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Immediate impact of child maltreatment on mental, developmental, and physical health trajectories

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Objective: The immediate impact of child maltreatment on health and developmental trajectories over time is unknown. Longitudinal studies starting in the direct aftermath of exposure with repeated follow-up are needed. **Method:** We assessed health and developmental outcomes in 6-month intervals over 2 years in 173 children, aged 3–5 years at study entry, including 86 children with exposure to emotional and physical abuse or neglect within 6 months and 87 nonmaltreated children. Assessments included clinician-administered, self- and parent-report measures of psychiatric and behavioral symptoms, development, and physical health. Linear mixed models and latent growth curve analyses were used to contrast trajectories between groups and to investigate the impact of maltreatment features on trajectories. **Results:** Maltreated children exhibited greater numbers of psychiatric diagnoses ($b = 1.998$, $p < .001$), externalizing ($b = 13.29$, $p < .001$) and internalizing ($b = 11.70$, $p < .001$) symptoms, impairments in cognitive ($b = -11.586$, $p < .001$), verbal ($b = -10.687$, $p < .001$), and motor development ($b = -7.904$, $p = .006$), and greater numbers of medical symptoms ($b = 1.021$, $p < .001$) compared to nonmaltreated children across all time-points. Lifetime maltreatment severity and/or age at earliest maltreatment exposure predicted adverse outcomes over time. **Conclusion:** The profound, immediate, and stable impact of maltreatment on health and developmental trajectories supports a biological embedding model and provides foundation to scrutinize the precise underlying mechanisms. Such knowledge will enable the development of early risk markers and mechanism-driven interventions that mitigate adverse trajectories in maltreated children. **Keywords:** Child development; follow-up studies; maltreatment; somatic problems; psychopathology.

Introduction

Maltreatment of children in the form of physical, emotional, and sexual abuse as well as physical and emotional neglect is an unfortunately common and highly prevalent problem throughout societies worldwide (Stoltenborgh, Bakermans-Kranenburg, Alink, & van IJzendoorn, 2015). Substantial evidence from epidemiological and clinical studies suggests that exposure to maltreatment not only strongly and robustly increases the risk for psychiatric diseases, including depression and anxiety disorders, and impaired cognitive development, but also induces lifelong risk for chronic physical disease outcomes, including cardiovascular disease, obesity, diabetes, lung cancer, chronic pain, headaches, and immune-related diseases, resulting in reduced longevity (Brown et al., 2009; Felitti et al., 1998; Heim & Binder, 2012; Norman et al., 2012; Wegman & Stetler, 2009). While several mechanisms may underlie a link between maltreatment exposure and adverse health outcomes, such as aberrations in cognition, learning, and attachment, there is profound evidence for a role of biological mediators: The developing brain and its adaptation systems are shaped by experience, and adversity during sensitive periods of developmental plasticity can lead to profound and persistent changes in regulatory systems that leave these individuals at lifelong risk to develop a wide range of diseases and adverse developmental outcomes. Hence, one current model posits that experiences of maltreatment are 'biologically embedded' during early development and that these early processes lead to stable changes across multiple systems that interfere with the ability to successfully adapt to or cope with challenge and lead to disease (Weiss & Wagner, 1998).

Accordingly, a large number of retrospective studies in adults with histories of child maltreatment

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[†]This paper is dedicated to Imke Moebus, MS.

have provided compelling evidence for long-term changes in regulatory systems at neural, physiological, and molecular levels. While this research has provided major insights into potential biological and molecular mechanisms that mediate the persistent effects of child maltreatment on disease risk, most human studies have been cross-sectional and rely on retrospective self-reports in adult samples, not allowing for causal inferences. Cross-sectional studies further do not allow for the identification of developmental trajectories of biological and behavioral changes over time, nor do they inform about early embedding processes. While a handful of longitudinal studies exist that assessed maltreatment in cohorts followed from childhood into adulthood, such as the E-Risk (Fisher et al., 2015) and Dunedin studies (Silver, Arseneault, Langley, Caspi, & Moffitt, 2005), these often started decades ago and did not collect biological data in the immediate aftermath of exposure to maltreatment and across development. Most studies, cross-sectional or longitudinal, did not adopt a multisystem approach. Thus, there is a significant gap of translation between insights into the neurobiological and molecular mechanisms that link maltreatment exposure with long-term risk for stress-related disorders and the use of this knowledge to develop new diagnostic markers to identify cases at risk or to develop novel interventions that target specific processes of biological embedding.

In order to increase our understanding of the impact of maltreatment exposure on disease risk across the lifespan, it is crucial to understand the early impact of maltreatment in the immediate aftermath of exposure and over time across multiple levels of regulation and to link these trajectories to clinical and developmental trajectories. As noted above, while there is a large evidence base for biological and clinical correlates of maltreatment in adults, there is a remarkable paucity of data in children that provide insights into early immediate processes of stress regulation and the emergence of symptoms. Elucidating these immediate developmental events will provide insight into the early mechanisms that are responsible to produce a persistent and pronounced programming of stress systems and risk for disorders. Only once we have mapped and understood these early events can we identify targets for specific interventions. By focusing on the early-life period, we may be able to take advantage of developmental plasticity to positively impact on long-term trajectories of health and adaption, by targeting early risk mechanisms and emerging pathology. Thus, there is an urgent need for prospective studies that map biological, clinical, and developmental trajectories in young children, starting immediately after they have been identified as maltreated and to follow these children over time.

A number of cross-sectional studies in young children have shown that exposure to maltreatment is associated with increased internalizing and externalizing behavior, developmental deficits, social deficits, chronic medical conditions, as well as increased health care use and emergency medical admissions (Crozier & Barth, 2005; Enlow, Blood, & Egeland, 2013; Hunt, Slack, & Berger, 2017; McKelvey, Conners Edge, Fitzgerald, Kraleti, & Whiteside-Mansell, 2017; Naughton et al., 2013; Vachon, Krueger, Rogosch, & Cicchetti, 2015). Available prospective studies in maltreated children report on selected clinical symptoms, health risks, or developmental deficits, but do not adopt a comprehensive approach across mental, physical, and developmental domains, starting in the immediate aftermath and assessing stability over time (Briggs-Gowan, Carter, & Ford, 2012; Éthier, Lemelin, & Lacharité, 2004; Lansford et al., 2002; Sternberg, Lamb, Guterman, & Abbott, 2006; Villodas et al., 2015). Indeed, no prospective study to date has evaluated the impact of maltreatment on medical diseases over time in children. While a number of cross-sectional and prospective studies in children report selected biological changes in stress-regulatory, metabolic, immune, or neural systems, such as cortisol dysregulation, inflammation, and grey matter changes (Danese et al., 2011; King, Mandansky, King, Fletcher, & Brewer, 2001; Lim, Radua, & Rubia, 2014; Slopen et al., 2015), generally replicating findings in adults, these studies did not integrate measures across multiple systems nor did they implement measures over time in short intervals directly after exposure. In terms of the assessments, the majority of available studies rely on parent- or self-report questionnaires to assess psychiatric symptoms or developmental deficits rather than conducting in-person clinician-administered diagnostic interviews and neurocognitive tests. Oftentimes, there is only limited information on timing or severity of maltreatment (White et al., 2015).

Taken together, there is a lack of prospective studies in young children providing a standardized and detailed clinician-based assessment of the immediate impact of maltreatment in young children on mental, developmental, and physical health trajectories in the direct aftermath of exposure with follow-up over time and there is no knowledge as to how such trajectories associate with biological embedding processes. Towards that end, we implemented a longitudinal multisystem study on the immediate biological embedding of maltreatment in children aged 3–5 years. We here report first results from this prospective study, focusing exclusively on the immediate impact of maltreatment exposure on mental, developmental, and physical health trajectories over time in these children. These results provide foundation to scrutinize biological mechanisms that underlie these clinical and developmental trajectories in future analyses and underscore the need for developing early risk markers as well as mechanistic targeted early interventions.

Methods

This report is part of the Berlin Longitudinal Children Study that investigates the immediate biological embedding of maltreatment in children, funded by the Federal Ministry of Education and Research (01KR1301) and conducted at Charité – Universitätsmedizin Berlin, Germany. The aim of the larger study was to identify biological processes at multiple levels of regulation in the immediate aftermath of exposure and over time (every 6 months for up to 2 years) and to associate these processes with clinical and developmental trajectories over time. The present report presents clinical and developmental data obtained in this study.

Approval for the study was obtained from the local medical ethics committee. All procedures are in accordance with the Ethical Principles for Medical Research as established by the Medical Association Declaration of Helsinki. Written informed consent was obtained from all participants after the procedures were fully explained. Children gave consent by painting or signing a form that was appropriate for the children's age range. Caregivers received monetary compensation for participation. Children received a small gift. Caregivers received diagnostic results and referral for psychosocial or medical follow-up, where necessary.

Participants and study design

We recruited 173 children aged 3–5 years at study entry (T0) and their caregivers. The sample includes 86 children who had been exposed to maltreatment within 6 months and 87 nonmaltreated children. Maltreatment and control groups were frequency-matched for sex. General exclusion criteria for all children included parents under the age of 18 years, neurodevelopmental disorders, serious medical disease as well as serious medical disease of the parents.

Maltreated children were recruited from a broad range of local child welfare and protection services, including government offices for child welfare, family assistants and counselors, and agencies of the child welfare sector. Sixty-one percent of the sample of maltreated children was recruited through these offices and can be considered as corroborated cases. To increase the sample size, we further recruited maltreated children from pediatric clinics and the community through advertisements and letters sent to families with children aged 3–5 years mainly identified through public census records (39%)[1]. For inclusion into the maltreatment group, children had to have experienced maltreatment in the form of physical or emotional abuse or neglect within 6 months, according to the Maltreatment Classification System (Barnett, Manly, & Cicchetti, 1993) [for cutoff scores, see below]. We did not specifically recruit for sexual abuse, as sexual abuse usually leads to removal of the child from the home, which we considered would be a significant intervention. Nonmaltreated children were recruited from the community using advertising as well as letters directed to families with children between 3 and 5 years of age using census records. For assignment to the control group, children were screened to exclude maltreatment, exposure to violence or any severe critical or traumatic life events.

We screened 525 families for inclusion. Of those, 325 were not interested in participating or did not meet the inclusion criteria, resulting in 200 families participating in T0. Of these 200 families, 27 families were excluded after the detailed assessments in T0 (as they did not meet inclusion criteria) resulting in a total sample of $N = 173$ at T0 (86 with and 87 without maltreatment)[2]. Follow-up time-points took place in 6-month intervals sequentially for each child over the course of 2 years (T1–T4). At each time-point, children and caregivers underwent a battery of clinician-administered interviews, questionnaires, and neuropsychological testing. Children also provided biological and genetic samples and a subset of maltreated children underwent repeated brain scans (data not included here). Dependent on the timing of the initial study entry (T0) and due to dropout, not all families reached T4. Attrition and noncompletion rates (due to drop-out or termination of the study before the child reached T4) were higher among maltreated children compared to nonmaltreated children ($n = 48$ vs. $n = 35$; $\chi^2(df = 1) = 4.208$, $p = .040$). For the overall study design and N per time-point, see Figure 1.

Assessments

Assessments included standardized clinician-administered interviews regarding maltreatment features and diagnostic interviews and questionnaires to assess psychiatric and behavioral outcome variables. In addition, the child underwent a medical examination as well as neuropsychological testing for developmental outcomes.

Maltreatment assessment. The occurrence and features of maltreatment were assessed at all time-points. At each follow-up visit, the maltreatment assessment was repeated to collect information on ongoing maltreatment for each 6-month interval as well as for safety purposes. To assess features of maltreatment, we used the Maternal Interview for the Classification of Maltreatment (Cicchetti, Toth, & Manly, 2003). The interview was administered by trained clinicians and based on caregiver reports. Responses were coded according to the Maltreatment Classification System (Barnett et al., 1993), which provides specific criteria for classifying and quantifying the occurrence and features of subtypes of maltreatment. The interview covers a range of subtypes, including emotional maltreatment (i.e., emotional abuse and/or emotional neglect), physical neglect (i.e., failure to provide and/or lack of supervision), physical abuse, and moral-legal and/or educational maltreatment. In our sample, the latter subtype overlapped with lack of supervision due to excessive video gaming or keeping the child busy, which we therefore assigned to the physical neglect category. For each incidence, severity is rated on a 5-point scale ranging from mild (1) to severe or life-threatening maltreatment (5). In addition, onset age was specified for each incidence. Severity cutoff scores were used to include children in the maltreatment group (emotional maltreatment ≥ 2, physical abuse ≥ 1, and physical neglect ≥ 2). As noted above, we did not recruit for sexual abuse; however, co-incident mild forms of sexual abuse were detected in 8 of 86 maltreated children.

Outcome measures. Mental health outcomes: Psychiatric disorders were assessed at T0, T2, and T4. To assess psychiatric disorders, we administered the electronic version of the Preschool Age Psychiatric Assessment (Egger & Angold, 2004), which provides a developmentally sensitive and fully structured assessment based on caregiver reports. The interview assesses the presence, frequency, duration, and onset of symptoms for a 3-month period and diagnoses are generated according to DSM-IV, including depressive disorders (i.e., major depression and dysthymia), anxiety disorders (i.e., social phobia, specific phobia, separation anxiety disorder, generalized anxiety disorder, and posttraumatic stress disorder), attention deficit hyperactive disorder, conduct disorder, oppositional defiant disorder, and mutism. All interviews were conducted by specifically trained clinicians. For 10% of the sample, interviews were conducted by several raters and interrater reliability was assessed (kappa coefficient = .64 and 1).

Behavioral and emotional problems were rated at each time-point (T0–T4) using the age-appropriate caregiver-report versions of the Child Behavior Checklist depending in the child's age, that is, 1.5–5 years or 6–18 years (Achenbach & Rescorla, 2000, 2001; Esser, Hänsch-Oelgart, & Schmitz, 2018; Plück et al., 2013). Because there are no published norm values for

Figure 1 Study design of the Berlin Longitudinal Children Study and N per time-point. Grey shaded area marks the clinical variables considered in this report (Federal Ministry of Education & Research 01KR1301)

the 1.5–5 years version for the German population, we used T values based on US norms for both versions to ensure comparability.

Developmental outcomes: Children underwent standardized neuropsychological testing for cognitive, verbal, and motor developmental domains at T0, T2, and T4. All tests were conducted by trained clinicians. To assess nonverbal cognitive development, we administered the Snijders Oomen Nonverbal Test for the age range of 2½–7 years (Tellegen, Snijders, Wijnberg-Williams, & Winkel, 1996). This well-validated test provides standardized intelligence quotient (IQ) scores. To assess verbal development, we used subtests of the Wechsler Preschool and Primary Scale of Intelligence – Fourth Edition (Wechsler, 2012). These verbal subtests result in two verbal IQ scores, reflecting vocabulary and verbal comprehension. We used the mean of both scores in our analyses. To assess motor development, we used the Movement Assessment Battery for Children – Second Edition (Henderson et al., 2007) that identifies impairments in motor performance and is validated for the age range of 3–16 years. Percentiles were converted into standardized IQ scores for our analyses.

Physical health outcomes: Children underwent a physician-administered full medical anamnesis and examination at T0, T2, and T4. Using a structured examination form, we coded symptoms in internal systems (i.e., cardiovascular, respiratory and/or abdominal symptoms or disorders) and neurological symptoms (i.e., headaches, seizures, and abnormal muscle tone). At all time-points (T0–T4), a brief physical examination was conducted to check for physical signs of severe physical abuse or neglect, for safety purposes.

Additional assessments for demographics and covariates. Child age and sex: To account for potential sex differences and the impact of age on effects, we entered sex and age at study entry as covariates in all analyses.

Socioeconomic status: Socioeconomic status has a well-established impact on mental and physical health and development in children (Bradley & Corwyn, 2002; Reiss, 2013). Socioeconomic status was assessed at all time-points (T0–T4) based on the Winkler and Stolzenberg Index (Lampert & Kroll, 2006; Lange et al., 2007; Winkler & Stolzenberg, 1999). The multi-dimensional index score represents the sum (range 3–21) of three metric components, that is, education and occupational qualification, occupational status, and net income of the household (range 1–7 each). The dimensional sum score was entered in our analyses.

Critical life events: We assessed critical life events other than maltreatment using the life event list included in the Preschool Age Psychiatric Assessment (Egger & Angold, 2004) at all time-points (T0–T4). The PAPA assesses minor and major critical life events. Minor critical life events include, for example, divorce, moving, change in school or daycare, death of pet, hospitalization of a parent, and others. Major critical life events include hospitalization of the child, death of loved adult (including grandparents), car accident, injury, natural disaster, and others. Because both groups of children scored in the life event scale and life events could plausibly impact on outcomes, we used the sum of life events as covariate in all analyses and models.

Maternal or caregiver depression: Maternal or caregiver depression may bias the rating of the child's emotional symptoms in caregivers and may have an adverse impact on the child's mental health (Boyle & Pickles, 1997; Saveanu & Nemeroff, 2012). Maternal or caregiver depression was assessed using the German self-report version (Kühner, Bürger, Keller, & Hautzinger, 2007) of the Beck Depression Inventory (Hautzinger, Keller, & Kühner, 2009). The score was used as covariate in all analyses with child mental health outcomes.

Adherence to psychosocial and medical recommendations: As noted above, families received feedback about the child's health and developmental status and recommendation for follow-up, where necessary (e.g., psychological consultation, dentist visit, etc.). Care seeking can be considered a confounder. Therefore, we recorded at each time-point whether or not these recommendations were followed and entered percent adherence as a covariate in our analyses.

Statistical analysis

Group differences regarding sample characteristics were estimated using *t*-tests, χ^2 tests, and Fisher exact tests. All analyses were controlled for potential cofounders, including age, sex, socioeconomic status, critical life events, caregiver depressive symptoms, and percent adherence to recommendations. For trajectory analyses, child sex and age at study entry were entered as time-invariant covariates along with the socioeconomic status, critical life events, depressive symptoms of the caregiver, and adherence to recommendations as time-varying covariates (T0–T4).

To estimate group differences regarding presence of psychiatric disorders over time, we used generalized linear mixed models with a binominal distribution. The presence or absence of a psychiatric disorder (yes/no) in a child served as the primary outcome, with Group, Time, the interaction term between Group and Time, and covariates as fixed predictors. We used generalized linear mixed models to estimate effects of lifetime severity and onset of maltreatment (analyses within the maltreatment group) on the presence or absence of psychiatric disorders over time.

To examine group differences regarding internalizing and externalizing symptom trajectories and developmental status over time, linear growth curve analyses within the structural equation modeling (SEM) framework were conducted with Group as predictor for the random intercept and slope (see Figure 2). We first identified the unconditional functional form of the growth curve model before entering any predictors or covariates. The latent intercept was positioned at the first measurement occasion (i.e., baseline assessment). Model fit was assessed using the comparative fit index (CFI; Bentler, 1990), root-mean-square error of approximation (RMSEA; Browne & Cudeck, 1993), and the χ^2 difference test.

To test whether change in maltreatment severity over time would be associated with internalizing and externalizing symptom trajectories and trajectories of developmental status over the course of the study, we estimated correlation coefficients between the latent growth factor scores of maltreatment and internalizing and externalizing symptoms as well as developmental status. Of note, these analyses could only be carried out for child outcomes that allowed the application of growth curve analyses. To estimate whether lifetime maltreatment accumulation in the maltreatment group or onset of the first maltreatment experience would predict symptom levels and trajectories over time, both were entered as predictors in separate linear growth curve models with internalizing and externalizing symptoms and each development type (cognitive, verbal, and motor) as outcomes, along with the above-mentioned covariates.

To estimate group differences in the number of medical symptoms over time, we ran a generalized mixed linear model with a Poisson distribution for count data. The number of medical symptoms was the outcome in this model, with measurement occasions nested within individuals. Group,

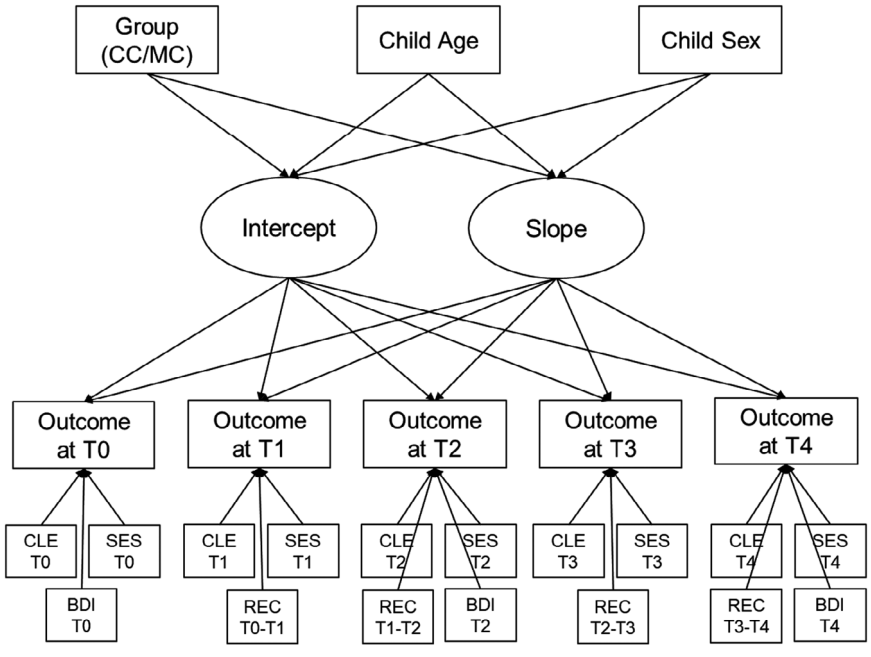

Figure 2 Growth curve model overview. CC = Control children. MC = Maltreated children. CLE = critical life events experienced by child. SES = socioeconomic status of family. BDI = Becks Depression Inventory (depressive symptoms of mother/caretaker). REC = percentage of not followed recommendations. Child age represents the age of the child at T0

Time, the interaction term between Group and Time, and covariates were included as fixed factors along with a random intercept. Likewise, we used generalized linear mixed models to estimate effects of lifetime severity and onset of maltreatment (analyses within maltreatment group) on the number of medical symptoms over time.

All model parameters were estimated by means of full information maximum likelihood as implemented in the *lavaan* package Version 0.5-22 (Rosseel, 2012) and package *lme4* Version 1.1-12 (Bates, Mächler, Bolker, & Walker, 2014) for R 3.2.2 (R Foundation, Vienna, Austria). Other analyses were performed in IBM SPSS Statistics 24 for Windows (IBM, Armonk, NY, USA). Full information maximum likelihood was used both in our SEM-based growth curve and linear mixed models to handle missing data. We report unstandardized (b) and (partially) standardized estimates (β). Please note that only metric variables were standardized, but not binary variables (e.g., group and age) or count variables (medical symptoms) to ease interpretation. In case the independent variable is non-metric, β can be considered partially standardized, in case it is metric, β is fully standardized.

Results

Demographic features and sample characteristics

Table 1 presents demographic features and sample characteristics at study entry. At T0, children were $M = 4.24$ years old ($SD = 0.79$). The mean age of maltreated children was slightly higher than the mean age of nonmaltreated children ($t = -2.066$, $p = .040$). Socioeconomic status differed significantly between groups with lower levels among maltreated children compared to nonmaltreated children ($t = 10.895$, $p<.001$). Eighty-three percent of children participated in the study with their biological mother, including 74.4% of maltreated children and 92% of nonmaltreated children ($\chi^2 = 56.597$, $p < .001$). All children attended daycare at T0. Significantly more maltreated children compared to nonmaltreated children received special support in daycare ($\chi^2 = 21.946$, $p<.001$), psychiatric treatment ($\chi^2 = 7.928$, $p = .005$), or psychotherapy ($\chi^2 = 5.782$, $p = .022$). Groups differed significantly with respect to the frequency of critical life events which was expected given that severe critical life events were exclusionary for the control group ($\chi^2 = 7.640$, $p = .006$). Parents of maltreated children were significantly more often separated or divorced as compared to parents of nonmaltreated children ($\chi^2 = 15.136$, $p<.001$). Finally, caregivers of maltreated children had more often been diagnosed with a mental disorder when compared to caregivers of nonmaltreated children ($\chi^2 = 21.728$, $p < .001$) and exhibited higher levels of depressive symptoms ($t = -5.651$, $p < .001$).

Maltreatment features

Frequency, co-occurrence, and severity of maltreatment types. Table 2 depicts the current and lifetime distribution of each subtype of maltreatment within the group of maltreated children at T0. Of note, for these children who had a mean age of $M = 52.36$ months ($SD = 10.0$) at T0, the mean exposure duration to maltreatment was $M = 44.16$ months ($SD = 16.71$) at T0. The mean onset of earliest maltreatment experiences was $M = 5.56$ months ($SD = 10.8$). Sixty-two percent of

Table 1 Sample characteristics at baseline

	Mean (*SD*) / count (percentage)			
	Control children	Maltreated children	χ^2/t	*p*
Children				
Age	4.12 (.73)	4.36 (.83)	−2.066[c]	.040
Female sex	41 (47.1%)	41 (47.7%)	.005[d]	.942
Citizenship				
German	84 (96.6%)	84 (97.7%)	.994[e]	1.000
EU	2 (2.3%)	2 (2.3%)		
Other (USA and Ukraine)	1 (1.1%)	0 (0%)		
Ethnicity[a]				
Black	0	1 (1.2%)	1.520[e]	.692
White	81 (93.1%)	77 (89.5%)		
Black-white	5 (5.7%)	6 (7.0%)		
Asian-white	1 (1.1%)	2 (2.3%)		
Attending day care	87 (100%)	86 (100%)	-	-
Integration status at day care (special support)	1 (1.2%)	22 (26.2%)	21.946[e]	<.001
Psychotherapy				
Current	0	3 (4.0%)	5.782[e]	.022
Past	0	2 (2.7%)		
Psychiatric treatment				
Current	0	3 (4.1%)	7.928[e]	.005
Past	0	4 (5.4%)		
Number of children with at least one critical life event				
Group A (mild to moderate life events)	16 (18.4%)	32 (37.2%)	7.640[d]	.006
Group B (severe life events)	44 (50.6%)	53 (61.6%)	2.145[d]	0.143
Participating caregivers				
Relation caregiver to child				
Biological mother	80 (92.0%)	64 (74.4%)	15.136[e]	.001
Biological father	6 (6.9%)	6 (7.0%)		
Foster mother	0	6 (7.0%)		
Other[b]	1 (1.1%)	10 (11.6%)		
Age	36.4 (5.8)	36.4 (8.6)	0.028	.977
N of people household	3.83 (.90)	3.99 (1.70)	−0.776[c]	.439
Children < 18 years	1.86 (.73)	2.37 (1.45)	−2.918[c]	.004
Status biological parents				
Living together	76 (87.4%)	23 (31.1%)	56.597[e]	<.001
Separated/divorced	6 (6.9%)	37 (50.0%)		
Never lived together	4 (4.6%)	14 (18.9%)		
Other (long distance relationship)	1 (1.1%)			
Single parent (without partner living in household)	6 (7.0%)	43 (52.4%)	41.993[d]	<.001
Socioeconomic status	16.10 (3.60)	9.40 (4.57)	10.895[c]	<.001
Mental disorder of participating caregiver (past/present)	10 (11.5%)	37 (43.0%)	21.728[e]	<.001
Maternal or caretaker depressive symptoms (BDI score)	5.16 (5.77)	14.16 (12.68)	−5.651[c]	<.001

Data on parent citizenship were missing in two cases (1 maltreatment and 1 control group), on integration status in six cases (4 control, 2 maltreatment), child psychotherapy in 14 cases (3 control, 11 maltreatment), child psychiatric treatment in 19 cases (7 control, 12 maltreatment), status of biological parents missing in 12 cases (all maltreatment group), BDI missing in 13 cases (2 control, 11 maltreatment), and parent age in two cases (both maltreatment).

[a]Ethnicity was assessed during interviews with the parent by enquiring about the origin of relatives for further genetic analyses (categories were Black, White, and Asian).

[b]Other included grandparent, adoptive parent, and child participating with an educator from a child protection facility.

[c]*t*-test.

[d]χ^2-*test*.

[e]Fisher's exact test.

maltreated children had experienced some form of maltreatment since birth. Figure 3 provides an overview of the co-occurrence and substantial overlap of different maltreatment types within the group of maltreated children at T0. The mean severity of maltreatment (lifetime since birth) within the maltreatment group was mild to moderate at T0 [emotional maltreatment, $M = 2.46$ ($SD = 0.81$); physical neglect, $M = 2.05$ ($SD = 0.98$); physical abuse, $M = 1.16$ ($SD = 0.48$); sexual abuse, $M = 1.13$ ($SD = 0.35$)]. For detailed descriptive information on maltreatment features, see Table S1.

Maltreatment trajectory over time. We estimated a growth curve model with a linear slope for the trajectory of the severity of maltreatment exposure over the course of the study. The sum severity score combining all the maltreatment events experienced during the last 6 months before baseline (T0) and between each of the assessments (T1–T4) was used.

Table 2 Maltreatment types experienced in maltreatment group

Maltreatment type	Frequency at time of baseline assessment *N* (%)	Lifetime (since birth) *N* (%)
Any abuse	77 (89.5%)	86 (100%)
Frequency of maltreatment types overall		
Emotional maltreatment	74 (86%)	85 (98.8%)
Physical neglect	12 (14.0%)	38 (44.2%)
Physical maltreatment	24 (27.9%)	36 (41.9%)
Sexual abuse	-	8 (9.3%)
Overlap of maltreatment types		
Emotional maltreatment only	47 (54.7%)	29 (33.7%)
Physical maltreatment only	1 (1.2%)	-
Physical neglect only	2 (2.3%)	1 (1.2%)
Neglect and emotional maltreatment	4 (4.7%)	15 (17.4%)
Physical abuse and emotional maltreatment	17 (19.8%)	18 (20.9%)
Sexual abuse and emotional maltreatment	-	1 (1.2%)
Neglect, physical abuse, and emotional maltreatment	6 (7.9%)	15 (17.4%)
Neglect, sexual abuse, and emotional maltreatment	-	4 (4.7%)
Neglect, physical abuse, sexual abuse, and emotional maltreatment	-	3 (3.5%)

Within maltreatment group (n = 86). No missing data.

The mean intercept i (mean level of experienced maltreatment during 6 months before T0) was $M(i)$ = 3.317 (p < .001). The average linear slope s was negative with $M(s)$ = −0.450 (p < .001). Thus, a slight decrease of maltreatment severity was apparent over time. There was no significant variance in the latent intercept ($\sigma^2(i)$ = 0.917, p = .059) and the latent slope ($\sigma^2(s)$ = 3.088, p = .870). Thus, our sample showed relatively homogeneous maltreatment severity levels at baseline and trajectories over time.

This model with a linear slope to describe the trajectory of maltreatment over time showed a mediocre fit (*RMSEA* = 0.109, *CFI* = 0.524, $\chi^2(df = 14) = 28.193$, p = .013). Further analyses showed that a complex model with a linear, quadratic, and cubic slope would result in a better fit. However, in favor of interpretability, we conducted further analyses with the parsimonious model with the linear slope. Details on a more complex model with higher order terms is included in Figure S1. Of note, results from the more complex models did not change any conclusions (see Table S2: Correlation of Factor Scores).

Mental health outcomes

Psychiatric disorders. Frequencies of psychiatric diagnoses at all time-points are presented in Table 3. Generalized linear mixed models with a binominal distribution revealed that maltreated children had a markedly higher likelihood to suffer from any psychiatric disorders compared to nonmaltreated children (b(group)=1.998, standardized β = 1.998, p < .001), both at baseline and across all follow-up time-points, with no significant moderation effect over time (b(group*time) = −.028, β = −.028, p = .883). This indicates a significant and stable increased prevalence of psychiatric disorders among children with maltreatment experience across the 2-year observational period. Twenty-four maltreated children (27.9%) were not diagnosed with any psychiatric disorder at any of the five study visits, whereas 59 nonmaltreated children (67.8%) were not diagnosed with any psychiatric disorder at any of the five study visits (χ^2 = 27.60, p < .001). Generalized linear mixed models did not reveal significant effects of severity of lifetime maltreatment exposure (b(severity) = .037, β = .164, p = .631) or onset age of first maltreatment (b(onset) = −.029, β = −.313, p = .278) on the likelihood of psychiatric disorders within the maltreatment group.

Internalizing and externalizing symptoms. Descriptive data on symptoms over time are depicted in Table 3 and statistical models are presented in Table 4. For a depiction of predicted trajectories, see Figure S2. We first estimated basic growth models for the course of internalizing and externalizing symptoms over time (Models 1a and 2a). For internalizing symptoms, a linear growth curve model (Model 1a) showed a good fit (*RMSEA* = 0.065, *CFI* = 0.972, $\chi^2(df = 14) = 24.216$, p = .043). The mean intercept (mean level of internalizing symptoms at baseline) was $M(i)$ = 48.51 (p < .001). The mean of the latent linear slope was slightly negative $M(s)$ = −0.837 (p < .001). There were significant interindividual differences in both the intercept ($\sigma^2(i)$ = 108.35, p < .001) and the slope ($\sigma^2(s)$ = 3.379, p = .001), indicating that there is variability inasmuch as children differed in the level of their internalizing symptoms at baseline as well as in their changes over time. Likewise, for externalizing symptoms, a linear growth curve model (Model 2a) showed good fit (*RMSEA* = 0.076, *CFI* = 0.971, $\chi^2(df = 14) = 27.88$, p = .015). The mean intercept was $M(i)$ = 47.52 (p < .001). The average linear slope was slightly negative $M(s)$ = −0.382, but not significantly (p = .088). There were significant interindividual differences in both intercept ($\sigma^2(i)$ = 125.89, p < .001) and slope ($\sigma^2(s)$ = 2.81, p = .004).

Next, the Group variable was entered as a predictor in these models (Model 1b and 2b) as were the covariates (Figure 2). For internalizing symptoms (Model 1b), we found a significant effect of Group on the intercept with markedly higher symptom levels at T0 in the group of maltreated children as compared to nonmaltreated children (b_i(group) = 11.70, p < .001). There was also a significant Group effect on the linear slope of internalizing symptoms, with a slightly

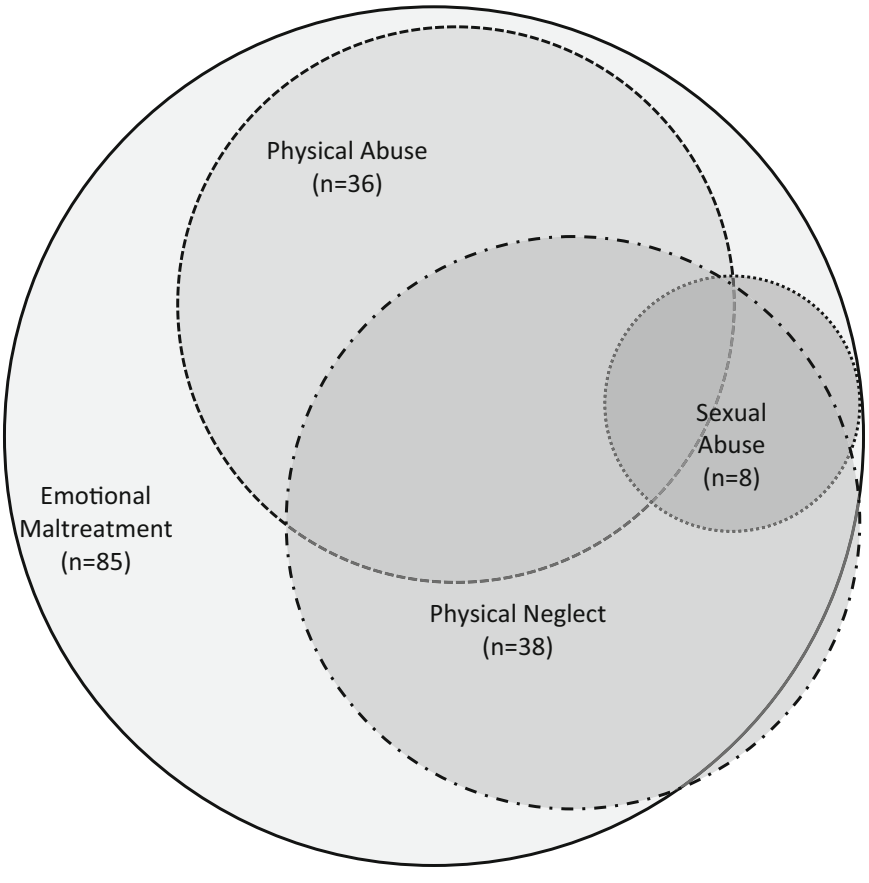

Figure 3 Co-occurrence and overlap of different maltreatment types within the group of maltreated children

stronger decrease in internalizing symptoms over time in the group of maltreated children relative to nonmaltreated children (b_s(group) = −1.50, p = .005). The applicable fit indices showed a good model fit (*RMSEA* = 0.070, $\chi^2(df = 91) = 167.29$, $p < .001$)[3]. To test whether mean level differences between maltreated and nonmaltreated children remained stable across all time-points, despite of the decrease of internalizing symptoms in the maltreatment group, we moved the position of the intercept of the growth curve model to the last time-point. We found that mean level differences between the two groups remained significant at T4 (b_i(group) = 5.708, p = .004). For externalizing symptoms (Model 2b), there was a significant effect of Group on the intercept with markedly higher symptom levels at baseline (T0) in maltreated children as compared to nonmaltreated children (b_i(group) = 13.29, $p < .001$). Group did not have an effect on the linear slope of symptoms, indicating that symptom level change over time did not differ between groups. The applicable fit indices showed a good model fit (*RMSEA* = 0.059, $\chi^2(df = 91) = 146.164$, $p < .001$)[1]. Taken together, maltreated children exhibited markedly increased internalizing and externalizing symptoms at T0 and at all follow-up visits across the 2-year follow-up period (T1–T4) as compared to nonmaltreated children.

We next evaluated predictors of symptom trajectories. Of note, change in maltreatment severity over time was not associated with internalizing and externalizing symptom trajectories. Correlation analyses showed that the latent growth factor of maltreatment was not associated with the latent growth factors of internalizing (Pearson's r=−0.017, p=.878) and externalizing symptoms (r = −.067, p = .542). However, the severity of lifetime maltreatment exposure (Model 1c) predicted internalizing symptoms (b_i(severity) = 0.734, p = .001), but not the slope (b_s(severity) = −0.140, p = .060). Onset age at first maltreatment (Model 1d) had a significant effect on the intercept (b_i(onset) = −0.207, p = .031) with earlier onset predicting higher internalizing symptoms levels, but not on the slope of internalizing symptoms (b_s(onset) = 0.041, p = .221). Severity of lifetime maltreatment exposure (Model 2c) had a significant effect on externalizing symptoms (b_i(severity) = 0.938, $p < .001$) with higher severity predicting higher symptom as well as slope (b_s(severity) = −0.152, p = .047) with children with higher severity showing a slightly stronger decrease over time. Onset age at first maltreatment (Model 2d) had a significant effect on the intercept (b_i(onset) = −0.275, p = .016) with earlier onset predicting higher externalizing symptoms levels, but not on the slope of externalizing symptoms (b_s(onset) = 0.029, p = .378).

Table 3 Description of clinical and developmental outcomes over time in nonmaltreated control children (CC) and maltreated children (MC). For statistical models, see text and Tables 4 and 5

Count (percentage) / mean (*SD*)	T0		T1		T2		T3		T4	
	CC (n = 87)	MC (n = 86)	CC (n = 80)	MC (n = 66)	CC (n = 70)	MC (n = 60)	CC (n = 64)	MC (n = 47)	CC (n = 52)	MC (n = 38)
Any psychiatric diagnosis	18 (20.7%)	49 (57.0%)			10 (14.7%)	36 (60%)			9 (17.6%)	17 (44.7%)
Major depression	0	4 (4.7%)			0	2 (3.3%)			0	2 (5.3%)
Dysthymic disorder	0	3 (3.5%)			0	1 (1.7%)			0	4 (10.5%)
Specific phobia	2 (2.3%)	3 (3.5%)			2 (2.9%)	2 (3.3%)			1 (2.0%)	1 (2.6%)
Social phobia	5 (5.7%)	10 (11.8%)			3 (4.4%)	3 (5.0%)			1 (2.0%)	3 (7.9%)
Generalized anxiety disorder	6 (6.9%)	15 (17.4%)			3 (4.4%)	8 (13.3%)			6 (18.6%)	2 (5.3%)
Separation anxiety disorder	5 (5.7%)	23 (26.7%)			4 (5.9%)	16 (26.7%)			3 (5.9%)	7 (18.4%)
Selective mutism	0	5 (5.8%)			0	2 (3.3%)			1 (2.0%)	1 (2.6%)
ADHD	5 (5.7%)	13 (15.1%)			1 (1.5%)	11 (18.3%)			0	10 (26.3%)
Conduct disorder	2 (2.3%)	14 (16.3%)			0	10 (16.7%)			0	2 (5.3%)
Oppositional defiant disorder	1 (1.1%)	16 (18.6%)			1 (1.5%)	13 (21.7%)			0	7 (18.4%)
Internalizing symptoms	42.86 (9.42)	54.89 (10.90)	42.88 (10.47)	52.42 (10.75)	41.63 (7.82)	50.67 (10.05)	43.03 (8.77)	49.91 (10.74)	43.00 (9.07)	49.27 (9.90)
Externalizing symptoms	41.49 (8.84)	53.58 (13.05)	41.96 (8.95)	53.78 (11.60)	40.19 (8.40)	51.55 (12.72)	41.80 (8.50)	52.53 (11.99)	41.19 (8.57)	52.43 (12.90)
Cognitive development	106.32 (12.22)	90.09 (17.33)			109.14 (13.00)	93.45 (17.40)			113.73 (13.30)	95.50 (16.74)
Verbal development	105.09 (11.96)	90.42 (13.33)			106.19 (9.36)	92.46 (14.24)			107.69 (8.24)	93.37 (15.29)
Motor development	98.31 (13.05)	90.13 (15.95)			99.26 (13.02)	94.30 (15.42)			103.17 (12.45)	88.78 (18.80)
Medical symptoms	24 (27.6)	49 (57)			31 (35.6)	35 (40.7)			18 (20.7)	19 (22,1)
Heart	4 (4.6)	6 (7)			3 (3.4)	3 (3.5)			1 (1.1)	2 (2.3)
Lung	1 (1.1)	7 (8.1)			2 (2.3)	1 (1.2)			1 (1.1)	2 (2.3)
Abdominal	1 (1.1)	0			1 (1.1)	0			0	0
Skeletal	2 (2.3)	3 (3.5)			4 (4.6)	5 (5.8)			0	1 (1.2)
Neurological	9 (10.9)	36 (41.9)			26 (29.9)	33 (38.4)			11 (12.6)	16 (18.6)

The structured interview to assess mental disorders, developmental testing and detailed physical assessment was conducted at T0, T2, T4 only. Information on missing data can be found in the Supporting Information.

Table 4 Results of growth curve analyses on internalizing and externalizing symptoms

	Internalizing symptoms				Externalizing symptoms			
	Model 1a	Model 1b	Model 1c	Model 1d	Model 2a	Model 2b	Model 2c	Model 2d
Parameters								
Intercept *M(i)*	48.51, $p < .001$				47.52, $p < .001$			
Linear Slope *M(s)*	−0.84, $p < .001$				−0.382, $p = .088$			
Intercept Variance $\sigma^2(i)$	108.35, $p < .001$				125.89, $p < .001$			
Slope Variance $\sigma^2(s)$	3.38, $p = .001$				2.81, $p = .004$			
b_i and β_i (group)		11.70, 1.17, $p < .001$ [b]				13.29, 1.18, $p < .001$		
b_s and β_s (group)		−1.50, −0.95, $p = .005$				−0.59, −0.40, $p = .268$		
b_i and β_i (severity)			0.73, 0.45, $p = .001$				0.94, 0.41, $p < .001$	
b_s and β_s (severity)			−0.14, −0.92, $p = .060$				−0.15, −0.70, $p = .047$	
b_i and β_i (onset)				−0.21, −0.29, $p = .031$				−0.28, −0.29, $p = .016$
b_s and β_s (onset)				0.04, 0.74, $p = .221$				0.03, 0.40, $p = .378$
Fit indices								
RMSEA	0.065	0.070	0.155	0.149	0.076	0.059	0.185	0.152
CFI[a]	0.972	-	-	-	0.971	-	-	-
χ^2 *(df)*	24.216 (14), $p = 0.043$	167.29 (91), $p < .001$	286.30 (93), $p < .001$	263.66 (93), $p < .001$	27.88 (14), $p = 0.015$	146.164 (91), $p < .001$	366.62 (93), $p < .001$	278.74 (93), $p < .001$

b = unstandardized parameter estimates. β = standardized parameter estimate. To ease interpretation parameter estimates for binary predictors (Group) have only been partially standardized.

[a]For some models the missing value pattern on the predictor variables prevented us from defining a standard baseline model. For this reason, we do not report CFI for these analyses.

[b]To test whether mean level differences between maltreated and nonmaltreated children remained stable across all time-points, despite of the decrease of internalizing symptoms in the maltreatment group, we moved the position of the intercept of the growth curve model to the last time-point. We found that mean level differences between the two groups remained significant at T4 (b_i(group) = 5.708, $p = .004$).

These models showed a comparatively lower fit: internalizing (severity) – Model 1c: *RMSEA* = 0.155, $\chi^2(df = 93) = 286.30$, $p < .001$; internalizing (onset) – Model 1d: *RMSEA* = 0.149, $\chi^2(df = 91) = 263.66$, $p < .001$; externalizing (severity) – Model 2c: *RMSEA* = 0.185, $\chi^2(df = 93) = 366.62$, $p < .001$; externalizing (onset) – Model 2d: *RMSEA* = 0.152, $\chi^2(df = 93) = 278.74$, $p < .001$[3].

Developmental outcomes

Descriptive data on developmental outcomes over time are depicted in Table 3 and statistical models are presented in Table 5. For a depiction of predicted trajectories, see Figure S2. Growth models for the trajectories of cognitive, verbal, and motor development over time were determined (Models 3–5a). For cognitive development, a linear growth curve model (Model 3a) showed an excellent fit (*RMSEA* = 0.000, *CFI* = 1.00, $\chi^2(df = 3) = 0.888$, $p = .828$). The mean intercept (mean *IQ* level at baseline) was *M(i)* = 98.080 ($p < .001$). The mean of the latent linear slope was slightly positive *M(s)* = 3.374 ($p < .001$). There were significant interindividual differences in the intercept ($\sigma^2(i) = 230.545$, $p < .001$), but not the slope. This indicates that children differed in *IQ* at baseline, but not in change over time. Likewise, for verbal development, a linear growth curve model (Model 4a) showed good fit (*RMSEA* = 0.075, *CFI* = 0.989, $\chi^2(df = 3) = 5.908$, $p = .116$). The mean intercept was *M(i)* = 97.697 ($p < .001$). The average linear slope was slightly positive *M(s)* = 1.590 ($p<.001$). There were significant interindividual differences in both intercept ($\sigma^2(i) = 178.192$, $p < .001$) and slope ($\sigma^2(s) = 8.114$, $p = .049$). This indicates that children differed in the verbal IQ at baseline as well as in their changes over time. For motor development, a linear growth curve model (Model 5a) showed an excellent fit (*RMSEA* = 0.000, *CFI* = 1.000, $\chi^2(df = 3) = 2.345$, $p = .504$). The mean intercept was *M(i)* = 94.175 ($p < .001$). The linear slope was not significant *M(s)* = 1.229 ($p = .085$). There were significant interindividual differences in the intercept ($\sigma^2(i) = 133.558$, $p < .001$), but not the slope, indicating that children differed in their motor developmental status at baseline, but not in change over time.

Next, Group was entered as a predictor in these models (Models 3–5b) as were the covariates. For cognitive development (Model 3b), there was a significant effect of Group on the intercept with a markedly lower cognitive developmental status in maltreated children compared to nonmaltreated children (b_i(group) = −11.586, $p < .001$). Groups did not differ in the slope of cognitive developmental status over time. The model showed an excellent fit (*RMSEA* = 0.003, $\chi^2(df = 28) = 28.054$, $p = .462$)[1]. For verbal development (Model 4b), there was a significant effect of Group on the intercept with markedly lower verbal developmental status in maltreated children relative to nonmaltreated children (b_i(group) = −10.687, $p < .001$). The groups did not differ in the linear slope of verbal developmental status. The model showed a good fit (*RMSEA* = 0.040, $\chi^2(df = 28) = 35.765$, $p = .149$)[3]. For motor development (Model 5b), there was a significant effect of Group on the intercept with markedly lower motor developmental status in maltreated children versus nonmaltreated children (b_i(group) = −7.904, p=.006). The groups did not differ in the linear slope of motor developmental status. The model showed a good fit (*RMSEA* = 0.051, $\chi^2(df = 28) = 40.752$, p=.057)[3]. Taken together, maltreated children exhibited markedly decreased cognitive, verbal and motor developmental status at baseline (T0) and at all follow-up visits across the 2-year follow-up period (T1–T4) as compared to nonmaltreated children.

We next evaluated predictors of trajectories of developmental status. Correlation analyses showed that the latent growth factor of maltreatment was not associated with the latent growth factors of cognitive development (Pearson $r = .021$, $p = .847$) or verbal development (Pearson $r = -.069$, $p = .531$). Because of insufficient variance in the latent slope, no correlations with changes in motor development were computed[4]. There was a significant effect of the severity of lifetime maltreatment exposure (Model 3c) on cognitive developmental status (b_i(severity) = −0.896, $p = .020$) with higher severity predicting lower cognitive developmental status, but no significant effect on the slope (b_s(severity) = −0.302, $p = .130$). Onset age at first maltreatment (Model 3d) did not have a significant effect on the intercept (b_i(onset) = 0.038, $p = .818$) nor on the slope of cognitive development (b_s(onset) = 0.089, $p = .285$). Severity of lifetime maltreatment exposure (Model 4c) predicted lower verbal developmental status (b_i(severity) = −1.003, $p = .001$), but there was no significant effect on the slope (b_s (severity) = −0.282, $p = .108$). Onset age at first maltreatment (Model 4d) did not have a significant effect on the intercept (b_i(onset)=.0.052, p=.695) nor on the slope of verbal development (b_s(onset)= 0.132, p=.069). There was no significant effect of the severity of lifetime maltreatment exposure (Model 5c) on motor developmental status neither on the intercept (b_i(severity) =−0.569, p=.137) nor on the slope (b_s(severity) = −0.304, $p = .256$). Onset age at first maltreatment (Model 5d) did not have a significant effect on the intercept (b_i(onset) = −0.065, $p = .697$) but on the slope of motor development (b_s(onset) = 0.219, $p = .038$), with later onset predicting a slightly stronger increase in motor development over time.

Some of the models within the group of maltreated children showed a comparatively lower fit: cognitive (severity) – Model 3c: *RMSEA* = 0.091, $\chi^2(df = 28) = 48.03$, $p = .011$; cognitive (onset) – Model 3d: *RMSEA* = 0.116, $\chi^2(df = 28) = 60.34$, $p < .001$; verbal (severity) – Model 4c: *RMSEA* = 0.045,

Table 5 Results of growth curve analyses on cognitive, verbal, and motor development

	Cognitive development				Verbal development				Motor development			
	Model 3a	Model 3b	Model 3c	Model 3d	Model 4a	Model 4b	Model 4c	Model 4d	Model 5a	Model 5b	Model 5c	Model 5d
Parameters												
Intercept *M(i)*	98.08, $p < .001$				97.70, $p < .001$				94.18, $p < .001$			
Linear slope *M(s)*	3.37, $p < .001$				1.59, $p < .001$				1.23, $p = .085$			
Intercept Variance $\sigma^2(i)$	230.55, $p < .001$				178.19, $p < .001$				133.558, $p < .001$			
Slope Variance $\sigma^2(s)$	2.27, $p = .713$				8.11, $p = .049$				9.72, $p = .357$			
b_i and β_i (group)		−11.59, −0.85, $p < .001$				−10.69, −0.87, $p < .001$				−7.90, −0.65, $p = .006$		
b_s and β_s (group)		−0.72, −0.48, $p = .591$				0.05, 0.02, $p = .965$				−1.10, −0.28, $p = .541$		
b_i and β_i (severity)			−0.90, −0.27, $p = .020$				−1.00, −0.38, $p = .001$				−0.57, −0.19, $p = .137$	
b_s and β_s (severity)			−0.30, −0.46, $p = .130$				−0.28, −0.35, $p = .108$				−0.30, −0.92, $p = .256$	
b_i and β_i (onset)				0.04, 0.03, $p = .818$				0.05, 0.05, $p = .695$				−0.07, −0.05, $p = .697$
b_s and β_s (onset)				0.09, 0.34, $p = .285$				0.13, 0.40, $p = .068$				0.22, 0.98, $p = .038$
Fit indices												
RMSEA	0.000	0.003	0.091	0.116	0.075	0.040	0.045	0.066	0.000	0.051	0.105	0.109
CFI[a]	1.000	—	—	—	0.989	—	—	—	1.000	—	—	—
χ^2 *(df)*	0.888 (3), $p = .828$	28.05 (28), $p = .462$	48.03 (28), $p = .011$	60.34 (28), $p < .001$	5.908 (3), $p = .116$	35.77 (28), $p = .149$	2.87 (28), $p = .241$	38.57 (28), $p = .088$	2.345 (3), $p = .504$	40.75 (28), $p = .057$	58.34 (30), $p = .001$	60.52 (30), $p = .001$

b = unstandardized parameter estimates. β = standardized parameter estimate. To ease interpretation parameter estimates for binary predictors (Group) have only been partially standardized.

[a]For some models the missing value pattern on the predictor variables prevented us from defining a standard baseline model. For this reason, we do not report CFI for these analyses.

$\chi^2(df = 28) = 2.87, p = .241$; verbal (onset) – Model 4d: $RMSEA = 0.066, \chi^2(df = 28) = 38.57, p = .088$); motor (severity) – Model 5c: $RMSEA = 0.105$, $\chi^2(df = 30) = 58.34$, $p = .001$; motor (onset) – Model 5d: $RMSEA = 0.109$, $\chi^2(df = 30) = 60.52$, $p = .001$[3].

Physical health outcomes

Descriptive data on physical health outcomes over time are depicted in Table 3. A generalized linear mixed model with Poisson distribution showed significantly higher numbers of medical symptoms and abnormalities at baseline ($b = 1.001$, standardized $\beta = 1.001$, $p < .001$) and over time in the maltreatment group with no significant effects in the interaction of group and time (b(group*time) = −0.136, $\beta = -0.136$, $p = .142$). Generalized linear mixed models within the maltreatment group did not reveal significant effects of severity of lifetime maltreatment exposure or onset age of first maltreatment on medical symptoms (b(severity) = 0.049, $\beta = -0.220$, $p = .109$; b(onset) = −0.012, $\beta = -0.125$, $p = .355$).

Information on missing data is included in Table S3.

Discussion

We here examined the immediate effects of maltreatment exposure within 6 months on longitudinal mental health, developmental status, and physical health trajectories, assessed over 2 years, in very young children aged 3–5 years. We report pronounced, immediate and stable, adverse effects of maltreatment exposure on outcomes across domains. Specifically, children who had been maltreated within 6 months exhibited markedly greater numbers of internalizing and externalizing symptoms as well as more syndromal clinician-diagnosed psychiatric disorders when compared to control children. In addition, these maltreated children exhibited pronounced developmental deficits, with lower verbal, motor and cognitive IQ, as well as increased numbers of medical symptoms as assessed in a standardized medical examination. These markedly adverse impacts of maltreatment on mental and physical health and developmental status were already present at study entry, in children as young as 3–5 years, and the effects remained remarkably stable over the course of the 2-year study. Hence, a detailed clinician-administered multi-domain assessment revealed immediate and stable impairments after maltreatment, already observable early in life. These strong effects were present despite of a relative low-to-moderate severity of maltreatment, suggesting that the well-known effects of maltreatment on mental and medical disease vulnerability across the lifespan are already embedded early in life.

The severity of mental health symptoms and developmental deficits demonstrated individual variability over time in the group of maltreated children. Importantly, using growth curve models, we were able to test whether changes over time in the severity of symptoms and developmental deficits associate with maltreatment severity slopes or whether the course of symptoms and deficits associates as a function of lifetime severity of maltreatment exposure or onset age. We found that lifetime severity and/or onset age of earliest maltreatment exposure predicted internalizing and externalizing symptom levels and developmental status over time. Trajectories of maltreatment severity within the maltreatment group were relatively homogeneous and were not related to changes in symptom levels or developmental deficits over time. These results may plausibly suggest that there is an early developmental biological embedding event, resulting in clinical and developmental phenotypic outcomes and that, once embedded, there is no evidence that these phenotypic changes are related to changes in the severity of maltreatment exposure. This result might underscore the notion of an early sensitive period for the biological embedding of maltreatment and the developmental programming of subsequent disease manifestation (Heim, Entringer, & Buss, 2019). That said, it will be critical to assess whether – and by what means – these processes are reversible.

Because maltreatment exposure exerts cross-domain effects on mental health, neurodevelopment, and physiological-somatic systems, it is conceivable that a core effect of maltreatment consists of a fundamental change at the level of neural networks implicated on the regulation of stress and emotion, involving cortical and limbic circuits, as well as impact on downstream regulatory systems, including the stress hormone and immune systems. Dysregulation of stress hormones and immune mediators may, in turn, signal back into the brain and promote further change in neural structure and function. Mechanistically, such effects are likely mediated by molecular processes that regulate gene expression, including epigenetic changes (Czamara et al., 2021). While there is little knowledge about such biological embedding processes in the immediate aftermath of maltreatment exposure as well as the sequence of biological embedding events over time, leading to stable clinical phenotypes, such knowledge will be critical to develop targeted interventions that reverse, mitigate or counter-regulate these processes in order to promote resilience and will aid in defining time windows of susceptibility for specific interventions (Entringer et al., 2021; Heim & Binder, 2012; Heim et al., 2019).

While considerable evidence suggests that the link between maltreatment and adverse health outcomes may be explained by biological embedding processes, this is only one of many possible mechanisms. There are manifold explanations for the impact of maltreatment on adverse health outcomes, including theories rooted in cognitive psychology, learning theory,

attachment theory, or evolutionary theory. For example, cognitive factors, such as negative inferential styles, low self-esteem, and high impulsivity may contribute to symptoms after maltreatment (Li, Luyten, & Midgley, 2020; Weissman et al., 2019). Altered learning processes, such as potentiated fear conditioning or lack of extinction may contribute to symptoms after maltreatment (McLaughlin et al., 2016). Insecure attachment and failure of the caretaker to regulate a child's emotions can contribute to symptoms (Spruit et al., 2020). We content that these factors are not mutually exclusive and arguably have neurobiological correlates. One more recent theoretical model that has gained considerable attention posits that early adversity changes the pace of brain and physiological development, which is advantageous for survival and reproduction in an early threatening environment. It has been suggested that accelerated maturation of emotion circuits and enhancement of detection of threat may occur at the cost of more general cognitive abilities and long-term health (Callaghan & Tottenham, 2916; Ellis & Giudice, 2019; Frankenhuis, Young, & Ellis, 2020; Roubinov, Meaney, & Boyce, 2021). Longitudinal studies starting in the immediate aftermath of exposure are needed to test, refine, and integrate such theories and derive strategies for augmenting resilience and mitigating adverse outcomes.

Our current clinical findings on the adverse impacts of maltreatment on multiple outcome domains are well in line with previous research in adult samples as well as in cross-sectional child samples (Felitti et al., 1998; Naughton et al., 2013; Norman et al., 2012). A limited number of studies report perpetuation of externalizing and internalizing symptoms into adolescence after maltreatment exposure during early childhood and preschool age (Éthier et al., 2004; Lansford et al., 2002; Villodas et al., 2015), and our findings are concordant with these reports. Of note, we controlled for several potential confounders that could impact on the observed effects, including SES, age, sex, other critical life events, parental or caretaker depression, and implementation of medical or psychosocial interventions. As noted above, lifetime severity of maltreatment and onset age were predictors of symptom severity over time, whereas symptoms slopes did not correlate with maltreatment severity slopes. This finding contrasts with previous reports suggesting that maltreatment has no persistent effects in the absence of continued abuse (Éthier et al., 2004; Sternberg et al., 2006). As noted above, our findings would support an early developmental programming effect, where a vulnerability for disease is biologically embedded and exerts stable effects over time. Further longitudinal studies, integrating data on biological pathways, are needed to scrutinize this hypothesis.

Of note, while maltreated children had higher levels of internalizing symptoms compared to nonmaltreated children at all time-points, the severity of internalizing symptoms slightly decreased over time in the total sample, and more so in the group of maltreated children as compared to nonmaltreated children. Several factors may account for this decrease, including larger attrition of cases with severe symptoms or decreases of maltreatment exposure over time. We found no evidence to difference in baseline symptom severity between children who completed all time-points of the study and those who did not (total sample: $t(170) = 1.122$, $p = .263$; maltreatment group: $t(83) = 0.247$, $p = .806$). Further, we did not find an association between latent slope factors of maltreatments severity and symptom levels. We speculate that participation in the study may have had an intervention effect, which would underscore the need to devise targeted interventions and provides incidental support that targeted early interventions could be effective.

In terms of developmental deficits in relation to maltreatment exposure, our findings are in line with cross-sectional studies in adults and children, suggesting that maltreatment is associated with cognitive impairments (Cowell, Cicchetti, Rogosch, & Toth, 2015; Crozier & Barth, 2005; Lupien, McEwen, Gunnar, & Heim, 2009). Such developmental deficits may be at least in part attributable to neurotoxic effects of stress hormones and immune mediators on neural plasticity, synaptogenesis, and neurogenesis (Lupien et al., 2009). The stable manifestation of these deficits in early childhood, as shown in our study, may have relevant impact on emotional and social competence (Enlow et al., 2013), school performance and subsequent academic and socioeconomic outcomes (Crozier & Barth, 2005; Lansford et al., 2002). Therefore, early targeted interventions are urgently needed.

In terms of somatic health, the current results are also in line with studies in adults suggesting that early life adversity potently induces increased risk for a wide range of medical diseases and early mortality (Brown et al., 2009; Felitti et al., 1998; Wegman & Stetler, 2009). A number of studies report greater numbers of acute and chronic somatic health issues in maltreated children (McKelvey et al., 2017). Substantial evidence further associates psychosocial stress with higher incidence of immune disorders and other chronic disease among children (Booster, Oland, & Bender, 2016; Johnson, Riley, Granger, & Riis, 2013; Wilson & Sato, 2014). As noted above, it can be assumes that fundamental change in the brain's regulatory adaptation systems, including the neuroendocrine and immune systems, as well as impact of both on metabolic systems, promotes somatic disease vulnerability in these children (Heim et al., 2019; Lupien et al., 2009). An additional explanation would encompass the hypothesis that parents of maltreated children are less sensitive to somatic health problems resulting in more frequent medical

neglect and lower adherence to treatments and thus an adverse somatic health status.

Our study has several important limitations: The sample size is small, highly selective, and not representative of the general population, limiting generalizability of results. In addition, there was considerable attrition that may have affected trajectories over time. Further limitations of the study include a potential participation bias due to voluntary participation as well as a systematic difference between cases and controls in terms of socioeconomic status, which was controlled for in all analyses. Moreover, details of the maltreatment experience were assessed based on a caregiver interview, as we could not access files from child welfare services, which is a limitation. Despite of this limitation, Sierau et al. (2016) demonstrated that interviews with caregivers provide valid information on specific maltreatment features. Clinicians who assessed outcomes were not blinded to maltreatment status, which is a limitation. There were a number of differences between groups in terms of demographics, which are in part linked to maltreatment, and a small percentage of maltreated children received interventions, which may have affected results. On the other hand, important strengths of our study include a large degree of corroborated cases identified in the immediate aftermath of exposure and enrolled in the study within 6 months with follow-up in 6-month intervals over 2 years. A further strength of our study is our detailed assessment procedure in which all assessments were administered by trained clinicians during a clinic visit and all children underwent a full medical evaluation by a physician. An additional strength is the recruitment of a control group with no severe or traumatic life stressors from the community as well as control of a multitude of potentially confounding variables in all longitudinal growth curve models, including controlling for socioeconomic status differences.

In conclusion, we here demonstrate that maltreatment has a profound and stable impact on mental health, developmental status, and somatic health, and these effects occur already in the immediate aftermath and are persistent over the course of the 2-year follow-up. Symptoms and developmental deficits are predicted by lifetime severity and onset age of maltreatment, supporting a biological embedding and developmental programming of disease concept. Our findings underscore the urgent need for early screening for all forms of child maltreatment as well as in-depth diagnostic and therapeutic care in children at risk in order to prevent adverse health trajectories. Further investigation of vulnerability versus resilience factors as well as scrutiny of the biological processes contributing to these outcomes are needed in order to enable targeted and personalized interventions for maltreated children. A precise understanding of the biological embedding mechanisms will enable the development of novel interventions to reverse or prevent negative outcomes as well as the development of biological markers that identify children in need of specific interventions, leading towards precision medicine in pediatrics.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Table S1. Detailed descriptive information on maltreatment types.
Table S2. Correlation of factor scores (comparison parsimonious model vs. complex model).
Table S3. Missing data in main outcomes.
Figure S1. Trajectory of maltreatment experience across the five visits in the study.
Figure S2. Predicted trajectories from latent growth curve analyses.

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Key points

- Child maltreatment is a risk factor for mental and physical disorders across the lifespan.
- We here report stable trajectories of marked mental and physical–medical symptoms as well as developmental impairments in the immediate aftermath of exposure to maltreatment and over 2 years in very young children.
- Marked symptoms and impairments can be observed even after mild forms of maltreatment at all time points.
- Clinical trajectories are best predicted by onset age and lifetime severity.
- This observation supports an early biological embedding model that may provide direct mechanism-driven targets for intervention.

Notes

[1]Recruitment groups did not differ in terms of maltreatment severity, age, sex, socioeconomic status, life events, maternal depression, symptoms, disorders, physical health or verbal and motor development. Groups differed in cognitive development (lower IQ in corroborated vs. noncorroborated children (t(84)=2.488, p=.015).
[2]The sample included one family with three siblings and 11 families with two siblings. We repeated all analyses by randomly including one child per family. The analyses indicated robustness of main findings.
[3]The missing value pattern on the predictor variables prevented us from defining a standard baseline model. For this reason, we do not report CFI for these analyses.
[4]The ML estimate of the slope variance in motor development was negative and thus manually constrained to zero.

References

Achenbach, T.M., & Rescorla, L.A. (2000). *Manual for the ASEBA preschool forms and profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, and Families.

Achenbach, T.M., & Rescorla, L.A. (2001). *Manual for the ASEBA school-age forms and profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, and Families.

Barnett, D., Manly, J.T., & Cicchetti, D. (1993). Defining child maltreatment: The interface between policy and research. In D. Cicchetti & S.L. Toth (Eds.), *Child abuse, child development, and social policy* (pp. 7–73). Norwood, NJ: Ablex.

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2014). Fitting linear mixed-effects models using lme4. *Journal of Statistical Software*, arXiv:1406(1).

Bentler, P.M. (1990). Comparative fit indexes in structural models. *Psychological Bulletin*, *107*, 238–246.

Booster, G.D., Oland, A.A., & Bender, B.G. (2016). Psychosocial factors in severe pediatric asthma. *Immunology and Allergy Clinics of North America*, *36*, 449–460.

Boyle, M.H., & Pickles, A. (1997). Maternal depressive symptoms and ratings of emotional disorder symptoms in children and adolescents. *Journal of Child Psychology and Psychiatry*, *38*, 981–992.

Bradley, R.H., & Corwyn, R.F. (2002). Socioeconomic status and child development. *Annual Review of Psychology*, *53*, 371–399.

Briggs-Gowan, M.J., Carter, A.S., & Ford, J.D. (2012). Parsing the effects violence exposure in early childhood: Modeling developmental pathways. *Journal of Pediatric Psychology*, *37*, 11–22.

Brown, D.W., Anda, R.F., Tiemeier, H., Felitti, V.J., Edwards, V., Croft, J.B., & Giles, W.H. (2009). Adverse childhood experiences and the risk of premature mortality. *American Journal of Preventive Medicine*, *37*, 389–396.

Browne, M.W., & Cudeck, R. (1993). Alternative ways of assessing model fit. In K.A. Bollen & J.S. Long (Eds.), *Testing structural equation models* (Vol. *154*, pp. 136–162). Newbury Park, CA: Sage Focus Editions.

Callaghan, B.L., & Tottenham, N. (2016). The stress acceleration hypothesis: Effects of early-life adversity on emotion circuits and behavior. *Current Opinion in Behavioral Sciences*, *7*, 76–81.

Cicchetti, D., Toth, S., & Manly, J. (2003). *Maternal maltreatment classification interview*. Unpublished manuscript, Mt. Hope Family Center, Rochester, NY.

Cowell, R.A., Cicchetti, D., Rogosch, F.A., & Toth, S.L. (2015). Childhood maltreatment and its effect on neurocognitive functioning: Timing and chronicity matter. *Development and Psychopathology*, *27*, 521–533.

Crozier, J.C., & Barth, R.P. (2005). Cognitive and academic functioning in maltreated children. *Children & Schools*, *27*, 197–206.

Czamara, D., Tissink, E., Tuhkanen, J., Martins, J., Awaloff, Y., Drake, A.J., … & Binder, E.B. (2021). Combined effects of genotype and childhood adversity shape variability of DNA methylation across age. *Translational Psychiatry*, *11*, 88.

Danese, A., Caspi, A., Williams, B., Ambler, A., Sugden, K., Mika, J., … & Arseneault, L. (2011). Biological embedding of stress through inflammation processes in childhood. *Molecular Psychiatry*, *16*, 244–246.

Egger, H.L., & Angold, A. (2004). The Preschool Age Psychiatric Assessment (PAPA): A structured parent interview for diagnosing psychiatric disorders in preschool children. In R. Delcarmen-Wiggins & A. Carter (Eds.), *Handbook of infant, toddler, and preschool mental health assessment* (pp. 223–243). New York: Oxford University Press.

Ellis, B.J., & del Giudice, M. (2019). Developmental adaptation to stress: An evolutionary perspective. *Annual Review of Psychology*, *70*, 111–139.

Enlow, M.B., Blood, E., & Egeland, B. (2013). Sociodemographic risk, developmental competence, and PTSD symptoms in young children exposed to interpersonal trauma in early life. *Journal of Traumatic Stress*, *26*, 686–694.

Entringer, S., De Punder, K., Overfeld, J., Karaboycheva, G., Dittrich, K., Buss, C., … & Heim, C. (2021). Immediate and longitudinal effects of maltreatment on systemic inflammation in young children. *Development and Psychopathology*, *32*, 1725–1731.

Esser, G., Hänsch-Oelgart, S., & Schmitz, J. (2018). Deutsche Schulalter-Formen der child behavior checklist von Thomas

M. Achenbach. Elternfragebogen über das Verhalten von Kindern und Jugendlichen (CBCL/6-18R), Lehrerfragebogen über das Verhalten von Kindern und Jugendlichen (TRF/6-18R), Fragebogen für Jugendliche (YSR/11-18R). *Psychologische Rundschau*, *69*, 144–146.

Éthier, L.S., Lemelin, J.P., & Lacharité, C. (2004). A longitudinal study of the effects of chronic maltreatment on children's behavioral and emotional problems. *Child Abuse and Neglect*, *28*, 1265–1278.

Felitti, V.J., Anda, R.F., Nordenberg, D., Williamson, D.F., Spitz, A.M., Edwards, V., … & Marks, J.S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*, *14*, 245–258.

Fisher, H.L., Caspi, A., Moffitt, T.E., Wertz, J., Gray, R., Newbury, J., … & Arseneault, L. (2015). Measuring adolescents' exposure to victimization: The Environmental Risk (E-Risk) Longitudinal Twin Study. *Development and Psychopathology*, *27*, 1399–1416.

Frankenhuis, W.E., Young, E.S., & Ellis, B.J. (2020). The hidden talents approach: Theoretical and methodological challenges. *Trends in Cognitive Sciences*, *24*, 569–581.

Hautzinger, M., Keller, F., & Kühner, C. (2009). *BDI-II. Beck-Depressions-Inventar. Revision. 2, Auflage*. Frankfurt, Germany: Pearson Assessment.

Heim, C., & Binder, E.B. (2012). Current research trends in early life stress and depression: Review of human studies on sensitive periods, gene-environment interactions, and epigenetics. *Experimental Neurology*, *233*, 102–111.

Heim, C.M., Entringer, S., & Buss, C. (2019). Translating basic research knowledge on the biological embedding of early-life stress into novel approaches for the developmental programming of lifelong health. *Psychoneuroendocrinology*, *105*, 123–137.

Henderson, S., Sugden, D., Barnett, A., Petermann, F., Bös, K., & Kastner, J. (2007). *Movement assessment battery for children–Second edition (Movement ABC-2)–Deutschsprachige Adaptation*. London: Harcourt Assessment.

Hunt, T.K.A., Slack, K.S., & Berger, L.M. (2017). Adverse childhood experiences and behavioral problems in middle childhood. *Child Abuse and Neglect*, *67*, 391–402.

Johnson, S.B., Riley, A.W., Granger, D.A., & Riis, J. (2013). The science of early life toxic stress for pediatric practice and advocacy. *Pediatrics*, *131*, 319–327.

King, J.A., Mandansky, D., King, S., Fletcher, K.E., & Brewer, J. (2001). Early sexual abuse and low cortisol. *Psychiatry and Clinical Neurosciences*, *55*, 71–74.

Kühner, C., Bürger, C., Keller, F., & Hautzinger, M. (2007). Reliabilität und validität des revidierten beck-depressionsinventars (BDI-II). *Der Nervenarzt*, *78*, 651–656.

Lampert, T., & Kroll, L.E. (2006). Messung des sozioökonomischen Status in sozialepidemiologischen Studien. In M. Richter & K. Hurrelmann (Eds.), *Gesundheitliche Ungleichheit*. VS Verlag für Sozialwissenschaften.

Lange, M., Kamtsiuris, P., Lange, C., Schaffrath, R.A., Stolzenberg, H., & Lampert, T. (2007). Messung soziodemographischer Merkmale im Kinder- und Jugendgesundheitssurvey (KiGGS) und ihre Bedeutung am Beispiel der Einschätzung des allgemeinen Gesundheitszustands. *Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz*, *50*, 578–589.

Lansford, J.E., Dodge, K.A., Pettit, G.S., Bates, J.E., Crozier, J., & Kaplow, J. (2002). A 12-year prospective study of the long-term effects of early child physical maltreatment on psychological, behavioral, and academic problems in adolescence. *Archives of Pediatrics & Adolescent Medicine*, *156*, 824–830.

Li, E.T., Luyten, P., & Midgley, N. (2020). Psychological mediators of the association between childhood emotional abuse and depression: A systematic review. *Frontiers in Psychiatry*, *11*, 559213.

Lim, L., Radua, J., & Rubia, K. (2014). Gray matter abnormalities in childhood maltreatment: A voxel-wise meta-analysis. *American Journal of Psychiatry*, *171*, 854–863.

Lupien, S.J., McEwen, B.S., Gunnar, M.R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, *10*, 434–445.

McKelvey, L.M., Conners Edge, N.A., Fitzgerald, S., Kraleti, S., & Whiteside-Mansell, L. (2017). Adverse childhood experiences: Screening and health in children from birth to age 5. *Families, Systems & Health*, *35*, 420–429.

McLaughlin, K.A., Sheridan, M.A., Gold, A.L., Duys, A., Lambert, H.K., Peverill, M., … & Pine, D.S. (2016). Maltreatment exposure, brain structure, and fear conditioning in children and adolescents. *Neuropsychopharmacology*, *41*, 1956–1964.

Naughton, A.M., Maguire, S.A., Mann, M.K., Lumb, R.C., Tempest, V., Gracias, S., & Kemp, A.M. (2013). Emotional, behavioral, and developmental features indicative of neglect or emotional abuse in preschool children: A systematic review. *JAMA Pediatrics*, *167*, 769–775.

Norman, R.E., Byambaa, M., De, R., Butchart, A., Scott, J., & Vos, T. (2012). The long-term health consequences of child physical abuse, emotional abuse, and neglect: A systematic review and meta-analysis. *PLoS Med*, *9*, e1001349.

Plück, J., Beiling, M., Hautmann, C., Kuschel, A., Heinrichs, N., Schmeck, K., & Döpfner, M. (2013). Die Erfassung von Verhaltensauffälligkeiten im Vorschulalter mit dem Elternfragebogen für Klein- und Vorschulkinder (CBCL/1 ½-5). *Diagnostica*, *59*, 155–166.

Reiss, F. (2013). Socioeconomic inequalities and mental health problems in children and adolescents: A systematic review. *Social Science and Medicine*, *90*, 24–31.

Rosseel, Y. (2012). Lavaan: An R package for structural equation modeling and more. Version 0.5–12 (BETA). *Journal of Statistical Software*, *48*, 1–36.

Roubinov, D., Meaney, M.J., & Boyce, W.T. (2021). Change of pace: How developmental tempo varies to accommodate failed provision of early needs. *Neuroscience and Biobehavioral Reviews*, *131*, 120–134.

Saveanu, R.V., & Nemeroff, C.B. (2012). Etiology of depression: Genetic and environmental factors. *Psychiatric Clinics of North America*, *35*, 51–71.

Sierau, S., Brand, T., Manly, J.T., Schlesier-Michel, A., Klein, A.M., Andreas, A., … & White, L.O. (2016). A multisource approach to assessing child maltreatment from records, caregivers, and children. *Child Maltreatment*, *22*, 45–57.

Silver, E., Arseneault, L., Langley, J., Caspi, A., & Moffitt, T.E. (2005). Mental disorder and violent victimization in a total birth cohort. *American Journal of Public Health*, *95*, 2015–2021.

Slopen, N., Loucks, E.B., Appleton, A.A., Kawachi, I., Kubzansky, L.D., Non, A.L., … & Gilman, S.E. (2015). Early origins of inflammation: An examination of prenatal and childhood social adversity in a prospective cohort study. *Psychoneuroendocrinology*, *51*, 403–413.

Spruit, A., Goos, L., Weenink, N., Rodenburg, R., Niemeyer, H., Stams, G.J., & Colonnesi, C. (2020). The relation between attachment and depression in children and adolescents: A multilevel meta-analysis. *Clinical Child and Family Psychology Review*, *23*, 54–69.

Sternberg, K.J., Lamb, M.E., Guterman, E., & Abbott, C.B. (2006). Effects of early and later family violence on children's behavior problems and depression: A longitudinal, multiinformant perspective. *Child Abuse and Neglect*, *30*, 283–306.

Stoltenborgh, M., Bakermans-Kranenburg, M.J., Alink, L.L.R., & van IJzendoorn, M.H. (2015). The prevalence of child maltreatment across the globe: Review of a series of meta-analyses. *Child Abuse Review*, *24*, 37–50.

Tellegen, P.J., Snijders, J.T., Wijnberg-Williams, B.J., & Winkel, M. (1996). *Snijders-Oomen non-verbaler intelligenztest: SON-R 2 1/2-7; Anleitung zur testdurchführung und interpretation*. Swets Test Services.

Vachon, D.D., Krueger, R.F., Rogosch, F.A., & Cicchetti, D. (2015). Assessment of the harmful psychiatric and behavioral effects of different forms of child maltreatment. *JAMA Psychiatry*, *72*, 1135–1142.

Villodas, M.T., Litrownik, A.J., Thompson, R., Jones, D., Roesch, S.C., Hussey, J.M., … & Dubowitz, H. (2015). Developmental transitions in presentations of externalizing problems among boys and girls at risk for child maltreatment. *Development and Psychopathology*, *27*, 205–219.

Wechsler, D. (2012). *Wechsler preschool and primary scale of intelligence- fourth edition (WPPSI-IV)*. San Antonio, TX: Psychological Corporation.

Wegman, H.L., & Stetler, C. (2009). A meta-analytic review of the effects of childhood abuse on medical outcomes in adulthood. *Psychosomatic Medicine*, *71*, 805–812.

Weiss, M.J., & Wagner, S.H. (1998). What explains the negative consequences of adverse childhood experiences on adult health? Insights from cognitive and neuroscience research. *American Journal of Preventive Medicine*, *14*, 356–360.

Weissman, D.G., Bitran, D., Miller, A.B., Schaefer, J.D., Sheridan, M.A., & McLaughlin, K.A. (2019). Difficulties with emotion regulation as a transdiagnostic mechanism linking child maltreatment with the emergence of psychopathology. *Development and Psychopathology*, *31*, 899–915.

White, L.O., Klein, A.M., Kirschbaum, C., Kurz-Adam, M., Uhr, M., Müller-Myhsok, B., … & von Klitzing, K. (2015). Analyzing pathways from childhood maltreatment to internalizing symptoms and disorders in children and adolescents (AMIS): A study protocol. *BMC Psychiatry*, *15*, 126.

Wilson, S.M., & Sato, A.F. (2014). Stress and paediatric obesity: What we know and where to go. *Stress Health*, *30*, 91–102.

Winkler, J., & Stolzenberg, H. (1999). Social class index in the Federal Health Survey. *Gesundheitswesen*, *61*, S178–183.

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