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Review article

Prenatal alcohol exposure and traumatic childhood experiences: A systematic review

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ABSTRACT

Prenatal alcohol exposure (PAE) and traumatic childhood experiences (trauma) such as abuse or neglect can each cause central nervous system neurobiological changes or structural damage which can manifest as cognitive and behavioural dysfunction. In cases where both exposures have occurred, the risk of neurodevelopmental impairment may be greater, but this interaction has not been well studied. Here we present a systematic review that identified five primary research studies which investigated either the impact of trauma in children with PAE, or of PAE in children with trauma. Due to the heterogeneity of studies, narrative analysis was applied. Children in these cohorts with both exposures were more likely to show deficits in language, attention, memory and intelligence, and exhibit more severe behavioural problems than children with one exposure in absence of the other. However, the current literature is scarce and methodologically flawed. Further studies are required that: assess dual exposure in other neurodevelopmental domains; feature developmentally impaired yet non-exposed controls; and account for the wide spectrum of effects and different diagnostic criteria associated with PAE.

1. Introduction

Prenatal alcohol exposure (PAE) can lead to a range of neurodevelopmental disorders collectively known as Fetal Alcohol Spectrum Disorder (FASD), and is a leading preventable cause of learning difficulties, with around 2% of all live births worldwide estimated to be affected (Roozen et al., 2016; Westrup, 2013). Alcohol is a teratogen which, when consumed by a pregnant woman, passes easily through the placenta and into the developing fetus, where it can disrupt healthy growth across the body, including in the brain (Goodlett et al., 2005). The type and scale of fetal damage depends on the amount, frequency and timing of alcohol exposures, as well as several other factors including maternal nutrition and metabolism, genetics and possibly epigenetics, and unknown fetal vulnerability factors (Mattson et al., 2001; Ungerer et al., 2013). The whole fetus is at risk of damage, and many somatic defects are seen in children prenatally exposed to alcohol, including low birthweight, microcephaly, craniofacial abnormalities and skeletal and organ defects (Hofer and Burd, 2009; O'Leary et al., 2010; Sawada Feldman et al., 2012). However, of particular interest here is damage to the brain and central nervous system. Improper brain development associated with prenatal exposure to alcohol can lead to a range of cognitive, behavioural and emotional difficulties (Greenbaum et al., 2009; Kingdon et al., 2015). These deficits can lead to a diagnosis of one or more of a range of disorders within the fetal alcohol spectrum, including Foetal Alcohol Syndrome (FAS; Jones & Smith, 1973).

The pathway by which prenatal exposure to alcohol can impact cognitive and behavioural development is illustrated by Kodituwakku & Kodituwakku (2014), who present a causal modelling framework adapted from Morton and Frith's (1995) model of autism. In its simplest terms, the framework describes how an initial exposure can cause organic brain damage, leading to simple and complex cognitive deficits in abilities such as attention and social cognition. These impairments can lead to a wide range of social and behavioural problems, especially as the child approaches adolescence.

Alcohol in the fetal compartment can disrupt development via a number of mechanisms, including programmed and unprogrammed cell death, oxidative stress, constriction of blood vessels, and disruption of neurotransmitter systems (Goodlett and Horn, 2001; Guerri et al., 2009). There is also increasing evidence of the role of epigenetic factors – prenatal and perinatal exposure to exogenous substances, including alcohol, can alter the expression of genes without altering their structure (Lussier et al., 2017). These and other mechanisms can lead to improper growth of the corpus callosum, hippocampus, basal gang-

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lia, dentate nucleus, thalamus, and parietal and frontal cortices (Donald et al., 2015). Damage to these areas is associated with a wide range of issues, including deficits in overall intelligence, learning, memory, (Davis et al., 2011) speech and language (O'Keeffe et al., 2014), executive functioning (Kingdon et al., 2015), social cognition, emotional processing (Greenbaum et al., 2009), and motor skills (Kalberg et al., 2006). These kinds of issues can become more apparent as the child reaches school age, where they are likely to struggle with academic and social demands. Executive functioning difficulties can lead to children being labelled as disruptive and they may be removed from the learning environment (Koren, 2015). Meanwhile, deficits in social cognition and language skills can prevent the development of positive peer relationships, leaving the child socially isolated (Kully-Martens et al., 2012).

Traumatic childhood experiences (trauma) such as maltreatment can lead to markedly similar neurological, cognitive and behavioural deficits as those caused by PAE (Norman et al., 2012; Rutter, 1998). Child maltreatment, as defined by the World Health Organisation, covers episodes of physical, sexual or psychological abuse, or physical or emotional neglect (Butchart et al., 2006). Other adverse childhood experiences, such as living with a drug user, or witnessing violence, may also be responsible for a wide range of physical and psychological problems (Felitti et al., 1998).

One explanation for the deficits seen following early trauma is that these experiences occur at such an age when the child is unable to regulate their own emotions. Infants rely on their caregivers to assist in the development of emotional self-regulation by attending, distracting or soothing during periods of stress, however, abusive or neglectful caregivers may fail to provide this assistance, instead leaving the infant in a prolonged and potentially harmful elevated psychophysiological state (Glaser, 2000). During periods of stress, the hypothalamic-pituitary-adrenal (HPA) axis is activated, involving the release of norepinephrine, adrenocorticotropic hormone (ACTH) and cortisol from the sympathetic nervous system, pituitary gland, and adrenal glands respectively (Neigh et al., 2009). Prolonged or frequent activation of this system during infancy is associated with immune and endocrine system dysfunction, and neurodevelopmental delay in adults (Neigh et al., 2009). Meanwhile, MRI studies suggest that abuse can have specific neuroanatomical outcomes. In one study, female victims of childhood sexual abuse were found to have a thinner than usual layer of cortical tissue in the genital representation area of the somatosensory cortex, suggesting that a lack of sensation has resulted from this traumatic event. Similarly, women with a history of emotional abuse showed reduced thickness in the regions associated with self-awareness (Heim et al., 2013).

The complex and covert nature of child maltreatment may prohibit accurate measurement of prevalence, but a recent review of international meta-analyses estimated that 13% of children had been sexually abused (8% of boys and 18% of girls), 23% of children had been physically abused, 36% had been emotionally abused, 16% had been physically neglected, and 18% had been emotionally neglected (Stoltenborgh et al., 2015). Studies into FASD prevalence rely on detection of CNS damage, and significant misdiagnosis is suspected (e.g. Chasnoff et al., 2015; Morleo et al., 2011). Estimated prevalence rates from a recent meta-analysis show around a 2% global prevalence of FASD, with rates of up to 11% in parts of South Africa, and around 3–4% in North America and Europe (Roozen et al., 2016). When considering rates of exposure of the fetus to alcohol, a recent meta-analysis estimated a global average of 9.8% of pregnant women who drink alcohol during pregnancy, with rates of more than 50% in some western countries (Popova et al., 2017).

A history of either PAE or trauma has the potential to cause permanent brain damage, leading to deficits in cognitive, social and behavioural domains, but the interaction of both exposures has been largely overlooked. It is possible that a compounding relationship exists here, where children born following PAE are more vulnerable to the impact of trauma, leading to more likely or more severe developmental deficit than expected following a single exposure. A potential mechanism for this is that PAE is associated with an increased stress response, which results from damage caused to the HPA axis (Hellemans et al., 2010). With a compromised HPA axis, trauma may have a greater impact on development following PAE, than in children without PAE. The potential overlap of exposures within the population also has implications for research methodology. Participants with a history of both exposures appear in databases labelled with either FASD or trauma, but their deficits and other characteristics may be the result of the other exposure, or the interaction of both (Henry et al., 2007). The present study reviewed all published research which sought to assess the interaction of both exposures, or provided evidence of the likelihood of both presenting together.

2. Methods

The review was conducted and reported according to the standards set out in Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher et al., 2009). Titles and abstracts were searched in online databases PubMed, Psycinfo, Medline, Cinahl, Web of Science, Academic Search Premier, Child Development and Adolescent Studies, and Maternity and Infant Care up to 16th August 2016. The same search terms were entered into each database. Terms relating to prenatal alcohol exposure such as FASD, fetal alcohol and prenatal exposure were searched for alongside terms relating to trauma such as abuse, maltreatment and neglect (see Appendix A for full search terms).

The abstracts of scholarly, peer-reviewed journal articles were searched. The following inclusion criteria were used: 1. Articles had to describe primary research into a) the effects of prenatal alcohol exposure and b) the impact of maltreatment including neglect and/or abuse in childhood; 2. Only studies using human participants were included; 3. All studies published before 16th August 2016 were included. Articles were excluded if they only compared participants suffering the effects of both exposures with non-affected, healthy controls. Articles were not screened based on outcome variable because the purpose of this review was to identify any and all outcome variables associated with the specific risk factors in question. Whilst no specific limits were set on language, only articles with an abstract available in English would have been returned.

3. Results

3.1. Study characteristics

The search returned 15,193 records, of which, 2369 were duplicates. Title and abstract screening led to the removal of a further 12,785 records, leaving 39 full-text articles to be assessed. Of these, three articles were found to meet the criteria. The reference sections of these three articles were searched for other relevant records, as well as Google Scholar options: 'Cited by' and 'Related articles'. These ensuing searches yielded a further two relevant articles which were not identified by the online database searches (Fig. 1).

Childhood maltreatment as we have defined above covers episodes of neglect and emotional, sexual and physical abuse. The five articles in this review differ somewhat in terms of their definitions, but all include the variable of maltreatment, albeit as part of a wider definition of trauma in some cases. Coggins et al. (2007) include maltreatment as we define it, although they use the term 'environmental risk'. Hyter (2012) uses the term 'complex trauma' which results from abuse or neglect. Henry et al. (2007) use the term 'traumatic stress' which they have based on the DSM-IV (APA, 1994) criteria for post-traumatic stress disorder, and the Traumagenic Impact of Maltreatment Rating (James, 1989). Koponen et al. (2009) and Koponen et al., (2013) use 'traumatic experiences', which as well as abuse and neglect, includes drug abuse by parents, witnessing violence, death of parents, criminal behaviour of

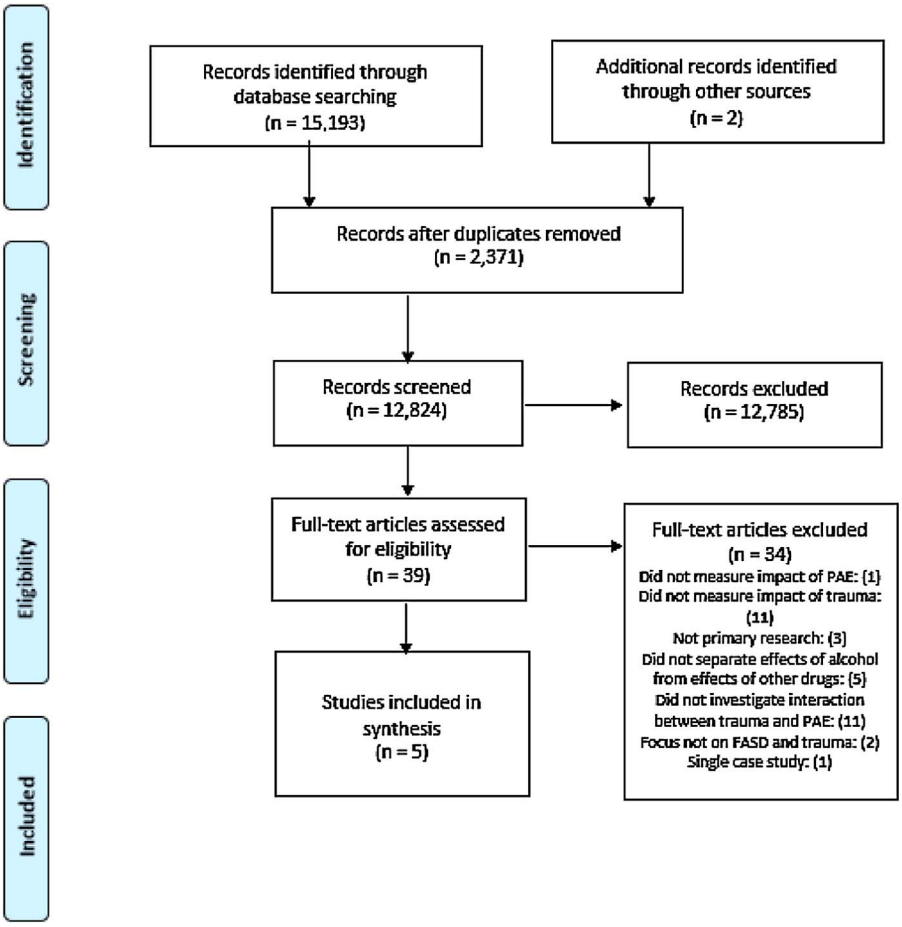

Fig 1. Flow diagram showing selection procedure.

parents, unemployment of parents, divorce of parents, mental health problems of parents, several placements in care system, and having lived in a children's home. Unless otherwise stated, for the purpose of this article we will use the term 'trauma' to refer to the range of definitions given by the authors of the reviewed articles.

Koponen et al. (2009) and Koponen et al. (2013) categorised patients as FAS and fetal alcohol effects (FAE; now mostly replaced by ARND), as well as undiagnosed children with prenatal alcohol exposure (PAE). Information on diagnoses and prenatal exposure was obtained from foster parents and social workers, and no details were given about which diagnostic codes were used. Children were not diagnosed by the study authors in either of these studies. Henry et al. (2007), Coggins et al. (2007) and Hyter (2012) used the FAS/DPN diagnostic code system for FASD (Astley, 2004), and their participants were diagnosed in-house. Coggins et al. report diagnoses of their participants (FAS, pFAS, etc. See Table 2) but Henry et al. and Hyter simply report FASD without giving diagnoses. The use of different diagnostic codes is an issue within FASD research, since it can be difficult to compare groups of participants whose diagnoses and neurodevelopmental profiles exist on a wide spectrum (Coles et al., 2016). The lack of diagnostic detail provided by some of the articles in this review restricts any conclusions, since participants with a diagnosis of FAS or pFAS may have a more severe neurodevelopmental impairment, and this may affect results from one study to another. Unless otherwise stated, for the purpose of this article we will use the term prenatal alcohol exposure (PAE) to refer to any diagnosis on the FASD spectrum as well as undiagnosed cases where damage related to prenatal alcohol exposure is suspected.

The five articles were assessed based on the extent to which they answered the research question: What is known about the compounding effects of prenatal alcohol exposure and childhood maltreatment? Two of the articles are reports of studies which compared a group exposed to both variables, to a group exposed to one variable. Henry et al. (2007), compared a group exposed to both to a group exposed to trauma only. Koponen et al. (2013) compared a group of foster children who were adopted at birth to a group of children who spent the first years of their lives with their birth parents. All children in this study were prenatally exposed to alcohol, and the authors report that those children who had lived with their birth parents had more traumatic experiences than the children adopted at birth. Henry et al. (2007) therefore examined the impact of prenatal alcohol exposure on children with history of trauma, whereas Koponen et al. (2013) examined the impact of trauma on children with prenatal alcohol exposure. A similar article, Hyter (2012), is a review which includes a short case study and preliminary results of a comparison which are not published elsewhere. The comparison is a follow up of Henry et al. (2007), using some of the same participants and comparing trauma and FASD with just trauma. Coggins et al. (2007) and Koponen et al. (2009) report cross-sectional studies into prenatal alcohol exposure and childhood maltreatment without using defined groups. Table 1 shows a breakdown of the five studies included in this review. Due to the heterogeneity of the articles featured, this review will be conducted in a narrative format, beginning with an assessment of the comorbidity of both disorders, leading to findings pertaining to speech and language, other cognitive deficits such as intelligence and memory, and finally social and behavioural problems. A selection of related studies, which came close to matching inclusion criteria, will then be summarised.

3.2. Comorbidity

Koponen et al. (2009) report that 58% of their sample of 38 fostered children with PAE were neglected by their birth parents; 36% witnessed violence, 16% were physically abused, and 5% were sexually abused. 40% of the sample of children with a history of trauma in Henry et al. (2007) were also prenatally exposed to alcohol, as were 32% of Hyter's (2012) sample of 106 children from the same cohort. Comorbidity data of this kind was unavailable for Koponen et al. (2013), who grouped their FASD participants based on whether they had been taken into care at birth or had lived with their birth parents. The mean number of traumatic experiences in the group adopted at birth was 0.6 (*SD* 0.5), and for the group who had lived with their birth parents this figure was 2.9 (*SD* 1.4). The sample of 573 children with FASD in Coggins et al. (2007) were assessed for trauma. Initially, 180 participants were removed as postnatal environment data was unavailable. Coggins et al. report that of the remaining 393 children, 19 had an unremarkable level of trauma, 39 had an unknown level, 162 had some level, and 173 had a high level of trauma. According to this analysis, more than 85% of the sample of children with FASD had experienced at least some level of trauma. However, the initial removal of data may be a factor here, especially since there was no data available for some of the remaining participants. If we include the whole original sample of 573 children, the rate of documented trauma becomes 58%; notably the same rate reported by Koponen et al. (2009). More worryingly perhaps, if we remove all the participants whose environmental data was unknown, the rate becomes 95% .

Of these studies, only Coggins et al. (2007) set out to assess rates of comorbidity in trauma and FASD, and this study appears to show a rate of between 58% and 95% of children with FASD having also experienced some form of trauma. However, the sample was taken from a clinic database, rather than the general population. Koponen et al. (2009), Koponen et al. (2013) used self-selecting samples of children from within the care system, and Henry et al. (2007) and Hyter (2012) recruited mostly through social services. These findings will therefore likely reflect the clinical situation, however the extent to which they can be extrapolated to the wider population is limited.

3.3. Comparisons

The five articles in this review featured some measure of the impact of one exposure on the other. Coggins et al. (2007) and Koponen et al. (2009) present correlational measurements of outcomes in children with FASD and trauma. Koponen et al. (2013) present a qualitative comparison between children with FASD who were taken into foster care at birth and children who lived with their birth parents before being fostered. Henry et al. (2007) and Hyter (2012) present quantitative comparisons between children with both exposures and children with just trauma. All five articles covered speech and language, three covered other cognitive deficits such as intelligence and memory, and four covered psychopathological, social and behavioural issues.

3.3.1. Speech and language

Coggins et al. (2007) measured language performance and narrative discourse performance in their cohort of children aged 6–12 years. Language performance was assessed using various measures, since data were collected over a number of years. Scores were categorised as either normal (< 1.25 standard deviations below the mean), mildly impaired (1.25–2 *SD* below *M*), or moderately to severely impaired (> 2 SD below M). 31% of children (n = 393) were found to be mildly impaired, while 38% were moderately to severely impaired. 85% of this sample had at least some experience of trauma, but no investigation of the relationship between language performance and trauma is presented. The figures suggest no significant correlation between language performance and level of trauma. In the narrative discourse tasks, children either re-told a story or generated a story from pictures depending on their age. The amount of information which children correctly reproduced was translated into a score. Children who obtained an information score above the 10th percentile (approximately 1.25 *SD* from the mean) were considered within the expected range of performance; children who scored at or below the 10th percentile were considered impaired. Of the younger children (age 6–7 years, n = 115), 50% re-told a story with an adequate level of detail, while the performance of the other 50% was considered impaired. 27% of the older children (age 8–12, n = 198), who generated a story from pictures, showed sufficient cohesion and coherence, whereas the remaining 73% were considered impaired. The authors report that no relationship was found between trauma and narrative discourse performance.

Koponen et al.'s (2009) cross-sectional study, and Koponen et al.'s (2013) qualitative comparison, both based on samples of children with FASD in foster care, also show some evidence of language problems associated with FASD. 12 out of Koponen et al.'s (2009) sample of 37 children showed difficulties with speech or language, but there is no indication of a relationship with trauma. Koponen et al. (2013) found that children in care from birth (who were much less likely to have

Table 1
Study characteristics.

Authors	Year	Country	Study design	Sample size	Age range	Items measured	Instruments
Coggins, Timler & Olswang	2007	USA	Cross-sectional	573	6–12	Prenatal risk Postnatal risk Language Social communication	Official records, caregiver interviews, language severity scale, narrative discourse performance tasks
Henry, Sloane & Black-Pond	2007	USA	Case-control	274	6–16	Motor function, language, memory, visual processing, intelligence, emotional, social and behavioural problems	PEEX 2, PEERAMID 2, Kaufman Brief Intelligence Test, Connors Rating Scales
Koponen, Kalland & Autti-Rämö	2009	Finland	Cross-sectional	38	1–15	Emotional, social and behavioural problems, somatic health, caregiving environment.	Caregiver & social worker questionnaires Caregiver interviews Child Behaviour Checklist
Hyter	2012	USA	Review featuring case study and preliminary results of case-control	106 + 1	6–16	Speech and language performance	PEEX 2, PEERAMID 2
Koponen, Kalland, Autti-Rämö, Laamanen & Suominen	2013	Finland	Case control	34	0–15	Behavioural problems, caregiving environment, socio-emotional development	Caregiver & social worker questionnaires Children's life stories written by caregivers Caregiver interviews

Table 2
Aims and methods of studies.

Study	Aims	Groups	FASD diagnostic criteria	Diagnoses of participants	Evidence of prenatal exposure	Method of evaluation	Robustness of evidence
Coggins et al., 2007	To assess the levels of environmental risk, language performance, and narrative discourse data within a clinical database of school-age children with fetal alcohol spectrum disorder.	Single cohort of 573 children with FASD and some level of trauma.	Participants diagnosed at clinic using the 4-digit diagnostic system.	FAS = 63 pFAS = 0 SE = 194 ND = 290 NCNSD = 26	Evidence was used in diagnosis, but data source is unclear.	Language severity scale, based on various commonly used speech and language pathology tests. Narrative discourse performance was measured using The bus story for 6–8 year olds and Frog, where are you? for 8–12 year olds. These tasks are ecologically valid measures of social communication and the child's ability to spontaneously produce meaningful language.	Large sample size. Language performance data was collected over a ten-year period, and as a result by several different tests. Rating system for traumatic experiences may be misleading − Scale of 1–4 where 2 represents unknown level of trauma.
Henry et al., 2007	To assess the impact on childhood neurodevelopment of prenatal alcohol exposure and postnatal traumatic experience compared to postnatal traumatic experience alone.	Two groups: 161 children who had experienced trauma, and 113 children with trauma and FASD.	Participants diagnosed at clinic using the 4-digit diagnostic system.	FASD group only reported as FASD.	Evidence was used in diagnosis, but data source is unclear.	Data was collected using a series of psychometric inventories and interviews including patient, parent, and teacher report forms. Children were assessed during a two-day clinic in language, intelligence, motor skills, memory, emotional social and behavioural problems.	Large sample size. Quasi-experimental design. Possible confound of ethnicity: 'Both' group 80% Caucasian, 9% African-American; 'just trauma' group 61% Caucasian, 26% African-American.
Koponen et al., 2009	To investigate the role of the postnatal caregiving environment in the socio-emotional development of children under the age of 16 who had been exposed to alcohol in utero and placed in foster family care.	Single cohort of 38 children living in foster care, all prenatally exposed to alcohol.	No diagnostic criteria given. Participants had either FAS, FAE or no diagnosis.	FAS = 22 FAE = 9 ND = 7	Information supplied by foster parents and social workers.	Informant questionnaires sent to foster carers and social workers to assess caregiving environment, illnesses, disabilities, attachment behaviour, and behavioural problems	Questionnaires were largely designed by the authors and relied mostly on the opinions of caregivers and social workers − uncertain validity of measures. Small sample size.
Hyter, 2012	This article is a review which features previously unpublished preliminary data from a study which sought to compare the impact of prenatal alcohol exposure and postnatal traumatic experience with postnatal traumatic experience alone on children's language and social communication.	Two groups: 72 children who had experienced trauma, and 34 children with trauma and FASD.	Participants diagnosed at clinic using the 4-digit diagnostic system.	FASD group only reported as FASD.	Evidence was used in diagnosis, but data source is unclear.	A follow up study to Henry et al. (2007; above), using a sample of the same participants. Language and social communication were assessed using standardised speech and language pathology tasks.	The findings in this review were previously presented at a conference, but were not published elsewhere. No methods section.
Koponen et al., 2013	To investigate the socio-emotional development of children with FASD in long-term foster family care, and assess the impact of age at first placement away from the biological family	Two groups, all with PAE: 7 children who were taken into care at birth, and 27 children who spent the first years of their lives with their biological parents.	No diagnostic criteria given. Participants had either FAS, FAE or no diagnosis.	FASD and trauma group: FAS = 16 FAE = 6 NDs = 5 Just FASD group: FAS = 4 FAE = 1 NDs = 2	Information supplied by foster parents and social workers.	This study grouped participants based on the amount of time they spent with their birth families: One group spent no time (fostered at birth) and the other group spent some time living with their birth family. Written life stories, interviews and questionnaires were used to assess socio-emotional development.	Participants taken from the same larger sample of 93 children from which Koponen et al. (2009; above) took their sample. Small sample size.

For the purpose of their study, Coggins et al. (2007) organised their participants into five diagnostic categories using the 4-digit code system. These were: Fetal Alcohol Syndrome (FAS), partial Fetal Alcohol Syndrome (pFAS), Static Encephalopathy (SE), Neurobehavioural Disorder (ND), and No Central Nervous System Dysfunction (NCNSD).
Koponen et al. (2009) and Koponen et al. (2013) use the diagnoses Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE) as well as the category of no diagnosis (NDs).

experienced trauma) had delays in understanding and producing speech. Problems found in those who had lived with their birth parents included: delay in speech development, naming problem, stammering, inability to converse, excessive speech, excessively loud speech, and absence of speech .

Henry et al. (2007) and Hyter (2012) divided their participants into two groups, who had: a) FASD and experience of trauma, or b) experience of trauma without FASD. Both studies measured differences in language using the Pediatric Early Elementary Examination (PEEX 2; Levine, 1996a) for children aged 6–8, and the Pediatric Examination of Educational Readiness at Middle Childhood (PEERAMID 2; Levine, 1996b) for children aged 9–15. This standardised measure gives a narrative description of a child's neurodevelopmental profile. Two tasks below age norms indicate a moderate delay for that specific domain, and three or more tasks below age norms indicate a major delay for that domain. Henry et al. report that 57% of children with just trauma ($n = 161$) showed moderate to major delays in receptive language, compared to 81% of children with both exposures ($n = 113$; $p < 0.001$), and that 50% of children with just trauma showed moderate to major delays in expressive language, compared to 72% of children with both exposures ($p = 0.001$). Hyter (2012) reports that children with both exposures ($n = 34$) were more likely to show deficits in phonological awareness (Cohen's $d = 0.12$, $p = 0.003$), semantics ($d = 0.31$, $p = 0.004$), syntax ($d = 0.47$, $p = 0.015$), and comprehension ($d = 0.31$, $p = 0.018$) than children with just trauma ($n = 72$).

3.3.2. Other cognitive deficits

Henry et al. (2007) measured intelligence using the Kaufman Brief Intelligence Test (Kaufman & Kaufman, 1990), which gives scores for verbal, non-verbal, and overall intelligence with a population mean of 100, and a standard deviation of 15. Children with history of trauma and FASD ($n = 113$) scored significantly lower in verbal intelligence ($d = 0.31$, $p = 0.007$), nonverbal intelligence ($d = 0.22$, $p = 0.04$), and in the composite score ($d = 0.42$, $p = 0.01$) than children with history of trauma only ($n = 161$). Mean scores in each group, and for each subtest, were within one standard deviation of the population mean and not clinically significant.

Koponen et al. (2009) asked foster parents to assess their children's developmental level compared to children of the same age on a three-point scale (better than average, average, worse than average) in the following areas: speech, interaction skills, obeying given orders, expressing own wishes, telling about own experiences, expressing attachment, expressing disappointment, understanding cause and effect, and physical exercise. Scores were found to correlate ($r = 0.47$, $p < 0.01$) with the child's age at his or her first placement away from the birth family. Children who were younger at the time of their first placement showed fewer deficits according to this measure, which suggests that trauma and FASD are predictive of developmental delay to a greater extent than FASD alone.

Henry et al. (2007) and Koponen et al. (2009) both found that deficits in attention were more likely with both exposures. Children with fewer than three traumatic experiences had fewer attention problems than those who had more, in a sample of children with FASD (Koponen et al., 2009), and 74% of children with history of trauma ($n = 161$) had moderate to major delays in attention compared to 89% of children with both exposures ($n = 113$; $p = 0.004$; Henry et al., 2007). Henry et al. also found deficits in memory were more likely in children with both exposures (87%) than in children with just trauma (71%; $p = 0.005$).

Henry et al. (2007) also measured differences between groups in visual processing, fine motor skills, gross motor skills, and graphomotor skills. Children with FASD as well as trauma were more likely to show deficits in each of these domains, but these differences were not statistically significant.

3.3.3. Social, emotional and behavioural problems

Hyter (2012) measured social communication skills using the PEEX 2 and PEERAMID 2 in 106 children with history of trauma, 34 of whom had FASD. Children with both exposures showed more deficits in conversational skills, narrative retelling, generated narrative, second order belief attribution, and comprehending other's intentions than children with trauma alone, but the differences were not statistically significant. Both groups showed clinically significant deficits compared to population norms.

Henry et al. (2007) used the Connors' Rating Scales − Revised (CRS-R; Connors, 1997), which consist of caregiver and teacher report forms, to measure emotional, social and behavioural problems in their sample of 274 children with history of trauma, 113 of whom also suffered from FASD. CRS-R scores are standardised, with a mean of 50 and a standard deviation of 10. Scores over 65 indicate significant problems, with those at 66–70 considered moderately atypical and those over 70 considered markedly atypical (Connors, 1997). In the caregiver report form, children with both exposures were rated as significantly more problematic in the domains of: oppositional ($d = 0.26$, $p = 0.04$), social problems ($d = 0.35$, $p = 0.02$), ADHD index ($d = 0.47$, $p = 0.004$), restless/impulsive ($d = 0.40$, $p = 0.01$), global index ($d = 0.46$, $p = 0.02$), DSM-IV criteria for inattention ($d = 0.50$, $p = 0.004$), DSM-IV criteria for hyperactivity/impulsivity ($d = 0.33$, $p = 0.03$), and DSM-IV total ($d = 0.27$, $p = 0.005$) than children with trauma alone. In the teacher report version, children with both exposures were rated as significantly more problematic in the domains of: cognitive problems/inattention ($d = 0.40$, $p = 0.006$), ADHD index ($d = 0.36$, $p = 0.02$), restlessness/impulsivity ($d = 0.38$, $p = 0.03$), DSM-IV criteria for inattention ($d = 0.27$, $p = 0.009$), and DSM-IV total ($d = 0.46$, $p = 0.01$). There was therefore agreement between caregivers and teachers that children with both exposures were more likely to exhibit behaviours associated with ADHD, and more specifically were more restless, impulsive, and less able to sustain attention than children with trauma alone. Scores across the two forms showed that children with both exposures were in the atypical range in 20 out of 27 domains − 8 of which fell in the markedly atypical range; compared to children with trauma only, who were in the atypical range in 6 out of 27 domains − none of which were in the markedly atypical range.

Koponen et al. (2009), in their sample of 38 children with FASD, found that children who had been removed from the care of their birth parents (where they were most likely maltreated) before the age of three were much less likely to have emotional problems as diagnosed by their psychologist than those placed later (0%/33%, $p < 0.01$). The authors used the Child Behaviour Checklist (CBCL; Achenbach, 1991) to assess caregiver's ratings of children's behaviour. Results showed that children's age at first placement ($r = 0.43$, $p < 0.05$), age at placement into their present foster family ($r = 0.34$, $p < 0.05$), and number of traumatic experiences ($r = 0.45$, $p < 0.01$), all showed moderate correlations with scores on the CBCL, meaning that trauma in early childhood is predictive of behavioural problems later on (Koponen et al., 2009). The authors also found that the number of traumatic experiences a child had suffered correlated with problematic attachment behaviour such as being unselectively friendly, and ready to leave with strangers ($r = 0.39$, $p < 0.05$) and bullying behaviour towards other children ($r = 0.37$, $p < 0.05$).

Koponen et al. (2013) collected qualitative information about children with FASD who had either been taken into care at birth ($n = 7$) or who had lived with their birth parents ($n = 27$). 26 out of the 27 children who had lived with their birth parents had experienced some form of trauma. The authors did not measure the impact of trauma in any statistical sense, but a wider variety of socio-emotional problems was reported from within the group of children who had lived with their birth parents. Problems reported by this group, which were not reported by the other group, included: fearfulness, nightmares, continence problems, delays in multiple daily activities such as washing

and eating, excessive need for affection, fear of losing foster parents, willingness to go with strangers, no sense of pain, disinhibited attachment disorder, violence toward other children, submissiveness, aggression, tantrums, breaking things, head banging, smearing stool on wall, low self-esteem, and inappropriate interest in sex.

3.4. Related studies

In addition to the five articles synthesised in this review, the literature search identified a number of studies which came close to answering the research question, or whose results were relevant without focussing on the impact of both exposures. A selection of these studies will be described here, since they provide a valuable contribution to the conclusions of this review.

Streissguth et al. (2004) assessed adverse life outcomes: disrupted school experiences, trouble with the law (TWL), confinement (CNF), inappropriate sexual behaviours (ISB), and alcohol or drug problems (ADP) in a large cohort of children and adults (n = 415, age range 6–51) with FAS or FAE, although no control group was studied for comparison. Less time spent in a stable nurturing home increased the risk of ISB (Odds Ratio = 4.06, $p < 0.001$), DSE (OR = 4.67, $p < 0.001$), TWL (OR = 2.69, $p = 0.01$), and ADP (OR = 4.10, $p = 0.001$). Fewer years per household by age 18 increased the risk of CNF (OR = 7.35, $p = 0.001$). Having been the victim of sexual or physical assault or domestic violence increased the risk of ISB (OR = 3.37, $p < 0.001$) and ADP (OR = 2.56, $p < 0.05$). A diagnosis of FAS protected against all five adverse outcomes. The authors suggest that the diagnosis of FAS protects against adverse outcomes due to the opportunity it affords caregivers to effectively advocate for their child's needs. The finding that young people with FASD who are abused are more likely to develop behavioural problems conforms to the findings of other articles in this review.

Mauren (2007) measured the impact of foster home stability (number of placements) and age at separation from birth family on cognitive and behavioural functioning in children (n = 88, age 6–18) with FASD. Adaptive functioning, academic achievement, executive functioning and behavioural problems were measured with a series of psychometric scales. Few significant relationships were identified between risk factors and outcomes, although number of placements had some impact on adaptive functioning, and age at first removal was related to academic achievement. The author suggests that certain characteristics of the data set may have confounded the findings of the study. Quality of placement was not evaluated, nor length of each placement. Such factors could have a greater impact on development as well as affecting the accuracy of parent-report scales. Such considerations should be taken into account when assessing environmental effects on children in foster care.

Gerteisen (2008) describes art therapy sessions with a group of seven children aged 10–14 with FASD and histories of trauma, who were living in a residential facility in Alaska. One of the children, an 11-year-old Native Alaskan boy with FAE, had suffered physical abuse as well as multiple foster placements and had witnessed the domestic abuse and suicide of his mother. During art therapy sessions lasting nine weeks, Tommy (pseudonym) apparently made some remarkable development. According to the author, who delivered the sessions, Tommy became progressively able to express himself through his drawings. The descriptions of Tommy's progress are encouraging; however, no mention is made of any progress in the remaining six children who attended the sessions. Further investigation into the efficacy of art therapy in children with FASD and a history of trauma is clearly necessary.

Huggins et al. (2008) interviewed six adults (age 18–29) with FASD from the same cohort as Streissguth et al. (2004. Six had attempted suicide at some point, whereas the remaining five had not. Five of the six suicide attempters had a history of physical or sexual abuse, compared to three out of five of those who had never attempted suicide. This small pilot study suggests that a history of trauma in people with FASD might increase the risk of suicidality, but larger studies are required to properly investigate this relationship.

Victor et al. (2008) studied children ($n = 136$, age 6–12) with FASD from the same archive as Mauren (2007. Participants were grouped based on their domestic history: 19 lived with their biological parents, 40 had one foster care placement, and 77 had more than one foster care placement. Cognitive functioning, academic achievement, executive functioning and behavioural status were assessed using a series of psychometrics similar to those used by Mauren (2007. Although not all subtest score differences were significant, children with a single placement achieved higher cognitive results and exhibited fewer behavioural problems than children with multiple placements and children who had remained with their biological families. This study provides more credible evidence that environmental factors such as foster home stability have influence over cognitive and behavioural development in children with FASD.

Fagerlund et al. (2011) examined risk and protective factors associated with behavioural problems in children and adolescents ($n = 73$, age 8–21) with FASD. More time spent living in a residential care unit (rather than biological or foster home) was associated with more internalising and externalising behavioural problems. Diagnosis of FAS offered more protection from behavioural problems than a diagnosis of ARND. This study provides further evidence that quality of care has an impact on behavioural development in children with FASD, and supports the conclusion of Streissguth (2004; above) that the visible dysmorphology associated with FAS still acts as a label which can increase the chances of a child receiving appropriate medical or educational assistance due to diagnosis being more likely and/or earlier. Efforts to increase the rate of support for children with fewer or no physical features, in particular those living in residential care, are required.

4. Discussion

4.1. Summary of main findings

The studies in this review provide some suggestion that prenatal exposure to alcohol coupled with traumatic childhood experiences may compound to result in a higher risk of difficulties in speech, language comprehension, intelligence, attention, memory, and a range of emotional and behavioural issues compared to prenatal alcohol or trauma alone. The methods used and results found by the articles in this review are mixed, and are representative of the wide range of difficulties faced by individuals who suffer from the effects of these exposures, and their definitional and diagnostic complexities.

The most common findings presented here pertain to speech and language difficulties and social and behavioural problems, but this may tell us more about the design of the studies than the effects of the exposures in question. Henry et al. (2007) and Hyter (2012), whose shared sample was the second largest here, found moderate differences between groups showing that the compound of exposures is associated with a higher risk of difficulties in speech and language than in trauma alone. However, Coggins et al. (2007), whose sample size was the largest, found no significant difference. Similarly, Koponen et al. (2009) found no significant effect of trauma on language in children with FASD, but Koponen et al. (2013) found many more language related problems, based on parent and teacher reports, in their group of children who had suffered both exposures.

Four out of the five articles measured some form of social, emotional or behavioural outcome, and three of these found notable or significant differences. Hyter (2012) failed to find an effect in social communication, but Henry et al. (2007) and Koponen et al. (2009) found significant differences in social and behavioural difficulties. Koponen et al. (2013) found many more social and behavioural difficulties were faced by children with both exposures. Only Henry et al. (2007) and Koponen et al. (2009) measured other cognitive

deficits. Significant differences were found in attention, memory, intelligence and developmental level, but not in motor skills or visual processing.

The related articles discussed in Section 3.4 provide further evidence that disruptive or adverse environments can increase the risk of problematic cognitive or behavioural development in children with FASD. Quality of care, number of foster placements, and length of time per placement were predictive of adverse outcomes in children and adults with FASD although, as above, the differences between groups were usually moderate and not always significant. One study discussed the potential of art therapy to help affected children to express their emotions, and two studies found that a diagnosis of FAS protected against adverse outcomes, probably because of its visibility, the increased likelihood of an earlier diagnosis, and the opportunity for parents to more effectively advocate for their child's needs.

4.2. Strengths and limitations

The most valuable article in this review is the comparison of traumatised children with and without FASD by Henry et al. (2007). Their large sample size, recognised methods of assessment based on predetermined criteria, quasi-experimental design with similar group sizes, and comprehensive assessment of cognitive and behavioural outcomes sets their study apart within this review. However, the main problem with the group comparisons in this review, including that in Henry et al., is that there are too few groups to properly determine the impact of the independent variables. The comparisons are based on two groups: one group with one exposure in absence of the other, and another group with both exposures; for sake of example – FASD vs both. If the 'both' group shows greater deficits in, say, speech, we determine that the presence of both exposures is to blame, and that they compound each other. However, this could be explained by the fact that trauma – the independent variable – has a greater impact on speech than FASD, and this therefore is the real cause of the greater deficit. In order to overcome this limitation, a study would require at least three groups: FASD, trauma, and both together; ideally with a group of carefully sampled, non-exposed controls. Furthermore, studies are required which feature a control group of children with neurodevelopmental impairment without trauma or PAE. Since children with FASD and/or a history of trauma often present with common neurobehavioural disorders (such as ADHD) it is necessary to better define any differences between type and magnitude of neurodevelopmental impairment from different exposures. Also missing from this review is any study which methodologically accounted for the impact of other drug exposures (cf. Eze et al., 2016). It is crucial to separate the effects of alcohol from the effects of other drugs, in order to better understand the harm caused by each.

The two Finnish studies (Koponen et al., 2009; Koponen et al., 2013) measure to varying extents, the impact of PAE and trauma on children from within the foster care system of Finland. As mentioned above, the definition of trauma in these articles goes beyond maltreatment to include factors such as parental divorce and unemployment. Whilst there is little doubt that these experiences can be disruptive, their inclusion may lead to participants in these studies being labelled as 'traumatised', when no such trauma exists. Not all children who experience parental divorce show increased cognitive and behavioural problems as a result (Lansford et al., 2006). This can depend on many factors, including the age of the child at parental separation, and the extent to which the marriage was in conflict prior to and during separation (Amato et al., 1995). Similarly, the impact of unemployment is not necessarily traumatic; this depends on socio-economic status and gender of the unemployed parent amongst other factors (Rege et al., 2011).

Koponen et al. (2009) asked foster parents to assess their children in terms of their developmental level, behavioural problems, attachment behaviour, ability to communicate worries, and bullying behaviour compared to other children of the same age. Behavioural problems were assessed by the CBCL (Achenbach, 1991) criteria, but the reliance on caregiver report data here is problematic due to its subjectivity. Koponen et al. (2013) present a qualitative study with rich, individual data in the form of a comparison between two groups – children fostered at birth, and children who lived with their birth parents before being fostered. As a qualitative investigation this gives valuable insights into the experiences and socio-emotional development of children with FASD in the Finnish foster-care system. As a comparison between groups however, this article may be somewhat misleading due to its group sizes. The group of children who lived with their birth parents number 27, whereas only 7 children in this sample were fostered at birth. This may explain the greater incidence of negative socio-emotional outcomes in the 'lived with parents' group, as raw data was reported, rather than any kind of 'per capita' assessment.

The findings of Coggins et al. (2007) are useful in terms of their assessment of the comorbidity of FASD and trauma, which appears to be substantial. Their study used recognised measures and the largest sample size in this review, and although the data presented supports previous research indicating that PAE and trauma are predictive of deficits in language, contrary to the other studies in this review it does not show a compounding effect where both exposures are present compared to one exposure. Some further studies would have been useful, given the opportunity to test such a large sample. Hyter's (2012) preliminary findings, presented within a review and not published elsewhere, lack a distinct method section, although as a follow-up to Henry et al. (2007), there may be little need. The findings in relation to speech and language are significant and valuable.

A problem which is pervasive throughout research into FASD is that methods of diagnosis and assessment of alcohol exposure are not uniform. Individuals with FASD form a heterogeneous population with widely varying levels of alcohol exposure and neurodevelopmental impairment. Moreover, a number of diagnostic systems are currently in use, each with their own criteria (see for example the five systems assessed by Coles et al., 2016). The articles in this review are impacted by these issues, since each of them presents an assessment of their sample of children with FASD as though they compose a homogenous group, whereas in reality, the differences in terms of neurological impairment within a group of children with FASD may be wide. Future studies should aim to present as detailed a description of their participants' diagnoses, their neurodevelopmental profiles and/or rates of alcohol exposure as possible. It is also possible that extraneous variables such as genetics, epigenetics and/or postnatal experiences unique to alcoholic families could lead to greater neurodevelopmental impairment in those with prenatal alcohol exposure. While we acknowledge the practical challenges of setting up such studies, researchers should aim to control as many potential variables as possible.

4.3. Implications

Individuals with prenatal exposure to alcohol or who have experienced early traumatic events are heterogeneous groups who present with a wide range of neurobiological, cognitive and behavioural difficulties. The range of domains in which deficits have been studied cover most aspects of neurodevelopmental functioning, regardless of exposure. These include: speech and language, executive function, memory, intelligence, empathy, attachment, emotional and behavioural issues, attention, social communication and peer relationships.

There is some evidence that problems with speech and language, attention, intelligence, memory, and emotional and behavioural issues can occur to a greater extent when both exposures present together, indicating a compounding relationship. However, five articles published on the impact of two highly prevalent, overlapping and debilitating risks is clearly insufficient. There is as yet no research that has investigated the lifetime outcomes of adults with both exposures, nor the neurological correlates of cognitive or behavioural deficits. The

studies presented here relied on cross-sectional or case-control measures, whose designs do not allow causal inferences. Studies with longitudinal designs should also be considered, which would provide stronger evidence for causal mechanisms. The apparently high levels of comorbidity between the two exposures coupled with a lack of studies which have sought to investigate their interaction leaves a significant risk that studies into each exposure separately have been impacted by contamination.

Further research in the immediate future should assess the following neurodevelopmental domains: executive functioning deficits including response inhibition, working memory and attention shifting; social communication; peer relationships; empathy or theory of mind; and neurological correlates of cognitive and/or behavioural deficits. Future research should also provide population-based comorbidity data, to employ more consistently defined FASD diagnoses across studies, and to assess differences between exposed children and those with neurodevelopmental impairment without exposures. Research that investigates the role of the stress response system as a possible mechanism for increased impairment following both exposures would be useful. It is also suggested that three or four-way group comparisons are employed (i.e. control, trauma, PAE, both exposures) as described in Section 4.2.

5. Conclusion

The five studies included in this review represent the current published body of knowledge on the compounding effects of prenatal alcohol exposure and traumatic childhood experiences. These studies present some rich qualitative descriptions of the problems faced by individuals who experience both trauma and FASD, and go some way to investigating the particular issues faced by such individuals in comparison to those who present with one exposure in absence of the other. On this evidence, it appears that deficits in speech and language, attention, intelligence, memory, and emotional and behavioural issues occur to a greater extent where both exposures are present. However, more research is urgently required to investigate how the nature and extent of the difficulties differ depending on whether the individual is exposed to both trauma and prenatal alcohol or prenatal alcohol alone. There are certain practical constraints to research in this area – for example, it may be difficult to identify and recruit many participants with PAE in absence of prenatal exposure to other drugs, poor maternal diet and any kind of post-natal trauma. However, methods further to those presented here are available and currently missing from the published literature. Further research should compare children with prenatal alcohol exposure and traumatic experiences to both non-exposed controls and children with neurodevelopmental deficits without these exposures. Studies should methodologically account for the impact of prenatal drug exposure, and the heterogeneity of children with FASD, in terms of diagnoses, diagnostic codes, and, as far as possible, levels of prenatal alcohol exposure.

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Appendix A. : Search terms

"fetal alcohol" OR "fetal alcohol" OR "fetal-alcohol" OR "fetal-alcohol" OR "alcohol-related neuro-developmental disorder" OR "alcohol-related neurodevelopmental disorder" OR "alcohol related neuro-developmental disorder" OR "alcohol related neurodevelopmental disorder" OR "alcohol related birth defects" OR "alcohol-related birth defects" OR "prenatal alcohol" OR "pre-natal alcohol" OR "pre natal alcohol" OR FAS OR PAE OR FASD OR ARND OR ARBD OR FAE OR PFAS OR pFAS OR ND-PAE OR NDPAE

Co-occurring with one or more of the following (using the Boolean operator AND):

neglect OR neglected OR abuse OR abused OR abusive OR trauma OR traumatic OR maltreated OR maltreatment OR mistreated OR mistreatment OR attachment OR adverse OR adopt OR adopted OR foster OR fostered OR environment

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