Cognitive variations following exposure to childhood adversity: Evidence from a pre-registered, longitudinal study

Tochukwu Nweze,[a,b,*] Michael Ezenwa,[c] Cyriacus Ajaelu,[c] Jamie L. Hanson,[d,e] and Chukwuemeka Okoye[c]

[a]MRC Cognition and Brain Sciences Unit, University of Cambridge, Cambridge, United Kingdom
[b]Department of Psychology, University of Nigeria, Nsukka, Nigeria
[c]Department of Psychology, Nnamdi Azikiwe University, Awka, Nigeria
[d]Department of Psychology, University of Pittsburgh, Pittsburgh, PA, USA
[e]Learning Research & Development Center, University of Pittsburgh, Pittsburgh, PA, USA

eClinicalMedicine
2023;56: 101784
Published Online XXX
https://doi.org/10.1016/j.eclinm.2022.101784

Summary

Background Different methodological approaches to studying the effects and timing of childhood adversity have been proposed and tested. While childhood adversity has primarily been operationalized through specificity (effects of individual adversity types) and cumulative risk (sum of all adversities reported by an individual) models, dimensional models (probeable through latent class and other cluster analyses) have recently gained traction given that it can overcome some of the limitations of the specificity and cumulative risk approaches. On the other hand, structured lifecourse modelling is a new statistical approach that examines the effects of the timing of adversity exposure on health outcomes by comparing sensitive periods and accumulation hypotheses. In this study, we apply these sets of methodological approaches and theoretical models to better understand the complex effects of childhood adversity on cognitive outcomes.

Methods We analysed data obtained from the Avon Longitudinal Study of Parents and Children for 2965 participants (Male = 1125; Female = 1840). This included parental report of 11 types of childhood adversity when participants were between 8 months and 8.7 years, and performance on inhibition, working memory and emotion recognition neurocognitive tasks when participants were 24 years of age (April 1, 1992–October 31, 2017). We used latent class analysis to classify the participants into subgroups, while we used Kruskal–Wallis test to examine differences in cognitive performance among the adversity subgroups. Additionally, to test whether sensitive period or accumulation models better explain the effects of childhood adversity on cognitive functioning, we carried out separate analyses using structured lifecourse modelling approaches.

Findings Latent class analysis showed evidence of 5 classes, namely: low adversity (71.6%), dysfunctional family (9.58%); parental deprivation (9.65%); family poverty (6.07%) and global adversity (3.1%). We observed group differences in cognitive performance among the adversity classes in an inhibition control task, $\chi^2(4) = 15.624$, $p = 0.003$ and working memory task, $\chi^2(4) = 15.986$, $p = 0.003$. Pairwise comparison tests showed that participants in the family poverty class performed significantly worse than those in the low adversity class, for the inhibition control task ($p = 0.007$) while participants in the global adversity class significantly performed worse than participants in the low adversity class ($p = 0.026$) and dysfunctional family class ($p = 0.034$) on the working memory task. A further analysis revealed that the associations between each individual adversity type and cognitive outcomes were mostly consistent with the observed class performance in which they co-occurred. Follow-up analyses suggested that adversity during specific sensitive periods, namely very early childhood and early childhood, explained more variability in these observed associations, compared to the accumulation of adversities.

Interpretation These findings suggest that dimensional approaches e.g., latent class analysis or cluster analysis could be good alternatives to studying childhood adversity. Using latent class analysis for example, can help reveal the population distribution of co-occurring adversity patterns among participants who may be at the greatest health risk and thus, enable a targeted intervention. In addition, this approach could be used to investigate specific pathways that link adversity classes to different developmental outcomes that could further complement the specificity or cumulative risk approaches to adversity. On the other hand, findings from a separate analysis using structured lifecourse modelling approaches also highlight the vital developmental timeframes in childhood during which the impact of adversity exposure on cognitive outcomes is greatest, suggesting the need to provide comprehensive academic and mental health support to individuals exposed during those specific timeframes.

*Corresponding author. MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge, United Kingdom.
E-mail address: ejiofortochukwunweze@gmail.com (T. Nweze).

Funding T.N. received funding from Cambridge Trust (University of Cambridge).

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Keywords: Childhood adversity; Cognitive functioning; Sensitive period; Structured lifecourse modelling approach; Latent class analysis

Research in context

Evidence before this study

This study was initially designed and pre-registered between November 01, 2019 and January 31, 2020. During this period, we searched for scientific papers published in PubMed before January 01, 2020 using the following keywords: "*childhood adversity*", OR "*early-life adversity*", OR "*early-life stress*", OR "*childhood maltreatment*", OR "*adverse childhood experiences*", AND "*cognition*" OR "*cognitive functioning*" OR "*cognitive abilities*", AND "*latent class analysis*", OR "*latent class profile*", OR "*cluster analysis*", "dimensional model", AND "*latent class regression*". Although the search engine identified at least 5 empirical studies that have examined the adversity latent classes, no empirical study published in any scientific journal before April 2022 has attempted to establish specific pathways to cognitive functioning from these adversity classes. We later added "*structured life course modelling approach*" to our search and found one study that used this modelling approach to test the sensitive period of adversity on recognition of facial emotions. We, therefore, included this modelling in our analysis to provide a comprehensive test of sensitive periods of adversity on multiple cognitive outcomes.

Added value of this study

We found 5 distinct subgroups of adversity exposed individuals, with varying performance in two cognitive outcomes of inhibition and working memory. We found no group differences for emotion recognition. To deal with challenges of specificity, we conducted sensitivity analyses examining the association between each adversity type and cognitive outcomes, before and after controlling for the effect of shared variance with other adversity types. Findings showed that the most significant associations between the adversity types (e.g., sexual abuse, maternal victimization, financial distress) and working memory lessened, to non-significant effects, after controlling for shared variance with other adversity predictors in a multivariate regression analysis. Finally, using structured lifecourse modelling approaches, we found that adversity exposure at specific sensitive periods explained greater variability in poorer cognitive performance compared to the adversity accumulated in childhood.

Implications of all the available evidence

Testing the theoretical models of dimensional approach, sensitive periods and accumulation hypotheses provided additional insight into the complex associations between childhood adversity and cognitive functioning.

Introduction

Several previous studies have shown that childhood adversity is associated with poorer developmental outcomes.[1,2] Other work has, however, observed certain improved outcomes linked to adaptation among individuals exposed to adversity.[3–7] These variations in findings may be driven partly, by the type of adversity measured and the way it was measured, timing of exposure, or even the cultural context of the sampled population. For instance, studies have shown that individuals exposed to different types of unpredictable childhood stress (e.g., caregiving instability or neighbourhood violence) may have better performance in some cognitive outcomes (e.g., set shifting; working memory) by developing relevant adaptive features needed for environmental survival. At the same time, after exposure to adversity, these same individuals also perform poorer in other outcomes that are not essential to basic survival in such unpredictable environments (e.g., inhibition).[3,4,8,9] Here, to examine the differential and time-sensitive effects of childhood adversity on cognitive functioning in adulthood, we leveraged a large-scale, longitudinal study with multi-measures of adversity across development.

Cognitive functioning has been shown to be a good predictor of many life outcomes at adulthood,[10] and studies have shown that individuals exposed to childhood adversity may struggle in one or more facets of cognitive functioning in later adolescence or adulthood. Several studies have shown that adversity globally impairs cognitive functioning with individuals exposed to adversity considerably showing worse performance in tests measuring general executive functioning such as inhibition,[11,12] working memory,[13,14] shifting[12] and affective processing.[15,16] However, these findings are not perfectly uniform, as some projects have noted individuals exposed to specific types of adversity have improved performance in specific cognitive domains likely to be adaptive for their survival and matched to their environments, including memory,[3,8,17] shifting,[9] as well as enhanced ability in detecting negative threatening emotional expressions.[18–21] These findings taken together, suggest that the effects of adversity on cognitive functioning may be quite heterogenous in nature.

Yet, despite the compelling evidence from these empirical studies, important gaps that limit our understanding remain. First, most studies of childhood adversity have used either specificity or cumulative risk score approaches when operationalizing adversity. In specificity approaches, the effects of specific types of childhood adversity are examined while cumulative risk score approaches involve tallying up all the adversities reported by an individual to create a risk score. As noted in previous studies,[22,23] each of these approaches have significant limitations. This is because childhood adversity mostly co-occurs[24,25] with varying effects; this fact is ignored by both specificity and risk score approaches. Second, many of the past studies have often relied on cross-sectional data, making it difficult to examine the effect of timing of adversity exposure on cognitive outcomes. Similarly, because of a paucity of longitudinal studies, there is limited insight on the developmental timeframes in which children's cognitive abilities are most vulnerable to adversity exposure. While theoretical models of sensitive periods (time-dependent effect of adversity) and accumulation (greater effect of adversity, as a result of greater number of occurrences) have been tested on a limited set of developmental outcomes,[26–28] these models have not adequately examined key cognitive outcomes (e.g., executive function tasks). To the best of our knowledge, only one study[28] tested these models on recognition of facial emotions.

In the current study, we first attempted to address these limitations by examining rich measurements of adverse childhood experiences using a combination of specificity approaches and dimensional models of adversity.[22,23] Specifically, we use latent class analysis to classify participants into adversity subgroups based on their response patterns of adversity exposure. The value of using dimensional models (e.g., latent class) lies in its ability to expose the dominant pattern of childhood adversity exposure. Rarely do we see individuals exposed to one adversity type that do not also report, at least, another type of adversity.[1] Studying adversity using a specificity approach is suitable for investigating a single adversity type in isolation. That is, when individuals in a population are reporting only one type of adversity. In practice, this is not robust as many other adversity types are left out. Studying multiple adversity types separately will help, but not completely solve this problem. Thus, latent class analysis is one technique that could provide insight into the pattern of responses among those reporting multiple adversity types, so that closely related adversities cluster together. In addition to examining the subgroups of adversity, we also probe the specific effects of individual types of adversity (specificity approach). By using both specificity and dimensional approaches, we can compare the effects of individual adversity types in relation to the clusters or classes in which they co-occurred, as well as disentangle the specific pathways linking childhood adversity to cognitive functioning. Previous studies testing dimensional models using latent class analysis found a varying number of latent classes, predominantly populated by participants reporting low levels of adversity.[29–34] However, no previous study, to our knowledge, has attempted to connect different adversity subgroups or classes to differences in cognitive functioning.

Second, guided by the theoretical models of sensitive periods and stress accumulation, we examine the timing effects of adversity exposure on cognitive functioning. To achieve this, we use structured lifecourse modelling approach (SLCMA)[26–28,35] to examine the time of exposure in which adversity is likely to have the greater effect on cognitive functioning. By using SLCMA, we can directly compare the two theoretical models and determine whether sensitive periods or accumulation models better explain the observed variability between childhood exposure and cognitive functioning. Sensitive period hypothesis assumes that for observed effects of childhood adversity on cognitive outcomes, a greater portion of the variance will be explained by the particular timing of the adversity exposure. This particular time of (adversity) exposure in our study could be between 8 months and 8.7 years when exposure to adversity was reported. Accumulation hypothesis, on the other hand, argues that it is the number of times an individual was exposed to adversity across these exposure timepoints that would explain the more variance in the observed effects between adversity exposure and cognitive outcomes. It is important to note that latent classes cannot be used to examine SLCMA as there are typical assumptions that must be met before analysis of SLCMA can take place (e.g., use of dichotomized manifest variables). These manifest variables must be measured across multiple timepoints from which SLCMA model can examine which specific timepoints (sensitive periods) or accumulation models have the greater explanatory power for the observed effect. Full methodological and statistical description of SCLMA has been detailed elsewhere.[35] Previous studies that have tested these theoretical models on other health outcomes have shown that sensitive period models explained more of the observed effects than the accumulation models.[26,27] Therefore, replicating these findings on cognitive outcomes will lead to a holistic appreciation of the impact of timing of adversity exposure on a broader range of outcomes and specifically, provide more informed knowledge to better support children who may be at high risk during these important developmental stages.

Thus, using the Avon Longitudinal Study of Parents and Children (ALSPAC), a population cohort study,[36–38] we addressed the following research questions:

1. What are the distinct patterns of childhood adversity exposure?
2. Are there differences in cognitive performance among different adversity subgroups?
3. Is sensitive periods or accumulation hypothesis better at explaining the independent associations between adversity types and cognitive outcomes?

The current study benefits from a large longitudinal panel dataset, as well as multiple adversity and cognitive measures. This will not only provide an informed understanding of the nuanced effects of adversity but also help demystify the effect of timing of adversity exposure on cognitive outcomes. More importantly, it will enable a direct comparison between previously used measurement models (specificity versus dimensional approaches), as well as disentangle between two popular but largely untested theoretical models (sensitive periods versus accumulation). Such an approach could provide a better insight into whether specific timing of adversity exposure or greater number of adversity occurrences better explains the observed variability between childhood adversity and cognitive functioning. Given previous studies,[22,23] we hypothesize the existence of, at least, four adversity classes that include the dimensions of threat, deprivation, low adversity and global or pervasive adversity. We also hypothesize that adversity will have differential effects on different facets of cognitive functioning (e.g., impair inhibition and positive emotions but improve working memory and recognition of negative emotions) and these effects will vary according to different adversity subgroups.

Methods

Participants

Data came from the Avon Longitudinal Study of Parents and Children (ALSPAC),[36–38] a multi-wave population cohort study that prospectively sampled mothers living in Avon county, United Kingdom. A pre-birth cohort of 14,541 pregnant women residing in Avon, with the expected delivery between 1 April 1991 and 31 December 1992, accepted to participate in the study designed to investigate the influence of environmental risk factors on the health and development of children. Data from mailed questionnaires and clinic visits were routinely obtained at regular intervals, of which 75% of participants completed at least one follow up. Ethical approval for the study 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 the participants while as appropriate, children were invited to give assent.[38] The data dictionary of the ALSPAC study website has full details of all the data that are available at every assessment wave (http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/).

The final analytic sample in this study consists of 2965 participants (Male = 1125; Female = 1840) whose mothers responded to a set of childhood adversity measures between 8 months and 8.7 years and who at age 24 visited the clinic and completed three cognitive measures of stop signal task (inhibition), N-back task (working memory) and emotional recognition task.

Measures

Childhood adversity

Eleven types of childhood adversity have been extensively examined in the ALSPAC cohort[27,28,39–43] and were used in the study. They include: 1. Physical abuse (by anyone); 2. Sexual abuse (by anyone); 3. Inconsistent caregiving; 4. Family instability; 5. Caregivers abuse; 6. Maternal psychopathology; 7. Maternal victimization; 8. Parental legal problems; 9. Parental separation or divorce; 10. Financial distress; and 11. Neighbourhood stress. These adversity measures were obtained from questionnaires mailed to mothers when participants were between 8 months and 8.7 years. Each adversity type was assessed between 2 and 8 timepoints. (See Supplement 1 to learn how the adversity measures were derived, including the sub-variable questions and coding as well as the assessment timepoints for each adversity type). Exposure to each adversity type at each timepoint was initially coded 1 if reported, or 0 if no exposure occurred at that assessment timepoint. To examine exposure to adversity across childhood, each adversity type was recoded across all timepoints, rather than at each timepoint. That is, each adversity type was coded 1, if a participant was reported to have been exposed at any of the assessment timepoints; otherwise a participant with no exposure at any of the assessment timepoints was coded 0. Additionally, to examine the theoretical models of sensitive periods and accumulation, we remodelled the adversity data accordingly. The sensitive periods hypothesis assumes that childhood adversity has developmental time-dependent effects on outcomes. Thus, for each type of adversity assessed, exposure to adversity types was modelled at each assessment timepoints (1 = exposed; 0 = non-exposed) to determine the effects of adversity timing ranging from 8 months to 8.7 years. Accumulation, on the other hand, involved summing the number of exposures to each adversity type reported across all the assessment timepoints.

Cognitive measures

At age 24, participants in the study attended a clinic session and completed three computerized cognitive batteries, namely stop signal task,[44] N-back task[45] and emotion recognition task.[46] These cognitive data were collected and managed by REDCap electronic data capture tools.[47] By using multiple cognitive measures, we can examine whether the effect of adversity is limited to executive functioning (e.g., N-back and stop signal task) or also extends to general affective processing (e.g., emotion recognition task). Prior to the main assessment, participants completed practice trials to familiarize themselves with the cognitive tasks described below:

Stop signal task

This is a measure of inhibition which assesses the ability to withhold prepotent responses. The task consists of two trial blocks. In the first block of the initial "go" trials, participants were shown a fixation cross at the centre of the screen, followed by the letter "X" or "O". They were asked to press the left arrow of their keyboard whenever the letter "X" appears or the right arrow when "O" appears. In the second trial block, the procedure is the same as the first, except that the "stop signal" is introduced in 25% of the trials. This involves random loud audio bleeps following the presentation of the letter "X" or "O". Participants were asked to withhold their responses whenever they hear the bleep. An estimate of stop signal reaction time (SSRT) was derived as the primary dependent outcome with higher scores indicating poorer inhibitory control.[44] However, participants scores were reverse coded, so that higher values indicate better performance.

N-back task

Widely used as a measure of working memory, participants in this study completed the N-back task that requires them to monitor a series of stimuli (consisting of letters and numbers) presented on the screen and respond by pressing 1 on the keyboard whenever a stimulus presented match the one presented in two trials earlier or press 2 whenever the stimulus is different. The task consists of 48 experimental trials with 8 targets of matching trials. The derived discriminability (d') score was the primary dependent outcome with higher scores indicating higher net accuracy and better working memory ability.

Emotional recognition task

Here, participants were asked, across 96 trials, to correctly identify a given displayed emotion from possible 6 basic emotions of happiness, sadness, surprise, anger, fear and disgust. On each trial, a facial image is shown on the screen for 200 ms and participants were asked to select from the 6 options, the emotion that best describes the displayed face. Each emotion type was presented for 16 times and varied in intensity (i.e., low and high intensities). The primary dependent outcome in this task is the sum of correctly identified emotions in the total trials. The scores for each emotion sub-types were also obtained. Higher scores indicate better performance and greater ability to identify emotions in facial expressions.

Missing data

In the ALSPAC study and as previously reported, participants from disadvantaged households were more likely to skip follow-ups[48]; thus to deal with this issue, we used multiple imputation methods available in the MICE package in R[49] to account for missing data on adversity exposures. A total of 0.46% of missing adversity data were imputed in our study. Cognitive data was, however, not imputed as only participants with complete cognitive data were selected in the final analytic sample.

Analyses

The research questions and analytic strategies were specified in a pre-registration document located here: https://osf.io/5dxqm/. However, see Supplement 2 for how the pre-registered plans deviated from the study analytic strategies.

To address the three research questions, we conducted five statistical analyses, namely, latent class analysis, Kruskal–Wallis test, zero-order correlation, multivariate regression and structured lifecourse modelling approach (SLCMA). All analyses were carried out in R[50] and R studio version 3.6.3.

To answer our first research question, we used latent class analysis to establish distinct patterns of adversity exposure. Latent class analysis is a multivariate technique which can classify response patterns across categorical data into classes or clusters, using probability profiles across each possible response. Participants (N = 2965) binarized scores (*ever exposed* = 1 versus *never exposed* = 0) of childhood adversity were initially entered into poLCA package.[51] To determine the best number of classes that explained our data, we carried out initial exploratory models for 1–8 classes. A 5-class solution was preferred because it yielded comparatively better estimates of BIC and entropy[52] after 50 repetitions at 5000 iterations per model (see Table S1 and Fig. S1).

To test our second research question of whether group differences in cognitive scores exist among the adversity classes, we carried out a non-parametric Kruskal–Wallis test. This test was preferred over ANOVA given the violation of normality assumption in the N-back scores in our study.[53] To undertake this test, we first extracted the 5 predicted latent class memberships for every participant and then fitted three separate Kruskal–Wallis test models for each cognitive score of SSRT, N-back scores and total emotions correctly identified. If the global Kruskal–Wallis test model showed a statistically significant difference, a Wilcoxon rank-sum test was further used to examine the pairwise comparisons among the 5 adversity classes. p-values were adjusted for multiple comparisons using Benjamini-Hochberg correction.

Third, to examine whether sensitive periods or accumulation hypothesis better explain the independent associations between adversity types and cognitive outcomes, we first conducted a zero-order correlation analysis before fitting a multivariate regression model. We conducted zero-order correlation and multivariate regression analyses to establish evidence of associations between the 11 adversity types and cognitive outcomes before we used SLCMA to test whether sensitive periods or accumulation hypothesis better explain these associations. To test zero-order correlation and multivariate regression, we entered the binarized scores of 11 childhood adversity types as the predictors and the scores of all cognitive outcomes including scores of the 6 sub-types of facial emotions, as the outcomes. Lastly, we modelled SLCMA.[35] By fitting SLCMA, we can compare the two competing theoretical models of sensitive periods (before age 3 = Very early childhood, 3–5 = Early childhood, 6–8 = middle childhood) and accumulation models to determine which of them better explain the observed association between the 11 adversity types and cognitive outcomes. As noted in past literature, SLCMA uses least angle regression (LAR) and covariate tests to identify the single model (or potentially the combination of more than one model) that has the highest parsimonious explanation for the observed outcome variation. In this analysis, the 11 adversity types at all assessment timepoints were modelled as the predictors, and the cognitive scores as the outcomes. LAR was then able to identify for each adversity type, the assessment timepoint (or the theoretical model) that had stronger association with the cognitive outcome. This would allow us to identify whether sensitive periods or accumulation models better explained variation in each cognitive outcome.

For all analyses, we applied a nominal significance threshold of $\alpha = 0.05$.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation or writing of the report. All authors accept responsibility for the decision to submit for publication.

Results

Descriptive results displayed in Table S2 show the proportion (number and percentage) of participants exposure to different adversity types across assessment timepoints as well as Pearson correlations between different adversity types (Table S3). Below, we present the results of tests of our research questions.

Research question 1: What are the distinct patterns of childhood adversity exposure?

To answer the first research question of whether participants' responses to childhood adversity follow distinct patterns of exposures, we entered the participants (N = 2965) scores of all 11 adversity types into latent class analysis. The initial exploratory analysis showed that the 5 class model is the most optimal and interpretable class solution with better fit indices (lowest BIC score and relatively high entropy value). See Table S1 and Fig. S1. Next, we inspected the population shares and the prevalence of exposure to each adversity measure for each of the 5 latent classes as well as any unique profiles or characterizations that defined the classes.

Class 1 (Fig. 1, top left), referred to as "*low adversity*", consists of 71.6% of the population. Members in this class have very low probability of being exposed to any of the 11 adversity measures. For these participants, most were not exposed to any adversity (~89%), with the exception of inconsistent caregiving (reported by 21% of participants) or family instability (reported by 39% of participants). Class 2 (Fig. 1, top centre), made up of 9.58% of all participants is referred to as "dysfunctional family" because members have medium to high probability of exposure to one or more adversity measures characterized by dysfunctional family rearing. Specifically, members in this class reported relatively high probability of exposure to family instability (59%), caregivers' abuse (53%), maternal psychopathology (47%), maternal victimization (61%) and inconsistent caregiving (39%). Class 3 (Fig. 1, top right) consists of 9.65% of the population. We refer to this class as "*parental deprivation*" because members uniformly responded to being exposed to parental divorce or separation (100%) as well as extremely high probability of exposure to family instability (91%) made up of the following variable questions: child separated from mother or father; child taken into care; child acquired new parent. We called Class 4 (Fig. 1, bottom left) "*family poverty*" because participants commonly reported extremely high exposure to various degrees of socioeconomic disparities and financial deprivation. Consisting of 6.07% of the total samples, members in this class have 97% and 60% probability of exposure to financial distress and neighbourhood stress respectively. Lastly, Class 5 (Fig. 1, bottom right) is referred to as "*global adversity*" because members in this class (3.1%) have very high probabilities of being exposed to all the adversity measures in our study. Probability of exposure to adversity measures in this class range from 17% (sexual abuse) to 95% (family instability). See Table S4 for all the class-conditional response probability for the adversity exposures in the 5 adversity classes. Taken together, these findings provide additional empirical evidence of classes or dimensions of adversity which have been theoretically classified in previous literature.[22,23]

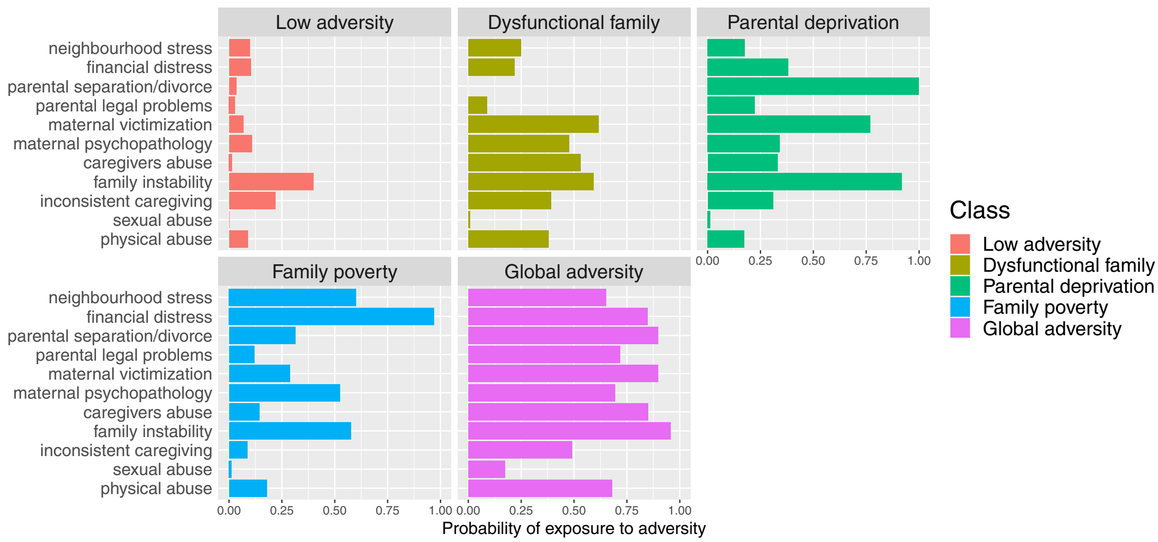

Fig. 1: Latent class analysis showing the five adversity classes and the corresponding class-conditional response probability for all the adversity measures.

See Supplement 3 for sensitivity analysis involving a larger sample size.

Research question 2: Are there group differences in cognitive performance among the adversity subgroups?

We used Kruskal–Wallis test to examine whether group differences exist in cognitive performance among the 5 adversity subgroups. Result showed that there was a statistically significant difference in cognitive performance among the adversity classes in SSRT, $\chi^2(4) = 15.624$, $p = 0.003$ and accuracy in N-back task, $\chi^2(4) = 15.986$, $p = 0.003$, but not in the total emotions correctly identified, $\chi^2(4) = 3.190$, $p = 0.526$. After correcting for multiple comparisons, a further pairwise test using Wilcoxon rank-sum test showed that participants in the family poverty subgroup (Mean = –0.237) performed significantly worse than participants in the low adversity subgroup (Mean = 0.034, $p = 0.007$) in SSRT. There was no significant difference between other adversity classes in SSRT (all, $p > 0.060$). Similarly, a second pairwise test showed that participants in the global adversity subgroup (Mean = –0.221) significantly performed worse than participants in the low adversity subgroup (Mean = 0.030, $p = 0.026$) and participants in the dysfunctional family subgroup (Mean = 0.071, $p = 0.034$) in the N-back task. No other group differences reached statistical significance in the N-back task (all, $p > 0.059$). Taken together, findings suggest that there are differences in cognitive performance among the adversity classes with poorer performance observed in inhibition and working memory among participants in the family poverty and global adversity subgroups respectively. See Table S5 and Fig. 2 for comparisons.

Research question 3: Is sensitive periods or accumulation hypothesis better at explaining the independent associations between adversity types and cognitive outcomes?

To examine the third research question, we first present (Table S6) the result of zero-order correlation involving the binarized scores (ever exposed = 1 versus never exposed = 0) of the 11 adversity measures and all cognitive scores, including the 6 emotion sub-types. To control for the effects of shared variance explained by other adversity predictors, we fit a multivariate regression model. Results of multivariate regression analysis displayed in Table 1 (and Fig. S2a–c) revealed that exposure to sexual abuse was associated with poorer performance in inhibition ($\beta = -0.450$, $p = 0.018$) and emotion recognition (total emotion: $\beta = -0.619$, $p = 0.001$; surprise: $\beta = -0.637$, $p < 0.001$; anger: $\beta = -0.413$, $p = 0.030$). Exposure to inconsistent caregiving on the other hand was associated with higher performance in working memory ($\beta = 0.125$, $p < 0.001$) and emotion recognition (total emotion: $\beta = 0.157$, $p < 0.001$; fear: $\beta = 0.126$, $p = 0.003$; anger: $\beta = 0.127$, $p = 0.003$). Exposure to family instability ($\beta = -0.080$, $p = 0.039$) and financial distress ($\beta = -0.132$, $p = 0.006$) were both associated with poorer inhibition while exposure to parental separation or divorce ($\beta = -0.115$, $p = 0.002$) was associated with poorer working memory. All other adversity measures yielded little evidence of significant association with cognitive outcomes.

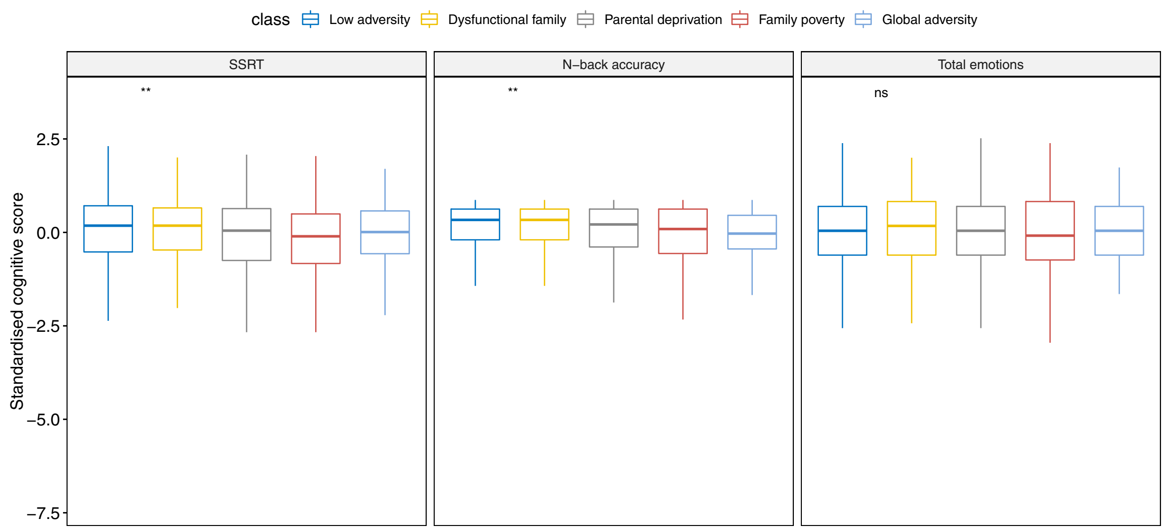

Fig. 2: Boxplots showing performance distributions across the adversity subgroups. The lower and upper whiskers represent the first and third quartiles of the performance distribution while the horizontal box lines indicate the groups' medium performance in cognitive tasks. SSRT = stop signal reaction time. Higher values indicate higher cognitive ability.

To justify the limitation against specificity approach of adversity study (i.e., the co-occurring pattern of adversity), we compared the results of zero-order correlation and multivariate regression. Result of zero-order correlations showed that neighbourhood stress, for example, was negatively associated with both inhibition and working memory but after controlling for all the adversity variables in the multivariate regression, these significant associations disappeared. This suggests that these effects were driven by the shared variance with financial distress from which neighbourhood stress co-occurred in "family poverty" class in the latent class analysis. Several other significant associations in the zero-order correlation analysis did not hold after controlling for other adversity effects in the multivariate regression. Similarly, it should be noted that the strength of the significant correlation coefficients between the 11 adversity types and cognitive outcomes were very modest (negative or positive correlations between 0.04 and 0.07, see Table S6). This suggests that the proportion of variance in cognitive outcomes significantly explained by the independent adversity types range from 4.95% in SSRT (financial distress) to 1.33% in recognition of sad emotions (inconsistent caregiving). See Supplement 4 for description of proportion of variance independently explained by adversity types and see Table 1, Table S6 & Fig. S2a–c for full comparison.

To test whether sensitive periods or accumulation hypotheses better explain the observed associations described above, we fit the SLCMA models. In this

	SSRT	N-back correct	Emotion Total	Happy	Surprise	Fear	Sad	Anger	Disgust
Physical abuse	−0.027	0.039	0.069	−0.044	0.009	0.123[c]	0.082	0.011	−0.004
Sexual abuse	−0.450[c]	−0.322	0.619[b]	−0.243	−0.637[a]	−0.264	−0.303	−0.413[c]	−0.313
Inconsistent caregiving	0.042	0.125[b]	0.157[a]	0.047	0.049	0.126[b]	0.073	0.127[b]	0.060
Family instability	−0.080[c]	0.001	0.022	0.034	0.032	0.005	0.020	0.043	−0.052
Caregivers abuse	0.017	0.058	0.079	−0.034	−0.042	−0.010	0.126[c]	0.061	0.159[b]
Maternal psychopathology	−0.010	−0.018	0.021	0.029	−0.031	0.032	0.033	0.019	−0.033
Maternal victimization	0.007	−0.050	−0.083	−0.000	−0.024	−0.026	−0.092	−0.056	−0.077
Parental legal problems	0.015	−0.030	−0.101	−0.028	0.012	−0.160[c]	0.008	0.004	−0.099
Parental separation/divorce	0.007	−0.115[c]	0.000	0.018	−0.021	−0.040	0.041	−0.054	0.080
Financial distress	−0.132[b]	−0.083	−0.059	0.058	0.028	−0.054	−0.142[b]	0.014	−0.044
Neighbourhood stress	−0.078	−0.033	0.023	−0.067	0.082	0.040	0.007	0.002	0.019

SSRT = stop signal reaction time. [a]Significant at $p < 0.001$. [b]Significant at $p < 0.01$. [c]Significant at $p < 0.05$.

Table 1: **Result of multivariate regression analysis examining association between binarized (ever exposed versus never exposed) score of each childhood adversity measure and cognitive outcomes.**

study, we fit 99 SCLMA models - consisting of 11 adversity types and the 9 cognitive outcomes. That is, each adversity type (e.g., physical abuse by anyone) was modelled with each cognitive outcome (e.g., inhibition). For each model, we both examined the time of adversity exposure or theoretical model (sensitive periods or accumulation) first selected by SLCMA and whether the selected theoretical model was within threshold of statistical significance ($p < 0.05$). Result of SLCMA shown in Fig. 3 and Table 2 revealed that among the 99 models examined, only 11 of the models first selected by SLCMA reached statistical significance (9 sensitive periods models and 2 accumulation models). Within sensitive periods, very early childhood was first selected in 3 significant models, while early childhood and middle childhood had 5 and 1 significant models respectively. Specifically, exposure to adversity at very early childhood (before age 3) significantly explained greater variability in poorer working memory performance observed among participants exposed to parental separation or divorce (age = 2.9 years, $\beta = -0.335$; $p < 0.001$) as well poorer performance in the emotion recognition task (total emotions: age = 1.9 years; $\beta = -0.163$; $p = 0.012$; fearful emotion: age = 1.9 years, $\beta = -0.450$; $p = 0.036$) observed among participants exposed to financial distress. Along similar lines, adversity exposure at early childhood (3–5 years) significantly explained more variability in the association between exposure to parental separation or divorce and poorer recognition of surprised emotional expression (age = 3.11 years; $\beta = -0.344$; $p = 0.026$) as well as poorer performance in working memory observed among participants exposed to parental legal problems (age = 5.1 years; $\beta = -0.421$; $p = 0.003$). The same timeframe explained greater variability in the higher performance observed among those exposed to inconsistent caregiving in the emotion recognition task: angry faces (age = 3.6 years, $\beta = 0.546$; $p = 0.039$), disgust faces (age = 3.6 years, $\beta = 0.439$; $p = 0.050$) and total emotions (age = 3.6 years, $\beta = 0.261$; $p = 0.038$). On the other hand, variability in poorer SSRT scores was explained by middle childhood exposure to parental separation or divorce (age = 6.1 years, $\beta = -0.245$; $p = 0.034$) but accumulation model mostly accounted for poorer performance in SSRT among participants exposed to neighbourhood distress ($\beta = -0.104$; $p = 0.011$) and better working memory in those exposed to inconsistent caregiving ($\beta = 0.054$; $p = 0.032$). Overall, these findings provide further evidence of more time-sensitive effects of childhood adversity on cognitive outcomes, compared to accumulation models. See Fig. 3 and Table 2 for full details.

Discussion

In a large longitudinal sample, this study examined the co-occurrence of adverse childhood experiences and whether differences in cognitive performance exist

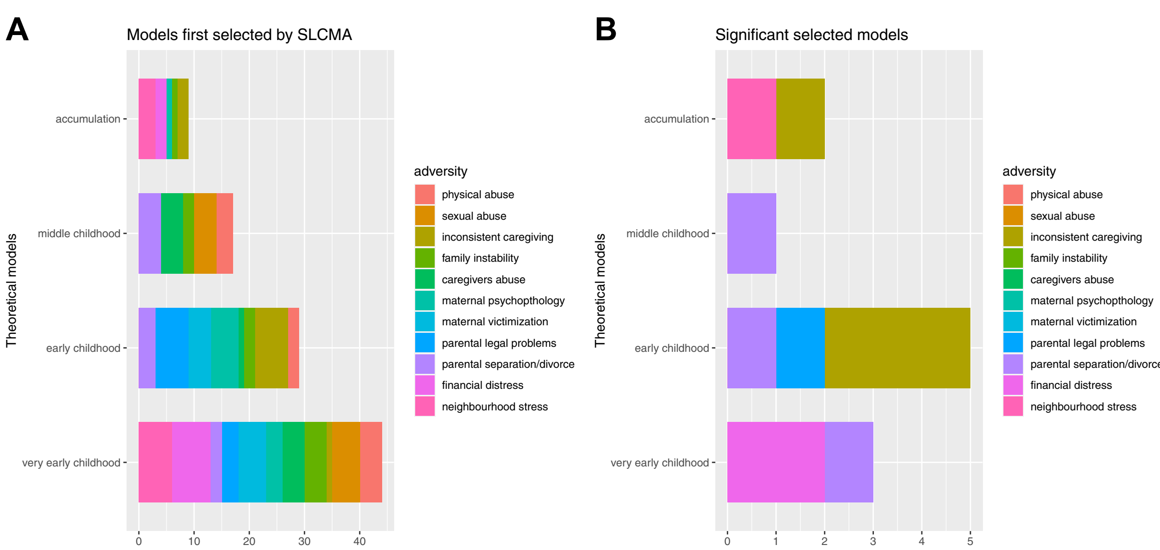

Fig. 3: The figure shows the results of the structural life course modelling approach comparing two theoretical models of sensitive periods (very early childhood = before age 3; early childhood = 3–5 years; middle childhood = 6–8 years) and accumulation models selected by different adversity types. **Panel A** illustrates the frequency by which these two theoretical models were first chosen by SLCMA. Out of the total 99 models estimated, sensitive periods were first selected by SLCMA models in 90 models (very early childhood = selected by 44 models; early childhood = 29 models; middle childhood = 17 models) while accumulation was selected in only 9 SLCMA models. **Panel B** displays the SLCMA models that reached significant threshold (i.e., $p < 0.05$). Sensitive periods were statistical significant in 9 SLCMA models compared to just 2 model in accumulation.

among the distinct subgroups of adversity. Additionally, we also used structured lifecourse modelling approach to test whether sensitive periods or accumulation hypotheses better explained the associations between the independent adversity types and cognitive outcomes. Results of latent class analysis showed evidence of five classes of adversity in our sample, namely: low adversity, dysfunctional family, parental deprivation, family poverty and global adversity. These adversity classes differed in cognitive functioning with participants in the family poverty class performing worse than those in the low adversity class in inhibition, while participants in the global adversity class also performed worse than those in the low adversity and dysfunctional family classes in the working memory task. In a separate analysis using regression model, we found that individual adversity types had distinct associations with cognitive functioning. However, structured lifecourse modelling approach showed that greater variability in these observed associations was explained by sensitive periods (specific timing of adversity exposure) compared to accumulation hypotheses.

	SSRT			N-back accuracy			Emotion total		
	Selected model	Estimate	95% CI	Selected model	Estimate	95% CI	Selected model	Estimate	95% CI
Physical abuse	4.9 years	−0.192	−0.309, 1.856	3.6 years	−0.181	−0.372, 0.506	1.6 years	0.212	−0.237, 0.445
Sexual abuse	8.7 years	−1.228	−2.076, 0.967	2.6 years	−2.855	−4.790, 0.823	2.6 years	−2.475	−5.479, 21.313
Inconsistent caregiving	3.6 years	0.130	−1.339, 0.230	Accumulation	0.054[b]	−0.004, 0.099	3.6 years	0.261[b]	−0.035, 0.398
Family instability	6.9 years	−0.180	−0.294, 0.241	4.9 years	−0.039	−0.182, 0.935	2.6 years	0.092	−0.154, 0.176
Caregivers abuse	8 months	−0.142	−0.348, 0.805	2.9 years	−0.164	−0.344, 0.703	6.1 years	−0.093	−0.169, 2.844
Maternal psychopathology	1.9 years	−0.111	−0.212, 0.518	Accumulation	−0.040	−0.082, 0.172	3.11 years	0.365	−7.491, 0.846
Maternal victimization	8 months	−0.142	−0.286, 0.152	1.9 years	−0.157	−0.238, 2.003	5.1 years	−0.124	−0.244, 0.154
Parental legal problems	5.1 years	−0.213	−0.397, 1.448	5.1 years	−0.421**	−0.648, −0.138	5.1 years	−0.245	−0.466, 0.319
Parental separation/divorce	6.1 years	−0.245[b]	−0.395, 0.022	2.9 years	−0.335[a]	−0.491, −0.176	6.1 years	−0.147	−0.295, 0.179
Financial distress	Accumulation	−0.072	−0.106, 0.085	Accumulation	−0.057	−0.090, 0.128	1.9 years	−0.163[b]	−0.282, −0.024
Neighbourhood stress	Accumulation	−0.104[b]	−0.168, 0.017	2.9 years	−0.109	−0.206, 0.490	2.9 years	−0.059	−0.167, 0.205
	Happy			Surprise			Fear		
	Selected model	Estimate	95% CI	Selected model	Estimate	95% CI	Selected model	Estimate	95% CI
Physical abuse	6.9 years	−0.519	−0.965, 1.113	8.7 years	0.208	−0.996, 0.463	1.6 years	0.764	−4.368, 1.420
Sexual abuse	2.6 years	−4.622	−7.999, 26.121	2.6 years	−4.731	−7.605, 4.245	8.7 years	−2.997	−5.824, 6.070
Inconsistent caregiving	5.9 years	−0.184	−0.323, 6.805	4.9 years	0.206	−0.913, 0.393	2.6 years	0.483	−8.858, 0.707
Family instability	5.9 years	0.258	−0.402, 0.479	1.6 years	0.151	−0.381, 0.310	2.6 years	0.181	−5.122, 0.343
Caregivers abuse	6.1 years	−0.227	−0.526, 0.652	6.1 years	−0.166	−0.385, 0.392	6.1 years	−0.468	−0.899, 2.215
Maternal psychopathology	2.9 years	0.177	−0.480, 0.385	1.9 years	−0.126	−0.306, 0.186	3.11 years	1.318	−21.625, 3.054
Maternal victimization	1.9 years	0.172	−4.536, 0.340	8 months	−0.202	−0.412, 0.403	5.1 years	−0.389	−0.740, 2.085
Parental legal problems	8 months	0.466	−6.765, 1.134	8 months	−0.611	−1.211, 0.840	5.1 years	−0.908	−1.638, 1.511
Parental separation/divorce	3.11 years	0.354	−13.890, 0.422	3.11 years	−0.344[b]	−0.590, 0.006	6.1 years	−0.465	−0.937, 1.696
Financial distress	2.9 years	0.148	−0.900, 0.372	1.9 years	−0.133	−0.302, 0.639	1.9 years	−0.450[b]	−0.855, 0.052
Neighbourhood stress	Accumulation	−0.118	−0.254, 0.191	Accumulation	0.066	−0.197, 0.162	1.9 years	0.096	−2.139, 0.410
	Sad			Anger			Disgust		
	Selected model	Estimate	95% CI	Selected model	Estimate	95% CI	Selected model	Estimate	95% CI
Physical abuse	1.6 years	0.697	−1.155, 1.155	6.9 years	0.363	−4.638, 0.778	1.6 years	0.545	−0.522, 1.064
Sexual abuse	6.9 years	−1.100	−2.307, 9.008	2.6 years	−5.363	−8.415, 62.221	8.7 years	−2.287	−4.175, 3.600
Inconsistent caregiving	Accumulation	0.120	−0.193, 0.210	3.6 years	0.546[b]	−0.080, 0.887	3.6 years	0.439[b]	−0.106, 0.751
Family instability	Accumulation	0.062	−0.073, 0.118	2.6 years	0.221	−0.686, 0.418	8.7 years	−0.301	−0.554, 0.684
Caregivers abuse	2.9 years	0.342	−1.491, 0.733	8 months	0.436	−0.862, 0.977	5.1 years	0.342	−0.300, 0.684
Maternal psychopathology	5.1 years	−0.891	−2.118, 4.947	5.1 years	−1.483	−3.061, 2.340	3.11 years	2.342	−0.576, 3.886
Maternal victimization	1.9 years	−0.240	−0.444, 2.804	5.1 years	−0.275	−0.576, 0.221	3.11 years	0.264	−0.683, 0.549
Parental legal problems	5.1 years	−0.240	−0.636, 3.188	5.1 years	−0.352	−0.867, 2.024	8 months	−0.994	−1.864, 1.460
Parental separation/divorce	8 months	−0.253	−0.628, 3.177	6.1 years	−0.314	−0.689, 0.301	5.1 years	0.376	−3.184, 0.655
Financial distress	1.9 years	−0.325	−0.571, 0.215	8 months	−0.184	−0.462, 0.581	1.9 years	−0.249	−0.509, 0.439
Neighbourhood stress	1.9 years	−0.117	−0.344, 0.467	2.9 years	−0.246	−0.519, 0.243	2.9 years	−0.112	−0.342, 0.945

CI = confidence interval; LAR = Least angle regression; SSRT = stop signal reaction time. Note that we refer to sensitive periods as very early childhood (adversity exposure before age 3), early childhood (exposure between 3 and 5 years) and middle childhood (exposure between 6 and 8 years). *p < 0.05; **p < 0.01; ***p < 0.001. [a]Significant at p < 0.001. [b]Significant at p < 0.050.

Table 2: **Result of SLCMA showing the theoretical model of adversity measures first selected by LAR for all 9 cognitive outcomes.**

Firstly, using latent class approach, the current study found five distinct patterns of participants' responses to childhood adversity, which provides empirical evidence of dimensions or subgroups of adversity exposure. As noted in previous studies,[22,23] the specificity and cumulative risk approaches of adversity studies have some shortcomings, because childhood adversities mostly co-occur, and different types of adversities have distinct effects. Thus, by examining adversity in their classes or clusters, we may gain a better understanding of the specific adversity subgroups (classes or clusters) driving specific observed effects. The past studies that have used clustering techniques (e.g., latent class analysis) have found between 3 and 5 classes of adversity.[29–34] While the number of classes and the corresponding co-occurring adversity types will likely vary across studies based on the number and severity of individual adversity types examined, there is little doubt that the clustering technique provides an alternative or complementary approach to studying childhood adversity, leading to a more nuanced understanding of the effects of adversity on outcomes, obtained through the pathways of adversity classes. Using latent class approach could further reveal the population distribution of the co-occurring adversity patterns among participants who may be at the greatest health risk and thus, prompt some form of intervention that targets the developmental areas of need for such high-risk groups.

Secondly, when we compared cognitive performance among the different adversity classes using Kruskal–Wallis test, results showed that performance differed among the classes in inhibition and working memory. Notably, participants in the family poverty class performed worse than participants in the low adversity class in inhibition. This finding was slightly contrary to initial predictions, as we expected participants in the global adversity class to have the worst performance metrics across all our cognitive measures. Previous studies have noted child poverty to be one of the most potent predictors of poorer cognitive outcomes in high income countries[54]; with some past studies suggesting that the poorer cognitive outcomes observed in people reared in poverty may be comparable to severely neglected or institutionalised children.[55] Connected to this finding, one previous study found that low family income and neighbourhood poverty were both independently correlated with poorer performance in response inhibition.[56] This was consistent with the observed negative correlation in inhibition among participants exposed to financial distress and neighbourhood stress in our study; the two adversity measures in our sample that constituted the family poverty class in our latent class analysis. Less surprising on the other hand is the finding that showed that participants in the global adversity class performed poorer than participants in the low adversity and dysfunctional family classes in working memory. Participants in the global adversity class reported over 65% probabilities of being exposed to all the measured adversity types except sexual abuse and inconsistent caregiving. Thus, poorer working memory ability found in this group may likely be a reflection of the impact of exposure to multiple adversities. These findings further demonstrate the added value of using latent class analysis as a complementary approach to studying childhood adversity; such methods can be used to quantify the population distribution of co-occurring adversity types to examine how the predicted high-risk groups perform in developmental measures, such as cognition or mental health. This would provide nuanced insight into the effects of adversity at a clustering level, and thus enable targeted academic or clinical interventions in the developmental area of need among the high-risk groups in the population.

On the other hand, to justify the limitations of specificity approaches to studying childhood adversity due to co-occurring patterns,[22,57] we compared the results of associations between each adversity types and cognitive outcomes before and after accounting for shared variance with other adversity measures. Findings show that some of the significant associations observed between each adversity type and cognitive outcomes lessened after controlling for shared variance with other adversity predictors. This was principally observed in the working memory measure. For example, the negative association observed for performance on this task with sexual abuse, maternal victimization and financial distress were not significant after accounting for shared variance in multivariate regression. Similarly, neighbourhood stress lost its significant association with inhibition. These findings suggest that some cognitive tasks (e.g., executive functioning) may be more sensitive to the effects of shared variance from other adversity measures. It is also possible that broader non-severe adversity types may more significantly impact executive functioning measures (e.g., n-back task) as opposed to the (non-significant) effects on general affective processing (e.g., emotion recognition).

In an important and novel set of analyses, we compared the theoretical models of sensitive periods and accumulation to ascertain which model has greater explanatory power for the observed associations between adversity and cognitive outcomes. For these comparisons, results showed that the observed variances were predominantly explained by sensitive periods. In all 11 models (estimating different adversity types on cognitive outcomes) that were significantly selected in SLCMA, 9 models were identified by sensitive periods. Consistent with previous studies on childhood adversity and DNA methylation,[27] sensitive periods in very early childhood (3) and early childhood (5) explained a greater number of the observed associations, than middle childhood (1). Accumulation hypotheses were significantly selected in only two models, suggesting that the timing of adversity exposure (sensitive periods), especially during early childhood, may be of greater importance; thus, the need for parents and caregivers to safeguard the childhood environment against any potential stressors. Overall, these findings provide additional evidence of sensitive periods of adversity on cognitive outcomes.

The current study should be interpreted in the light of some limitations. First, the adversity measures used in this study were parent-completed, and thus may have been underreported.[58] Second, because this is a longitudinal study, there may be attrition effects as certain participants dropped out overtime. In the ALSPAC study, it was reported that participants from disadvantaged households were more likely to skip follow-ups,[48] thus, the generalization of these findings may be limited. Third, it should be noted that while the study modelled different adversities longitudinally, the cognitive data used in this study was cross-sectional as it was obtained at one time point. Finally, the long interval between the adversity measurements and cognitive assessments may have contributed to the relatively modest correlations observed between adversity and cognitive outcomes. See Supplementary Material for additional study limitations.

In conclusion, the study found evidence of five adversity classes in a population-based sample. These adversity classes had varying levels of cognitive performance with poorer performance coming from participants in the family poverty class and global adversity class in inhibition and working memory respectively. We reported the independent associations between each adversity type and cognitive outcomes but observed that it was the timing of exposure to these adversity types (sensitive periods) that appears to explain these observed associations more than the number of times an individual was exposed (accumulation). Examined collectively, our results suggest important impact of adversity that could subsequently inform the development of novel targets for intervention and prevention for high-risk groups.

Contributors

T.N., M.E., C.A., and C.O. drafted or edited the manuscript; T.N., M.E., C.A. and C.O. revised the manuscript; T.N. conceptualized the study, analysed and verified the data; J.L.H. revised the manuscript and aided with variable re-conceptualization and data interpretation. Only T.N. has full access to the data – in line with ALSPAC policy, other co-authors do not have access to the data as they joined the project after data approval has been granted by ALSPAC. All authors accept responsibility for the decision to submit this paper for publication.

Data sharing statement

There is a restricted access to the data used in this study. To access the supporting data for this study, please contact the ALSPAC team http://www.bristol.ac.uk/alspac/researchers/access/ and request for data access. R scripts used in this study are available here https://osf.io/5dxqm/.

Declaration of interests

Jamie L. Hanson received research grant from the US National Institute of Health. He is a member of board of directors Project Destiny, Pittsburgh, PA, Non-profit and also received consultancy fees from OASIS Mental Health.

Acknowledgements

The UK Medical Research Council and Wellcome (Grant ref: 217065/Z/19/Z) and the University of Bristol provide core support for ALSPAC. This publication is the work of the authors who will serve as guarantors for the contents of this paper. A comprehensive list of grants funding is available on the ALSPAC website (http://www.bristol.ac.uk/alspac/external/documents/grant-acknowledgements.pdf); This research was specifically funded by Cambridge Trust. 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, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses. We thank Dr Erin Dunn and Dr Florian Lange for providing general feedback on our manuscript. Dr Dunn (and her lab) also provided the R script used for SLCMA analysis.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2022.101784.

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