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Developmental trajectories of ADHD symptoms in a large population-representative longitudinal study

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Abstract

Background: Previous research has suggested that there is substantial heterogeneity in the developmental trajectories of ADHD symptoms. Sometimes qualitative distinctions between trajectories with different ages of onset and/or patterns of remission are made; however, little is known about the predictors and broader clinical meaningfulness of these candidate 'developmental subtypes' of ADHD symptoms. Methods: We applied latent class growth analysis to data from the UK Millennium Cohort Study (MCS; N=11,316; ages 3,5,7,11 and 14) to evaluate whether developmental trajectories of ADHD symptoms differing in early life predictors could be identified. Our optimal model included six trajectory groups, labelled unaffected (34.9% of the sample), mildly affected (24.1%), subclinical remitting (12.8%), pre-school onset partially remitting (14.1%), developmentally increasing (7.6%), and pre-school onset persistent (6.4%). Results: Factors such as gender, conduct problems, cognitive ability, maternal education, premature birth, peer problems, and school readiness scores differentiated between specific ADHD symptom trajectories. Conclusions: Taken together, our findings provide preliminary evidence that distinguishing different trajectories of ADHD symptoms could be clinically informative.

Keywords: attention deficit/hyperactivity disorder, developmental trajectories, onset, remission, persistence, latent class growth analysis

Developmental trajectories of attention-deficit/hyperactivity disorder (ADHD) symptoms can be highly heterogeneous (Asherson & Agnew-Blais, 2019) and there have been attempts to parse this into developmental. Traditional approaches have been based on *a priori* criteria such as whether supra-clinical threshold symptoms have an onset (or resolve) before a given age. Studies in this tradition have, for example, identified symptom severity, comorbidities, family disadvantage, and lower IQ as predicting belong to a 'persistent' rather than 'remitting' subtype (e.g., Caye, Spadini, et al., 2016); and poorer executive functions and comorbidities as predictors of 'later onset' symptoms among those who show few symptoms early in life (e.g., Manfro et al., 2019). Comparisons of 'late onset' and 'early onset' subtypes (defined as onset before age 7 in DSM-IV and before age 12 in DSM 5) have meanwhile mostly suggested similar patterns of impairment and treatment response but with some evidence for greater impairments among those with an earlier onset (e.g., Faraone et al., 2009; Reinhardt et al., 2007).

These *a priori* defined developmental subtypes may not, however, optimally reflect variation in ADHD symptom trajectories. Cut-offs for late onset ADHD, for example, are necessarily arbitrary, as symptoms can cross into the clinically significant range at a range of ages (Asherson & Agnew-Blais, 2019). Similarly, it is likely that there is long-term continuous variation in symptoms rather than abrupt onsets or remissions. An alternative approach that can take these forms of variation into account is to explore the trajectories of symptoms that emerge from longitudinal data drawing on data-driven techniques such as growth mixture modelling, latent class growth analysis, or group-based trajectory analysis (henceforth collectively 'trajectory analysis').

Only a small number of previous studies have used trajectory analysis to examine developmental subtypes of ADHD symptoms (Murray, Booth, Auyeung, et al., 2018; Murray et al., 2019; Pingault et al., 2011; Riglin et al., 2016; Sasser et al., 2015, 2016). In

many but not all cases, groups corresponding to the 'late onset', 'early onset persistent', 'early onset remitting', and 'unaffected' groups commonly specified in *a priori* definitions have emerged using these more data-driven approaches. However, the specific developmental trajectories that correspond to these groups vary dependent on characteristics such as the nature of the sample, measurement methods, and developmental period covered.

Irrespective of the approach used to define the trajectory groups, making qualitative distinctions between different trajectories is arguably only clinically useful to the extent that these distinctions are related to etiological and risk factors, prognoses, and treatment responses such that they can help provide guidance on the best treatment options and likely support needs of an individual. Within the trajectory analysis approach; however, only a handful of studies have examined the clinically relevant correlates of group membership. Riglin et al., (2016) found that low IQ, social communication problems, pragmatic language impairment, and conduct problems in childhood, as well as polygenic risk scores for ADHD were higher in their persistent relative to childhood-limited (remitting) category, while Sasser et al. (2016) identified aggression and hyperactivity at school and emotional dysregulation at home as predictors of being in their persistent relative to remitting category. Pingault et al., (2011) identified poorer academic outcomes in their early onset persistent compared to their later onset group while Murray et al. (2017) found that their later onset group had lower levels of childhood anxiety, reactive aggression, and risk-taking as compared to their earlier onset/persistent group. The latter was, however, true only for inattention and not hyperactivity/impulsivity trajectories. In the same sample, Murray et al. (2018) found that psychosocial impairments in late adolescence tended to be more severe for those who had early onset/persistent symptoms compared to a later onset. There is also preliminary evidence that females are more likely to show later onsets of ADHD symptoms than males (Malone et al., 2010; Murray et al., 2019). Finally, Sasser et al. (2015) found that poor executive function skills and elevated opposition-aggression differentiated those who showed later onset versus stably low inattention developmental trajectories, while Murray et al. (2017) similarly found that high levels of sensation-seeking predicted being in a later onset group compared to a group with stably low symptoms.

Building on these initial trajectory analysis findings, we investigate which developmental trajectory classes emerge from a large UK-population representative longitudinal study and whether the resultant classes can be differentiated on the basis of clinically relevant factors such as child gender, prematurity, low birth weight, maternal education, early life cognitive ability, infant temperament, and co-occurring early childhood peer, emotional, and conduct problems (Frazier et al., 2004; Russell et al., 2014; Willoughby et al., 2017). While these factors have previously been associated with ADHD symptoms, it is not clear whether they differentiate specific developmental trajectories. We hypothesised that symptom trajectories associated with persistently high levels of symptoms from early in life would tend to be associated with a broader range of risk factors, reflecting a higher overall etiological load; that higher cognitive ability in particular would be associated with a more delayed onset of symptoms, reflecting the fact that children of higher cognitive ability may be better able to compensate for their difficulties until the demands of the late childhood to adolescence transition; and that among those who show no early evidence of ADHD symptoms, those who showed later onsets of symptoms would tend to score higher on established ADHD risk markers early in life.

Method

Participants

Participants (N=11,315) were from the Millennium Cohort Study (MCS) who participated up to sweep 6 when the children were aged 14. Families were sampled using a

stratified sampling procedure from the United Kingdom. Ethnic minority groups and disadvantaged families were oversampled in order to ensure adequate representation of these groups, with sampling weights used to post hoc correct model parameters to population-representativeness. MCS is fully documented and accessed at: https://ukdataservice.ac.uk. The current study uses the sweeps where the children are aged 9 months, 3,5,7,11 and 14 years.

Ethical considerations

All participants provided informed consent/assent as relevant.

Measures

ADHD symptoms

ADHD symptoms were measured at ages 3,5,7,11 and 14 using the hyperactivity/inattention subscale of the parent-reported Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997). Items refer to: being restless, overactive, being unable to stay still for long; constantly fidgeting or squirming; being easily distracted; thinking before acting; and seeing tasks through to their end. The SDQ version administered at age 3 was adapted slightly to improve its age-appropriateness with the item 'can stop and think before acting' used in place of 'thinks things out before acting'. Longitudinal invariance and reliability of the items over ages 3,5,7,9 and 14 was confirmed, with omega values: .80, .84, .86, .86, and .85. Previous research in UK samples has also shown that the SDQ hyperactivity/inattention scale is highly correlated with ADHD diagnosis (Caye et al., 2020; Riglin et al., 2016). For a sample and age groups similar to those in the present study, Riglin et al., (2016) found an optimal cut-point for identifying clinically significant symptoms (based on DSM-IV diagnostic interview) to be a score of 7, with 6 representing a borderline score.

Predictors of developmental trajectories

Prematurity, low birth weight, maternal educational level, and early child temperament were based on information reported in the caregiver interview when the child was 9 months. Infants were classified as premature if born before 37 weeks of gestation. We did not make a further distinction between very premature (born before 32 weeks) and premature infants in this study because we did not expect comparisons involving this group to be adequately powered. Infants were classified as having a low birth weight if they weighed less than 2500g on delivery. Maternal educational level was based on an item in which participants reported their highest academic qualification: 'higher degree', 'first degree', 'diplomas in higher education', 'A/AS/S levels', 'O level/GCSE grades A-C', 'GCSE grades D-G', 'Other academic qualifications' and 'None of these qualifications'. A/AS/A levels, O levels, and GCSEs all refer to qualifications taken in secondary school with A/AS/S levels representing higher qualification levels than O levels and GCSE levels. Given that these levels do not form a hierarchy in all cases, this variable was treated as nominal-categorical.

Early child temperament at age 9 months was measured using the Carey Infant Temperament Scale (Carey & McDevitt, 1978). Five items were used to assess mood, adaptability, regularity, and crying a sum of item scores used for each domain.

Early child cognitive ability, conduct problems, peer problems, and emotional problems were assessed in caregiver interviews when the child was aged 3. Early child cognitive ability was measured using the composite percentile score on the Bracken School Readiness Assessment (Bracken, 2002) and the percentile score on the British Ability Scales – II (BAS-II; Elliott et al., 1996) Vocabulary Naming test. The Bracken scales assess colours, letters, numbers, sizes, comparisons, and shapes while the BAS-II Vocabulary Naming Test

measures vocabulary. Conduct problems, peer problems, and emotional problems were assessed using the parent-reported SDQ, with 5 items in each subscale.

Data analysis

Model selection

Latent class growth analysis models were fit with linear and quadratic growth because previous research has suggested that ADHD symptom trajectories tend to be curvilinear (e.g., Murray, Booth, et al., 2019). Intercept factor loadings were fixed to one; slope factor loadings were fixed proportional to the distance between measurement waves; and quadratic slope factor loadings were fixed to the square of the linear slope factor loadings. Fixing the loadings in this pattern results in the intercept factor for each group capturing age 3 levels of symptoms, the linear slope factor capturing linear change over time, and the quadratic slope factor capturing quadratic change over time. Factor variances were fixed to zero to reflect the assumption of a mixture distribution and the corresponding assumption that the groups are a convenient discretisation of continuous distribution, rather than necessarily 'true' subtypes (see e.g., Nagin & Odgers, 2010). Models were fit for between 1 and 8 classes, with the decision to test no more than 8 classes made a priori to preserve parsimony/interpretability and to ensure group sizes would be large enough to ensure adequate statistical power for comparisons. All models were fit in *Mplus 8.4* using robust maximum likelihood estimation used to account for the complex sampling design of the MCS (including weights, stratification, and clustering). The attrition weights provide unbiased parameter estimates provided data are missing at random (MAR; Rubin, 1976), i.e., that missingness is predictable and that this is captured in the weights.

Model selection was based on the Lo-Mendall-Rubin (LMR) test where a *p*-value <.05 indicates that the k-class model is significantly better fitting than the k-1 class model.

We also examined Akaike's Information Criterion (AIC), Bayesian Information Criterion (BIC) and sample size adjusted BIC (saBIC) to provide supplementary information on model fit. Smaller (more negative) values of AIC, BIC and saBIC indicate better fit.

Predictors of class membership

After identifying an optimal latent class growth analysis model, the nominal class membership variable was regressed on candidate predictors in a multiple multinomial regression model, with all predictors entered at once. We did not adjust for multiple comparisons because of the exploratory nature of the study. Raw *p*-values for the complete set of comparisons are provided in Supplementary Materials. To account for uncertainty of class membership, the three-step method described by Asparouhov and Muthén (2014) was used. Missing data were dealt with using multiple imputation, using an 'H0' approach in which the imputation model was specified to match the main analysis model. Twenty imputations were used to strike a balance between using a sufficient number of imputations for variance estimation and computation time and parameter estimates and standard errors pooled according to Rubin's rules (Rubin, 2004). This method provides unbiased parameter estimates provided that MAR holds.

Results

Descriptive Statistics

Descriptive statistics for all study variables are provided in Table S1 of Supplementary Materials.

Latent class growth analysis models

Table S2 of Supplementary Materials provides model fits for the longitudinal latent class models without any predictors. The LMR test suggested a 6-class model as optimal.

This model is summarised in Table S3 and plotted in Figure 1. Figure 1 also shows the reference line for borderline (=6) and clinically significant (=7) ADHD symptoms based on a cut-point established in previous research (Riglin et al., 2016). The entropy value of .713 suggests that this model provides sufficient class separation for the 3-step method of analysing predictors of class membership (Asparouhov & Muthén, 2014). The full table of classification probabilities is provided in Table S4 of Supplementary Materials. A pre-school onset persistent class showed a trajectory characterised by consistently high scores from age 3 and had symptom scores in the clinically significant range for the entire developmental period studied. A pre-school onset partially remitting class showed scores that began in the borderline range but which declined into the non-clinical range by around age 7. A subclinical remitting class showed initially elevated but sub-clinical scores at age 3 that declined over development. A developmentally increasing class showed initially moderate (sub-clinical) symptom levels that increased over development to reach borderline levels by age 11 and clinically significant levels by age 14. A mildly affected class showed slightly elevated but sub-clinical symptom levels that remained fairly constant over development. Finally, an *unaffected* class showed consistently low levels of symptoms over development.

Predictors of class membership

The results of the regression of class membership on gender, prematurity, low birth weight, maternal education, infant temperament, early cognitive ability, and early emotional, conduct and peer problems are provided in Tables S5-S10 of Supplementary Materials and summarised in Figures 2 and 3. To compare each class against all others, classes 1 to 5 were used as the reference class in turn; however, key comparisons are highlighted.

Individuals in the *developmentally increasing* class were more likely to be male, to have been born prematurely, to have a mother in the 'GCSE Grades D-G' or 'None of these

qualifications' education categories, and to have higher levels of age 3 conduct and peer problems than those in the *unaffected* class. The *developmentally increasing* group were more likely to be female, had lower levels of conduct problems and higher school readiness scores than those in the *pre-school onset persistent*. Those in both the *subclinical remitting* and *pre-school onset partially remitting* classes were more likely to be female and had lower levels of conduct problems than those in the *pre-school onset persistent* class.

Discussion

We evaluated whether it was possible to summarise developmental trajectories of ADHD symptoms from age 3 to 14 in terms of a small number of potentially clinically meaningful developmental subtypes. Using latent class growth analysis, we found the optimal characterisation of ADHD symptom trajectories in a large UK-representative sample was a model with groups: *unaffected*, *mildly affected*, *subclinical remitting*, *pre-school onset partially remitting*, *developmentally increasing*, and *pre-school onset persistent*.

The groupings were largely consistent with existing evidence, with the majority of the sample (86%) falling into a trajectory group that did not reach clinically significant levels at any point in development (the later onset group accounting for 7.6% of the sample exceeded this threshold only at age 14). For the trajectories characterised by borderline or clinically significant levels of symptoms at some stage of development, most individuals were assigned to a group in which these were already evident at age 3, with approximately one third of these falling into a group with persistent symptoms (Caye et al., 2016). The remaining group was characterised by symptoms that increased over the course of development, reaching borderline levels around age 11 and clinically significant levels around age 14.

We explored the differences between all trajectory groups emerging in this study with all others, on a set of perinatal, temperamental, cognitive, and comorbidity variables. Consistent with previous research, trajectory groups characterised by an elevation of symptoms at some stage of development tended to score higher on ADHD risk factors and co-occurring issues and were more likely to be male, to have mothers with lower levels of education, and to show conduct problems, lower levels of school readiness, and score lower on ability tests. The more severely affected trajectories characterised by higher and/or more persistent ADHD levels also tended to show more difficult infant temperaments (e.g., worse mood, poorer adaptability, lower regularity, and more crying) and more peer and emotional problems than the *unaffected* group. They were also more likely to be born low birth weight. One counter-intuitive finding was that the *mildly affected* group but not more severely affected trajectory groups was more likely to be born premature than the *unaffected* group This will require further replication in independent data but may point to a specific prematurity phenotype involving mild ADHD-like difficulties that are etiologically dissociable from ADHD symptoms that are rooted in specific genetic and neurobiological risks for ADHD.

Other comparisons provided insights into the predictability of later onset symptoms among those who show few symptoms early in life; possible differences between individuals with later versus earlier onsets of symptoms; and predictors of remission. Comparisons of the *developmentally increasing* and *unaffected* group suggested that key predictors of later developing ADHD symptoms were male gender, low maternal education, premature birth, and peer and conduct problems at age 3. These findings provide further confirmation that those with later onsets of symptoms may have many of the 'hallmarks' of ADHD despite not following a 'classical' trajectory.

When comparing the *developmentally increasing* category to the 'classical' ADHD symptom trajectory (*pre-school onset persistent*), we found that those in the *developmentally increasing* category were more likely to be female, to have lower levels of conduct problems

and higher school readiness scores at age 3. These findings are consistent with previous research suggesting that later onset ADHD symptoms are associated with a slightly milder – though still impaired – profile (e.g., Murray, Booth, Auyeung, et al., 2018). The higher school readiness scores in the *developmentally increasing* group are consistent with the hypothesis that a delayed onset may reflect the presence of compensatory strengths that allow an individual to function well until life demands intensify (Agnew-Blais et al., 2019). Future research that assesses whether increases in symptoms track specific changes around this time (e.g., puberty onset, transition to high school, decreasing parental supervision) will be valuable for illuminating the proximal factors that lead to possible escalations in symptoms around late childhood/adolescence. The fact that the *developmentally increasing* subtype was associated with fewer early issues could, however, contribute to the under-identification of these issues. It is important that teachers and frontline staff are aware that ADHD symptoms may appear later in the school-age years and possibly more subtly than in early childhood. The fact that females were more likely to show a 'later onset' trajectory is also consistent with previous research (Murray et al., 2019) and underlines the importance of ensuring that females with ADHD symptoms - who may already be more likely to be go undetected - are not missed.

Finally, we evaluated predictors of ADHD symptom persistence by comparing our *pre-school onset persistent* group to two groups characterised by initially elevated but declining symptoms. Only male gender and early conduct problems were associated with persistence. Conduct problems have previously been identified as a predictor of persistence (Caye et al., 2016; Riglin et al., 2016) as well as treatment resistance (Lee et al., 2012), suggesting that they may be a marker for more intractable ADHD symptoms.

Taken together, our results suggest that clinically-relevant early life perinatal, temperamental, cognitive factors, as well as early comorbidities differentiate individuals

following different trajectories of ADHD symptoms. This provides preliminary evidence for the potential clinical utility of attending to an individual's developmental trajectory of ADHD symptoms when seeking to understand their condition, not only their current levels. Future research would be beneficial to establish whether these trajectories also differ in other etiological factors, longer-term outcomes, and (where relevant), treatment responses. It will also be important to evaluate the generalisability of ADHD developmental trajectory groups across different cultures, settings and ethnicities.

Limitations

While the measure of ADHD used was well-validated, it does not distinguish inattention, hyperactivity and impulsivity and it does not provide diagnostic information. There is also no clear universal optimal cut-point on it to indicate clinically significant symptoms, partly reflecting the fact that the avoidance of false positives versus false negatives will differ in different populations and contexts. Similarly, only parent-reported data was available for all sweeps 2-6; however, symptoms may manifest differently across settings and in interaction with different informants (Murray, Booth, Ribeaud, et al., 2018). Further, data into adulthood is not yet available, therefore, how the trajectories develop in the long-term not yet known. Information on ADHD interventions were also not available, therefore, the impact of treatment on trajectories was not possible to ascertain. Finally, our missing data methods assumed MAR. Missing not at random (NMAR, i.e., missing over and above the mechanisms of missingness modelled in the weights/imputations) could not be tested and to the extent that data were NMAR, parameter estimates could be biased. Based on previous research showing a slight tendency for young people with elevated ADHD symptoms to drop out of cohort studies (Eisner et al., 2018), we would expect that the most likely form of bias would be an under-estimation of the class prevalence for the

developmentally increasing class as well as the attenuation of covariate associations involving this class.

Conclusion

IT may be possible to make clinically meaningful distinctions between a small number of ADHD trajectory groups, including pre-school onset persistent, pre-school onset remitting groups, and a developmentally increasing group

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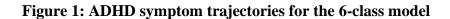
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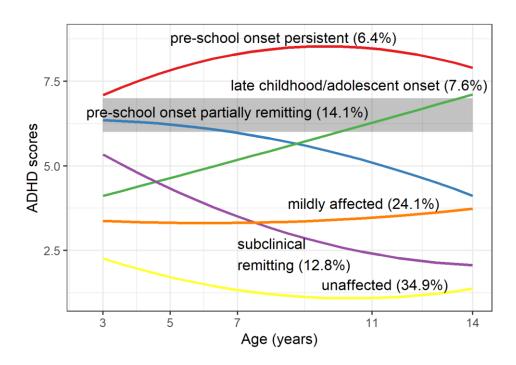
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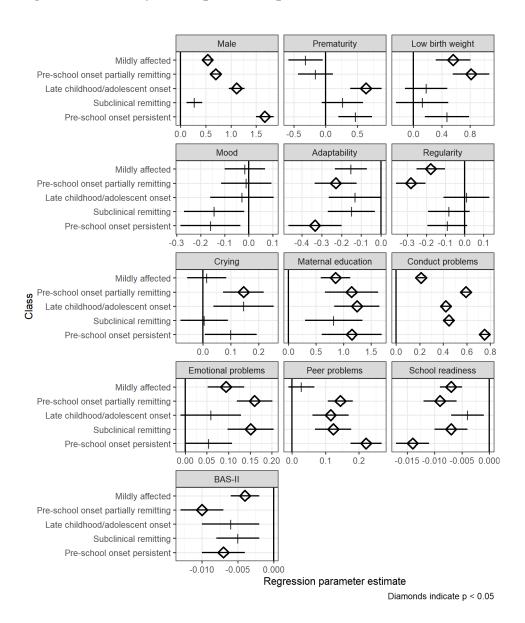
Figures





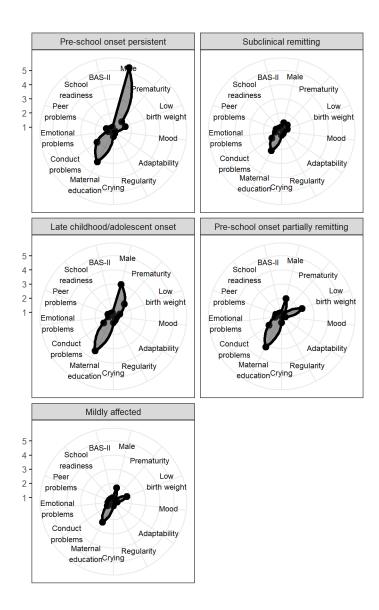
Note. Each solid line represents the trajectory for one of the six classes. The dashed line represents the optimal cut-point (6) for predicting a clinical diagnosis of ADHD established in a previous study.

Figure 2: Summary of comparison of predictors across classes



Note. Figures show b coefficients. Prematurity= born before 37 weeks; Low birth weight= born <2500g; Mood, Adaptability, Regularity, and Crying are subscale scores from the Carey Infant Temperament Scale measured at 9 months; Maternal education = educational qualifications of mother, with the effect of 'None of these qualifications' shown only for clarity; conduct problems, emotional problems, and peer problems are subscale scores from the SDQ measured at age 3; School readiness= Bracken School Readiness Assessment composite scores measured at age 3; and BAS-II = British Ability Scales score measured at age 3.

Figure 3: Predictor profiles (odds ratios) of all classes compared to the unaffected class



Note. Figure shows odds ratios for each predictor using the unaffected class as the reference class. BAS-II= British Ability Scale score; 'None of these qualifications' only displayed for maternal education for visual clarity.

Supplementary Materials

Table S1: Descriptive Statistics for ADHD items and trajectory predictors

	N	Mean	SD	Minimum	Maximum	Skewness	Kurtosis
Age 3 conduct problems	10377	2.77	2.03	0.00	10.00	0.74	0.30
Age 3 emotional problems	10359	1.36	1.49	0.00	10.00	1.51	2.92
Age 3 hyperactivity/inattention	10284	3.85	2.35	0.00	10.00	0.47	-0.31
Age 3 peer problems	10294	1.52	1.59	0.00	10.00	1.13	1.13
Age 5 hyperactivity/inattention	10796	3.23	2.36	0.00	10.00	0.70	0.01
Age 7 hyperactivity/inattention	10587	3.29	2.50	0.00	10.00	0.68	-0.17
Age 11 hyperactivity/inattention	11470	2.99	2.40	0.00	10.00	0.79	0.16

Age 14 hyperactivity/inattention	10762	3.08	2.46	0.00	10.00	0.78	0.06
Age 3 School readiness score	9782	58.61	30.33	0.20	100.00	-0.39	-1.13
Age 3 British Ability Scale - II score	10267	49.47	30.76	1.00	99.00	0.04	-1.31
Age 9 months Temperament - mood	10220	3.82	0.68	1.00	5.00	-0.64	0.43
Age 9 months Temperament -	7393	1.93	0.73	1.00	5.00	0.89	0.65
adaptability							
Age 9 months Temperament - regularity	10732	4.27	0.77	1.00	5.00	-1.43	2.25
Age 9 months Temperament - crying	10834	2.77	0.88	1.00	5.00	0.13	-0.51
Gender	Male		Female				
	5920		5943				
Prematurity	Preterm		Term				
	880		10436				

Low birth weight	<2500g		>2500g					
	886		10556					
Maternal education	Higher	First	Diploma	A/AS/S	O level/	GCSE	Other	None of
	degree	degree	in higher	level	GCSE	D- G		these
			education		A-C			
	451	1753	1075	1131	3714	1121	320	1845

Table S2: Model fits for 1-6 class linear + quadratic latent class growth analysis models

Model	LMR	p	AIC	BIC	saBIC	Entropy
(number of						
classes)						
1	-	-	234359.641	234418.313	234392.890	-
2	15956.616	<.001	217983.645	218071.653	218033.518	.826
3	4295.104	<.001	213581.501	213698.845	213647.999	.787
4	1235.533	<.001	212320.876	212467.555	212403.998	.738
5	1217.621	<.001	211078.642	211254.657	211178.388	.748
6	405.801	.0438	210669.972	210875.323	210786.343	.713
7	288.462	.3338	210381.784	210616.471	210514.779	.697
8	293.078	.3249	210088.856	210352.879	210238.475	.711

Note. Optimal model indicated in boldface. LMR= Lo-Mendell-Rubin value; AIC= Akaike
Information Criterion; BIC= Bayesian Information Criterion; saBIC= sample size adjusted
BIC

Table S3: Intercept and linear slope parameters for the selected model

Class Label	%	Intercept	SE	Linear	SE	Quadratic	SE
	sample*			Slope		Slope	
Pre-school onset persistent	6.4	7.090	0.136	4.802	0.591	-3.993	0.541
Subclinical remitting	12.8	5.339	0.396	-6.049	1.327	2.779	0.969
Developmentally increasing	7.6	4.115	0.300	2.885	1.685	0.115	1.492
Pre-school onset partially remitting	14.1	6.350	0.149	-0.344	0.878	-1.888	0.834
Mildly affected	24.1	3.376	0.120	-0.466	0.482	0.821	0.427
Unaffected	34.9	2.263	0.051	-3.502	0.152	2.609	0.145
	Pre-school onset persistent Subclinical remitting Developmentally increasing Pre-school onset partially remitting Mildly affected	Pre-school onset persistent 6.4 Subclinical remitting 12.8 Developmentally increasing 7.6 Pre-school onset partially 14.1 remitting Mildly affected 24.1	Sample* Pre-school onset persistent 6.4 7.090 Subclinical remitting 12.8 5.339 Developmentally increasing 7.6 4.115 Pre-school onset partially 14.1 6.350 remitting Mildly affected 24.1 3.376	Sample* Pre-school onset persistent 6.4 7.090 0.136 Subclinical remitting 12.8 5.339 0.396 Developmentally increasing 7.6 4.115 0.300 Pre-school onset partially 14.1 6.350 0.149 remitting Mildly affected 24.1 3.376 0.120	sample* Slope Pre-school onset persistent 6.4 7.090 0.136 4.802 Subclinical remitting 12.8 5.339 0.396 -6.049 Developmentally increasing 7.6 4.115 0.300 2.885 Pre-school onset partially 14.1 6.350 0.149 -0.344 remitting Mildly affected 24.1 3.376 0.120 -0.466	Sample* Slope Pre-school onset persistent 6.4 7.090 0.136 4.802 0.591 Subclinical remitting 12.8 5.339 0.396 -6.049 1.327 Developmentally increasing 7.6 4.115 0.300 2.885 1.685 Pre-school onset partially 14.1 6.350 0.149 -0.344 0.878 remitting Mildly affected 24.1 3.376 0.120 -0.466 0.482	sample* Slope Slope Pre-school onset persistent 6.4 7.090 0.136 4.802 0.591 -3.993 Subclinical remitting 12.8 5.339 0.396 -6.049 1.327 2.779 Developmentally increasing 7.6 4.115 0.300 2.885 1.685 0.115 Pre-school onset partially 14.1 6.350 0.149 -0.344 0.878 -1.888 remitting Mildly affected 24.1 3.376 0.120 -0.466 0.482 0.821

Note. *based on estimated posterior probabilities. SE= standard error.

Table S4: Classification probabilities for the optimal latent class growth analysis model

Class	1	2	3	4	5	6	
1	.894	.000	.044	.060	.001	.000	
2	.000	.547	.001	.068	.250	.133	
3	.046	.002	.709	.135	.107	.001	
4	.023	.043	.053	.790	.090	.001	
5	.000	.078	.020	.046	.750	.106	
6	.000	.025	.000	.000	.061	.914	

Note. Classification probabilities are for the most likely class membership (in columns) by latent class (rows)

Table S5: Regression parameters using the unaffected class as the reference group

	В	OR	SE	P
Pre-school onset persistent				
Gender	1.67	5.32	0.17	<.001
Prematurity	0.47	1.60	0.27	.077
Low birth weight	0.47	1.61	0.31	.131
Mood	-0.16	0.85	0.13	.204
Adaptability	-0.33	0.72	0.13	.012
Regularity	-0.09	0.91	0.10	.387
Crying	0.10	1.11	0.09	.286
Maternal education (first degree)	-0.52	0.60	0.58	.372
Maternal education (Diploma in higher				
education)	0.20	1.23	0.59	.730
Maternal education (A/AS/S level)	0.67	1.96	0.56	.225
Maternal education (O level/GCSE grades A-				
C)	0.80	2.22	0.51	.115
Maternal education (GCSE grades D-G)	1.22	3.39	0.53	.020
Maternal education (Other academic				
qualifications)	0.34	1.40	0.79	.669

Maternal education (None of these				
qualifications)	1.15	3.16	0.54	.034
Conduct problems	0.75	2.12	0.04	<.001
Emotional problems	0.05	1.06	0.05	.320
Peer problems	0.22	1.25	0.05	<.001
School readiness	-0.01	0.99	0.00	<.001
BAS-II	-0.01	0.99	0.00	.036
Subclinical remitting				
Gender	0.28	1.32	0.15	.071
Prematurity	0.26	1.30	0.33	.416
Low birth weight	0.12	1.13	0.37	.738
Mood	-0.14	0.87	0.13	.249
Adaptability	-0.15	0.86	0.12	.205
Regularity	-0.08	0.92	0.11	.454
Crying	0.01	1.01	0.09	.957
Maternal education (first degree)	-0.08	0.92	0.52	.872
Maternal education (Diploma in higher				
education)	0.33	1.39	0.54	.545
Maternal education (A/AS/S level)	0.45	1.57	0.53	.392

Maternal education (O level/GCSE grades A-				
C)	0.28	1.33	0.51	.579
Maternal education (GCSE grades D-G)	0.43	1.54	0.53	.411
Maternal education (Other academic				
qualifications)	1.05	2.86	0.64	.098
Maternal education (None of these				
qualifications)	0.82	2.28	0.52	.113
Conduct problems	0.45	1.56	0.04	<.001
Emotional problems	0.15	1.16	0.05	.004
Peer problems	0.12	1.13	0.05	.023
School readiness	-0.01	0.99	0.00	.039
BAS-II	-0.01	1.00	0.00	.142
Late childhood/adolescent onset	ON			
Gender	1.11	3.04	0.16	<.001
Prematurity	0.63	1.89	0.25	.010
Low birth weight	0.18	1.20	0.30	.548
Mood	-0.03	0.97	0.13	.831
Adaptability	-0.13	0.88	0.13	.325

0.01

1.01

0.12

.932

Regularity

Crying	0.15	1.16	0.11	.175
Maternal education (first degree)	-0.27	0.76	0.41	.511
Maternal education (Diploma in higher				
education)	-0.11	0.89	0.42	.792
Maternal education (A/AS/S level)	0.19	1.20	0.45	.678
Maternal education (O level/GCSE grades A-				
C)	0.27	1.32	0.38	.466
Maternal education (GCSE grades D-G)	1.17	3.22	0.42	.005
Maternal education (Other academic				
qualifications)	-0.15	0.86	0.69	.831
Maternal education (None of these				
qualifications)	1.25	3.47	0.41	.002
Conduct problems	0.42	1.53	0.04	<.001
Emotional problems	0.06	1.06	0.07	.397
Peer problems	0.12	1.12	0.05	.031
School readiness	0.00	1.00	0.00	.175
BAS-II	-0.01	0.99	0.00	.080
Pre-school onset partially remitting				
Gender	0.70	2.01	0.11	<.001
Prematurity	-0.16	0.85	0.28	.558

Low birth weight	0.81	2.26	0.26	.002
Mood	-0.01	0.99	0.11	.923
Adaptability	-0.23	0.80	0.11	.031
Regularity	-0.28	0.76	0.08	<.001
Crying	0.15	1.16	0.07	.046
Maternal education (first degree)	-0.53	0.59	0.52	.306
Maternal education (Diploma in higher				
education)	0.38	1.46	0.51	.456
Maternal education (A/AS/S level)	0.58	1.78	0.47	.221
Maternal education (O level/GCSE grades A-				
C)	0.78	2.19	0.46	.086
C) Maternal education (GCSE grades D-G)	0.78	2.192.98	0.46	.086
Maternal education (GCSE grades D-G)				
Maternal education (GCSE grades D-G) Maternal education (Other academic	1.09	2.98	0.46	.017
Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications)	1.09	2.98	0.46	.017
Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these	1.09 0.73	2.982.08	0.46	.017
Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these qualifications)	1.09 0.73	2.982.083.15	0.46 0.53	.017
Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these qualifications) Conduct problems	1.09 0.73 1.15 0.59	2.982.083.151.81	0.46 0.53 0.48 0.04	.017 .169 .017 <.001

BAS-II	-0.01	0.99	0.00	<.001
Mildly affected				
Gender	0.54	1.71	0.10	<.001
Prematurity	-0.32	0.73	0.27	.242
Low birth weight	0.56	1.75	0.24	.022
Mood	-0.02	0.98	0.08	.846
Adaptability	-0.15	0.86	0.08	.063
Regularity	-0.18	0.84	0.08	.019
Crying	0.01	1.01	0.07	.839
Maternal education (first degree)	-0.30	0.74	0.26	.237
Maternal education (Diploma in higher				
education)	0.25	1.28	0.26	.339
Maternal education (A/AS/S level)	0.08	1.09	0.28	.763
Maternal education (O level/GCSE grades A-				
C)	0.37	1.45	0.24	.122
Maternal education (GCSE grades D-G)	0.68	1.98	0.28	.013
Maternal education (Other academic				
qualifications)	0.13	1.14	0.41	.753
Maternal education (None of these				
qualifications)	0.86	2.36	0.27	.001

Conduct problems	0.21	1.24	0.03	<.001
Emotional problems	0.09	1.10	0.04	.024
Peer problems	0.03	1.03	0.04	.481
School readiness	-0.01	0.99	0.00	.005
BAS-II	0.00	1.00	0.00	.047

Note. SEs are on the scale of the B coefficients. The reference category for gender is female and the reference category for maternal education is 'higher degree'.

Table S6: Regression parameters using pre-school onset persistent group as the reference class

	В	OR	SE	p
Subclinical remitting				
Gender	-1.40	0.25	0.22	<.001
Prematurity	-0.20	0.82	0.36	.574
Low birth weight	-0.35	0.70	0.39	.372
Mood	0.02	1.02	0.15	.917
Adaptability	0.18	1.20	0.16	.243
Regularity	0.01	1.01	0.12	.946
Crying	-0.10	0.91	0.11	.395
Maternal education (first degree)	0.44	1.54	0.64	.498
Maternal education (Diploma in higher				
education)	0.13	1.13	0.66	.849
Maternal education (A/AS/S level)	-0.22	0.80	0.67	.740
Maternal education (O level/GCSE grades A-				
C)	-0.51	0.60	0.61	.401
Maternal education (GCSE grades D-G)	-0.79	0.45	0.65	.228
Maternal education (Other academic				
qualifications)	0.71	2.04	0.82	.383

Maternal education (None of these						
qualifications)	-0.33	0.72	0.63	.606		
Conduct problems	-0.30	0.74	0.05	<.001		
Emotional problems	0.10	1.10	0.06	.124		
Peer problems	-0.10	0.91	0.06	.080		
School readiness	0.01	1.01	0.00	.081		
BAS-II	0.00	1.00	0.00	.495		
Late childhood/adolescent onset						
Gender	-0.56	0.57	0.23	.013		
Prematurity	0.17	1.18	0.32	.609		
Low birth weight	-0.30	0.74	0.35	.403		
Mood	0.13	1.14	0.17	.437		
Adaptability	0.20	1.23	0.19	.284		
Regularity	0.10	1.11	0.15	.497		
Crying	0.05	1.05	0.14	.735		
Maternal education (first degree)	0.25	1.28	0.73	.732		
Maternal education (Diploma in higher						
education)	-0.32	0.73	0.70	.650		
Maternal education (A/AS/S level)	-0.49	0.61	0.71	.494		

Maternal education (O level/GCSE grades A-				
C)	-0.52	0.59	0.62	.398
Maternal education (GCSE grades D-G)	-0.05	0.95	0.66	.940
Maternal education (Other academic				
qualifications)	-0.49	0.62	1.05	.642
Maternal education (None of these				
qualifications)	0.10	1.10	0.66	.885
Conduct problems	-0.33	0.72	0.05	<.001
Emotional problems	0.01	1.01	0.09	.954
Peer problems	-0.11	0.90	0.06	.091
School readiness	0.01	1.01	0.01	.032
BAS-II	0.00	1.00	0.01	.840
Pre-school onset partially remitting				
Gender	-0.98	0.38	0.18	<.001
Prematurity	-0.63	0.53	0.35	.075
Low birth weight	0.34	1.41	0.33	.296
Mood	0.15	1.16	0.14	.282
Adaptability	0.11	1.11	0.15	.482

-0.19

0.83

0.10

.065

Regularity

Crying	0.05	1.05	0.09	.616
Maternal education (first degree)	-0.01	0.99	0.64	.986
Maternal education (Diploma in higher				
education)	0.18	1.19	0.65	.788
Maternal education (A/AS/S level)	-0.10	0.91	0.61	.876
Maternal education (O level/GCSE grades A-				
C)	-0.01	0.99	0.56	.979
Maternal education (GCSE grades D-G)	-0.13	0.88	0.58	.823
Maternal education (Other academic				
qualifications)	0.40	1.48	0.79	.618
Maternal education (None of these				
qualifications)	0.00	1.00	0.55	.994
Conduct problems	-0.16	0.85	0.04	<.001
Emotional problems	0.11	1.11	0.06	.067
Peer problems	-0.08	0.93	0.05	.117
School readiness	0.01	1.01	0.00	.205
BAS-II	0.00	1.00	0.00	.502
Mildly affected				
Gender	-1.13	0.32	0.17	<.001
Prematurity	-0.79	0.46	0.34	.021

Low birth weight	0.09	1.09	0.35	.805
Mood	0.14	1.15	0.12	.231
Adaptability	0.18	1.20	0.13	.174
Regularity	-0.09	0.92	0.10	.397
Crying	-0.09	0.92	0.09	.329
Maternal education (first degree)	0.22	1.24	0.60	.719
Maternal education (Diploma in higher				
education)	0.04	1.04	0.60	.943
Maternal education (A/AS/S level)	-0.59	0.55	0.57	.299
Maternal education (O level/GCSE grades A-				
•				
C)	-0.43	0.65	0.51	.407
_	-0.43 -0.54	0.65 0.58	0.51	.407
C)				
C) Maternal education (GCSE grades D-G)				
C) Maternal education (GCSE grades D-G) Maternal education (Other academic	-0.54	0.58	0.53	.307
C) Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications)	-0.54	0.58	0.53	.307
C) Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these	-0.54 -0.21	0.58	0.53	.307
C) Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these qualifications)	-0.54 -0.21 -0.29	0.58 0.81 0.75	0.53 0.77 0.53	.307 .786
C) Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these qualifications) Conduct problems	-0.54 -0.21 -0.29 -0.54	0.58 0.81 0.75 0.58	0.53 0.77 0.53 0.04	.307 .786 .584 <.001

BAS-II	0.00	1.00	0.00	.427
Unaffected				
Gender	-1.67	0.19	0.17	<.001
Prematurity	-0.47	0.63	0.27	.077
Low birth weight	-0.47	0.62	0.31	.131
Mood	0.16	1.17	0.13	.204
Adaptability	0.33	1.40	0.13	.012
Regularity	0.09	1.09	0.10	.387
Crying	-0.10	0.90	0.09	.286
Maternal education (first degree)	0.52	1.68	0.58	.372
Maternal education (Diploma in higher				
education)	-0.20	0.82	0.59	.730
Maternal education (A/AS/S level)	-0.67	0.51	0.56	.225
Maternal education (O level/GCSE grades A-				
C)	-0.80	0.45	0.51	.115
Maternal education (GCSE grades D-G)	-1.22	0.30	0.53	.020
Maternal education (Other academic				
qualifications)	-0.34	0.71	0.79	.669
Maternal education (None of these				
qualifications)	-1.15	0.32	0.54	.034

Conduct problems	-0.75	0.47	0.04	<.001
Emotional problems	-0.05	0.95	0.05	.320
Peer problems	-0.22	0.80	0.05	<.001
School readiness	0.01	1.01	0.00	<.001
BAS-II	0.01	1.01	0.00	.036

Table S7: Regression parameters using subclinical remitting as the reference group

	В	OR	SE	p
Pre-school onset persistent				
Gender	1.40	0.22	6.27	<.001
Prematurity	0.20	0.36	0.56	.574
Low birth weight	0.35	0.39	0.89	.372
Mood	-0.02	0.15	-0.10	.917
Adaptability	-0.18	0.16	-1.17	.243
Regularity	-0.01	0.12	-0.07	.946
Crying	0.10	0.11	0.85	.395
Maternal education (first degree)	-0.44	0.64	-0.68	.498
Maternal education (Diploma in higher				
education)	-0.13	0.66	-0.19	.849
Maternal education (A/AS/S level)	0.22	0.67	0.33	.740
Maternal education (O level/GCSE grades A-				
C)	0.51	0.61	0.84	.401
Maternal education (GCSE grades D-G)	0.79	0.65	1.20	.228
Maternal education (Other academic				
qualifications)	-0.71	0.82	-0.87	.383

Maternal education (None of these				
qualifications)	0.33	0.63	0.52	.606
Conduct problems	0.30	0.05	6.62	<.001
Emotional problems	-0.10	0.06	-1.54	.124
Peer problems	0.10	0.06	1.75	.080
School readiness	-0.01	0.00	-1.74	.081
BAS-II	0.00	0.00	-0.68	.495
Late childhood/adolescent onset				
Gender	0.84	0.20	4.24	<.001
Prematurity	0.37	0.34	1.10	.272
Low birth weight	0.06	0.37	0.15	.879
Mood	0.12	0.15	0.80	.425
Adaptability	0.02	0.15	0.13	.900
Regularity	0.09	0.14	0.68	.498
Crying	0.14	0.12	1.16	.246
Maternal education (first degree)	-0.19	0.60	-0.31	.759
Maternal education (Diploma in higher				
education)	-0.44	0.60	-0.73	.465
Maternal education (A/AS/S level)	-0.27	0.62	-0.43	.667

Maternal education (O level/GCSE grades A-				
C)	-0.01	0.58	-0.02	.986
Maternal education (GCSE grades D-G)	0.74	0.60	1.23	.218
Maternal education (Other academic				
qualifications)	-1.20	0.83	-1.44	.149
Maternal education (None of these				
qualifications)	0.42	0.58	0.73	.464
Conduct problems	-0.03	0.05	-0.47	.638
Emotional problems	-0.09	0.08	-1.18	.239
Peer problems	-0.01	0.06	-0.12	.904
School readiness	0.00	0.00	0.64	.522
BAS-II	0.00	0.00	-0.41	.685
Pre-school onset partially remitting				
Gender	0.42	0.17	2.50	.012
Prematurity	-0.43	0.37	-1.16	.246
Low birth weight	0.69	0.38	1.81	.071
Mood	0.13	0.15	0.92	.360
Adaptability	-0.08	0.14	-0.56	.577

-0.20

0.11

-1.75

.080

Regularity

Crying	0.14	0.10	1.45	.147
Maternal education (first degree)	-0.45	0.65	-0.68	.495
Maternal education (Diploma in higher				
education)	0.05	0.67	0.07	.941
Maternal education (A/AS/S level)	0.13	0.66	0.19	.849
Maternal education (O level/GCSE grades A-				
C)	0.50	0.63	0.79	.432
Maternal education (GCSE grades D-G)	0.66	0.64	1.02	.306
Maternal education (Other academic				
qualifications)	-0.32	0.68	-0.47	.642
Maternal education (None of these				
qualifications)	0.32	0.65	0.50	.618
Conduct problems	0.15	0.04	3.39	.001
Emotional problems	0.01	0.06	0.14	.886
Peer problems	0.02	0.06	0.35	.725
School readiness	0.00	0.00	-0.59	.556
BAS-II	-0.01	0.00	-1.49	.137
Mildly affected				
Gender	0.26	0.19	1.39	.164
Prematurity	-0.58	0.45	-1.30	.193

Low birth weight	0.44	0.45	0.97	.331		
Mood	0.13	0.15	0.88	.380		
Adaptability	0.00	0.14	-0.01	.993		
Regularity	-0.10	0.12	-0.78	.436		
Crying	0.01	0.11	0.09	.927		
Maternal education (first degree)	-0.22	0.58	-0.38	.705		
Maternal education (Diploma in higher						
education)	-0.08	0.61	-0.14	.890		
Maternal education (A/AS/S level)	-0.37	0.59	-0.63	.531		
Maternal education (O level/GCSE grades A-						
C)	0.09	0.55	0.16	.874		
_	0.09	0.55	0.16 0.43	.874		
C)						
C) Maternal education (GCSE grades D-G)						
C) Maternal education (GCSE grades D-G) Maternal education (Other academic	0.25	0.59	0.43	.669		
C) Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications)	0.25	0.59	0.43	.669		
C) Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these	0.25	0.59	0.43	.669		
C) Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these qualifications)	0.25 -0.92 0.04	0.59 0.69 0.56	0.43 -1.33 0.06	.669 .184 .949		
C) Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these qualifications) Conduct problems	0.25 -0.92 0.04 -0.24	0.59 0.69 0.56 0.05	0.43 -1.33 0.06 -4.59	.669 .184 .949 <.001		

BAS-II	0.00	0.00	0.05	.959			
Unaffected							
Gender	-0.28	0.15	-1.81	.071			
Prematurity	-0.26	0.33	-0.81	.416			
Low birth weight	-0.12	0.37	-0.34	.738			
Mood	0.14	0.13	1.15	.249			
Adaptability	0.15	0.12	1.27	.205			
Regularity	0.08	0.11	0.75	.454			
Crying	-0.01	0.09	-0.05	.957			
Maternal education (first degree)	0.08	0.52	0.16	.872			
Maternal education (Diploma in higher							
education)	-0.33	0.54	-0.61	.545			
Maternal education (A/AS/S level)	-0.45	0.53	-0.86	.392			
Maternal education (O level/GCSE grades A-							
C)	-0.28	0.51	-0.56	.579			
Maternal education (GCSE grades D-G)	-0.43	0.53	-0.82	.411			
Maternal education (Other academic							
qualifications)	-1.05	0.64	-1.65	.098			
Maternal education (None of these							
qualifications)	-0.82	0.52	-1.59	.113			

Conduct problems	-0.45	0.04	-10.70	<.001
Emotional problems	-0.15	0.05	-2.86	.004
Peer problems	-0.12	0.05	-2.28	.023
School readiness	0.01	0.00	2.07	.039
BAS-II	0.01	0.00	1.47	.142

Table S8: Regression parameters with late childhood/adolescent onset as reference group

	В	OR	SE	p
Pre-school onset persistent				
Gender	0.56	0.23	2.48	.013
Prematurity	-0.17	0.32	-0.51	.609
Low birth weight	0.30	0.35	0.84	.403
Mood	-0.13	0.17	-0.78	.437
Adaptability	-0.20	0.19	-1.07	.284
Regularity	-0.10	0.15	-0.68	.497
Crying	-0.05	0.14	-0.34	.735
Maternal education (first degree)	-0.25	0.73	-0.34	.732
Maternal education (Diploma in higher				
education)	0.32	0.70	0.45	.650
Maternal education (A/AS/S level)	0.49	0.71	0.68	.494
Maternal education (O level/GCSE grades A-C)	0.52	0.62	0.85	.398
Maternal education (GCSE grades D-G)	0.05	0.66	0.08	.940
Maternal education (Other academic				
qualifications)	0.49	1.05	0.47	.642

Maternal education (None of these						
qualifications)	-0.10	0.66	-0.14	.885		
Conduct problems	0.33	0.05	6.14	<.001		
Emotional problems	-0.01	0.09	-0.06	.954		
Peer problems	0.11	0.06	1.69	.091		
School readiness	-0.01	0.01	-2.14	.032		
BAS-II	0.00	0.01	-0.20	.840		
Subclinical remitting						
Gender	-0.84	0.20	-4.24	<.001		
Prematurity	-0.37	0.34	-1.10	.272		
Low birth weight	-0.06	0.37	-0.15	.879		
Mood	-0.12	0.15	-0.80	.425		
Adaptability	-0.02	0.15	-0.13	.900		
Regularity	-0.09	0.14	-0.68	.498		
Crying	-0.14	0.12	-1.16	.246		
Maternal education (first degree)	0.19	0.60	0.31	.759		
Maternal education (Diploma in higher						
education)	0.44	0.60	0.73	.465		
Maternal education (A/AS/S level)	0.27	0.62	0.43	.667		

Maternal education (O level/GCSE grades A-C)		0.58	0.02	.986
Maternal education (GCSE grades D-G)	-0.74	0.60	-1.23	.218
Maternal education (Other academic				
qualifications)	1.20	0.83	1.44	.149
Maternal education (None of these				
qualifications)	-0.42	0.58	-0.73	.464
Conduct problems	0.03	0.05	0.47	.638
Emotional problems	0.09	0.08	1.18	.239
Peer problems	0.01	0.06	0.12	.904
School readiness	0.00	0.00	-0.64	.522
BAS-II	0.00	0.00	0.41	.685
Pre-school onset partially remitting				
Gender	-0.42	0.20	-2.12	.034
Prematurity	-0.80	0.32	-2.47	.014
Low birth weight	0.64	0.33	1.94	.052
Mood	0.02	0.17	0.10	.917
Adaptability	-0.10	0.18	-0.54	.587
Regularity	-0.29	0.13	-2.20	.028
Crying	0.00	0.13	0.00	.999

Maternal education (first degree)	-0.26	0.63	-0.41	.681			
Maternal education (Diploma in higher							
education)	0.49	0.66	0.75	.455			
Maternal education (A/AS/S level)	0.39	0.64	0.61	.540			
Maternal education (O level/GCSE grades A-C)	0.51	0.56	0.91	.365			
Maternal education (GCSE grades D-G)	-0.08	0.60	-0.13	.895			
Maternal education (Other academic							
qualifications)	0.88	0.85	1.04	.301			
Maternal education (None of these							
qualifications)	-0.10	0.60	-0.17	.869			
Conduct problems	0.17	0.05	3.35	.001			
Emotional problems	0.10	0.08	1.24	.214			
Peer problems	0.03	0.06	0.49	.625			
School readiness	-0.01	0.00	-1.19	.235			
BAS-II	0.00	0.01	-0.79	.429			
Mildly affected							
Gender	-0.58	0.18	-3.24	.001			
Prematurity	-0.95	0.34	-2.81	.005			
Low birth weight	0.38	0.36	1.07	.287			

Mood	0.01	0.14	0.09	.933
Adaptability	-0.02	0.15	-0.13	.895
Regularity	-0.19	0.13	-1.47	.142
Crying	-0.13	0.12	-1.08	.278
Maternal education (first degree)	-0.03	0.43	-0.08	.938
Maternal education (Diploma in higher				
education)	0.36	0.44	0.81	.420
Maternal education (A/AS/S level)	-0.10	0.48	-0.21	.831
Maternal education (O level/GCSE grades A-C)	0.10	0.38	0.26	.795
Maternal education (GCSE grades D-G)	-0.49	0.42	-1.15	.249
Maternal education (Other academic				
qualifications)	0.28	0.80	0.35	.729
Maternal education (None of these				
qualifications)	-0.39	0.40	-0.97	.335
Conduct problems	-0.21	0.06	-3.85	<.001
Emotional problems	0.04	0.08	0.43	.668
Peer problems	-0.09	0.06	-1.57	.116
School readiness	0.00	0.00	-0.59	.557
BAS-II	0.00	0.00	0.49	.627

Unaffected

Gender	-1.11	0.16	-7.08	<.001
Prematurity	-0.63	0.25	-2.58	.010
Low birth weight	-0.18	0.30	-0.60	.548
Mood	0.03	0.13	0.21	.831
Adaptability	0.13	0.13	0.99	.325
Regularity	-0.01	0.12	-0.09	.932
Crying	-0.15	0.11	-1.36	.175
Maternal education (first degree)	0.27	0.41	0.66	.511
Maternal education (Diploma in higher				
education)	0.11	0.42	0.26	.792
Maternal education (A/AS/S level)	-0.19	0.45	-0.42	.678
Maternal education (O level/GCSE grades A-C)	-0.27	0.38	-0.73	.466
Maternal education (GCSE grades D-G)	-1.17	0.42	-2.80	.005
Maternal education (Other academic				
qualifications)	0.15	0.69	0.21	.831
Maternal education (None of these				
qualifications)	-1.25	0.41	-3.05	.002
Conduct problems	-0.42	0.04	-9.68	<.001
Emotional problems	-0.06	0.07	-0.85	.397

Peer problems	-0.12	0.05	-2.15	.031
School readiness	0.00	0.00	1.36	.175
BAS-II	0.01	0.00	1.75	.080

 $\begin{tabular}{ll} Table S9: Regression parameters with pre-school onset partially remitting as reference \\ group \end{tabular}$

	В	OR	SE	p
Pre-school onset				
Gender	0.98	0.18	5.38	<.001
Prematurity	0.63	0.35	1.78	.075
Low birth weight	-0.34	0.33	-1.05	.296
Mood	-0.15	0.14	-1.08	.282
Adaptability	-0.11	0.15	-0.70	.482
Regularity	0.19	0.10	1.84	.065
Crying	-0.05	0.09	-0.50	.616
Maternal education (first degree)	0.01	0.64	0.02	.986
Maternal education (Diploma in higher				
education)	-0.18	0.65	-0.27	.788
Maternal education (A/AS/S level)	0.10	0.61	0.16	.876
Maternal education (O level/GCSE grades A-				
C)	0.01	0.56	0.03	.979
Maternal education (GCSE grades D-G)	0.13	0.58	0.22	.823
Maternal education (Other academic				
qualifications)	-0.40	0.79	-0.50	.618

Maternal education (None of these							
qualifications)	0.00	0.55	0.01	.994			
Conduct problems	0.16	0.04	3.88	<.001			
Emotional problems	-0.11	0.06	-1.84	.067			
Peer problems	0.08	0.05	1.57	.117			
School readiness	-0.01	0.00	-1.27	.205			
BAS-II	0.00	0.00	0.67	.502			
Subclinical remitting							
Gender	-0.42	0.17	-2.50	.012			
Prematurity	0.43	0.37	1.16	.246			
Low birth weight	-0.69	0.38	-1.81	.071			
Mood	-0.13	0.15	-0.92	.360			
Adaptability	0.08	0.14	0.56	.577			
Regularity	0.20	0.11	1.75	.080			
Crying	-0.14	0.10	-1.45	.147			
Maternal education (first degree)	0.45	0.65	0.68	.495			
Maternal education (Diploma in higher							
education)	-0.05	0.67	-0.07	.941			
Maternal education (A/AS/S level)	-0.13	0.66	-0.19	.849			

Maternal education (O level/GCSE grades A-				
C)	-0.50	0.63	-0.79	.432
Maternal education (GCSE grades D-G)	-0.66	0.64	-1.02	.306
Maternal education (Other academic				
qualifications)	0.32	0.68	0.47	.642
Maternal education (None of these				
qualifications)	-0.32	0.65	-0.50	.618
Conduct problems	-0.15	0.04	-3.39	.001
Emotional problems	-0.01	0.06	-0.14	.886
Peer problems	-0.02	0.06	-0.35	.725
School readiness	0.00	0.00	0.59	.556
BAS-II	0.01	0.00	1.49	.137
Late childhood/adolescent onset				
Gender	0.42	0.20	2.12	.034
Prematurity	0.80	0.32	2.47	.014
Low birth weight	-0.64	0.33	-1.94	.052
Mood	-0.02	0.17	-0.10	.917
Adaptability	0.10	0.18	0.54	.587

0.29

0.13

2.20

.028

Regularity

Crying	0.00	0.13	0.00	.999
Maternal education (first degree)	0.26	0.63	0.41	.681
Maternal education (Diploma in higher				
education)	-0.49	0.66	-0.75	.455
Maternal education (A/AS/S level)	-0.39	0.64	-0.61	.540
Maternal education (O level/GCSE grades A-				
C)	-0.51	0.56	-0.91	.365
Maternal education (GCSE grades D-G)	0.08	0.60	0.13	.895
Maternal education (Other academic				
qualifications)	-0.88	0.85	-1.04	.301
Maternal education (None of these				
qualifications)	0.10	0.60	0.17	.869
Conduct problems	-0.17	0.05	-3.35	.001
Emotional problems	-0.10	0.08	-1.24	.214
Peer problems	-0.03	0.06	-0.49	.625
School readiness	0.01	0.00	1.19	.235
BAS-II	0.00	0.01	0.79	.429
Mildly affected	ON			
Gender	-0.16	0.13	-1.28	.202
Prematurity	-0.16	0.38	-0.42	.678

Low birth weight	-0.26	0.33	-0.78	.434
Mood	-0.01	0.13	-0.05	.961
Adaptability	0.08	0.12	0.66	.509
Regularity	0.10	0.09	1.18	.237
Crying	-0.13	0.08	-1.64	.102
Maternal education (first degree)	0.23	0.50	0.46	.649
Maternal education (Diploma in higher				
education)	-0.13	0.51	-0.26	.793
Maternal education (A/AS/S level)	-0.50	0.48	-1.04	.299
Maternal education (O level/GCSE grades A-				
C)	-0.41	0.44	-0.93	.352
C) Maternal education (GCSE grades D-G)	-0.41 -0.41	0.44	-0.93 -0.88	.352
Maternal education (GCSE grades D-G)				
Maternal education (GCSE grades D-G) Maternal education (Other academic	-0.41	0.46	-0.88	.379
Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications)	-0.41	0.46	-0.88	.379
Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these	-0.41 -0.61	0.46	-0.88 -1.09	.379
Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these qualifications)	-0.41 -0.61 -0.29	0.46 0.56 0.45	-0.88 -1.09 -0.64	.379
Maternal education (GCSE grades D-G) Maternal education (Other academic qualifications) Maternal education (None of these qualifications) Conduct problems	-0.41 -0.61 -0.29 -0.38	0.46 0.56 0.45 0.04	-0.88 -1.09 -0.64 -9.23	.379 .278 .525 <.001

BAS-II	0.01	0.00	1.75	.080
Unaffected				
Gender	-0.70	0.11	-6.13	<.001
Prematurity	0.16	0.28	0.59	.558
Low birth weight	-0.81	0.26	-3.16	.002
Mood	0.01	0.11	0.10	.923
Adaptability	0.23	0.11	2.15	.031
Regularity	0.28	0.08	3.64	<.001
Crying	-0.15	0.07	-2.00	.046
Maternal education (first degree)	0.53	0.52	1.02	.306
Maternal education (Diploma in higher				
education)	-0.38	0.51	-0.75	.456
Maternal education (A/AS/S level)	-0.58	0.47	-1.22	.221
Maternal education (O level/GCSE grades A-				
C)	-0.78	0.46	-1.72	.086
Maternal education (GCSE grades D-G)	-1.09	0.46	-2.39	.017
Maternal education (Other academic				
qualifications)	-0.73	0.53	-1.38	.169
Maternal education (None of these				
qualifications)	-1.15	0.48	-2.38	.017

Conduct problems	-0.59	0.04	-17.05	<.001
Emotional problems	-0.16	0.04	-3.90	<.001
Peer problems	-0.14	0.04	-3.88	<.001
School readiness	0.01	0.00	3.23	.001
BAS-II	0.01	0.00	3.50	<.001

Table S10: Regression parameters with mildly affected as reference group

	В	OR	SE	p
Pre-school onset persistent				
Gender	1.13	0.17	6.54	<.001
Prematurity	0.79	0.34	2.30	.021
Low birth weight	-0.09	0.35	-0.25	.805
Mood	-0.14	0.12	-1.20	.231
Adaptability	-0.18	0.13	-1.36	.174
Regularity	0.09	0.10	0.85	.397
Crying	0.09	0.09	0.98	.329
Maternal education (first degree)	-0.22	0.60	-0.36	.719
Maternal education (Diploma in higher				
education)	-0.04	0.60	-0.07	.943
Maternal education (A/AS/S level)	0.59	0.57	1.04	.299
Maternal education (O level/GCSE grades				
A-C)	0.43	0.51	0.83	.407
Maternal education (GCSE grades D-G)	0.54	0.53	1.02	.307
Maternal education (Other academic				
qualifications)	0.21	0.77	0.27	.786

Maternal education (None of these							
qualifications)	0.29	0.53	0.55	.584			
Conduct problems	0.54	0.04	12.61	<.001			
Emotional problems	-0.04	0.06	-0.72	.471			
Peer problems	0.19	0.05	3.72	<.001			
School readiness	-0.01	0.00	-2.08	.038			
BAS-II	0.00	0.00	-0.79	.427			
Subclinical remitting							
Gender	-0.26	0.19	-1.39	.164			
Prematurity	0.58	0.45	1.30	.193			
Low birth weight	-0.44	0.45	-0.97	.331			
Mood	-0.13	0.15	-0.88	.380			
Adaptability	0.00	0.14	0.01	.993			
Regularity	0.10	0.12	0.78	.436			
Crying	-0.01	0.11	-0.09	.927			
Maternal education (first degree)	0.22	0.58	0.38	.705			
Maternal education (Diploma in higher							
education)	0.08	0.61	0.14	.890			
Maternal education (A/AS/S level)	0.37	0.59	0.63	.531			

Maternal education (O level/GCSE grades				
A-C)	-0.09	0.55	-0.16	.874
Maternal education (GCSE grades D-G)	-0.25	0.59	-0.43	.669
Maternal education (Other academic				
qualifications)	0.92	0.69	1.33	.184
Maternal education (None of these				
qualifications)	-0.04	0.56	-0.06	.949
Conduct problems	0.24	0.05	4.59	<.001
Emotional problems	0.06	0.06	0.90	.367
Peer problems	0.10	0.06	1.55	.121
School readiness	0.00	0.00	-0.09	.928
BAS-II	0.00	0.00	-0.05	.959
Late childhood/adolescent onset	ON			
Gender	0.58	0.18	3.24	.001
Prematurity	0.95	0.34	2.81	.005
Low birth weight	-0.38	0.36	-1.07	.287
Mood	-0.01	0.14	-0.09	.933
Adaptability	0.02	0.15	0.13	.895
Regularity	0.19	0.13	1.47	.142

Crying	0.13	0.12	1.08	.278
Maternal education (first degree)	0.03	0.43	0.08	.938
Maternal education (Diploma in higher				
education)	-0.36	0.44	-0.81	.420
Maternal education (A/AS/S level)	0.10	0.48	0.21	.831
Maternal education (O level/GCSE grades				
A-C)	-0.10	0.38	-0.26	.795
Maternal education (GCSE grades D-G)	0.49	0.42	1.15	.249
Maternal education (Other academic				
qualifications)	-0.28	0.80	-0.35	.729
Maternal education (None of these				
qualifications)	0.39	0.40	0.97	.335
Conduct problems	0.21	0.06	3.85	<.001
Emotional problems	-0.04	0.08	-0.43	.668
Peer problems	0.09	0.06	1.57	.116
School readiness	0.00	0.00	0.59	.557
BAS-II	0.00	0.00	-0.49	.627
Pre-school onset partially remitting	ON			
Gender	0.16	0.13	1.28	.202
Prematurity	0.16	0.38	0.42	.678

Low birth weight	0.26	0.33	0.78	.434
Mood	0.01	0.13	0.05	.961
Adaptability	-0.08	0.12	-0.66	.509
Regularity	-0.10	0.09	-1.18	.237
Crying	0.13	0.08	1.64	.102
Maternal education (first degree)	-0.23	0.50	-0.46	.649
Maternal education (Diploma in higher				
education)	0.13	0.51	0.26	.793
Maternal education (A/AS/S level)	0.50	0.48	1.04	.299
Maternal education (O level/GCSE grades				
A-C)	0.41	0.44	0.93	.352
			0.88	.379
Maternal education (GCSE grades D-G)	0.41	0.46	0.88	.575
Maternal education (GCSE grades D-G) Maternal education (Other academic	0.41	0.46	0.88	.579
	0.41	0.46	1.09	.278
Maternal education (Other academic				
Maternal education (Other academic qualifications)				
Maternal education (Other academic qualifications) Maternal education (None of these	0.61	0.56	1.09	.278
Maternal education (Other academic qualifications) Maternal education (None of these qualifications)	0.61	0.56	1.09 0.64	.278
Maternal education (Other academic qualifications) Maternal education (None of these qualifications) Conduct problems	0.61 0.29 0.38	0.56 0.45 0.04	1.09 0.64 9.23	.278 .525 <.001

BAS-II	-0.01	0.00	-1.75	.080
Unaffected				
Gender	-0.54	0.10	-5.69	<.001
Prematurity	0.32	0.27	1.17	.242
Low birth weight	-0.56	0.24	-2.30	.022
Mood	0.02	0.08	0.19	.846
Adaptability	0.15	0.08	1.86	.063
Regularity	0.18	0.08	2.35	.019
Crying	-0.01	0.07	-0.20	.839
Maternal education (first degree)	0.30	0.26	1.18	.237
Maternal education (Diploma in higher				
education)	-0.25	0.26	-0.96	.339
Maternal education (A/AS/S level)	-0.08	0.28	-0.30	.763
Maternal education (O level/GCSE grades				
A-C)	-0.37	0.24	-1.55	.122
Maternal education (GCSE grades D-G)	-0.68	0.28	-2.48	.013
Maternal education (Other academic				
qualifications)	-0.13	0.41	-0.32	.753
Maternal education (None of these				
qualifications)	-0.86	0.27	-3.21	.001

Conduct problems	-0.21	0.03	-6.74	<.001
Emotional problems	-0.09	0.04	-2.26	.024
Peer problems	-0.03	0.04	-0.70	.481
School readiness	0.01	0.00	2.80	.005
BAS-II	0.00	0.00	1.99	.047