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How does childhood maltreatment influence ensuing cognitive functioning among people with the exposure of childhood maltreatment? A systematic review of prospective cohort studies

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Abstract

Background

Childhood maltreatment is closely related to normal cognitive development and ensuing adverse mental health outcomes and cognitive dysfunction. Our current comprehensive systematic review examines the relationship between childhood maltreatment and cognitive functioning focusing only on prospective studies, which allow us to draw inferences about the temporal relationships among the constructs and make causal inferences.

Methods

The databases, EMBASE, HealthStar, PsychoInfo, Medline, and Cochrane Library, were searched using a systematic methodology to identify prospective studies published up to December, 2017 to explore the relationship between childhood maltreatment and cognitive functioning. Quality assessment of each study was rated using Newcastle-Ottawa-Scale (NOS).

Results

10 articles with 11 studies were included evaluating cognitive development, memory, academic achievement, literacy/verbal comprehension, intelligence, executive function, processing speed, perceptional reasoning, and non-verbal reasoning among children exposed to abuse, neglect or domestic violence either individually or combined. Intelligence and executive function were the most frequently reported cognitive impairments. The findings of this review collectively indicated that nine domains of the cognitive functioning impairments were significantly related to multiple forms of maltreatment and that significance remained in multivariable analyses after controlling for potential confounders.

Limitations

A high degree of heterogeneity of various domains of cognitive functioning and different measurements among selected studies precluded the use of meta-analysis.

Conclusions

Childhood maltreatment is considered as one of the most consistent factors related to later life cognitive dysfunction. The study outcomes provide direction for future research on children who have experienced child abuse and have implications for the delivery of health and mental health services to develop clinical practice and intervention for maltreated children.

Keywords: childhood abuse; cognitive functioning; intelligence; prospective studies; systematic review

1. Introduction

1.1 Childhood maltreatment

Childhood maltreatment, including physical abuse, sexual abuse, psychological abuse and neglect, has a wide range of negative consequences on physical and mental health (Corso et al., 2008; Draper et al., 2008; Gould et al., 2012). WHO estimates that 1 in 5 women and 1 in 13 men worldwide have been sexually abused during childhood, and around 25% of adults having being exposed to physical abuse in their early life (WHO, 2014). Maltreatment in the early life is a major threat to the optimal development and functioning of the human being. As a complex stressor, it disrupts a number of important cognitive functioning, such as threat processing, reward processing, emotion regulation and executive function (McCrory et al., 2017). Both retrospective and prospective studies have consistently found that early life exposure to maltreatment: 1) alters the neural reactivity of the threat system, even in resilient children and adolescents who are not presenting with psychopathology, and the degree of reactivity appears to be associated with the severity of childhood adversity (Mueller et al., 2010); 2) reduces activity in subcortical reward-related areas, such as the striatum, which is linked to neuroanatomical and neurochemical brain reward systems, and triggers the onset of psychopathology (Forbes and Dahl, 2012; Ubl et al., 2015b, 2015a); and, 3) indicates functional alteration in brain regions and networks associated with emotional regulation and executive function attributes that are closely connected with the risk of psychopathology (Heleniak et al., 2016; McLaughlin et al., 2015; Snyder et al., 2015). It is estimated that over one-half of depression and anxiety cases are potentially attributable to self-reported childhood maltreatment worldwide (Li et al., 2016).

1.2 Relationship between childhood maltreatment and cognitive impairment

Maltreatment in early life alters a range of neurocognitive functioning, especially daily functioning (i.e. processing and psychomotor speed, attention, executive function, memory, and learning, etc.), which may implant susceptibility to later mental health problems (McCrory et al., 2017). The enduring effect of maltreatment on cognitive impairments has been investigated across the life span (De Bellis, 2005). Childhood maltreatment can alter both functional and structural brain maturation and organizational processes, most notably in the hippocampus (De Bellis et al., 2013; Juster et al., 2010; Lupien et al., 2009). Small hippocampal volume has been found in people with histories of childhood maltreatment and cognitive impairments (Hart and Rubia, 2012; Teicher et al., 2012). It is plausible that people with early life adversities are at a higher risk of psychopathology with small hippocampal volume acting as a preexisting risk factor (Gilbertson et al., 2002; Heim and Nemeroff, 2009; Krystal and Neumeister, 2009). Additionally, studies have also consistently found that childhood maltreatment predicts poorer executive function, with inconsistent findings on the mediating or moderating role of psychopathology in this relationship (Nikulina and Widom, 2013; Yanos et al., 2010; Young and Widom, 2014).

1.3 Mediating and moderating factors in the relationship between childhood maltreatment and cognitive impairment

The role of psychopathology has always been an area of interest in the research on the relationship between childhood maltreatment and cognitive impairments (Masson et al., 2015). Certain psychiatric disorders (i.e. depression, anxiety, and schizophrenia) are closely related to a wide range of cognitive impairments, such as cognitive deficits in executive function, memory, and attention (Castaneda et al., 2008; Rock et al., 2014; J. Schaefer et al., 2013; T. L. Schaefer et

al., 2013). Studies have also suggested childhood maltreatment predicts a higher risk of future psychopathology, and different types of maltreatment have differential influences on individual psychiatric disorders (Li et al., 2016). Cognitive deficits are common to people with the history of maltreatment and those suffering from psychopathology. Noteworthy, the small group of people, with the severe childhood maltreatment who never go on to develop psychiatric or behavioral problems. It has been reported that 48.1% of abused or neglected children did not meet criteria for psychiatric disorders or internalizing behavior problems including depression, dysthymia, generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), and antisocial personality disorder (ASPD). While the figure turned to 38.2% for substance abuse (McGloin and Widom, 2001). A comprehensive review of 45 empirical studies on the impact of sexual abuse on children reported that about 20% to 50% of the sexually abused children will not have symptoms of psychopathology associated with the maltreatment (Kendall-Tackett et al., 1993). Research on resilience and protective factors against psychopathology among people with early adversity has uncovered multilevel dynamic processes of child developmental outcomes in abused /neglected as well as non-abused children (Alink et al., 2012; Cicchetti and Rogosch, 2012). Epigenetic marks, especially DNA methylation, have recently been used to explain the mechanism by which early life environment (maltreatment) impacts later health (Mitchell et al., 2016). Interactions between susceptible genes and psychosocial environmental factors also play a role in the relationship between early life adversity and later health outcomes. These studies raise the intriguing question of how these factors lead to the alterations of cognitive functioning.

Studies have found that the exposure to maltreatment in early life increases the risk of later on psychopathology (Li et al., 2016; Rehan et al., 2017). Psychopathology has been associated with neurocognitive deficits (Cowell et al., 2015), and early life maltreatment significantly associates

with ensuing abnormal cognitive functioning (McCrory et al., 2017). There have been a lot of discussions in the literature about the underlying mechanisms of relationships among childhood maltreatment, ensuing psychopathology, and alternations in cognitive functioning. Two not mutually inclusive hypotheses have been mooted: 1) cognitive impairments may be directly caused by the exposure of childhood maltreatment, independent of secondary comorbid psychopathology; 2) early life adversity may increase the risk of psychopathology, which then triggers changes in cognitive functioning.

There is an urgent need to have a clear examination on the relationship between childhood maltreatment and ensuing cognitive functioning. While two systematic reviews have been published on this general topic (Irigaray et al., 2013; Kavanaugh et al., 2017), each has its own limitations in terms of providing robust evidence which renders them being incomplete in their review of the literature. The study by Kavanaugh et al. (2017) only searched two databases (PubMed and PsycINFO) and the literature up to 2015, and included retrospective study designs which limit the inferences of the temporal order between maltreatment and cognitive functioning. Such studies are more prone to recall bias as the assessment of maltreatment. Another study (Irigaray et al., 2013) only selected articles published between 1995 and 2011 and included a wide range of study designs, including cross-sectional studies, and randomized clinical trials. Given that many more studies have been published in the last five years on child maltreatment and many others have identified multiple factors in the relationship between child maltreatment and cognitive functioning, such as, epigenetic marks, interplay between gene and environment, comparisons between resilient and susceptible survivors of child maltreatment. It is critical to conduct a systematic review update or understanding of the relationship between childhood maltreatment and cognitive functioning.

This systematic review aims to summarize the literature from prospective cohort studies of childhood maltreatment and cognitive functioning, and to explore the moderating and mediating role of psychiatric disorders in this relationship. By only including prospective cohort studies in this review, a clear temporal order between maltreatment and cognitive functioning can be determined. A sensitive searching strategy to include all relevant articles will be employed. This present review extends the findings of existing systematic reviews by expanding the coverage of literature (up to December 2017) and more databases to reflect a rising interest in the area of childhood maltreatment and cognitive functioning in the past five years. It is hoped the findings of this review will provide further evidence on the relationship between maltreatment in childhood and ensuing cognitive functioning.

2. Methods

The process and results reporting of systematic review was guided by the PRISMA guidelines, 2009 revision (Moher et al., 2009).

2.1 Search strategy

To ensure a thorough and systematic search of the literature, two methods were used to retrieve relevant articles. First, we conducted a computerized search for relevant articles in five bibliographic databases: EMBASE, HealthStar, PsychoInfo, Medline, and Cochrane Library. Appendix 1 describes the detailed search strategies for each database. We searched up to December 2017. Second, a snowball technique was used whereby the reference lists of selected articles were scanned in order to identify further potential articles. In addition, we manually searched other resources for relevant studies through the screening of reference lists of review

articles and gray literature.

2.2 Selection criteria

Articles were eligible for this review if the article: 1) used a prospective cohort study design; 2) examined the relationship between child maltreatment and ensuing cognitive functioning; 3) used well-accepted measurements for cognitive functioning and child maltreatment; 4) had comparison groups (including both maltreatment exposed and non-exposed groups) to examine the difference between the influence of child maltreatment on cognitive functioning; and, 5) provided statistical indicators to examine the impact of childhood maltreatment on ensuing cognitive functioning.

Articles were excluded if they: 1) did not measure child maltreatment or cognitive functioning; 2) were not written in English; or, 3) did not have comparison data.

We chose to study only prospective cohort studies in this systematic review because prospective cohort studies allowed us to test the temporal order that childhood maltreatment occurred before the measurement of cognitive functioning. These included studies also measured cognitive functioning using validated batteries of neuropsychological tests covering various domains including cognitive development, memory, academic achievement, literacy/verbal comprehension, intelligence, executive function, processing speed, perceptional reasoning, and non-verbal reasoning, which were deemed relevant for this systematic review.

2.3 Data collection and management

2.3.1 Selection of studies

Three review authors (SY, YS and XM) independently conducted the literature retrieval and articles evaluations. If all authors deemed an article to be irrelevant, it was discarded, and vice versa. Inconsistencies in interpretation were resolved through group of discussion with other coauthors. Endnote, RefWorks and Mendeley were used as the bibliographic software. Figure 1 provides the details of the selection process.

2.3.2 Data extraction and management

Data on author(s), country, year of publication, sample size, characteristics of study cohort, measurements of cognitive functioning, scales and questionnaires of child maltreatment, maltreatment subtypes, and major findings, were independently extracted. Inconsistencies were solved by group discussions. If there were multiple reports of a single study, they were coded onto a single data extraction form. The latest report was extracted first and then additional reports were used to fill in the gaps. If there were discrepancies in reports, we contacted the study authors for clarification.

2.4 Study quality

Study quality was evaluated by the Newcastle-Ottawa-Scale (NOS) (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp), which was designed to assess study quality of case-control and cohort studies. The NOS rating is composed of eight specific items covering three domains: selection of study groups, comparability of case and comparison groups, and ascertainment of outcome or exposure. The total score on the NOS rating system ranges between 0 and 9. Details on NOS scores for the selected articles are presented in Appendix 2.

2.5 Data synthesis

We assessed the heterogeneity of selected studies in terms of their study characteristics: study subjects, measurements of childhood maltreatment, subtypes of childhood maltreatment, measurements of cognitive functioning, different domains of cognitive functioning, and statistical analyses used. A high heterogeneity in these study characteristics across selected studies precluded the use of meta-analysis in this review. Meta-analyses, including random-effects models, make the assumption of different studies which are drawn from a normal distribution (Higgins et al., 2009). High heterogeneity significantly violates this underlying assumption. As recommended by Cochrane review, a qualitative approach was then used to synthesize the relationship between childhood maltreatment and ensuing cognitive functioning.

3. Results

The initial search produced 2328 titles, and 1467 literatures were excluded due to duplicate, then 861 abstracts were evaluated, and 242 articles were fully retrieved for full assessments. A total of 10 articles including 11 studies, which met the eligibility criteria were included. Table 1 provides an overview of the characteristics of selected studies by study domains of cognitive functioning. Of the eleven studies, five were from the United States (Enlow et al., 2012; Manly et al., 2013; Nikulina and Widom, 2013; Nikulina, 2014; Rudo, 1997), two from Australia (Mills et al., 2011; Strathearn et al., 2001), two from Britain (Danese et al., 2017; Geoffroy et al., 2016), one from Canada (Berthelot et al., 2015), and one from New Zealand (Danese et al., 2017). Only two studies collected data on both cognitive functioning and psychiatric disorders (Geoffroy et al., 2016; Nikulina and Widom, 2013). In total, nine domains of cognitive functioning as well as multiple types of maltreatment were reported, furthermore, different cognitive functioning

measurement scales were applied. The selected studies also used different statistical approaches to summarize their original findings. Therefore, a qualitative approach was used to synthesize the association between the history of childhood maltreatment and cognitive functioning. The NOS quality score for included studies ranged from 6 to 9 with the average score of 7.9. Any study scored above the average score was considered as a good quality study. Seven (64%) of included studies exceeded this threshold for good quality.

The review reports on study findings by various subtypes of maltreatment including physical/sexual/emotional abuse, neglect, domestic violence and poly-victimization and their independent and/or combined effects on nine subdomains of cognitive functioning. Intelligence and executive function were the most frequently studied cognitive functioning.

3.1 Cognitive development

Three studies (Enlow et al., 2012; Geoffroy et al., 2016; Strathearn et al., 2001) compared children with histories of maltreatment to participants without maltreatment in terms of cognitive development. All studies consistently found the exposure of maltreatment was linked with delayed cognitive development. Strathearn et al. (2001) used the Griffiths general quotient and the McCarthy general cognitive index scales to measure cognitive development among low birthweight children. They found that emotional abuse, sexual abuse and neglect showed significant associations with delayed cognitive development. The most pronounced differences were found in the association between substantiated neglect and cognitive development but no association was found for substantiated physical abuse. The significant associations remained after controlling for confounders (different types of maltreatment, birth weight < 750 g, male gender, incomplete high school education, and public hospital status). Enlow et al. (2012)

showed that children exposed to physical, emotional abuse, neglect, sexual abuse, or interpersonal trauma (IPT) -witnessing maternal partner violence between birth and 64 months were more likely to have lower cognitive development scores (0-24 months: r=-0.31; $p<0.001$; 24-64 months: r=0.19; $p<0.01$). In addition, children exposed to IPT during infancy only and those exposed both during infancy and preschool had lower scores than those exposed in preschool and unexposed children. Another study (Geoffroy et al., 2016) based on the 1958 British birth cohort which included a series of tests for reading, arithmetic and general ability at ages of 7, 11, and 16 found negative associations between child neglect and cognitive functioning scores in both childhood and adolescence. These significant associations were slightly attenuated after adjusting for confounders including maternal age, maternal smoking of ≥1 cigarette per day in pregnancy, birth weight, birth order, father's social class in 1958, parental education, and household amenities. *Childhood physical abuse, sexual abuse, emotional abuse,* and *domestic witnessed abuse* also predicted lower cognitive functioning in childhood and adolescence. However, no association was found between emotional abuse and cognitive functioning at the age of 7. Although the majority of these abuse associations, as opposed to neglect, became non-significant after controlling confounders, the relationships between sexual abuse in childhood and cognitive functioning remained significant. The study quality of these three studies was good.

3.2 Memory

Two studies (Berthelot et al., 2015; Danese et al., 2017) identified reduced memory performance among children following the exposure to maltreatment compared to non-exposed groups. One (Danese et al., 2017) of these two studies evaluating memory functions, participants who had experienced abuse as a child (maternal rejection and harsh discipline) between age of 3 and 11,

had poor performance on several tests of memory at midlife. However, these differences were no longer significant after adjusting preexisting cognitive functioning. Another memory study (Berthelot et al., 2015) demonstrated that offspring exposed to abuse/neglect had lower memory performance scores than non-exposed offspring for visual episodic memory ($F_{1,61.9}$=7.26; *p=0.009*), but not for verbal memory ($F_{1,62.0}$=2.30; *p=0.140*) or working memory ($F_{1,45.8}$=1.86; *p=0.180*). There were 67% of offspring exposed to abuse having visual episodic memory impairments, compared to non-abused individuals. Offspring exposed to abuse were 5.2 times more likely to report poorer memory performance. When intelligence quotient (IQ), socio-economic status, substance abuse or dependence and nonpsychotic DSM (Diagnostic and Statistical Manual) diagnoses were considered as covariates, the effect of maltreatment on visual episodic memory remained. The study quality for this group was mixed.

3.3 Academic achievement

Two studies (Manly et al., 2013; Rudo, 1997) found maltreatment predicted lower academic performance. Academic achievement was measured by math and reading scores of the Wide Range Achievement Test-Revised (WRAT-R) and final grades in language arts and mathematics. Rudo (1997) found that there were significant differences between physically abused children and non-abused children in terms of their reading achievement but not for math achievement. Another study (Manly et al., 2013) found that childhood neglect was associated with decreased language arts (in kindergarten) and math grades (in first grade), and lower scores overall on first-grade academic performance. However, neglect severity was not directly associated with first-grade academic performance, but rather indirectly related to cognitive performance. The study quality of this group ranged from fair to good.

3.4 Literacy/Verbal comprehension

Two studies (Danese et al., 2017; Mills et al., 2011) examined the influence of childhood maltreatment on literacy or verbal comprehension, and found that lower performance in literacy and verbal comprehension among maltreated children. The Wide Range Achievement Test (WRAT) reading test was used to measure reading, spelling, and arithmetic computation ability in the Mater University study (Mills et al., 2011). Lower WRAT scores were associated with any maltreatment including abuse and neglect both individually and combined. The magnitude of association was similar for substantiated abuse or neglect. Denese et al. (2017) assessed verbal comprehension using the Wechsler Adult Intelligence Scale (WAIS) Verbal Comprehension Index, and identified that children abused between age of 3 and 11 had poorer performance on verbal comprehension tests in midlife, however, no verbal comprehension differences were found after controlling for preexisting cognitive functioning. The study quality in this group was mixed.

3.5 Intelligence

Five studies assessed IQ examined the relationship between cognitive functioning and childhood maltreatment (Berthelot et al., 2015; Danese et al., 2017; Enlow et al., 2012; Manly et al., 2013). All studies identified the negative association between child abuse and IQ score even after adjusting confounders. Multiple well-known IQ measures were applied across five studies. One longitudinal twins study enrolled same-sex 5-year-old twins as participants and found that childhood victimization predicted impaired IQ both in adolescence and young adulthood (Danese et al., 2017). Similarly, the Dunedin study found that both physical abuse and domestic violence were related to adolescent and adulthood neurodevelopmental deficits (Danese et al., 2017). However, this relationship was attenuated or became insignificant after adjusting preexisting cognitive functioning. Overall, all five studies reported significant adverse impact of childhood

abuse on adult IQ scores in univariate analyses. The association remained significant in two studies (40%, 5) after adjusting confounders. The study quality of this group was mixed with only one study for fair quality.

3.6 Executive function

Four studies (Berthelot et al., 2015; Danese et al., 2017; Nikulina and Widom, 2013) examined the relationship between childhood maltreatment and executive function. Consistently, they found that childhood maltreatment, especially *neglect* was significantly associated with lower cognitive performance at a univariate level. In three studies (Berthelot et al., 2015; Danese et al., 2017), even when adjusted socio-demographic variables, childhood maltreatment still predicted poorer performance on executive function. While Danese et al. (2017) in the E-Rsik Study found that these maltreated/non-maltreated differences were significantly attenuated at young adulthood after considering preexisting differences in IQ at age 5 and family socioeconomic status. Nikulina and Widom (2013) used a prospective cohort study to evaluate the effect of *physical abuse, sexual abuse* and *neglect* on executive function in middle adulthood, and found that only childhood maltreatment in general and *neglect*, were related to poor executive function. Neither sexual nor physical abuse predicted cognitive scores. At age of 29, none of the types of childhood maltreatment interacted with Post-traumatic stress disorder (PTSD) to predict poorer executive performance after controlling for confounders (age, race, sex, and IQ). The study quality of this group was mixed with two studies for good and two for fair.

3.7 Processing speed

Two studies (Danese et al., 2017; Nikulina and Widom, 2013) found significant associations between childhood maltreatment and performance on processing speed tests both in early and

middle adulthood. Although both of them identified maltreatment as lowering processing speed in univariate analyses, after controlling for preexisting cognitive functioning and other covariates, Danese et al. (2017) did not find any significant associations. Similarly, Nikulina and Widom (2013) found no relationship between childhood maltreatment in general and neglect with processing speed after controlling for IQ at age of 29 and PTSD. Furthermore, when IQ was considered in the analyses, *physical and sexual abuse* no longer predicted processing speed. The study quality in this group was mixed.

3.8 Perceptual reasoning

Two studies (Danese et al., 2017; Mills et al., 2011) reported on perceptual reasoning outcomes and showed statistically significant results using either the WAIS Perceptual Reasoning Index or Raven's Standard Progressive Matrices (RSPM) scales. The Dunedin study (Danese et al., 2017) found that childhood maltreatment (between age of 3 and 11) predicted lower scores on perceptual reasoning tests in midlife. Consistent with that finding, Mills et al. (2011) in a birth cohort study (from birth to age of 14) found that children experiencing abuse or neglect either independently or combined had lower RSPM scores compared to those without the exposure. The study quality of this group was mixed.

3.9 Non-verbal reasoning

Two studies (Nikulina and Widom, 2013; Nikulina, 2014) assessed cognitive impairments using the Matrix Reasoning test, found that children exposed to *physical abuse* and/or *neglect* performed poorly on this test. More specifically, childhood maltreatment in general and neglect, in particular, were associated with lower non-verbal reasoning scores even after adjustments for demographic variables. Nikulina (2014) assessed cognitive functioning with the Trail Making A test for processing speed, Trail Making B test for cognitive flexibility, and Matrix Reasoning for

nonverbal reasoning and found that maltreated children had poorer cognitive flexibility and nonverbal reasoning. However, physical abuse no longer predicted Matrix Reasoning scores after adjusting for IQ covariate. One study did not have enough information to make judgement as to study quality, and another study had only fair quality.

Table 2 provides a summary of all the relationships between subtypes of maltreatment and different domains of cognitive functioning.

3.10 Moderators and Mediators

Only two studies (Geoffroy et al., 2016; Nikulina and Widom, 2013) examined the role of psychopathology in the maltreatment-cognitive functioning relationship. Nikulina and Widom (2013) found that post-traumatic stress disorder was not a significant mediator for the relationship between any childhood maltreatment (physical abuse, sexual abuse and neglect) and executive function after controlling for age, race, sex, IQ, depressive symptoms, and excessive alcohol consumption. Another study found that when considering mental health as a covariate in the neglect-cognition association, the role of mental health in the relationship attenuated slightly for cognition measured both at 16 years and in adulthood at age of 50 (Geoffroy et al., 2016). Similarly, the study by Manly et al. (2013) found that neighborhood poverty did not play a moderating role in the relationship between child neglect and cognitive functioning.

4. Discussion

4.1 Summary of major findings

This systematic review included 10 eligible articles examining the relationship between childhood maltreatment and cognitive functioning. Nine cognitive functioning domains were

associated with different subtypes of maltreatment. Generally, childhood maltreatment had a significant and direct impact on ensuing cognitive functioning. Few additional factors were also significantly associated with cognitive functioning, such as sociodemographic characteristics and the presence of mental disorder.

Child maltreatment is known as one of the most consistent factors related to cognitive dysfunction (Crozier and Barth, 2005; Majer et al., 2010). Many cross-sectional studies have found that adulthood neurodevelopmental impairments are one of the most common lasting and ensuing consequences of childhood maltreatment (Bücker et al., 2012; De Bellis et al., 2013; Gould et al., 2012; Ritchie et al., 2011). Children who exposed to maltreatment may also experience adverse growth environment, such as lack of responsive and sensitive care, family dysfunction and social deprivation, which can pose substantial threats to neurobiological function and brain development (Burrus, 2013; Glaser, 2014; Norman et al., 2012).

In general, we found that *physical abuse* was linked with poor memory. Danese et al. (2017) found that physical abuse was only associated with visual episodic memory but not verbal or working memory. In addition, physical abuse was associated with cognitive development, academic achievement, literacy/verbal comprehension, IQ scores at age of 12, 18 and 38, executive function, proceeding speed, perceptual reasoning as well as non-verbal reasoning in adolescence and adulthood. *Sexual abuse* was associated with cognitive development, memory, literacy/verbal comprehension, IQ scores at age of 12, 18 and 38, executive function, proceeding speed, perceptual reasoning and non-verbal reasoning. *Emotional abuse* was associated with cognitive development and lower IQ scores at age of 2 and 18. Furthermore, *emotional abuse* was associated with literacy/verbal comprehension, executive function, proceeding speed and perceptual reasoning. *Neglect* (both physical and emotional combined or independently) - was

related to cognitive development, memory, academic achievement, literacy/verbal comprehension, IQ, executive function, proceeding speed, perceptual reasoning and non-verbal reasoning. *Domestic violence* was related to cognitive development, memory, literacy/verbal comprehension, IQ (at age of 38), executive function, proceeding speed and perceptual reasoning in the literature available. *Poly-victimization* was associated with IQ at age of 2 and 18, as well as with executive function and proceeding speed.

The underlying mechanisms of the relationship between cognitive dysfunction and childhood maltreatment have been extensively studied. Cognitive deficits of maltreated children may be influenced by genetic background and prenatal experience, such as poor intrauterine environment, lacking of medical intervention during pregnancy, and adverse postnatal conditions, which could mutually determine the impact of maltreatment on ensuing cognitive functioning, since brain regions related to extended postnatal development are especially vulnerable to long-term effects of adverse experiences (Crozier and Barth, 2005; Teicher et al., 2003). Furthermore, animal studies have found that early traumatic events such as maternal separation or loss, abuse or neglect are related to long-term alterations in cognitive functioning (Sánchez et al., 2001). Likewise, human studies have also shown that maltreatment or other adverse experiences could pose a cascade of detrimental effects on children who are in the periods of rapid creation or modification of neuronal connections (Cicchetti et al., 2006), due to structural alterations in the brain which had reduced medial prefrontal cortex volume and gray matter volume in the hippocampus (Frodl et al., 2010; Kitayama et al., 2005). For instance, Tomoda et al. (2009) found that children exposed to harsh corporal punishment had smaller volume of the prefrontal cortex, which was associated with cognitive processing (Miller and Cohen, 2001). Additionally, long and lasting stress can cause dysregulations of hypothalamic-pituitary adrenal (HPA) axis,

and makes its product- cortisol not to regulate normal brain functions, such as learning, memory, and other cognitive functions (Lupien et al., 2009; Marin et al., 2011). In addition, epigenetic mechanisms may also contribute to the relationship between early life stress and cognitive impairments. The HPA axis is epigenetically regulated by stress, particularly during development (Zovkic et al., 2013). A considerable amount of research has found that histone acetylation in long-term has a long-term effect on brain and learning behavior functions, such as spatial memory (Fischer et al., 2007; Guan et al., 2009).

There are several studies in this review reported significant associations in univariate analyses, but the associations were attenuated or no longer significant after adjusting for confounders, such as IQ. There are many possible reasons for this phenomenon. Antecedent or concurrent third factors, including psychiatric disorders, potentially mediated and moderated the development of cognitive functioning after maltreatment during childhood, thereby contributing to the onset of neurodevelopmental deficits. Berthelot et al. (2015) found a potential mediating developmental role for cognitive domains in the established association between childhood maltreatment and later psychiatric illnesses. However, whether psychiatric disorders served as mediators for this relationship remained to be determined. Only two studies (Geoffroy et al., 2016; Nikulina and Widom, 2013) explored the mediating and moderating role of mental disorders in this review and the majority of selected studies did not explore psychiatric disorders or investigate their potential mediating roles in the association between childhood maltreatment and cognitive functioning. Future studies should consider factors potentially contributed to causal pathways in their research, and have capacity to investigate the mediating and moderating effect of these factors.

4.2 Strengths and limitations

This review provides robust evidence to support relationships between domains of cognitive functioning and subtypes of maltreatment. From methodological perspective, this present review only included prospective cohort studies, which can offer clearly temporal order between the exposure of child maltreatment and ensuing cognitive functioning. In addition, we used a systematic and comprehensive searching strategy to ensure all potential articles were objectively evaluated.

There are several limitations to be noted. Firstly, a high degree of heterogeneity was identified among selected studies in terms of various domains of cognitive functioning, and measurements used for cognitive functioning and childhood maltreatment. A qualitative approach, as recommended, was used to evaluate the association between childhood maltreatment and cognitive functioning. Secondly, maltreatment was largely measured by self-reported questionnaires and scales. Only few studies used institutional records. Accuracy of maltreatment may be influenced by measurement bias introduced by self-reported measures. Thirdly, only two eligible studies investigated the mediating and moderating role of psychiatric disorders in the relationship between childhood maltreatment and cognitive impairments. Fourthly, data on age onset of child maltreatment, severity, duration and frequency, were not available in the selected studies. Future studies should collect more detailed information on child maltreatment and introduce neurobiological markers to facilitate exploration of underlying mechanisms of cognitive dysfunction caused by maltreatment. Finally, most of studies included in our review were conducted in developed countries, therefore, more studies on the maltreatment-cognitive functioning relationship from low /middle -income countries are warranted.

4.3 Implications for research and practice

The implementation of this research is that health policy and programs focused on childhood maltreatment prevention and intervention and aimed at providing better care and reducing negative consequences of maltreatment are urgently required. In addition, it is critical to develop an in-depth understanding of connections between various subtypes of maltreatment and different domains of cognitive functioning and apply to a network approach to better prevent and intervene those negative consequences caused by maltreatment.

4.4 Conclusions

The present review provides a robust evidence to support childhood maltreatment is a risk factor linked with ensuing adverse cognitive functioning. More specifically, different maltreatment subtypes have independent and/or combined detrimental effects on various domains of cognitive functioning. Findings of this review highlight the importance for developing public health strategies to prevent childhood maltreatment and mitigate its negative consequences. Effective prevention targeted on childhood maltreatment can receive tremendous benefits in terms of long-term cognitive functioning. Further studies are needed to better understand the underlying mechanisms of this maltreatment-cognitive functioning relationship. This review observes a high degree of heterogeneity and lack of data existed in the literature. More multi-centred longitudinal cohort studies are needed to provide more robust evidence on causation, mechanisms of action and strategic leverage points for prevention.

Highlights

- This review provides robust evidence on relationships between domains of cognitive functioning and maltreatment subtypes.
- Intelligence and executive function were the most frequently studied cognitive functioning.
- Maltreatment subtypes have independent/combined/synergistically adverse effects on domains of cognitive functioning.
- The importance of public health strategies to prevent child maltreatment and mitigate its negative effects is highlighted.

Declarations of interest

None.

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Author contributions

YS and SY conducted the search, together with XM reviewed the articles returned by the search for eligibility and reviewed all data extraction. YS prepared the draft of this manuscript. XM and

CD designed this review. XM oversaw the project, provided feedback on all steps of the search and data extraction and interpretation. All authors contributed to the writing and editing of the manuscript.

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Table 1. Characteristics of studies that have investigated the relationship between childhood maltreatment and cognitive functioning.

Authors	Country	Year	Age of study sample	Sample size	Timing of mental disorders and cognitive functioning	Neuropsychological tests	Assessment of maltreatment	Maltreatment subtype	Significant findings	Non-significant findings
Cognitive development										
Strathearn *et al.*	Australia	2001	Infants were followed for 4 years	352	NM	Griffiths general quotient (GQ); McCarthy general cognitive index (GCI)	IR/OR	PA/SA/EA/N	All categories of child maltreatment, except substantiated physical abuse, were associated with cognitive delay; After adjustment for confounding variables, neglect was found to be the only one that was associated with cognitive delay.	No results
Enlow *et al.*	United States	2012	Birth cohort study followed to 64 months	206	NM	Bayley Mental Development Scale (BMD)	OR	PA/EA/N/DV	IPT (interpersonal trauma) groups differed on BMD scores at 24 months; IPT exposure during infancy was associated with cognitive outcomes.	IPT exposure during preschool was not associated with cognitive outcomes.
Geoffroy *et al.*	Britain	2016	Birth cohort study followed to adulthood	18558	ST	Tests of reading, arithmetic, general ability and immediate and delayed word lists, animal naming, and letter cancellation	OR	PA/SA/EA/N/ DV	A negative association between childhood neglect and cognitive score at each age in childhood and adolescence persisted into adulthood. Associations remained after adjusting for confounders. Childhood physical, psychological, sexual, and witnessed abuse, were associated with lower cognitive score during childhood and adolescence. Only associations between sexual abuse and childhood/ adolescence cognition remained after adjustments.	No results
Memory										
Berthelot *et al.*	Canada	2015	6–22 years	66	NA	Rey Complex Figure Test ; California Verbal Learning Test; WISC-III or WAIS-III subtest	OR	PA/SA//N	Exposed offspring had lower performance than non-exposed offspring in visual episodic memory. When covariate (IQ, socioeconomic status, substance abuse or dependence and DSM diagnoses) was entered in the model, separately, the effect of trauma on visual episodic memory remained.	No difference was found among exposed offspring and non-exposed offspring in terms of verbal memory or working memory.
Danese *et al.*	New Zealand	2017	3 years of age	1037	NM	Cambridge Neuropsychological Test Automated Battery (CANTAB) Paired Associates Learning; Wechsler Memory Scale-III; Rey Auditory Verbal Learning Test	OR	PA/DV	Children exposed to maltreatment between ages 3 and 11 had lower scores on several tests of memory at midlife.	Differences were attenuated when considered indicators of preexisting cognitive functioning.

Academic achievement										
Rudo *et al.*	United States	1997	8-18 years	94	BT	Math and reading scores on the Wide Range Achievement Test-Revised (WRAT-R)	IR	PA	Physically abused children had significantly lower reading scores of WRAT-R than non-abused children at year 7.	Children with serious emotional disturbances and a history of physical abuse and those non-abused did not differ in math achievement.
Manly *et al.*	United States	2013	4 years of age	170	NM	Final grades in Language Arts and Math	IR	N	Neglect was associated with decreased language, arts effort in kindergarten, and math grades in the first grade. Results showed that neglected children had significantly lower factor scores on first-grade academic performance.	Neglect severity was not related to classroom behaviors or academic performance directly, but indirectly through cognitive performance.
Literacy/Verbal comprehension										
Mills *et al.*	Australia	2010	Birth cohort study followed to 14 years	7214	NM	Wide Range Achievement Test (WRAT) reading test	OR	PA/SA/EA/N	WRAT scores were significantly lower for the children who exposed to any maltreatment and both abuse and neglect independently. Notification of any child maltreatment was associated with a significantly lower score on both reading ability.	For WRAT, both notification and substantiation, the interaction variable was not statistically significant.
Danese *et al.*	New Zealand	2017	3 years of age	913	NM	WAIS Verbal Comprehension Index	OR	PA/DV	Children exposed to maltreatment between ages 3 and 11 performed more poorly in midlife on several tests of verbal comprehension.	Differences were attenuated when considered indicators of preexisting cognitive functioning.
Intelligence										
Enlow *et al.*	United States	2012	Birth cohort study followed to 64 months	206	NM	Wechsler Preschool and Primary Scale of Intelligence (WPPSI); Wechsler Intelligence Scale for Children-Revised (WISC-R)	OR	PA/EA/N/DV	IPT groups differed significantly on WPPSI scores at 64 months and WISC-R scores at 96 months.	No results
Manly *et al.*	United States	2013	4 years of age	170	NM	Wechsler Preschool and Primary Scale of Intelligence–Revised (WPPSI-R), The Peabody Picture Vocabulary Test (PPVT-III), and Expressive Vocabulary test (EVT scores)	IR	N	Neglect was significantly associated with lower intelligence performance.	Neighborhood poverty moderation of the link between child neglect and cognitive performance as well as moderation of the link from cognitive performance to classroom behavior and academic performance were insignificant.
Berthelot *et al.*	Canada	2015	6–22 years	66	NA	Wechsler Intelligence Scale for Children-III [WISC-III]; Wechsler Adult Intelligence Scale-III [WAIS-III]	OR	PA/SA//N	A lower IQ was found in exposed than in non-exposed offspring. When covariates (socioeconomic status, substance abuse or dependence) were entered in the model, the effect of trauma on IQ remained significant.	No results

Danese *et al.*	Britain	2017	Same-sex 5-year-old twins	2112	NM	Wechsler Intelligence Scale for Children-Revised (WISC-R)	OR	PA/SA/EA/N/ DV/P	Children who experienced **poly-victimization**, **physical domestic violence, bullying victimization, physical harm, sexual harm, emotional abuse and physical neglect** between ages 5 and 12 had lower IQ test scores at age 12 than non-victimized children; Children with no history of victimization before age 5 years who experienced **poly-victimization** between ages 5 and 12 had lower IQ test scores at age 12 than non-victimized children.	No results
Danese *et al.*	Britain	2017	Same-sex 5-year-old twins	2045	NM	Wechsler Adult Intelligence Scale-IV (WAIS-IV)	OR	PA/SA/EA/N/ DV/P	Children who experienced **poly-victimization, physical domestic violence, bullying victimization, physical harm, sexual harm, emotional abuse and physical neglect** between ages 5 and 12 had lower IQ at age 18 than non-victimized children. Children with no history of victimization before age 5 years who experienced **poly-victimization** between ages 5 and 12 had lower IQ at age 18 than non-victimized children.	Differences were attenuated when considered preexisting differences in IQ at age 5 and family socioeconomic status.
Danese *et al.*	New Zealand	2017	3 years of age	899	NM	Wechsler Intelligence Scale for Children-Revised (WISC-R)	OR	PA/DV	Children who experienced maltreatment between ages 3 and 11 had lower IQ at ages 11–13 than non-maltreated children.	Differences were attenuated when considered indicators of preexisting cognitive functioning.
Danese *et al.*	New Zealand	2017	3 years of age	913	NM	Wechsler Adult Intelligence Scale-IV (WAIS-IV)	OR	PA/DV	Children exposed to maltreatment between ages 3 and 11 had lower IQ scores at age 38, than non-maltreated children.	Differences were attenuated when considered indicators of preexisting cognitive functioning.
Executive function										
Nikulina *et al.*	United States	2013	0-11 years	1575	PTSD:BT; Depression: ST	Trail Making tests B	IR	PA/SA/N	Childhood maltreatment in general predicted poorer performance on executive function. Childhood maltreatment overall and neglect, in particular, predicted lower Trail Making B scores.	Neither sexual nor physical abuse predicted Trail Making B scores. None of subtypes of maltreatment interacted with PTSD diagnosis at mean age 29 to predict Matrix Reasoning or Trail Making B.
Berthelot *et al.*	Canada	2015	6–22 years	66	NA	Verbal Fluency Test	OR	PA/SA//N	Exposed offspring had lower performance than non-exposed offspring in executive functions.	No results

Danese *et al.*	Britain	2017	Same-sex 5-year-old twins	2232	NM	Rapid Visual Processing (RVP), Spatial Working Memory (SWM), Spatial Span (SSP)	OR	PA/SA/EA/N/ DV/P	Children who experienced different subtypes of maltreatment between ages 5 and 12 performed more poorly on executive function at age 18. Children with no history of victimization before age 5 who experienced poly-victimization between ages 5 and 12 performed more poorly on executive function at age 18.	Differences were also attenuated when considered indicators of preexisting cognitive functioning.
Danese *et al.*	New Zealand	2017	3 years of age	1037	NM	CANTAB Rapid Visual Information Processing; WAIS Working Memory Index: Wechsler Memory Scale-III; Trails-B test	OR	PA/DV	Children exposed to maltreatment between ages 3 and 11 performed more poorly in midlife on executive function tests.	Differences were attenuated when considered indicators of preexisting cognitive functioning.
Processing speed										
Nikulina *et al.*	United States	2013	0-11 years	1575	PTSD:BT; Depression: ST	Trail Making tests A	IR	PA/SA/N	Childhood maltreatment in general, neglect, physical abuse, and sexual abuse predicted poorer performance on processing speed.	Maltreatment and neglect did not predict Trail Making A after controlling for IQ at age 29. When IQ and PTSD diagnosis were introduced, physical and sexual abuse no longer predicted Trail Making A.
Danese *et al.*	Britain	2017	Same-sex 5-year-old twins	2232	NM	CANTAB tests (Rapid Visual Processing; Spatial Working Memory)	OR	PA/SA/EA/N/ DV/P	Children who experienced **poly-victimization**, **physical domestic violence, bullying victimization, physical harm, sexual harm, emotional abuse and physical neglect** performed more poorly on processing speed tests at age 18. Children with no history of victimization before age 5 years who experienced **poly-victimization** performed more poorly on processing speed tests at age 18.	Differences were significantly attenuated when considered preexisting differences in IQ at age 5 and family socioeconomic status.
Perceptual reasoning										
Mills *et al.*	Australia	2010	Birth cohort study followed to 14 years	7214	NM	Raven's Standard Progressive Matrices (RSPM)	OR	PA/SA/EA/N	RSPM scores were lower for children exposed to any kind of maltreatment and both abuse and neglect, independently. Notification of any child maltreatment was associated with a significant lower score on perceptual reasoning tests.	For RSPM, both notification and substantiation, the interaction was not significant.
Danese *et al.*	New Zealand	2017	3 years of age	911	NM	WAIS Perceptual Reasoning Index	IR/OR	PA/DV	Children exposed to maltreatment between ages 3 and 11 performed more poorly in midlife on perceptual reasoning tests.	No results

Non-verbal reasoning

Nikulina *et al.*	United States	2013	0-11 years	1575	PTSD:BT; Depression: ST	The Matrix Reasoning test, a subtest of the WAIS-III	IR	PA/SA/N	Childhood maltreatment, neglect and physical abuse were related to poorer performance on Matrix Reasoning. Childhood maltreatment overall and neglect, in particular, predicted lower Matrix Reasoning scores despite adjusting demographic factors.	Childhood physical abuse no longer predicted poorer performance on Matrix Reasoning after IQ was introduced. None of subtypes of maltreatment interacted with PTSD diagnosis at mean age 29 to predict Matrix Reasoning or Trail Making B.
Nikulina *et al.*	United States	2014	0-11 years	1185	NA	Matrix Reasoning	NA	PA/SA/N	Childhood maltreatment predicted poorer cognitive flexibility and nonverbal reasoning.	No results

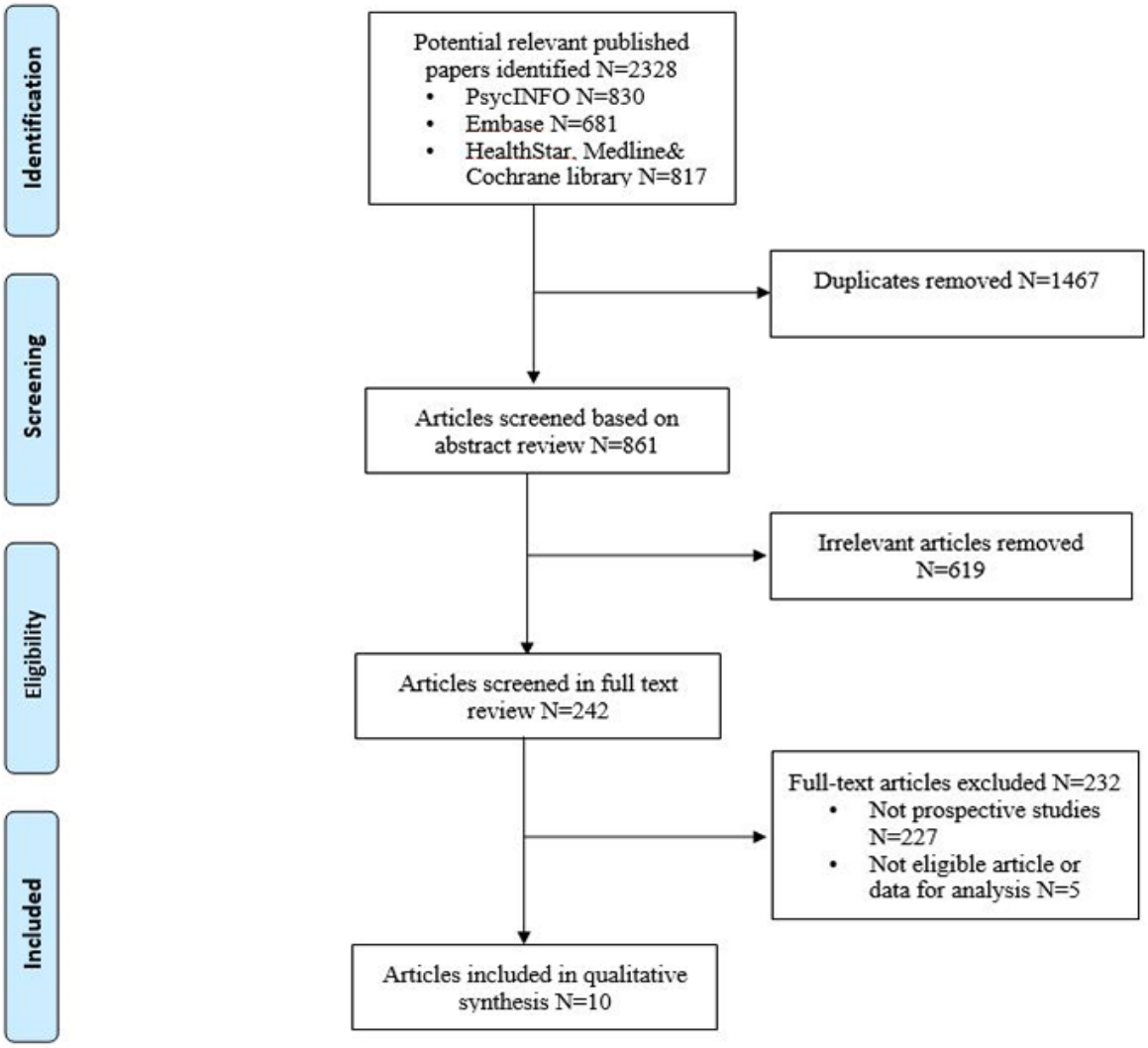
Note: IQ= Intelligence quotient; PTSD = Posttraumatic stress disorder; ST=Measured at the same time; BT= Mental disorders measured before cognitive functioning; NM=No mention on mental disorders; IR=Institutional record; OR= Self-report scale/questionnaire/questions; PA=Physical abuse; SA=Sexual abuse; EA=Emotional abuse; N=Neglect (physical or emotional); DV=Domestic violence; P=Poly-victimization; NA=Not available.

Table 2. A Summary of research findings by subtypes of maltreatment and nine domains of cognitive functioning.

Maltreatment	Cognitive functioning								
	Cognitive development	Memory	Academic achievement	Literacy/Verbal comprehension	Intelligence	Executive function	Processing speed	Perceptual reasoning	Non-verbal reasoning
Physical abuse	√*	√*	√*	√*	√*	√*	√*	√*	√*
Sexual abuse	√*	√*		√*	√*	√*	√*	√*	√*
Emotional abuse	√*			√*	√*	√*	√*	√*	
Neglect (physical/emotional or both)	√*	√*	√*	√*	√*	√*	√*	√*	√*
Domestic violence	√*	√*		√*	√*	√*	√*	√*	
Poly-victimization					√*	√*	√*		

√*indicated negative association

Figure 1. A summary of selection process of this systematic review



Appendix 1. A summary of search strategy

To ensure a thorough and systematic review of the literature, two methods were used to retrieve relevant studies. First, we used computerized bibliographic databases EMBASE, HealthStar (1966-2017), PsychoInfo, Medline, Cochrane Library, using the following combinations of search terms for title and abstract: "(cognitive [Text Word] OR neurocognitive [Text Word] OR intellectual [Text Word] OR intelligence [Mesh term] OR IQ [Text Word] OR language* [Text Word] OR visual spatial [Mesh term] OR memory [Mesh term] OR motor [Text Word] OR psychomotor [Text Word] OR attention [Text Word] OR executive [Text Word]) **AND** (control [Text Word] OR dysfunction [Mesh term] OR functioning [Text Word] OR function [Text Word] OR deficit* [Text Word] OR impairment* [Text Word]) **AND** (childhood [Text Word] OR early life [Text Word] OR infan* [Text Word] OR children [Text Word]) **AND** (childhood [Text Word] OR early life [Text Word] OR infan* [Text Word] OR children [Text Word]) **AND** (maltreatment* [Mesh term] OR neglect [Mesh term] OR abuse [Text Word] OR mistreatment* [Text Word] OR adversity* [Text Word] OR trauma* [Text Word]), Limits: Humans [MeSH Terms]". No constraints were placed on the publication date. The literature search comprised articles up to December, 2017. Second, a snowball technique was applied whereby the reference lists of all relevant studies were scanned in order to identify further studies. We manually searched other resources for other relevant studies. The reference lists of selected articles, review articles on relevant topic, and the gray literatures were also screened.

Appendix 2. A summary of the Newcastle-Ottawa Scale (NOS) quality assessment for selected studies.

Assessment item	Study										
	Strathearn (2001)	Enlow (2012)	Geoffroy (2016)	Mills (2010)	Danese (2017)[#]	Danese (2017)[*]	Manly (2013)	Berthelot (2015)	Rudo (1997)	Nikulina (2013)	Nikulina (2014)
Selection											NA
1. Representativeness of the intervention cohort											
a) truly representative of the average, elderly, community-dwelling resident	0	0	1	0	0	1	1	0	1	0	
b) somewhat representative of the average, elderly, community-dwelling resident	1	1	0	1	1	0	0	1	0	1	
c) selected group of patients, e.g. only certain socio-economic groups/areas	0	0	0	0	0	0	0	0	0	0	
d) no description of the derivation of the cohort	0	0	0	0	0	0	0	0	0	0	
2. Selection of the non-intervention cohort											
a) drawn from the same community as the intervention cohort	1	1	0	1	1	1	1	1	1	1	
b) drawn from a different source	0	0	0	0	0	0	0	0	0	0	
c) no description of the derivation of the non-intervention cohort	0	0	0	0	0	0	0	0	0	0	
3. Ascertainment of intervention (exposure)											
a) secure record (e.g. health care record)	1	0	0	1	0	0	1	0	1	1	
b) structured interview	0	1	1	0	1	0	0	1	0	0	
c) written self report	0	0	0	0	0	0	0	0	0	0	
d) other / no description	0	0	0	0	0	0	0	0	0	0	
4. Demonstration that outcome of interest was not present at start of study											
a) yes	1	1	1	1	0	0	1	1	0	0	
b) no	0	0	0	0	0	0	0	0	0	0	

Comparability											NA
1. Comparability of cohorts on the basis of the design or analysis											
a) study controls for age, sex, marital status	1	1	1	1	1	1	0	1	0	1	
b) study controls for any additional factors (e.g. socio-economic status, education)	1	1	1	1	1	1	1	1	0	1	
Outcome											NA
1. Assessment of outcome											
a) independent blind assessment	1	1	1	1	1	1	1	1	1	1	
b) record linkage	0	0	0	0	0	0	0	0	0	0	
c) self report	0	0	0	0	0	0	0	0	0	0	
d) other / no description	0	0	0	0	0	0	0	0	0	0	
2. Was follow up long enough for outcomes to occur											
a) yes, if median duration of follow-up >= 6 month	1	1	1	1	1	1	1	1	1	1	
b) no, if median duration of follow-up < 6 months	0	0	0	0	0	0	0	0	0	0	
3. Adequacy of follow up of cohorts											
a) complete follow up: all subjects accounted for	0	1	0	0	0	0	1	1	1	0	
b) subjects lost to follow up unlikely to introduce bias: number lost <= 20%, or description of those lost suggesting no different from those followed	1	0	1	0	1	1	0	0	0	0	
c) follow up rate < 80% (select an adequate %) and no description of those lost	0	0	0	0	0	0	0	0	0	0	
d) no statement	0	0	0	0	0	0	0	0	0	0	
Overall	Good quality	Good quality	Good quality	Good quality	Good quality	Fair quality	Good quality	Good quality	Fair quality	Fair quality	NA

Note: # * two studies in one article;# Study 1: The E-Risk Study;*Study 2: The Dunedin Study