Psychological Medicine

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Harsh parenting, amygdala functional connectivity changes across childhood, and behavioral problems

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Original Article

Cite this article: Koyama Y, Tiemeier H, Huang P, Chan SY, Sudo M, Kyeong Y, Meaney M, Setoh P, Tan AP (2024). Harsh parenting, amygdala functional connectivity changes across childhood, and behavioral problems. *Psychological Medicine* 1–12. https://doi.org/10.1017/S003329172400196X

Received: 28 February 2024
Revised: 15 June 2024
Accepted: 24 June 2024

Keywords:
amygdala functional connectivity; emotional processing; externalizing behaviors; harsh parenting

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Abstract

Background. Harsh parenting in early childhood is related to offspring's adverse behavioral outcomes. Due to the scarcity of longitudinal neuroimaging data, few studies have explored the neurobiological underpinnings of this association, focusing on within-person variability. This study examined the temporal associations among harsh parenting, later behavioral problems, and the developmental trajectories of amygdala volume and amygdala resting-state functional connectivity (RSFC) profiles, using longitudinal neuroimaging data.

Methods. The study was embedded in the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort. T1-weighted (296 children, 642 scans) and resting-state functional scans (256 children, 509 scans) were collected at ages 4.5, 6, 7.5, and 10.5 years. Amygdala volume and RSFC between the amygdala and six brain regions that have leading roles in emotional regulation were extracted. Harsh parenting at 4.5 years and child behavioral problems at 10.5 years were assessed via parent-report questionnaires. Linear regression and linear mixed models were applied.

Results. Harsh parenting was associated with more severe externalizing problems in girls ($\beta = 0.24$, 95% CI 0.08–0.40) but not boys ($p_{int} = 0.07$). In the overall sample, harsh parenting was associated with the developmental trajectories of amygdala-ACC, amygdala-OFC, and amygdala-DLPFC RSFC. In addition, the developmental trajectory of amygdala-ACC RSFC mediated the harsh parenting–externalizing problems association in girls (indirect effect = 0.06, 95% CI 0.01–0.14).

Conclusions. Harsh parenting in early childhood was associated with amygdala neurocircuitry development and behavioral problems. The developmental trajectory of amygdala-ACC RSFC is a potential neural mechanism linking harsh parenting and externalizing problems in girls.

Introduction

Adverse experiences in early childhood are associated with enduring effects on brain development and child outcomes including behavioral problems (McLaughlin, Weissman, & Bitrán, 2019). These adverse experiences can be broadly categorized into two distinct dimensions that have different impacts on the brain: threat and deprivation (McLaughlin et al., 2019). Harsh parenting, including both physical punishments and negative emotional expressions, is considered a form of threat experience for children. Harsh parenting can negatively impact children's socioemotional development and predispose children to poor psychosocial developmental outcomes, including behavioral problems. Childhood behavioral problems which include internalizing (e.g. depression, anxiety) and externalizing (e.g. conduct disorder, hyperactivity, aggression) disorders (Cui & Liu, 2020; Gruhn & Compas, 2020; May, Younan, & Pilkington, 2022; Todorov, Devine, & De Brito, 2023) have extended impacts on the socioemotional aspects of adult life (Aebi, Giger, Plattner, Metzke, & Steinhausen, 2014; Jung et al., 2017; Nowicki et al., 2018; Offord & Bennett, 1994). A recent meta-analysis shows concurrent and longitudinal associations between harsh parenting and offspring's externalizing problems (Pinquart, 2021). Conversely, authoritative parenting has been linked to lower levels of

depression and internalizing problems (Yap & Jorm, 2015) while supportive parenting decreases the levels of both internalizing and externalizing problems (Vazsonyi, Ksinan, Javakhishvili, Scarpate, & Kahumoku-Fessler, 2022). Nevertheless, it is important to acknowledge that the effects of harsh parenting are not uniform across contexts. This parenting approach has been shown to have positive effects on academic performance within the Asian community (Lea Bornstein, 2007).

A growing body of research that investigates the neural underpinnings of behavioral problems has perpetually highlighted the role of the amygdala (Dugré et al., 2020; Long et al., 2023). Both structural and functional abnormalities of the amygdala have been reported in individuals with behavioral problems (Padgaonkar et al., 2020; Sukhodolsky et al., 2022; Waller et al., 2020). Moreover, reduced amygdala volume and heightened reactivity of the amygdala toward threat experiences have been observed in multiple studies of childhood adverse experiences (Cassiers et al., 2018; McLaughlin et al., 2019; Paquola, Bennett, & Lagopoulos, 2016). These observations are likely related to the amygdala's central role in emotional processing (Dugré et al., 2020). However, emotional processing is an intricate process whereby the amygdala, while playing a critical role, does not function in isolation. The generation of an emotional response involves the perception of stimuli, the deployment of attention, and the appraisal of the significance of stimuli, taking into account both positive and negative valence (Buhle et al., 2014). Top-down control processes governed by the cognitive control network are critical for successful emotional regulation (Buhle et al., 2014). For these reasons, this study will focus not only on volumetric changes in the amygdala but also on the functional connectivity between the amygdala and other major brain regions involved in emotional processing. Core brain regions of the emotional processing network (hippocampus, anterior cingulate cortex (ACC)) (Phillips, Drevets, Rauch, & Lane, 2003), the reward processing network (nucleus accumbens (NAcc), orbital frontal cortex (OFC)) (Jia et al., 2016), and the cognitive control network (dorsolateral prefrontal cortex (DLPFC), posterior parietal cortex (PPC)) (Niendam et al., 2012) were selected as regions of interest in our current study. Prior research has indicated that the amygdala's functional connectivity plays a mediating role in the association between exposure to negative parenting and later internalizing problems (Brieant, Sisk, & Gee, 2021; Jiang et al., 2021).

To date, little empirical attention has been devoted to examining the associations among parenting practices, brain developmental trajectories across childhood, and later behavioral problems in a comprehensive manner. An analysis of longitudinal data from preadolescents aged 9–10 years in the United States reported that early life adversities including child maltreatment and family dysfunction were associated with decreased changes in cortico-limbic–amygdala resting-state functional connectivity, which in turn was associated with internalizing problems (Brieant et al., 2021). A separate longitudinal study conducted on an Australian cohort aged between 8 and 13 years discovered an association between harsh/inconsistent parenting and a reduction in cortical thinning in some brain regions, although this reduction was not associated with later psychopathology (Whittle et al., 2022). While both studies utilized a longitudinal design, the acquisition of neuroimaging data at only two time points restricts their capacity to detect non-linear changes in brain development. Moreover, the time window between the baseline and follow-up imaging in both studies was short and centered around the late childhood and adolescent periods, precluding the assessment of developmental changes in early childhood which is a critical period for brain development.

We leveraged data from the deeply-phenotyped Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort to address these critical knowledge gaps. Specifically, using multimodal magnetic resonance imaging (MRI) of the brain at four time points, spanning the ages 4.5–10.5 years, we examined differences in brain developmental trajectories across early to late childhood in relation to harsh parenting and subsequent behavioral problems. Neuroimaging assessments at multiple time points across childhood are crucial as the brain undergoes progressive changes during this critical period of neurodevelopment (Gee et al., 2013b; Uematsu et al., 2012). The longitudinal neuroimaging data utilized in our study for the assessment of brain developmental trajectories is highly notable as it allows us to distinguish between-subject from within-subject variability (Bethlehem et al., 2022), in contrast to the more commonly used approach of estimating neurodevelopmental trajectory from cross-sectional imaging data, adopting age as a proxy for time. This is especially important when studying brain development across childhood as within-subject variability has been reported to be more prominent in children compared to adults (Bethlehem et al., 2022). A recent study also revealed that age-related brain changes estimated from cross-sectionally mapped brain charts can significantly underestimate actual changes measured longitudinally (Di Biase et al., 2023).

In this study, we first examined the association between harsh parenting in early childhood assessed at age 4.5 years, and child behavioral problems assessed at age 10.5 years. As our interests lie in the exploration of the neural underpinnings of the associations between harsh parenting and child behavioral problems, subsequent analyses were driven by our findings on the harsh parenting–child behavioral problems associations. Next, we examined the association between harsh parenting and brain developmental trajectories across childhood, focusing on (1) amygdala volume and (2) amygdala resting-state functional connectivity profiles, which were subsequently examined as a path between harsh parenting and behavioral problems in a mediation analysis. We hypothesized that harsh parenting in early childhood would be associated with later behavioral problems and an accelerated pattern of development of the amygdala. We also hypothesized that variations in developmental trajectories of the amygdala would mediate the association between harsh parenting and behavioral problems. Specifically, increased exposure to harsh parenting will lead to accelerated development of the amygdala, which will in turn lead to more severe behavioral problems. Previous studies have reported that parenting style differs by a child's sex (Morawska, 2020); also girls and boys may exhibit distinct responses to stress (Adrián-Ventura, Costumero, Parcet, & Ávila, 2019; Whittle et al., 2022). More importantly, brain developmental trajectories differ between girls and boys (DeCasien, Guma, Liu, & Raznahan, 2022; Giedd, Raznahan, Mills, & Lenroot, 2012; Kaczkurkin, Raznahan, & Satterthwaite, 2019). For these reasons, we repeated the aforementioned analyses with the inclusion of sex interaction terms, followed up with separate analyses in males and females. There exists a scarcity of research that has examined the potential sex differences in the association between parenting styles and child outcomes.

https://doi.org/10.1017/S003329172400196X Published online by Cambridge University Press

Method

Participants

Participants were recruited from GUSTO (Soh et al., 2014), a large longitudinal, Singaporean birth cohort study. The GUSTO study was approved by the National Healthcare Group Domain Specific Review Board (NHG DSRB) and the SingHealth Centralized Institutional Review Board (CIRB). Written informed consent was obtained from all guardians on behalf of the children enrolled in this study. The original GUSTO cohort comprises 1466 participants. Among them, 408 participants with usable parenting assessment at the age of 4.5 years were included in our study. A subset of these participants had good quality neuroimaging datasets: structural MRI (sMRI) (parenting-sMRI analytical sample: $n = 296$, 642 scans) and resting-state functional MRI (rsfMRI) (parenting-fMRI analytical sample: $n = 256$, 509 scans). Assessment for childhood behavioral problems (Child Behavior Checklist; CBCL) and depressive symptoms (Children's Depression Inventory 2nd Edition; CDI-2) were completed for 256 and 311 participants respectively. We subsequently excluded one of the twins ($n = 2$), obtaining the final analytical sample of 254 children for the parenting-CBCL analytical sample and 309 children for the parenting-CDI analytical sample. The sampling flow chart is included in online Supplementary Figure S1 and the current analytical sample characteristics are shown in Table 1. For the comparison between the original cohort and analytical sample, please refer to online Supplementary Table S1. The study design and aims are delineated in Fig. 1.

Table 1. Demographics of analytical samples

		Children in any analysis ($n = 379$)	Children in mediation analysis ($n = 174$)
Child sex, *N* (%)	Girl	180 (47.5%)	85 (48.9%)
	Boy	199 (52.5%)	89 (51.1%)
Marital status, *N* (%)	Living with husband	369 (97.4%)	170 (97.7%)
	Not living with husband	10 (2.6%)	4 (2.3%)
Maternal ethnicity, *N* (%)	Chinese	213 (56.2%)	101 (58.0%)
	Malay	109 (28.8%)	54 (31.0%)
	Indian	57 (15.0%)	19 (10.9%)
Household highest education, *N* (%)	Primary or secondary	53 (14.0%)	25 (14.4%)
	ITE/NITEC	52 (13.7%)	25 (14.4%)
	GCE A levels/ Polytechnic/ Diploma	109 (28.8%)	57 (32.8%)
	University (Bachelor, Master, PhD)	165 (43.5%)	67 (38.5%)
Household monthly income, *N* (%)	SGD 0–1999	52 (13.7%)	22 (12.6%)
	SGD 2000–3999	119 (31.4%)	59 (33.9%)
	SGD 4000–5999	97 (25.6%)	44 (25.3%)
	SGD ⩾ 6000	111 (29.3%)	49 (28.2%)
Maternal depressive symptoms, mean (s.d.)		6.4 (7.5)	6.8 (8.4)
Age at MRI measurement, mean (s.d.)	Wave 1	4.6 (0.1)	4.6 (0.1)
	Wave 2	6.0 (0.1)	6.0 (0.1)
	Wave 3	7.5 (0.1)	7.4 (0.1)
	Wave 4	10.7 (0.2)	10.7 (0.2)
Number of usable sMRI scans, *N* (%)[a]	4 (all)	38 (12.8%)	33 (19.2%)
	3 only	67 (22.6%)	51 (29.7%)
	2 only	98 (33.1%)	61 (35.5%)
	1 only	93 (31.4%)	27 (15.7%)
Number of usable rsfMRI scans, *N* (%)[b]	4 (all)	22 (8.6%)	19 (10.9%)
	3 only	51 (19.9%)	43 (24.7%)
	2 only	85 (33.2%)	59 (33.9%)
	1 only	98 (38.3%)	53 (30.5%)

ITE, institute of technical education; NITEC, national institute of technical education certificate; GCE, General Certificate of Education; SGD, Singapore dollar; sMRI, structural magnetic resonance imaging; rsfMRI, resting-state functional magnetic resonance imaging. Values shown here were derived from the first imputed dataset.
[a]Proportions were calculated based on children in any analysis with sMRI scans ($n = 296$) and for children in mediation analysis ($n = 172$).
[b]Proportions were calculated based on children in any analysis with fMRI scans ($n = 256$).

https://doi.org/10.1017/S003329172400196X Published online by Cambridge University Press

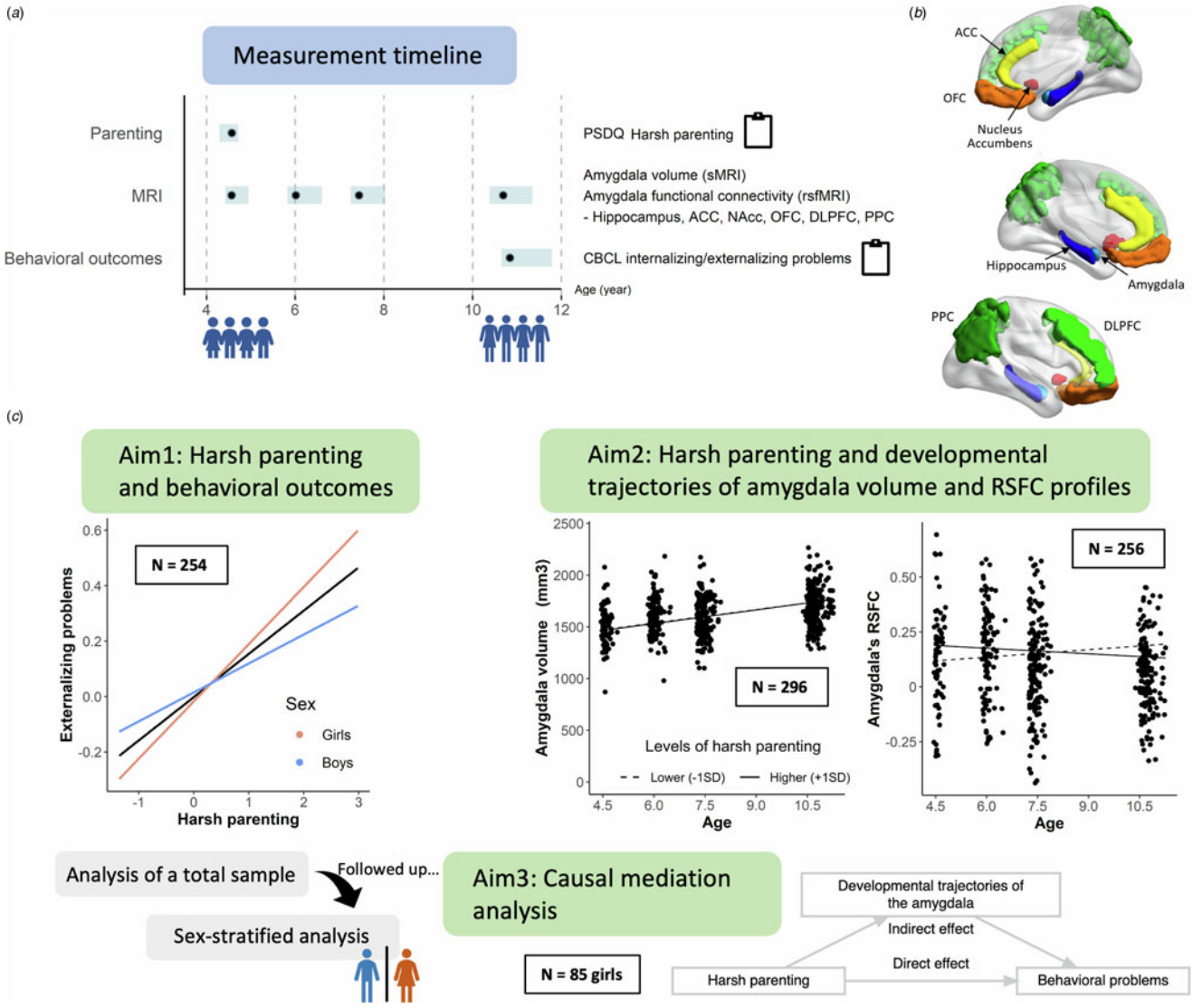

Figure 1. Study design and study aims. (A) The timeline of the assessments of parenting, brain imaging, and behavioral outcomes. The median (black dots) and range of age (light blue bar) for each measurement are shown. (B) Core brain regions of the emotional processing network (hippocampus, anterior cingulate cortex (ACC)), the reward processing network (nucleus accumbens (NAcc), orbital frontal cortex (OFC)), and the cognitive control network (dorsolateral prefrontal cortex (DLPFC), posterior parietal cortex (PPC)) were selected as regions of interest. (C) Aim 1 is to investigate the association between harsh parenting and child behavioral outcomes, followed up with the inclusion of sex interaction terms and sex-stratified analyses. Aim 2 is to investigate the associations between harsh parenting and developmental trajectories of amygdala volume and resting-state functional connectivity (RSFC) profiles. Aim 3 is to examine the associations among harsh parenting, developmental trajectories of the amygdala, and behavioral problems in later childhood through a causal mediation analysis approach.

Harsh parenting measures

The Parenting Style & Dimensions Questionnaire – Short version (PSDQ) (Robinson, Mandleco, Olsen, & Hart, 2001) was utilized to assess parenting practice. PSDQ is a 32-item parenting questionnaire and mothers provided a self-report of their parenting behaviors when their children were 4.5 years old. We defined the harsh parenting score used in our analyses as the mean score of the physical coercion, verbal hostility, and nonreasoning/punitive dimensional subscales. These are the same three subscales used to define the authoritarian parenting style. Therefore, the term 'harsh parenting' used in our study is equivalent to authoritarian parenting. The Cronbach's alpha of harsh parenting scores (authoritarian parenting scores) for the current sample was 0.82.

Child psychological outcome measures

Child behavioral problems were assessed with the Child Behavior Checklist (CBCL/6-18) (Achenbach, 1991) and childhood depressive symptoms were assessed using the Children's Depression Inventory 2nd Edition (CDI-2) (Kovacs & Staff, 2011) at age 10.5. CBCL is a parent-report 113-item assessment of children's behavioral and emotional problems. We used the internalizing problems score (the sum of anxious/depressed, withdrawn/depressed, and somatic complaints scales; the Cronbach's alpha of the current sample was 0.87) and the externalizing problems score (the sum of rule-breaking behavior and aggressive behavior scale scores; the Cronbach's alpha of the current sample was 0.88) for the main analysis. As externalizing problems are more likely to be observed directly by parents, whereas internalizing problems

https://doi.org/10.1017/S003329172400196X Published online by Cambridge University Press

such as anxiety and depression are less observable in nature, we utilized self-report CDI-2 at age 10.5 years to validate the absence of significant results for internalizing difficulties assessed with the parent-report CBCL. CDI-2 is a 28-item self-report questionnaire assessing cognitive, affective, and behavioral symptoms of depression in children and adolescents. We utilized the two scale scores of emotional problems (the sum of subscales of negative mood/physical symptoms and negative self-esteem; the Cronbach's alpha of the current sample was 0.78) and functional problems (the sum of subscales of ineffectiveness and interpersonal problems; the Cronbach's alpha of the current sample was 0.80) in our sensitivity analysis.

Brain MRI data acquisition

Neuroimaging data were acquired at ages 4.5, 6, 7.5, and 10.5 years with a 3.0 Tesla MRI scanner (for 4.5 and 6 years: Siemens Magnetom Skyra; for 7.5 and 10.5 years: Siemens Magnetom Prisma). For each subject, T1-weighted Magnetization Prepared Rapid Gradient Recalled Echo (MPRAGE) images and single-shot echo-planar imaging (EPI-BOLD) rsfMRI were collected. Full details of the imaging protocol are delineated in online Supplementary Table S2.

MRI pre-processing

T1 structural images underwent the standard recon-all pipeline using FreeSurfer version 7.1.1. The output was manually inspected for registration accuracy, and poor-quality datasets were excluded, resulting in the exclusion of 28 children. The amygdala was segmented using the Desikan–Killiany atlas in FreeSurfer (Desikan et al., 2006), and the resultant mask was used to extract the volumetric measurements.

The rsfMRI data was preprocessed using the default MNI pipeline in the CONN toolbox (release 20b) and SPM12 in Matlab R2020a as previously described (Chan et al., 2024; Huang et al., 2023). The procedure includes temporal alignment, motion correction, alignment with sMRI, outlier detection, nuisance regression, and bandpass filtering. Details of rsfMRI preprocessing are described in online Supplementary Text S1. A total of 51 subjects were excluded from the analysis due to low-quality data. A table comparing the sample characteristics between excluded participants and the PSDQ-fMRI analytical sample has been included in online Supplementary Materials (online Supplementary Table S3).

Region-of-interests (ROIs) and functional connectivity matrices

The Mindboggle 101 atlas was used to delineate the set of predetermined ROIs (amygdala, hippocampus, ACC, NAcc, OFC, DLPFC, and PPC). Functional connectivity matrices were computed by measuring the bivariate correlation coefficients of the BOLD time series between the amygdala and target ROIs (hippocampus, ACC, NAcc, OFC, DLPFC, and PPC) through a hemodynamic response factor (hrf)-weighted general linear model, obtaining a total of six RSFC profiles.

Covariates

The collection of data pertaining to maternal ethnicity, maternal and paternal educational attainment, marital status, and household income was conducted by the administration of self-report questionnaires at recruitment. Maternal depressive symptoms were measured with the Beck Depression Inventory 2nd edition (Beck, Steer, & Brown, 1987) at 4.5 years of child age. Missing data of covariates were imputed using multiple imputations with chained equations with the R package 'mice' (van Buuren & Groothuis-Oudshoorn, 2011). The imputation model includes the exposure, outcome, and confounders as well as the auxiliary variables. We obtained 30 imputed datasets with a maximum of 25 iterations using classification and regression trees.

Statistical analysis

All statistical analyses were performed in R (v4.2.3) (R core Team, 2023). The alpha level was set at $\alpha < 0.05$ (two-tailed). Analyses were adjusted for child sex, child age at outcome measurement, maternal ethnicity, differences in scanners (for brain measures), household education, and maternal depressive symptoms. Statistical models for amygdala volume were also adjusted for total intracranial volume, and those for RSFC were also adjusted for mean head motion during scans. Child outcome scores as well as harsh parenting scores were standardized; therefore, we obtained standardized coefficients for the child outcome and RSFC models. Results were obtained for each imputed dataset and aggregated using Rubins' rule (Rubin, 1987). The summary of the statistical analysis procedure is shown in Fig. 1B.

(i) **Associations between harsh parenting and child behavioral outcomes** (CBCL; internalizing problems and externalizing problems scores, CDI-2; emotional problems and functional problems scores) were analyzed with linear regression. All the analyses were repeated with a sex interaction term and subsequently in a sex-stratified manner.

(ii) **Associations between harsh parenting and developmental trajectories of the amygdala** (change in amygdala volume and amygdala RSFC profiles) were investigated with linear mixed models (LMMs). To assess whether harsh parenting was associated with developmental trajectories of amygdala volume, volumetric measures were regressed over harsh parenting score, age at scans, and harsh parenting × age at scans interaction term with random intercept for individual participants. This way, we can take into account the between- and within-individual variability separately and examine the associations of harsh parenting with change over time in the amygdala volume within individuals. A similar approach was used to assess whether harsh parenting was associated with the developmental trajectories of amygdala RSFC. The *p*-values for RSFC analyses were corrected for multiple comparisons with the Benjamini-Hochberg false discovery procedure accounting for a total of six tests. As a secondary analysis, all the analyses were repeated in a sex-stratified manner (therefore, exempted from the multiple comparison corrections).

(iii) **Mediation analysis** was carried out to investigate the extent to which the association between harsh parenting and child behavioral outcomes obtained in (i) was mediated by amygdala measure(s) from (ii). Changes in amygdala measures were the age effects derived from random effects of age terms in the LMMs. The LMMs applied here included a random intercept and age slope for individual participants and age, sex, age × sex, mean head motion, and differences in

https://doi.org/10.1017/S003329172400196X Published online by Cambridge University Press

scanner as fixed effect terms. We conducted a statistical mediation analysis (Tingley, Yamamoto, Hirose, Keele, & Imai, 2013) to obtain the average mediation effect (indirect effect), average direct effect, average total effect, and proportion of mediated effect using the nonparametric bootstrapping with 1000 simulations for variance estimation with the imputed dataset obtained by single imputation using the expectation-maximization algorithm from the R package 'amelia' (Honaker, King, & Blackwell, 2011).

Results

Association between harsh parenting and child behavioral outcomes

Table 2 shows the prospective associations between harsh parenting and child behavioral problems. Harsh parenting in early childhood was associated with externalizing problems ($\beta = 0.14$, 95% CI 0.02 to 0.25), but not with internalizing problems at age 10.5 years ($\beta = 0.02$, 95% CI −0.09 to 0.13) in the total sample (Fig. 2A). Similarly, we did not find any association between harsh parenting and child-reported depressive symptoms at age 10.5 years (online Supplementary Table S4), consistently demonstrating a lack of evidence of the association between harsh parenting and internalizing problems across reporters (emotional subscale: $\beta = -0.02$, 95% CI −0.12 to 0.09; functional subscale: $\beta = -0.03$, 95% CI −0.14 to 0.07). Analyses including a sex-interaction term (i.e. harsh parenting × sex) indicated no statistical differences by sex in both externalizing problems (interaction (ref. girls): $\beta = -0.21$, 95% CI −0.44 to 0.02, p for interaction = 0.07) and internalizing problems ($\beta = -0.09$, 95% CI −0.31 to 0.13, p for interaction = 0.43). Sex-stratified analysis indicated that the association between harsh parenting and externalizing problems was explained by the associations in girls ($\beta = 0.24$, 95% CI 0.08 to 0.40) but not that in boys ($\beta = 0.01$, 95% CI −0.16 to 0.17). To address the possibility of reverse causality, we examined the association between harsh parenting and externalizing problems by additionally adjusting externalizing scores at age 4 years. This adjustment did not alter the finding (girls: $\beta = 0.21$, 95% CI 0.05 to 0.37), demonstrating the robustness of the association. The current sample also did not show any sex differences in harsh parenting raw scores (girls v.s. boys: 2.25 v.s. 2.33, $p = 0.46$), showing that findings in sex differences were not a result of sex differences in parenting. Descriptive statistics of harsh parenting and child behavioral measures are shown in online Supplementary Table S5. Correlations between harsh parenting and child behavioral measures across all the evaluated time points are delineated in online Supplementary Table S6.

Association between harsh parenting and developmental trajectory of amygdala volume

Harsh parenting was not associated with the amygdala volume at baseline (age 4.5 years) ($B = -6.64$, 95% CI −25.35 to 12.08), and its change over time ($B = 0.31$, 95% CI −2.69 to 3.32) (Fig. 2B, online Supplementary Table S7). The observed results were not attributable to the adjustment of total brain volumes since harsh parenting was not associated with any global brain measures (online Supplementary Table S8).

Association between harsh parenting and developmental trajectories of amygdala resting-state functional connectivity (RSFC) profiles

Harsh parenting was associated with the developmental trajectories (slope of the change) of amygdala-ACC RSFC ($\beta = -9.95$, 95% CI −17.94 to −1.96), amygdala-OFC RSFC ($\beta = -8.63$, 95% CI −16.03 to −1.22), and amygdala-DLPFC RSFC ($\beta = -9.36$, 95% CI −16.71 to −2.02), all of which survived multiple comparison corrections ($p_{FDR-adjusted} < 0.05$) (Table 3). In children exposed to higher levels of harsh parenting (+1S.D.), amygdala-ACC RSFC and amygdala-DLPFC RSFC decreased over time, while children exposed to lower levels of harsh parenting (−1S.D.) demonstrated a relatively stable trajectory. For amygdala-OFC RSFC, children exposed to higher levels of harsh parenting showed a lower rate of increase compared to children exposed to lower levels of harsh parenting (−1S.D.) (Fig. 2C). Secondary sex-stratified analyses revealed that the association between harsh parenting and the developmental trajectory of amygdala-ACC RSFC was only significant in girls ($\beta = -14.58$, 95% CI −26.08 to −3.08) while the association between harsh parenting and the developmental trajectory of amygdala-OFC RSFC was only significant in boys ($\beta = -11.78$, 95% CI −2.39 to −1.16).

Mediation analysis

Given the aforementioned results on the association between harsh parenting and externalizing problems in girls, we conducted a causal mediation analysis to examine the mediating role of amygdala-ACC RSFC, using the slopes from the LMMs ($n = 85$). The descriptive statistics of the amygdala measures used in this mediation analysis are shown in online Supplementary Table S9 along with the other amygdala-based measures. A significant mediation effect was observed (indirect effect: $\beta = 0.06$, 95% CI 0.01 to 0.14, 20%), indicating that girls who were exposed to higher levels of harsh parenting showed a higher rate of decrease in amygdala-ACC RSFC, which in turn was associated with more severe externalizing problems (Fig. 2D, online Supplementary Table S10).

Table 2. Associations between harsh parenting and child behavioral outcomes

	Total ($n = 254$)			Girls ($n = 113$)			Boys ($n = 141$)			
	β	95% CI	p-Values	β	95% CI	p-values	β	95% CI	p-values	P_{int}
Internalizing problems	0.02	−0.09 to 0.13	0.67	0.07	−0.14 to 0.26	0.48	−0.04	−0.17 to 0.09	0.53	0.43
Externalizing problems	0.14	0.02 to 0.25	0.02	0.24	0.08 to 0.40	<0.01	0.01	−0.16 to 0.17	0.93	0.07

Model adjusted for child sex, child age at psychological outcome measurement, maternal ethnicity, household education, and maternal depressive symptoms (BDI) at 4.5YR.
The analyses were repeated with a mediation analysis sample ($n = 174$), finding the associations between harsh parenting and externalizing problems only in girls ($\beta = 0.17$, 95% CI: 0.04 to 0.31, $p = 0.01$).

https://doi.org/10.1017/S003329172400196X Published online by Cambridge University Press

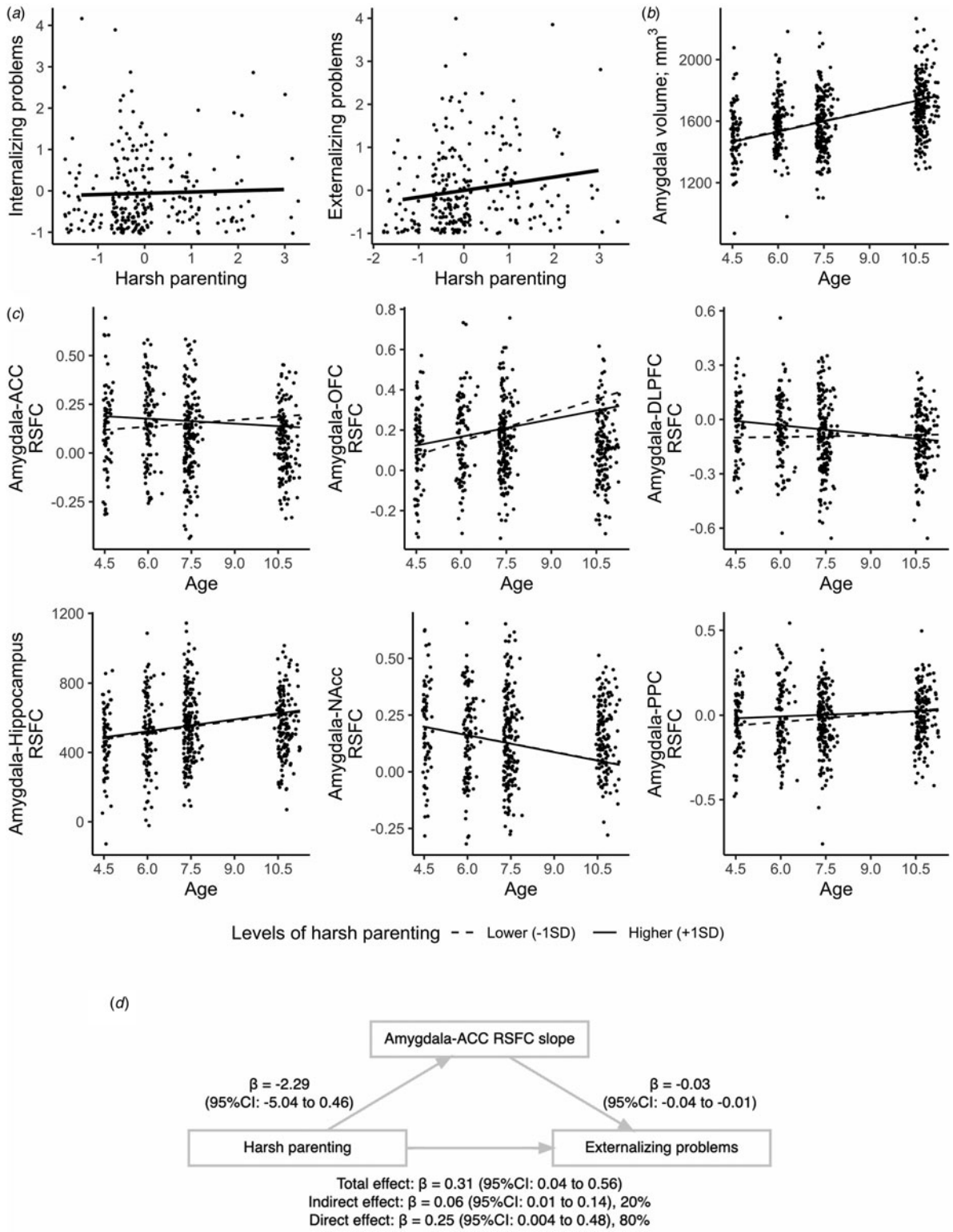

Figure 2. Associations among harsh parenting, child behavioral outcomes, and developmental trajectories of the amygdala. Note that the analyses presented in the text were conducted with continuous harsh parenting scores, and the figures illustrate associations of harsh parenting and brain development for two levels (+1S.D., −1S.D.) for descriptive purposes only. (A) Linear regression showed no association between harsh parenting and internalizing problems while there is an association with externalizing problems. (B) Linear mixed modeling showed no differences in the amygdala volumes by the levels of harsh parenting. (C) Linear mixed modeling revealed that children exposed to higher levels of harsh parenting (+1S.D. harsh parenting score) exhibited a decreasing trend (negative slope) for amygdala-ACC RSFC and amygdala-DLPFC RSFC (solid black line) while those exposed to lower levels of harsh parenting (−1S.D. harsh parenting score) exhibited an increasing trend (positive slope) for amygdala-ACC RSFC and amygdala-DLPFC RSFC (dashed black line). As for the amygdala-OFC RSFC, children exposed to higher levels of harsh parenting showed a slower increase while those exposed to lower levels of harsh parenting showed a higher increase. There are no differences in the amygdala-hippocampus RSFC, amygdala-NAcc RSFC, and amygdala-PPC RSFC by the levels of harsh parenting. In plots, each point shows individual observations. D) Causal mediation analysis ($n = 85$) showed that the accelerated decrease in amygdala-ACC RSFC, which may indicate accelerated development, could be a potential neural mechanism underlying the association between harsh parenting and externalizing problems in girls. Standard errors were estimated using a nonparametric bootstrap with 1000 simulations. Analyses were conducted using the imputed dataset from a single imputation with the expectation-maximization algorithm.

https://doi.org/10.1017/S003329172400196X Published online by Cambridge University Press

Table 3. Associations between harsh parenting and amygdala resting-state functional connectivity development

	Amygdala-hippocampus			Amygdala-ACC				Amygdala-NAcc				Amygdala-OFC				Amygdala-DLPFC				Amygdala-PPC		
(× 1/1000)	*β*	95% CI	*p*	*β*	95% CI	*p*		*β*	95% CI	P		*β*	95% CI	P		*β*	95% CI	*p*		*β*	95% CI	*p*
Total (*n* = 256)																						
Harsh parenting	3.41	−30.43 to 37.25	0.84	36.58	2.20 to 70.95	0.04		0.25	−30.79 to 31.30	0.99		24.37	−7.39 to 56.13	0.13		46.76	15.40 to 78.12	<0.01		21.78	−8.68 to 52.24	0.16
Age	22.23	−17.07 to 61.53	0.27	0.58	−38.17 to 39.32	0.98		−25.25	−61.10 to 10.61	0.17		38.13	2.44 to 73.82	0.04		−7.24	−42.60 to 28.12	0.69		11.16	−24.16 to 46.47	0.54
Harsh parenting × age	0.13	−8.05 to 8.30	0.98	−9.95	−17.94 to −1.96	0.01	*	−0.18	−7.64 to 7.27	0.96		−8.63	−16.03 to −1.22	0.02	*	−9.36	−16.71 to −2.02	0.01	*	−3.76	−11.13 to 3.60	0.32
Girl (*n* = 136)																						
Harsh parenting	37.91	−11.24 to 87.05	0.13	55.17	−0.35 to 110.69	0.05		−4.07	−51.00 to 42.87	0.87		−0.54	−48.99 to 47.90	0.98		46.98	0.58 to 93.38	0.05		47.37	2.19 to 92.54	0.04
Age	37.17	−15.92 to 90.25	0.17	−4.06	−58.53 to 50.42	0.88		−43.41	−94.20 to 7.34	0.09		67.85	19.81 to 115.88	0.01		−3.44	−50.69 to 43.81	0.89		9.07	−39.44 to 57.58	0.71
Harsh parenting × age	−3.40	−14.79 to 8.00	0.56	−14.58	−26.08 to −3.08	0.01		0.85	−10.08 to 11.78	0.88		−4.63	−14.94 to 5.69	0.38		−10.07	−20.27 to 0.12	0.05		−7.79	−18.27 to 2.69	0.15
Boy (*n* = 120)																						
Harsh parenting	−21.93	−70.73 to 26.88	0.38	23.25	−22.40 to 68.91	0.32		3.74	−39.35 to 46.84	0.86		40.28	−3.58 to 84.13	0.07		42.22	−4.17 to 88.61	0.07		0.38	−43.24 to 44.00	0.99
Age	−2.71	−61.94 to 56.51	0.93	3.41	−52.67 to 59.49	0.91		−3.75	−55.41 to 47.91	0.89		13.04	−39.72 to 65.79	0.63		−10.51	−66.25 to 45.23	0.71		8.86	−43.48 to 61.20	0.74
Harsh parenting × age	2.36	−9.51 to 14.23	0.70	−5.47	−16.71 to 5.78	0.34		−1.45	−11.77 to 8.88	0.78		−11.78	−2.39 to −1.16	0.03		−8.35	−19.16 to 2.47	0.13		−0.72	−11.20 to 9.75	0.89

Model adjusted for child sex, maternal ethnicity, mean head motion, household education, and maternal depressive symptoms (BDI) at 4.5YR.
Random intercept is included.
Results are for fixed effects aggregated across imputed datasets using Rubin's rule.
*Indicated FDR adjusted *p*-values <0.05.
The analyses were repeated with a mediation analysis sample ($n = 174$), showing the consistent associations between harsh parenting and amygdala-ACC RSFC in girls ($\beta = -18.74$, 95% CI −31.68 to −5.80, $p = 0.005$).

Discussion

Our study addressed critical gaps in the neurodevelopment literature by highlighting a potential unifying model of the associations among harsh parenting in early childhood, developmental trajectories of amygdala RSFC, and behavioral problems in later childhood. Specifically, harsh parenting was found to be associated with externalizing problems at age 10.5 years and with the developmental trajectories of amygdala-ACC RSFC, amygdala-OFC RSFC, and amygdala-DLPFC RSFC, in a sex-dependent manner. Our causal mediation analysis showed that girls who experienced harsher parenting exhibited a greater rate of decline in amygdala-ACC RSFC, which in turn was associated with more severe externalizing problems.

Our findings highlighted the association between harsh parenting in early childhood and later externalizing, but not internalizing problems. The observed associations between harsh parenting and externalizing problems are aligned with a meta-analysis showing concurrent and longitudinal associations between harsh parenting and offspring's externalizing problems (Pinquart, 2021). The absence of evidence of the association between harsh parenting and internalizing problems may be related to age differences in the prevalence of internalizing and externalizing problems. The emergence of internalizing problems is more common in adolescence while externalizing problems are more common in childhood (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Kessler et al., 2007). Therefore, the developmental window assessed in our study (between ages 4.5 and 10.5 years) may not be able to capture the emergence of internalizing problems. The potential reverse pathway that more externalizing problems provoke parental use of harsh parenting was tested by including baseline externalizing problems. This additional adjustment only slightly attenuated the associations, confirming the temporal associations between harsh parenting and externalizing problems in later childhood. Importantly, sex stratification suggested modest sex differences in the associations, whereby the association between harsh parenting and externalizing problems was primarily attributable to the association observed in girls.

The sex differences in the response of children to harsh parenting at the behavioral level may be attributed to genetic, hormonal, developmental, and social factors (Adrián-Ventura et al., 2019). A social model of the development of disruptive behavior in girls emphasizes the sex differences not only from biological perspectives but also social perspectives including sensitivity toward interpersonal relationships and rejection compared to boys (Kroneman, Loeber, Hipwell, & Koot, 2009). This indicates that girls may view harsh parenting as more fearful and threatening compared to boys, thus leading to more externalizing problems. One study of a combined cohort of over 1300 children reported that the influence of early child maltreatment on girls' behavioral problems was weakest at the most proximal assessment (age 4) and became stronger throughout follow-ups till the most recent assessment (age 12), while the opposite relations were observed among boys (Godinet, Li, & Berg, 2014). There is another possibility that parents are more sensitive to externalizing behaviors in girls compared to that in boys and hence rate it accordingly. The differences in parenting styles between girls and boys may also play a role (Kroneman et al., 2009) although a previous study using the same cohort showed no differences in the prevalence of physical discipline, one facet of harsh parenting, by child sex (Sudo et al., 2023). The current sample also did not show any sex differences in harsh parenting scores. We failed to establish the neurocircuitry differences in response to harsh parenting by sex. However, considering the sex differences in brain development during childhood and adolescence (Bethlehem et al., 2022), early life adversities such as harsh parenting could affect the neurocircuitry development of girls and boys differently. Future analyses with a larger sample size are warranted.

Harsh parenting was found to be associated with the developmental trajectories of fronto-amygdala circuits, namely the amygdala-ACC, amygdala-OFC, and amygdala-DLPFC circuits. Distinct fronto-amygdala circuits play critical roles in emotion regulation and have all been linked to early life stress (Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Gao, Biswal, Chen, Wu, & Yuan, 2021; Thomason et al., 2015). As the brain matures, there is a reduction in coupling between the amygdala and PFC, representing the enhanced top-down inhibitory processing of the prefrontal system and age-related cognitive maturity in emotion regulation (Gee et al., 2013b; Silvers et al., 2017). Hence, it is plausible that the higher rate of decrease in amygdala-ACC and amygdala-DLPFC RSFC (steeper slope) observed in children exposed to higher levels of harsh parenting may represent an element of accelerated development, in keeping with the stress acceleration hypothesis (Callaghan & Tottenham, 2016). More importantly, we provided evidence that this pattern of accelerated development subsequently resulted in higher levels of externalizing behaviors, in concordance with the established link among early life adversities, accelerated development, and psychopathologies in later life (Colich & McLaughlin, 2022). Although the definitive mechanisms underlying the possible accelerated development of fronto-amygdala RSFC remain unknown, one plausible explanation is that stress related to harsh parenting may lead to modifications of the hypothalamic–-pituitary–adrenal axis, and thereby affects the maturation of emotion-related brain circuitry (Gee et al., 2013a; Tottenham & Galván, 2016). Interestingly, we found that children exposed to high levels of harsh parenting showed a lower rate of increase in amygdala-OFC RSFC. This may seem counterintuitive at first glance, and it may appear to contradict the stress acceleration hypothesis. However, it is important to note that the impact of early life stress on developmental pace varies across brain regions and circuits (Herzberg & Gunnar, 2020). The same early life stress might result in accelerated development in some brain circuits while delayed development in others.

Our study has several strengths. First, our longitudinal study offers a unique opportunity to investigate the temporal link between harsh parenting, brain development, and later behavioral problems. Second, neuroimaging was performed at multiple time points, allowing the evaluation of longitudinal changes in brain development. Existing knowledge on the associations between early life adversities and brain development primarily stems from cross-sectional research, which is limited in its ability to distinguish variations within individuals from variations across individuals. Causal associations are best inferred with the consideration of within-individual variability. Third, we employed multimodal MRI to evaluate changes at the macrostructural and functional connectivity levels. However, several limitations should be considered when interpreting the findings. First, our sample size is relatively small for sex-stratified analyses. Therefore, validation of our findings in a larger sample is necessary. Second, parenting practice was assessed via a self-reported questionnaire which is vulnerable to self-reporting and recall biases. Although self-reported questionnaires offer the benefits of being efficient in terms of time and offering a wide range of behaviors, attitudes,

https://doi.org/10.1017/S003329172400196X Published online by Cambridge University Press

and beliefs in a systematic and standardized manner, it is best to supplement these questionnaires with observational measures in an experimental setting in future studies. Observational measures provide valuable insights into actual behaviors and dynamics of parent–child interactions. Also, as we only assessed the impacts of harsh parenting at one time point (age 4.5 years), associations reported in our current study do not take into account the duration or chronicity of harsh parenting. Third, motion is a possible confounder in neuroimaging studies, and collecting high-quality neuroimaging data is especially challenging in pediatric populations. Thus, we accounted for motion in our pre-processing and analysis. Fourth, our study lacks imaging data before age 4.5 years, thus we were unable to establish the developmental trajectory prior to age 4.5 years. However, we included the exposure measured at the relevant timing (harsh parenting at around 4 years) and the brain imaging onward, when the brain still undergoes a large proportion of changes. The difficulty in measuring and defining parenting practice in the newborn to toddler stages highlights the importance of examining the impact of parenting in the preschool period on brain development. Further, our brain assessment includes a maximum of four time points within 4.5–10.5 years, which is appropriate to capture brain development longitudinally. Lastly, our study sample is a Singaporean population, consisting of Chinese, Malay, and Indians, thus the results might not be generalizable to other populations. However, this investigation in the multi-ethnic Asian population was a contribution to neuroimaging studies predominantly targeting Western and US populations. Replications in other cohorts are needed to assess the generalizability of our findings.

Conclusions

The present study provided evidence that harsh parenting in early childhood is prospectively associated with both externalizing behavior and the developmental trajectories of functional connectivity profiles of the amygdala, with some support for sex differences at the behavioral and neurocircuitry levels. Notably, our study adds to the existing body of literature by providing a unifying model of the associations among harsh parenting in early childhood, developmental trajectories of amygdala RSFC, and behavioral problems in girls. Specifically, our findings suggest that the accelerated decrease in amygdala-ACC RSFC, which may indicate accelerated development, could be a potential neural mechanism underlying the association between harsh parenting and externalizing problems. This aligns with the established link among early life adverse experiences, accelerated development, and psychopathologies in later life.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S003329172400196X.

Acknowledgements. This research was supported by grants NMRC/TCR/004-NUS/2008 and NMRC/TCR/012-NUHS/2014 from the Singapore National Research Foundation (NRF) under the Translational and Clinical Research Flagship and grant OFLCG/MOH-000504 from the Open Fund Large Collaborative Grant Programmes and administered by the Singapore Ministry of Health's National Medical Research Council (NMRC), Singapore. In RIE2025, GUSTO is supported by funding from the NRF's Human Health and Potential (HHP) Domain, under the Human Potential Programme. Additional funding was provided by the Singapore Institute for Clinical Sciences, Agency for Science Technology and Research (A*STAR), Singapore. YK is supported by funding from the JSPS Overseas Research Fellowship. SYC is supported by funding from the NMRC Open Fund – Young Individual Research Grant (MOH-001149-00). MM is supported by funding from the Hope for Depression Research Foundation, USA, the Toxic Stress Network of the JPB Foundation, USA, the Jacobs Foundation, Switzerland, and the NRF and A*STAR's Human Potential Programme (H22P0M0001), Singapore. PS is supported by funding from Yong Loo Lin School of Medicine, National University of Singapore, NUHSRO/2021/093/NUSMed/13/LOA and Singapore Ministry of Education Academic Research Fund Tier 1 RG39/22. APT is supported by funding from the NMRC Transition Award (MOH-001273-00) and A*STAR (Brain-Body Initiative, iGrants call ID #21718).

Competing interests. There is no conflict of interest to declare.

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