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The association of early regulatory problems with behavioral problems and cognitive functioning in adulthood: two cohorts in two countries

Dieter Wolke,[1,2] Nicole Baumann,[3,4] Julia Jaekel,[1,5] Riikka Pyhälä,[6] Kati Heinonen,[7] Katri Räikkönen,[8] Christian Sorg,[9,10,11] and Ayten Bilgin[1,12]

[1]Department of Psychology, University of Warwick, Coventry, UK; [2]Warwick Medical School, University of Warwick, Coventry, UK; [3]Department of Health Sciences, University of Leicester, Leicester, UK; [4]Turner Institute for Brain and Mental Health, School of Psychology Sciences, Monash University, Melbourne, Victoria, Australia; [5]Psychology, University of Oulu, Oulu, Finland; [6]Maternity and Child Health Clinics, City of Helsinki, Helsinki, Finland; [7]Psychology/Welfare Sciences, Faculty of Social Sciences, Tampere University, Tampere, Finland; [8]Department of Psychology and Logopedics, University of Helsinki, Helsinki, Finland; [9]Department of Neuroradiology and Klinikum rechts der Isar, Technische Universität München, Munich, Germany; [10]Department of Psychiatry, Klinikum Rechts der Isar, Technische Universität München, Munich, Germany; [11]TUM-NIC Neuroimaging Center Technische Universität München, Munich, Germany; [12]School of Psychology, University of Kent, Canterbury, UK

Background: Regulatory problems (RPs; excessive crying, sleeping, or feeding difficulties) that co-occur (i.e., multiple) or are persistent have been associated with cognitive and behavioral problems in childhood. However, it remains unknown if multiple or persistent RPs are associated with cognitive and behavioral problems in adulthood. **Methods:** This large prospective longitudinal study ($N = 759$) was conducted in two cohorts in Germany ($N = 342$) and Finland ($N = 417$). RPs were assessed at 5, 20, and 56 months via the same standardized parental interviews and neurological examinations. In young adulthood, questionnaires were used to assess behavioral problems. Cognitive functioning was assessed with IQ tests. We examined the effects of multiple or persistent RPs on the outcomes via analysis of covariance tests and logistic regression controlled for the influence of cohort. **Results:** Of 163 participants with RPs, 89 had multiple and 77 had persistent RPs. Adults who had early multiple or persistent RPs ($N = 151$) reported more internalizing ($p = .001$), externalizing ($p = .020$), and total behavioral problems ($p = .001$), and, specifically, more depressive ($p = .012$), somatic ($p = .005$), avoidant personality ($p < .001$), and antisocial personality problems ($p = .006$) than those who never had RPs ($N = 596$). Participants with multiple or persistent RPs were more likely to receive any ADHD diagnoses ($p = .017$), particularly of hyperactive/impulsive subtype ($p = .032$). In contrast, there were no associations between multiple or persistent RPs and IQ scores in young adulthood. **Conclusions:** The results indicate long-lasting associations between multiple or persistent RPs and behavioral problems. Thus, screening for early RPs could help to identify children who are at risk for later behavioral problems. **Keywords:** Regulatory problems; crying; sleeping; feeding; Bavarian Longitudinal Study (BLS); Arvo Ylppö Longitudinal Study (AYLS).

Introduction

Excessive crying beyond 3 months of age and feeding and sleeping problems beyond 6 months of age may be labeled as infant or early regulatory problems (RPs) (Bilgin et al., 2020; Cook et al., 2019). Approximately 20% of infants experience any of these RPs in the first year of life (Bilgin et al., 2020; Hemmi, Wolke, & Schneider, 2011), whereas a smaller group (i.e., 2–8%) have several RPs concurrently (i.e., multiple RPs) in infancy or persistently across more than one assessment point during early childhood (Bilgin et al., 2020; Cook et al., 2019; Winsper, Bilgin, & Wolke, 2020). It has been suggested that early RPs may indicate emerging problems in self-regulation with a core feature of having difficulties inhibiting a current state, such as self-soothing when crying, settling back to sleep at night and overcoming neophobia to new food (Cook et al., 2019; Hemmi et al., 2011). Furthermore, RPs are stressful and challenging for parents and can result in parental depression, stress, and fatigue (Petzoldt, Wittchen, Einsle, & Martini, 2016).

Although most early RPs are transient with no long-term consequences, there is increasing evidence that multiple RPs in infancy or persistent RPs are associated with an increased risk of dysregulation and behavioral and attention problems during childhood (Baumann et al., 2019; Cook et al., 2019; Hemmi et al., 2011; Hyde, O'Callaghan, Bor, Williams, & Najman, 2012; Schmid, Schreier, Meyer, & Wolke, 2010; Winsper et al., 2020). In addition, new evidence shows that this association between early multiple or persistent RPs and behavioral, psychiatric, and attention problems lasts into adolescence (Winsper et al., 2020) and even into adulthood (Bäuml et al., 2019; Bilgin et al., 2020; Jaekel et al., 2020). Moreover, studies focusing on temperamental traits related to multiple or persistent RPs such as negative emotionality and self-regulation

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provided evidence for long-term associations regarding the development of psychopathology in childhood and adolescence (Kostyrka-Allchorne, Wass, & Sonuga-Barke, 2020). On the other hand, the evidence regarding the association between early RPs and cognitive functioning in childhood has been contradictory with no studies investigating this link into adulthood (Baumann et al., 2019; Rao, Brenner, Schisterman, Vik, & Mills, 2004; Short et al., 2018).

Currently, the existing evidence on the association between multiple or persistent RPs and adult behavioral outcomes is limited to attention problems (self-report of attention problems, observed attention span, ADHD diagnoses) from one study in Germany (the Bavarian Longitudinal Study; BLS; Bilgin et al., 2020). In the current study, we use data from two large prospective longitudinal cohorts in two countries (Germany and Finland) that assessed RPs with identical measures in the early childhood years and have harmonized data on behavioral and cognitive outcomes in adulthood. Only those with multiple or persistent RPs were followed into adulthood given that the current study used a case–control design, and it was not possible to follow-up every participant until adulthood (i.e., lack of required funds). This decision was based on the evidence that multiple or persistent RPs have stronger associations with later behavioral problems than single RPs (Bilgin & Wolke, 2016; Cook et al., 2019; Hemmi et al., 2011). The aim of the current study was to investigate whether multiple RPs at age 5 months or persistent RPs over three time points (at least two of the following points: 5, 20 and 56 months) are associated with behavioral problems, and cognitive functioning in adulthood. We further aimed to replicate our previous finding of higher ADHD diagnoses in adults who had multiple or persistent RPs than those who never had RPs (Bilgin et al., 2020) in a larger sample.

Methods

Study design and participants

The Bavarian-Finnish Longitudinal Study (BFLS; Riegel, Ohrt, Wolke, & Österlund, 1995) is a prospective geographically defined birth cohort study of neonatal at-risk children born in Southern Bavaria, Germany (The Bavarian Longitudinal Study, BLS), between January 1985 and March 1986 (N = 7,505, 10.6% of all live births) and in the county of Uusimaa, Finland (Arvo Ylppö Longitudinal Study, AYLS) between March 1985 and March 1986 (N = 1,535), who required admission to a children's hospital within the first 10 days after birth. In addition, 916 and 658 healthy infants born at term in the same obstetric hospitals were recruited as controls in Germany and Finland, respectively.

Parents were approached within 48 h of the infant's hospital admission and asked to give written informed consent to participate. Ethical approval for the studies was granted by the ethics committees of the University of Munich Children's Hospital, the Bavarian Health Council (Landesärztekammer Bayern), the University Hospital Bonn, the Helsinki City Maternity Hospital, the Helsinki University Central Hospital, the Jorvi Hospital, and the Coordinating Ethics Committee of the Helsinki and Uusimaa Hospital District. Informed consent was obtained from parents (childhood) and participants (adulthood).

Bavarian Longitudinal Study. After the first phase of the study (birth to 56 months), the decision was made to reduce the sample size to allow for more intensive psychological and neurological assessments while preserving sufficient statistical power. Sampling criteria and dropout rates are provided elsewhere (Jaekel, Baumann, & Wolke, 2013).

For the prospective case–control follow-up study, we excluded (a) those participants who at any time had a single or non-persistent RPs, and (b) all cases with any missing data on crying, sleeping, or feeding problems at assessments 5, 20, and 56 months (N = 787, see Figure 1). Of the remaining eligible 708 participants (N = 138 with multiple or persistent RPs and N = 570 without any RPs at any time), we were able to follow up N = 83 with multiple or persistent RPs and N = 259 without RPs into adulthood.

Arvo Ylppö longitudinal study. Of the initial sample (N = 2,193), 2,086 participants were identified as alive and living in Finland in adulthood. For the prospective case–control study, 705 participants were identified with data on multiple or persistent RPs (crying, sleeping, or feeding/eating problems) measured at age 5, 20 and 56 months (N = 167 with multiple or persistent RPs and N = 538 without any RPs; Figure 1). Of those, 417 participants were assessed in adulthood, including N = 80 with multiple or persistent RPs and N = 337 without RPs.

In both cohorts, to ascertain that the controls were comparable to the group with multiple or persistent RPs, controls were selected and stratified according to gestational age, sex, and SES with a 3:1 ratio (Figure 1). Descriptive characteristic of the BLS and AYLS study participants are shown in Table 1.

Measures and outcomes

Multiple or persistent RPs from 5 to 56 months. At 5 months of age, pediatricians asked parents about their infant's crying, feeding, and sleeping problems via a standardized interview as part of a neurodevelopmental assessment. At 20 and 56 months, sleeping and eating problems were assessed via standardized parental interview and neurological examination of oral motor function both conducted by pediatricians, who were trained to achieve an inter-rater reliability >90% and received three-monthly booster workshops. The assessments at 5 and 20 months were carried out corrected for prematurity, and the assessment at 56 months was carried out according to chronological age. The definitions for crying, feeding, and sleeping problems at 5 months and sleeping and eating problems at 20 and 56 months have been described previously (Schmid et al., 2010) and are shown in Table S1.

Children with multiple RPs were those who had two or three RPs at 5 months (BLS: 13.2%, AYLS: 12.0%). Persistent RPs were defined as having at least one RP at 5, 20 and at 56 months of age (BLS: 14.3%, AYLS: 8.6%). Subsequently, multiple and/or persistent RPs were combined into one binary variable: 0 = never RPs, 1 = multiple or persistent RPs. For a detailed description of frequencies of RPs, see Table 1.

Behavioral problems in adulthood. At 26–30 years, participants reported on their behavioral problems using the German version of the Young Adult Self Report (YASR) (Achenbach, 1997) and the Finnish version of the Adult Self Report (ASR; Achenbach & Rescorla, 2003). Both questionnaires are part of the same Achenbach Assessment suite (ASEBA) with items of the same format. The YASR is composed of 116, while the ASR has 123 items on a scale ranging from 0 (not true) to 2 (very or often true).

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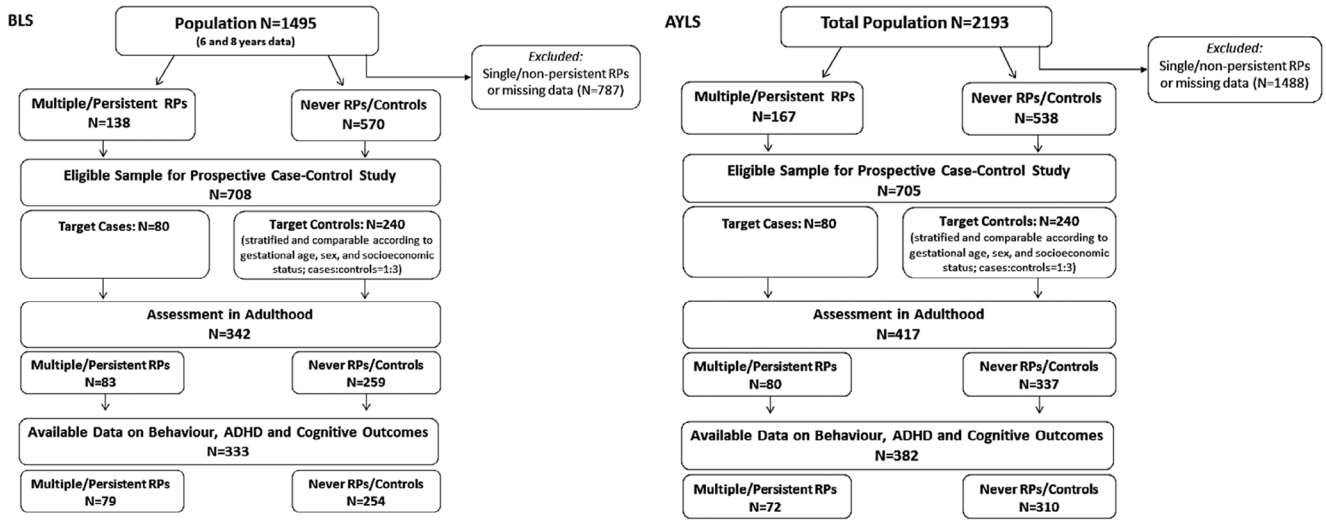

Figure 1 Flow diagram of Bavarian Longitudinal Study and Arvo Ylppö Longitudinal Study participants

The Ratings to Scores software by ASEBA (Achenbach, 2005) was used to compute raw scores and *T*-scores for scales according to the ASR form for both the ASR and YASR data. Consequently, all scores across both cohorts are based on the same items (Pyhälä et al., 2017). The ASR/YASR scales yielded three sum scales: internalizing, externalizing and total problems; and six Diagnostic and Statistical Manual of Mental Diseases, Fourth Edition (DSM-IV)-oriented scales: depressive, anxiety, somatic, avoidant personality, attention deficit/hyperactivity, and antisocial problems. Higher scores indicate more problems. Scores could be computed for 676 participants (BLS: $N = 333$, AYLS: $N = 343$).

Attention deficit/hyperactivity disorder (ADHD) diagnoses in adulthood. ADHD was assessed in adulthood with the DSM-IV based adult ADHD rating scales completed by participants in the BLS (Kooij et al., 2005) and AYLS (Kessler et al., 2005). These ADHD rating scales are considered a valid measure of ADHD and associated psychosocial impairment in adulthood (Kooij et al., 2005). Following guidelines by Kooij et al. (2005) adults exhibiting four out of nine inattentive symptoms or four out of nine hyperactivity/impulsivity symptoms 'often' or 'very often' are considered significantly impaired and classified as predominantly inattentive (ADHD-IA), predominantly hyperactive/impulsive (ADHD-HI), or ADHD combined type (ADHD-C). Complete data on ADHD scores in adulthood were available for 675 participants (BLS: $N = 333$, AYLS: $N = 342$). The harmonization of both ADHD rating scales is described in Appendix S1.

Cognitive functioning in adulthood. IQ in adulthood was tested using the short German version of the Wechsler Adult Intelligence Scale (WAIS III; von Aster, Neubauer, & Horn, 2006) and the short Finnish version of the Wechsler Adult Intelligence Scale-Revised (Ward, 1990).

In the BLS, intelligence tests were carried out by psychologists. The 6 subtests were vocabulary, similarities, letter-number-sequence, block design, matrix reasoning, and digit symbol coding. Cognitive functioning scores of the subtests were converted into age-normed IQ scores. In the AYLS, tests were carried out by psychology graduate students under the supervision of a licensed psychologist, and the 7 subtests were information, similarities, arithmetics, digit span, picture completion, matrix reasoning, and digit symbol. IQ scores were calculated according to Ward (1990). Complete verbal, performance and full-scale IQ Scores were available for $N = 647$, $N = 648$, $N = 646$ participants, respectively (BLS: $N = 302$, AYLS: $N = 347$, 346, 344).

Confounding variables. GA at birth was determined from maternal reports of the last menstrual period and serial ultrasounds during pregnancy. Information on family SES at birth was collected via structured parental interviews and computed as a weighted composite score derived from the occupation of the self-identified head of each family together with the highest educational qualification held by either parent into three categories of low, medium, and high SES. Evidence of childhood neurosensory impairment was collated from data indicating severe visual impairment (blindness), hearing impairment (uncorrected by assistive devices), severe cerebral palsy (grade 3 or 4), or childhood cognitive impairment (IQ < 2*SD*). If data regarding a certain neurosensory impairment variable were missing for a participant, the individual was categorized as having no evidence of the presence of that impairment. Data indicating the presence of neurosensory impairment were combined into a binary childhood neurosensory impairment variable (any evidence of impairment vs. no evidence of impairment; Eves et al., 2021). We also included participant's sex, age at assessment in adulthood, and cohort membership (BLS and AYLS) as further confounding variables.

Statistical analysis

All analyses were conducted with SPSS Version 22 (IBM SPSS Statistics, IBM Corporation). First, we conducted t-tests and chi-square tests to document sample characteristics and to investigate differences between those who had multiple or persistent RPs and who never had RPs. Statistical significance level was set at $p < .05$.

Second, to test the main effects of RPs on adulthood outcomes, we performed Analyses of Covariance (ANCOVAs) for behavioral symptoms (YASR/ASR) and IQ (WAIS-III/WAIS-R) and logistic regressions for ADHD diagnoses. Gestational age, sex, socioeconomic status, age at assessment in adulthood, neurosensory impairment, and cohort membership (BLS and AYLS) were included as covariates in all analyses. Effect sizes (η_p^2) were interpreted as follows: 0.02 = small, 0.13 = medium, 0.26 = large effects. To correct for the influence of multiple comparisons, the Benjamini–Hochberg procedure (Yoav & Yosef, 1995) was applied (i.e., using 25% false discovery rate). Two sets of sensitivity analyses were conducted. First, given the high percentage of preterm born individuals in our sample, main analyses were repeated using data of term (≥37 weeks gestational age) born adults only (see Table S2). Second, the main analyses were repeated separately for individuals with multiple versus persistent RPs (Tables S3 and S4).

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Table 1 Comparison of those with multiple or persistent regulatory problems (RPs) and those who never had RPs

	Never RPs $N = 596$ (78.5%)	Multiple/Persistent RPs $N = 163$ (21.5%)	p
Gestation (weeks): *M* (*SD*)	37.64 (3.57)	37.42 (3.83)	.50
Birth weight (g): *M* (*SD*)	3,042 (916)	2,904 (927)	.09
SGA <10%: *N* (%)	88 (14.8%)	37 (22.7%)	.016
Multiple births: *N* (%)	38 (6.4%)	10 (6.1%)	.91
Sex: *N* (%)			
Male	288 (48.3%)	86 (52.8%)	.32
Female	308 (51.7%)	77 (47.2%)	
Socioeconomic status: *N* (%)			
High	201 (33.8%)	55 (34.4%)	.10
Middle	265 (44.6%)	59 (36.9%)	
Low	128 (21.5%)	46 (28.7%)	
Complication scores: *M* (*SD*)			
Pre-pregnancy	1.23 (0.86)	1.31 (0.88)	.34
Prenatal	1.31 (1.22)	1.34 (1.39)	.73
Perinatal	2.95 (1.66)	2.88 (1.61)	.64
Neonatal	2.98 (3.35)	3.57 (3.64)	.053
Hospitalization (days): *M* (*SD*)	16.33 (24.82)	21.28 (30.21)	.06
Neurosensory impairment in childhood[a]: *N* (%)	17 (2.9%)	16 (9.8%)	<.001
Participant's age at assessment in adulthood: *M* (*SD*)	26.37 (1.61)	26.92 (1.92)	.001

SGA, Small for Gestational Age.
[a]Evidence of childhood neurosensory impairment was collated from data indicating severe visual impairment (blindness), hearing impairment (uncorrected by assistive devices), severe cerebral palsy (grade 3 or 4), or childhood cognitive impairment (IQ $< 2SD$).

Role of the funding source

The views expressed are those of the authors and not necessarily those of the German Federal Ministry of Education and Science (BMBF), the Academy of Finland, and the German Research Foundation (DFG). The funders had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. Two of the authors (DW; NB) have full access to all study data, and all authors take responsibility for the decision to submit for publication. All authors have approved the final version of the paper.

Results

Sample characteristics

There were no significant differences between adults with multiple or persistent RPs in infancy and early childhood and those who never had RPs with regards to the majority of perinatal, neonatal and childhood characteristics. However, more participants in the multiple or persistent RPs group were born small for gestational age (SGA) and had neurosensory impairment in childhood than participants in the never RPs group. In addition, those who had multiple or persistent RPs in early childhood were older at the time of the follow-up assessment in adulthood compared to those who never had RPs (Table 1).

Multiple or persistent RPs and adulthood behavioral problems, ADHD, and cognitive functioning

Adults who experienced multiple or persistent RPs reported more internalizing, externalizing, and total behavioral problems in adulthood in comparison to those who never had RPs (Table 2). Among the behavioral problems, only internalizing and total problems remained significant after correction for multiple comparisons. Moreover, multiple, or persistent RPs were associated with a higher risk of any ADHD diagnoses in adulthood, particularly of the hyperactive/impulsive subtype with only any ADHD diagnoses remaining significant after correction for multiple comparisons. In contrast, there were no significant differences between those with multiple RPs in infancy and those who never had RPs in terms of IQ scores in adulthood. (Table 2).

When we conducted the sensitivity analysis using only term-born participants (GA ≥ 37 weeks), the findings remained the same, except no associations were found between multiple or persistent RPs and ADHD diagnoses (Table S2). When we repeated the analyses separately for multiple RPs, there were significant differences between the two groups in internalizing, externalizing and total behavioral problems, but no associations with ADHD diagnoses (except a marginal significance for hyperactivity/impulsive subtype) and IQ scores (Table S3). Those with persistent RPs had more internalizing and total behavioral problems, as well as more any and inattentive ADHD diagnoses than those who never had RPs, but no associations were found with IQ scores in adulthood (Table S4).

Multiple or persistent RPs and adulthood scores in DSM-oriented scales (YASR/ASR)

Figure 2 illustrates that those who had multiple or persistent RPs in early childhood scored higher on depression, somatic symptoms, avoidant personality, and antisocial personality problems in adulthood than those who never had RPs.

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Table 2 Early *multiple or persistent* regulatory problems and adult behavioral and cognitive outcomes

	Never RPs ($N = 596$)	Multiple/ Persistent RPs ($N = 163$)	Main effect RPs p-value[a]	Main effect RPs partial η^2	Significant covariates (η^2)
YASR/ASR (T-scores)	$N = 535$	$N = 141$			
Sum scales					
Total problems	42.95 (10.12)	45.50 (10.06)	**.001**	.02	Male sex (.02), cohort (.07)
Internalizing problems	45.57 (11.30)	49.30 (12.09)	**.001**	.02	Male sex (.02)
Externalizing problems	45.64 (9.52)	47.30 (9.44)	**.020**	.01	Gestation (.01), male sex (.01), cohort (.04)
DSM-oriented Scales					
Depressive	53.92 (6.60)	55.23 (7.81)	**.012**	.01	Male sex (.03), cohort (.02)
Anxiety	51.56 (3.61)	52.06 (4.68)	.116	.00	Gestation (.01), male sex (.02)
Somatic	52.12 (4.58)	53.69 (5.41)	**.005**	.01	Male sex (.01), cohort (.01)
Avoidant personality	53.36 (5.86)	55.53 (7.15)	**<.001**	.02	Male sex (.01)
Attention deficit/ hyperactivity	52.43 (5.25)	52.93 (5.56)	.106	.00	Neurosensory impairment (.01), cohort (.10)
Antisocial personality	52.26 (4.31)	53.22 (5.62)	**.006**	.01	Male sex (.02), low SES (.01), cohort (.04)
ADHD, *n* (%)[b]	$n = 534$	$n = 141$			
Any	59 (11.0%)	27 (19.1%)	**.017**	n/a	./.
Inattentive	31 (5.8%)	14 (9.9%)	.086	n/a	Cohort[c]
Hyperactive/impulsive	42 (7.9%)	20 (14.2%)	**.032**	n/a	./.
Combined	14 (2.6%)	7 (5.0%)	.166	n/a	./.
IQ	$n = 507$/ 506/ 504	$n = 142$			
Verbal IQ	99.31 (14.68)	97.48 (15.15)	.934	.00	All covariates: gestation (.01), neurosensory impairment (.04), male sex (.02), low SES (.02), high SES (.05), age (.07), cohort (.03)
Performance IQ	97.51 (14.97)	96.48 (16.42)	.991	.00	Gestation (.02), neurosensory impairment (.08), low SES (.01), high SES (.01)
Overall IQ	98.27 (14.46)	96.58 (16.38)	.964	.00	Gestation (.02), neurosensory impairment (.07), male sex (.01), low SES (.02), high SES (.04), age (.02)

ASR, Adult Self Report; RPs, Regulatory Problems Data are mean (SD); YASR, Young Adult Self Report. Means are unadjusted, and all p-values are adjusted for gestational age, male sex, socioeconomic status, age at assessment in adulthood, neurosensory impairment in childhood and cohort effects. Partial η^2: 0.01 = small, 0.09 = medium and 0.25 = large effect. Bold indicates statistically significant p-values.

[a]Please note that the presented p-values are not corrected for multiple comparisons.

[b]To be consistent with the values for the other outcomes (unadjusted means and SDs and adjusted p-values), the Ns and percentages are based on chi-square (unadjusted) and the p-values on logistic regressions (adjusted for gestational age, male sex, socioeconomic status, age at assessment in adulthood, neurosensory impairment in childhood and cohort effects).

[c]Please note that η^2 is not available for ADHD diagnoses. However, the Odds Ratio (OR) for the covariate 'cohort' was OR = 3.41 (95% Confidence Interval: 1.30–8.97).

Analyses of term born adults showed that those with multiple or persistent RPs had higher scores on avoidant and antisocial personality scores than those who never had RPs, but no significant differences were found between the two groups on depressive, somatic and attention deficit/hyperactivity scores (Table S2). When individuals with multiple and persistent RPs were investigated separately, avoidant personality symptoms were found to be consistently higher in those who had RPs compared to those who never had RPs (Tables S3 and S4).

Discussion

This study investigated the association of multiple or persistent RPs in early childhood with adulthood behavioral problems and IQ using a combined sample of two cohorts in two countries. Adults who experienced multiple or persistent RPs in early childhood reported more internalizing and total behavioral problems, and any ADHD diagnoses in comparison with those who never experienced early RPs. In contrast, no differences in IQ scores were

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found between those who had multiple or persistent RPs and those who never had RPs.

The results support previous findings of the associations between early multiple or persistent RPs and behavioral problems in adulthood (Jaekel et al., 2020), and these effects were found in a combined sample of two cohorts in two countries. The associations between multiple or persistent RPs and internalizing and total behavioral problems were stronger than the association with externalizing problems which diminished after correction for multiple comparisons. The same pattern was found when the analyses were repeated including only term-born adults. The effect sizes were statistically significant but small explaining around 1–2% of unique variance. However, these effect sizes should be considered within the long timespan of individual development from infancy to adulthood. To illustrate, even the most stable characteristics in individuals, such as cognitive abilities or intelligence, have a correlation of r = .03 when tested with structured developmental assessment at 5 months and IQ at 26 years, which was not significant in the general population (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2015). The new findings presented here extend the results of previous studies which showed a link between early RPs and behavioral problems in childhood and adolescence (Baumann et al., 2019; Cook et al., 2019; Winsper et al., 2020).

Long-term follow up studies that span from infancy to adulthood and focus on early childhood crying, sleeping, and feeding problems and behavioral problems are rare. Currently, the only other additional evidence comes from a study in the UK that followed individuals from early childhood to adulthood and reported that severe but not moderate sleeping difficulties in early childhood were associated with depression in adulthood (Greene, Gregory, Fone, & White, 2015). This finding is in line with the results of the current study which indicate that adults who had multiple or persistent RPs are more likely to have DSM-oriented depressive symptoms than adults who did not have early multiple or persistent RPs. Furthermore, our results show that those who had early multiple or persistent RPs are more likely to have DSM-oriented somatic, avoidant, and antisocial personality symptoms, but not anxiety and attention deficit/hyperactivity symptoms. Furthermore, when we included only adults born at term, the results on behavioral problems and DSM-oriented scales remained similar, although term born adults with multiple or persistent RPs reported higher scores only in avoidant and antisocial personality symptoms compared to those who never had RPs. Thus, in line with the findings of a previous study (Bäuml et al., 2019), there is evidence that early RPs may be particularly associated with avoidant personality symptoms.

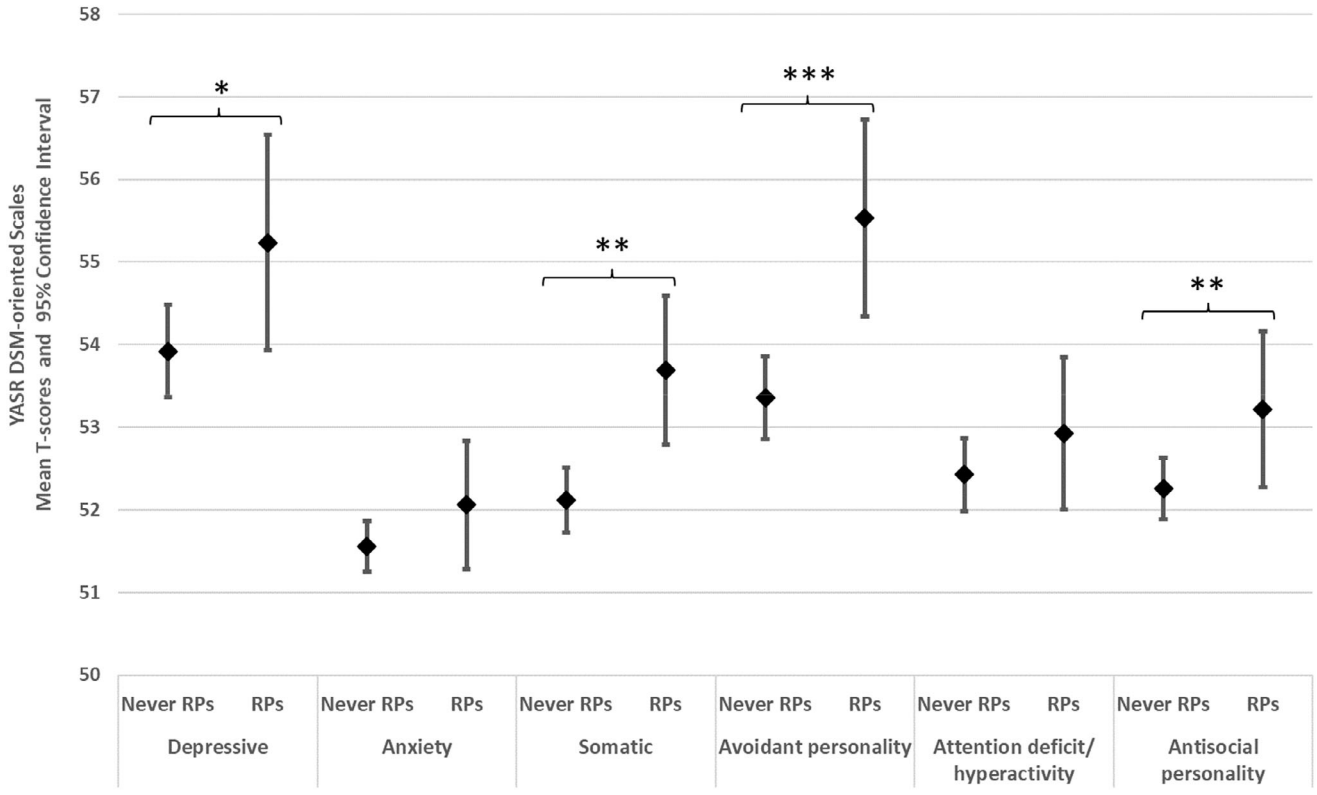

Figure 2 Early *multiple or persistent* regulatory problems and YASR/ASR DSM-oriented scales in adulthood. ASR, Adult Self Report; YASR, Young Adult Self Report. Please note that regulatory problems reflect multiple or persistent regulatory problems. Means are unadjusted, and all *p*-values are adjusted for gestational age, sex, socioeconomic status, age at assessment in adulthood, neurosensory impairment in childhood, and cohort effects. *p < .05, **p < .01, ***p < .001. Please note that the presented *p*-values are not corrected for multiple comparisons

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This particular association between early multiple or persistent RPs and personality disorder symptoms could be due to the comorbidities between anxiety (particularly social anxiety) and avoidant personality symptoms (Isomura et al., 2015), and between attention deficit/hyperactivity (particularly impulsivity symptoms) and antisocial personality symptoms (Cumyn, French, & Hechtman, 2009). We may speculate that personality disorder symptoms may indicate more severe difficulties than anxiety and attention deficit/hyperactivity symptoms. Furthermore, both avoidant and antisocial personality symptoms include difficulties in close relationships and are associated with parental neglect during the early years (Waxman, Fenton, Skodol, Grant, & Hasin, 2014). Parental neglect is also associated with the development of disorganized attachment, which predicts difficulties in social competence (Groh et al., 2014). Considering the evidence that multiple RPs are associated with disorganized attachment (Bilgin & Wolke, 2020), early multiple or persistent RPs might be particularly associated with the development of problems in social skills reflected as personality disorder symptoms (Winsper et al., 2020) in adulthood, particularly avoidant symptoms.

However, considering symptomatology in the context of normative development, it should be noted that these findings could also be attributed to the fact that symptoms of both externalizing problems and ADHD tend to decrease as individuals get older (Pyhälä et al., 2017). This and comorbidities with antisocial personality symptoms could further explain the variation of findings regarding ADHD in DSM-oriented and diagnostic scores. Adults who had early multiple or persistent RPs had more ADHD diagnoses than those who never had RPs as documented previously (Bilgin et al., 2020), while there were no significant differences on the DSM-oriented ADHD symptoms scale. However, when multiple and persistent RPs were analyzed separately, higher DSM-oriented ADHD symptoms were found in those who had multiple RPs, while higher diagnoses of ADHD were found in those who had persistent RPs. Thus, both multiple and persistent RPs might reflect underlying neurodevelopmental differences.

Although individuals with multiple or persistent RPs had, on average, higher behavioral problems in adulthood, they were not different than adults who never had early RPs in terms of their IQ scores. No previous studies have reported on the link between early multiple or persistent RPs and IQ scores in adulthood. However, a small association between sleep duration and cognitive development in children ($r = .06$) has been reported, suggestive of a link with verbal IQ but not fluid IQ (Short et al., 2018). Our results suggest that this small association between RPs in early childhood and cognitive functioning may not last into adulthood (Rao et al., 2004).

While we report here on direct associations of early RPs with behavioral problems in adulthood, a cascade model of the associations between early multiple or persistent RPs and behavioral problems across the life course has been recently suggested (Winsper et al., 2020). The cascade model suggests that early risk predictors cumulatively affect the development of maladaptive outcomes over time via influencing the regulation of behaviors in the next proximate phase of development, which in turn will dynamically affect the following stage (Bornstein, Hahn, & Wolke, 2013). Within this framework, we previously showed that the association of early RPs with attention problems in childhood is partly mediated by impaired inhibitory control in the second year of life (Baumann et al., 2019). Furthermore, in a large UK population study it was shown that early RPs in infancy/toddlerhood increased the risk of co-occurring internalizing and externalizing problem trajectories across childhood, which in turn increased the risk of psychopathology in adolescence such as depression and borderline personality disorder (Winsper et al., 2020). Thus, there is evidence that early RPs may be a risk factor for having problems in self-regulation affecting early inhibitory control, organization of attachment formation (Bilgin & Wolke, 2020), and subsequent dysregulation in behavioral and emotional control across childhood (Winsper et al., 2020). However, this requires further testing using data across multiple time points across the life course. Moreover, consistent with the theory of multifinality (Cicchetti & Rogosch, 1996), early RPs may be a global risk factor for various dysregulation trajectories with different psychopathological outcomes over the life course.

There are several potential explanations for how early multiple or persistent RPs can cascade into later psychopathological outcomes in adulthood. First, it is plausible that early RPs disrupt the quality of interaction between parent-infant dyads and socio-emotional relationships, which in turn influence the development of later psychological problems (Bilgin & Wolke, 2020; Jaekel et al., 2020). Second, early RPs may be linked to adulthood behavioral outcomes due to dysregulation of the Hypothalamic Pituitary–Adrenal (HPA) axis considering the evidence that RPs are associated with HPA axis dysregulation, and dysregulation of the HPA axis correlates with internalizing and attention problems (Scher, Zukerman, & Epstein, 2005). Third, there is evidence that early RPs are associated with reduced intrinsic functional connectivity of the default mode network in the brain, which is a domain general network involved in a wide range of functions and particularly relevant for the interactions of the individual with the social environment (Bäuml et al., 2019). Fourth, genetic vulnerability may explain the increased risk of behavioral problems and ADHD in children who had early RPs (Poustka et al., 2015), suggesting that early RPs might reflect manifestations of a genetic profile which first expresses itself as problems in self-

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regulation and then as behavioral problems at later stages of development. Finally, it has been suggested that disruptions in brain stem development during the prenatal period might be associated with the development of infant RPs (Geva & Feldman, 2008), which might contribute to the longitudinal associations between multiple or persistent RPs and adult behavioral problems. These suggested mechanisms call for future research.

The current study has several strengths, including the prospective design from infancy to adulthood, harmonized data from two cohorts in two countries, repeated measurement of early childhood RPs and a relatively large sample size that includes participants across the full spectrum of gestational age. Furthermore, the assessment of RPs was made via both clinical parent interviews and neurological examinations in both countries. However, there are also limitations. First, RPs were not assessed via structured diaries. However, this was not feasible in these two long-term prospective cohorts due to the often-reported high attrition rates in diary studies. Second, we reported adulthood outcomes only for individuals who had multiple or persistent RPs excluding those who had single RPs. This was due to lack of funding to follow up the whole sample until adulthood which resulted in a decision to focus on the highest risk group based on previous evidence (Hemmi et al., 2011). Third, the samples of both cohorts included participants who were born preterm (i.e., born before 37 weeks of gestation). However, we controlled for the influence of preterm birth in all analyses and conducted sensitivity analyses that replicated the findings while excluding those born preterm. Fourth, we were unable to consider the role of other potential conditions such as Autism Spectrum Disorder due to unavailability of this information across cohorts.

Conclusions

Multiple or persistent RPs experienced during early childhood are associated with increased behavioral problems and ADHD diagnoses in adulthood, but not with differences in IQ. These findings suggest that children with early RPs should be included in screening and intervention programs to help prevent long-term behavioral problems.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1. Description of the assessment of ADHD diagnoses.
Table S1. Definition of crying, feeding, and sleeping problems at 5, 20 and 56 months and assessment mode.
Table S2. Early ***multiple or persistent*** regulatory problems and adult behavioral and cognitive outcomes (Gestational age ≥ 37 weeks).
Table S3. Early ***multiple*** regulatory problems (at 5 months) and adult behavioral and cognitive outcomes.
Table S4. Early ***persistent*** regulatory problems (from 5 to 56 months) and adult behavioral and cognitive outcomes.

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Correspondence

Dieter Wolke, Department of Psychology, University of Warwick, Coventry CV4 7AL, UK;
Email: d.wolke@warwick.ac.uk

Key points

- Early childhood regulatory problems (RPs; excessive crying, sleeping, and feeding difficulties) occurring concurrently (i.e., multiple) or persistently are associated with behavioral problems in childhood and adolescence.
- The current study showed that multiple or persistent RPs are associated with more behavioral problems in adulthood, particularly internalizing problems. However, there were no associations between multiple or persistent RPs and cognitive functioning in adulthood.
- This evidence suggests that having multiple RPs as early as 5 months or persistent RPs spanning from infancy to early childhood may be the starting point of a pathway of dysregulation leading to behavioral problems still detectable in adulthood.
- The clinical implication of this finding is that screening for RPs could help identify children who are at risk for later behavioral problems.

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