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Emotion regulation trajectories in childhood, anorexia nervosa and atypical anorexia nervosa in early adolescence: a UK general population cohort study.

Mariella Henderson¹ MSc, Helen Bould^{2,3} PhD, Eirini Flour⁴ PhD, Amy Harrison⁴ PhD, Gemma Lewis¹ PhD, Glyn Lewis¹ PhD, Ramya Srinivasan¹ BMBCh, Jean Stafford¹ PhD, Naomi Warne² PhD, Francesca Solmi¹ PhD

¹ *UCL Division of Psychiatry, London, UK*

² *Centre for Academic Mental Health, Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK*

³ *Gloucestershire Health and Care NHS Foundation Trust, Gloucester, UK*

⁴ *UCL Institute of Education, London, UK.*

Corresponding author:

Francesca Solmi, PhD

UCL Division of Psychiatry,

Maple House, 6th floor, wing A

148 Tottenham Court Road

W1T 7NF, London, UK.

Email: Francesca.solmi@ucl.ac.uk

Phone: +44(0)2076799643

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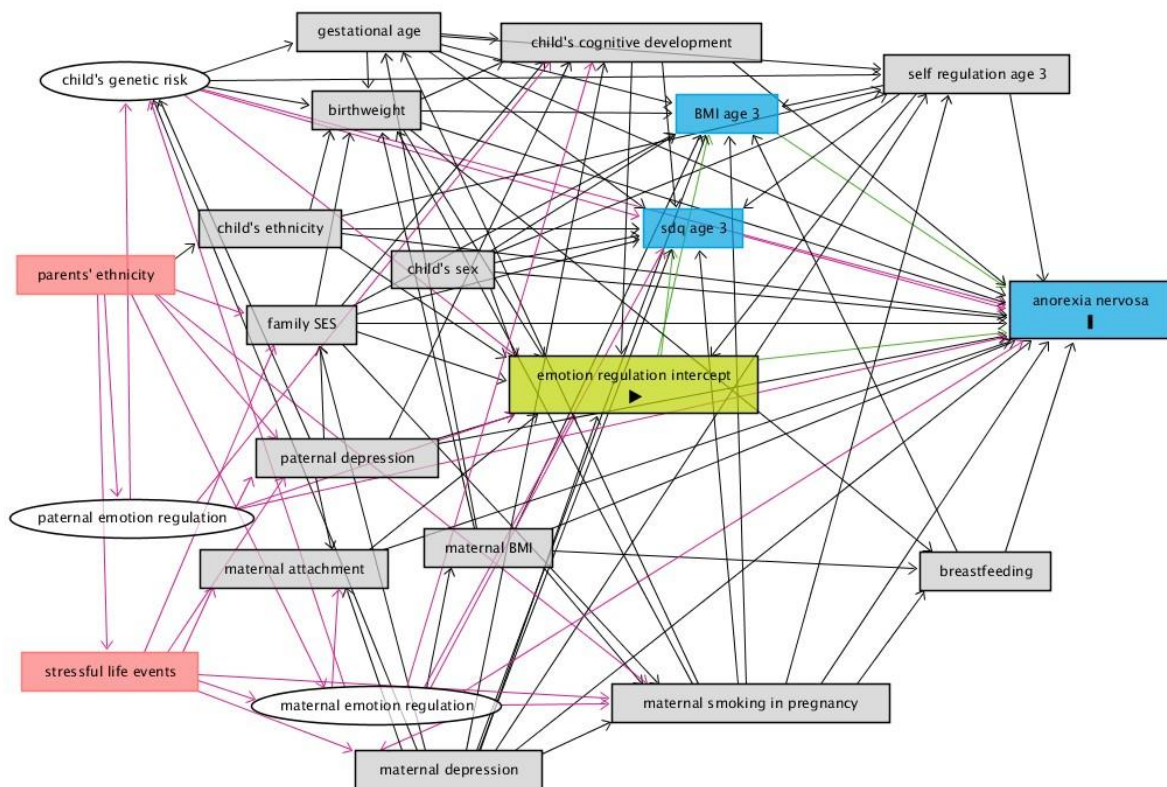
e-Method 1: Millennium Cohort study details

The Millennium Cohort Study (MCS) is an ongoing longitudinal population-based birth cohort study of children born between September 2000 and January 2002 who were living in the UK at nine months of age, and their families.¹ The latter were selected from the Department of Social Security's Child Benefit register, using a clustered stratified sampling design to ensure greater representation of infants from ethnic minority backgrounds and those living in more deprived areas of the UK. The initial recruited sample at MCS sweep one consisted of 18,552 families (72% of all eligible), including 18,818 children, 246 pairs of twins, and 10 sets of triplets². A further 692 eligible families (50% of those eligible for inclusion, but not included at sweep one) were recruited at MCS sweep two in 2004/2005 bringing the total sample to 19,244 families.² The Multi-Centre Research Ethics Committee (MREC) gave ethics approval for MCS.

e-Table 1. Child Social Behaviour Questionnaire (CSBQ) items

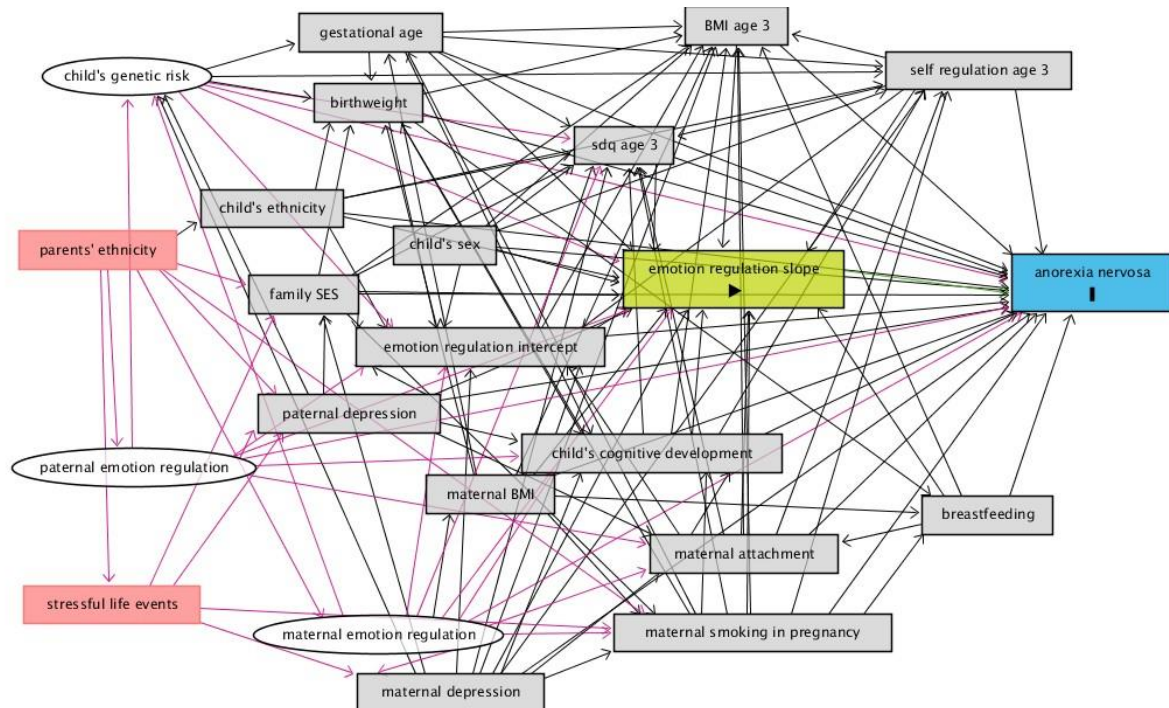
Subscale	Items	Scoring
Emotion Regulation	<p>Child:</p> <ul style="list-style-type: none"> a. Shows wide mood swings b. Gets over excited c. Is easily frustrated d. Gets over being upset quickly e. Is impulsive, acts without thinking 	<p>Caregiver scored how appropriate the statement was on a 3-point Likert scale:</p> <ul style="list-style-type: none"> 0. Not true 1. Somewhat true 2. Certainly true <p><i>Item d. is reversely scored.</i></p>
Cognitive Self-Regulation	<p>Child:</p> <ul style="list-style-type: none"> a. Likes to work things out for self b. Does not need much help with tasks c. Chooses activities on their own d. Persists in the face of difficult tasks e. Can move to a new activity after finishing a task 	<p>Caregivers scored how appropriate the statement was on a 3-point Likert scale:</p> <ul style="list-style-type: none"> 0. Not true 1. Somewhat true 2. Certainly true

e-Figure 1: Direct Acyclic Graph outlining our causal assumptions on the potential confounders of the association between predicted emotion regulation at age three years and broad anorexia nervosa at 14 years.



In this DAG the green rectangle represents the exposure (i.e. predicted emotion regulation intercept at age three years) and the blue rectangle with black borders is the outcome (i.e. anorexia nervosa). Blue rectangles are hypothesised mediators, which do not need to be controlled for in the analyses. All other variables in rectangles and circles represent potential confounders and the associations between them, which we explored. Variables in grey rectangles are those we were able to control for and those in white circles those that are not recorded in MCS and therefore cannot be adjusted for. Variables in red rectangles are those we considered, but which are not required to calculate the total effect of exposure on outcome. The earliest BMI and SDQ measurements were available at age 3 years, that is at the same time of our emotion regulation intercept measurement. When two variables are measured at the same time, it is difficult to disentangle the temporality of the association and ensure that confounder measurement refers to a factor preceding and causing the exposure. Hence, here, we had to impose our assumptions on the data. We assumed that at age 3 years BMI and mental health difficulties would be consequences, rather than causes, of emotion dysregulation, as there is evidence that the latter is associated with onset of mental health difficulties and high BMI.³⁻⁵ Nevertheless, we could also not exclude that emotion dysregulation could be a manifestation of mental health difficulties. Furthermore, there is evidence of potentially bi-directional associations between externalising symptoms and BMI.⁶ For this reason, in sensitivity analyses we also included these factors as confounders.

e-Figure 2: Direct Acyclic Graph outlining our causal assumptions on the potential confounders of the association between predicted change in emotion regulation between age three and seven years and broad anorexia nervosa at 14 years.



In this DAG the green rectangle represents the exposure (i.e. predicted emotion regulation intercept at age three years) and the blue rectangle with black borders is the outcome (i.e. anorexia nervosa). Blue rectangles are hypothesised mediators, which do not need to be controlled for in the analyses. All other variables in rectangles and circles represent potential confounders and the associations between them, which we explored. Variables in grey rectangles are those we were able to control for and those in white circles those that are not recorded in MCS and therefore cannot be adjusted for. Variables in red rectangles are those we considered, but which are not required to calculate the total effect of exposure on outcome.

e-Method 2: Confounder measurements

In order to obtain unbiased causal estimates of the association between emotion dysregulation and anorexia nervosa, it was necessary to control for any variable which could be hypothesised to cause both the exposure and the outcome and not lie on the causal pathway between exposure and outcome.^{7,8} We identified these measures based on previous literature and clinical observations and made our assumptions clear using DAGs (see eFigure 1 and eFigure 2).⁹ Below we provide a list of all confounders we included in the analyses and how these were measured. Child and family socio-economic and socio-demographic characteristics.^{10,11} Mothers reported on child's sex (male/female) and ethnicity (grouped according to Office for National Statistics categories: white/Black African or Caribbean/Asian/mixed/other). To measure family's socio-economic status, we used: maternal highest education (compulsory/non-compulsory), property ownership (own/rent/rent-free), family weekly income equivalised for number of family members using Organisation for Economic Co-operation and Development (OECD) criteria, and highest parental social class (manual/non-manual occupation). We also included a continuous indicator of maternal age. All of these were measured at the first MCS sweep when the child was nine months old.

Prenatal and perinatal confounders.¹²⁻¹⁸ At the first data collection sweep mothers also reported on child's birthweight (in Kilograms), gestational age (in weeks), their pre-pregnancy weight and their height from which we derived a measure of pre-pregnancy BMI, whether they ever breastfed their child (no/yes), and whether they smoked during pregnancy (never smoked/smoked but stopped during pregnancy/smoked during pregnancy).

Child's physical, cognitive and psychological confounders.^{6,19-22} Trained research assistants measured child's height and weight at age three years, from these we derived age- and sex-standardised BMI using IOTF growth charts.²³ At this age, mothers also reported on their child's cognitive self-regulation and mental health difficulties (i.e. internalising and

externalising behaviours). Cognitive self-regulation was assessed using five questions from the CSBQ (previously described in the section: *exposure* and **e-table 1**) and child's mental health using the Strengths and Difficulties Questionnaire (SDQ).²⁴ The SDQ is a validated scale capturing internalising (emotional symptoms and peer problems) and externalising (conduct, hyperactivity and inattention) problems through 20 questions scored on a three-point Likert scale (range 0 "not true" to 2 "certainly true"). Here, we used the total score ranging from 0 to 40, with higher scores denoting greater mental health difficulties. To capture child's cognitive development at baseline we also controlled for language development and school readiness. Trained researchers administered the British Ability Scales (BAS) naming vocabulary subtest, measuring child's expressive language ability,²⁵ and the Bracken School Readiness Test (BRST), measuring child's performance on six subtests relating to letters, numbers, colours, sizes, comparisons, and shapes. We used t scores for the BAS and the composite standard score of the BRST.

Parental psychological factors²⁶⁻²⁸: At the first sweep of data collection, when the child was 9 months, maternal attachment was measured using the sum of six items from the Condon maternal attachment questionnaire.²⁹ When the child was three years old, mothers and their partners reported their depressive symptoms, using the Kessler-6 scale.³⁰ The Kessler-6 scale includes six questions (scored 0 to 4) aimed at measuring psychological distress in the past month, and has strong psychometric properties and good internal consistency. We used the sum of the six questions, ranging from zero to 24, to measure parental psychological distress (higher scores indicating more symptoms).

e-Method 3: Multiple imputation.

In multiple imputation models we imputed 50 datasets using all variables included in the main models as well as a number of auxiliary variables. These were: child's BMI at age five, seven, 11, and 14 years; measures of self-harm, social support, social media use, sexual orientation, and depressive symptoms at age 14 years; child's total mental health difficulties

scores at ages age five, seven, 11, and 14 years; child's self-regulation scores at ages five and seven; maternal marital status; stratum and population weight variables.

e-Table 2: Characteristics of children with missing outcome data among those with complete exposure data (n=15,896)

	Missing outcome data at age 14 years		
	No n (%) n= 9,912	Yes n (%) n=5,984	p-value
Child's sex			
<i>Male</i>	4,976 (61.4%)	3,134 (38.6%)	
<i>Female</i>	4,936 (63.4%)	2,850 (36.6%)	0.008
Child's ethnicity			
<i>White</i>	8,355 (62.2%)	5,077 (37.8%)	
<i>Black</i>	289 (56.0%)	227 (44.0%)	
<i>Asian</i>	896 (68.8%)	407 (31.2%)	
<i>Mixed</i>	250 (54.4%)	210 (45.6%)	
<i>Other</i>	122 (65.9%)	63 (34.1%)	<0.0001
Highest parental social class			
<i>Non-manual</i>	6,511 (68.0%)	3,061 (32.0%)	
<i>Manual</i>	2,968 (54.4%)	2,491 (45.6%)	<0.0001
Housing tenure			
<i>Own</i>	6,528 (68.2%)	3,054 (31.9%)	
<i>Rent</i>	2,817 (52.9%)	2,510 (47.1%)	
<i>Living rent free</i>	552 (57.7%)	405 (42.3%)	<0.0001
Child was ever breastfed			
<i>No</i>	2,719 (54.1%)	2,306 (45.9%)	
<i>Yes</i>	7,184 (66.3%)	3,654 (33.7%)	<0.0001
Mother smoked during pregnancy			
<i>Never smoked</i>	6,781 (66.3%)	3,450 (33.7%)	
<i>Smoked but quit in pregnancy</i>	1,180 (58.2%)	846 (41.8%)	
<i>Smoked throughout pregnancy</i>	1,941 (53.7%)	1,677 (46.3%)	<0.0001
Maternal highest education			
<i>Compulsory</i>	5,853 (57.3%)	4,365 (42.7%)	
<i>Non-compulsory</i>	4,032 (71.8%)	1,584 (28.2%)	<0.0001
	Mean (SD)	Mean (SD)	
Maternal age at child's birth	29.84 (5.7)	28.43 (6.1)	<0.0001
Maternal pre-pregnancy BMI	23.69 (4.4)	23.72 (4.6)	0.761
Child's standardised BMI at age 3 years	0.58 (1.1)	0.67 (1.1)	0.0001
Child's SDQ total score at age 3 years	9.21 (5.1)	10.18 (5.5)	<0.0001
Child's emotion regulation intercept	4.34 (1.50)	4.60 (1.50)	<0.0001
Child's emotion regulation slope	-0.21 (0.17)	-0.19 (0.14)	<0.0001
Child's self-regulation score at age 3 years	2.47 (0.3)	2.45 (0.4)	0.0003
Child's birthweight (in Kg)	3.36 (0.6)	3.34 (0.6)	0.005
Child's gestation age (in weeks)	39.44 (1.9)	39.33 (2.1)	0.0002
Maternal depression (Kessler 6 scale)	3.14 (3.6)	3.43 (3.9)	<0.0001
Paternal depression (Kessler 6 scale)	2.80 (2.9)	2.85 (3.3)	0.460
Family weekly OECD-equivalised income	319.62 (206.2)	260.19 (180.0)	<0.0001
BAS-language scale at age 3 years	50.4 (11.3)	48.3 (11.1)	<0.0001
Maternal attachment	18.5 (2.5)	18.8 (2.5)	<0.0001
Bracken school readiness scale	105.4 (16.1)	101.1 (16.1)	<0.0001

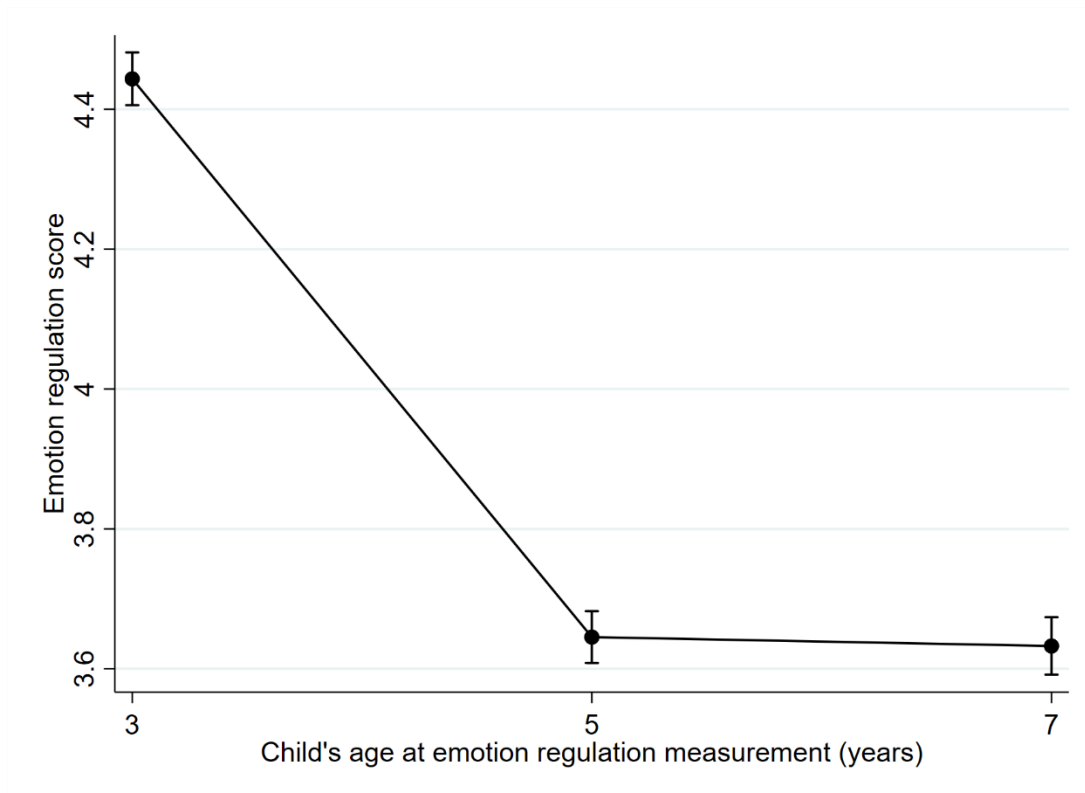
List of abbreviations: SDQ = strengths and difficulties questionnaire, OECD=Organisation for Economic Co-operation and Development, SD= standard deviation

e-Table 3: unconditional multilevel models used derive the exposures

	Models with age centred at 3 years (used to predict the random intercept)		Models with age centred at 5 years (used to predict the linear random slope)	
	Unconditional model 1	Unconditional model 2	Unconditional model 1	Unconditional model 2
Fixed effects				
<i>Age</i>	-0.20 (-0.21 to -0.19) p<0.0001	-0.59 (-0.63 to -0.56) p<0.0001	-0.20 (-0.21 to -0.19) p<0.0001	-0.20 (-0.21 to -0.19) p<0.0001
<i>Age</i> ²	-	0.10 (0.09 to 0.11) p<0.0001	-	0.10 (0.09 to 0.11) p<0.0001
<i>Constant</i>	4.30 (4.27 to 4.34)	4.44 (4.41 to 4.48)	3.89 (3.86 to 3.93)	3.64 (3.61 to 3.68)
Random effects				
<i>SD (age)</i>	0.30 (0.29 to 0.32)	0.32 (0.31 to 0.34)	0.30 (0.29 to 0.32)	0.32 (0.31 to 0.34)
<i>SD (constant)</i>	1.76 (1.72 to 1.79)	1.79 (1.75 to 1.82)	1.77 (1.75 to 1.80)	1.78 (1.76 to 1.81)
<i>covariance (age, constant)</i>	-0.08 (-0.11 to -0.05)	-0.11 (-0.14 to -0.08)	0.10 (0.08 to 0.12)	0.10 (0.08 to 0.12)
<i>AIC</i>	163799.6	163176.8	163799.6	163176.8
<i>BIC</i>	163850.9	163236.7	163850.9	163236.7

Fixed effects of these models show that emotion regulation scores decline overall between age 3 and 5, and remain stable afterwards between 5 and 7 years. Random effects coefficients indicate that there is greater variability between children in intercept values than there is in slope values.

e-Figure 3: overall emotion regulation trajectory in the sample (mean scores at each time point)



Error bars represent 95% confidence intervals. Higher scores represent greater emotion regulation difficulties.

e-Table 4: Proportion of sample with symptoms consistent with broad anorexia nervosa at age 14 years

	Total n(%)	Child's sex		Child's ethnicity	
		Males n(%)	Females n(%)	White n(%)	Ethnic minority ^a n(%)
<i>Anorexia nervosa (among those with complete exposure and available data at 14 n=9,912)</i>	97 (0.98%)	11(0.22%)	86 (1.74%)	85 (1.00%)	14 (0.80%)

^a Here we grouped all ethnic minority groups together, as – due to sample size – some cell sizes would have been n<5

e-Table 5: Results of univariable and multivariable logistic regression models testing the association between increases in emotion regulation *intercept* and *slope* and broad anorexia nervosa at age 14 years. Based on participants with complete exposure and outcome, imputing confounders (n=9,912)

Anorexia nervosa, 14 years	
Odds Ratio (95% confidence intervals), p-value	
Emotion regulation intercept	
Univariable model	1.25 (1.03 to 1.78), p=0.032
Adjusted model 1: child's sex and ethnicity	1.35 (1.03 to 1.78), p=0.032
Adjusted model 2: model 1 + birth-weight, gestational age, breastfeeding status; self-regulation, BAS language score, school readiness at age 3	1.35 (1.01 to 1.80), p=0.038
Adjusted model 3: model 2 + family SES ^a	1.31 (0.93 to 1.84), p=0.120
Adjusted model 4: model 3 + maternal pre-pregnancy BMI, smoking in pregnancy, maternal and paternal depression, maternal attachment	1.28 (0.90 to 1.80), p=0.160
Emotion regulation slope	
Univariable model	1.47 (1.19 to 1.98), p=0.001
Adjusted model 1: child's sex and ethnicity	1.53 (1.19 to 1.98), p=0.001
Adjusted model 2: model 1 + self-regulation & SDQ scores, BAS language score, school readiness, and BMI at age 3 years; gestational age, birthweight, breastfeeding status	1.51 (1.18 to 1.93), p=0.001
Adjusted model 3: model 2 + family SES ^a	1.50 (1.17 to 1.93), p=0.002
Adjusted model 4: model 3 + maternal pre-pregnancy BMI, maternal smoking in pregnancy, maternal & paternal depression, maternal attachment	1.49 (1.16 to 1.92), p=0.002
Adjusted model 5: model 4 + emotion regulation intercept	1.48 (1.16 to 1.88), p=0.002

^a includes maternal education and age, highest parental social class, weekly family OECD equivalised income, and housing tenure.

e-Table 6: Results of univariable and multivariable logistic regression models testing the association between increases in emotion regulation *intercept* and *slope* and broad anorexia nervosa at age 14 years. Based on participants with complete data.

	Anorexia nervosa, 14 years Odds Ratio (95% confidence intervals), p-value
Emotion regulation intercept (n=4,004)^a	
Univariable model	1.19 (0.85 to 1.67), p=0.312
Adjusted model 1: child's sex and ethnicity	1.26 (0.90 to 1.79), p=0.176
Adjusted model 2: model 1 + birth-weight, gestational age, breastfeeding status; self-regulation, BAS language score, school readiness at age 3	1.22 (0.83 to 1.79), p=0.310
Adjusted model 3: model 2 + family SES ^b	1.17 (0.75 to 1.83), p=0.483
Adjusted model 4: model 3 + maternal pre-pregnancy BMI, smoking in pregnancy, maternal and paternal depression, maternal attachment	1.14 (0.73 to 1.79), p=0.550
Emotion regulation slope (n=3,768)^a	
Univariable model	1.27 (0.88, 1.83), p=0.208
Adjusted model 1: child's sex and ethnicity	1.32 (0.91 to 1.91), p=0.139
Adjusted model 2: model 1 + self-regulation & SDQ scores, BAS language score, school readiness, and BMI at age 3 years; gestational age, birthweight, breastfeeding status	1.32 (0.93 to 1.89), p=0.122
Adjusted model 3: model 2 + family SES ^b	1.30 (0.92 to 1.85), p=0.138
Adjusted model 4: model 3 + maternal pre-pregnancy BMI, maternal smoking in pregnancy, maternal & paternal depression, maternal attachment	1.29 (0.93 to 1.81), p=0.132
Adjusted model 5: model 4 + emotion regulation intercept	1.29 (0.93 to 1.79), p=0.130

^a Sample size differs across models as analyses of emotion regulation slope also included BMI and SDQ scores at age 3, which are not included in intercept models and have different missingness patterns

^b includes maternal education and age, highest parental social class, weekly family OECD equivalised income, and housing tenure.

e-Table 7: Results of univariable and multivariable logistic regression models testing the association between emotion regulation scores at age 3, 5, and 7 years and symptoms of broad anorexia nervosa at age 14 years. Based on participants with complete exposure and imputed confounders and outcome at each individual time point.

	Exposure: emotion regulation		
	Age 3 years N=12,830	Age 5 years N=13,322	Age 7 years N=12,357
	Odds Ratio (95% confidence intervals), p-value	Odds Ratio (95% confidence intervals), p-value	Odds Ratio (95% confidence intervals), p-value
Outcome: Anorexia nervosa at 14 years			
Univariable model	1.01 (0.92 to 1.12), p=0.776	1.11 (0.98 to 1.25), p=0.085	1.17 (1.06 to 1.29), p=0.002
Adjusted model 1: child's sex and ethnicity	1.04 (0.95 to 1.15), p=0.433	1.15 (1.01 to 1.30), p=0.029	1.22 (1.10 to 1.35), p<0.0001
Adjusted model 2: model 1 + birth-weight, gestational age, breastfeeding status; self-regulation, BAS language score, school readiness at age 3	1.03 (0.93 to 1.14), p=0.558	1.14 (1.00 to 1.31), p=0.046	1.22 (1.10 to 1.36), p<0.0001
Adjusted model 3: model 2 + family SES ^a	1.00 (0.90 to 1.12), p=0.949	1.13 (0.97 to 1.31), p=0.120	1.21 (1.07 to 1.35), p=0.002
Adjusted model 4: model 3 + maternal pre-pregnancy BMI, smoking in pregnancy, maternal and paternal depression, maternal attachment	0.99 (0.89 to 1.11), p=0.910	1.12 (0.97 to 1.31), p=0.132	1.20 (1.06 to 1.35), p=0.003
Adjusted model 5: model 4+ BMI and SDQ at at previous wave	-	1.11 (0.95 to 1.31), p=0.199	1.19 (1.05 to 1.36), p=0.007

^a includes maternal education and age, highest parental social class, weekly family OECD equivalised income, and housing tenure.

e-Table 8: Results of univariable and multivariable linear mixed models, modelling trajectories of emotion regulation scores for adolescents with and without broad anorexia nervosa at age 14 years. Age centred at 5 years (n=15,896).

	Emotion regulation			
	Model 1: Univariable mean difference (95% CI)	Model 2: Multivariable mean difference (95% CI)	Model 3: Multivariable mean difference (95% CI)	Model 4: Multivariable mean difference (95% CI)
Fixed effects				
Broad anorexia nervosa at age 14 years				
No	Reference	Reference	Reference	Reference
Yes	0.25 (-0.14 to 0.64) P=0.215	0.25 (-0.09 to 0.60) P=0.150	0.33 (-0.05 to 0.67) P=0.061	0.38 (-0.05 to 0.80) p=0.080
Broad anorexia nervosa*age interaction		-	P=0.001	P=0.001
Broad anorexia nervosa*age ² interaction		-		P=0.652
Random effects				
SD (age 5)	0.32 (0.31 to 0.34)	0.32 (0.31 to 0.34)	0.32 (0.31 to 0.34)	0.32 (0.31 to 0.34)
SD (constant)	1.78 (1.76 to 1.81)	1.52 (1.50 to 1.55)	1.52 (1.50 to 1.55)	1.52 (1.50 to 1.55)
Corr (age 5/constant)	0.18 (0.14 to 0.21)	0.19 (0.15 to 0.22)	0.19 (0.15 to 0.22)	0.19 (0.15 to 0.22)

Univariable model also includes an indicator of child's age (centred at age 5 years) and age squared.

Multivariable model2 includes an indicator of child's age (centred at age 5 years) and age squared; child's: sex, ethnicity, birthweight, gestational age, self-regulation at age 3 years, British Ability Scale language score at age 3 years, school readiness at age 3. Maternal: age at child's birth, highest education, pre-pregnancy BMI, smoking in pregnancy, depressive symptoms at child's age 3, maternal attachment at child's age 9 months. Parental highest social class. Weekly family OECD equivalised income and housing tenure. Paternal depressive symptoms at child's age 3 years.

Multivariable model 3 = model 2 + interaction between linear age and broad anorexia nervosa

Multivariable model 4 = model 3 + interaction between quadratic age and broad anorexia nervosa

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