Internalizing and externalizing problems across childhood and psychotic-like experiences in adulthood: The role of developmental period

¹ Keri Ka-Yee Wong, Ph.D.

² Marta Francesconi, Ph.D.

³ Eirini Flouri, Ph.D.

¹²³ Department of Psychology and Human Development, University College London, London WC1H 0AA, United Kingdom

Word count = 3,788

Author Notes

This manuscript has been submitted for publication and is likely to be edited as part of the peer-review process. Correspondence regarding this paper should be addressed to Keri Ka-Yee Wong, keri.wong@ucl.ac.uk.

Abstract

Background Psychopathology in childhood and adolescence, commonly indexed by co-occurring internalizing and externalizing problem behaviors, has been found to predict psychotic-like experiences (PLEs) in adults. However, studies to date have rarely examined internalizing and externalizing problem behaviors simultaneously or identified in which developmental period do these problem behaviors predict PLEs in adults. This study tests to what extent internalizing and externalizing problem behaviors in childhood (4–9 years) or adolescence (11–16 years) predict PLEs in adulthood (18 years).

Methods Parent-rated child internalizing and externalizing problems on the Strengths and Difficulties Questionnaire at ages 4, 6, 8, 9, 11, 13, and 16 years from the Avon Longitudinal Study of Parents and Children (N=4717) were modelled using two-piece latent growth curve modelling to predict clinician-rated PLEs at age 18 years, controlling for confounders (gender, ethnicity, socio-economic status, parental education and stressful life events) assessed prior to baseline at age 4 years.

Results Controlling for confounders, an increase in childhood internalizing problems from 4 to 9 years and externalizing problems at baseline (at 4 years) predicted PLEs at 18 years, explaining 9.5% of the variance in adult PLEs. These associations were independent to controls for any changes in adolescent internalizing and externalizing problems from 11 to 16 years.

Conclusions High baseline levels of externalizing problems and increasing internalizing problems throughout childhood can predict PLEs at 18 years. Externalizing problems around the transition to primary school and internalizing problems throughout childhood may be particularly helpful in informing risk of PLEs in adulthood.

Keywords: ALSPAC; psychotic-like experiences; internalizing; externalizing; developmental; childhood.

1. Introduction

Psychotic symptoms exist in adult patients, young adults, and community youths at varying degrees of severity (Bebbington et al., 2013; Bird et al., 2017; Wong et al., 2014). A systematic review of 19 general population studies showed that younger children (9-12 years) generally report higher prevalence rates than older children (13-18 years), at 17% and 7.5%, respectively (Kelleher et al., 2012). More recent cross-sectional studies of school children have either replicated this age contrast - reporting higher prevalence rates in childhood at 8 to 10 years and a leveling off in adolescence, at 11 to 14 years (Wong et al., 2014) - or reported no age contrast in the same age range (Zhou et al., 2018). Why more psychotic-like experiences (PLEs) may be reported in childhood than in adolescence may be explained by three reasons: First, it may be due to the still developing subcortical regions of children's brains. For example, research on children's ability to read others' minds – or theory of mind – suggests that social cognition is still developing beyond the preschool years, with theory of mind shown to increase across 7 to 13 years over and above verbal ability (Devine & Hughes, 2013). This would suggest that, compared to adolescents, children may have more limited cognitive abilities to make sense of their social interactions with others (e.g., they may be more affected by negative peer experiences because they lack the reasoning skills to understand others' minds) and have less control over their own behaviors (e.g., they show poorer emotional regulation). Second, children may misunderstand questions on PLEs, often endorsing more symptoms compared to interviewer assessed PLEs as demonstrated by low informant agreement ($\kappa = .46$) (Wong et al., 2015). Third, there is some evidence to suggest that the turning point observed in PLEs at age 11 years may reflect changes in the school environment as children transition from primary to secondary school (Wong et al., 2014; Wong et al., 2018).

Although PLEs may be difficult to assess properly in early development, they have been found to co-occur with childhood psychopathology (Lancefield et al., 2016), commonly indexed by internalizing and externalizing problem behaviors. While limited research has explored the early childhood psychopathology/later PLEs relationship, the prospective and cross-sectional studies that do exist have found internalizing and externalizing problems in both younger children and adolescents in the community to predict later PLEs (Bird et al., 2017; Gin et al., 2020; Wong et al., 2014; Liu et al., 2019). However, whether it is internalizing and externalizing problems in childhood or adolescence or *both* that may be related to later PLEs and whether any relationships found are not confounded have yet to be

addressed. This is, respectively, due to the narrow assessment points in most studies and the lack of control for other risk factors associated with both internalizing/externalizing problems and PLEs including: *social risks* (i.e., childhood trauma (Kelleher et al., 2008), urbanicity and disadvantaged homes (Polanczyk et al., 2010)), *biological risks* (family history of psychosis (Zammit et al., 2008), *inflammation* (Francesconi et al., 2019), and *cognitive impairments* (poorer motor skills and lower intelligence (Cannon et al., 2002; Horwood et al., 2008)).

There are another two limitations in the extant literature. First, the available evidence suggests that internalizing problems, especially anxiety, are more strongly associated with PLEs, like paranoia, than are externalizing problems like aggression and callous-unemotional traits (Wong et al., 2014). However, with few exceptions (Francesconi et al., 2019; Gjone & Stevenson, 1997), most studies assess internalizing or externalizing problems in separate models without accounting for the high comorbidity between them (Lancefield et al., 2016) or for the fluctuation of these problems throughout different developmental periods. Given that externalizing problems tend to be more observable in childhood and internalizing problems in adolescence (Bongers et al., 2004; Wolff, & Ollendick, 2006), it may also be suggested that *levels* and *changes* in levels of these problems within developmental stage may independently predict PLEs in adulthood. Second, the few available longitudinal studies have typically aggregated change across a few narrow assessment timepoints and modeled data assuming stable linear trajectories of problems. Even the one study, to our knowledge, modelling risk of PLEs by symptom trajectory group over time (e.g., high, low, remitting, persisting, desisting) could not, given its analytic approach, identify the developmental period most predictive of later PLEs (Polanczyk et al., 2010).

Consequently, it is unclear if *levels* and *changes* in internalizing and externalizing problems during different early developmental periods – like childhood and adolescence – may predict psychosis risk in adult life - the aim of our study. Knowing however whether childhood and/or adolescent internalizing and/or externalizing problems predict PLEs may be important for informing early preventive interventions for psychosis with greater precision. Our study, aiming to add this knowledge, reports findings from the Avon Longitudinal Study of Parents and Children (ALSPAC) testing the hypothesis that both internalizing and externalizing problem behaviors across ages 4 to 16 years will be positively associated with levels of PLEs at age 18 years, controlling for covariates such as child's gender, paternal socioeconomic status, maternal education and stressful life experiences. To test our hypothesis, we apply a flexible modelling technique, two-piece growth modelling (2-PGM) to understand which developmental period (childhood and/or adolescence) of internalizing

and externalizing problems, jointly modelled, predicts PLEs in adulthood. 2-PGM estimates change across time whilst controlling for confounders, allowing us to test the specific influences (levels/changes in symptoms) of a-priori development periods that may predict PLEs, a feature that is not available in growth curve modelling or growth mixture modelling which estimate growth trajectories over an entire developmental period. This technique therefore should be particularly useful in capturing the progression of internalizing and externalizing problems behaviors that are known to fluctuate throughout distinct stages of development (Lee & Bukowski, 2012) and be highly comorbid (Lilienfeld, 2003; Willner et al., 2016).

2. Method

2.1. Participants

Ethical approval of the ALSPAC cohort was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time (details at www.alspac.bris.ac.uk). In all, 14,541 pregnant women living in Bristol, UK, and surrounding areas, were enrolled for the study (details of all the data that is available at <http://www.bristol.ac.uk/alspac/researchers/our-data/>). Children were invited to attend annual assessment clinics, including face-to-face interviews and psychological and physical tests from age 7 years onward (Fraser et al., 2012). Additional children were recruited using the original enrolment definition from the participating children's age 7 years onwards, allowing us to have available study data for 15,445 fetuses. Of those, 14,684 were alive at 1 year of age. In an attempt to bolster the initial sample size, new pregnancies have been enrolled since then resulting in additional children being enrolled as well. To date, the total sample size for analyses using any data collected after the age of 7 years is 15,454 pregnancies, resulting in 15,589 fetuses. Of these 14,901 were alive at 1 year of age. In this study our analytic sample was those with full data on PLEs at 18 years ($n = 4,717$). Missing data on all other study variables are found in Table 1.

2.2 Measures

Internalizing and externalizing problem behaviors at ages 4, 6, 8, 9, 11, 13, and 16 years. Internalizing and externalizing problems were assessed via the mother-reported 25-item Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997). The SDQ is a valid

and reliable tool for measuring emotional and behavioral difficulties in children (Goodman, 2001). Excluding the 5 prosocial items, 20 items on children's difficulties (in the past 6 months) were summed to create a 10-item *internalizing* (emotional problems and peer relationship problems) problems scale and a 10-item *externalizing* (conduct problems and hyperactivity-inattention) problems scale (Goodman et al., 2010). The sum of the two scales gives a total difficulties score. The items are scored on a 3-point scale with 0 = 'not true', 1 = 'somewhat true' and 2 = 'certainly true'. These subscales demonstrated good internal reliability at all ages we considered.

Psychotic-like experiences (PLEs) at age 18 years. Problems of psychosis were assessed through the clinician-administered 12-item semi-structured Psychosis-Like Symptom Interview (PLIKSi) (Zammit et al., 2013). The PLIKSi is a widely used assessment of the presence of delusions and hallucinations through 7 items from the Diagnostic Interview Schedule for Children Version IV (Shaffer et al., 2000) and 5 items from the Schedules for Clinical Assessment in Neuropsychiatry version 2 (WHO, 1994). Psychotic experiences were coded as not present, suspected, or definitely psychotic. For suspected or definite psychotic experiences, interviewers also reported the frequency; impact on affect, impact on social function, impact on educational/occupational function; help seeking from professionals; and attributions, such as fever, hypnopompic/hypnogogic state, or substance use. In our analysis, we defined individuals with psychotic-like experiences at age 18 years as those with definite psychotic experiences compared with everyone else.

Covariates. We adjusted our models for a number of baseline (up to about age 4 years, when SDQ was first measured in our sample) covariates known to be associated with children's internalizing and externalizing problems but also with PLEs. These included gender, ethnicity (white, non-white), parental socioeconomic status (approximated by maternal education (below O-level, O-level only, A-level only, university degree) and paternal social class (I, II, III (non-manual), III (manual), IV, V)), and child's stressful life events until age 4 years. In our study these were measured using a 14-item upsetting events checklist (Barnett et al., 1983; Brown et al., 1973; Brown et al., 1973; Honnor et al., 1994), completed by the mother for the child, at the following timepoints in ALSPAC: 18 months (covering events since the child was 6 months), 30 months (events since the child was 18 months), and 42 months (since the child was 30 months). We derived a life events total score for the period of 6 months to 42 months which was the sum of the item scores at all these timepoints (see Online Supplementary Materials Table 2).

2.2.Data Analysis

A latent growth modelling (LGM) and two-piece growth modelling (2-PGM) were conducted using *MPlus* 7.4 for Mac (Muthén, & Muthén, 1998-2015) to test how a single trajectory over childhood and adolescence compared against different trajectories across the two stages: childhood (4-9 years) and adolescence (11-16 years). Applying 2-PGM to our data allows the calculation of a latent variable for the baseline (intercept) level of psychopathology and separate growth time scores to estimate if changes in psychopathology across theoretically-identified transition periods, such as *childhood* (slope 1) and *adolescence* (slope 2), may predict PLEs at age 18 years. Therefore, our 2-PGM produces three latent variables (intercept, slope 1, slope 2) with associated means and variances that can be used to predict our outcome, PLEs in adulthood at 18 years. In our data, the *intercept* represents the baseline level of internalizing or externalizing problems at age 4 years. *Slope 1* represents the average rate of change in internalizing/externalizing problems over time and individual variability about that change in childhood (4-9 years). Likewise, *slope 2* represents the change in adolescence (11-16 years). Weighted least square mean and variance adjusted (WLSMV) estimators were requested as the dependent variable was categorical.

First, LGMs were fitted to examine the role of the average trajectories of combined internalizing and externalizing problems (total difficulties score) across 4 to 16 years in predicting PLEs at 18 years. Second, parallel 2-PGMs were developed to examine the differential developmental effects of childhood and adolescent internalizing and externalizing psychopathology on PLEs at age 18 years. Third and finally, the same models were rerun controlling for potential confounders. Five goodness-of-fit indices were used for model comparison: chi-square statistic (χ^2), root mean squared error of approximation (RMSEA), comparative fit index (CFI), Tucker-Lewis index (TLI), BIC and the AIC (Akaike, 1974) calculated by $\chi^2 - 2*(\text{degrees of freedom})$. High CFI (>0.90), high TLI (>0.90), low RMSEA (<0.06) and the lowest AIC among nested model comparisons indicate a good-fitting model (Brown & Cudeck, 1993; Hu & Bentler, 1999).

2.3.Missing data

We ran our models on complete data available on the PLIKSi at 18 years and used full information maximum likelihood (FIML) estimation (Enders, 2010) to include those with data on at least one confounder variable. FIML makes the assumption that data are missing-at-random (i.e., given the observed data included in the model, the missingness mechanism

does not depend on the unobserved data). Missing data for study variables is detailed in Table 1.

[Insert Table 1]

3. Results

3.1. Descriptive analyses.

Table 1 shows the means, standard deviations, and sample sizes (where appropriate) for all study variables. Online Supplementary Table 1 presents the intercorrelations between all study variables. Internalizing and externalizing problems across all timepoints (4 to 16 years) were generally positively associated with PLEs at age 18 years, as were being female, low maternal education and low paternal socioeconomic status.

Preliminary analysis testing an LGM with the total difficulties score was conducted to explore the average trajectory of combined internalizing and externalizing problems. This demonstrated a poor fitting model (CFI/TLI = .858/858, $\chi^2(28) = 1513.702$, $p < .001$, RMSEA = .106, 90%CI [.102-.111], WRMR = 4.532, $N = 4717$, see Online Supplementary Figure 1). From here onwards, and in line with our hypothesis for the importance of considering different trajectories for internalizing and externalizing problems, we estimate the trajectories of internalizing and externalizing problems in parallel.

3.2. LGM of parallel internalizing and externalizing problem behaviors predicting PLEs at age 18 years.

The LGM of internalizing and externalizing problems measured at 4 to 16 years which assumes a uniform rate of change relative to age (as we specified a linear slope for the whole period) predicting PLEs at age 18 years demonstrated a mediocre fit to the data (see Model 1, Table 2). Above and beyond concurrent externalizing problem behaviors assessed at each timepoint, this model showed that baseline (age 4 years) externalizing problems ($b = .111$, $SE = .047$, $p = .019$) and changes in internalizing problems across childhood and adolescence (ages 4-16 years) ($b = .207$, $SE = .051$, $p < .001$) predicted PLEs at 18 years, but baseline internalizing ($p = .095$) or changes in externalizing problem behaviors ($p = .074$) did not (see Online Supplementary Figure 2). This model explained 6.4% of the variance in PLEs at age 18 years.

[Insert Table 2, Online Supplementary Figure 2]

3.3. 2-PGM of childhood (4-9 years) and adolescent (11-16 years) internalizing and externalizing problem behaviors predicting PLEs at age 18 years.

The 2-PGM of internalizing and externalizing problems during childhood and adolescence predicting PLEs at age 18 years demonstrated a good fit to the data (see Model 2, Table 2). Above and beyond concurrent problem behaviors across development, baseline externalizing problems ($b = .137$, $SE = .066$, $p = .037$) and changes in *childhood* internalizing problems ($b = .223$, $SE = .059$, $p = .001$) predicted PLEs at 18 years (Figure 1). Baseline internalizing problems ($p = .311$), slope of *adolescent* internalizing problems ($p = .099$), slope of *childhood* externalizing problems ($p = .111$), and slope of *adolescent* externalizing problems ($p = .329$) did not predict PLEs at 18 years. This model explained 7.1% of the variance in PLEs at age 18 years.

[Insert Figure 1]

3.4. LGM and 2-PGM controlling for covariates assessed prior to baseline (age 4 years).

Rerunning the same models controlling for covariates assessed before age 4 years produced a poor model fit for the LGM (see Model 3 in Table 2) with none of the latent variables predicting PLEs at 18 years (all $ps > .05$). On the other hand, rerunning the 2-PGM controlling for covariates improved the model fit to the data (see Model 4, Table 2), with the slope of childhood internalizing problems ($b = .207$, $SE = .059$, $p < .001$) and baseline externalizing problems ($b = .139$, $SE = .068$, $p = .040$) predicting PLEs at 18 years, as in the unadjusted model. Baseline internalizing problems ($p = .376$), slope of adolescent internalizing problems ($p = .133$), slope of childhood externalizing problems ($p = .080$), and slope of adolescent externalizing problems ($p = .407$) however, did not predict PLEs at 18 years. Of the covariates included, gender significantly predicted PLEs at 18 years, where females were more likely than males to be in the definite/suspected PLEs group ($b = .228$, $p = .001$), as did lower maternal education ($b = -.064$, $p = .033$). This final model estimating childhood and adolescent levels and changes in levels of internalizing and externalizing psychopathology was an excellent fit, explaining 9.5% of the variance in PLEs at age 18 years (see Figure 2 for the standardized and unstandardized model results).

[Insert Figure 2]

4. Discussion

4.1. *Main Findings.*

In this large-scale study of modelling childhood (4 – 9 years) and adolescent (11 - 16 years) trajectories of internalizing and externalizing problems simultaneously using two-piece growth modelling (2-PGM), we found that baseline externalizing problems at age 4 years and changes in internalizing problems in childhood predicted psychotic-like experiences (PLEs) at age 18 years, above and beyond baseline internalizing and changes of either type of problems in adolescence. These findings suggest that information about the changes in emotional problems in childhood (4-9 years) and about the level of externalizing problems as early as 4 years of age, rather than information about mental health in adolescence, has greater utility in predicting clinician-assessed PLEs in adulthood.

We argue that high levels of externalizing problems – hyperactivity and conduct problems – very early in childhood and increasingly more internalizing problems– emotional symptoms and peer problems - in childhood may represent a set of prodrome symptoms for PLEs. One explanation may be that by age 4 years most of the toddlers with very early externalizing symptoms would have shown symptom reduction, suggesting that those with high levels of externalizing symptoms at age 4 may be those more likely to be in the stable-high group (Fanti & Henrich, 2010). In turn, the persistent trajectory of externalizing behavior, which is also more easily observable than internalizing problems (Bongers et al., 2004; Wolff, & Ollendick, 2006), has been associated with prenatal and perinatal medical risks, and these problems have been found to be related to neuropsychological deficits, in turn related to cognitive impairment and PLEs (Gin et al., 2020). Children exhibiting increasing internalizing problems on the other hand are often unable to form good peer relationships and are more likely to engage in isolating behaviors and social withdrawal, related to later PLEs (Matheson et al., 2013). At the same time, internalizing and externalizing problems may also be seen as the product of early childhood adversity, neglect, and abuse (Trotta et al., 2015; Wong et al., 2018) which are speculated to lead to structural and functional brain changes that give rise to schizophrenia-like problems (Cannon et al., 1994). However, if this were a pathway, we would see our effects lose significance after controlling for stressful life events.

Rather than identifying groups of individuals most vulnerable for developing PLEs in adulthood based on their childhood trajectories of psychopathology (as a latent class growth analysis would do), this study is the first general-population study in the field of schizophrenia spectrum disorders to use 2-PGM to understand *when* assessments or

intervention of comorbid childhood internalizing/externalizing problems may take place in order to reduce PLEs in adulthood for the entire population. 2-PGM allowed us to test which development period(s) - childhood or adolescence - (a feature unique to this modelling technique) best predicts PLEs in adulthood whilst controlling for levels and changes in levels of internalizing/externalizing problems across time. To our knowledge, no study to date has applied 2-PGM to modelling trajectories of childhood and adolescent psychopathology to predict PLEs, although this technique has been used in other areas of developmental psychopathology (Jones & Meredith, 2000). Thus, it is our hope that other researchers in the field of schizophrenia will replicate these findings in other samples.

A final rather interesting but unexpected finding from this study is the gender difference in risk of PLEs. Contrary to the literature suggesting that prevalence rates in schizophrenia do not differ between men and women (Ochoa et al., 2012), the young women in our study were more likely than young men to be in the definite PLEs group. Similarly, studies of clinical high-risk populations, on balance, do not document gender differences in the conversion rate to psychosis (Walder et al., 2013), while studies of patient samples do report gender contrasts in the symptom presentation of patients, where women present with more affective problems while men present with more disorganized and negative problems (Cotton et al., 2009). Some explanations for this discrepant finding could be due to methodological differences in both sampling (e.g., community vs patient samples, where gender differences may be more pronounced in the latter group but not in the former) and assessment (e.g., Psychosis-Like Symptom Interview which is not a diagnostic tool vs clinical diagnostic tools). But presently, this remains an unexpected difference and one which would need to be replicated in future studies.

4.2. Strengths & Limitations.

This study begins to answer how trajectories of change in broad psychopathology across childhood and adolescence may predict psychotic-like experiences in adulthood. To our knowledge, this is also the first study to explore this using an analytic approach, two-piece growth modelling, that could appropriately capture the independent contributions of internalizing and externalizing problems across two distinct stages of development. Thus, our study was able to incorporate flexibly transitional periods (in our case, the transition, broadly speaking, to school and that to adolescence), often encountered in longitudinal data. This modeling technique provides a nuanced understanding of potentially critical developmental windows for assessment and intervention. Another strength of this study is the use of a large,

general population sample with consistent assessments across 7 timepoints (throughout a 14-year period) – a unique feature of our dataset, ALSPAC.

This study is not without limitations, however. First, although our clinician-assessment PLIKSi at age 18 years is widely used in research, it is not a diagnostic tool. While it is conceivable that PLEs may exist or co-occur with internalizing and externalizing problems earlier in development, as shown in previous studies, PLIKSi at age 18 years in ALSPAC was the most complete and reliable, capturing those who have been ‘persistently’ experiencing PLEs over the years (Thaper et al., 2012). Second, our effect sizes are small though significant, and thus may be a result of the analyses being overpowered. Third, *why* early externalizing problems and childhood changes in internalizing problems, but not adolescent internalizing/externalizing problems, may be predictive of psychotic-like experiences in adulthood remains to be clarified. Nonetheless, these study findings spanning a wide developmental period of 14 years highlight childhood years as a potential critical developmental window for early assessment and preventive interventions.

References

- Akaike, H., 1974. A new look at the statistical model identification. *IEEE T Automat Contr.* 19(6), 716-723.
- Barnett, B.E, Hanna, B., Parker, G., 1983. Life event scales for obstetric groups. *J. Psychosom. Res.* 27(4), 313-320.
- Bebbington, P.E., McBride, O., Steel, C., Kuipers, E., Radovanović, M., Brugha, T., Jenkins, R., Meltzer, H.I., Freeman, D., 2013. The structure of paranoia in the general population. *Brit J Psychiat.* 202(6), 419-427.
- Bird, J.C., Waite, F., Rowsell, E., Fergusson, E.C., Freeman, D., 2017. Cognitive, affective, and social factors maintaining paranoia in adolescents with mental health problems: a longitudinal study. *Psychiat. Res.* 257, 34-39.
- Bongers, I.L., Koot, H.M., Van Der Ende, J., Verhulst, F.C., 2004. Developmental trajectories of externalizing behaviors in childhood and adolescence. *Child Dev.* 75(5), 1523-1537.
- Brown, G.W., Harris, T.O., Peto, J., 1973. Life events and psychiatric disorders 1 Part 2: nature of causal link. *Psychol. Med.* 3(2), 159-176.
- Brown, G.W., Sklair, F., Harris, T.O., Birley, J.L. 1973. Life-events and psychiatric disorders 1 Part 1: some methodological issues. *Psychol. Med.* 3(1), 74-87.
- Brown, M.W., Cudeck, R., 1993. *Alternative Ways of Assessing Model Fit*. In K. A. Bollen, & J. S. Long (Eds.), *Testing Structural Equation Models*. Newbury Park, CA: Sage, 136-162.
- Cannon, M., Caspi, A., Moffitt, T.E., Harrington, H., Taylor, A., Murray, R.M., Poulton, R., 2002. Evidence for early-childhood, pan-developmental impairment specific to schizophreniform disorder: results from a longitudinal birth cohort. *Arch. Gen. Psychiat.* 59(5), 449-456.
- Cannon, T.D., Mednick, S.A., Parnas, J., Schulsinger, F., Praestholm, J., Vestergaard, A., 1994. Developmental brain abnormalities in the offspring of schizophrenic mothers: II. Structural brain characteristics of schizophrenia and schizotypal personality disorder. *Arch. Gen. Psychiat.* 51(12), 955-962.
- Cotton, S.M., Lambert, M., Schimmelmann, B.G., Foley, D.L., Morley, K.I., McGorry, P.D., Conus, P., 2009. Gender differences in premorbid, entry, treatment, and outcome characteristics in a treated epidemiological sample of 661 patients with first episode psychosis. *Schizophr. Res.* 114(1-3), 17-24.

- Devine, R.T., Hughes, C., 2013. Silent films and strange stories: Theory of mind, gender, and social experiences in middle childhood. *Child Dev.* 84(3), 989-1003.
- Enders, C. K., 2010. *Applied missing data analysis*. Guilford press.
- Fanti, K.A., Henrich, C.C., 2010. Trajectories of pure and co-occurring internalizing and externalizing problems from age 2 to age 12: findings from the National Institute of Child Health and Human Development Study of Early Child Care. *Dev. Psychol.* 46(5), 1159-1175.
- Francesconi, M., Minichino, A., Khandaker, G.M., Midouhas, E., Lewis, G., Flouri, E., 2019. Internalising problems mediate the longitudinal association between childhood inflammation and psychotic-like experiences in adulthood. *Schizophr. Res.* 15, 424-429.
- Fraser, A., Macdonald-Wallis, C., Tilling, K., Boyd, A., Golding, J., Davey Smith, G., Henderson, J., Macleod, J., Molloy, L., Ness, A., 2012. Ring, S. Cohort profile: the Avon Longitudinal Study of Parents and Children: ALSPAC mothers' cohort. *Int. J. Epidemiol.* 42(1), 97-110.
- Gin, K., Stewart, C., Jolley, S., 2020. A systematic literature review of childhood externalising psychopathology and later psychotic symptoms. *Clin. Psychol. Psychother.* 1-23.
- Gjone, H., Stevenson, J., 1997. The association between internalizing and externalizing behavior in childhood and early adolescence: genetic or environmental common influences?. *J Ab. Child Psychol.* 25(4), 277-286.
- Goodman, R., 1997. The Strengths and Difficulties Questionnaire: a research note. *J Child Psychol. Psychiat.* 38(5), 581-586.
- Goodman, R., 2001. Psychometric properties of the strengths and difficulties questionnaire. *J Am Acad. Child Adoles. Psychiat.* 40(11), 1337-1345.
- Honnor, M.J., Zubrick, S.R., Stanley, F.J., 1994. The role of life events in different categories of preterm birth in a group of women with previous poor pregnancy outcome. *Eur. J. Epidemiol.* 10(2), 181-188.
- Horwood, J., Salvi, G., Thomas, K., Duffy, L., Gunnell, D., Hollis, C., Lewis, G., Menezes, P., Thompson, A., Wolke, D., Zammit, S., 2008. IQ and non-clinical psychotic problems in 12-year-olds: results from the ALSPAC birth cohort. *Br. J. Psychiat.* 193(3), 185-191.
- Hu, L.T., Bentler, P.M., 1999. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Struc. Eq Model.* 6(1), 1-55.

- Jones, C.J., Meredith, W., 2000. Developmental paths of psychological health from early adolescence to later adulthood. *Psychol. Aging*, 15(2), 351–360. <https://doi.org/10.1037/0882-7974.15.2.351>
- Kelleher, I., Connor, D., Clarke, M.C., Devlin, N., Harley, M., Cannon, M., 2012. Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. *Psychol. Med.* 42(9), 1857-1863.
- Kelleher, I., Harley, M., Lynch, F., Arseneault, L., Fitzpatrick, C., 2008. Cannon, M. Associations between childhood trauma, bullying and psychotic symptoms among a school-based adolescent sample. *Br. J. Psychiat.* 193(5), 378-382.
- Lancefield, K.S., Raudino, A., Downs, J.M., Laurens, K.R., 2016. Trajectories of childhood internalizing and externalizing psychopathology and psychotic-like experiences in adolescence: a prospective population-based cohort study. *Dev. Psychopathol.* 28(2), 527-536.
- Lee, E.J., Bukowski, W.M., 2012. Co-development of internalizing and externalizing problem behaviors: Causal direction and common vulnerability. *J Adoles.* 35(3), 713-729.
- Lilienfeld, S.O. 2003. Comorbidity between and within childhood externalizing and internalizing disorders: Reflections and directions. *J. Ab. Child Psychol.* 31(3), 285-291.
- Linscott, R.J., Van Os, J., 2013. An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychol Med.* 43(6):1133-49.
- Liu, J., Wong, K.K., Dong, F., Raine, A., Tuvblad, C., 2019. The Schizotypal Personality Questionnaire–Child (SPQ-C): Psychometric properties and relations to behavioral problems with multi-informant ratings. *Psychiatr. Res.* 275, 204-211.
- Matheson, S.L., Vijayan, H., Dickson, H., Shepherd, A.M., Carr, V.J., Laurens, K.R., 2013. Systematic meta-analysis of childhood social withdrawal in schizophrenia, and comparison with data from at-risk children aged 9–14 years. *J Psychiatric Res.* 47(8), 1061-1068.
- Muthén, L.K., Muthén, B.O., 1998-2015. Mplus User’s Guide. Seventh Edition. Los Angeles, CA: Muthén & Muthén.
- Ning, L., Luo, W., 2017. Specifying turning point in piecewise growth curve models: challenges and solutions. *Front. App. Math. Stat.* 3, 19.

- Ochoa, S., Usall, J., Cobo, J., Labad, X., Kulkarni, J., 2012. Gender differences in schizophrenia and first-episode psychosis: a comprehensive literature review. *Schizophr. Res. Treat.* 1-9.
- Polanczyk, G., Moffitt, T.E., Arseneault, L., Cannon, M., Ambler, A., Keefe, R.S., Houts, R., Odgers, C.L., Caspi, A., 2010. Etiological and clinical features of childhood psychotic problems: results from a birth cohort. *Arch. Gen. Psychiatr.* 67(4), 328-338.
- Shaffer, D., Fisher, P., Lucas, C. P., Dulcan, M.K., Schwab-Stone, M.E., 2000. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. *J. Am. Acad. Child Adoles. Psychiatr.* 39(1), 28-38.
- Thapar, A., Heron, J., Jones, R.B., Owen, M.J., Lewis, G., Zammit, S., 2012. Trajectories of change in self-reported psychotic-like experiences in childhood and adolescence. *Schiz. Res.* 140(1-3), 104-109.
- Trotta, A., Murray, R.M., Fisher, H.L., 2015. The impact of childhood adversity on the persistence of psychotic problems: a systematic review and meta-analysis. *Psychol. Med.*, 45(12), 2481-2498.
- Walder, D.J., Holtzman, C.W., Addington, J., Cadenhead, K., Tsuang, M., Cornblatt, B., ... & Seidman, L.J., 2013. Sexual dimorphisms and prediction of conversion in the NAPLS psychosis prodrome. *Schiz. Res.* 144(1-3), 43-50.
- WHO., 1994. Geneva. Psychiatric Publishers International/American Psychiatric Press Inc.; Switzerland: 1994. SCAN: schedules for clinical assessment in neuropsychiatry version 2.0.
- Willner, C.J., Gatzke-Kopp, L.M., Bray, B.C., 2016. The dynamics of internalizing and externalizing comorbidity across the early school years. *Dev.l Psychopathol.* 28(4pt1), 1033-1052.
- Wolff, J.C., Ollendick, T.H., 2006. The comorbidity of conduct problems and depression in childhood and adolescence. *Clin. Child Fam. Psychol. Rev.* 9(3-4), 201-220.
- Wong, K.K., 2015. *Paranoia and social mistrust in UK and Hong Kong children* (Doctoral dissertation, University of Cambridge). <https://doi.org/10.17863/CAM.16650>
- Wong, K.K., Freeman, D., Hughes, C., 2014. Suspicious young minds: paranoia and mistrust in 8-to 14-year-olds in the UK and Hong Kong. *Br. J. Psychiatr.* 205(3), 221-309.
- Wong, K.K., Raine, A., Venables, P., 2018. The effect of being left home alone at age 3 years on schizotypy and antisocial behavior at ages 17 and 23 years. *J. Psychiatr. Res.* 105, 103-112.

- Zammit, S., Horwood, J., Thompson, A., Thomas, K., Menezes, P., Gunnell, D., Hollis, C., Wolke, D., Lewis, G., Harrison, G., 2008. Investigating if psychosis-like problems (PLIKS) are associated with family history of schizophrenia or paternal age in the ALSPAC birth cohort. *Schizophr. Res.* *104*(1-3), 279-286.
- Zammit, S., Kounali, D., Cannon, M., David, A.S., Gunnell, D., Heron, J., Jones, P.B., Lewis, S., Sullivan, S., Wolke, D., Lewis, G., 2013. Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study. *Am. J. Psychiatr.* *170*(7), 742-750.
- Zhou, H.Y., Wong, K.K., Shi, L.J., Cui, X.L., Qian, Y., Jiang, W.Q., Du, Y.S., Lui, S.S.Y., Luo, X.R., Yi, Z.H., Cheung, E.F.C., Docherty, A.R., Chan, R.C., 2018. Suspiciousness in young minds: Convergent evidence from non-clinical, clinical and community twin samples. *Schizophr. Res.* *199*, 135-141.

Tables

Table 1. Means, standard deviations, and sample sizes for all study variables.

Descriptive Statistics		
Analytic sample (n = 4717)	<i>N</i>	<i>M (SD)</i>
Continuous variables		
Internalizing, 4 years	3895	2.88 (2.35)
Internalizing, 6 years	3767	2.53 (2.50)
Internalizing, 8 years	3728	2.95 (2.74)
Internalizing, 9 years	3897	2.59 (2.68)
Internalizing, 11 years	3809	2.51 (2.69)
Internalizing, 13 years	3744	2.58 (2.73)
Internalizing, 16 years	3451	2.54 (2.72)
Externalizing, 4 years	3884	5.59 (3.14)
Externalizing, 6 years	3757	4.67 (3.15)
Externalizing, 8 years	3726	4.51 (3.30)
Externalizing, 9 years	3893	3.90 (3.01)
Externalizing, 11 years	3804	3.66 (2.90)
Externalizing, 13 years	3739	3.87 (3.01)
Externalizing, 16 years	3458	3.35 (2.88)
Stressful Life Events Score		
Total score, summed 18m, 30m, 42m	3761	4.00 (2.48)
Categorical variables		
Paternal social class (I to V)		
I (non-manual)	577	12.23%
II (non-manual)	1484	31.46%
III (non-manual)	481	10.20%
III (manual)	1018	21.58%
IV (manual)	311	6.59%
V (manual)	86	1.82%
Missing	760	16.11%
Maternal education		
Below O-level	667	14.14%
O-level	1463	31.02%
A-Level	1193	25.29%
University degree	826	17.51%
Missing	568	12.04%
Ethnicity		
White	4045	85.75%
Non-white	179	3.79%
Missing	493	10.45%
Gender		
Male	2051	43.48%
Female	2665	56.50%
Missing	1	.02%
Psychotic-like experiences, 18 years		
Definite	229	4.85%
None definite	4488	95.15%

Table 2. Model fit indices for linear and piecewise growth curve models of internalizing and externalizing problem behaviors.

Model	free	AIC (χ^2 -2df)	χ^2 (df)	RMSEA [95%CI]	CFI/TLI	WRMR
Model 1. Int/Ext Linear Parallel Growth Curve Model	33	2292.341	2494.341 (101) ***	.071 [.068 - .073]	.873/.868	3.966
Model 2. Int/Ext Parallel 2-Piece Growth Curve Model	53	486.277	648.277 (81) ***	.039 [.036 - .041]	.970/.961	1.727
Model 3. Int/Ext Linear Parallel Growth Curve Model with covariates	78	3022.016	2879.301 (151) ***	.062 [.060 - .064]	.882/.852	3.084
Model 4. Int/Ext Parallel 2-Piece Growth Curve Model with covariates	108	518.236	760.236 (121) ***	.033 [.031 - .036]	.972/.957	1.374

Notes. *** $p < .000$. Dependent variable = PLEs at age 18 years. N = 4717. Estimator = WLSMV, Iterations = 10,000, Coverage = 0.05.

Figure 1 Two-piece latent growth curve model (2-PGM) (unadjusted) of parallel internalizing and externalizing problem behaviors predicting PLEs at 18 years (standardized beta).

Figure 2 Two-piece latent growth curve model (2-PGM) of parallel internalizing and externalizing problem behaviors predicting PLEs at 18 years controlling for covariates assessed before age 4 years with standardized (above) and unstandardized (below) betas.

Online Supplementary Table 1. Summing a list of 15 mother-reported childhood upsetting life events when the child was 18 months, 30 months, and 42 months.

1. Child was taken into care
2. A pet died
3. Child moved home
4. Child had a shock or fright
5. Child was physically hurt by someone
6. Child was sexually abused
7. Child was separated from her mother for at least a week
8. Child was separated from her father for at least a week
9. Child acquired a new parent
10. Child had a new brother or sister
11. Child was admitted to hospital
12. Child changed carer/care giver
13. Child was separated from someone else
14. Child started creche or nursery
15. Something else

Online Supplementary Table 2. Correlations between all study variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. Gender (Male = 1, Female = 2)	-	-.02	-.01	-.04**	.04**	-.01	.01	.01	.02	.02	.02	.10**	-.07**	-.11**	-.12**	-.10**	-.11**	-.11**	-.06**	.06**
2. Stressful Life Events		-	.01	.13**	-.07**	.07**	.12**	.12**	.13**	.10**	.08**	.07**	.07**	.09**	.11**	.10**	.08**	.09**	.07**	.01
3. Ethnicity (White = 1, non-White = 2)			-	.01	.03*	.00	.01	.00	.01	.00	.00	.01	.00	.00	-.02	.00	.00	.00	.00	.01
4. Maternal Education				-	-.34**	-.05**	-.03*	.00	.00	-.05**	-.03*	-.03*	-.12**	-.08**	-.06**	-.07**	-.07**	-.06**	-.07**	-.05**
5. (Low) Paternal Social Class					-	.04**	.02	.02	-.01	.04**	.04**	.04**	.10**	.08**	.07**	.06**	.07**	.09**	.08**	.04**
6. Internalizing Age 4						-	.47**	.44**	.36**	.34**	.30**	.27**	.25**	.20**	.22**	.20**	.17**	.19**	.13**	.01
7. Internalizing Age 6							-	.58**	.54**	.46**	.42**	.37**	.18**	.28**	.25**	.24**	.21**	.23**	.18**	.03*
8. Internalizing Age 8								-	.59**	.53**	.48**	.40**	.22**	.28**	.34**	.27**	.27**	.26**	.21**	.04**
9. Internalizing Age 9									-	.58**	.53**	.43**	.20**	.27**	.28**	.34**	.28**	.27**	.22**	.05**
10. Internalizing Age 11										-	.61**	.47**	.21**	.27**	.29**	.28**	.35**	.29**	.24**	.06**
11. Internalizing Age 13											-	.51**	.22**	.26**	.26**	.29**	.29**	.34**	.24**	.07**
12. Internalizing Age 16												-	.15**	.20**	.18**	.20**	.22**	.21**	.30**	.08**
13. Externalizing Age 4													-	.59**	.58**	.53**	.47**	.46**	.37**	.03
14. Externalizing Age 6														-	.73**	.71**	.64**	.60**	.47**	.03*
15. Externalizing Age 8															-	.73**	.68**	.63**	.50**	.05**
16. Externalizing Age 9																-	.72**	.69**	.56**	.04**
17. Externalizing Age 11																	-	.74**	.59**	.06**
18. Externalizing Age 13																		-	.61**	.06**
19. Externalizing Age 16																			-	.06**
20. Psychotic-Like Experiences (PLEs) Age 18 (None Def = 0; Def = 1)																				-

Notes. **. $p < 0.01$; * $p < 0.05$. Kendall's tau correlations between a continuous/categorical variable. Spearman's rho between skewed continuous variables. Pearson's correlation between normally distributed variables.

Online Supplementary Figure 1. Latent growth curve model (LGM) of total difficulties score (on the SDQ) predicting PLEs at 18 years (standardized beta). CFI/TLI = .858/858, $\chi^2(28) = 1513.702$, $p < .001$, RMSEA = .106, 90%CI[.102-.111], WRMR = 4.532, $N = 4717$.

Online Supplementary Figure 2. Linear latent growth model (LGM) (unadjusted) of parallel internalizing and externalizing problem behaviors predicting PLEs at 18 years (standardized beta).

Role of Funding Source

The UK Medical Research Council and Wellcome (Grant ref: 217065/Z/19/Z) and the University of Bristol provide core support for ALSPAC. PLIKSi assessments were funded by MRC G0701503/85179. A comprehensive list of grants funding is available on the ALSPAC website (<http://www.bristol.ac.uk/alspac/external/documents/grant-acknowledgements.pdf>).

This publication is the work of the authors and Professor Eirini Flouri, Dr. Keri Wong and Dr. Marta Francesconi will serve as guarantors for the contents of this paper. This research was specifically funded by the UK Economic and Social Research Council (Grant ref: ES/P001742/1; PI Eirini Flouri). The authors report no biomedical financial interests or potential conflicts of interest.

Contributors

K.W. was involved with conception of the research question, analysing the data, drafting, writing, reviewing, and final approval of the article.

M.F. was involved with drafting, writing, reviewing, and final approval of the article.

E.F. was involved with the management of the project, supervision of the work, writing up, and final approval of the article.

Acknowledgements

We are extremely grateful to all the families who took part in this study, the midwives for their help in recruiting them, and the whole ALSPAC team, including interviewers, computer and laboratory technicians, clerical workers, research scientists, statisticians, volunteers, managers, receptionists and nurses. This publication is the work of the authors. Professor Eirini Flouri, Dr. Keri Wong and Dr. Marta Francesconi will serve as guarantors for the contents of this paper.