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The Relationship Between Early Life Stress and Working Memory in Adulthood: A Systematic Review and Meta-Analysis

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Abstract

Exposure to early life stress has been linked to impairment in cognitive functioning in adulthood. The aim of this study was to systematically review the literature on the relationship between early life stress and working memory, a central component of cognitive functioning. Database searches yielded 358 abstracts matching the search terms. Abstract screening followed by full-text review resulted in 26 publications suitable for inclusion, of which 23 were included in the meta-analysis. Results of the meta-analysis suggested exposure to early life stress was associated with poorer working memory. Even though there were a wide variety of working memory tasks used, this effect was significant for both phonological and visuospatial working memory tasks, and both visual and aural task presentation modalities. The effect was also found in samples with and without clinical psychopathology. This review provides recommendations for future research and implications for clinical practice.

Keywords: Working Memory; Short-Term Memory; Early Life Stress; Childhood Trauma; Childhood Experiences.

The Relationship Between Early Life Stress and Working Memory in Adulthood: A Systematic Review and Meta-Analysis

Early life stress, also known as childhood trauma or maltreatment, refers to adverse events occurring before the age of 18, including physical and emotional abuse, physical and emotional neglect, sexual abuse, adverse family environment, peer violence and witnessing community or collective violence (World Health Organisation [WHO], 2009). A study by Felitti et al. (1998) examined the prevalence of early life stress in a sample of over 9,000 adult participants. They found that over half the participants reported experiencing at least one of these categories of early life stress, with 6% of participants reporting having experienced four or more categories of early life stress. More recent estimates indicate this prevalence rate has remained relatively stable, with Sacks, Murphy and Moore (2014) reporting that 46% of people have experienced some form of early life stress.

Early life stress has been associated with health-related problems in adulthood, including increased risk of cardiovascular disease (Lei, Beach, & Simons, 2018), poor general health, asthma, stroke, and disability (Gilbert et al., 2015), and poorer mental health, including anxiety, depression, and emotional problems (Schneider, et al., 2017). There is also evidence to suggest early life stress is related to impaired cognitive functioning in adulthood (Irigaray et al., 2013; Lu et al., 2017; Mason, Bussieres, East-Richard, R-Mercier, & Cellard, 2015). The relationship between early life stress and working memory, which is a fundamental component of cognitive functioning, has been examined in several recent studies, with some reporting a significant association (Fuge et al., 2014; Majer, Nater, Lin, Capuron & Reeves, 2010; Rivera-Velez, Gonzales-Viruet, Martinez-Taboas, & Perez-Mojica, 2014) and others finding no association (Dunn et al., 2016; Gonzales, Jenkins, Steiner & Fleming, 2012).

Working memory is the cognitive system responsible for the transient storage and manipulation of task-relevant information during concurrent processing demands (Baddeley, 2017). In the original model of working memory proposed by Baddeley and Hitch (1974), there are three main components; an attentional control system, referred to as the central executive, and two slave systems, the phonological loop and the visuospatial sketchpad. This model describes the domain-specific nature of working memory, whereby phonological information (e.g., letters, numbers, and words) is briefly stored in the phonological loop, separate from visuospatial information (e.g., shapes, colours, and locations), which is briefly stored in the visuospatial sketchpad. Neurological studies have provided support for the domain-specific nature of working memory (see D'Esposito & Postle, 2015, for a review).

There is a growing body of literature examining the relationship between early life stress and cognition in general. A meta-analysis conducted by Mason et al. (2015) included 50 studies reporting on the relationship between some forms of early life stress (i.e., sexual abuse, physical abuse, neglect or emotional/psychological abuse) and cognition in adults. Of these studies, 12 examined the relationship between early life stress and working memory. Their findings revealed an association between early life stress and cognitive functioning, including working memory. While the overall effect size for the relationship between early life stress and working memory was reported in the meta-analysis, effect sizes for individual studies were not. The different measures used to assess early life stress and working memory were also not examined. Indeed, to date, no studies of which we are aware have systematically reviewed the literature on early life stress with a specific focus on working memory.

A number of working memory tasks have been developed. However, there is often a lack of consensus among researchers as to whether some of these tasks actually assess working memory. Working memory tasks can differ on a number of dimensions, including complexity (i.e., load on the central executive), presentation modality (i.e., auditory or visual), or the working memory domain (e.g., visuospatial or phonological) the task is assumed to assess. If there is a relationship between early life stress and working memory, it is uncertain from the current literature whether the relationship is dependent on the working memory measure employed. It is important to ascertain whether differences in findings reported in the extant literature may be partially due to differences in the type of working memory tasks used.

If early life stress is related to working memory, then the consequences of that deficit should be considered for those who have experienced early life stress. Working memory has been shown to be related to many everyday skills, such as language acquisition (Baddeley, Gathercole, & Papagno, 1998) and expression (Henry & MacLean, 2003), reading comprehension (Chiappe, Hasher, & Siegal, 2000), mathematical ability (Bull, Epsey, & Weibe, 2008), and higher cognitive skills such as reasoning (Conway, Kane, & Engle, 2003) and problem solving (Bull & Scerif, 2001). If a relationship between early life stress and poor working memory exists, especially in clinical populations, it is important for clinicians to have a good understanding of this association. Many of the skills taught in clinical therapies such as cognitive behaviour therapy (e.g., identifying maladaptive automatic thoughts, cognitive restructuring, and self-monitoring of thoughts and behaviours outside of therapy) likely require working memory for execution.

The goals of this study were preregistered with PROSPERO. In line with this preregistration, the main aim of the present study was to conduct a systematic review and meta-analysis of the literature reporting on the relationship between early life stress and working memory. We also examined whether the strength of the relationship between early life stress and working memory is moderated by: 1) the type of task used to assess working memory; 2) the type of early life stress experienced; or 3) clinical status.

Method

Protocol Registration

The protocol outlining the aims and scope of this systematic review and meta-analysis was registered with PROSPERO on the 15th July 2016 (Citation: Chalmers, K., Freeman, E., & Goodman, J. (2016). The Relationship Between Early Life Stress and Working Memory in Adulthood: a Systematic Review and Meta-Analysis. PROSPERO 2016:CRD42016042995). The protocol is available from: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016042995.

Search Strategy

The PsycINFO, PubMed, ProQuest, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Published International Literature on Traumatic Stress (PILOTS), and Science Direct electronic bibliographic databases were searched. The search strategy used included key terms and Medical Subject Headings (MeSH) relating to early life stress (“early life stress”, “early experience”, “emotional trauma”, “child* trauma”, “child* abuse”, “divorce”, “sexual abuse”, “adverse child* experience”, “child* neglect”, “emotional abuse”, and “early trauma”) and working memory (“working memory”, “short term memory” and “executive function”.) The search strategy was created by the authors in the PsycINFO database and adapted for use with the other bibliographic databases. Given the broad range of eligible studies, and varied nomenclature, we did not use any additional search filters. The final database search was conducted in July 2017.

Study Selection and Data Extraction

The titles and abstracts retrieved from the search were independently screened by two reviewers to identify empirical studies that included: 1) a human adult sample, 2) a measure of at least one form of early life stress, and 3) a clear measure of working memory as classified by a statement from the author, or general consensus in the literature, that it is measuring working memory. The WHO (2009) definition of early life stress was used to assess suitable early life stress categories to include in this study. As a result, the following interpersonal early life stress types were considered for inclusion: physical abuse, emotional abuse, physical neglect, emotional neglect, sexual abuse, peer violence (i.e., experiencing physical or emotional bullying), living in an adverse family environment (i.e., a household member was incarcerated, had a substance use disorder, or had a mental illness; or the child had witnessed domestic violence, or had only one parent/caregiver). Where non-interpersonal early life stress types (e.g., medical trauma, experiencing a natural disaster) were the only early life stress type reported, the study was excluded.

Potentially eligible studies were retrieved for full-text review and independently assessed for eligibility for inclusion by two reviewers. Any disagreement between the two reviewers at any point in the review process was resolved through discussion with a third reviewer. All publication records retrieved throughout the review process were stored in an electronic database and the reasons for exclusion were recorded.

Data were extracted from the included studies for assessment of study quality and data synthesis. Extracted information included the study sample, details of study methodology (early life stress measure, working memory measure, and study design) and results (e.g., means, SDs, effect sizes, correlation coefficients). Where the data required for analysis were unclear, or not reported in the included publications, the corresponding authors were contacted. Of the six authors contacted, three provided additional information, which allowed for the publication to be included in the meta-analysis. Data extraction was completed by one reviewer and checked by a second reviewer.

Assessment of Study Quality

All included publications were assessed for research quality by two reviewers, using the following criteria: 1) presence of a valid and objective measure of early life stress, 2) presence of a valid and objective measure of working memory, 3) appropriate sample size for the statistical analyses used, and 4) sufficient data reported to include in the meta-analysis. Each publication was given a score of 0, 1, or 2 for each criterion, where a score of 0 represented 'not met', a score of 1 represented 'partially met' or 'required further information from authors' and a score of 2 represented 'fully met'. Each publication was given a total score out of a possible 8 points. The points allocated to each criteria are presented in Table 1. Study quality descriptors were applied, based on the following cut off scores: Poor = 0-2; Fair = 3-5; Good = 6-8.

Data Analysis

Where available, outcomes for each individual working memory task were used. In cases where only a composite working memory score was reported (i.e., scores from different working memory tasks were combined), the composite score was used. Comprehensive Meta-Analysis (CMA) software (Borenstein, Hedges, Higgins, & Rothstein, 2011) was used to calculate effect sizes. Hedge's *g*, an effect size suitable for small samples, calculated as the difference between the means of two groups (e.g., early life stress vs. non-early life stress) divided by the pooled standard deviation, was calculated for each available outcome, collapsed across early life stress type. CMA was used to transform correlational data to this shared effect size estimate. Hedge's *g* with 95% confidence intervals can be interpreted using Cohen's (1988) convention of small (.20), medium (.50), and large (.80) effect sizes (Ellis, 2010).

To account for variability in study characteristics, a random effects model was used to analyze effect sizes. Distributions of effect sizes were examined using tests of heterogeneity. Significant heterogeneity estimates indicate variance can be partly attributed to differences in study characteristics, rather than the result of within-study sampling error alone (Thompson & Sharp, 1999).

Three moderator analyses were conducted to examine whether the domain (phonological vs. visuospatial) assessed by the working memory task, the presentation modality (visual vs. auditory) of the working memory task, or clinical status (clinical vs. non-clinical) of the sample could explain variability in effect sizes across outcomes. Moderator tests in meta-analysis are analogous to analysis of variance (ANOVA) and result in a between-studies heterogeneity estimate (*Q*) that can be used to interpret moderator effects (Hedges & Pigott, 2004). A significant between-studies homogeneity estimate indicates that effect sizes are significantly different across different categories of the moderator variable.

Analysis of Publication Bias

To address publication bias, Egger's test was used to examine if the likelihood of studies being published depended on the direction of the observed effect. The test employs linear regression, whereby the slope of the regression line (B1) represents the treatment effect and the intercept value (B0) represents symmetry. Significant B0 values indicate bias (Egger, Smith, Schnieder & Minder, 1997). Duval and Tweedie's (2000) Trim and Fill method was used to assess whether the observed overall effect size would change if asymmetry caused by the identified publication bias was corrected for by trimming the asymmetric studies from the right of the mean and re-inserting them to the left of the mean.

Results

Literature Search Process

A flowchart depicting the search and selection process is presented in Figure 1. The initial search yielded 540 abstracts of which 358 were unique. After the abstract screening procedures, 276 publications were excluded due to: being a case study, a review article, a conference abstract, an animal study, a child study, or written in a non-English language; having no working memory measure, or no measure of early life stress. The remaining 82 publications were retrieved for full-text review to assess eligibility. At the full-text review stage, 56 publications were excluded for the following reasons: non-unique sample (i.e., the same sample's data had been published in a more recent journal), no clear working memory measure, no early life stress measure, or insufficient data to analyse the relationship between early life stress and working memory. A total of 26 publications containing 29 samples and

75 outcomes were included in this systematic review. The methodology, results, and assessment of study quality for each of the included publications are presented in Table 2.

Assessment of Early Life Stress

The complete data set from the 26 included publications consisted of 26,976 adult participants, of whom 16% had experienced early life stress and 76% had reported never to have experienced early life stress. Presence versus absence of early life stress was not categorised in 9 studies that used a correlational approach (8% of participants).

The majority of studies were observational/exploratory in design with regards to the analysis of early life stress. A total of 11 different self-report measures were used in the included studies. The measures differed in the type and number of early life stress categories assessed. The full range of early life stress categories assessed were: abuse (unspecified, physical, or emotional), neglect (unspecified, physical, or emotional), sexual abuse or harassment, loss (separation, divorce, or death in the family), bullying, bodily threat, witnessing family violence or conflict, and exposure to illicit substances via a parent with a substance use disorder.

Early life stress data were conceptualised in two different ways. While over a third kept the different forms of early life stress separate in their data analysis, the majority of studies (60%) combined two or more forms of early life stress into a single measure in their data analysis. The latter approach precludes investigation into whether working memory deficits can be better predicted by childhood exposure to a specific type of early life stress. None of the publications that looked at specific types of early life stress reported the consideration of co-occurrence of other types of early life stress (e.g., by including it as a covariate in the analyses). As a result, an analysis of the strength of the relationship between working memory and specific types of early life stress could not be completed in the present research. Type of early life stress was therefore not included as a moderator in the meta-analyses below.

Measures of Working Memory

Ten different working memory measures were used in the included studies. A brief description of each working memory measure is presented in Table 3. Of the 26 included publications, 25 used objective performance-based measures of working memory and one study used a subjective self-report measure of working memory (i.e., Mugge et al., 2016).

Each performance-based measure of working memory was classified according to working memory domain (visuospatial or phonological) and presentation modality (visual or auditory). Tasks were considered to assess visuospatial working memory if they used stimuli that were defined by shape, colour, or position in space. Tasks were considered to assess phonological working memory if they used verbal stimuli, defined as words, letters or numbers. Thirty-one percent of the outcomes were derived from visuospatial working memory tasks, 64% were derived from phonological working memory tasks, and 5% were based on working memory composites that included tasks tapping both visuospatial and phonological domains.

When classified by presentation modality, 44% of the outcomes were from visually presented tasks and 51% were from aurally presented tasks. The remaining 5% were reported as working memory composites that combined scores from both visually and aurally presented tasks.

Outcome metrics varied over studies, with some reporting accuracy, some reporting reaction time, and some reporting both. Of the identified working memory tasks, only the *n*-back task allows for calculation of signal detection theory indices such as discriminability and bias. Of the six studies that used an *n*-back task, all reported ‘accuracy’ as an outcome measure, yet only two papers clearly defined how accuracy was calculated. Fuge et al. (2014) defined accuracy as [(hits – false alarms) / number of targets] and Quide et al. (2017) defined accuracy as [correct responses / total possible responses]. Viola et al. (2013) stated that accuracy was the sum of correct responses, however it is unclear if this included both hits and correct rejections. Phillip et al. (2013), Phillip et al. (2016) and Ucok et al. (2015) did not specify how their accuracy outcome was calculated.

Clinical Status

Almost half (47%) of the outcomes were from clinical samples, representing a range of formal mental disorder diagnoses described in the *Diagnostic and Statistical Manual of Mental Disorders Fifth Edition* (American Psychiatric Association, 2013), including schizophrenia spectrum and other psychotic disorders, bipolar disorders, major depressive disorder, and substance-related disorders. The remaining outcomes were based on non-clinical samples (i.e., without a formal mental disorder diagnosis), with the one exception being a study in which the outcome reported was for a combined clinical and non-clinical sample.

Meta-Analysis of the Relationship Between Early Life Stress and Working Memory

Outcomes from 23 publications were included in the meta-analysis. Three publications (Selah et al., 2017; Parolin, Simonelli, Mapelli, Sacco, & Cristofalo, 2016; Ucok et al., 2015) were excluded due to insufficient data. Effect size for each working memory outcome, collapsed over early-life stress type, is presented in Table 4.

Four analyses were conducted. The first examined the combined effect size over all of the outcomes reported in Table 4. The combined effect size (Hedge's $g = 0.22$, 95% CI [0.16, 0.27]; $z = 7.68$, $p < .001$) showed those who had experienced early life stress were significantly more likely to show impaired working memory ability in adulthood than those who had not experienced early life stress. Moderate to substantial inconsistency between studies was found ($Q = 147.5$, $p < .001$; $I^2 = 53\%$). A visual representation of the contribution of each publication to the overall effect size is shown in Figure 2.

The second analysis examined effect size as a function of working memory domain (i.e., tasks designed to assess phonological working memory, and tasks designed to assess visuospatial working memory). The outcomes contributing to this analysis are identified in the ‘Domain’ column (in Table 4). This analysis revealed a significant negative association between early life stress and working memory ability in both the phonological domain (Hedge’s *g* = 0.18, 95% CI [0.11, 0.25]; *z* = 5.07, $p < .001$) and the visuospatial domain (Hedge’s *g* = 0.24, 95% CI [0.18, 0.31]; *z* = 7.10, $p < .001$). While the effect size for visuospatial tasks was greater than that for phonological tasks, the heterogeneity estimate between the domains was not significant (*Q* =1.43, *p* =.232, I^2 = 30%), suggesting the relationship between early life stress and working memory is not moderated by working memory domain.

The third analysis examined effect size as a function of presentation modality (i.e., auditory vs. visual presentation). Outcomes contributing to this analysis are identified in the ‘Modality’ column of Table 4. A significant negative association between early life stress and working memory was found for both auditory tasks (Hedge’s *g* = 0.17, 95% CI [0.10, 0.24]; z = 4.47, $p < .001$) and visual tasks (Hedge’s *g* = 0.25, 95% C: [0.19, 0.31]; *z* = 7.76, $p < .001$). While the effect size was greater for visual than auditory tasks, the heterogeneity estimate between presentation modalities was not significant (*Q* = 2.49, *p* = 0.114, I^2 = 60%), suggesting the relationship between early life stress and working memory is not moderated by presentation modality.

The final analysis examined effect size as a function of clinical status (i.e., clinical vs. non-clinical participants; see final column of Table 4 for outcomes included in this analysis). A significant negative relationship between early life stress and working memory was found in both clinical (Hedge’s *g* = 0.21, 95% CI [0.13, 0.29], *z* = 5.06, $p < .001$) and non-clinical samples (Hedge’s *g* = 0.23, 95% CI [0.15, 0.30], *z* = 5.68, $p < .001$). The heterogeneity between clinical and non-clinical samples was not significant (*Q* = 0.07, *p* = .793, I^2 = 0%), suggesting the relationship between early life stress and working memory is not moderated by clinical status.

Publication bias. Egger's test identified a significant intercept (B0; $t = 3.11$, $p = .001$) suggesting that publication bias may have affected the estimates. Figure 3 shows a relatively high number of observed outcomes fall to the right of the observed mean effect, suggesting that small sample studies that do not find the expected relationship between early life stress and working memory are less likely to be published. The trim-and-fill procedure identified 14 missing outcomes to the left of the observed mean, resulting in a corrected mean effect size of $g = 0.15$, 95% CI [0.10, 0.21] when asymmetry (bias) was taken into account.

Discussion

The results of this systematic review and meta-analysis showed a significant association between early life stress and working memory ability in adulthood. Those who reported exposure to early life stress performed more poorly on working memory tasks than those who had not experienced early life stress. While some publication bias was indicated, the observed relationship remained robust after publication bias was taken into consideration.

A high level of inconsistency was observed between the studies, as indicated by the I^2 statistic, providing support for the need to explore potential moderators. Three moderation analyses were conducted to explore the complexities of the relationship between early life stress and working memory performance. The first analysis revealed the relationship between early life stress and working memory performance was not moderated by the domain (phonological vs. visuospatial) of the working memory task. The relationship between early life stress and working memory was significant both for tasks designed to assess phonological working memory and for tasks designed to assess visuospatial working memory, but there was no significant difference in the strength of the relationship for phonological and visuospatial tasks.

The second moderation analysis showed the presentation modality of the working memory task was not a significant moderator of the relationship between early life stress and working memory. While there was a significant association between early life stress and working memory both for visually presented tasks and for aurally presented tasks, the strength of the relationship did not differ as a function of presentation modality.

The third moderation analysis examined whether the strength of the relationship between early life stress and working memory was moderated by clinical status. The relationship between early life stress and working memory was significant in both clinical and non-clinical samples. There was no significant difference in the strength of the relationship for clinical and non-clinical samples, indicating the relationship between early life stress and working memory is not moderated by clinical status.

The final aim of the present research, as submitted in the PROPERO preregistration, was to examine whether the relationship between early life stress and working memory varied as a function of the type of early life stress experienced. Unfortunately, we were unable to answer this research question with the current metadata. There were two reasons for this, which both pertain to the way that early life stress was measured and reported across studies. First, many of the included studies reported a single, cumulative measure of early life stress (i.e., the data were combined over two or more categories of early life stress). Second, of the studies that did report an outcome for a specific type of early life stress, none examined the unique contribution of the specific type of early life stress (e.g., by including measures of other types of early life stress as covariates in their analysis) to working memory ability in adulthood.

Practical and Theoretical Implications

The results of the analyses examining whether the type of task used to assess working memory moderated the relationship between early life stress and working memory have provided useful information about how the relationship between early life stress and working memory could be studied in future research. As significant results were identified for both visually (e.g., visual *n*-back, spatial span) and aurally (e.g., digit span, letter-number sequencing) presented working memory tasks, and the modality of presentation did not moderate the relationship between early life stress and working memory, these findings suggest visual or auditory tasks are both suitable for examining this relationship. From a research perspective, this could allow researchers more flexibility in experimental design decisions such as choice of platform, delivery, and setting for their research studies. For example, visually presented tasks may be more convenient than auditory tasks in large online studies, whereas auditory tasks may be more suitable than visual tasks in some populations.

The moderation analysis examining whether the domain (phonological vs. visuospatial) assessed by the working memory task moderated the relationship between early life stress suggested that the relationship is independent of working memory domain. From a theoretical perspective, in terms of Baddeley and Hitch's (1974) model of working memory, this suggests early life stress may affect both the phonological loop and the visuospatial sketchpad components of the working memory system. Alternatively, as suggested in a recent systematic review conducted by Morey (2018), there is little evidence to support the existence of domain-specific short-term memory stores (see also Macken, Taylor, & Jones, 2015).

This review also identified that not only were working memory tasks different by design, but where design was comparable, the metric for assessing working memory ability was not. This was particularly pertinent for tasks that allow for sensitivity analyses, such as the *n*-back task, which allow for collection of data on hits, misses (or 'omission errors'), false alarms (or 'commission errors'), and correct rejections (Meule, 2017). These data can be combined in a number of ways to create outcome metrics that differ in their sensitivity to performance. In this review, only two of the six studies that used the *n*-back working memory task (Fuge et al., 2014; Quide et al., 2017) explicitly stated how they defined accuracy. Furthermore, only three of the six studies that used *n*-back tasks reported on reaction time (Phillip et al., 2013; Phillip et al., 2016; Quide et al., 2017). Ucok et al. (2015) stated that reaction time was assessed, but was not reported. In line with suggestions previously made (e.g., Meule, 2017), this review highlights the need for researchers to clearly define their outcome metric when describing the working memory task, to enable an accurate interpretation of the findings and comparability of task performance across studies.

The analysis examining whether clinical status moderated the relationship between early life stress and working memory suggested the relationship exists in both clinical and non-clinical samples. As cognitive deficits are often associated with mental illnesses such as depression and bipolar disorder (MacQueen & Memedovich, 2017), and schizophrenia (Kochunov, Coyle, & Rowland, 2017), the possible confound that mental illness poses has been raised as a methodology concern in some studies included in this review. For example, Majer et al. (2010) highlighted the lack of research examining the relationship between early life stress and working memory outside of clinical populations and suggested that future studies should focus on case-control designs in order to disentangle the complex interrelationships between mental illness, working memory and early life stress. While the results of the present study suggest early life stress may affect working memory ability in adulthood, independent of the presence or absence of mental illness, we too suggest that further research using case-control designs is needed.

We were unable to answer the question as to whether the relationship between early life stress and working memory varied as a function of the type of early life stress experienced, as the unique contribution of a particular type of early life stress was generally not able to be ascertained from the current data. As co-occurrence of early life stressors is reportedly highly prevalent (Felitti et al., 1998), we acknowledge that finding a sample of individuals with only one form of early life stress is difficult. One study included in this review (Cromheeke et al., 2014) attempted to control for other types of stress by comparing working memory performance among individuals with early life stress (i.e., sexual and/or physical abuse) with two control groups; a non-interpersonal abuse group (i.e., life threatening accident or illness) and a traditional control group (i.e., no abuse or stress). While this approach allows for a more nuanced analysis of the effect of early life stress on working memory, the effects of specific forms of early life stress (e.g., sexual vs. physical abuse) cannot be disentangled.

The results of this review also have implications for clinical practice. Clinicians working with clients who have experienced early life stress need to be aware of possible cognitive difficulties faced by these clients. This is important in psychology practice as many of the therapeutic interventions used to manage psychopathology commonly associated with early life stress, such as anxiety and depression (Heim & Nemeroff, 2001), have a cognitive-based component (e.g., cognitive behaviour therapy, CBT; Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012). As working memory is involved in many everyday tasks such as reading, comprehension (Chiappe et al., 2000) and problem solving (Bull & Scerif, 2001), a deficit in this area may reduce a client's ability to engage with these kinds of therapy, particularly CBT skills such as thought challenging and cognitive restructuring. Future research is needed to gain an understanding of the role of working memory in cognitive-based therapies.

In conclusion, the results of this systematic review and meta-analysis provide support for a relationship between early life stress and working memory. While a number of different measures of working memory were used in the included studies, the way in which working memory was assessed did not affect the strength of this relationship. These results suggest that both visuospatial and phonological working memory tasks, and both visually and aurally presented tasks may be used to assess this relationship, allowing for flexibility in future research design. It was also found that early life stress affects working memory performance similarly in individuals with and without a diagnosed mental health disorder. Due to the way in which early life stress data has been collected and categorised, questions regarding the unique contribution of specific types of early life stress could not be addressed. Further research into the co-occurrence of different forms of early life stress is needed to further our understanding of the relationship between early life stress and working memory.

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References

Aas, M., Steen, N. E., Agartz, I., Aminoff, S. R., Lorentzen, S., Sundet, K., Andreassen, O. A. Melle, I. (2012). Is cognitive impairment following early life stress in severe mental disorders based on specific or general cognitive functioning? *Psychiatry Research, 198*(3), 495-500. doi: 10.1016/j.psychres.2011.12.045

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (5th Edition*). Arlington, VA: Author.

Baddeley, A. D. (2017). Exploring Working memory: Selected works of Alan Baddeley. London, UK: Routledge. Baddeley, A. D., & Hitch, G. (1974). Working memory. *Psychology of Learning and Motivation, 8*, 47-89. doi: 10.1016/S0079-7421(08)60452-1

Baddeley, A., Gathercole, S., & Papagno, C. (1998). The phonological loop as a language learning device. *Psychological Review, 105*(1), 158. doi: 10.1037/0033-295X.105.1.158

Baddeley, A. D., & Hitch, G. (1974). Working memory. Psychology of Learning and Motivation, 8, 47–89.

Begemann, M., Daalman, K., Heringa, S., Schutte, M., & Sommer, I. (2016). Childhood trauma as a risk factor for psychosis: The confounding role of cognitive functioning. *Psychological Medicine, 46*(5), 1115-1118. doi: 10.1017/S003329171500255X

Borenstein, M., Hedges, L., Higgins, J., & Rothstein, H. (2011). Comprehensive Meta-Analysis Version 2. Englewood, NJ: Biostat.

Bull, R., Espy, K. A., & Wiebe, S. A. (2008). Short-term memory, working memory, and executive functioning in preschoolers: Longitudinal predictors of mathematical achievement at age 7 years. *Developmental Neuropsychology, 33*(3), 205-228. doi: 10.1080/87565640801982312

Bull, R., & Scerif, G. (2001). Executive functioning as a predictor of children’s mathematics ability: Inhibition, switching, and working memory. *Developmental Neuropsychology*, *19*(3), 273–293.

Bücker, J., Kozicky, J., Torres, I. J., Kauer-Sant’anna, M., Silveira, L. E., Bond, D. J., Lam, R. W., Yatham, L. N. (2013). The impact of childhood trauma on cognitive functioning in patients recently recovered from a first manic episode: Data from the Systematic Treatment Optimization Program for Early Mania (STOP-EM). *Journal of Affective Disorders, 148*(2–3), 424-430. doi: 10.1016/j.jad.2012.11.022

Campbell, C. Barrett, S., Shannon, C., Hoy, K., Rushe, T., Cooper, S., Mulholland, C. (2013). The relationship between childhood trauma and neuropsychological functioning in first episode psychosis. *Psychosis: Psychological, Social and Integrative Approaches, 5*(1), 48-59. doi: 10.1080/17522439.2012.660982

Chiappe, P., Siegel, L. S., & Hasher, L. (2000). Working memory, inhibitory control, and reading disability. *Memory & Cognition, 28*(1), 8-17.

Conway, A. R., Kane, M. J., & Engle, R. W. (2003). Working memory capacity and its relation to general intelligence. *Trends in Cognitive Sciences, 7*(12), 547-552. doi: 10.1016/j.tics.2003.10.005

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences (2nd ed.)*. Hillsdale, NJ: Erlbaum.

Cromheeke, S., Herpoel, L., & Mueller, S. C. (2014). Childhood abuse is related to working memory impairment for positive emotion in female university students. *Child Maltreatment, 19*(1), 38-48. doi: 10.1177/1077559513511522

Danese, A., Moffitt, T. E., Arseneault, L., Bleiberg, B. A., Dinardo, P. B., Gandelman, S. B., Houts, R., Ambler, A., Fisher, H. L., Poulton, R., Caspi, A. (2017). The origins of cognitive deficits in victimized children: Implications for neuroscientists and clinicians. *The American Journal of Psychiatry, 174*(4), 349-361. doi: 10.1176/appi.ajp.2016.16030333

Dannehl, K., Rief, W., & Euteneuer, F. (2017). Childhood adversity and cognitive functioning in patients with major depression. *Child Abuse & Neglect, 70*, 247-254. doi:10.1016/j.chiabu.2017.06.013

D'Esposito, M., & Postle, B. R. (2015). The cognitive neuroscience of working memory. *Annual Review of Psychology, 66*, 115-142. doi: 10.1146/annurev-psych-010814-015031

Dunn, E. C., Busso, D. S., Raffeld, M. R., Smoller, J. W., Nelson, C. A., Doyle, A. E., & Luk, G. (2016). Does developmental timing of exposure to child maltreatment predict memory performance in adulthood? Results from a large, population-based sample. *Child Abuse & Neglect, 51*, 181-191. doi: 10.1016/j.chiabu.2015.10.014

Duval, S., & Tweedie, R. (2000). Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics, 56*(2), 455–463.

Fuge, P., Aust, S., Fan, Y., Weigand, A., Gartner, M., Feeser, M., Bajbouj, M., & Grimm, S. (2014). Interaction of early life stress and corticotropin-releasing hormone receptor gene: Effects on working memory. *Biological Psychiatry, 76*(11), 888-894. doi: 10.1016/j.biopsych.2014.04.016

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ*, *315*(7109), 629–634. doi: 10.1136/bmj.315.7109.629

Ellis, P. (2010). *The Essential Guide to Effect Sizes: Statistical Power, Meta-Analysis, and the Interpretation of Research Results.* Cambridge, UK: Cambridge University Press

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., & 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*(4), 245-258. doi: 0.1016/S0749-3797(98)00017-8

Gilbert, L. K., Breiding, M. J., Merrick, M. T., Thompson, W. W., Ford, D. D., Dhingra, S. S., & Parks, S. E. (2015). Childhood adversity and adult chronic disease: an update from ten states and the District of Columbia, 2010. *American Journal of Preventative Medicine, 48*(3), 345-349. doi: 10.1016/j.amepre.2014.09.006.

Gonzalez, A., Jenkins, J. M., Steiner, M., & Fleming, A. S. (2012). Maternal early life experiences and parenting: The mediating role of cortisol and executive function. *Journal of the American Academy of Child & Adolescent Psychiatry, 51*(7), 673-682. doi: 10.1016/j.jaac.2012.04.003

Hedges, L. V., & Pigott, T. D. (2004). The power of statistical tests for moderators in meta-analysis. *Psychological methods*, *9*(4), 426.

Heim, C., & Nemeroff, C. B. (2001). The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. *Biological Psychiatry, 49*(12), 1023-1039. doi:

Henry, L., & MacLean, M. (2003). Relationships between working memory, expressive vocabulary and arithmetical reasoning in children with and without intellectual disabilities. *Educational and Child Psychology, 20*(3), 51-63.

Hofmann, S. G., Asnaani, A., Vonk, I. J., Sawyer, A. T., & Fang, A. (2012). The efficacy of cognitive behavioral therapy: A review of meta-analyses. *Cognitive Therapy and Research, 36*(5), 427-440. doi: 10.1007/s10608-012-9476-1.

Irigaray, T. Q., PachecoI, J. B., Grassi-Oliveira, R., Fonseca, R. P., de Carvalho Leite, J. C., & Kristensen, C. H. (2013). Child maltreatment and later cognitive functioning: A systematic review. *Psychology: Reflection and Criticism, 26*(2), 376-387. doi:10.1590/S0102-79722013000200018

Kochunov, P., Coyle, T. R., Rowland, L. M., Jahanshad, N., Thompson, P. M., Kelly, S., … Hong, L. E. (2017). Association of White Matter With Core Cognitive Deficits in

Patients With Schizophrenia. JAMA Psychiatry, 74(9), 958–966. Doi: 10.1001/jamapsychiatry.2017.2228

Lei, M. K., Beach, S. R. H., & Simons, R. L. (2018). Childhood trauma, pubertal timing, and cardiovascular risk in adulthood. *Health Psychology, 37*(7), 613–617. Doi: 10.1037/hea0000609

Lu, S., Pan, F., Gao, W., Wei, Z., Wang, D., Hu, S., Huang, M., Xu, Y., & Li, L. (2017). Neural correlates of childhood trauma with executive function in young healthy adults. *Oncotarget, 8*(45), 79843-79853. Doi: 10.18632/oncotarget.20051

Lysaker, P. H., Meyer, P., Evans, J. D., & Marks, K. A. (2001). Neurocognitive and symptom correlates of self-reported childhood sexual abuse in schizophrenia spectrum disorders. *Annals of Clinical Psychiatry, 13*(2), 89-92. doi: 10.1023/A:1016667624487

Macken, B., Taylor, J., & Jones, D. (2015). Limitless capacity: a dynamic object-oriented approach to short-term memory. *Frontiers in Psychology, 6*. Doi: 10.3389/fpsyg.2015.00293

MacQueen, G. M., & Memedovich, K. A. (2017). Cognitive dysfunction in major depression and bipolar disorder: Assessment and treatment options. *Psychiatry and Clinical Neurosciences, 71*(1), 18–27. Doi: 10.1111/pcn.12463

Majer, M., Nater, U. M., Lin, J. M., Capuron, L., & Reeves, W. C. (2010). Association of childhood trauma with cognitive function in healthy adults: a pilot study. *BMC Neurology, 10*, 61. doi:10.1186/1471-2377-10-61

Masson, M., Bussieres, E.-L., East-Richard, C., R-Mercier, A., & Cellard, C. (2015). Neuropsychological profile of children, adolescents and adults experiencing maltreatment: A meta-analysis. *The Clinical Neuropsychologist, 29*(5), 573-594. doi:10.1080/13854046.2015.1061057

Meule, A. (2017). Reporting and Interpreting Working Memory Performance in n-back Tasks. *Frontiers in Psychology, 8*. Doi: 10.3389/fpsyg.2017.00352

Miller, S., McTeague, L. M., Gyurak, A., Patenaude, B., Williams, L. M., Grieve, S. M., . . . Etkin, A. (2015). Cognition-chilhood maltreatment interactions in the prediction of antidepressant outcomes in major depressive disorder patients: Results from the iSPOT-D trial. *Depression and Anxiety, 32*(8), 594-604. doi: 10.1002/da.22368

Morey, C. C. (2018). The case against specialized visual-spatial short-term memory. *Psychological Bulletin, 144*(8), 849–883. Doi: 10.1037/bul0000155

Mugge, J. R., Chase, S. L., & King, A. R. (2016). Child peer abuse and perceptions of executive-functioning competencies. *Applied Neuropsychology: Child, 5*(1), 67-75. doi: 10.1080/21622965.2014.986327

Narvaez, J. C., Magalhaes, P. V., Trindade, E. K., Vieira, D. C., Kauer-Sant'anna, M., Gama, C. S., von Diemen, L., Kapczinski, N. S., & Kapczinski, F. (2012). Childhood trauma, impulsivity, and executive functioning in crack cocaine users. *Comprehensive Psychiatry, 53*(3), 238-244. doi:10.1016/j.comppsych.2011.04.058

Parolin, M., Simonelli, A., Mapelli, D., Sacco, M., & Cristofalo, P. (2016). Parental substance abuse as an early traumatic evnt. Preliminary findings on neuropsychological and personality functioning in young drug addicts exposed to drugs early. *Frontiers in Psychology, 7,* 887. Doi: 10.3389/fpsyg.2016.00887.

Philip, N. S., Sweet, L. H., Tyrka, A. R., Price, L. H., Carpenter, L. L., Kuras, Y. I., Clark, U. S., & Niaura, R. S. (2013). Early life stress is associated with greater default network deactivation during working memory in healthy controls: a preliminary report. *Brain Imaging and Behavior, 7*(2), 204-212. doi:10.1007/s11682-012-9216-x

Philip, N. S., Sweet, L. H., Tyrka, A. R., Carpenter, S. L., Albright, S. E., Price, L. H., & Carpenter, L. L. (2016). Exposure to childhood trauma is associated with altered n-back activation and performance in healthy adults: implications for a commonly used working memory task. *Brain Imaging and Behavior, 10*(1), 124-135. doi: 10.1007/s11682-015-9373-9

Quide, Y., O'Reilly, N., Rowland, J. E., Carr, V. J., Elzinga, B. M., & Green, M. J. (2017). Effects of childhood trauma on working memory in affective and non-affective psychotic disorders. *Brain Imaging and Behavior, 11*(3), 722-735. doi:10.1007/s11682-016-9548-z

Rivera-Velez, G. M., Gonzalez-Viruet, M., Martinez-Taboas, A., & Perez-Mojica, D. (2014). Post-traumatic stress disorder, dissociation, and neuropsychological performance in Latina victims of childhood sexual abuse. *Journal of Child Sexual Abuse, 23*(1), 55-73. doi:10.1080/10538712.2014.864746

Sacks, V. H., Murphey, D., & Moore, K. (2014). Adverse childhood experiences: National and state-level prevalence. *Child Trends, 28*. 1-11. doi: 10.13140/2.1.1193.8087

Saleh, A., Potter, G. G., McQuoid, D. R., Boyd, B., Turner, R., MacFall, J. R., & Taylor, W. D. (2017). Effects of early life stress on depression, cognitive performance and brain morphology. *Psychological Medicine, 47*(1), 171-181. doi: 10.1017/s0033291716002403

Schalinski, I., Teicher, M. H., Carolus, A. M., & Rockstroh, B. (2017). Defining the impact of childhood adversities on cognitive deficits in psychosis: An exploratory analysis. *Schizophrenia Research*, 351-356. doi: 10.1016/j.schres.2017.05.014

Schneider, F. D., Loveland Cook, C. A., Salas, J., Scherrer, J., Cleveland, I. N., Burge, S. K., & for the Residency Research Network of Texas Investigators. (2017). Childhood Trauma, Social Networks, and the Mental Health of Adult Survivors. *Journal of Interpersonal Violence*, 1-23. Doi: 10.1177/0886260517696855

Shannon, C., Douse, K., McCusker, C., Feeney, L., Barrett, S., & Mulholland, C. (2011). The association between childhood trauma and memory functioning in schizophrenia. *Schizophrenia Bulletin, 37*(3), 531-537. doi: 10.1093/schbul/sbp096

Spies, G., Ahmed-Leitao, F., Fennema-Notestine, C., Cherner, M., & Seedat, S. (2016). Effects of HIV and childhood trauma on brain morphometry and neurocognitive function. *Journal of Neurovirology, 22*(2), 149-158. doi: 10.1007/s13365-015-0379-2

Thompson, S. G., & Sharp, S. J. (1999). Explaining heterogeneity in meta-analysis: a comparison of methods. *Statistics in medicine*, *18*(20), 2693-2708.

Üçok, A., Kaya, H., Uğurpala, C., Çıkrıkçılı, U., Ergül, C., Yokuşoğlu, Ç., Bülbül, Ö., Direk, N. (2015). History of childhood physical trauma is related to cognitive decline in individuals with ultra-high risk for psychosis. *Schizophrenia Research, 169*(1), 199-203. doi:10.1016/j.schres.2015.08.038

Viola, T. W., Tractenberg, S. G., Pezzi, J. C., Kristensen, C. H., & Grassi-Oliveira, R. (2013). Childhood physical neglect associated with executive functions impairments in crack cocaine-dependent women. *Drug and Alcohol Dependence, 132*(1-2), 271-276. doi:10.1016/j.drugalcdep.2013.02.014

World Health Organisation [WHO]. (2009). Adverse Childhood Experiences International Questionnaire (ACE-IQ). Retrieved from: http://www.who.int/violence_injury_prevention/violence/activities/adverse_childhood_experiences/en/

Table 1.

Explanations of point allocation for each study quality criterion.

Criterion		0 Points	1 Point	2 Points
1) Early Life Stress Measure		Neither objective nor validated	Objective OR validated	Objective AND validated
2) Working Memory Task		Neither objective nor validated	Objective OR validated	Objective AND validated
3) Sample Size:	Means	< 15 per group	15 - 30 per group	> 30 per group
	Correlation	< 30	30 - 50	> 50
	Regression	< 10 per predictor	10 - 20 per predictor	> 20 per predictor
4) Data Availability		Insufficient for meta-analysis AND not provided by author on request	Insufficient for meta-analysis but provided by author on request	Sufficient data for meta-analysis included in the publication

Note. Possible total scores ranged from 0 to 8. Descriptors were applied based on total score: Poor = 0-2, Fair = 3-5, Good = 6-8.

Table 2.
Characteristics and summary of results from each included publication.

Study First author (year)	Sample	ELS Category	WM Task	Design	Relevant Findings	Study Quality
Aas (2012)	Mental illness with psychotic features (*n*=406)	PA, SA, EA, EN, PN (Specified)	WM Composite (LNS, DSF & DSB)	Comparison of means (low & high ELS groups)	Low PA, SA, & PN category participants performed better on WM than the high PA, SA & PN groups. No differences in WM between high and low EA and EN groups.	Good
Begermann (2016)	Psychosis (*n*=101) and non-clinical controls (*n*=101)	PA, SA, EA, EN, PN (Combined)	DSB	Regression	ELS was not a significant predictor of WM performance in both samples.	Good
Bucker (2013)	Bipolar disorder (*n*=26) and non-clinical controls (*n*=38)	PA, SA, EA, PN, EN (Combined)	LNS	Correlation	No relationship.	Good
			CANTAB Spatial WM task	As above	High ELS was related to better WM performance for the bipolar group only.	
Campbell (2014)	First episode psychosis (*n*=30)	EN, EA, bodily threat, sexual harassment, SA (Combined)	SS	Comparison of means (ELS group & non-ELS group)	The non-ELS group performed better than the ELS group.	Fair
			DSF	As above	No significant difference.	
			DSB	As above	As above	
Cromheeke (2014)	Non-clinical participants (*n*=38)	PA & SA (Combined) & *life-threatening accident/illness*	Spatial emotional match to sample task	Comparison of means (Abuse ELS, Non-abuse ELS, & non-ELS groups)	No significant difference.	Fair

Danese et. al. (2016)	E-Risk Longitudinal Twin Study (*n*=2,044)	PN, EA, PA,SA (Combined)	CANTAB Spatial WM	Regression	ELS predicted poorer performance.	Good
			SSF	As above	As above	
			SSB	As above	As above	
	Dunedin Multidisciplinary Health and Development Study (*n*=2,037)	EA, PA, SA, EN, PN (Combined)	WAIS WM Index	Regression	ELS predicted poorer performance.	
Dannehl (2017)	Major depression (*n*=91) and non-clinical controls (*n*=40)	SA, PA, EA, PN, EN (specified)	DSF	Regression	Only SA predicted worse performance on DSF for the depression group. EN predicted poorer performance for the control group	Good
			DSB	Regression	No significant relationships for DSB for depression group. EN predicted poorer performance for the control group.	
Dunn (2016)	National Longitudinal Study of Adolescent to Adult Health (*n*=10,788)	PA, SA (specified)	DSB	Regression	PA & SA were not significant predictors of WM performance.	Good
Fuge (2014)	Non-clinical participants (*n*=541)	PA, SA, EA, PN, EN (Combined)	*n*-Back (2-back)	Comparison of means (No ELS, Low ELS, Moderate ELS, & Severe ELS groups)	Significant main effect of ELS on *n*-back performance. Higher *n*-back accuracy in participants with no exposure to ELS.	Good
Gonzalez (2012)	Postpartum mothers (*n*=89)	PA, SA, EA, PN, EN, inconsistent care (Combined)	CANTAB Spatial WM task	Correlation	No Significant relationship.	Good
Lysaker (2001)	Schizophrenia & schizoaffective disorder (*n*=43)	SA	LNS	Comparison of means (non-SA group & SA group)	The non-SA group performed significantly better on the WM tasks compared to the SA group.	Fair
Majer (2010)	Non-clinical participants (*n*=47)	PA, SA, EA, PN, EN (specified)	CANTAB Spatial WM task	Regression	EA, PA, & PN were significantly associated with double errors in the Spatial WM task.	Good

Miller (2015)	Major Depressive Disorder (*n*=91)	Abuse, neglect, bullying*, medical illnesses, natural disasters* (Combined)	WM Composite (DSF & DSB)	Comparison of means (ELS group & non-ELS group)	The non-ELS group performance better on WM tasks (WM composite) than those in the ELS group. No significant difference when controlling for current depressive symptomology.	Good
Mugge (2016)	Non-clinical students and general population (*n*=96)	Bullying	BRIEF-A: WM subscale	Correlation and contrasts (bullied group & controls)	Higher bullying severity was associated with lower WM performance. Group contrasts were not significant.	Good
Narvaez (2012)	Substance use disorder (*n*=84)	PA, SA, EA, PN, EN (Combined)	WM Composite (DSF & DSB)	Comparison of means (ELS group & non-ELS group)	WM performance (WM composite) was significantly greater in the non-ELS group.	Good
Parolin (2016)	SUD & childhood drug exposure (*n*=15), SUD & no exposure (*n*=15), & non-clinical controls (*n*=15)	Adverse family environment: biological parent with SUD	DS	Comparison of impairment rates (Early exposure & no early exposure)	No group differences on DS.	Fair
Philip (2016)	Non-clinical participants (*n*=26)	PA, SA, EA, PN, EN (Combined)	*n*-back (2-back)	Comparison of means (ELS & non-ELS groups)	The control group had significantly better accuracy on the WM task compared to the ELS group.	Fair
Philip (2013)	Non-clinical participants (*n*=19)	19 ELS categories including PA, SA, death in family, divorce (Combined)	*n*-back (2-back)	Comparison of means (ELS & non-ELS groups)	No significant differences.	Fair
Quide (2017)	Various mental illnesses (*n*=92) and non-clinical participants (*n*=45)	PA, SA, EA, PN, EN (Combined)	*n*-back (2-back)	Comparison of means (ELS & non-ELS groups for both samples)	No significant differences.	Good
Rivera-Velez (2014)	Females with SA (*n*=12) and No-SA controls (*n*=12)	SA	LNS	Comparison of means (SA & non-SA groups)	The non-SA group performed better on the LNS task than the SA group.	Fair

			DSF	As above		
			DSB	As above	No significant difference.	
Saleh (2017)	Major Depressive Disorder (*n*=64) & Healthy participants (*n*=65)	19 ELS Categories including PA, SA, EA, Neglect (Combined)	WM Composite (DSF & DSB)	Regression	No significant main effect of total ELS score on WM.	Fair
Schalinski (2017)	Psychosis (*n*=168) & Non-clinical controls (*n*=50)	EA, PA (specified)	WM Composite (SS & LNS)	Regression	Abuse at age 2 and age 3 predicted WM composite performance.	Fair
Shannon (2009)	Schizophrenia (*n*=85)	PA, SA, EA, PN, EN (Combined)	LNS	Comparison of means (ELS & non-ELS groups)	The non-ELS group displayed higher WM performance, compared to the ELS group.	Good
Spies (2017)	Non-clinical HIV^{+} women (*n*=67), HIV^{-} women (*n*=50)	EA, PA, SA, EN, PN (Combined)	SS	Relevant statistics not reported in published article.	-	Fair
Ucok (2015)	Psychosis (*n*=53)	PA, SA, EA, PN, EN (specified)	*n*-back (2-back)	Comparison of means (ELS & non-ELS groups for each ELS category)	No significant differences.	Fair
			DSF	As above	The non-PA group performance significantly better than the PA group.	
			DSB	As above	No significant differences.	
Viola (2013)	Substance abuse (*n*=85)	PN (specified)	*n*-back (1-back)	Comparison of means (PN & non-PN)	No significant difference.	Good
			n-back (2-back)	As above	The non-PN group performed better than the PN group.	

	n-back (3-back)	As above	As above
	LNS	As above	As above

Note. PA = Physical abuse. SA = Sexual abuse. EA = Emotional abuse. PN = Physical neglect. EN = Emotional neglect. Non-interpersonal early life stress is italicised. WM = working memory. CANTAB = Cambridge Neuropsychological Test Automated Battery. LNS = Letter-number sequencing. DSF = Digit span forwards. DSB = Digit span backwards. SS = Spatial span. WAIS = Weschler Adult Intelligence Scale. BRIEF-A = Behavior Rating Inventory of Executive Function (adult version). NS = Not specified. ELS specified = analyses were completed on specific ELS variables. ELS cumulative = analyses were completed on a cumulative ELS variable. SUD = Substance Use Disorder. Non-personal trauma types are in italics.

Table 3.
A summary of the working memory (WM) measures used in the included publications, classified by domain and presentation modality.

WM Task	Description	Domain	Modality	Outcomes	Used in *n* (*k*)
Self-report measures					
Behaviour Rating Inventory of Executive Function	A self-report questionnaire of executive functioning. The WM subscale consists of 10 statements such as, "*I have trouble with jobs or tasks with more than one step*", to which participants respond on a 3-point scale.	N/A	N/A	WM subscale score	1 (1)
Performance-based Measures					
CANTAB Spatial WM Task	Participants are presented with 'boxes' on screen. By process of elimination they are required to search the boxes to find 'tokens', without revisiting boxes already searched.	VS	V	Strategy score No. of errors	4 (9) 3 (8)
Digit Span (forward & backward)	A string of digits is presented. Participants are required to repeat the digits in the same (forward) order or in the reverse (backward) order.	P	A	Accuracy	10 (29)
Letter-Number Sequencing	A string of digits and letters is presented. Participants must repeat the stimuli in alphabetical and numerical order.	P	A	Accuracy	7 (14)
n-Back	A series of stimuli (letters or digits) are presented one after another. Participants are required to indicate if they saw/heard the current item *n* items ago.	P	V or A	Accuracy Reaction time	6 (8) 3 (4)
Spatial Emotional Match to Sample Task	Participants are presented with a face in 1 of 24 locations on screen, followed by a distractor and then a target face. Participants are required to indicate if the target face was in the same location as the cue face presented at the start of the trial.	VS	V	Miss score Match score	1 (1) 1 (1)
Spatial Span (forward & Backward)	A string of stimuli (dots or shapes) are presented. Participants indicate where each item appeared in the same (forward) or reverse (backward) order.	VS	V	Accuracy	4 (7)
WAIS WM Index	A standardised composite score including digit span and arithmetic (aurally presented mathematics problems).	P	A	WM index score	1 (1)

Note. Domain: P = Phonological, VS = Visuospatial. Modality: A = auditory, V = visual. Used in *n* = number of studies, *k* = number of outcomes (including tasks in WM composites). CANTAB = Cambridge Neuropsychological Test Automated Battery. WAIS = Weschler Adult Intelligence Scale.

Table 4.
Effect sizes (Hedge's g and 95% CI) showing the strength of the relationship between early life stress and working memory, and classification by working memory domain, presentation modality and clinical status. Positive values indicate early life stress is related to poorer working memory.

First author (year)	Outcome	Effect size & 95% CI			Classification		
		Hedges *g*	Lower	Upper	Domain	Modality	Clinical Status
Aas (2012)	WM composite	0.19	-0.01	0.39	P	A	NC
Begermann (2016)	Digit span backwards	0.16	-0.12	0.44	P	A	-
Bucker (2016)	CANTAB spatial WM task: Errors	0.28	-0.22	0.78	VS	V	C
	CANTAB spatial WM task: Strategy	0.51	-0.01	1.02	VS	V	C
	Letter number sequencing	-0.30	-0.80	0.20	P	A	C
	CANTAB spatial WM task: Errors	0.63	-0.17	1.43	VS	V	NC
	CANTAB spatial WM task: Strategy	0.57	-0.23	1.36	VS	V	NC
	Letter number sequencing	-0.10	-0.86	0.67	P	A	NC
Campbell (2013)	Digit span forwards	0.33	-0.44	1.09	P	A	C
	Digit span backwards	0.12	-0.64	0.88	P	A	C
	Spatial span	0.36	-0.40	1.13	VS	V	C
Cromheeke (2014)	Spatial emotional match to sample: Match	0.00	-0.63	0.63	VS	V	NC
	Spatial emotional match to sample: Miss	-0.01	-0.64	0.61	VS	V	NC
Danese (2016)	CANTAB spatial WM task: Errors	0.26	0.18	0.35	VS	V	NC
	CANTAB spatial WM task: Strategy	0.24	0.15	0.33	VS	V	NC
	Spatial span forwards	0.18	0.09	0.27	VS	V	NC
	Spatial span backwards	0.22	0.13	0.31	VS	V	NC
Dannehl (2017)	Digit span forwards	0.05	-0.67	0.47	P	A	C
	Digit span backwards	0.01	-0.41	0.42	P	A	C
	Digit span composite	0.99	0.28	1.70	P	A	NC
Dunn (2016)	Digit span backwards	0.03	-0.05	0.10	P	A	NC
Fuge (2014)	2-back accuracy	0.46	0.19	0.73	P	V	NC
Gonzalez (2012)	CANTAB spatial WM task: Strategy	0.16	-0.26	0.58	VS	V	NC
Lysaker (2001)	Letter number sequencing	0.55	-0.08	1.17	P	A	C
Majer (2010)	CANTAB spatial WM task: Errors	0.76	0.12	1.39	VS	V	NC
	CANTAB spatial WM task: Strategy	0.03	-0.55	0.61	VS	V	NC
Miller (2015)	Digit span composite	0.54	0.12	0.95	P	A	C
Mugge (2016)	BRIEF-A: WM subscale	0.47	0.06	0.88	-	-	NC
Narvaez (2012)	Digit span	0.50	0.04	0.96	P	A	C

Philip (2013)	2-back accuracy	-0.28	-1.14	0.59	P	V	NC
	2-back reaction time	-0.35	-1.22	0.42	P	V	NC
Philip (2016)	2-back accuracy	0.85	0.07	1.63	P	V	NC
	2-back reaction time	0.56	-0.20	1.32	P	V	NC
Quide (2017)	2-back accuracy	0.28	-0.14	0.69	P	V	C
	2-back reaction time	0.06	-0.35	0.48	P	V	C
	2-back accuracy	0.27	-0.32	0.85	P	V	NC
	2-back reaction time	0.09	-0.50	0.67	P	V	NC
Rivera-Velez (2013)	Digit span backwards	0.32	-0.46	1.10	P	A	NC
	Digit span forwards	0.18	-0.60	0.95	P	A	NC
	Letter number sequencing	0.78	-0.02	1.59	P	A	NC
Schalinski (2017)	WM composite	0.45	-0.09	0.99	-	-	C
Shannon (2009)	Letter number sequencing	0.23	-0.20	0.65	P	A	C
Spies (2017)	Spatial span	0.02	-0.55	0.59	VS	V	NC
Viola (2012)	2-back accuracy	0.45	0.02	0.89	P	A	C
	3-back accuracy	0.57	0.14	1.01	P	A	C
	Letter number sequencing	0.64	0.20	1.07	P	A	C

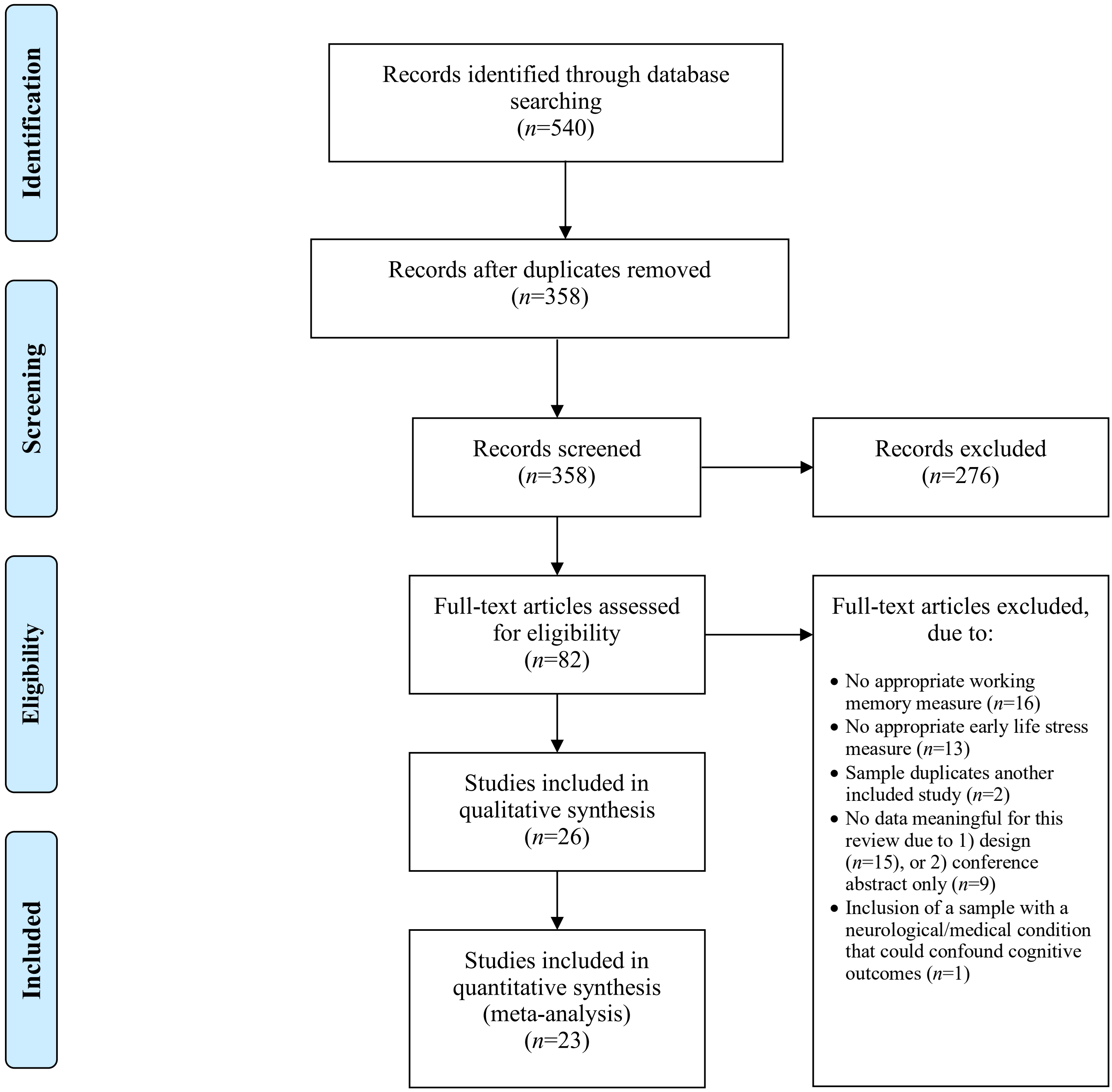
Note. Domain: P = Phonological, VS = Visuospatial. Modality: A = auditory, V = visual. Clinical Status: C = clinical, NC = non-clinical. Outcomes that were not solely defined by one of the two options in each classification are represented by a dash and were not included in the moderation analyses.

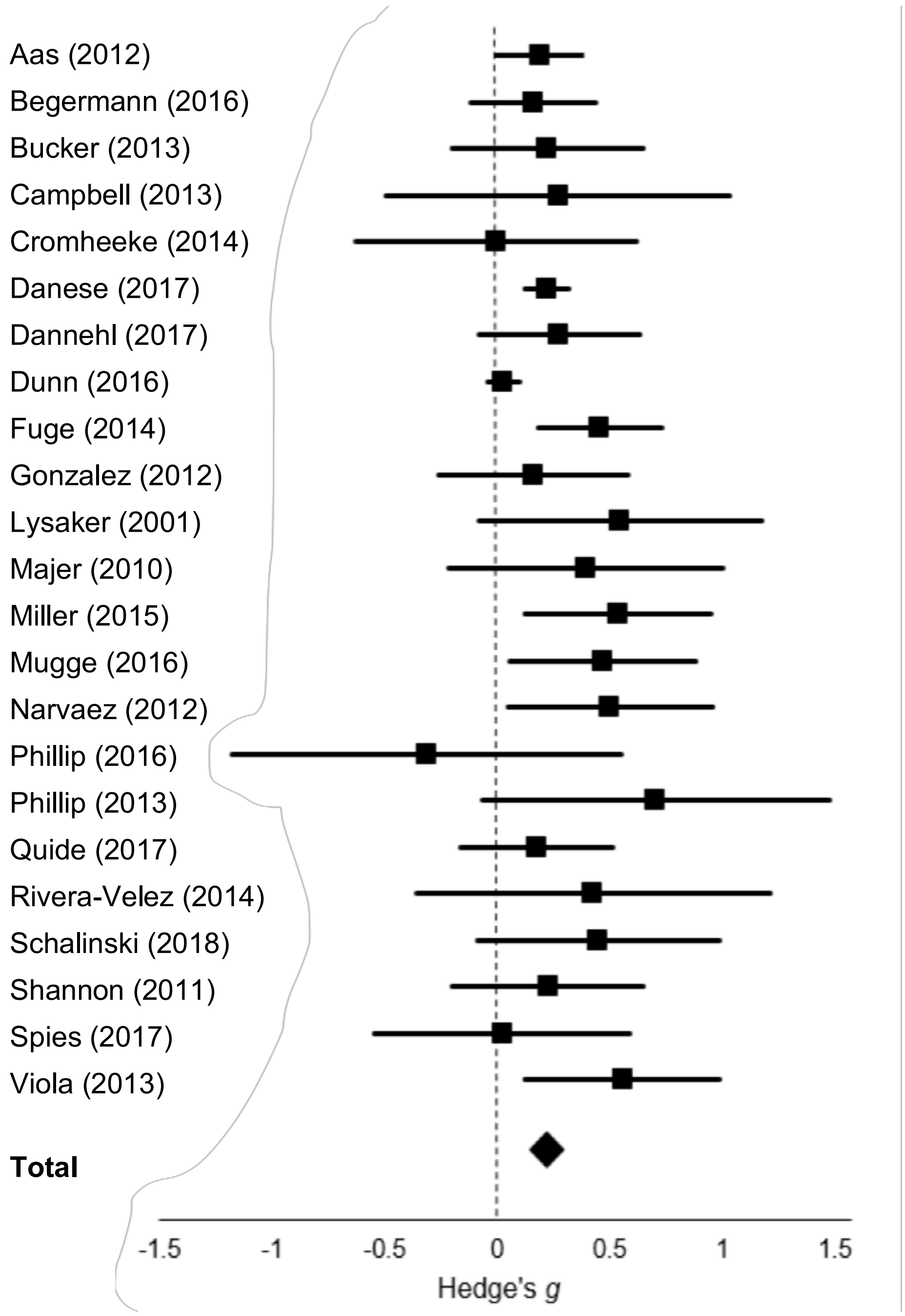
Figure Captions

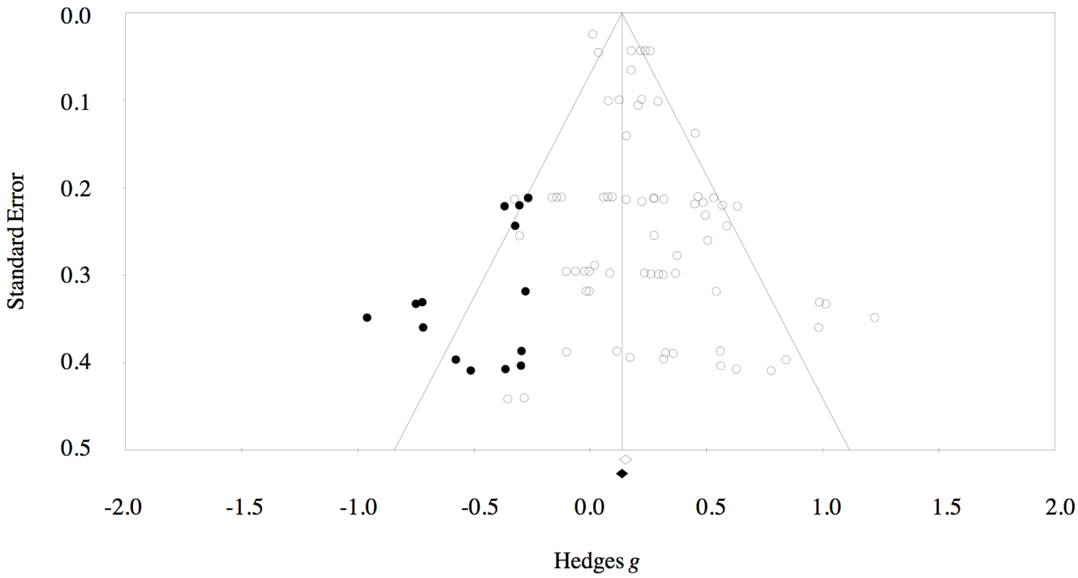
Figure 1. PRISMA flowchart illustrating the selection process for publications included in this systematic review and meta-analysis.

Figure 2. Forrest plot of the mean effect size (Hedge's *g*) and 95% CI for each included publication. Larger positive effect sizes indicate that increased early life stress is related to poorer working memory.

Figure 3. Funnel plot of standard error by Hedge's *g* of observed (open circles) and imputed (closed circles) outcomes and observed (open diamond) and corrected (closed diamond) mean effect size based on Duval and Tweedie's (2000) trim-and-fill procedure.


Identification
Screening
Eligibility
Included
Records identified through database searching (n=540)
Records after duplicates removed (n=358)
Records screened (n=358)
Records excluded (n=276)
Full-text articles assessed for eligibility (n=82)
Full-text articles excluded, due to:
• No appropriate working memory measure (n=16)
• No appropriate early life stress measure (n=13)
• Sample duplicates another included study (n=2)
• No data meaningful for this review due to 1) design (n=15), or 2) conference abstract only (n=9)
• Inclusion of a sample with a neurological/medical condition that could confound cognitive outcomes (n=1)
Studies included in qualitative synthesis (n=26)
Studies included in quantitative synthesis (meta-analysis) (n=23)


Aas (2012)
Begermann (2016)
Bucker (2013)
Campbell (2013)
Cromheeke (2014)
Danese (2017)
Dannehl (2017)
Dunn (2016)
Fuge (2014)
Gonzalez (2012)
Lysaker (2001)
Majer (2010)
Miller (2015)
Mugge (2016)
Narvaez (2012)
Phillip (2016)
Phillip (2013)
Quide (2017)
Rivera-Velez (2014)
Schalinski (2018)
Shannon (2011)
Spies (2017)
Viola (2013)
Total
-1.5
-1
-0.5
0
0.5
1
1.5
Hedge's g


0.0
0.1
0.2
0.3
0.4
0.5
Standard Error
-2.0
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
Hedges g