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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