, Mogan J. Early infant crying: child and family follow-up at three years. *Can. J. Nurs. Res.* 1997; **29**: 47–67.
- Vik T, Grote V, Escubano J *et al.* Infantile colic, prolonged crying and maternal postnatal depression. *Acta Paediatr.* 2009; **98**: 1344–8.
- Howard CR, Lanphear N, Lanphear BP *et al.* Parental responses to infant crying and colic: the effect on breastfeeding duration. *Breastfeed. Med.* 2006; **1**: 146–55.
- Reijneveld SA, van der Wal MF, Brugman E *et al.* Infant crying and abuse. *Lancet* 2004; **364**: 1340–2.
- Levitzky S, Cooper R. Infant colic syndrome—Maternal fantasies of aggression and infanticide. *Clin. Pediatr.* 2000; **39**: 395–400.
- Smarius LJCA, Strieder TGA, Loomans EM *et al.* Excessive infant crying doubles the risk of mood and behavioral problems at age 5: Evidence for mediation by maternal characteristics. *Eur. Child Adolesc. Psychiatry* 2017; **26**: 293–302.
- Canivet C, Jakobsson I, Hagander B. Infantile colic. Follow-up at four years of age: Still more “emotional”. *Acta Paediatr.* 2000; **89**: 13–7.
- 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**: 129–32.
- Hemmi MH, Wolke D, Schneider S. Associations between problems with crying, sleeping and/or feeding in infancy and long-term behavioural outcomes in childhood: A meta-analysis. *Arch. Dis. Child.* 2011; **96**: 622–9.
- van Sleuwen BE, L'hoir MP, Engelberts AC *et al.* Comparison of behavior modification with and without swaddling as interventions for excessive crying. *J. Pediatr.* 2006; **149**: 512–7.
- Wessel MA, Cobb JC, Jackson EB *et al.* Paroxysmal fussing in infancy, sometimes called colic. *Pediatrics* 1954; **14**: 421–35.
- Anon. Standaard Onderwijsindeling (SOI). Available from: <https://www.cbs.nl/nl-nl/onze-diensten/methoden/classificaties/onderwijs-en-beroepen/standaard-onderwijsindeling-soi> [accessed 1 February 2020].
- Achenbach T, Rescorla L. Manual for the ASEBA preschool forms & profiles: An integrated system of multi-informant assessment; Child Behavior Checklist for Ages 1 1/2-5; 2000.
- Brock De A, Vermulst A, Gerris J *et al.* NOSI-Nijmeegse Ouderlijke Stress Index, Handleiding experimentele versie [NOSI-Nijmeegse Parenting Stress Index, Manual experimental version]. Lisse: Swets & Zeitlinger; 1992.
- Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. *Psychol. Med.* 1979; **9**: 139–45.
- Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd edn. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
- 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**: 522–39.
- Stifter CA, Spinrad TL. The effect of excessive crying on the development of emotion regulation. *Infancy* 2002; **3**: 133–52.
- Southam-Gerow MA, Kendall PC. Emotion regulation and understanding: implications for child psychopathology and therapy. *Clin. Psychol. Rev.* 2002; **22**: 189–222.
- Eisenberg N, Cumberland A, Spinrad TL *et al.* The relations of regulation and emotionality to children's externalizing and internalizing problem behavior. *Child Dev.* 2001; **72**: 1112–34.
- Rieffe C, Oosterveld P, Miers AC *et al.* Emotion awareness and internalising symptoms in children and adolescents: The Emotion Awareness Questionnaire revised. *Personal. Individ. Differ.* 2008; **45**: 756–61.
- Korja R, Huhtala M, Maunu J *et al.* Preterm infant's early crying associated with child's behavioral problems and parents' stress. *Pediatrics* 2014; **133**: e339–45.
- Räihä 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.
- Scholten L, Willemsen A, Last B, *et al.* Behavior Problems in Children with Chronic Illness Applying for Psychosocial Care: Risk and Protective Factors. Available from: pdfs.semanticscholar.org
- Achenbach TM, Rescorla LA. *Manual for the ASEBA School-Age Forms & Profiles*. Burlington, VT: University of Vermont Research Center for Children, Youth, and Families; 2001.
- Leis JA, Heron J, Stuart EA *et al.* Associations between maternal mental health and child emotional and behavioral problems: Does

- prenatal mental health matter? *J. Abnorm. Child Psychol.* 2014; **42**: 161–71.
- 33 Gjerde LC, Eilertsen EM, Hannigan LJ *et al.* Associations between maternal depressive symptoms and risk for offspring early-life psychopathology: The role of genetic and non-genetic mechanisms. *Psychol. Med.* 2021; **51**: 441–9.
- 34 Hartman S, Eilertsen EM, Ystrom E *et al.* Does prenatal stress amplify effects of postnatal maternal depressive and anxiety symptoms on child problem behavior? *Dev. Psychol.* 2020; **56**: 128–37.
- 35 Breeman LD, Jaekel J, Baumann N *et al.* Infant regulatory problems, parenting quality and childhood attention problems. *Early Hum. Dev.* 2018; **124**: 11–6.
- 36 Nath S, Pearson RM, Moran P *et al.* The association between prenatal maternal anxiety disorders and postpartum perceived and observed mother-infant relationship quality. *J. Anxiety Disord.* 2019; **68**: 102148.
- 37 Bell G, Hiscock H, Tobin S *et al.* Behavioral outcomes of infant colic in toddlerhood: A longitudinal study. *J. Pediatr.* 2018; **201**: 154–9.
- 38 Toledano MB, Smith RB, Brook JP *et al.* How to establish and follow up a large prospective cohort study in the 21st century – Lessons from UK COSMOS. *PLoS One* 2015; **10**: e0131521.
- 39 Tick NT, van der Ende J, Koot HM *et al.* 14-year changes in emotional and behavioral problems of very young Dutch children. *J. Am. Acad. Child Adolesc. Psychiatry* 2007; **46**: 1333–40.
- 40 Popp L, Fuths S, Schneider S. The relevance of infant outcome measures: A pilot-RCT comparing baby triple P positive parenting program with care as usual. *Front. Psychol.* 2019; **10**: 2425.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Data S1. Description of Child Behavior Checklist (CBCL), NOSI-K and GHQ-28 questionnaires.

Data S2. Dutch normative sample of the Child Behaviour Checklist (CBCL)

Table S1. Baseline characteristics of the cases versus norm group

Table S2. Mean (SD) raw scale scores of cases compared to the Dutch normative sample on the Child Behaviour Checklist (CBCL) scales

Table S3. Logistic regression model of factors associated with behavioral problems in children with a history of infant colic