

The impact of traumatic childhood experiences on cognitive and behavioural functioning in children with foetal alcohol spectrum disorders

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Abstract

Prenatal alcohol exposure (PAE) can cause lasting physical damage to the developing foetus including the brain. This brain damage can manifest as cognitive dysfunction and behavioural difficulties, which can be diagnosed as foetal alcohol spectrum disorders (FASD). FASD is thought to be common in the UK, with estimates ranging from 3.24% up to 17% of the population affected, although rates of diagnosis are much lower than this. Children with FASD are at increased risk of a range of traumatic or adverse childhood experiences, such as neglect or abuse. Studies into the long-term effects of neglect or abuse show a similar range of cognitive dysfunction and behavioural difficulties as those seen in FASD, but there is a lack of evidence on the impact of a dual exposure of PAE and trauma. This is especially necessary for clinicians, who may need to use the presence of trauma to inform and potentially exclude a diagnosis on the foetal alcohol spectrum. This aim of this thesis was to investigate the impact of childhood trauma on the cognitive and behavioural functioning of children with FASD. A wide-ranging overview of the literature on the effects of PAE and trauma as separate exposures was conducted and was followed by a systematic literature review of studies into the dual exposure of PAE and trauma. The reviews showed that only five studies had investigated the impact of both exposures, although one further study was published more recently. The literature reviews, including the one new study showed that, although there had only been a small number of studies conducted, a pattern was emerging that children with both FASD and trauma were more similar to children with just FASD than they were to children with just trauma, in terms of their cognitive and behavioural functioning.

The findings of the reviews were used to develop four original studies, which advanced the evidence in this area. The studies were designed to assess the damage caused by dual exposure at four levels: neurological, cognitive, behavioural, and finally the effect of behavioural problems on other people. A neuroimaging study measured task-related blood oxygenation in the prefrontal cortex in 15 children aged 8-14 years with FASD with and without a history of trauma. A series of cognitive tasks assessed verbal, non-verbal and overall intelligence, working memory and inhibitory control in 25 children aged 8-14 years with FASD with and without a history of trauma. An informant-report survey that assessed Adverse Childhood experiences, cognitive, affective and overall empathy, behavioural strengths and difficulties, and comorbid diagnoses was completed by the carers of children aged 4-16 years with FASD. A series of semi-structured interviews was conducted with caregivers of children aged 8-14 years with FASD, with and without a history of trauma.

Children with FASD had high levels of adverse childhood experiences including neglect and abuse, poor empathy, high levels of behavioural difficulties, and high levels of comorbid diagnoses, particularly attention deficit hyperactivity disorder (ADHD). They also had verbal, non-verbal and overall intelligence in the average range, and working memory and inhibitory control scores that were similar to the scores of typically developing children of the same age. Children with both FASD and a history of trauma were found not to be significantly different from children with FASD without trauma in terms of their task-related prefrontal activity, verbal, non-verbal and overall intelligence, working memory, inhibitory control, and empathy. There was a slight tendency for children with higher numbers of adverse childhood experiences to exhibit more severe behavioural difficulties, particularly conduct problems. Caregivers of children with both exposures described experiences with the same themes as those whose children had FASD without trauma. Caregivers described their children as difficult to manage, but also described many strengths and rewarding moments. Caregivers were critical of service providers including medical and educational services, social services, adoption agencies and local authorities, who lacked knowledge and understanding of FASD. This led to their children being misunderstood and offered insufficient or inappropriate services.

The findings of this thesis support previous research showing that children with FASD have high levels of behavioural difficulties, poor empathy, and high levels of comorbid diagnoses. It provides the first data on levels of adverse childhood experiences in children with FASD, which are also high. The main finding of the thesis is that the impact of traumatic childhood experiences on the cognitive and behavioural functioning of children with FASD may be very subtle, especially in terms of cognitive functioning. Clinicians and other professionals should be aware that a history of neglect or abuse does not appear to be a better explanation for cognitive dysfunction or behavioural difficulties than prenatal alcohol exposure. Where children have a history of both exposures, they should primarily be treated as children with FASD, and provided appropriate support and interventions specifically designed for FASD.

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Chapter 1: General Introduction

1.1 Background

Prenatal alcohol exposure (PAE) is one of the world's leading causes of birth defects and neurodevelopmental impairment (May et al., 2009). Infants prenatally exposed to alcohol can develop one of a range of adverse outcomes known collectively as foetal alcohol spectrum disorders (FASD). At the severe end of the spectrum, associated with higher levels of alcohol exposure, is foetal alcohol syndrome (FAS), which is characterised by deficient growth, craniofacial anomalies, and neurodevelopmental impairment. The effects of PAE are permanent and there is considerable variation amongst affected individuals. There are often no visible defects, but cognitive impairment is pervasive and is associated with emotional and behavioural difficulties which can lead to secondary conditions including disrupted school experiences, trouble with the law, imprisonment, drug or alcohol addiction, and risky sexual behaviours (Streissguth et al., 2004).

The prevalence of PAE is very high in many western countries, and the UK has one of the highest rates of drinking during pregnancy in the world at over 40% (Popova et al., 2017), but no high-quality prevalence studies of FASD have been conducted here. The most recent meta-analysis of international studies used rates of alcohol consumption in pregnancy to produce an estimated prevalence rate of 3.24% for the UK (Lange et al., 2017). Recent studies in the United States (May et al., 2018) and Canada (Popova et al., 2018) have shown that rates of FASD in those countries may be significantly higher than previously thought, with estimates at 1-5% and 2-3% respectively.

Some, but not all parents of infants born with FASD will suffer from alcohol misuse issues and addiction. Children born into families where alcoholism and other addictions are present are at increased risk of suffering traumatic childhood experiences including neglect and abuse. Even in the absence of alcohol exposure during foetal development, these traumatic experiences during early childhood are associated with an increased risk of cognitive impairment, emotional and behavioural difficulties, and many of the same adverse health and social outcomes that are seen in individuals with FASD (Dube, Anda, Felitti, Croft, et al., 2001). This may be due to a similar pattern of neurobiological and neuroendocrine damage, but there may also be an issue regarding research methods – it is possible that, due to a significant amount of comorbidity between childhood trauma and prenatal alcohol exposure, many of the research participants in those studies would have significant exposures that were not considered by the researchers. The likelihood of this may be increased by the fact that very few published studies have sought to control both prenatal alcohol exposure and early childhood trauma.

Clinicians from the only specialist FASD clinic in the UK (UK National FASD Clinic; www.fasdclinic.com) noticed that a significant proportion of the children seen were adopted or fostered following state intervention and removal from their biological parents. In these cases, alcohol and substance misuse by the birth mother or birth parents was common. This is unsurprising given that the children who present at this clinic have suspected prenatal alcohol exposure, but this is seldom the reason for state intervention. In England, more than half of children taken into care are removed from their birth parents due to physical, psychological or sexual abuse, or emotional or physical neglect (Department for Education, 2015). Many of the children seen in the clinic had suffered some form of abuse or neglect prior to adoption, but some initial literature searches appeared to show very few articles that specifically described the relationship between prenatal alcohol exposure and postnatal abuse or neglect, and the way that these exposures might interact to impact development.

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), there is a section with the proposed criteria for diagnosis of Neurobehavioural Disorder associated with Prenatal Alcohol Exposure (ND-PAE; APA, 2013). Part of the proposed requirements for diagnosis are that factors that better explain the characteristics of ND-PAE must be excluded, and one of these is neglect. In other words, under the proposed diagnostic methods, if an individual has a history of neglect, this may prevent them from a diagnosis of ND-PAE as it is seen as a better explanation of their presentation. Studies are therefore needed to investigate the relationship between prenatal alcohol exposure and postnatal neglect.

Early diagnosis and interventions can help to prevent or reduce secondary conditions associated with FASD: early diagnosis is associated with fewer adverse and more positive life outcomes in individuals with FASD (Streissguth et al., 2011) and emerging data on interventions are showing a similar effect (Carmichael-Olson & Montague, 2011). Interventions generally include pharmacological, behavioural and educational treatments, and many of these have shown promising results, but much more data are required in order to inform and develop theoretical foundations, methods and outcomes (Chandrasena, Mukherjee, & Turk, 2009; Mukherjee, Cook, Fleming, & Norgate, 2016). Moreover, risk factors such as abuse and neglect have received little attention within the FASD literature, leaving a risk that these factors are confounding results and conclusions. This thesis was proposed in a collaboration between the National FASD Clinic and the University of Salford in order to develop the limited understanding of the expected presentation and development of children with exposure to both prenatal alcohol and postnatal trauma, with the long-term aim of improving interventions in this population.

1.2 Aims and objectives

The overall aim of this thesis is to investigate how traumatic experiences impact cognitive and behavioural functioning in children with FASD. The developmental trajectory of an individual with FASD is difficult to predict and may depend on many factors including early childhood experiences. The identification of any differences between individuals with FASD who do and do not have histories of traumatic experiences could help healthcare professionals, social workers, educators and parents to better understand what to expect of a young person with FASD, given their environmental history.

The first objective of the thesis is to describe what is currently known about the relationship between FASD and traumatic experiences and identify the most pressing gaps in the research literature. The second stage of the project employs primary research methodologies to fill these gaps and advance the knowledge base of this subject.

1.3 A note on language

This thesis is largely concerned with the long-term effects of two exposures: prenatal exposure to alcohol, and postnatal exposure to traumatic experiences such as abuse and neglect. Prenatal alcohol exposure is abbreviated to PAE, and refers specifically to the exposure, not the effects. The long-term effects of PAE are known as foetal alcohol spectrum disorders; this is abbreviated to FASD and refers to the effects, not the exposure. Not all the participants in this study had a diagnosis on the foetal alcohol spectrum. However, those who did not were all children whose parents/carers perceived them to have difficulties caused by PAE. In this thesis, the term 'FASD' refers to the range of harm caused by PAE, whether diagnosed or not. Traumatic childhood experiences are a little more complicated. Neglect can be physical or emotional; abuse can be psychological, physical or sexual; and the word 'maltreatment' refers to abuse and/or neglect (for detailed definitions of abuse and neglect, see [section 2.7](#)). The systematic review presented in chapter three describes published studies that use the phrases 'environmental risk', 'complex trauma', 'traumatic experiences', and 'traumatic stress' when describing the potentially traumatic childhood experiences in the histories of their participants. These are largely synonymous; all refer to at least maltreatment, but the potential range of exposures is not definitive. It is best defined by Henry, Sloan and Black-Pond (2007), who define 'trauma' as childhood experiences that can lead to a diagnosis of post-traumatic stress disorder. In chapter five of this thesis, the 10-item Adverse Childhood Experiences (ACE) questionnaire (Dube et al., 2003) is identified as a useful tool to assess a history of traumatic experiences in children, via caregiver report. ACEs include maltreatment, as well as five other environmental exposures such as witnessing domestic violence and living though

parental separation. Due to differences in research design, the study described in chapter five is largely concerned with the impact of ACEs (scale data), whereas the studies described in chapters six and seven are concerned with maltreatment (categorical data). In this thesis, the phrase 'traumatic childhood experiences' is abbreviated as 'trauma'; it describes exposures rather than effects and refers to the full range of potentially traumatic experiences from both the ACE questionnaire and the studies described in the systematic review.

- PAE: Prenatal alcohol exposure
- FASD: Foetal alcohol spectrum disorder – the range of effects caused by PAE
- Maltreatment: Neglect and/or abuse
- ACEs: Any of the 10 Adverse Childhood Experiences
- Trauma/ Traumatic childhood experiences: Any ACEs or any other traumatic childhood experiences described in the systematic review

1.4 Thesis structure

The wider literature overview in chapter two provides a general introduction to the topic of FASD, with some history of the early clues about alcohol-related harm in pregnancy, up to the first published papers in the 1960s and 1970s. This leads to an overview of the biological mechanisms of PAE, the cognitive and behavioural profile of FASD, and the difficulties that can be experienced by parents and carers of children with FASD. Next, literature on the impact of traumatic childhood experiences is discussed, again with a focus on the cognitive and behavioural profile of individuals with a history of trauma, and the potential impact on carers. The chapter ends with a short section on the combination of FASD and a history of trauma, and this is followed by chapter three, which describes the first piece of original research in this project – a systematic literature review of studies into the dual exposure of PAE and traumatic childhood experiences. The overview (chapter 2) demonstrates that there is a lack of research into the long-term effects of a dual exposure of PAE and trauma, and that studies should investigate cognitive and behavioural functioning and the impact of difficulties on carers in children, by comparing children with dual exposure with children with only one of those exposures. The systematic review (chapter 3) shows five studies where this has been done, and identifies gaps left in the literature, where the difference between dual and single exposure has not yet been investigated. Following a short introduction to the primary research stage (chapter 4), chapters five, six, seven and eight describe four original studies into specific differences between children with dual and single exposure. These four studies were logically conducted in parallel, in other words, the conclusions of one study do not lead to the next, rather the conclusions of the literature reviews form the rationales for all the primary studies. They

are presented here in the chronological order in which they were conducted. Chapter five describes an online caregiver survey, chapters six and seven describe neurocognitive assessments with a subsample of the children whose caregivers responded to the survey, and chapter eight describes interviews with some of their caregivers. Finally, chapter nine provides a discussion of the overall findings and conclusions of the thesis. Figure 1.1 shows a schematic representation of the thesis.

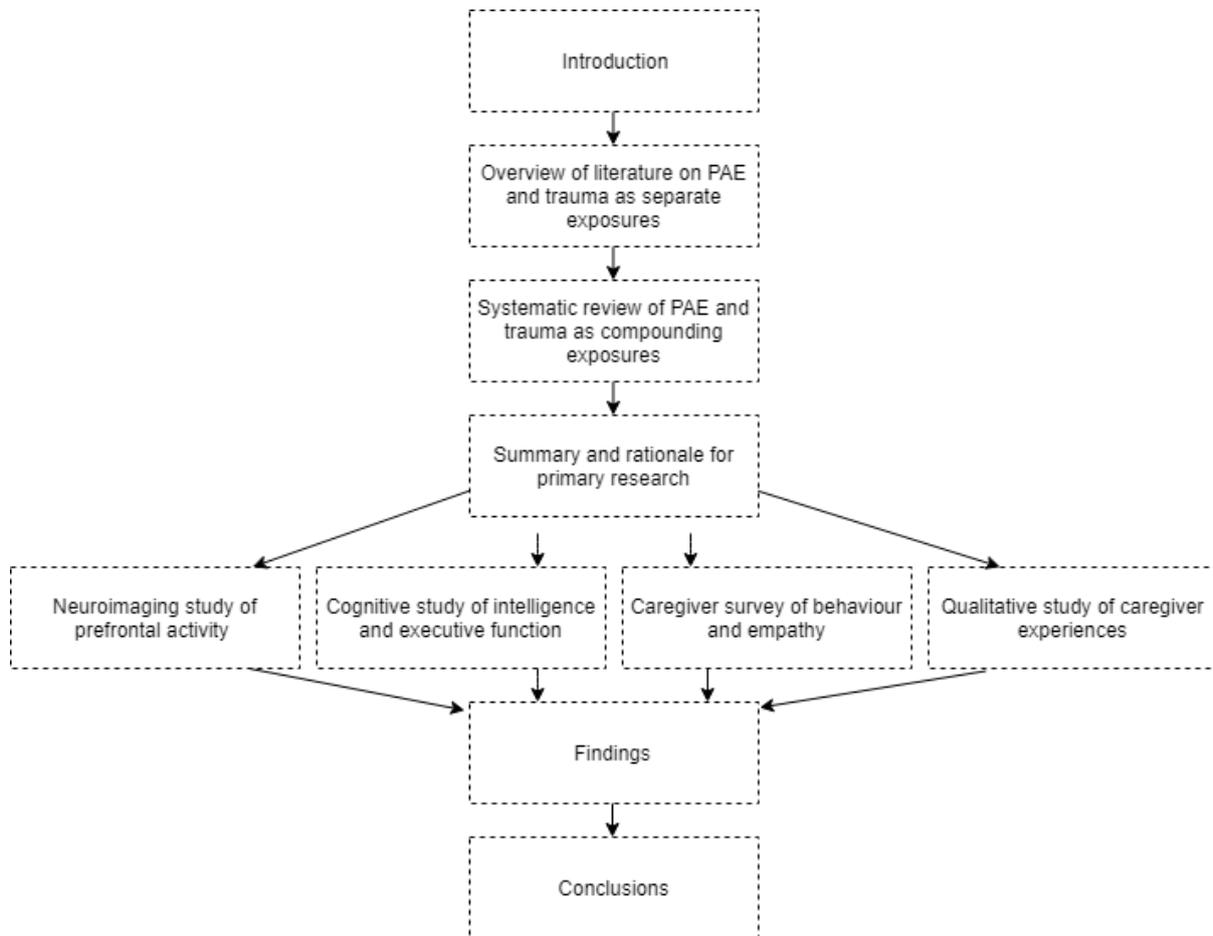


Figure 1.1 Schematic diagram of thesis structure

Chapter 2: Prenatal alcohol exposure and traumatic childhood experiences as separate exposures: an overview of the published literature

2.1 History of FASD

The contemporary investigation into the impact of prenatal alcohol exposure is most often traced back to a series of articles by Kenneth Jones and colleagues at the University of Washington in the early 1970's (Jones & Smith, 1973a; Jones & Smith, 1973b; Jones & Smith, 1975; Jones, Smith, Streissguth & Myriantopoulos, 1974; Jones, Smith, Ulleland, and Streissguth, 1973), and to a lesser extent to an article published in French five years earlier (Lemoine, Harousseau, Borteyru, & Menuet, 1968). However, these publications have been described as rediscoveries of the harmful effects of alcohol on pregnancy, and such knowledge may have existed for hundreds or even thousands of years.

The earliest known warning concerning alcohol and pregnancy appears in the Old Testament Book of Judges, which is thought to have been written during or before the 6th century BCE. The Angel of the Lord appears to the Wife of Manoah to inform her that she will become pregnant, and warns her, amongst other instructions, to “...*drink no wine, nor other fermented drink...*” (Judges, 13:2, New International Version). The woman gives birth to Samson, who becomes renowned for his strength and intellect. Whilst some have suggested that this represents knowledge of the harmful impact that alcohol may have on an unborn baby (Calhoun & Warren, 2007; Davis, 1980), others have argued that this may not be the case, and that the instructions were most probably given to ensure that proper religious rites were followed (Abel, 1997; Sanders, 2009).

Similarly, the following quote has been attributed to Aristotle (384–322 BCE): “*Foolish, drunken, or haire brain women most often bring forth children like unto themselves, morose and feeble*” (Abel, 1999, pp. 869), and has been held as evidence that the Ancient Greeks had at least a rudimentary knowledge of the ill effects of alcohol consumed during pregnancy (Lemoine, 1968; Smith & Jones, 1973; Warner & Rosett, 1975). It turns out though that renaissance scholar Robert Burton fabricated the quote, along with several others, in *The Anatomy of Melancholy* (1621). Aristotle did in fact discuss the influence of alcohol on conception in *Problemata* (reprinted 1927), but only in terms of its effect on the male libido, and that as a result of cooling the male body prior to intercourse, a couple might have the ‘misfortune’ to conceive a girl (Abel, 1999; Sanders, 2009).

There is little evidence of attention to the issue of prenatal alcohol exposure between these ancient clues and the end of the 1600s, when the abolishment of a monopoly on distillation in

England coincided with a levy on the import of French brandy. By the early 1720's, the price of domestically produced gin had fallen so sharply that even the working classes could afford to consume several pints each of the strong liquor per year (Warner & Rosett, 1975; Warren & Hewitt, 2009). During the next thirty years, the widely documented public drunkenness on the streets of the English capital became known as the London gin epidemic. Warner and Rosett (1975) document several observations from that era, which appear to show that physicians were well aware of the harm that alcohol was having on unborn babies:

“Half the train of chronical diseases with which we see children afflicted are only the secondary sighs and groanings...of parentive ill-spent life. These consequences...will be brought on infants by the debauchery of the Mother.”
(Sedgewick, 1725, pp. 368-369).

“What must become an infant, who is conceived in gin? With the poisonous distillations of which it is nourished, both in the womb and at the breast.”
(Fielding, 1751, pp. 19-20).

“...the enormous use of spirituous liquors...renders such infants as are born meagre and sickly, and unable to pass through the first stages of life.” (Morris, 1751, pp. 89).

Such quotes have generally been held as fairly strong evidence that the dangers of prenatal exposure to alcohol, or at least to gin, were well known during the early to mid-1700s (Coffey, 1966; Rodin, 1981; Warner & Rosett, 1975). Others have noted that these complaints about drunkenness only applied to the 'inferior classes' (Abel, 2001a, 2001b). Many social and economic forces influenced the lives of the working classes, the health of their children, and how they were perceived by upper class physicians and politicians. It is also interesting to note that cheap, home-made gin was widely available on the black market, especially after a tax rise in 1736, which often contained additives such as sulphuric acid, lime oil and turpentine (Solmonson, 2012), and that prenatal exposure to turpentine has recently been shown to damage neurobehavioural function in rats (Fortier, Luheshi & Boksa, 2007). Exposure to turpentine, or other chemicals in bootleg gin during the 18th century could therefore go some way to explaining the problems seen in working class children born during this time.

During the 19th century, public attitudes towards alcohol in Europe and North America became less favourable, fuelled in part by the temperance movement. The first epidemiological studies on alcohol's harmful effects were published, such as Sullivan's (1899) study of 120 pregnant

inmates at a Liverpool women's prison. Maternal alcoholism was found to be associated with a higher rate of stillbirth or infant mortality than in cases where mothers had been denied alcohol. Sullivan also noted that paternal and grandparental alcoholism were less damaging than maternal exposure (Sanders, 2009; Sullivan, 1899). Such research was supported by, and conducted in support of the temperance movement, whose attitude toward alcohol was based primarily on religious teachings (Sanders, 2009). Prohibition of alcohol in the United States was accompanied by often sensational claims about the harms of alcohol and dependency, so much so that following the end of prohibition in 1933, warnings about the harmful effects of alcohol were largely denounced as propaganda. Any previous research that supported the temperance view of alcohol was therefore effectively discredited, which may go some way to explaining the surprise of medical professionals at more recent findings pertaining to prenatal alcohol exposure (Sanders, 2009; Warren & Hewitt, 2009).

In the second half of the 20th century, two articles written in French (Lemoine, 1968; Rouquette, 1957) described physical and behavioural deficits in over 200 babies born to alcoholic mothers. The authors of both articles noted the impact of prenatal exposure to alcohol on the developing fetuses, but neither article managed to make an impact (Calhoun & Warren, 2007; Lemoine, 2003). The issue remained hidden until 1970, when Christie Ulleland, a junior paediatrician at the University of Washington School of Medicine, noticed that maternal alcoholism was a factor in a significant number of infants suffering with failure to thrive. She wrote that: "*These observations indicate that infants of alcoholic mothers are at high risk for pre- and post-natal growth and developmental failure, and suggest that greater attention should be given to alcoholic women during the child bearing years.*" (Ulleland, Wennberg, Igo & Smith, 1970, pp. 474). This brief statement is arguably the true source of the modern investigation into the effects of prenatal exposure to alcohol. Eight of those infants from alcoholic mothers suffered from microcephaly, stunted growth, developmental delay, short palpebral fissures, joint anomalies and small jaws. This collection of defects was given the name Foetal Alcohol Syndrome and received global recognition in a series of articles written by Ulleland's colleagues Kenneth Jones and David Smith, whose names have become synonymous with the first descriptions of Foetal Alcohol Syndrome (Jones et al., 1973; Jones et al., 1974; Jones & Smith, 1973).

There was initial scepticism that such a ubiquitous substance as alcohol could do so much damage without previously coming to the attention of medical professionals. Since alcoholism frequently coincides with malnutrition, poverty and a chaotic home environment, many suggested that these environmental risks could explain a range of birth defects just as easily as alcohol (Jones et al., 1974; Warren & Hewitt, 2009). A steady increase in research attention mostly diminished

these concerns, although the interaction between prenatal alcohol exposure and early environmental risk is still not fully understood (Price, Cook, Norgate & Mukherjee, 2017). Animal models provided experimental evidence of the teratologic effects of alcohol (e.g. Chernoff, 1977; Sulik & Johnston, 1983), even finding the same distinctive facial anomalies in mouse pups as those described by Jones and colleagues in human infants. Meanwhile, human epidemiological studies (e.g. Harlap & Shiono, 1980; May, Hymbaugh, Aase, & Samet, 1983; Sokol, Miller, & Reed, 1980) provided evidence of prevalence, range of outcomes, and began to demonstrate a link between level of consumption and severity of outcome.

In the time since this increase in attention to the issue, the harmful effects of alcohol taken during pregnancy have become better understood and widely known to the general public, at least in societies where alcohol is widely used. Government warnings to reduce or avoid alcohol consumption during pregnancy in the United States in the 1970's and 1980's were followed by similar warnings in other western countries, but the extent to which these warnings are having the desired effect is the subject of some debate (Burton, 2015; Warren and Hewitt, 2009).

2.2 The impact of alcohol on foetal development

Alcohol is a teratogen – an agent that causes malformation to an embryo or fetus. There are several mechanisms by which alcohol can impact foetal development, as well as an increasing number of techniques that may be used to investigate these effects. Prenatal alcohol exposure (PAE) can impact development of the whole foetus, and exposed individuals can present with structural damage to such areas as the digestive system (Hofer & Burd, 2009), skeleton (Simpson, Duggal, & Keiver, 2005), heart (Burd et al., 2007), eyes (Strömmland & Pinazo-Durán, 2002), and the immune and endocrine systems (Zhang, Sliwowska & Weinberg, 2005). However, without completely overlooking the range of somatic anomalies and disabilities in children prenatally exposed to alcohol, this chapter and wider thesis will focus primarily on the impact of PAE on the developing brain and central nervous system.

Alcohol consumed during pregnancy enters the mother's bloodstream, passes freely through the placenta, and into the fetus and amniotic fluid (Gupta, Gupta, & Shirasaka, 2016). In adults, alcohol is metabolised by a pair of enzymes called cytosolic alcohol dehydrogenase (ADH) and hepatic CYP2E1. These enzymes begin to appear in the individual during gestation, but do not reach maximum efficacy until well into childhood (Zelner & Koren, 2013). Instead, the main elimination method available to the fetus is transfer of alcohol back into the maternal bloodstream, but this is a complex process which can be impeded by alcohol-related constriction of blood vessels (Gupta, Gupta, & Shirasaka, 2016). For these reasons, elimination of alcohol from the foetal compartment

only occurs at around 3-4% of the maternal rate, which leads to prolonged foetal exposure (Heller & Burd, 2014).

Whilst in the foetal compartment, alcohol can disrupt development of the fetus via a number of mechanisms. Apoptosis is the process of programmed cell death which is usually beneficial and necessary in organic growth, but this process can be inappropriately initiated or suppressed by some diseases or exposures to exogenous substances including alcohol (Elmore, 2007; Goodlett & Horn, 2001). Apoptotic cell death due to alcohol exposure has been demonstrated in animal fetus models (Cartwright, Tessmer & Smith, 1998; Ramachandran et al., 2001), animal infant models (Ikonomidou et al., 2000; Young & Olney, 2006), and *in vitro* cell culture experiments (Chen, Kuhn, Chaturvedi, Boyadjieva, & Sarkar, 2006; Katz, Shear, Malkiewicz, Valentino, & Neuman, 2001). This process is seen in the human (adult) liver following alcohol consumption (Wu & Cederbaum, 2003), but may be particularly harmful during foetal development since alcohol here is metabolised more slowly, and since damage to cells during organogenesis can lead to improper development of those organs (Gupta, Gupta, & Shirasaka, 2016).

Alcohol can induce apoptosis by promoting the generation or inhibiting the elimination of reactive oxygen species (ROS) – unstable molecules formed during metabolic processes, which can react with many other molecules including those involved with cellular processes such as DNA and proteins (Wu & Cederbaum, 2003). Moreover, alcohol exposure can reduce the number of antioxidant cells, whose functions include elimination of ROS (Wu & Cederbaum, 2003). Raised levels of ROS can lead to uncontrolled apoptosis, and animal models have suggested this as a mechanism for the characteristic craniofacial and neurodevelopmental abnormalities seen in FAS (Cartwright & Smith, 1995; Dunty, Chen, Zucker, Dehart, & Sulik, 2001).

Besides direct impact on cellular processes, PAE may affect gene expression. DNA molecules are present in every type of cell, and contain essentially the same information, most of which will be unnecessary to the functioning of a given cell. Epigenetic markers are molecules that develop during gestation, attach to DNA molecules, and whose role is to activate or inhibit certain genes or groups of genes, ultimately controlling gene expression (Mazzio & Soliman, 2012). Various environmental factors can influence epigenetic markers and gene expression, sometimes resulting in adverse outcomes such as cancers (Mazzio & Soliman, 2012). There is emerging evidence from animal fetus and cell culture studies that PAE can alter epigenetic markers, resulting in widespread changes in gene expression (Lussier, Weinberg & Kobor, 2017). Moreover, recent human clinical studies have shown expected epigenetic differences in children with FASD, which support the role of epigenetics as a mechanism for PAE-related harm in humans (Laufer et al., 2015; Portales-Casamar et al., 2016).

Children born prenatally exposed to alcohol can present with a wide variety of physical, cognitive and behavioural problems, and to varying degrees. The relative breadth and severity of deficits are associated with a number of risk factors which contribute to the impact of alcohol on a developing fetus. Perhaps the most influential of these is the drinking behaviour of the expectant mother. Consistently high levels of alcohol consumption throughout pregnancy and/or episodes of binge-drinking (more than six units per session for women; NHS, 2016) are associated with severe cognitive deficits (Flak et al., 2014), behavioural disorders (Fryer, McGee, Matt, Riley, & Mattson, 2007) and structural cortical abnormalities (Sowell et al., 2008) in humans. Animal models have shown that high-dose alcohol exposure can cause severe neurodevelopmental deficits in primates and rodents (Maier & West, 2001). Results from studies into the impact of mild to moderate PAE (defined by one review as 3-6 standard US drinks per week; Flak et al., 2014) in humans are less consistent, with some studies failing to find a significant detrimental effect on pregnancy outcome (Henderson, Gray, & Brocklehurst, 2007) or cognitive and behavioural development (Kelly et al., 2013). However, a recent meta-analysis found a small association between moderate PAE and behavioural issues in children (Flak et al., 2014). Timing of exposure also appears to be a factor, although fewer published studies have investigated this. Two human cohort studies have shown an increased risk of physical deficits (Sawada-Feldman et al., 2012) and behavioural problems (O'Leary et al., 2010) following high levels of exposure during the first trimester, compared with the second and third trimesters. A study using primates has also pointed to PAE during the first trimester of pregnancy as being especially harmful to brain development and cognitive function (Astley, Magnuson, Omnell, & Clarren, 1999).

There is some evidence of a genetic component in the teratogenic effects of alcohol. PAE has been experimentally shown to have differing effects on five distinct inbred strains of mice (Downing, Balderrama-Durbin, Broncucia, Gilliam, & Johnson, 2009). One strain showed severe global physical defects following maternal prenatal intubation of alcohol, whereas another strain showed no teratogenesis and the remaining three strains showed intermediate effects. A mechanism for these kinds of results may be the variation in rates of maternal or foetal metabolism of alcohol; the efficacy of enzymes such as those mentioned above - ADH and CYP2E1 - may be largely the result of genetic variation in humans as well as animals (Gemma, Vichi, & Testai, 2007). At least one human twin study has supported the role of genetics, with monozygotic alcohol-exposed twin pairs showing significantly greater concordance in terms of IQ and diagnosis than between dizygotic pairs (Streissguth & Dehaene, 1993), although these kinds of studies are scarce.

Many other maternal factors can also impact prenatal development. Risks relating to exposure to exogenous substances such as tobacco and street drugs are well known (Cornelius &

Day, 2009; Smith et al, 2006), and there is some evidence that prenatal polydrug use combined with alcohol exposure may be more harmful than alcohol exposure alone (Rivkin et al., 2008). Many women who consume alcohol during pregnancy, especially those who struggle with addiction, can be further affected by polydrug exposure (Harrison & Sidebottom, 2009) as well as other related issues such as malnutrition. Maternal diet or nutrient deficiency may also intensify the impact of PAE - low levels of iron (Rufer et al., 2012) and zinc (Keen et al., 2010) in maternal blood have been shown to exacerbate the teratogenic effects of alcohol in animal models. Choline supplements may be useful as an intervention during pregnancy as these have been shown to moderate the impact of PAE in rats (Thomas, Abou, & Dominguez, 2009), and multivitamin supplements have recently shown a similar effect in humans (Coles et al., 2015).

Much of the research into the specific dangers and mechanisms of alcohol related harm to a developing fetus is necessarily conducted using either *in vitro* tissue sample or animal model research methods. True experiments using human participants would clearly be harmful and unethical, so it is not possible to design a PAE study in humans where all relevant variables – genetics, drug exposure, pattern of alcohol exposure, environmental influences etc. – can be effectively controlled. Studies using tissue samples are useful under particular circumstances, and this method can be tightly controlled, uncomplicated, and cost-effective which can allow for multiple internally valid experiments (Wilson & Cudd, 2011). However, tissue studies are limited in terms of their ability to demonstrate the impact of PAE, which necessarily involves whole animals during pregnancy, with a digestive system and many bodily influences on alcohol consumed and its eventual impact on the fetus (Wilson & Cudd, 2011). Studies using live animals bridge this gap, and although no animal is a perfect surrogate for the human body, different animals can provide useful models for different research questions (Cudd, 2005). Smaller animals such as rodents are suitable for neurobiological or genetic studies, and their shorter gestation period allows a greater turnover of results (Schneider, Moore, & Adkins, 2011). Larger animals such as sheep and pigs provide a gestation period and some behaviours similar to humans, whereas non-human primates offer the most similar model to humans in terms of genetics, neurological and cognitive development, and social behaviours (Cudd, 2005; Kelly, Goodlett, & Hannigan, 2009). There are of course ethical issues inherent in the use of animals in this kind of research, but the impact that these studies can have on our understanding of PAE is substantial (Beydoun & Saftlas, 2008). Where observational studies of humans have provided tentative findings, the use of various animal models has been invaluable in the process of supporting evidence in a manner which would otherwise be unrealistic (Wilson & Cudd, 2011).

Early evidence of the physical impact of PAE on the human brain came entirely from post-mortem investigations of children born to alcoholic mothers following heavy PAE (Guerra, Bazinet, & Riley, 2009). By the late 1970s, alcohol had become widely accepted as a teratogen responsible for growth deficiency, craniofacial abnormalities, joint or skeletal defects, microcephaly, cardiac problems, and mental deficiency (Clarren, 1981). Further studies during this time began to produce more specific neurological findings including hydrocephalus (excess fluid on the brain), extensive neuroanatomical disorganisation, and leptomenigeal neuroglial heterotopia (an abnormal sheet of neural or glial tissue) around the meninges, cerebellum and brainstem (Clarren, Alvord, Sumi, Streissguth, & Smith, 1978). Such studies highlight the extent to which heavy PAE can impact brain development, often leading to stillbirth or infant mortality, but these findings may not be representative of the full range of deficits, especially those seen following moderate alcohol exposure (Sawada-Feldman et al., 2012). More recently, advances in brain imaging technologies have allowed the assessment of brain structure and function in live human patients. Magnetic resonance imaging (MRI) has shown that reductions in overall brain volume and surface area as well as malformations are common, but that certain brain areas appear to be particularly susceptible to PAE including the corpus callosum, cerebellum, basal ganglia, hippocampus, and the parietal and frontal lobes (Donald et al., 2015; Lebel, Roussotte, & Sowell, 2011).

Further to studies investigating changes in brain structure in FASD, functional neuroimaging studies allow the investigation of brain activity. In individuals with FASD, several types of brain imaging technologies have been employed, including electroencephalography (EEG), Positron Emission Tomography (PET), functional MRI (fMRI), and one recently published study has used functional near infra-red spectroscopy (fNIRS; Kable & Coles, 2017). Neuroimaging studies have shown a general inefficiency in brain functioning in individuals with FASD, where task performance is weaker than in typically developing participants. This is associated with differences in brain activity, such as the use of a wider volume of brain area or greater levels of activity, suggesting people with FASD use their brain in a different way to typically developing persons. This has been seen in studies of spatial working memory (Malisza et al., 2005), sustained visual attention (Li et al., 2008), and facial working memory (Astley et al., 2009). However, even where task performance is similar, brain imaging studies have shown that PAE is associated with differences in neurological functioning, both in terms of level and area of activity. This is shown by studies of inhibitory control (Fryer, Tapert, et al., 2007), working memory (O'Hare et al., 2009), and number processing (Meintjes et al., 2010), suggesting that individuals with FASD have to expend more energy than typically developing persons to achieve the same cognitive goal.

Related to neuroanatomical damage, and of particular interest to this thesis, is the impact of PAE on the endocrine system. Animal models and human observational studies have demonstrated a link between PAE, hormone imbalance, and an increased stress-response (Haley, Handmaker, & Lowe, 2006; Hellemans, Verma, Yoon, & Weinberg, 2008), and the link between alcohol exposure and an altered stress response is the hypothalamic-pituitary-adrenal (HPA) axis (Weinberg, Sliwowska, Lan, & Hellemans, 2008). The HPA axis is formed of the hypothalamus and pituitary gland in the brain, and the adrenal glands which are located at each kidney. The stress response begins with activation of the hypothalamus, and results in the release of cortisol, epinephrine and norepinephrine into the bloodstream. These hormones increase heart rate and glucose levels which may be needed during the stressful situation (Garret, 2011). PAE can increase activation of the HPA axis in humans (Haley, Handmaker, & Lowe, 2006), which means that individuals exposed to alcohol prenatally may be more susceptible to damage caused by stressful events during childhood or adulthood.

Fathers' drinking behaviour can also affect their unborn offspring, through both biological and environmental means. Alcohol consumption by biological fathers in the week leading up to IVF sperm collection has been found to predict failure to achieve live birth and spontaneous miscarriage in a large sample of Hungarian men, possibly due to the impact of alcohol on sperm count or quality (Czeizel, Czeizel, & Vereczkey, 2013). In a mouse model, males who were intubated with alcohol prior to the conception of their offspring were more likely than non-exposed controls to produce pups with teratogenic and developmental deficits (Lee et al., 2013). Sperm quality was also suggested as an explanation for these effects, but the authors report that such mechanisms are poorly understood. Transgenerational epigenetic inheritance – the biological inheritance of acquired characteristics from the previous generation via epigenetic means - has been suggested as a mechanism for passing on drug-seeking behaviours from male mice to their offspring (Finegersh, Rompala, Martin, & Homanics, 2015). Epigenetic inheritance is also seen in plants and smaller animals such as nematodes, but the extent to which it may occur in mammals is poorly understood (Heard & Martienssen, 2014; van Otterdijk & Michels, 2016). Further studies in humans have found associations between preconception paternal alcohol consumption and low birthweight (Passaro, Little, Savitz, & Noss, 1998), cognitive deficit (Roeleveld, Vingerhoets, Zielhuis, & Gabreëls, 1992), congenital heart defect (Steinberger, Ferencz, & Loffredo, 2002) and leukaemia (Milne et al., 2013). Sperm quality is currently a more likely explanation for such effects than transgenerational epigenetic inheritance.

Aside from biological mechanisms, there appears to be a significant social effect of male partners on maternal alcohol consumption during pregnancy, leading to an increased risk of a child

being born with FASD. Women who drink during pregnancy have been shown to be more likely to live with a male partner who consumed alcohol (Czeizel et al., 2013), and more than half of women whose male partner was a heavy drinker continued to drink during pregnancy (Bakhireva et al., 2011). The quality of a woman's relationship with her male partner has also been shown to influence her alcohol behaviour during pregnancy; women who reported higher relationship satisfaction were less likely to consume alcohol during pregnancy (Bakhireva et al., 2011), and when fathers were involved in pregnancy care protocols, their female partner was less likely to drink during pregnancy (Czeizel et al., 2013). Unfortunately, many of the findings relating to male partners' impact on FASD are taken from only a small number of high-quality studies (for a review, see McBride, & Johnson, 2016). The focus of investigations into the mechanisms of FASD has understandably been on *in utero* biological factors which necessarily implicate the biological mother, but there has been some concern that women have been unfairly villainised here, while the role of fathers, partners and others has been overlooked (Gearing, McNeill, & Lozier, 2005; McBride, & Johnson, 2016). There also appear to have been no studies into the prenatal influence of female partners on maternal alcohol consumption (McBride, & Johnson, 2016).

2.3 Diagnosis of FASD

The term foetal alcohol syndrome (FAS) was coined in 1973 by Jones and Smith, following their landmark description of eight infants born to alcoholic mothers (Jones & Smith, 1973; Jones et al., 1973). Those infants presented with microcephaly, prenatal and postnatal growth restriction, craniofacial, limb, and cardiovascular defects, and neurodevelopmental deficit including impaired motor function and behaviour (Jones et al., 1973). The diagnosis of FAS is still in use today but in the decades since these first descriptions of an emerging problem, it has become apparent that FAS is only part of the full spectrum of effects seen following PAE. FAS is now considered to be the most severe category of a range of outcomes best described as foetal alcohol spectrum disorders (FASD; Riley, Infante & Warren, 2011). The craniofacial anomalies first described by Jones and Smith have become key diagnostic features of FAS, three of these in particular – short palpebral fissures (eye openings), thin upper vermillion (of the top lip), and a smooth philtrum (groove between top lip and nose; see figure 1).

For a diagnosis of FAS, evidence is required of three criteria: the characteristic facial features discussed above; growth restriction - weight or height at or below the 10th percentile; and (Coles et al., 2016). Documented evidence of maternal alcohol consumption is required for all diagnoses

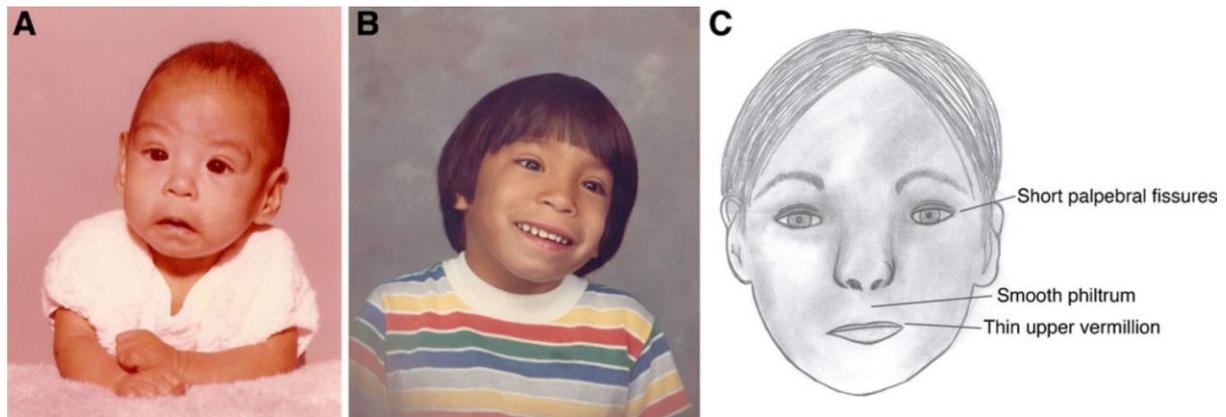


Figure 2.1: FAS facial features. From Riley, Infante & Warren (2011)

except FAS, neurodevelopmental deficit including microcephaly, cognitive deficit, and behavioural which can be diagnosed without confirmed PAE if all other criteria are met (Coles et al., 2016). Other diagnoses in use include partial foetal alcohol syndrome (pFAS), alcohol related neurodevelopmental disorder (ARND), and alcohol related birth defects (ARBD) as well as a number of less frequently used and often overlapping diagnoses. The reason for this variety in diagnostic practice is that a clinician may use one of several available diagnostic codes, each of which has its own set of diagnoses and criteria (Coles et al., 2016). During the 1980's and 1990's, a diagnosis of foetal alcohol effects (FAE) was typically used in cases where damage from PAE was evident, but the patient did not meet diagnostic criteria for FAS. FAE was poorly defined however, which led to the misdiagnosis of patients whose symptoms may not have been the result of PAE (Hoyme et al., 2005). Since then, several diagnostic guidelines have been proposed, and are used by clinicians today. These feature various distinct diagnoses, although they share many similarities. Complete descriptions of these guidelines and their diagnostic criteria are available elsewhere (see original citations below or Coles et al., 2016 for a review). A very brief description of some of the more commonly used guidelines is provided in table 2.1

Without any external standard, it is difficult to assess which, if any, of these diagnostic guidelines is more useful or valid than the others. Coles and colleagues (2016) reviewed four of these (Hoyme modifications, CDC, Canadian guidelines, and 4-digit code) as well as their own proposed system known as Emory Clinic. The authors concluded that these five systems produce only moderate agreement in terms of diagnostic outcome. The fact that a patient's choice of clinic or country of residence may be a deciding factor between one diagnosis and another, or between a diagnosis and no diagnosis, is clearly undesirable, especially since early diagnosis can reduce the risk of some adverse outcomes associated with PAE (Streissguth et al., 2004).

Table 2.1: Summary of diagnostic criteria for FASD

<p>Institute of Medicine and Hoyme modifications</p>	<p>In 1996, the Institute of Medicine (IOM) published the first detailed criteria for FASD and described five distinct diagnoses: foetal alcohol syndrome with confirmed alcohol exposure; foetal alcohol syndrome without confirmed alcohol exposure; partial foetal alcohol syndrome (pFAS); alcohol related neurodevelopmental disorder (ARND); and alcohol related birth defects (ARBD; Stratton, Howe, & Battaglia, 1996). These diagnoses differ in terms of their criteria – all except FAS require documented evidence of PAE, ARND does not require physical signs, and ARBD does not require neurodevelopmental delay. The IOM criteria were modified by Hoyme and colleagues (2005), who added a further category of pFAS without confirmed PAE.</p>
<p>Seattle 4-digit code</p>	<p>The 4-digit code diagnostic system (Astley & Clarren, 2000), uses a slightly different approach. Patients are still rated in terms of the four criteria used in the IOM system (PAE, growth, facial features and neurodevelopment), but a numerical system is used where patients are given a score of one to four, to signify the severity or likelihood of each of these criteria. This system therefore produces 256 possible combinations, from 1-1-1-1 (no diagnosis) up to 4-4-4-4 (foetal alcohol syndrome). The 4-digit code system does use the diagnoses of FAS and pFAS, but instead of ARBD and ARND, this system uses the diagnoses of sentinel physical findings, static encephalopathy, and neurobehavioural disorder (Astley & Clarren, 2000).</p>
<p>CDC and Canadian guidelines</p>	<p>The Centres for Disease Control and Prevention (CDC) published their own diagnostic guidelines in 2004 (Bertrand et al., 2004). This system is similar to the IOM criteria, except that it does not allow the diagnoses of ARND or ARBD. Finally, the Canadian guidelines (Chudley et al., 2005; Cook et al., 2016) use a numerical diagnostic procedure based on the 4-digit code system, but diagnostic categories are taken from the IOM criteria.</p>

The most recent (5th) edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) contains a proposed diagnosis of Neurobehavioural Disorder associated with Prenatal Alcohol Exposure (ND-PAE). This inclusion is not yet a recognised functioning diagnosis but is suggested as a condition that requires further research. According to Sanders (2013), the motivation behind a further diagnosis related to PAE is that the extant diagnoses are often insufficient in terms of providing medical or educational assistance to patients. Payment for such services, particularly in countries without universal access to healthcare, is a key issue since a recognised diagnosis can lead to vital state-funded support. The suggested diagnostic criteria for ND-PAE depart from those outlined above in that there is no requirement for the presence or absence of physical features. The diagnosis is based only on PAE and neurodevelopmental issues

including impaired self-regulation, cognitive deficit, and deficits in adaptive functioning (Kable et al., 2016). ND-PAE is therefore most similar to the already established ARND, but this system avoids any issues related to the presence or absence of physical features as well as any confusion with the various existing definitions of ARND (Kable & Mukherjee, 2017).

Diagnosis of any of the PAE-related conditions usually requires evidence of maternal alcohol consumption during pregnancy, and the most common source of this information is maternal self-report (Lange, Shield, Koren, Rehm, & Popova, 2014). This method may be problematic however, since retrospective accounts of alcohol consumption can be unreliable (Monk, Heim, Qureshi & Price, 2015) and in the case of drinking during pregnancy there is the added risk of stigmatisation leading to embarrassment or guilt (Zelner et al., 2012). Objective measures are available for the detection of PAE in newborns or mothers post-delivery and these may be used in conjunction with maternal self-report, although there is often discrepancy between these two sources (Bager, Christensen, Husby, & Bjerregaard, 2017). Objective methods include taking samples of blood, hair or urine from the infant or mother, or samples of meconium (infant's first stool), umbilical cord, or placenta (Bager et al., 2017; Joya et al., 2012). From these samples, many biochemical substances can show evidence of PAE due to their relative scarcity or abundance, and a recent review found that of these biomarkers, fatty acid ethyl esters, ethyl glucuronide, ethyl sulphate, and phosphatidylethanol were found to be the most effective at detecting PAE (Bager et al., 2017). No biomarker for the detection of PAE or PAE related damage in older children, adolescents or adults is currently available. There is emerging evidence that DNA methylation signatures (Portales-Casamar et al., 2016) or changes to histone modifications (Chater-Diehl, Laufer, & Singh, 2017) may enable researchers to develop diagnostic techniques that take advantage of more stable biomarkers, but this avenue of research is currently speculative.

2.4 Prevalence and financial cost of FASD

PAE is one of the world's leading known causes of birth defects and neurodevelopmental impairment, and one of the few that is entirely preventable (May et al., 2009; Popova, Lange, Probst, Gmel, & Rehm, 2017). The use of medical records to determine prevalence may be unreliable however, since the majority of cases of FASD are thought to be undiagnosed (Chasnoff, Wells, & King, 2015; Morleo et al., 2011). This view is supported by evidence from active case ascertainment studies, where systematic diagnosis is conducted on large samples of schoolchildren; studies such as this tend to produce far higher prevalence estimates than those relying on passive reporting systems (May et al., 2009).

The prevalence of FASD is unknown in the UK, but a recent meta-analysis found that the rate of alcohol consumption during pregnancy in the UK is among the highest in the world at an estimated 41.3% (Popova et al., 2017). Based on this figure, it has been estimated that the rate of FASD amongst UK children is approximately 3.24% (Lange et al., 2017). More recently, a screening algorithm was used to estimate prevalence of FASD from existing cohort data in the South-West of England (McQuire et al., 2019). Missing data was dealt with in three different ways, and three estimates were generated of 6%, 7.2% and 17%. In some countries, active case ascertainment methods, where a large sample of schoolchildren are actively screened for the condition, have been used to more reliably predict the rates of FASD, but this method has not currently been used in any UK study. European countries have some of the highest rates of alcohol exposure during pregnancy, with Ireland at the top of the list with 60.4% (Popova et al., 2017) and a consequent estimated FASD prevalence of 4.8% (Lange et al., 2017). These rates of exposure do not necessarily translate to levels of FASD however, which aside from methodological factors, may highlight the impact of issues such as dose, timing and pattern of exposure, as well as those genetic and other environmental factors discussed above. Some of the highest rates of FAS and FASD have been found in South Africa, and especially in the Western Cape province, where a number of historical, political and social factors have led to high levels of poverty and addiction to alcohol especially in some rural communities (May et al., 2000). Rates of FASD amongst schoolchildren here have been recorded at up to 20% (May et al., 2013). Elsewhere, high rates have been found in marginalised indigenous communities in Australia and North America. A study based on a community of Aboriginal Australians found a prevalence rate of 12% for FAS or pFAS (Fitzpatrick et al., 2015), whilst rates of up to 18.9% have been seen within indigenous Canadian communities (Popova, Lange, Probst, Parunashvili, & Rehm, 2017). FASD however is not just a problem in marginalised communities; the most recent meta-analysis to assess the prevalence of FASD in general population studies showed prevalence rate estimates of 1.5% in the United States, 4.5% in Italy, 4.8% in Ireland, 5.3% in Croatia, and 11.1% in South Africa (Lange et al., 2017). From these figures, the authors estimated a global prevalence for FASD at around 0.8% of all live births, although there is wide variation between international regions. In northern Africa and the Middle East for example, alcohol consumption is much lower than in western countries and estimated rates of FASD reflect this. Figures here are as low as 0.1 cases per 1000 in Libya and Tunisia, and 0 per 1000 in Saudi Arabia and the United Arab Emirates (Lange et al., 2017).

Damage from PAE is especially prevalent in children and young people living in foster care, children's homes, or otherwise under the supervision of Social Services or a similar state welfare system. Studies have found rates of FASD in looked after children of up to 28% in Brazil, 11% in

Canada, 16% in Chile, 40% in Russia, 52% in Sweden, 27% in the UK, and 34% in the USA (Lange, Shield, Rehm, & Popova, 2013; Gregory, Reddy, & Young, 2015).

Studies into the direct financial costs associated with PAE have been limited to those conducted in North America. A recent review of these estimated that costs are between 75 million and 5.4 billion US dollars annually for all individuals with FASD in the United States and Canada (Popova, Stade, Bekmuradov, Lange, & Rehm, 2011). These costs include healthcare, residential care, special education, and lost productivity, but crucially do not include costs associated with the criminal justice system, child welfare, or research and prevention which were absent from the literature at the time. The cost of incarceration has been assessed more recently in one Canadian study (Popova, Lange, Burd, & Rehm, 2015), which found that the cost of prison in 2011/12 for youths with FASD in Canada was 17.5 million Canadian dollars, whilst the cost for adults was over 350 million Canadian dollars. The largest studies on prevalence of FASD in prisons were two surveys of the entire correctional systems of the USA and Canada in 2001/02 (Burd, Selfridge, Klug, & Bakko, 2004; Burd, Selfridge, Klug, & Juelson, 2003). These surveys relied on official records, so undiagnosed cases would have been missed; rates of 0.91% were found for FASD in both countries. An active case ascertainment study of 287 Canadian inmates yielded a much higher estimate than this, at approximately 23% for FASD (Fast, Conry, & Loock, 1999). Despite the paucity of recent data, it is apparent that the cost of incarceration associated with FASD is significant in North America, and is presumably similar in other western countries.

2.5 Cognitive and behavioural deficits following PAE

Research into the cognitive and behavioural deficits seen in individuals prenatally exposed to alcohol has been ongoing since Jones and Smith's initial descriptions of Foetal Alcohol Syndrome (Jones & Smith 1973; Jones et al., 1973); yet almost half a century later, a distinct descriptive neurobehavioural profile is not yet complete (Kodituwakku, 2007; Kodituwakku & Kodituwakku, 2014). This may reflect the wide variation of damage seen within the foetal alcohol spectrum, but methodological limitations and inconsistencies may also be a factor here. There is, however, a fairly consistent picture emerging of the cognitive and behavioural strengths and weaknesses of children prenatally exposed to alcohol (Mattson, Crocker, & Nguyen, 2011).

One of the most common deficits in individuals with PAE is of general intellectual functioning. Studies have consistently shown lower IQ scores for children with FASD (e.g. Mattson, Riley, Gramling, Delis, & Jones, 1997; Streissguth, Clarren, & Jones, 1985; Streissguth, Herman, & Smith, 1978), and this effect appears to be a long-term or permanent deficit rather than developmental delay (Spohr, Willms, & Steinhausen, 2007; Steinhausen & Spohr, 1998; Streissguth,

Randels, & Smith, 1991). Moreover, lower IQ scores in children with FASD are related to poor academic achievement, which could lead to further adverse life outcomes (Howell, Lynch, Platzman, Smith, & Coles, 2006). Studies have tended to show that those individuals with dysmorphic features (e.g. smooth philtrum, thin upper vermillion, and short palpebral fissures) have IQ scores in the borderline intellectual disability range of approximately 70, whereas for those without dysmorphic features the average is approximately 80 (Ervalahti et al., 1997; Mattson et al., 1997; Streissguth et al., 1978). However it is not uncommon for individuals with FASD to exhibit IQ scores in the average and above average ranges (e.g. Chasnoff, Wells, Telford, Schmidt, & Messer, 2010). Measures of IQ tend to discriminate between verbal and non-verbal intelligence, and in FASD there is often a difference in terms of an individual's verbal and non-verbal scores, but the direction of this difference is inconsistent (Mattson et al., 2011; Mattson & Riley, 1998). Few published studies have investigated the impact of low to moderate levels of PAE on intelligence, and results have been inconsistent (Falgreen-Eriksen et al., 2012; Streissguth, Barr, & Sampson, 1990). Extraneous variables such as parental educational attainment (Alati et al., 2008) and ethnicity have been shown to moderate this effect (Willford, Leech, & Day, 2006).

Executive function (EF) is an umbrella term for the range of higher-order cognitive processes that involve conscious control and decision-making (Suchy, 2009), and these have consistently been identified as a central impairment of FASD (Khoury, Milligan, & Girard, 2015; Kodituwakku, Kalberg, & May, 2001). Measures of EF can take the form of informant report inventories such as the Behaviour Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy & Kenworthy, 2000), which attempt to give full accounts of an individual's EF in the real world, and cognitive procedures such as the Stroop (Stroop, 1935) or trial making tasks which generate a score based on accuracy or completion time (Anderson et al, 2002). Both of these approaches are used in research, but there is poor agreement between them, possibly due to parents' subjective perception of their child's abilities, or because children may struggle to implement their EF skills in daily life (Gross, Deling, Wozniak, & Boys, 2015). It appears that EF deficit in FASD is a long-term or permanent feature rather than a developmental delay, with some suggestion that deficits can worsen with age (Rasmussen & Bisanz, 2009). Few studies have explored cognitive functioning in adults with FASD but there is some evidence of EF deficit here too (Rangmar, Sandberg, Aronson & Fahlke, 2015). Most studies into EF in FASD have focussed on older children and adolescents, but there is some evidence that children with FASD under six years of age also show deficits in EF, and those with a diagnosis of FAS may be more severely affected than others (Fuglestad et al., 2015). Diagnosis is also a moderating factor in older children, with studies tending to show more deficient EF in those toward the more severe end of the spectrum with dysmorphic features (Astley et al., 2009; Khoury et al., 2015). EF may be one of

the cognitive deficits most keenly felt by parents and carers of children with FASD and may be a significant cause of stress (Paley, O'Connor, Frankel, & Marquardt, 2006). This is because deficit in EF is associated with problems in communication, externalising behaviour, adaptive functioning and social skills (Clark, Prior, & Kinsella, 2002; Schonfeld, Paley, Frankel, & O'Connor, 2006).

Language impairments appear to be common amongst children with FASD, but studies have not found a consistent profile of language deficit (McCabe, 2009). This is reflective of the wide variation of neurobiological damage associated with PAE, but methods used by such studies have been inconsistent and not always appropriate (Ganthous, Rossi, & Giacheti, 2015). Measures of language ability commonly discriminate between expressive (production of) and receptive (comprehension of) language, and although studies tend to find deficits in both domains in alcohol-exposed children, the relative strength of one or the other is inconsistent (McGee, Bjorkquist, Riley, & Mattson, 2009; Wyper & Rasmussen, 2011). Deficits in children with FASD have been found in many aspects of language including speech production, comprehension, grammar, pragmatics, and semantics (Mattson et al., 2011), and there is some evidence that language deficit may worsen during later childhood (Proven, Ens, & Beaudin, 2014). However there are very few data on language in adults with FASD. One study assessed affective prosody (the non-linguistic aspects of speech such as tone, cadence and volume) in adults with PAE, and found that they performed worse than healthy controls and on a par with adults with focal brain lesions (Monnot, Lovallo, Nixon, & Ross, 2002). This study also provides evidence for a link between PAE, damage to the right cortex and corpus callosum, and affective language deficits in adults, although other studies have identified a link between PAE, language deficit, and damage to the left temporo-parietal region of the cortex (Lindell, 2016). Another issue with research into language deficit in FASD is that intelligence has been consistently identified as a moderating variable – FASD children with higher IQ scores tend to perform better in language assessments (Mattson et al., 2011; McGee, Bjorkquist, Riley, & Mattson, 2009).

Other cognitive domains have been found to be deficient in FASD, including attention (Mattson, Calarco, & Lang, 2006), memory (Willford, Richardson, Leech, & Day, 2004), motor function (Connor, Sampson, Streissguth, Bookstein, & Barr, 2006), sensory processing (Franklin, Deitz, Jirikowic, & Astley, 2008) and visual-spatial abilities (Crocker, Riley, & Mattson, 2015). Together with intelligence, executive functioning and language, the range of cognitive deficits seen following PAE is substantial, and these are closely related and interconnected to a similarly wide range of problematic behavioural, emotional and social outcomes. Significant variation is seen here as well, but a profile is gradually taking shape (Kodituwakku & Kodituwakku, 2014; Matson et al., 2010). A particular feature of PAE that serves to demonstrate the relationship between cognitive

and behavioural deficits is social cognition. Children with FASD have difficulties with understanding social cues, show poor social judgement and decision making (Kodituwakku, 2007), and can be deficient in terms of empathy and social perspective taking (Stevens, Dudek, Nash, Koren, & Rovet, 2015). Moreover, deficits in social cognition following PAE tend to persist and may worsen with age (Kully-Martens, Denys, Treit, Tamana, & Rasmussen, 2012). Poor performance on measures of Theory of Mind (the ability to attribute and recognise different mental states in others) has been shown to correlate with deficits in executive functioning in children with FASD (Rasmussen, Wyper, & Talwar, 2009). A combination of difficulties with EF, social cognition, and language has been postulated more than once as a major cause of poor social and behavioural outcomes in children and adolescents with FASD, including a tendency to be disliked, ostracised or bullied by their peers (Coggins et al., 2003; Kully-Martens et al., 2012).

As well as having difficulties with social communication and peer relationships, children with FASD may struggle to cope with school or home life due to an extensive range of internalising (self-focused or emotional) and externalising (acting out) behavioural problems. These can include: acting young for their age (Nash et al., 2006), adaptive or daily living difficulties (Jirikowic, Kartin, & Olson, 2008), aggression (Sood et al., 2001), attention deficit (LaFrance et al., 2014), bedwetting or incontinence (Roozen et al., 2017), confabulation (Brown, 2017), cruelty or bullying of other children (LaFrance et al., 2014), depression or anxiety (Hellemans, Sliwowska, Verma, & Weinberg, 2010), disobedience, impulsivity, lack of guilt (Nash et al., 2006), lying or cheating, restlessness or hyperactivity (LaFrance et al., 2014), sleep disturbances (Chen, Olson, Picciano, Starr, & Owens, 2012), and stealing (LaFrance et al., 2014). Due to the varied and often significant behavioural outcomes seen, children with FASD frequently meet criteria for other developmental or mental health diagnoses including attention deficit hyperactivity disorder (ADHD; O'Malley & Nanson, 2002), autism spectrum disorder (ASD; Bishop, Gahagan, & Lord, 2007), conduct disorder (Disney, Iacono, McGue, Tully, & Legrand, 2008), mood disorder (O'Connor et al., 2002), and oppositional defiant disorder (Fryer, McGee, et al., 2007).

Most FASD research is conducted on children, but there is evidence of the persistence of behavioural difficulties associated with PAE in adolescents and adults, and the kinds of adverse life outcomes seen in this population. Prenatal alcohol exposure has been identified as a risk factor for alcohol misuse in adolescence (Baer, Barr, Bookstein, Sampson, & Streissguth, 1998) and young adulthood (Baer, Sampson, Barr, Connor, & Streissguth, 2003). Young adults who were prenatally exposed to binge drinking have been found to be more likely than typically developing peers to experience a range of psychiatric disorders and traits including drug or alcohol misuse, paranoia, and antisocial personality disorder (Barr et al., 2006). Adults with FASD have been found to display high

rates of secondary disabilities and adverse life outcomes including trouble with the law, drug or alcohol misuse, disrupted educational experiences, unemployment, homelessness, and inappropriate sexual behaviours (Brown, 2014; Clark, Lutke, Minnes, & Ouellette-Kuntz, 2004; Streissguth et al., 2004). Inappropriate sexual behaviours included promiscuity, public exposure, sexual harassment, voyeurism, bestiality, incest, or any other sexual behaviour that would likely result in prosecution. These types of behaviours, along with drug misuse issues and the fact that individuals with FASD are easily led or suggestible (Fast & Conry, 2009) add to the risk of arrest, prosecution and potentially imprisonment. Suggestibility may also be an issue when being questioned by police, and guidelines have been proposed for police in order to prevent individuals with FASD from falsely incriminating themselves (e.g. Brown, Gudjonsson, & Connor, 2011). Women with FASD may also be at increased risk of conceiving a child with FASD. There is little research on this, but in an American study of 30 women with FASD who were mothers (Streissguth, Barr, Kogan, & Bookstein, 1996), 40% reported drinking during pregnancy, 37% had their children removed by child protective services, and 17% had a child with a diagnosis on the foetal alcohol spectrum, with a further 13% with suspected PAE related damage. There is a lack of specific data on women with FASD drinking during pregnancy, but with an increased risk of alcohol misuse, risky sexual behaviours, difficulty with planning and decision-making, and a tendency to suggestibility, it would appear that there is a significant risk of a positive feedback cycle where higher rates of FASD, especially amongst women, could increase the rate further in the next generation.

Recently, prospective studies have attempted to assess cognitive and behavioural outcomes following low to moderate prenatal exposure to alcohol, but results have been inconsistent. The definitions of low or moderate exposure are not uniform, and this is complicated by the use of different unit measures across different countries. In the UK Millennium Cohort Study, Kelly and colleagues (2008, 2010, 2013) defined low exposure as more than zero, but no more than two UK units per week or per drinking session. They found no significant risk of cognitive or behavioural problems in children with low level PAE at ages three, five or seven. Similarly, in the Western Australian Pregnancy Cohort Study, Robinson and colleagues (2010) defined light drinking as between two and six standard drinks per week (Australian, equivalent to 1.3 – 7.6 UK units), and found no significant associated risk of behavioural problems in children up to 14 years. However, in an American study, Sood and colleagues (2001) found that low levels of exposure (between zero and 0.3 fluid ounces of pure alcohol - equivalent to between zero and one UK unit per day) were significantly correlated with adverse behavioural outcomes including aggression and externalising problems in children aged six to seven years, even after controlling for other factors known to predict behavioural problems.

The mixed results of studies into low to moderate PAE may be partly due to the influence of confounding variables. True experiments in humans, where pregnant women are randomly assigned to consume alcohol, would be deeply unethical. Therefore, research is limited to observational designs such as case-control or cohort studies, which are susceptible to confounding variables (Gray, Mukherjee & Rutter, 2009). For example, women who drink low to moderate amounts of alcohol during pregnancy tend to be more affluent than women who never drink and women who drink more heavily, and affluence is associated with advantages in offspring such as higher levels of intelligence and academic achievement (O'Leary & Bower, 2012). Factors such as affluence could therefore partly explain the mixed results of studies into low to moderate alcohol exposure on cognitive functioning in school-age children. One technique that can bridge the gap between observational studies and experimental studies in humans is Mendelian randomisation. Named after early geneticist Gregor Mendel, this technique relies on the random distribution of genes from each parent to their offspring. This leads to random variation within the population of genetic determinants of behaviour, including alcohol consumption. Variations of a gene that controls the production of alcohol dehydrogenase - rs1229984 (ADH1B) – have been shown to predict alcohol consumption before and during pregnancy (Zuccolo et al., 2009) and is considered the most useful tool to conduct quasi-randomisation to conditions of varying PAE in humans (Zuccolo et al., 2013). Studies that have employed this technique have demonstrated significant incremental differences between moderate, low, and zero alcohol exposure in pregnancy, where higher exposures were associated with deficits, in intelligence and academic achievement (Zuccolo et al., 2013), early-onset persistent conduct problems (Murray et al., 2016) and atopic conditions such as asthma, hay fever and eczema (Shaheen et al., 2014)

2.6 Attachment, trauma and addiction

It has been known for several decades that children of alcoholics are at an increased risk of drug and alcohol misuse, and various adverse emotional and behavioural outcomes compared with children of non-alcoholics (Berkowitz, & Perkins, 1988). This is not necessarily due to PAE, since there are many environmental risk factors related to families and environments where substance use is an issue. The Adverse Childhood Experiences (ACE) study (Felitti et al., 1998) identified seven categories (later made up to 10; Dube et al., 2003) of childhood experiences that are predictive of a range of health risk behaviours and diseases in adulthood. These include physical, sexual and psychological abuse, emotional and physical neglect, and having lived with an alcoholic or drug abuser. Subsequent studies have shown that children of alcoholics are at an increased risk of experiencing all categories of ACE, compared to children of non-alcoholics (Anda et al., 2002; Dube, Anda, Felitti, Croft, et al., 2001). According to a recent systematic review (Park & Schepp, 2015),

specific adverse outcomes seen in children of alcoholics have included externalising and internalising behavioural problems, depression and anxiety, low cognitive ability and academic performance, ADHD, anxiety, poor social skills, substance misuse, and suicidality. Surprisingly, the review did not mention any study that had considered the impact of PAE in these outcomes. Aside from the potential impact of prenatal exposures, postnatal experiences including neglect and abuse can lead to adverse outcomes via socio-developmental mechanisms including the infant-caregiver attachment relationship.

Attachment in infancy has a major impact on social information processing. The experiences of infants with their caregivers contribute to a mental representation of social interaction and the nature of other persons (Bowlby, 1969, 1973, 1980; Dykas & Cassidy, 2011). Most infants will benefit from the presence of an attentive, emotionally available caregiver and will develop a secure attachment, but this is less likely in families with low socioeconomic status, teenage mothers, parents with mental health issues, and parents with drug or alcohol misuse issues (Van Ijzendoorn, Schuengel, & Bakermans–Kranenburg, 1999). Children who are maltreated however, are among the most likely to develop harmful insecure or disorganised attachments to their caregivers, which can lead to a lifetime of dysfunctional relationships with authority figures, peers, partners, and ultimately their own children (Howe, 2005; Baer & Martinez, 2006). Attachment relationships and their behavioural consequences have been studied in depth for many years (e.g. Ainsworth & Bell, 1970; Hazan & Shaver, 1987); more recently though, the neurobiological and hormonal mechanisms of attachment have emerged, mostly based on data from animal models (Insel, & Young, 2001). Mammalian studies have shown that endorphins, dopamine, and oxytocin play a key role in attachment formation, and functional neuroimaging studies have supported this relationship in humans (Swain et al., 2014). The physical presence of an attachment figure stimulates the release of endorphins and oxytocin in the infant brain, and this appears to be necessary for the healthy development of related brain circuitry including the oxytocinergic and dopaminergic systems (Maté, 2012; Strathearn, 2011). Prolonged absence of a caregiver and neglectful caregiving are associated with major alterations in these systems, which can have serious long-term consequences for social development and emotion regulation (oxytocinergic system) and stimulus-reward learning and decision-making (dopaminergic system; Strathearn, 2011). Abusive caregiving can also cause this kind of damage to the infant brain; even though the caregiver may be present, an abusive caregiver is not a source of comfort and will instead provoke a stress response in the infant, characterised by increased release of cortisol and activation of the HPA axis (Tarullo, & Gunnar, 2006). Repeated or prolonged activation of the HPA axis during infancy and early childhood shapes the long-term

behaviour of that system, initiating a trajectory which can lead to long-term issues with stress-response, relationships and mental and physical health (Tarullo, & Gunnar, 2006).

Caregivers who are abusive and/or neglectful of their children are more likely to have been maltreated themselves as children than non-maltreating caregivers (Howe, 2005), although the predictive validity of this relationship may have been exaggerated at times (Kaufman & Zigler, 1987). The relationship between caregiver and child is complex, and there are many potential confounders of the likelihood that a caregiver will maltreat their child. Episodes tend to occur during stressful periods such as problematic child behaviour. Many parents find child misbehaviour difficult to manage, but a caregiver who themselves has a malfunctioning oxytocinergic or stress-response system, for whom the usual chemical attachment mechanisms are compromised, may be psychologically incapable of dealing with this stress and resort to either physically or psychologically lashing out at their child, or escaping the situation and leaving the child physically or emotionally neglected, or vulnerable to abuse by other adults (Howe, 2005; Wolfe, 1985). Sociopathic tendencies of the abuser – lying, stealing, violence and other criminal behaviour – along with a home environment characterised by poor social interaction, neglect of children and violence between adult partners, are predictive of an adult's sexual abuse of children (Howe, 2005). Although only a minority of sexual abusers appear to have been sexually abused themselves as children (Kaufman & Zigler, 1987), some factors may increase this risk in potential perpetrators. These include witnessing or experiencing violence in childhood, rejection or emotional neglect, lack of guilt or remorse, and the lack of a non-abusive father figure (Skuse et al., 1998).

Maltreated children are more likely than non-maltreated children to become substance-addicted adults (Elliot et al., 2014; Hovdestad, Tonmyr, Wekerle, & Thornton, 2011). A key factor in this relationship may be the role of the dopaminergic incentive-motivation system; rats separated from their mothers at an early age show an increased dopamine response to stress, and increased sensitivity to the effects of cocaine and amphetamine in adulthood (Meaney, Brake, & Gratton, 2002). Similarly, oxytocin, which is responsible for social affiliation and the regulation of mood and anxiety, is a key mechanism behind the effects of several popular recreational drugs, and is seen in diminished quantities in adults who were neglected as children (Teicher, 2000). Further studies in humans have indicated that childhood maltreatment is predictive of dependence on alcohol (Potthast, Neuner, & Catani, 2014), nicotine (Elliott et al., 2014), cocaine (Hyman, Garcia, & Sinha, 2006), heroin (Lau et al., 2005), and predicts gambling addiction (Petry, & Steinberg, 2005), internet addiction (Dong et al., 2010) and obesity (Danese & Tan, 2014). It would appear likely therefore, that the neurobiological and neuroendocrine system injuries sustained during a traumatic childhood can significantly increase the risk of developing addiction during adolescence or adulthood, and this

explanation has been postulated a number of times (e.g. Elton, Smitherman, Young, & Kilts, 2015; Enoch, 2011; Gerra et al., 2009; Maté, 2012; Sinha, 2008). Many maltreated children do not develop addictions however, and a number of potential protective factors have been identified, including genetic characteristics, female sex, high quality family and peer relationships, no family history of substance abuse, and low family or neighbourhood stress (Enoch, 2011).

2.7 Definitions of maltreatment, abuse and neglect

Child maltreatment is defined as physical, sexual or psychological abuse, or physical or emotional neglect. The most recent definitions used by the UK government (2015) are as follows:

Table 2.2: Definitions of abuse and neglect. (UK government, 2015)

Physical abuse	A form of abuse which may involve hitting, shaking, throwing, poisoning, burning or scalding, drowning, suffocating or otherwise causing physical harm to a child. Physical harm may also be caused when a parent or carer fabricates the symptoms of, or deliberately induces, illness in a child.
Emotional abuse	The persistent emotional maltreatment of a child such as to cause severe and persistent adverse effects on the child’s emotional development. It may involve conveying to a child that they are worthless or unloved, inadequate, or valued only insofar as they meet the needs of another person. It may include not giving the child opportunities to express their views, deliberately silencing them or ‘making fun’ of what they say or how they communicate. It may feature age or developmentally inappropriate expectations being imposed on children. These may include interactions that are beyond a child’s developmental capability, as well as overprotection and limitation of exploration and learning, or preventing the child participating in normal social interaction. It may involve seeing or hearing the ill-treatment of another. It may involve serious bullying (including cyber bullying), causing children frequently to feel frightened or in danger, or the exploitation or corruption of children. Some level of emotional abuse is involved in all types of maltreatment of a child, though it may occur alone.
Sexual abuse	Involves forcing or enticing a child or young person to take part in sexual activities, not necessarily involving a high level of violence, whether or not the child is aware of what is happening. The activities may involve physical contact, including assault by penetration (for example, rape or oral sex) or non-penetrative acts such as masturbation, kissing, rubbing and touching outside of clothing. They may also

	include non-contact activities, such as involving children in looking at, or in the production of, sexual images, watching sexual activities, encouraging children to behave in sexually inappropriate ways, or grooming a child in preparation for abuse (including via the internet). Sexual abuse is not solely perpetrated by adult males. Women can also commit acts of sexual abuse, as can other children.
Neglect	<p>The persistent failure to meet a child’s basic physical and/or psychological needs, likely to result in the serious impairment of the child’s health or development.</p> <p>Neglect may occur during pregnancy as a result of maternal substance abuse. Once a child is born, neglect may involve a parent or carer failing to:</p> <ul style="list-style-type: none"> • provide adequate food, clothing and shelter (including exclusion from home or abandonment) • protect a child from physical and emotional harm or danger; • ensure adequate supervision (including the use of inadequate care-givers) • ensure access to appropriate medical care or treatment. <p>It may also include neglect of, or unresponsiveness to, a child’s basic emotional needs.</p>

Similar definitions are given by the National Society for the Prevention of Cruelty to Children (NSPCC, 2017), World Health Organisation (WHO, 2017), and Centres for Disease Control and Prevention (Leeb, Paulozzi, Melanson, Simon, & Arias, 2008). The long-term cognitive and behavioural consequences of the trauma associated with maltreatment have been investigated extensively, although a full understanding may never be reached. An overview of some of the findings is provided in the following section of this chapter. Many maltreated children suffer multiple forms of abuse or neglect and to varying degrees of severity (Clemmons, Walsh, DiLillo, & Messman-Moore, 2007; Edwards, Holden, Felitti, & Anda, 2003). They may also suffer other adverse experiences such as a chaotic home environment, witnessing domestic violence, parental separation, war or neighbourhood violence, living with a family member who is mentally ill, addicted to drugs or alcohol, or who is incarcerated, and many other traumatic or adverse issues which are more difficult to define (Dube et al., 2003; Copeland, Keeler, Angold, & Costello, 2007).

2.8 The impact of traumatic childhood experiences on cognitive and behavioural development

In November 1989, a coup d'état in Romania saw the collapse of the ruling Ceauşescu government, and international media and humanitarian organisations were allowed in to the previously secretive state. It soon became apparent that over a hundred thousand orphans had been

kept in state institutions where conditions ranged “from poor to appalling” (Rutter, 1998, p. 467). Infants and young children were effectively warehoused with little or no access to any kind of physical or social stimulation, in rows of cots and with around 30 children to one, often untrained, caretaker (Kumsta et al., 2015). Upon release, many of the children were adopted by international families, and some were enrolled into research cohorts to make use of the rare opportunity to study a substantial cohort of similarly aged children who had moved from a situation characterised by severe neglect and deprivation, into caring and relatively prosperous families. The English and Romanian Adoptees (ERA) Study (Rutter, 1998) consisted of 144 Romanian institution orphans, 21 Romanian orphans from deprived, non-institutional care, and a control group of 52 English adoptees of the same age range (0-46 months). To date, assessments have been carried out at 4, 6, 11, 15, and 22-25 years (Kumsta et al., 2015; Sonuga-Barke et al., 2017).

One of the most enduring and significant findings from the ERA study is that children who spent less than their first six months in neglectful care appear to have been largely protected from the many adverse physical, emotional and cognitive outcomes seen in those who were older than six months at adoption, and the Romanian cohort in this study has therefore typically been divided into groups based on their age at adoption (Kumsta et al., 2015; Sonuga-Barke et al., 2017). At first, most children were developmentally delayed, but by six years of age those with less than six months of deprivation had caught up with the English controls in most aspects of cognitive and behavioural development (Rutter et al., 1999). Those who were adopted at over six months of age showed cognitive deficit (IQ < 80), problems with language and communication, inattention and hyperactivity. However, cognitive deficit tended to diminish through childhood and adolescence so that by young adulthood, those with more than six months’ deprivation had caught up with the other Romanian adoptees and English controls, but emotional problems such as depression and anxiety took the opposite trajectory, worsening with age (Sonuga-Barke et al., 2017). Behavioural problems (dishonesty, aggression, conduct problems, disobedience) were more consistent throughout childhood, adolescence and young adulthood. Those who were adopted from institutions at over six months of age were most likely to have low educational attainment, be unemployed, and use mental health services as young adults (Sonuga-Barke et al., 2017).

Other studies of post-institutionalised children have found similar results. Severe early deprivation is predictive of deficits in executive functioning, memory (Bos, Fox, Zeanah, & Nelson, 2009) and empathy (Tarullo, Bruce, & Gunnar, 2007), and is predictive of attachment disorder (O’Connor, Bredenkamp, & Rutter, 1999) and a range of emotional and behavioural difficulties (Hawk & McCall, 2010). Moreover, duration of institutional care is positively related to severity of cognitive and behavioural deficit (Hawk & McCall, 2010; O’Connor et al., 2009). Studies of non-

institutionalised children who were adopted or fostered following neglect or abuse have similar results. Children adopted or fostered from abusive or neglectful homes show high rates of internalising and externalising behavioural problems, cognitive deficit, mental disorders, learning difficulties, and emotional difficulties (Oswald, Heil, & Goldbeck, 2009; Smith, Howard, & Monroe, 2000; Van Ijzendoorn, Juffer, & Poelhuis, 2005).

Neuroimaging studies have shown structural differences in the brains of individuals with a history of childhood trauma, including global abnormalities such as smaller total volume (De Bellis et al., 2002). Structural abnormalities have also been seen in the prefrontal cortex (De Bellis and Keshavan, 2003), hippocampus (Weniger, Lange, Sachsse, & Irle, 2008), anterior cingulate cortex (Kitayama, Quinn & Bremner, 2006) and corpus callosum (Jackowski et al., 2008) which are associated with executive functioning, memory, emotion regulation, and neural integration respectively. Functional brain imaging studies have most often shown differences in activation in the prefrontal cortex and anterior cingulate cortex, both of which are involved in executive functioning, and which correlates with impaired executive function (Hart & Rubia, 2012).

The Adverse Childhood Experiences (ACE) study was based on a cohort of over 9,000 American adults from the general population and was the first to find that childhood maltreatment and other adverse experiences were strongly predictive of many of the leading causes of death in adults including cancer, heart disease, lung disease, liver disease, skeletal fractures, obesity, and sexually transmitted infections (Felitti et al., 1998). Since this initial report, several more publications have documented a relationship between the number of different adverse experiences in an individual's history, and likelihood of adverse outcomes. As well as somatic complaints, many studies have found an increased risk of emotional and behavioural difficulties. ACEs are associated with an earlier initiation of illicit drug use, more problematic drug use, drug addiction, and injection of drugs which carries the additional risk of the acquisition of infections such as HIV and hepatitis (Dube et al., 2003). Emotional abuse in childhood increases the risk of anxiety (Edwards, Holden, Felitti, & Anda, 2003) and depressive disorder in adulthood (Chapman et al., 2004), and a higher number of ACEs increases the risk of suicide attempts in adolescence and adulthood (Dube, Anda, Felitti, Chapman et al., 2001). Neglect and physical abuse in childhood significantly increase the risk of homelessness in adulthood (Herman, Susser, Struening, & Link, 1997), and presence of any ACEs in childhood is associated with risky sexual behaviours in women including having had more than 30 partners, becoming sexually active before the age of 15, and self-reported risk of contracting AIDS (Hillis, Anda, Felitti, & Marchbanks, 2001). A limitation of the ACE and similar studies is that it is difficult to reliably measure the severity of neglect or abuse (Litrownik et al., 2005). However, one of the most common findings of the entire ACE project was that a distinct dose-response relationship

exists between the number of different types of ACE and the risk or severity of adverse health and behavioural outcomes – as an individual's ACE score (0-10 for presence of each ACE) increases, so does the severity or likelihood of adverse outcomes (Anda et al., 2006).

In terms of the five defined categories of child maltreatment (physical, sexual, emotional abuse and physical and emotional neglect), there is wide variation in reported prevalence rates, some of which has to do with the use of either self-report or informant-report methods; self-report measures tend to produce much higher estimates than informant reports (Stoltenborgh, Bakermans-Kranenburg, Alink, & IJzendoorn, 2015). The latest meta-analysis of international data using self and informant-report, and in all five categories of maltreatment, estimates that 12.7 % of children have been sexually abused (7.6% for boys and 18% for girls), 22.6% have been physically abused, 36.3 % emotionally abused, 16.3% physically neglected, and 18.4 % emotionally neglected (Stoltenborgh et al., 2015). What is more difficult to calculate though, are the prevalence and outcomes associated with multiple types of maltreatment. Many maltreated children, and a majority of maltreated children in care, suffer two or more types of maltreatment (Pears, Kim, & Fisher, 2008), but there is a shortage of studies in this area. There is some evidence that: children who are neglected and physically abused are more likely to develop cognitive deficit; internalising behavioural difficulties are more strongly associated with physical and/or sexual abuse; and externalising behavioural difficulties are more likely following a combination of physical, emotional and sexual abuse and neglect together (Pears et al., 2008). Severity of maltreatment is also an issue here though; a history of multiple types of maltreatment is positively correlated with severity of maltreatment, and therefore severity and type of maltreatment are factors which can be difficult to separate (Clemmons, Walsh, DiLillo, & Messman-Moore, 2007).

Individuals who have experienced sexual abuse as children are more likely to be victims of sexual abuse as adults, become pregnant as teenagers, have high numbers of sexual partners (Lalor, & McElvaney, 2010), engage in unprotected sex, trade sex for money, drugs or shelter (Arriola, Loudon, Doldren, & Fortenberry, 2005) and perpetrate sexual abuse (Paolucci, Genuis, & Violato, 2001). They are also at an increased risk of developing many psychiatric disorders including depression, anxiety, eating disorders, post-traumatic stress disorder (PTSD), sleep disorders (Chen et al., 2010), and borderline personality disorder (Fossati, Madeddu, & Maffei, 1999). In terms of emotional and behavioural outcomes, individuals sexually abused as children are at increased risk of suicidal thoughts or suicide attempts (Chen et al., 2010) as well as non-suicidal self-injurious behaviours, which have been suggested as a maladaptive coping mechanism (Klonsky, & Moyer, A. (2008). The majority of findings are associated with emotional, pathological or behavioural consequences of sexual abuse, but academic achievement is also likely to suffer (Paolucci et al.,

2001). This suggests a direct effect of sexual abuse on cognitive development, but behavioural difficulties leading to disrupted school experiences may be a sufficient explanation for this.

Childhood physical abuse is associated with an increased risk of depressive disorder, anxiety disorder, PTSD, panic disorder, bulimia nervosa, obesity, and conduct disorder (Norman et al., 2012). As children, individuals with a history of physical abuse are more likely to be rated by peers as aggressive and disruptive compared with non-maltreated children and other maltreated children. Those children were also more likely to suggest aggressive responses to vignettes (Teisl & Cicchetti, 2008). Physical and violent sexual abuse is predictive of an increased risk of suicidal thoughts or attempts compared with non-maltreated and other maltreated children (Joiner et al., 2007), as well as poor emotion regulation compared with other maltreated children (Teisl & Cicchetti, 2008).

There is some crossover between emotional neglect and emotional abuse, and there has been some difficulty in operationalising definitions (Glaser, 2002). Broadly, emotional neglect can be seen as the omission of care whilst emotional abuse is associated more with actively causing harm (see definitions in [section 2.7](#)). These forms of maltreatment have mostly been studied alongside physical and/or sexual abuse, which have received more attention (Spertus, Yehuda, Wong, Halligan, & Seremetis, 2003). It is therefore more difficult to identify any adverse consequences of emotional neglect and psychological abuse without the contamination of other exposures in research samples. Studies have identified increased risks of sexually transmitted infections, risky sexual behaviours, drug or alcohol misuse, depression, anxiety, low self-esteem, personality disorder, and suicide attempts amongst adults with a history of childhood emotional abuse (Norman et al., 2012; Spertus, 2003). All categories of abuse are associated with adverse emotional, behavioural and pathological outcomes, whilst neglect is also associated with a risk of cognitive deficit. Although dated now, Hildyard and Wolfe (2002) have produced the most comprehensive review to delineate the adverse outcomes associated with physical and emotional neglect. They found that emotionally neglected children are more likely than non-maltreated children to show developmental delay, poor emotional regulation, negative affect, pathological behaviours (e.g. soiling, tantrums, tics) and social withdrawal. Physically neglected children were more likely to show externalising behavioural problems, poor academic achievement, poor emotional regulation, low ego control, and attention deficit. More recent studies have found further cognitive deficits associated with neglect without considering type. These have shown that neglected children and adolescents demonstrate more deficits in working memory, executive functioning, general intelligence, reading, mathematics, attention, language, planning, and problem solving compared with non-maltreated peers (De Bellis, Hooper, Spratt, & Woolley, 2009; Hanson et al., 2013).

2.9 The impact of behavioural problems in FASD and trauma on families

A consequence of adverse neurodevelopmental development that has received little attention is the impact of cognitive and behavioural difficulties on the people who care for those individuals. Caring for a child, adolescent or adult with a developmental disorder is a stressful role that has significant and tangible consequences on the wellbeing of the carer (Hastings, 2002). Carers of young people with FASD face unique challenges related to their children's specific set of difficulties, as well as a lack of support from health or education systems which may be linked to a poor understanding of FASD, even amongst medical professionals. Deficits in domains such as executive functioning, adaptive functioning, and externalising behaviours are common in FASD, and these have been reported as predictors of high levels of stress in parents and guardians (Green et al., 2014; Paley, O'Connor, Frankel, & Marquardt, 2006). Parents of children with FASD have consistently reported high levels of stress, not only elevated above average population levels, but above levels seen in parents of children with other developmental disorders including autism spectrum disorder (Bobbitt et al., 2016; Watson, Coons, & Hayes, 2013a). Apart from the stress of dealing with the behavioural challenges of their child or young person, FASD carers also struggle with related issues: families have reported becoming socially isolated due to their children's behavioural difficulties; stress within the family has led to marital breakdown; parents report being anxious about their child in the future when they are no longer able to care for them; parents have reported a lack of knowledge and understanding amongst medical professionals and that this has obstructed their pursuit of support from health and educational services (Brown & Bednar, 2004; Mukherjee, Wray, Commers, Hollins, & Curfs, 2013).

There are few published articles that have assessed the impact of a child's history of maltreatment on stress in their caregivers, but two studies have assessed stress in adoptive parents of post-institutionalised Romanian orphans (Judge, 2003; Mainemer, Gilman, & Ames, 1998). These studies both found a strong positive correlation between child externalising behavioural problems and parental stress in mothers and fathers. Fathers were more likely to report feeling socially isolated, withdrawal, depression, and suffering stress associated with their children's crying. Mothers felt responsible for their children's problems and this was associated with stress or depression. Parental stress was higher for adoptive parents of Romanian orphans than for adoptive parents of non-institutionalised children, but levels of stress were rarely in the clinical range. Interestingly, time spent by the child in institutional care did not predict parental stress in these studies, despite the common finding that time in an institution is associated with more severe behavioural problems (e.g. Rutter et al., 1999).

2.10 FASD and trauma

To summarise so far: Prenatal alcohol exposure (PAE) has been known to be harmful to a developing fetus for at least the last 50 years (Lemoine, 1968; Rouquette, 1957). Alcohol consumed during pregnancy easily enters the foetal compartment and can lead to permanent foetal injury via direct and indirect cell damage, neurochemical changes, disrupted brain development, and possible epigenetic changes (Guerra et al., 2009). The dose, timing and pattern of alcohol consumption have an impact on damage, with binge-drinking or steadily high consumption of alcohol associated with more severe damage than low levels, although even very low rates of consumption have occasionally been shown to cause some damage (Murray et al., 2016). Fathers' alcohol consumption can also affect their children's health by reducing preconception sperm quality and by the social facilitation of their female partner's alcohol consumption during pregnancy. Children born following PAE may be diagnosed early on with foetal alcohol syndrome (FAS) if they display a distinctive set of physical deformities (microcephaly, low birthweight, and craniofacial anomalies). Children without these physical markers may have equally severe damage to the central nervous system, but this is more difficult to diagnose, and these children may be identified later (often beyond 6-7 years) using one of many diagnoses and based on a variety of criteria depending on which system is used by their physician (Coles et al., 2016). The full range of diagnoses, including FAS, are known by the umbrella term foetal alcohol spectrum disorder (FASD). Rates of alcohol consumption during pregnancy are as high as 40-60% in many western countries. However, the difficulties involved with diagnosis, as well as a reluctance to admit prenatal exposure, mean that significant under-reporting and/or misdiagnosis of FASD is suspected. This view is supported by the discrepancy between medical records, which show low prevalence, and active case ascertainment methods, where a cross-section of children are examined. These methods have produced prevalence estimates of well over 1% of live births in western countries, with some community samples showing rates of over 10% (Lange et al., 2017). Individuals with FASD present with a variety of neurobiological damage, somatic complaints, cognitive deficits, and emotional or behavioural difficulties. These can range from mild to severe, and it has been difficult to establish an expected pattern, or phenotype, of cognitive and behavioural problems. Some of the more commonly reported deficiencies are in executive function, speech and language, general intelligence, social cognition, attention, and adaptive functioning, and individuals may display hyperactivity, conduct disorder, depression or anxiety, trouble with the law, and problems with addiction or substance misuse. There is a complex relationship between addiction and trauma: people who experience environmental trauma such as maltreatment as children are at an increased risk of developing addictions, including alcoholism, as adults (Maté, 2012). Meanwhile, maltreated children are more likely than non-maltreated children to become

abusive or neglectful parents themselves. This is not always the case and some protective factors have been identified, but there may be a cycle here, involving substance abuse, insecure or disorganised attachment relationships, and child abuse and neglect. Maltreated children often show many of the same neurochemical, cognitive, emotional, and behavioural deficits and difficulties as those seen in children with FASD, with abused children tending to show emotional, behavioural or pathological problems, and neglected children tending to show these problems as well as cognitive deficits (Hildyard and Wolfe, 2002). Finally, the people who care for children with FASD or a history of maltreatment may experience increased levels of stress and depression compared to other caregivers, and this seems to be especially pronounced in those carers of young people with FASD (Green et al., 2014).

To suggest a further component to the addiction-trauma-attachment damage cycle; women (and men, due to their social influence on maternal drinking) who abuse alcohol, who were maltreated themselves as children, and who struggle with planning, decision-making and social cognition, may be at increased risk of conceiving a child who is prenatally exposed to alcohol. This child with FASD is more likely than their typically developing peers to suffer abuse or neglect due to their parents' own inability to cope with the stress of parenthood, and the parents' own attachment traumas. That child is then at an increased risk of misusing alcohol and conceiving their own alcohol-exposed child, and the cycle continues as summarised in figure 2.2. The relationship between maltreatment and PAE is poorly understood at best, and the remainder of this thesis will attempt to identify what is currently known, and to develop the evidence-based understanding of the combination of the two exposures. Since a similar range of adverse outcomes are associated with each exposure, it may be the case that individuals with both exposures are at increased risk of deficits or difficulties compared to those with either one exposure.

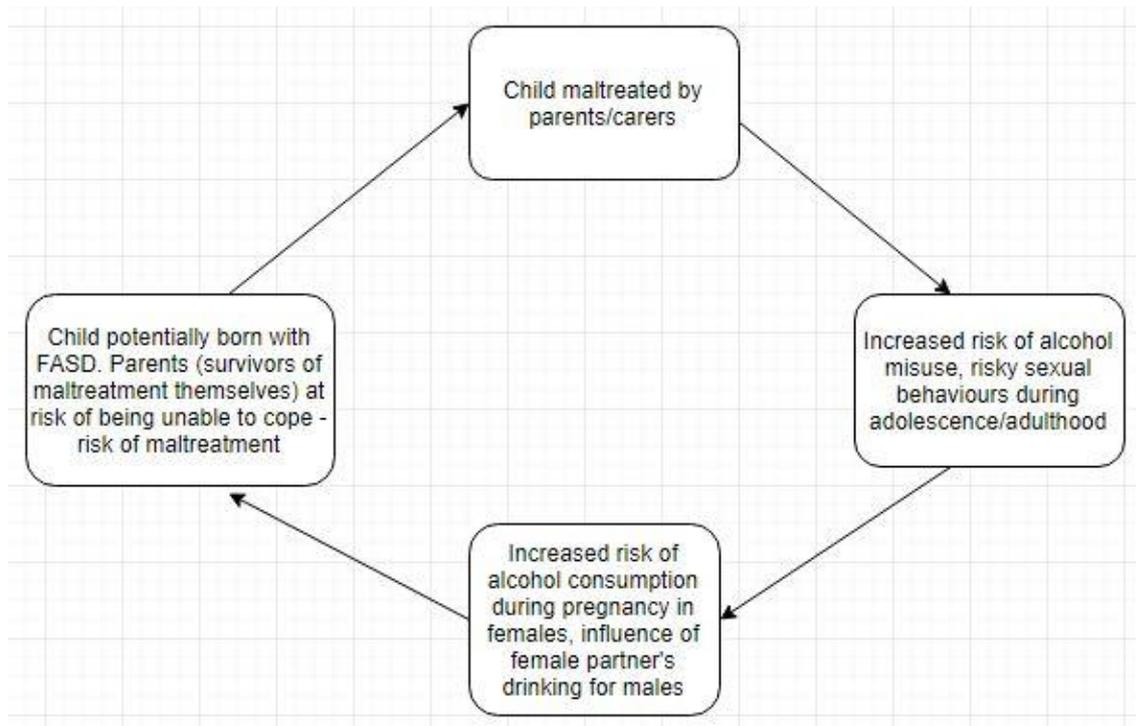


Figure 2.2: Flow diagram of cycle of maltreatment with PAE

With a lack of published studies on the dual impact of both exposures, it is very difficult to estimate the number of individuals with both FASD and a history of trauma. To take the UK as an example: as outlined above, FASD prevalence rates from high-quality studies in the UK are missing, though the best recent estimate is 3.24% (Lange et al., 2017). Traumatic childhood experiences are thought to be much more common, with up to 30% of British adolescents reporting at least one incident of neglect or abuse during their childhood (NSPCC, 2011). However, for both FASD and traumatic experiences, significant underreporting is suspected (Morelo et al, 2011; Gilbert et al, 2009). Prevalence rates of FASD and trauma are particularly high in children who have been fostered, adopted or who live in children’s homes. Within the UK population of looked after children it is estimated that at least 61% have a history of traumatic experiences (Adoption UK, 2015), and around 30% may have FASD (Gregory, Reddy & Young, 2015; Selwyn & Wijedesa, 2011). With a looked after population exceeding 90,000 (Adoption UK), this means that as many as 30,000 looked after children in the UK might suffer from both FASD and the impact of traumatic experiences.

A possible mechanism in the relationship between PAE, maltreatment, and adverse developmental outcomes, is the hypothalamic–pituitary–adrenal (HPA) axis. As outlined above, this component of the neuroendocrine system is involved in the stress response, also known as the fight-or-flight response. Neurotransmitters and hormones released by the hypothalamus, pituitary gland, and adrenal glands are necessary during stress, in order to provide energy to escape or engage a potential threat. Individuals with FASD, and individuals with a history of maltreatment, have both

shown increased activation of the stress response, which is associated with permanent emotional and behavioural difficulties. In the case of children with both exposures, it is possible that their already heightened stress-response could exacerbate the neurochemical reaction to abuse or neglect during childhood, leading to more severe permanent damage than in the case of children with a single exposure. Some sex differences have been found in the stress responses of individuals with PAE, including in human infants where males have shown greater activation than females in response to a social stressor (Haley et al., 2006). Due to the greater activation in males, if males with PAE were found to exhibit a more severe reaction to trauma than females, this would implicate the stress-response system as a possible mechanism for increased difficulties associated with trauma in children with PAE.

Another possibility is suggested by Henry, Sloan and Black-Pond (2007). Given the high numbers of children with FASD that are no longer looked after by their birth parents, studies into the adverse developmental outcomes associated with PAE will probably have unwittingly recruited participants who were also exposed to traumatic experiences as young children. Meanwhile, given the low estimated rates of diagnosis, studies into the adverse outcomes associated with maltreatment will probably have recruited some participants with undiagnosed FASD. These studies and their conclusions may therefore be affected by research contamination – unidentified confounding variables associated with attributes of the research population. These are just two examples of how findings related to individuals with a history of both exposures could be interpreted. It is likely that several interacting psychological and neurobiological mechanisms will explain the actual impact of both exposures, and many other factors including other adverse environmental experiences should not be overlooked.

2.11 Initial rationale aims and research question

The overview of literature on the effects of prenatal alcohol exposure and postnatal trauma above shows that each exposure is responsible for significant changes in neurobiological, cognitive and behavioural functioning, and that these deficits can lead to difficulties for family members. It seems intuitive that individuals with both exposures may experience more difficulties or more severe symptoms than those with just one exposure, but this appears to be currently unknown. The purpose of this thesis therefore, is to investigate the impact of the dual exposures of prenatal alcohol and postnatal trauma on cognitive and behavioural functioning, and to assess the impact of any difficulties on family members. There appears to be a paucity of published research on this, but in order to identify the actual number of published studies that have attempted to answer this question, it was decided that the first stage of this project would involve a systematic literature

review. The research question for this stage of the project is therefore: What is currently known about the combined effects of prenatal alcohol exposure and postnatal trauma?

Chapter 3: Prenatal alcohol exposure and traumatic childhood experiences: A systematic review of their combined effects

3.1 Introduction

This systematic review has been published in *Neuroscience and Biobehavioural Reviews* (Price, Cook, Norgate & Mukherjee, 2017), and is reproduced here largely in its original format with kind permission from publishers Elsevier. The published version is available online:

<https://www.sciencedirect.com/science/article/pii/S0149763416306510> and the accepted document is attached in [appendix 1](#).

To briefly recap the rationale for this chapter: There has been a substantial amount of research published on the effects of prenatal alcohol exposure and childhood trauma as separate exposures over the last several decades. However, the extent to which the impact of a dual exposure has been studied remains unclear. Therefore, before any primary research can be designed or conducted on this matter, it is imperative that any and all current knowledge is identified, collated and assessed. Once the extent of the current knowledge was recognised, gaps were identified, and the subsequent studies were built on this foundation. By far the most reliable form of literature review is the systematic literature review.

Non-systematic literature reviews may not report or employ an explicit search strategy, leaving their methods subjective and their findings unreliable (Uman, 2011). Systematic reviews and meta-analyses on the other hand are considered to be amongst the highest categories of scientific evidence (Glasziou, Vandenbroucke & Chalmers, 2004) due to their objectivity, rigorous methodologies, comprehensive literature search strategies, transparency, and explicit criteria for inclusion and exclusion of studies (Cronin, Ryan, & Coughlan, 2008). They are also used widely by clinicians and policymakers to inform decision making (Gopalakrishnan & Ganeshkumar, 2013), but perhaps most importantly for this project, they are superior to non-systematic reviews for identifying gaps in the literature (Schlosser, 2006).

A systematic literature review was therefore conducted, with the research question of: What is currently known about the dual exposure of prenatal alcohol and postnatal trauma?

3.2 Methods

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, foetal alcohol and prenatal exposure were searched for alongside terms relating to trauma such as abuse, maltreatment and neglect (for full search terms, see [appendix 1](#))

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.

Due to the heterogeneity of the articles featured, this review was 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, memory, and social and behavioural problems. Finally, a selection of related studies that came close to matching inclusion criteria are summarised.

3.3 Results

3.3.1 Study characteristics

The search returned 15,193 records, of which, 2,369 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 (see figure 3.1).

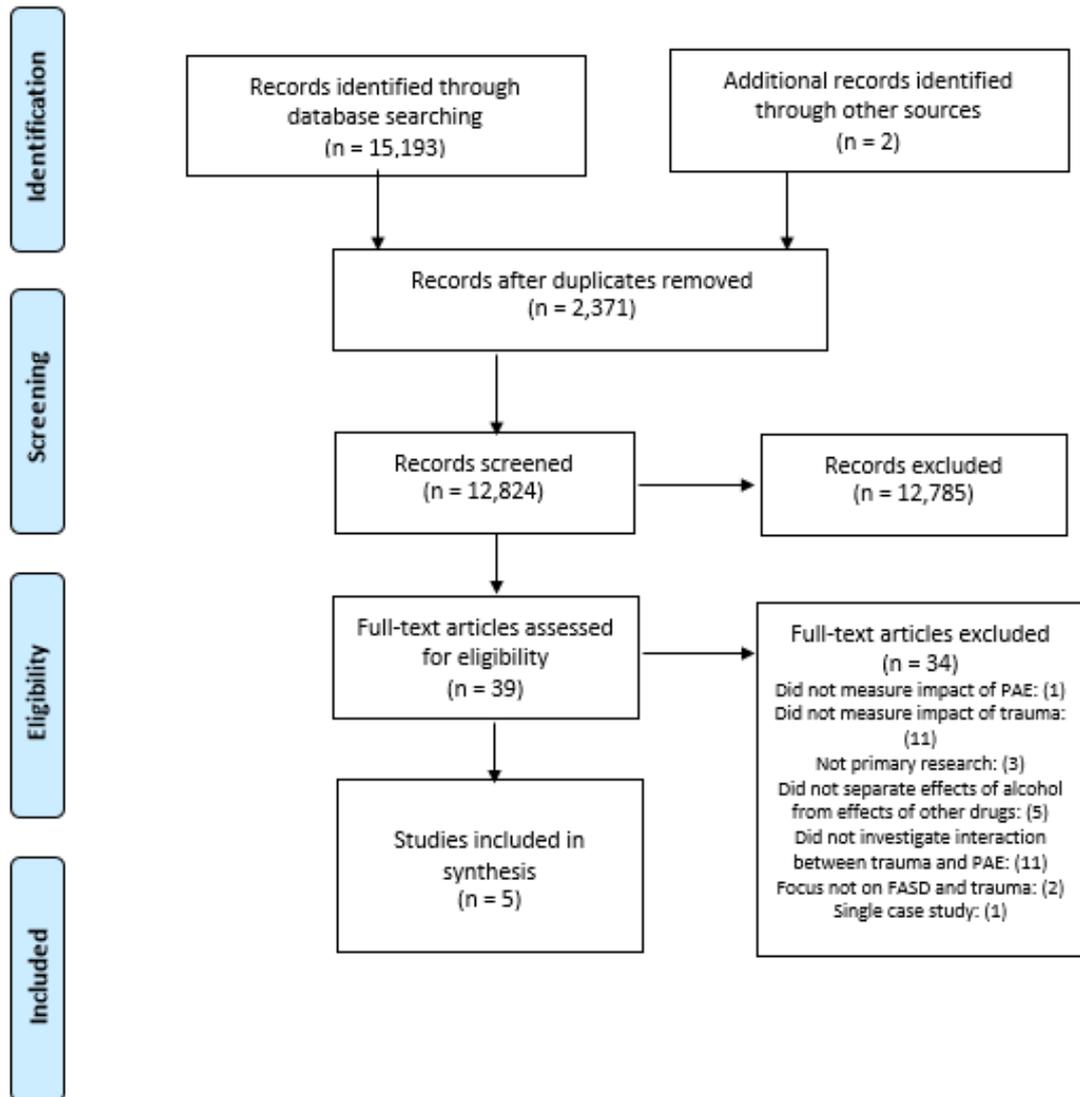


Figure 3.1: Flow diagram showing literature selection procedure

Of the five studies identified in the literature search, three were conducted in the United States (Coggins, Timler and Olswang, 2007; Henry et al., 2007; Hyter, 2012), and two in Finland (Koponen, Kalland & Autti-Rämö, 2009; Koponen, Kalland, Autti-Rämö, Laamanen and Suominen, 2013). Two studies had correlational designs (Coggins et al., 2007; Koponen et al., 2009), two had quasi-experimental designs (Henry et al., 2007; Hyter, 2012), and one used a qualitative design (Koponen et al., 2013). The combined sample size was 1,026, and the total age range of participants was 0-16 years. In terms of outcomes, the studies assessed speech and language, intelligence, memory, attention, developmental level, behavioural problems, attachment problems, and socio-emotional development.

Childhood maltreatment as defined in [section 2.7](#) covers episodes of physical and emotional 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 defined in [section 1.1](#) as abuse and/or neglect, although they use the term 'environmental risk'. Hyter (2012) uses the term 'complex trauma' which results from abuse or neglect. Henry, Sloane and Black-Pond (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 parents, unemployment of parents, divorce of parents, mental health problems of parents, several placements in the care system, and having lived in a children's home.

Koponen et al (2009) and Koponen et al (2013) categorised patients as FAS and FAE (foetal alcohol effects – a defunct diagnosis which was used to describe the wider foetal alcohol spectrum outside of FAS), 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 as part of the study. Coggins et al. report diagnoses of their participants (FAS, pFAS, etc. See table 4) 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.

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 traumatic experiences? Three of the articles are reports of studies that compared a group with both exposures, to a group with one exposure. Henry et al. (2007), compared a group of children exposed to both PAE and trauma, 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. Hyter (2012) is a review that 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. The other two articles report cross-sectional studies of children with PAE, where a sub-sample of participants had exposure to trauma (Coggins et al., 2007; and Koponen et al., 2009). Henry et al (2007), Hyter (2012) and Koponen et al., (2013) therefore examined the impact of prenatal alcohol exposure on children with history of trauma, whereas Coggins et al. (2007) and Koponen et al. (2009) examined the impact of trauma on children with prenatal alcohol exposure. Table 3 shows a breakdown of the five studies included in this review.

3.3.2 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 were 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

Table 3.1 Study characteristics - systematic review

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

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 also 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 of 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.

3.3.3 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 neglectful or abusive 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.

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 significant correlation between language performance and level of trauma was identified. 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 that 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 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 indicates a moderate delay for that specific domain, and three or more tasks below age norms indicates a major delay for that domain. Henry et al. (2007) 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 ($n = 113$; $p < .001$), and that 50% of children with just trauma showed moderate to major delays in expressive language, compared to 72% of children with both exposures ($p = .001$). Hyter (2012) reports that children with both exposures ($n = 34$) were more likely to show deficits in

Table 3.2 Aims and methods of studies in systematic review

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 foetal 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	Large sample size. Quasi-experimental design. Possible confound of ethnicity: 'Both' group 80% Caucasian, 9% African-American; 'just trauma' group 61%

during a two-day clinic in Caucasian, 26% African-
language, intelligence, American.
motor skills, memory,
emotional social and
behavioural problems.

Study	Aims	Groups	FASD diagnostic criteria	Diagnoses of participants	Evidence of prenatal exposure	Method of evaluation	Robustness of evidence
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	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	The findings in this review were previously presented at a conference, but were not published elsewhere. No methods section.

with postnatal traumatic experience alone on children's language and social communication.

standardised speech and language pathology tasks.

Study	Aims	Groups	FASD diagnostic criteria	Diagnoses of participants	Evidence of prenatal exposure	Method of evaluation	Robustness of evidence
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: Foetal Alcohol Syndrome (FAS), partial Foetal 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 Foetal Alcohol Syndrome (FAS) and Foetal Alcohol Effects (FAE) as well as the category of no diagnosis (NDs).

phonological awareness (Cohen's $d = .12$, $p = .003$), semantics ($d = .31$, $p = .004$), syntax ($d = .47$, $p = .015$), and comprehension ($d = .31$, $p = .018$) than children with just trauma ($n = 72$).

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 both a history of trauma and FASD ($n = 113$) scored significantly lower in verbal intelligence ($d = .31$, $p = .007$), nonverbal intelligence ($d = .22$, $p = .04$), and in the composite score ($d = .42$, $p = .01$) than children with a 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 ($r = .47$, $p < .01$) 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.

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 ($n = 113$; $p = .004$; Henry et al. 2007). Henry et al. also found that deficits in memory were more likely in children with both exposures (87%) than in children with just trauma (71%; $p = .005$).

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.

Social, emotional and behavioural problems

Hyter (2012) measured social communication skills using the PEEEX 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 to 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 ($d = .26, p = .04$), social problems ($d = .35, p = .02$), ADHD index ($d = .47, p = .004$), restless/impulsive ($d = .40, p = .01$), global index ($d = .46, p = .02$), DSM-IV criteria for inattention ($d = .50, p = .004$), DSM-IV criteria for hyperactivity/impulsivity ($d = .33, p = .03$), and DSM-IV total ($d = .27, p = .005$) 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 ($d = .40, p = .006$), ADHD index ($d = .36, p = .02$), restlessness/impulsivity ($d = .38, p = .03$), DSM-IV criteria for inattention ($d = .27, p = .009$), and DSM-IV total ($d = .46, p = .01$). 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%, $p < .01$). 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 ($r = .43, p < .05$), age at placement into their present foster family ($r = .34, p < .05$), and number of traumatic experiences ($r = .45, p < .01$), 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 ($r = .39, p < .05$) and bullying behaviour towards other children ($r = .37, p < .05$).

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. Table 1: Comparison of studies in systematic review by perspective

Perspectives

Table 3.3 shows one way of organising the studies in the systematic review – by their perspective. The left column shows the two studies that took a sample of children all with a history of trauma, some of whom also had PAE, and the right column shows the three studies that took a sample of children with PAE, some of whom also had a history of trauma. The two largest studies (Coggins et al., 2007 & Henry et al., 2007) took different perspectives and produced different results. Henry et al. (2007) found that children with both exposures had more severe difficulties in attention, memory, language, intelligence, hyperactivity, impulsivity, restlessness, oppositional behaviour and social problems than children with just trauma. Coggins et al. (2007) found no significant effect of trauma on language or social communication in their sample of children with PAE. Of the smaller studies: Koponen et al. (2009) found that children with both trauma and PAE had more severe behavioural, but not cognitive, difficulties compared with children with just PAE; and Hyter (2012) found children with both exposures had more severe language, but not social communication, deficits than children with just trauma. The qualitative study by Koponen et al., (2013) provided important details, but its disproportionate group sizes and lack of quantitative analysis prohibit inferences in the style of those above.

Table 3.3: Studies in systematic review by perspective

Trauma vs (PAE + trauma)	PAE vs (PAE + trauma)
<p>Hyter 2012 (quasi-experimental, <i>n</i>=106)</p> <p>Clinically significant language delays and social communication difficulties in both groups</p> <p>‘Both’ group had more language delays than ‘just trauma’ group</p> <p>No significant difference between groups in social communication</p>	<p>Coggins et al 2007 (cross-sectional, <i>n</i>=573)</p> <p>Substantial comorbidity between PAE and trauma</p> <p>Sample as a whole had poor language and social communication</p> <p>No relationship between trauma and severity of outcomes</p>
<p>Henry et al 2007 (quasi-experimental, <i>n</i>=274)</p> <p>‘Both’ group had more delays/deficits in: attention, memory, language.</p> <p>No difference between groups in: visual processing, motor control</p> <p>‘Both’ group had lower verbal, non-verbal and composite IQ scores.</p> <p>Children in ‘both’ group rated as more problematic than ‘just trauma’ group by parents and teachers in the following: hyperactivity, attention, impulsivity, restlessness; and by parents only in the following: oppositional behaviour, social problems.</p>	<p>Koponen et al 2009 (cross-sectional, <i>n</i>=38)</p> <p>Full sample had high levels of cognitive and behavioural problems.</p> <p>Being older when removed from abusive home predicted more cognitive and behavioural problems</p> <p>More traumatic experiences predicted attachment and behavioural problems, but not cognitive deficit.</p>
	<p>Koponen et al 2013 (qualitative, <i>n</i>=34)</p> <p>Children who lived with abusive parents appeared to have more difficulties with attachment, concentration, hyperactivity and developmental delay than those adopted at birth.</p> <p>Difficult to draw any conclusions due to study design</p>

3.3.4 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 years) 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, $p<.001$), DSE (OR=4.67, $p<.001$), TWL (OR=2.69, $p=.01$), and ADP (OR=4.10, $p=.001$). Fewer years per household by age 18 increased the risk of CNF (OR=7.35, $p=.001$). Having been the victim of sexual or physical assault or domestic violence increased the risk of ISB (OR=3.37, $p<.001$) and ADP (OR=2.56, $p<.05$). 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 years) 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 years 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 necessary.

Huggins et al (2008) interviewed 11 adults (age 18-29 years) with FASD from the same cohort as Streissguth et al (2004; above). 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 years) with FASD from the same archive as Mauren (2007; above). 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; above). 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 years) 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.

3.4 Discussion

3.4.1 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.'s qualitative study (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.

3.4.2 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 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 that 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 that 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, Loomis & Booth, 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, Telle, & Votruba, 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 better explain the greater number of negative socio-emotional outcomes in the ‘lived with parents’ group, as raw data were 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 measures 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 some of the methods are described in Henry et al. (2007), of which Hyter (2012) is a follow-up.

A problem that 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 widely varied. 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. Although this brings many practical challenges, researchers should aim to control as many potential variables as possible.

3.4.3 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.

The studies in this review took different perspectives to investigating the dual exposure of PAE and trauma – two compared only trauma with both exposures, and three compared only PAE with both exposures (as shown in table 5). The two contrasting perspectives appear to show an emerging pattern, where trauma may be having less of an impact on development, particularly cognitive development, than PAE. Very few studies have been conducted so far, and there are other differences between those studies that may be confounding this effect, for example the two ‘trauma vs PAE’ studies were of a quasi-experimental style, whereas the two studies with quantitative findings that took the ‘PAE vs both’ approach, were both cross-sectional studies. This potential pattern warrants further research using both perspectives, although given the large sample size and multiple assessments conducted by Henry et al (2007), studies that compare PAE with both

exposures may be a higher priority. Moreover, studies that compare groups of children with each exposure separately as well as a group with both exposures and one with neither, would be of great value.

Further research in the immediate future should also 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 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.

3.5 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.

The wider overview of literature on FASD and trauma in chapter two identified the need for studies that assess the dual impact of PAE and trauma in terms of neurological, cognitive and behavioural functioning, and the impact that these deficits can have on family members. The systematic review shows that this question has started to be investigated. There is now some evidence – all of which is synthesised in this thesis - that children with a dual exposure of PAE and trauma have been found to exhibit some more severe deficits in attention, memory, language, and intelligence, and have higher levels of some behavioural and social difficulties compared to children with just trauma. Conversely, children with dual exposure were found to have similar cognitive functioning and more behavioural difficulties than children with just PAE. But the review demonstrates that more studies are needed. Some gaps in the literature are now apparent, and the rest of this thesis will be devoted to filling in some of those gaps. Some domains, such as executive functioning and brain activity, have not yet been compared, and no study has investigated the impact of dual exposure on the families of affected children. The following chapter will briefly summarise what is known, and what gaps remain. A theoretical framework is provided, which helps

to illustrate the state of the current evidence and produce aims and hypotheses for a series of four primary research studies, which are presented in chapters five, six, seven and eight.

Chapter 4: Introduction to primary research

4.1 Introduction

Two years after the systematic review was completed, an article was published that described the impact of postnatal neglect on neurodevelopmental outcomes in young people with FASD (Mukherjee, Cook, Norgate & Price, 2019). The study was an audit of data from the UK National FASD Clinic and would have met criteria for inclusion in the systematic review. Data were presented on ADHD and ASD symptoms, social communication, sensory problems, daily living problems and language skills. The results were in keeping with the pattern identified by the systematic review; patients with both FASD and postnatal neglect had no more severe neurodevelopmental outcomes than patients with FASD without neglect. The study highlighted previous work (Mukherjee et al., 2013) that showed parents often feel blamed for the lack of development in their children with FASD, whose difficulties may be attributed to their early traumatic environments rather than PAE. If a child has both PAE and a history of trauma, it is sometimes assumed by professionals that a stable, nurturing home and parenting practices based on attachment theory should help, and in the case of children with a history of trauma without PAE this should be the case (Bick & Dozier, 2013; Stronach, Toth, Rogosch, & Cicchetti, 2013; Suchman, Decoste, McMahon, Rounsaville, & Mayes, 2011). However, if the profile of a child with both exposures is due more to a prenatally acquired brain injury, such strategies may be less effective. Moreover, parents who are told their attachment-based parenting strategies should work may blame themselves and become more stressed when their child shows no improvement.

Taken together, the study described above and the five studies described in the systematic review represent the extent of the published evidence on the impact of a dual exposure of PAE and trauma. The wider overview of literature presented in chapter two highlights the need for studies into this dual exposure, and particularly that focus on cognitive and behavioural functioning, as well as the impact of any difficulties on family members. The systematic literature review along with the clinical data audit (Mukherjee et al., 2019) provide evidence on specifically which questions have been addressed, and which have not. The next section of this chapter summarises the findings and gaps identified so far, and provides a theoretical framework based on what is known, which is used to develop the aims and hypotheses for the primary research studies of this thesis.

4.2 Interim summary of findings and theoretical framework

The wider literature overview in chapter two demonstrates that children with either FASD or a history of trauma tend to exhibit difficulties or deficits in a wide range of cognitive and behavioural

functions. It is presumably the case that children with both exposures, as a population, will tend to exhibit a similar range of cognitive and behavioural difficulties, but the severity of their difficulties may or may not be greater than children with one exposure. The systematic review and clinical audit data show that this question has been addressed from two perspectives. Children with both exposures have been compared to children with just trauma in terms of speech and language, social communication, attention, memory, intelligence, visual processing, motor control, oppositional behaviour, anxiety, hyperactivity, social problems, ADHD symptoms, and impulsivity (Henry et al., 2007; Hyter, 2012). Conversely, children with both exposures have been compared to children with just PAE in terms of language, social communication, developmental level, behavioural problems, attachment behaviour, self-expression, ASD symptoms, ADHD symptoms, sensory problems, daily living problems and language skills (Coggins et al., 2007; Koponen et al., 2009; Mukherjee et al., 2019). Overall, children with both exposures had more in common with children with PAE only, than they had with children with trauma only, but there are still several cognitive or behavioural areas that have not been assessed. Executive functioning and social cognitive deficits have been reported following each exposure but have not been assessed in studies of both FASD and trauma. Similarly, no study has employed brain imaging techniques to report differences in brain activity, nor used a recognised valid measure of intelligence to assess differences between children with both exposures and just PAE (Koponen et al used parent report). Measures of behavioural difficulties in these studies also either focused on the difference between both exposures and trauma or were conducted on small samples. Finally, no study has begun to assess the impact of any of these difficulties on the families of children with both exposures.

The causal modelling framework in figure 4.1 shows the pathway by which prenatal exposure to alcohol and postnatal trauma can each lead to cognitive and behavioural deficit, via neurological damage, and eventually leading to difficulties or stress in the family of the exposed individual. The framework is adapted from Kodituwakku and Kodituwakku (2014), who themselves adapted the framework of Morton and Frith (1995), which is based on the concept that the characteristics of neurodevelopmental conditions are best described in terms of three levels: neurobiological, cognitive, and behavioural. The framework used here also includes a fourth level: the interpersonal level, which describes the impact of cognitive or behavioural difficulties on other people. The evidence discussed in the opening chapters of this thesis show that PAE and trauma have each been shown to cause neurobiological changes, which lead to cognitive and behavioural deficits, which in turn can lead to difficulties for family members. The model in figure 4.1 goes beyond this, to propose that dual exposure will lead to differences in brain activity, greater cognitive and behavioural damage, and differences in the experiences of family members, compared to

individuals with a single exposure. The pattern that seems to be emerging is that children with both exposures are more similar to children with only PAE than they are to children with only trauma. Therefore, even though the framework could be employed to compare dual exposure to either single exposure, in this thesis it is used to compare dual exposure to only PAE.

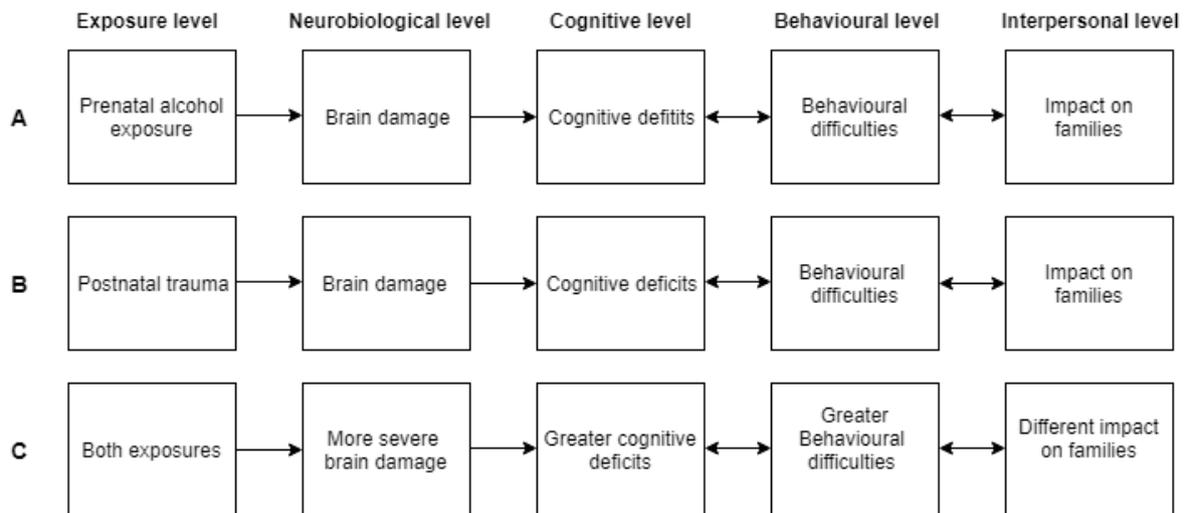


Figure 4.1 Causal modelling framework of PAE and trauma

The evidence in support of the first two rows (A and B) of the framework, was discussed in length in chapter two and is summarised above. The remainder of this thesis will attempt to provide evidence for row C, which represents dual exposure. Therefore, in order to provide some evidence of the neurological, cognitive and behavioural differences, and their effects on family members, the primary studies of this project were designed to measure at least one outcome in each of those four domains.

4.3 Planning primary studies

The few published studies that have so far addressed the dual exposure of PAE and trauma have either compared dual exposure with PAE or with trauma. No published study has yet featured groups of participants with a) PAE, b) trauma, c) both, and d) neither. Such a study would be valuable because it would allow the interaction between both exposures to be assessed. During the planning stage of this project, it was hoped that some or all of these studies would follow this four-group design. Enquiries were made to charities, adoption and fostering agencies as well as through informal and professional networks, but unfortunately no assistance was forthcoming, and it was not possible to recruit a group of participants with a history of trauma without PAE. Adoption and fostering agencies were also unable to help with the recruitment of an FASD group, but recruitment of these participants was achieved thanks to the significant online presence of support groups for

families affected by FASD. The primary studies conducted in this project therefore all compare children with both exposures to children with only PAE, and in those studies where normative data were not available, to typically developing children as well.

The studies in the systematic review were of quasi-experimental (Henry et al., 2007; Hyter, 2012), qualitative (Koponen et al., 2013) or cross-sectional design (Coggins et al., 2007; Koponen et al., 2009). This may confound their findings because the cross-sectional studies both took the 'PAE vs both' perspective and the quasi-experimental studies both took the 'trauma vs both' perspective. To avoid this potentially confounding issue, the primary studies in this project will use both cross-sectional and quasi-experimental designs.

Many decisions were made concerning the tools and measures used in the individual studies, and these are discussed in detail in each of the following chapters. One broad issue to present here though, is the difference between subjective and objective measures. For example, the methods of assessing executive functioning in children broadly fall into one of two categories: cognitive tasks in which the child takes part and receives a score for performance, such as the Tower of Hanoi task (e.g. Kotovsky, Hayes, & Simon, 1985); and behavioural measures, where a parent or teacher provides answers to a psychometric inventory based on their own experience of the child, such as the Behaviour Rating Inventory of Executive Functioning (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000). Cognitive tasks may be the more objective option but lack ecological validity (Anderson et al., 2002), whereas informant-report measures can provide more details about the child in the real world but may be vulnerable to parents' biases (Vriezen & Pigott, 2002). For this project, it was decided that a mix of objective and subjective measures would be used to restrict the influence of the limitations of either type.

When designing the series of primary studies for this project, the following methodological and practical issues were identified as essential criteria for this project:

1. The studies should investigate issues relating to the four stages of the causal modelling framework in figure 4: neurological, cognitive, behavioural, and the impact on families.
2. The studies should be a mix of both quasi-experimental and cross-sectional design.
3. The studies should use tools that rely on both informant report and direct measurement, for a balance between ecological validity and objectivity of measurement.
4. Study design was also limited to some extent by time limits, financial resources, difficulties with recruitment and limited equipment.
5. Ethical considerations were somewhat limiting. In particular, the issue of assessing children's histories of trauma.

Based on the findings of the literature overview, systematic review and audit of clinical data (Mukherjee et al., 2019), as well as methodological, ethical and practical considerations, the following six primary research questions were devised:

1. What is the impact of trauma on empathy in children with FASD?
2. What is the impact of trauma on behavioural difficulties in children with FASD?
3. What is the impact of trauma on intelligence in children with FASD?
4. What is the impact of trauma on executive functioning in children with FASD?
5. What is the impact of trauma on brain activity in children with FASD?
6. How are families of children with FASD and a history of trauma affected by their children's behavioural, emotional and social difficulties?

To answer these questions, four primary research studies were designed:

1. A cross-sectional caregiver-report survey to assess the impact of trauma on empathy and behavioural difficulties in children with FASD.
2. A quasi-experimental study to assess the impact of trauma on intelligence and executive functioning in children with FASD.
3. A functional brain imaging study to detect any differences in task-related brain activity associated with trauma in children with FASD.
4. A qualitative interview study of the experiences of parents of children with FASD and trauma, with a focus on the impact of behavioural difficulties.

Based on the wider literature overview, systematic review, and clinical audit data (Mukherjee et al., 2019), the overall null hypothesis of the thesis was that children with a history of both PAE and trauma will not differ significantly from children with only PAE in terms of executive functioning, empathy, intelligence, brain activity, and behavioural difficulties. The alternative hypothesis was that children with both exposures will differ, in negative ways where relevant (i.e. more severe cognitive and behavioural difficulties but a different pattern of brain activity) than children with only PAE. The investigation into the impact of behavioural difficulties on family members was qualitative and therefore did not test a hypothesis. However, some families discussed children with a history of trauma whereas other children had not experienced trauma, and some differences are discussed.

Chapter 5: Trauma, empathy and behavioural difficulties in children with foetal alcohol spectrum disorder

5.1 Introduction

This chapter describes a study that sought to measure the impact of trauma on empathy and behavioural difficulties in children with FASD. There are several potential confounders to these relationships, such as prenatal exposures to drugs and tobacco, or the age at which a child receives their FASD diagnosis, and these are also assessed. Data were collected using a caregiver-report online survey that was distributed to parents and guardians of children with FASD via social media. The survey consisted of previously published, validated parent-report measures of trauma, empathy, and behavioural difficulties, as well as questions about their children's histories.

Empathy has been defined as "sensitivity to, and understanding of, the mental states of others" (Smith, 2006, p.3). This definition is useful because it acknowledges that empathy is best conceptualised as two separate but related abilities: cognitive and affective empathy. Cognitive empathy, which is broadly synonymous with perspective taking and Theory of Mind, refers to the ability to understand and predict the thoughts, perspectives or behaviours of other people. Affective empathy on the other hand, describes the ability to vicariously experience the emotions of others (Smith, 2006). The two abilities have also been described by Frith & Blakemore (2005) as intentional empathy (cognitive), and instinctive empathy or sympathy (affective). Measures of empathy typically provide a score each for cognitive and affective empathy, as well as an overall, or total, empathy score (e.g. Dadds et al., 2008; Davis, 1980; Jolliffe & Farrington, 2006). Children with FASD (Stevens et al., 2015) and children with a history of trauma (Burack et al., 2006; Kairys et al., 2002) have been reported to show deficits in both cognitive and affective empathy compared to typically developing children. However, the systematic review (Chapter 4 of this thesis; Price et al., 2017) shows that no study has yet assessed the impact of a dual exposure of PAE and trauma on empathy.

Empathy has frequently been shown to relate to behaviour in typically developing children. Lower cognitive and affective empathy are each correlated with more bullying behaviour in children and adolescents (Mitsopoulou & Giovazolias, 2015), whereas defending others from bullying is associated with higher cognitive and affective empathy (Van Noorden et al., 2015). Prosocial, cooperative and socially competent behaviours are also positively related to empathy in children and adults (Eisenberg & Miller, 1987). Empathy is negatively related to aggressive, antisocial and externalising behavioural problems (those that are directed toward others or the environment) in children and adolescents (Miller & Eisenberg, 1988), but almost all studies have been based on self-

report or observational measures of empathy. Dadds et al (2008) developed the first caregiver-report measure of empathy (the Griffith Empathy Measure; GEM) and compared scores with those of the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) in children aged 4-16. Empathy scores tended to correlate negatively with emotional and behavioural problems, and positively with prosocial behaviour, supporting the results of self-report and observational studies.

Although no study has specifically examined the relationship between empathy and behavioural difficulties in children with FASD, one study has demonstrated that deficits in the wider domain of social cognition (of which empathy is one aspect) are predictive of behavioural problems in children aged 6-13 years with FASD (Greenbaum et al., 2009). Social cognition is the range of cognitive processes that involve other individuals, including empathy, social attribution, prejudice, group behaviour, and social influence (Frith & Blakemore, 2005). In the Greenbaum study, higher numbers of behavioural difficulties were predicted by higher levels of difficulty with false belief, intentions, deception, sarcasm, and strategic control of emotions. Similarly, few if any studies have specifically assessed the relationship between empathy and behavioural difficulties in children with a history of trauma, but there is some evidence of the role of other social cognitive domains. The hostile attribution bias (Crick & Dodge, 1994) is a cognitive bias where an individual is more likely than usual to attribute malice to an action or agent, regardless of whether it was intended. In a sample of 339 young adults, Richey et al (2016) identified a positive correlation between childhood maltreatment and reactive aggression, and this relationship was mediated by a hostile attribution bias. In other words, maltreated children are more likely than non-maltreated children to misattribute malice to an ostensibly aggressive act and react aggressively themselves.

Children with FASD have well-documented, multiple and varied behavioural difficulties, including internalising (directed toward the self) and externalising problems (Kodituwakku & Kodituwakku, 2014; Tsang et al., 2016). Commonly cited in the literature are hyperactivity or restlessness, problems with attention or concentration (Nash et al., 2006), conduct problems such as aggression, disobedience or stealing (Ruisch et al., 2018), problems with peer relationships and other social difficulties (Kully-Martens et al., 2012), and poor adaptive functioning or daily living skills (Jirikowic et al., 2008). Similarly, children with a history of trauma have been reported to have higher levels of internalising and externalising problems (Kim & Cicchetti, 2003), attention deficit, negative affect, emotion regulation (Shields & Cicchetti, 1998), aggression, anxiety, depression, dissociation, post-traumatic stress disorder symptoms, social problems, thought problems, and social withdrawal compared with children without a history of trauma (Lansford et al., 2002).

In contrast to the complete lack of studies on empathy, two studies have assessed differences in behavioural difficulties between children with both FASD and trauma, and a group with only one of those exposures. Henry et al (2007) used the revised Conners' Rating Scales (Conners, 2001) to measure behavioural difficulties in 274 children with histories of trauma, around half of whom also had prenatal exposure to alcohol. Children with both exposures were rated higher for hyperactivity, attention, impulsivity, restlessness, oppositional behaviour and social problems. Koponen et al (2009) took the opposing perspective and assessed the impact of trauma within a sample of children with FASD. Higher numbers of traumatic experiences were correlated with higher total score (more problems) on the Child Behaviour Checklist (Achenbach, 1991), although this study used a smaller sample of 38 Finnish children in foster care. From these two studies, it would appear that the combination of exposures can be expected to lead to more severe problems than either one on its own, but the difference between dual exposure and just PAE may be more subtle.

Given the wide range of social, behavioural and other difficulties that are characteristic of FASD, it is unsurprising that children and adults are at increased risk of a number of developmental or mental health diagnoses. These have been well-documented, and a recent systematic review identified the most common disorders and compared their prevalence in FASD to the general population. Weyrauch et al (2017) found that the most common comorbid mental or developmental diagnoses in children and adults with FASD were: Attention-deficit hyperactivity disorder (ADHD, 50.2% of people with an FASD diagnosis have this), intellectual disability (23%), learning disorder (19.9%), oppositional defiant disorder (ODD, 16.3%), depressive disorder (15.1%), psychotic disorder (12.3%), bipolar disorder (8.6%), anxiety disorder (7.8%), post-traumatic stress disorder (PTSD, 6%), obsessive compulsive disorder (4.9%), and reactive attachment disorder (4.7%). With the exception of PTSD and learning disorder, each of these prevalence rates is several times higher than in the general population: ADHD is ten times as prevalent in the FASD group compared to the general population, intellectual disability is 23 times as prevalent, and psychotic disorder is 25 times as prevalent. Another recent systematic review (Popova et al, 2016) calculated the prevalence of all other medical diagnoses comorbid with foetal alcohol syndrome (not the wider spectrum). Using ICD-10 criteria, they identified 428 comorbid conditions. Of the developmental and mental health diagnoses, the most common were: conduct disorder (90.9% prevalence in FAS), receptive language disorder (81.8%), expressive language disorder (76.2%), unspecified disorder of psychological development (69.2%), and developmental disorder of speech and language (76.2%). Studies into the developmental or mental health diagnoses associated with a history of trauma are less often compiled into comprehensive reviews, perhaps due to the diversity in type of trauma. Studies have found that childhood trauma is predictive of psychosis or schizophrenia (Read et al., 2005), PTSD,

ADHD, ODD (Ford et al., 2000), depression and anxiety (Hovens et al., 2010), personality disorders (Johnson, Cohen, Brown, Smailes, & Bernstein, 1999) and reactive attachment disorder (Zeanah et al., 2004). There is currently no evidence for the impact of trauma on mental or developmental diagnoses in individuals with FASD.

Previous studies have shown that the age at which a child is diagnosed with FASD can affect some outcomes. Streissguth et al (2004) found the odds of an individual with FASD experiencing an adverse life outcome increased if they received their diagnosis over the age of 12 years. The five adverse life outcomes were: Inappropriate sexual behaviours (Odds Ratio = 2.25 times more likely), disrupted school experiences (OR = 3.27), trouble with the Law (OR = 2.92), confinement (OR = 3.03), and alcohol or drug problems (OR = 4.16). Similarly, Alex and Feldmann (2012) found children diagnosed with an FASD at age five or younger had fewer social problems, were less aggressive, and were less likely to steal or play with fire than those diagnosed at age six or older. However, Fagerlund et al (2011) found no significant effect of age at diagnosis on behavioural difficulties. Foster or care placement history can also have an effect on outcomes in children with a history of trauma. A higher number of placements, and older age at first placement outside the birth family, have each been found to be related to a higher risk of criminality in male, but not female, adolescents with a history of trauma (Ryan & Testa, 2005). Children with FASD and a history of trauma have been found to exhibit fewer socio-emotional problems if they were removed from their birth family at an earlier age (Koponen et al., 2009), but no significant relationship was identified between number of placements and socio-emotional outcomes. The same study also found that having an FASD diagnosis was associated with fewer behavioural problems compared to an FAS diagnosis, although the effect was small (Koponen et al., 2009).

Prenatal exposures to drugs or tobacco can lead to adverse cognitive and behavioural outcomes by themselves and may compound the effects of prenatal alcohol exposure. For example: prenatal exposure to tobacco is associated with aggression, antisocial behaviour, impulsivity and ADHD; prenatal cocaine exposure is associated with a range of cognitive deficits, attention problems and disruptive behaviours; and prenatal exposure to opiates is associated with anxiety, aggression and disruptive behaviour (Minnes, Lang, & Singer, 2011). Few if any studies have investigated a potential compounding effect of prenatal alcohol, tobacco and/or other drugs on the social or behavioural development of the offspring, but some have assessed the impact on birth outcome. A structural brain imaging study of children aged 10-14 years (Rivkin et al., 2008) found that children exposed to either alcohol, tobacco, cannabis, or cocaine had lower mean cortical grey matter and total parenchymal volumes, and smaller mean head circumference than non-exposed children. For each additional exposure, the severity of neuroanatomical harm was increased, with those children

exposed to all four substances affected most severely. Similarly, a review of studies on combined prenatal alcohol and tobacco exposure (Odendaal, Steyn, Elliott, & Burd, 2009) found that preterm labour, low birthweight and growth restriction were each more likely following dual exposure compared to either one exposure. Further to this, a dual exposure carried a greater risk than the sum of both exposures, indicating a synergistic effect of alcohol and tobacco on birth outcome.

To summarise, the evidence above demonstrates a number of gaps in the current knowledge of the combined effects of prenatal alcohol exposure and trauma on empathy, behaviour and mental or developmental diagnoses. Children with FASD or a history of trauma have each demonstrated deficits in empathy, but no study has assessed the impact of trauma on empathy within children with FASD. Similarly, studies have shown links between those exposures and behavioural problems, but little is currently known about differences in behavioural problems related to trauma in children with FASD. Studies have demonstrated a link between empathy and behaviour in typically developing children, and between social cognition and behaviour in children with FASD or a history of trauma; but a specific relationship between empathy and behaviour in children with FASD and/or a history of trauma is yet to be established. Children with FASD or a history of trauma are more likely than non-exposed children to have one or more of a range of mental health or developmental diagnoses such as ADHD or conduct disorder, but no study has investigated the impact of trauma on diagnoses in children with FASD. Finally, absence of an FASD diagnosis, older age at diagnosis, older age at first placement, higher number of placements, and prenatal exposures to drugs or tobacco have all been shown to predict more severe adverse outcomes in children with either FASD or a history of trauma. It is possible that some or all of these factors will confound a relationship between trauma and social or behavioural outcomes in children with FASD.

The study described in this chapter tested the following hypotheses:

- Children with FASD will have lower empathy than children in the general population
- Children with FASD will have more behavioural difficulties than children in the general population
- Children with FASD will have higher levels of trauma than children in the general population
- There will be a negative relationship between trauma and empathy in children with FASD
- There will be a positive relationship between trauma and behavioural difficulties in children with FASD
- There will be a negative relationship between empathy and behavioural difficulties in children with FASD

- There will be a positive relationship between trauma and comorbid diagnoses in children with FASD
- The relationships between a) trauma and empathy, and b) trauma and behavioural difficulties, will be mediated by the presence of an FASD diagnosis, age at diagnosis, age at first placement, number of placements, and prenatal exposures to drugs and tobacco.

5.2 Methods

5.2.1 Design

The study was a cross-sectional, observational, caregiver-report survey of children aged 4-16 years with FASD or suspected FASD. Diagnosis was not required because a) the majority of individuals who would qualify for a diagnosis remain undiagnosed (Chasnoff, Wells & King, 2015; May et al., 2018; Morleo et al., 2011), and b) so that any differences between those with and without a diagnosis could be assessed.

5.2.2 Participants

Participants were recruited through FASD support groups on the social media platform Facebook. A link to the online survey was shared, with the permission of group administrators, amongst parents and carers of children aged 4-16 years with FASD or suspected FASD. Participants were not recruited based on country of residence, but the support groups catered mainly for English-speakers. Between October 2016 and October 2017, the URL was visited 1,446 times, and the full survey was completed by the parents or carers of 253 children and adolescents who were prenatally exposed to alcohol. Eight responses were excluded for age range violations, leaving 245 responses for inclusion in the study. Of the 245 children for whom caregivers provided information, 123 (50.2%) were male, 120 (49%) were female, and two (0.8%) did not fit into either category. The age range was 4.15 – 16.84 years ($M=10.65$, $SD=3.34$), and most of the children were residents of the United States (50.6%), the United Kingdom (32.7%), and Canada (12.2%). Most respondents (85.3%) reported that they had adopted their child or were foster carers (5.3%). Some children lived with their extended families (4.9%) or were cared for under other legal arrangements such as care orders (2.9%). Three respondents (1.2%) were their child's biological parent. Most children (80.4%) had a diagnosis on the foetal alcohol spectrum. The most common diagnosis was foetal alcohol syndrome (33.9%), followed by alcohol related neurodevelopmental disorder (17.1%). Participant characteristics are provided in table 5.1.

5.2.3 Measures

Trauma

Several validated caregiver-report measures of trauma or maltreatment were available for use in the survey. Definitions of trauma, traumatic experiences, adverse childhood experiences (ACE's), and maltreatment may be used almost interchangeably, and their definitions overlap. Maltreatment is defined (see section 2.7) as physical, sexual or psychological abuse or physical or emotional neglect. ACE's (defined originally by Felitti et al., 1998; updated by Dube et al., 2003) include these five items as well as 1) witnessing domestic violence, 2,3,4) living with a family member who is mentally ill, addicted to drugs or alcohol, or who is imprisoned, or 5) experiencing parental divorce or separation. Trauma or traumatic experiences are less well defined but often include either maltreatment or all ten ACEs plus other environmental factors such as having had multiple placements within the care system (e.g. Koponen et al., 2009). A number of potential measures were considered for this project - all of which covered maltreatment, and many of which covered more than this. The Childhood Trauma Questionnaire (short form; Bernstein et al., 2003) covers maltreatment with five questions per scale, for example under the physical abuse category: child was hit hard enough to see a doctor, hit hard enough to leave bruises, punished with hard objects, was physically abused, or was hit hard enough to be noticed. The measure was validated on a sample of 1,978 adults from clinical and non-clinical populations but was originally designed for adults to answer about themselves. The Comprehensive Childhood Maltreatment Scale (Higgins & McCabe, 2001) covers sexual abuse, physical abuse, psychological maltreatment, neglect, and witnessing family violence, with three questions for each subscale except sexual abuse which has 11 questions. Self-report and caregiver-report formats are available, validated on 313 adults (self-report form) and 100 parents (parent report form).

However, it was decided that the most appropriate measure of traumatic experiences was the 10-item Adverse Childhood Experiences (ACE) questionnaire (Felitti et al., 1998; updated by Dube et al., 2003). The ACE questionnaire covers the five maltreatment variables plus five other adverse experiences (witnessing domestic violence, living with a family member who is mentally ill, addicted to drugs or alcohol, or imprisoned, or experiencing parental divorce or separation). There are two questions per category, and the measure was validated on a sample of 13,949 adults. The scale was originally designed for self-report but has been used in caregiver report format by altering the subject of the question so that, for example, "did you ever..." becomes "did your child ever..." (Sacks, Murphey, & Moore, 2014). Test-retest reliability of the 10 ACE questions has been shown to be moderate, good, or substantial, and the reliability of the overall score has been identified as good (Dube, Williamson, Thompson, Felitti, & Anda, 2004), although no validity or reliability data exist for

its use as a caregiver-report tool. The ACE is a highly cited, well-recognised measure of childhood trauma, and its validity is demonstrated by its ability to predict a wide range of somatic and psychological adverse outcomes in many hundreds of studies (for reviews, see Carr et al., 2013; Kalmakis & Chandler, 2015). The ACE produces a score on a scale from 0-10, which enables the analysis of relationships between ACEs and adverse outcomes in cross-sectional studies; and it is useful that a dose-response effect has been established, where higher numbers of ACEs are associated with a higher risk of adverse outcomes (Anda et al., 2006).

Empathy

The validity of behavioural and self-report measures of empathy in children was criticised in a recent review which suggested the need for progress in this area (Lovett & Sheffield, 2007). In response to this, Dadds et al (2008) developed the first and only informant-report measure of cognitive, affective and total empathy. Based on a sample of 2,612 children aged 4-16, the Griffith Empathy Measure (GEM) is a 23-item parent-report measure of empathy in children and adolescents aged 4-16. In addition to providing a measure of empathy, the scale can be divided into cognitive and affective empathy subscales. Caregivers respond to statements such as “My child becomes sad when other children are sad”, and “My child doesn’t understand why other people cry out of happiness”, on a 9-point Likert scale where -4 is strongly disagree, and +4 is strongly agree. This gives a total empathy score from -92 to +92, with higher scores indicating a higher level of ability to recognise or vicariously experience the perspectives or emotions of other people. The GEM has good test-retest reliability over 1 week ($r > .89$) and over 6 months ($r > .69$); it is internally consistent, has a stable factor structure across age and genders, has good inter-parental agreement ($r > .47$), and has good convergence with child reports ($r = .41$; Dadds et al., 2008).

Behavioural difficulties

Several reliable parent-report measures of children’s behavioural difficulties are available, which measure overlapping aspects of behavioural, emotional and social functioning. The five to fifteen (FTF; Kadesjö et al, 2004) scale provides a measure of memory, learning, language, executive function, motor skills, perception, social skills, and emotional/behavioural problems for children aged six to fifteen years. It contains 181 questions, has high inter-parent agreement ($r = 0.77$ for behavioural problems) and test-retest reliability ($r = .83$), and includes opportunities for caregivers to elaborate on any positive aspects of their children’s characters. The Revised Conners' Parent Rating Scale (CPRS-R; Conners, Sitarenios, Parker, & Epstein, 1998) is available in short 27-question, or long 80-question formats. It provides scores for oppositional behaviour, cognitive Problems,

Table 5.1 Survey sample characteristics

Age (years)	Range	Mean, SD
	4.15 – 16.84	10.65, 3.34
Gender	Frequency	Percentage
Male	123	50.2
Female	120	49.0
Other	2	0.8
Country of residence	Frequency	Percentage
USA	124	50.6
UK	80	32.7
Canada	30	12.2
Australia	3	1.2
Belgium	2	0.8
Germany	2	0.8
New Zealand	2	0.8
Ireland	1	0.4
South Africa	1	0.4
Living arrangements	Frequency	Percentage
Adopted	209	85.3
Fostered	13	5.3
Lives with extended family	12	4.9
Other legal arrangement	7	2.9
Lives with biological parent(s)	3	1.2
FASD diagnosis	Frequency	Percentage
Foetal alcohol syndrome	83	33.9
No diagnosis	48	19.6
Alcohol related neurodevelopmental disorder	42	17.1
FASD without dysmorphic features	19	7.8
FASD with dysmorphic features	16	6.5
Partial foetal alcohol syndrome	16	6.5
Neurodevelopmental disorder associated with PAE	13	5.3
Foetal alcohol effects	7	2.9
Alcohol related birth defects	1	0.4

hyperactivity-impulsivity, anxiety, shyness, perfectionism, social problems, psychosomatic problems, ADHD symptoms, and an overall global scale, for children aged 3-17. The CPRS-R has high internal reliability ($\alpha = .75$ to $.94$ for males, $.75$ to $.93$ for females), and moderate to high test-retest reliability

($r = .42 - .78$) on all subscales except for perfectionism ($r = .13$). The Child Behaviour Checklist (CBCL; Achenbach, 1991) has caregiver and teacher report forms for all children aged from 18 months to 18 years, as well as a self-report version for adolescents. Both parent and teacher forms contain 132 questions that assess problem behaviour and adaptive behaviour as well as internalising and externalising problems. Internal consistency of the CBCL is high, with alpha values ranging from .72 for social problems, to .96 for total problems.

The Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) however, was the best fit for the current project. The SDQ is a 25-item questionnaire for the parents or teachers of children aged 4-17, designed to assess emotional and behavioural strengths and difficulties on five scales: conduct problems, hyperactivity, emotional problems, peer problems, and prosocial behaviour. The first four subscales can be grouped together to provide a total difficulties score, while prosocial behaviour is the one 'strength' subscale. The inclusion of the one 'strength' subscale allows respondents the opportunity to reflect on their child's positive characteristics and will hopefully make their participation a more positive experience. This aspect sets the SDQ apart from similarly valid tools such as the CBCL. The four difficulties can also be paired as externalising problems (conduct and hyperactivity) and internalising problems (peer problems and emotional problems). There are therefore eight possible scores from the SDQ: the five subscales, internalising problems, externalising problems, and total difficulties. Five statements are given for each of the five subscales, e.g. 'My child often has temper tantrums or hot tempers' or 'My child is nervous or clingy in new situations, easily loses confidence', and responses are given on a three-point scale: Certainly true, somewhat true, or not true. Scores are standardised and described on a four-point scale: Average (indicating behaviour is no more problematic than the average child), slightly raised, high, and very high (indicating that behaviour is highly problematic compared with the average child). The SDQ is a validated, highly cited measure with good internal consistency (Cronbach's $\alpha = .73$), retest stability after six months ($M = 0.62$) and established diagnostic predictability (Goodman, 2001). The SDQ was selected because: a) its validity and reliability are at least as high as similar measures; b) it is considerably shorter than its competitors with only 25 questions, which puts less pressure on respondents; and c) one of the five SDQ subscales concerns a positive characteristic – prosocial behaviour. This provides a more nuanced assessment of each child compared with measures that deal only with difficulties, and caregivers may benefit from the opportunity to reflect on their children's strengths.

Other questions

Aside from the three established measures of empathy, trauma and behaviour, the survey also asked respondents to state which, if any, mental or developmental diagnoses their children had.

They were also asked about some factors that were included due to their possible effect on the relationships between trauma, empathy and behaviour:

- Their child's age at first placement outside the birth family (if any)
- The number of placements their child had between leaving their birth family and arriving at their current home
- Their child's age at FASD diagnosis (if any)
- Whether their child was prenatally exposed to tobacco or drugs, and which drugs

For the full survey, see [appendix 2](#).

5.2.4 Procedure and ethics

Ethical approval for the study was granted by the University of Salford Health Research Ethical Approval Panel (reference number HSCR1682, see [appendix 3](#)). The online survey was created using Bristol Online Surveys (www.onlinesurveys.ac.uk), and participation was entirely online. The opening page provided full study information including participants' rights in accordance with the British Psychological Society Code of Human Research Ethics (BPS, 2014). Participation was voluntary and anonymous, and respondents were asked to provide a memorable word or phrase to identify their data in the event that they would like it to be removed. Participants were alerted to the fact that one section of the survey (ACEs) contained potentially upsetting questions. They were informed that they were under no pressure to take part, were able to stop or take a break at any point, and that they were able to request the removal of their data up to one month after completion of the survey. Participants provided their informed consent on the second page. On the third page, participants provided information about their country of residence, their child's age, gender, placement history, prenatal exposures and diagnoses. The fourth, fifth and sixth pages contained the GEM, SDQ and ACE questionnaires respectively. At the end of pages three, four, five and six, a free text box was provided, with the instruction: "If you would like to make any extra comments, please do so here". Finally, the last page of the survey provided contact details of the research team and charities that provide counselling and advice specific to FASD and childhood trauma.

5.2.5 Analysis

Pearson's correlation analyses were conducted to assess any relationships between ACE score, GEM empathy scores, and SDQ behaviour scores, including their sub-scales. Since hypotheses were directional (e.g. there will be a positive correlation between ACE score and SDQ score), correlation tests were one-tailed. The sample was also split into those living in the UK and those

living in North America (the USA and Canada combined), and into boys and girls, for sub-group analysis. In order to test the hypotheses that children with FASD have lower total, cognitive and affective empathy scores than children in the general population, a series of one-sample z-tests were conducted for each age group across both boys and girls. In order to assess the relationship between trauma and non-FASD diagnoses (e.g. ADHD), a categorical variable of maltreatment (abuse and/or neglect) was created. Children whose caregivers reported any maltreatment on the ACE questionnaire were compared with children whose caregivers reported that no maltreatment had occurred (children whose caregivers were unsure about this were removed from this analysis). Pearson's Chi-square tests were conducted to assess the relationship between maltreatment and non-FASD diagnoses, and chi-square goodness of fit tests were used to compare rates of ACEs between the FASD sample and population data. Goodness of fit tests were also used to compare rates of non-FASD diagnoses between the full sample and population data. Mann-Whitney-U tests were used to assess the relationship between having an FAS or FASD diagnosis, and the age at which a child received their FASD diagnosis, on GEM and SDQ scores. Multiple linear regression analysis was used to assess the combined impact of ACEs, age at first placement, number of placements, country of residence, gender, and age at FASD diagnosis on both GEM empathy scores and SDQ behavioural difficulties scores. All statistical analysis was conducted using SPSS version 25. Syntax for the one-sample z-tests was provided by how2stats.com.

5.3 Results

5.3.2 Empathy

Normative data for the Griffith Empathy Measure (Dadds et al, 2008) are not provided for the whole age range (4-16) but are divided into three age groups (4-6, 7-10, and 11-16 years) and by gender. Hence, data from the GEM in this report are presented in those age groups and between boys and girls for comparison with population data. Table 5.2 shows that boys and girls across all three age groups in this sample had significantly lower cognitive, affective and total empathy scores than children in the general population. The mean effect size (Cohen's *d*) was very high ($M = -1.47$, $SD = .71$), with a range of $-.3$ to -3 .

5.3.3 Behavioural strengths and difficulties

Table 5.3 and figure 5.1 show that the majority of children with PAE in this sample tend to have above average levels of internalising and externalising behavioural difficulties across all four subscales of the SDQ. The majority also had below average scores for prosocial behaviour. The percentage of children in this sample with high or very high levels of problems was 63.3% for

Table 5.2 Means, SDs, Z statistics and effect sizes of GEM scores for FASD sample (n=245) and normative data (n=8,613)

Age range	Empathy Scale	Gender					
		Male		Female			
		Population	FASD sample	Z statistic	Population	FASD sample	Z statistic
4-6 years	Total	M = 28.63	M = -11.64	Z = -9.60	M = 36.76	M = -14.53	Z = -13.06
		SD = 19.67	SD = 31.93	p < .001	SD = 17.12	SD = 38.38	p < .001,
			n = 22	d = -2.05		n = 19	d = -3.00
	Cognitive	M = 7.59	M = -6.91	Z = -5.40	M = 9.42	M = -5.89	Z = -9.41
		SD = 7.19	SD = 9.30	p < .001	SD = 7.09	SD = 10.11	p < .001
			n = 22	d = -1.15		n = 19	d = -2.16
	Affective	M = 5.96	M = -1.27	Z = -3.25	M = 8.55	M = -3.47	Z = -4.90
		SD = 10.45	SD = 15.21	p = .001	SD = 10.69	SD = 18.33	p < .001
			n = 22	d = -.69		n = 19	d = -1.12
7-10 years	Total	M = 30.28	M = 2.47	Z = -8.52	M = 39.78	M = 2.87	Z = -11.50
		SD = 21.89	SD = 35.83	p < .001	SD = 21.53	SD = 37.98	p < .001
			n = 45	d = -1.27		n = 45	d = -1.71
	Cognitive	M = 8.15	M = -4.22	Z = -10.45	M = 10.48	M = -3.33	Z = -11.86
		SD = 7.87	SD = 8.50	p < .001	SD = 7.81	SD = 9.54	p < .001
			n = 45	d = -1.57		n = 45	d = -1.77
	Affective	M = 6.00	M = 2.67	Z = -2.00	M = 8.99	M = 2.69	Z = -6.59
		SD = 11.17	SD = 17.05	p = .046	SD = 11.89	SD = 16.86	p < .001
			n = 45	d = -.30		n = 45	d = -.98
11-16 years	Total	M = 37.02	M = -.41	Z = -12.63	M = 42.19	M = .79	Z = -16.80
		SD = 22.18	SD = 33.37	p < .001	SD = 18.44	SD = 36.54	p < .001
			n = 56	d = -1.69		n = 56	d = -2.25
	Cognitive	M = 9.74	M = -4.48	Z = -12.97	M = 12.03	M = -6.14	Z = -14.54
		SD = 8.20	SD = 7.88	p < .001	SD = 9.35	SD = 9.73	p < .001
			n = 56	d = -1.73		n = 56	d = -1.94
	Affective	M = 7.90	M = .93	Z = -4.40	M = 7.51	M = 1.64	Z = -3.82
		SD = 12.16	SD = 17.09	p < .001	SD = 11.49	SD = 17.82	p < .001
			n = 56	d = -.57		n = 56	d = -.51

emotional problems, 72.5% for peer problems, 78.8% for conduct problems, 79.2% for hyperactivity, 70.2% for prosocial behaviour, and 91.5% for total difficulties.

Table 5.3: Frequencies and percentages of children with FASD (n = 245) by scores on Strengths and Difficulties Questionnaire

	Average	Slightly raised	High	Very high
Internalising problems				
Emotional problems	65 (26.5%)	25 (10.2%)	60 (24.5%)	95 (38.8%)
Peer problems	41 (16.7%)	26 (10.6%)	29 (11.8%)	149 (60.7%)
Externalising problems				
Conduct problems	37 (15.1%)	15 (6.1%)	54 (22%)	139 (56.7%)
Hyperactivity	19 (7.8%)	32 (13.1%)	30 (12.2%)	164 (67%)
Prosocial behaviour*	37 (15.1%)	36 (14.7%)	26 (10.6%)	146 (59.6%)
Total difficulties score	8 (3.3%)	13 (5.2%)	21 (8.6%)	203 (82.9%)

* Raised, high, and very high scores for prosocial behaviour indicate increased problems, or lower levels of prosocial behaviour

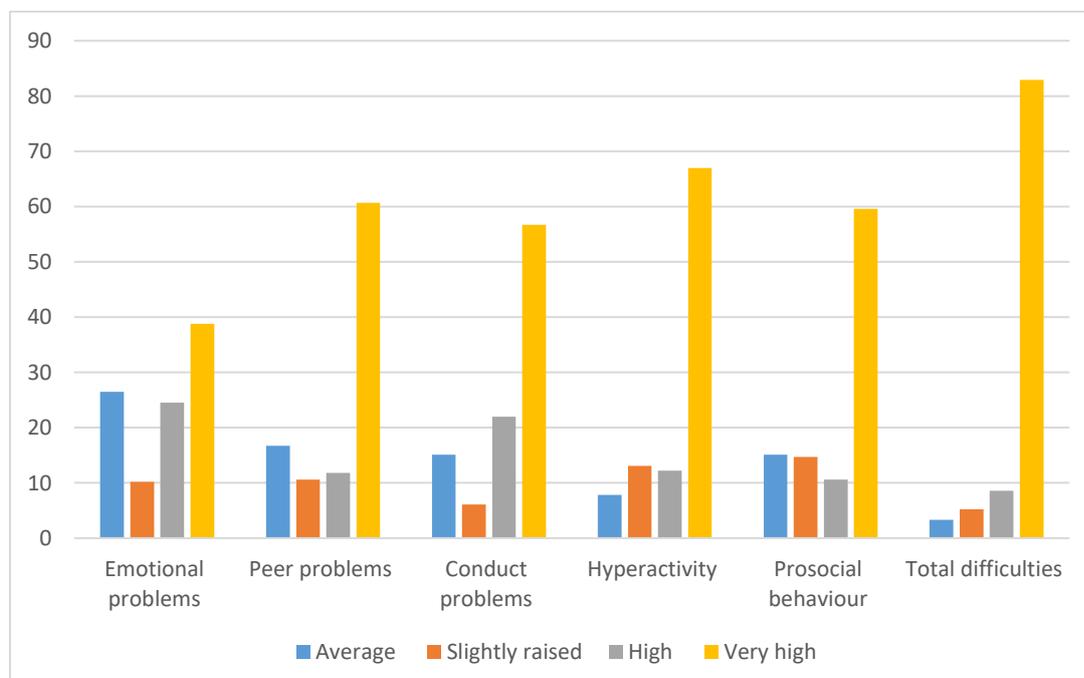


Figure 5.1 Percentages of children with FASD with average, raised, high, or very high scores on Strengths and Difficulties Questionnaire scales

5.3.4 Adverse childhood experiences

Table 5.4 and figure 5.2 show the percentages of this sample with a reported history of each Adverse Childhood Experience. Compared with normative data (Dube et al., 2003) children in this sample with FASD had significantly higher levels of all 10 ACEs, with the exception of physical abuse and sexual abuse. There was no difference between rates of reported physical abuse in the FASD sample (25.3%) and normative data (26.4%, $\chi^2 = .15$, $p = .70$), and reported sexual abuse was more common in the normative data (21%) compared with the FASD sample (11.4%, $\chi^2 = 13.29$, $p < .001$). There were also widely varying levels of uncertainty for the different types of ACE. Most respondents were able to report whether or not their child had been physically neglected (4.5% uncertainty) or lived with a parent who abused drugs or alcohol (6.5% uncertainty), but there were high levels of uncertainty for physical abuse (29% uncertainty) and sexual abuse (32.2% uncertainty).

Table 5.4: Percent of individuals with reported Adverse Childhood Experiences

Type of ACE	Population <i>n</i> =8,613	Sample <i>n</i> =245	Chi square	Parents of FASD sample who were unsure
Maltreatment				
Physical abuse	26.4	25.3	.15	29.0
Psychological abuse	10.2	40.4	221.25*	18.4
Sexual abuse	21.0	11.4	13.29*	32.2
Physical neglect	9.9	50.6	402.30*	4.5
Emotional neglect	14.8	34.7	72.52*	24.1
Others				
Parental divorce	24.1	44.5	53.28*	13.1
Violence against mother	13.0	32.2	75.36*	28.2
Parent misused alcohol or drugs	28.2	56.7	94.21*	6.5
Household member mentally ill	20.3	43.3	75.95*	21.2
Household member in prison	6.0	31.8	253.74*	19.6
ACE Score				
0	32.7	22.4		
1	25.6	9.8		
2	15.5	7.8		
3	9.9	11.8		
4	5.9	5.7		
5 or more	10.5	42.5		

* $p < .001$

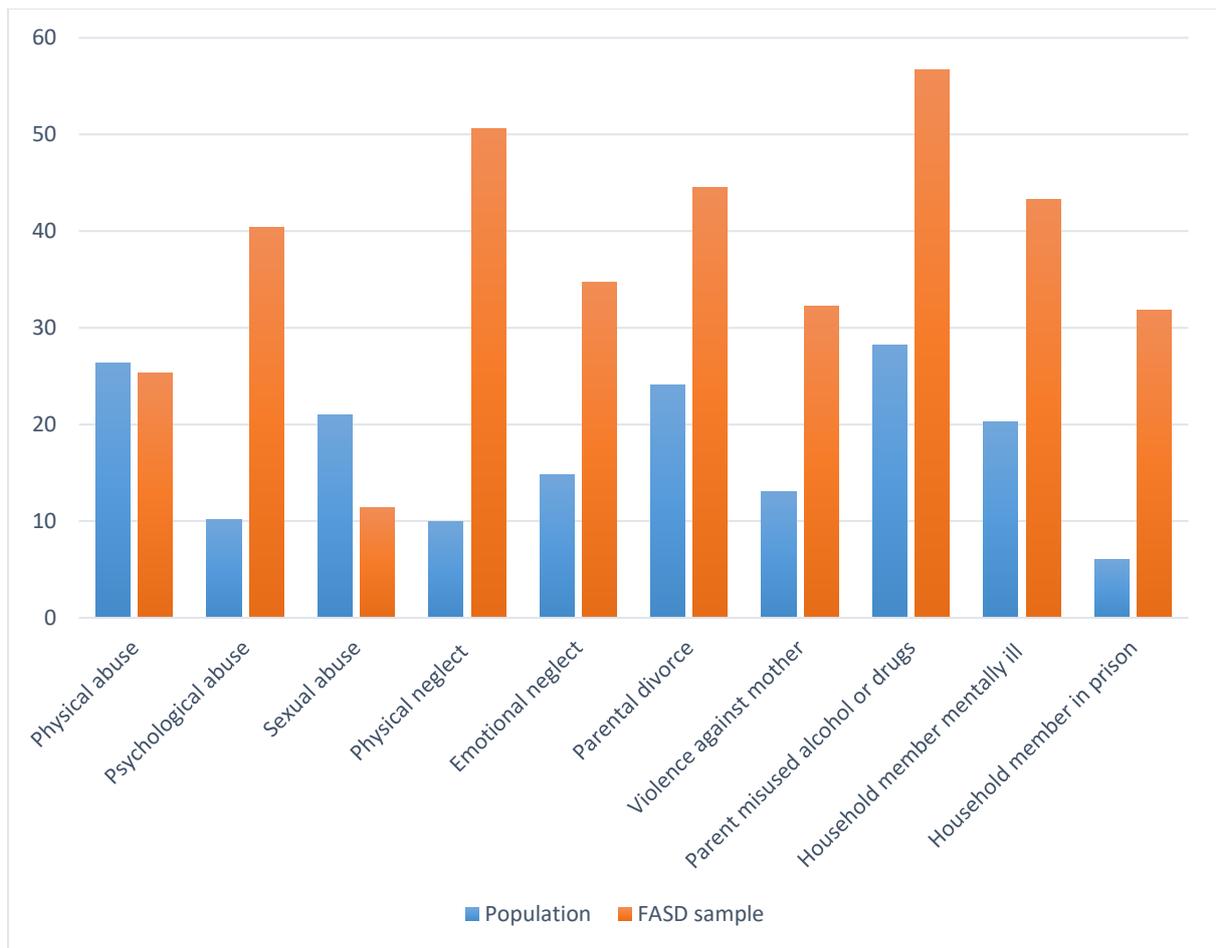


Figure 5.2 Percentage of individuals with reported Adverse Childhood Experiences

5.3.5 Comorbid diagnoses

Figure 5.3 shows the rate of comorbid diagnoses in the FASD sample, compared with international population data from a recent systematic review (Weyrauch et al., 2017). Most respondents (77.1%) reported that their child had at least one non-FASD mental or developmental diagnosis. The most common was attention-deficit hyperactivity disorder (38.8% comorbidity; population rate 5%), followed by intellectual disability (14.7%; population 1%), anxiety disorder (13.9%; population 0.9%), attachment disorder (13.9%; population 1.4%), and sensory processing disorder (11.4; population prevalence unknown). Goodness of fit tests showed the rates of ADHD ($p < .001$), intellectual disability ($p = .001$), anxiety disorder ($p = .001$), attachment disorder ($p = .001$), and Autism Spectrum Disorder ($p = .02$) were significantly more common in the FASD sample than in the general population data.

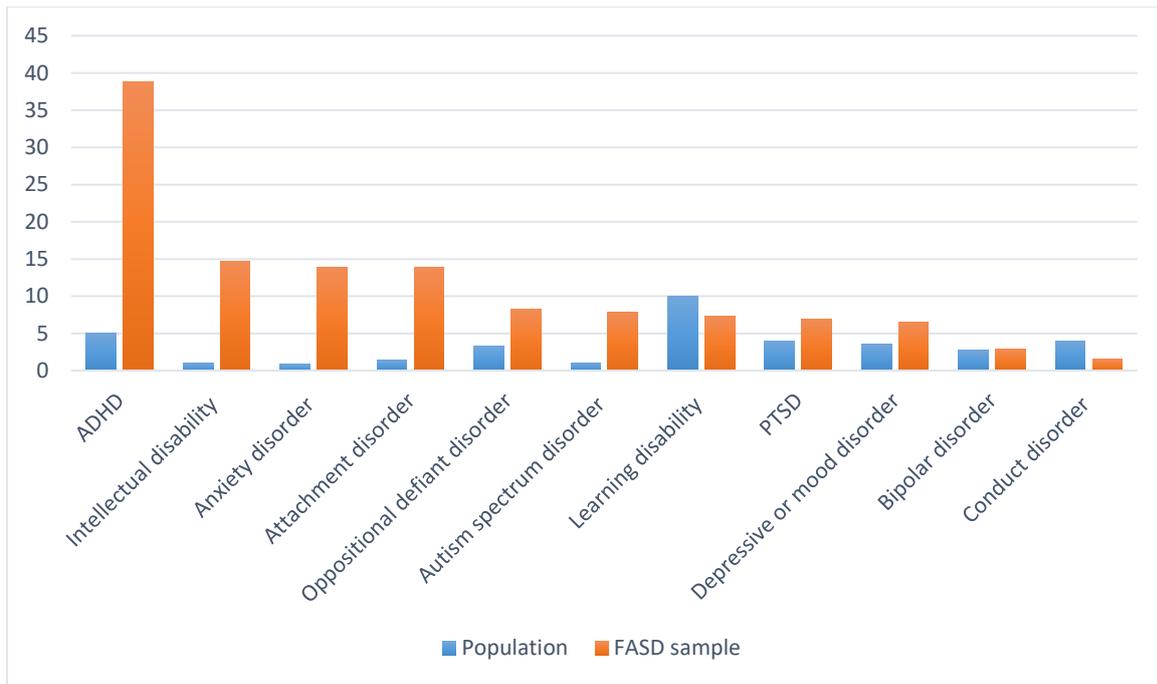


Figure 5.3 Percentage of FASD sample with comorbid diagnoses with population data

5.3.6 Potential confounding variables

Table 5.5 shows the percentage of children that were prenatally exposed to drugs or tobacco, and the ranges, means and standard deviations of children’s number of placements, age at first placement, and age at FASD diagnosis. Over half (50.6%) of respondents reported that their child had been prenatally exposed to recreational drugs, and many others (39.2%) were unsure. The most commonly reported drug that children had been exposed to was cannabis (11.8% of sample), followed by cocaine (9%), methamphetamine (6.5%), and opiates (6.5%). Most respondents (60.4%) reported that their child had been prenatally exposed to tobacco, but there was also a high level of uncertainty (32.7%). The mean number of placements was 4.40 years (SD = 1.98), the mean age at first placement was 1.28 years (SD = 1.86), and the mean age at FASD diagnosis was 7.26 years (SD = 3.92).

5.3.7 Correlations between ACEs, empathy and behavioural difficulties

Table 5.6 shows Pearson’s correlation coefficients of ACE scores, GEM empathy scores, SDQ behaviour scores, and the other mediating factors. There was no relationship between ACE score and GEM affective, cognitive or total empathy scores. None of the GEM empathy scores were associated with age at first placement, number of placements, or age at diagnosis. There was a weak positive correlation between ACE score (M=3.71, SD=3.00) and SDQ total difficulties (M=25.19,

Table 5.5 Potential confounding variables in sample of children with FASD (n=245)

Prenatal drug exposure	Frequency	Percentage
Yes	124	50.6
No	25	10.2
Unsure	96	39.2
Type of drug	Frequency	Percentage
Cannabis	29	11.8
Cocaine	22	9.0
Methamphetamine	16	6.5
Opiates	16	6.5
Crack cocaine	9	3.7
Amphetamine	5	2.0
Prescription painkillers	2	0.8
Prenatal tobacco exposure	Frequency	Percentage
Yes	148	60.4
No	17	6.9
Unsure	80	32.7
Others	Range	M, SD
Number of placements	0-13	4.40, 1.98
Age at first placement	0-10	1.28, 1.86
Age at FASD diagnosis	1-16	7.26, 3.92

$SD=6.00$; $r=.21$, $p<.001$, one-tailed). There was also a weak positive correlation between ACE score ($M=3.71$, $SD=3.00$) and SDQ conduct problems ($M=5.82$, $SD=2.72$; $r=.23$, $p<.001$, one-tailed). There was a weak positive correlation between age at diagnosis ($M = 7.26$, 3.92) and SDQ peer problems ($M=5.22$, $SD=2.52$; $r=.25$, $p<.001$, one-tailed). The relationships between ACE score and other SDQ subscales were either very weak or not significant.

Table 5.7 shows the relationships between GEM empathy scores and SDQ behaviour scores. Peer problems, conduct problems and total difficulties had moderate negative correlations with GEM empathy scores, with the exception of affective empathy ($M=1.30$, $SD=17.04$) and total difficulties ($M=25.19$, $SD=6.00$) which had a weak negative correlation ($r=-.19$, $p=.003$). Emotional problems ($M=5.51$, $SD=2.65$) had weak positive correlations with affective empathy ($M=1.30$, $SD=17.04$; $r=.21$, $p=.001$, one-tailed) and total empathy ($M=-.95$, $SD=35.70$; $r=.13$, $p=.04$, one-tailed).

Table 5.6 Correlation matrix showing relationships between ACEs, modifiers, empathy and behaviour in children with FASD (n=245)

	Empathy (GEM)			Behaviour (SDQ)					
	Affective	Cognitive	Total	Internalising		Externalising			
				Emotion Problems	Peer problems	Conduct problems	Hyper-activity	Prosocial behaviour	Total difficulties
Adverse childhood experiences score	.00	-.08	-.04	.06	.17**	.23***	.01	-.02	.21***
Age at first placement	-.04	-.13	-.10	.04	.15*	-.03	.07	-.02	.09
Age at diagnosis	-.02	-.02	-.02	.09	.25***	.15*	-.09	-.07	.19**
Number of placements	-.02	.00	-.03	-.01	.06	.12	.09	.01	.10

* $p < .05$, ** $p < .01$, *** $p < .001$

Hyperactivity ($M=8.65$, $SD=1.83$) had a weak negative correlation with cognitive empathy ($M=-4.87$, $SD=9.04$; $r=-.20$, $p=.001$, one tailed). Prosocial behaviour ($M=5.00$, $SD=2.46$) had strong positive correlations with GEM affective empathy ($M=1.3$, $SD=17.04$; $r=.63$, $p<.001$, one-tailed), cognitive empathy ($M=-4.87$, $SD=9.04$; $r=-.61$, $p<.001$; one-tailed), and total empathy ($M=-.95$, $SD=35.70$; $r=.75$, $p<.001$, one-tailed).

Correlations between ACE scores and SDQ behaviour scores differed depending on country of residence and gender. In the UK ($n=80$), ACE score ($M=3.55$, $SD=2.83$) was not correlated with SDQ total difficulties score ($M=26.15$, $SD=5.57$; $r=.05$, $p=.32$, one-tailed). However, in North America (the USA and Canada; $n=154$) ACE score ($M=3.86$, $SD=3.12$) had a weak positive correlation with SDQ total difficulties score ($M=24.69$, $SD=6.26$; $r=.29$, $p<.001$). In boys ($n=123$), there was a weak positive correlation between ACE score ($M=3.26$, $SD=3.05$) and SDQ total difficulties score ($M=25.42$, $SD=5.36$; $r=.31$, $p<.001$, one-tailed), whereas in girls ($n=120$), there was no relationship between ACE score ($M=4.18$, $SD=2.91$) and SDQ total difficulties score ($M=25.09$, $SD=6.57$; $r=.13$, $p=.08$, one-tailed).

Table 5.7 Correlation matrix showing relationships between GEM empathy scores and SDQ behaviour scores in children with FASD (n=245)

	Internalising		Externalising			Total difficulties
	Emotion problems	Peer problems	Conduct problems	Hyperactivity	Prosocial behaviour	
Affective Empathy	.21**	-.33***	-.30***	-.01	.63***	-.19**
Cognitive Empathy	-.04	-.28***	-.47***	-.20**	.61***	-.41***
Total empathy	.13*	-.38***	-.43***	-.10	.75***	-.33***

5.3.8 Relationships between maltreatment and comorbid diagnoses

Chi square tests of independence were conducted to compare the frequency of non-FASD diagnoses in children with and without a history of maltreatment. Only two significant relationships were identified: children who were maltreated were more likely to be diagnosed with attachment disorder ($\chi^2(1, n = 228) = 6.29, p = .01, \text{Cramer's } V = .17$), and post-traumatic stress disorder ($\chi^2(1, n = 228) = 3.86, p = .049, \text{Cramer's } V = .13$) compared with children who were not maltreated. Table 5.8 shows the frequencies and percentages of children with and without maltreatment, attachment disorder and post-traumatic stress disorder.

Table 5.8 Frequencies and percentages of children with and without maltreatment, attachment disorder, and post-traumatic stress disorder

	No diagnosis	Attachment disorder
No maltreatment	114 (50%)	11 (5%)
Maltreatment	82 (36%)	21 (9%)
	No diagnosis	PTSD
No maltreatment	120 (53%)	5 (2%)
Maltreatment	92 (40%)	11 (5%)

5.3.9 Group comparisons

In order to test the hypothesis that a diagnosis of FAS would protect against adverse outcomes, Mann-Whitney-U tests were conducted. 83 children had a diagnosis of FAS, and the remaining 162 children did not. There was no difference in SDQ total difficulties score between the FAS group (Mdn=26) and the non-FAS group (Mdn=25), $U=5999.00$, $p=.17$. There was also no difference in GEM total empathy score between the FAS group (Mdn=-3) and the non-FAS group (Mdn=2.5), $U=6246.50$, $p=.36$.

Mann-Whitney-U tests were also used to determine differences in outcome based on the presence or absence of any FASD diagnosis. 197 children had a diagnosis on the foetal alcohol spectrum, and the remaining 48 did not. There was no difference in SDQ total difficulties score between the diagnosed group (Mdn=25.00) and the non-diagnosed group (Mdn=26.00), $U=4214.5$, $p=.24$. There was also no difference in GEM total empathy score between the diagnosed group (Mdn=-1) and the non-diagnosed group (Mdn=6.50), $U=4342.00$, $p=.38$.

The sub-sample of children with a diagnosis on the foetal alcohol spectrum ($n=198$) was split into groups based on their age at diagnosis. A series of Mann-Whitney-U tests was conducted to find the cut-off age at which diagnosis made the biggest difference. Children diagnosed with an FASD at age eight or younger ($n=131$; Mdn=25) had significantly lower SDQ total difficulties scores than those diagnosed at age nine or older ($n=67$; Mdn=28), $U = 3091.50$ $p = .001$. There was no difference in GEM total empathy score between the eight or younger group (Mdn=-5) and the nine or over group (Mdn=2), $U = 4319.50$, $p=.86$.

5.3.10 Multivariate analysis

In order to assess the impact of ACEs and the other mediating factors on behaviour and empathy in children with FASD, two stepwise multiple linear regression analyses were conducted. Due to low reported numbers of children who were not prenatally exposed to drugs or tobacco, and high levels of uncertainty amongst respondents, the potential mediating factors of prenatal drugs and tobacco were left out of the regression equations. The first analysis was calculated to predict GEM total empathy score based on a) ACE score, b) age at first placement, c) number of placements, d) residence of North America or the UK, e) gender, f) FASD diagnosis age eight or younger, g) FASD diagnosis age nine or older. No significant regression equation was found, and none of the mediating factors correlated significantly with GEM total empathy score.

In the second analysis, a stepwise multiple linear regression was calculated to predict SDQ total behavioural difficulties score based on the same mediating factors as above: a) ACE score, b) age at first placement, c) number of placements, d) residence of North America or the UK, e) gender,

f) FASD diagnosis age eight or younger, g) FASD diagnosis age nine or older. A significant regression equation was found ($F(1, 140)=14.20, p<.001$), with an R^2 of .09. Participants' predicted SDQ total difficulties score is equal to $24.25 + 4.18$ (diagnosis at age nine or older) where diagnosis at age nine or older is a dummy variable coded as 0 or 1. Children diagnosed at age nine or older had an SDQ total difficulties score that was higher by 4.18 points compared to those who were not diagnosed at age nine or older (including those diagnosed at age eight or younger and those without a diagnosis). Diagnosis at age nine or older was the only significant predictor of SDQ total difficulties score. Table 5.9 shows the coefficients of the multiple regression model.

Table 5.9 Multiple regression coefficients for prediction of SDQ total difficulties

	B	SE	β
(Constant)	24.25	.59	
Diagnosis at age nine or older	4.18	1.11	.30

5.3.11 Open responses

At the end of each section of the survey, an open text box was included so that respondents would have the opportunity to disclose any further information or clarifications. The four prompts were identical: *"If you would like to provide any further information, please do so here"*, once at the end of each page. Many respondents took the opportunity to provide further details, often to provide clarifications for their responses.

In reference to the GEM, many caregivers explained that their child would demonstrate empathy for some people, but not others. These responses tended to emphasise that familiarity was an important factor, with children unable to empathise with unfamiliar persons. For example:

"My child's responses depend on if he knows the other person or people involved. He has very strong reactions to people he knows when they are upset but seems not to notice if it is a stranger."

In reference to both the GEM and the SDQ, parents explained how their child's empathy or behaviour varied depending on their current mood, or whether they were medicated:

"These answers would be different if...she wasn't on her ADHD meds, which help [keep] her calm and regulated..."

"Emotional awareness really varies depending on her mood"

Some caregivers reported that their children could feign empathy by copying their peers' empathic behaviour, or would otherwise demonstrate empathy whilst lacking a genuine understanding of the perspective of others:

"My child mimics others around him when he doesn't understand what has happened"

Similarly, some respondents explained that the reason for their child's low scores on the GEM may have been due to a more general problem with failing to understand a situation:

"The majority of answers are followed by "if she notices" she's oblivious to the world around her unless it directly affects her"

On lying, cheating and stealing, some caregivers reported that these behaviours were more likely the result of a lack of awareness or memory issues, with more than one respondent referring to confabulation:

"She does not lie deliberately. She does not understand the concept of lying. The truth often gets mixed up with fantasy. I prefer to call it confabulation. That would be a better definition."

Many respondents explained that behavioural problems could be context-dependent, and that behaviour could be controlled during the school day, but not at home.

"These answers would be different if...relationships were differentiated between immediate family / school mates & teachers / strangers. Her behaviour at home is significantly worse than elsewhere"

5.4 Discussion

The aims of this study were: to describe the levels of and relationships between trauma, empathy and behavioural difficulties; describe the range of comorbid diagnoses; and assess the extent to which a number of potentially mediating factors affect the relationship between trauma, empathy and behavioural difficulties in an international caregiver-report survey of children with FASD. The main findings of the study are as follows. Children aged 4-16 years with confirmed or suspected developmental damage from prenatal alcohol exposure appear to have higher levels of adverse childhood experiences, lower empathy, higher levels of behavioural difficulties, and higher numbers of some mental or developmental disorders compared with children in the general population. The number of ACEs had no relationships or weak relationships with behavioural outcomes across the full sample, and no relationship with empathy across the full sample or any subsamples. When divided into groups based on gender and country of residence, there was a weak

positive relationship between ACEs and behavioural difficulties in children living in the USA and Canada, but no relationship in UK children. There was also a weak positive relationship between ACEs and behaviour in boys, but no relationship in girls. Neither a diagnosis of foetal alcohol syndrome nor any diagnosis on the foetal alcohol spectrum protected against difficulties with empathy or behaviour, and neither was associated with greater difficulties. Children who received their FASD diagnosis at a younger age tended to have fewer peer problems than those diagnosed later. Children who had been maltreated were more likely than children in the general population to be diagnosed with attachment disorder or post-traumatic stress disorder. Children with PAE were more likely to be diagnosed with ADHD, intellectual disability, anxiety disorder, attachment disorder and Autism spectrum disorder than children in the general population. The potentially mediating factors that were added to regression analyses made no difference to the relationship between ACEs and empathy, and little difference to the relationship between ACEs and behavioural difficulties. Respondents took advantage of free text responses in the survey to clarify or expand on their responses. Empathy and behaviour were described as situation-dependent, and lying was described as sometimes being the result of memory issues – confabulation - rather than deliberate deception.

This study appears to be the first to measure ACEs in a sample of individuals with FASD. Over three quarters (77.6%) of this sample had at least one confirmed ACE compared with 67.3% of the general population; and 42.5% had five or more confirmed ACEs, compared with 10.5% of the general population. A major issue here though is that informant reporting of trauma tends to underestimate compared to self-report (Stoltenborgh, Bakermans-Kranenburg, Alink, & IJzendoorn, 2015), and the respondents in this study reported high levels of uncertainty. It seems likely that these results represent a significant underestimate of the true numbers of ACEs in children with FASD. Only two previous studies have measured the comorbidity of trauma within a sample of children with FASD. Coggins et al (2007) used official records rather than caregiver-report, and still reported high levels of uncertainty, but 58% of their sample of 576 children with FASD had a confirmed history of trauma. Koponen et al (2009) used caregiver and social worker report, and also reported some uncertainty. Of their sample of 38 children with FASD, 58% had been neglected, 36% witnessed violence, 16% were physically abused, and 5% were sexually abused.

The low levels of empathy and high levels of behavioural problems were expected and support previous findings. Previous studies (e.g. Greenbaum et al., 2009) have found that children with FASD have difficulties with social cognition, and one previous study (Stevens et al., 2015) has specifically found that children with FASD achieve lower scores than typically developing children on measures of empathy. The results of the present study support those findings by showing that children with FASD in this sample achieved substantially lower scores for affective, cognitive and

total empathy compared to normative data. Similarly, the results of the SDQ support previous studies (e.g. Kodituwakku & Kodituwakku, 2014; Tsang et al., 2016), which have shown that children with FASD have high levels of internalising and externalising behavioural problems.

The finding that there was no relationship between ACE score and empathy was contrary to the hypothesis but fits with the emerging pattern seen in the systematic review and clinical audit data (Mukherjee et al., 2019), that individuals with both exposures tend to be functionally more similar to those with only PAE than those with only trauma. This finding shows that the impact of PAE on empathy can be independent of trauma, and suggests that, where both are present, PAE may be the better explanation of low empathy. This finding has potential clinical implications. Adults with FASD are more likely than those in the general population to be diagnosed with a personality disorder (Barr et al., 2006). Deficient empathy forms part of the diagnostic criteria for some personality disorders (narcissistic and antisocial; APA, 2013), but a neurodevelopmental cause of deficient empathy could contaminate a diagnosis of personality disorder. Adults whose deficient empathy is the result of a prenatal exposure may have important differences in presentation compared to non-FASD patients and may not benefit from cognitive therapies (Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012, for a review) that are designed to help with personality disorders.

As hypothesised, there was a positive correlation between ACEs and behavioural difficulties, but the relationship was weak. This suggests that environmental exposures can moderate the relationship between PAE and behavioural outcomes to some extent, but differences in behavioural difficulties may be better explained by other factors such as the dose, timing or pattern of alcohol consumption during gestation (e.g. O'Leary et al., 2010). The data in the present study came from a self-selecting sample, whose alcohol-related damage was not assessed, and may have been highly varied.

The relationships between empathy and behaviour in this sample were also consistent with findings from general population studies and provide the first data on the relationships between these variables in children with FASD. Empathy has been shown to correlate negatively with behavioural problems (Miller & Eisenberg, 1988; Mitsopoulou & Giovazolias, 2015) and positively with prosocial behaviour (Dadds et al., 2008; Van Noorden et al., 2015) in non-FASD samples; in other words, lower empathy relates to more behavioural problems and less prosocial behaviour. The present study shows that cognitive and total empathy have strong positive correlations with prosocial behaviour, and that peer problems, hyperactivity and conduct problems were negatively correlated with cognitive and total empathy, all of which are consistent with non-clinical data. The relationship between affective empathy and behavioural problems is more complex in the general

population, with differences between behavioural subscales and some gender differences (Dadds et al., 2008). In this FASD sample, affective empathy was positively correlated with emotional problems. This lends support to the theory that empathic tendencies, in adverse environments, can lead to emotional problems such as empathic distress or guilt, possibly leading to depression and anxiety (Tone & Tully, 2014). The high levels of ACEs in this sample may explain the relationship between affective empathy and emotional problems, although it is possible that PAE is having an effect here. There is now strong evidence of a link between PAE and poor empathy (this chapter; Stevens et al., 2015), and there was no apparent effect of ACEs on empathy within this sample.

The range of other diagnoses in this sample is similar to those seen in previous studies, as demonstrated by a recent systematic review (Wayrauch et al., 2017). The pattern is similar, with attention-deficit hyperactivity disorder by far the most common comorbid diagnosis in children with FASD or suspected FASD. There are some differences here though, perhaps most notably that autism spectrum disorder (ASD) was diagnosed in 7.8% of the participants in this sample, but does not tend to reach these levels in meta-analyses (Popova et al., 2016; Wayrauch et al., 2017). ASD and FASD do share similarities in presentation, such as problems with social and communicative functioning (Stevens et al., 2013), and two UK clinical studies have found 72% (Mukherjee, Layton, Yacoub, & Turk, 2011) and 68% (Mukherjee et al., 2019) comorbidity rates, suggesting that other factors such as diagnostic guidelines or local clinical practice may be having an impact on this relationship.

The finding that children who received their FASD diagnosis at age eight years or younger had fewer behavioural difficulties than those who were older at diagnosis supports previous findings (Alex & Feldmann, 2012; Streissguth et al., 2004) that an earlier diagnosis can have a protective effect. In these previous studies, the cut-off ages were five and twelve respectively. Age eight was found to be the most powerful cut-off age here, but despite these differences, there is now a growing body of evidence that an earlier FASD diagnosis can act as an intervention to reduce adverse outcomes. This may be due to the increased support, behaviour management and other interventions that a diagnosis can allow. It has been suggested that the perceived stigma of FASD may explain a reluctance to diagnose amongst some clinicians (Mukherjee et al., 2015). This study and others demonstrate that, despite any impact of stigmatisation, an early diagnosis on the foetal alcohol spectrum can lead to a reduction in adverse outcomes in patients.

This study was not designed to assess cross-cultural differences, but since almost the full sample of respondents were based in the USA, Canada and the UK, it was possible to explore national or trans-Atlantic differences. Correlation analyses showed no relationship between ACEs and behaviour in the UK, a weak positive relationship in the USA, and a moderate positive

relationship when the USA was grouped together with Canada to form a North American group. There is therefore an unexpected difference in this data between the UK and North America: for children in the UK with PAE, ACEs make no apparent difference to behavioural outcomes; whereas in North America, ACEs have a significantly adverse impact on the behavioural functioning of children with PAE. The reason for this trans-Atlantic difference is not clear, and further studies will be necessary to confirm and suggest mechanisms for this effect. One possibility is that FASD is better-recognised and better-supported in North America than it is in the UK. A 2008 international survey of FASD diagnostic services (Peadon et al., 2008) found that of the 34 FASD clinics in the world at that time, 29 were in North America (24 in the USA and five in Canada). At the time of this study, there was only one clinic operating in the UK (UK National Clinic). If there is a significant difference in support for children with FASD in the UK compared to North America, this could explain the relationships between ACEs and behaviour in this study. With better support for the behavioural difficulties seen in FASD, we might expect to see differences related to ACEs in the North American sample, where those children with fewer or no ACEs make improvements. With fewer services for FASD in the UK, behavioural difficulties may be left unsupported, children across the board may be less likely to make improvements, and ACEs may make little detectable difference to behavioural difficulties.

The regression analyses showed that ACE score together with the factors of placement history, gender, age at diagnosis, and country of residence (which were identified as possible mediators), were not statistically significant predictors of GEM empathy score. For SDQ behavioural difficulties score, the only variable that remained statistically significant in the stepwise model was FASD diagnosis at age nine or older, which explained 9% of the variance in SDQ score. Taken together with the results of the correlation analyses, these results show that the environmental variables addressed in this study appear to make little difference to the psychological outcomes measured, within a sample of children with FASD. However, the children in this sample were different from the general population in terms of those outcomes. This suggests the high levels of behavioural problems and low empathy seen in this sample are more likely to be the result of PAE, than the result of any of the environmental factors that were addressed here. Finally, many respondents completed free text responses to elaborate on their children's characteristics in a way that was not allowed by the questionnaires. Empathy and behavioural problems were described as context-dependent or affected by medication. Empathy could be feigned, and what appeared to be deception may have been confabulation - the production of fabricated or distorted information due to a disturbance of memory. This has been reported previously in children with FASD (Brown, 2017) and may have had an effect on the validity of the questionnaires.

5.4.1 Limitations

The study has several limitations. First, it was based on a self-selecting sample, which may not be representative of the population of children with PAE. Survey participants responded to an online advertisement circulated in forums specific to FASD via social media. Respondents were therefore aware of their child's PAE, and we were unable to recruit from the significant section of that population whose children are undiagnosed, have unknown alcohol-related damage, or whose caregivers choose not to or are unable to participate in online FASD forums. Second, many of the children with PAE were not formally diagnosed. This is not uncommon in FASD, but there is therefore no certainty that they would in fact meet criteria for a diagnosis. Of those who were diagnosed, their clinicians may have used one of five or six different diagnostic criteria currently in use (Coles et al., 2016 for a review). This raises the possibility that, even amongst those with a diagnosis, there is variation in presentation or severity of damage. Third, the SDQ was chosen partly based on its ability to elicit positive responses and allow caregivers the opportunity to reflect on their child's strengths as well as their weaknesses. Unfortunately, this backfired somewhat, since the sample tended to score low on prosocial behaviour, effectively causing this subscale to represent a difficulty rather than a strength as intended. Fourth, the survey relied entirely on caregiver report of prenatal exposures, ACEs, placement history, behavioural difficulties and empathy. Only three (1.2%) respondents were their children's own biological parents, so knowledge of prenatal exposures would usually be at least second-hand. Informant-report measures of childhood trauma tend to underestimate the true extent of that trauma (Stoltenborgh et al., 2015), and this was evidenced here by the high number of 'unsure' responses to the ACE scale. Use of parent-report behavioural and empathy measures may be less limiting since both scales were designed for this purpose and their validity is well-evidenced (Dadds et al., 2008; Goodman, 2001). However, several respondents felt the need to offer clarifications on their answers, typically to explain that their children's characteristics were context-dependent and that the questionnaires did not allow this level of detail. Fifth, although this study did assess prenatal exposures to drugs and tobacco, there were high levels of uncertainty amongst respondents. No analysis of the effects of either of these exposures was therefore undertaken, but since studies have shown long-term effects of both (Cornelius & Day, 2009; Smith et al, 2006) these exposures are potential confounders to the results of this study. Sixth, some potential mediating factors that can affect the relationship between childhood trauma and adverse outcomes were not addressed in this study. Relationships with trustworthy adults in childhood (Werner, 1993) and differences in genetics (Byrd & Manuck, 2014) have been shown to protect against some adverse outcomes in children with ACEs. This study was unable to measure these variables. Finally, this study assessed the impact of ACEs in a sample of children with PAE. This

design prohibits the assessment of children with ACEs but without PAE – in other words, the study is missing a ‘just trauma’ group.

5.4.2 Conclusion

This study provides further evidence that children with PAE have an increased risk of childhood trauma, high levels of behavioural difficulties, poor empathy and high levels of comorbid mental or developmental disorders. It provides the first data on ACEs in children with PAE, and these are also at high levels. The impact of ACEs and other environmental experiences such as placement history on the behavioural difficulties and empathy of children with PAE may be relatively subtle. This suggests that PAE is responsible for at least some of the harmful outcomes observed, independently of environmental factors. For clinical practice, where patients have histories of PAE and ACEs, difficulties with behaviour and social cognition may be better explained by prenatal brain damage than by postnatal psychological trauma. Practitioners, educators and caregivers should be made aware, and training for professionals and parents should reflect this.

Chapter 6: The impact of trauma on intelligence and executive functioning in children with foetal alcohol spectrum disorder

6.1 Introduction

The wider literature review (chapter 2) showed that individuals with a history of prenatal alcohol exposure (PAE) or childhood trauma tend to have deficits in intelligence and executive functioning (EF) compared to typically developing individuals. However, the systematic review (chapter 3) found that there is currently only one published study on the impact of dual exposure on intelligence, and none on EF. Henry et al (2007) compared a group of children with dual exposure to PAE and childhood trauma, to a group of children with the single exposure of trauma. They found that children with dual exposure had significantly lower verbal, non-verbal and overall IQ scores than children with trauma only, although neither group's mean score was beneath the benchmark for intellectual disability (IQ<70). This finding suggests that, from an epidemiological point of view, 'adding' PAE to a model that already contains trauma has a significant detrimental effect on intelligence. The current study takes the alternative perspective; adding trauma to a model that already contains PAE, to assess the impact of trauma on intelligence and EF in children with PAE.

6.1.1 Intelligence

Intelligence is not always defined consistently, but most definitions state that intelligence is a measure of an individual's capacity for problem-solving and applying learned skills or knowledge across different contexts (Braaten & Norman, 2006). There has been some disagreement about whether intelligence is best described as one overarching construct or many separate abilities. However, the various abilities classified within the construct of intelligence tend to correlate with one another, lending support to the notion of an overall intelligence factor, often known as general intelligence, Spearman's *g*, or just *g* (Spearman, 1927). This forms the theory from which modern intelligence testing developed. Intelligence Quotient (IQ) tests are designed to assess an overall, or general intellectual functioning score, and are often formed from many subtests of spatial reasoning, arithmetic, verbal fluency, logical reasoning, and other abilities, whose scores can be combined to give an overall IQ score (e.g. Kaufman, Raiford & Coalson, 2015). Most IQ tests also give scores for verbal intelligence and non-verbal (also known as performance or visual) intelligence (e.g. Glutting, Adams & Sheslow, 2000), based on verbal (e.g. analogies) and non-verbal (e.g. spatial reasoning) tasks. These subscales also provide a measure of Horn and Cattell's (1966) fluid and crystallised subscales of intelligence. Fluid intelligence, measured by non-verbal IQ scales, is more strongly associated with *g*, and is defined as "The use of deliberate and controlled mental operations to solve novel problems that cannot be performed automatically" (McGrew, 2009, p. 5). Crystallised

intelligence is measured by the verbal scales, is less strongly associated with *g*, and includes learned knowledge, language comprehension and vocabulary (Kaya, Stough & Juntune, 2017).

Intelligence is a major field within psychology, and IQ tests are amongst the best-studied, most valid and reliable measures of any of the cognitive domains (Braaten & Norman, 2006). The score that an individual receives from their IQ test is predictive of numerous positive and negative life outcomes concerning education, employment, health and wellbeing. IQ scores have been shown to correlate positively with educational attainment (Kuncel, Hezlett, & Ones, 2004), vocational performance and occupational level (Schmidt & Hunter, 2004), life satisfaction (Stolarski, Jasielska, & Zajenkowski, 2015), social mobility (Tittle & Rotolo, 2000), and even physical attractiveness (Kanazawa, 2011). Lower IQ scores have been shown to predict antisocial behaviour in at-risk groups (Kandel et al., 1988), obesity (Yu, Han, Cao, & Guo, 2010), schizophrenia, depression (Zammit et al., 2004), and death from cancers and cardiovascular diseases (Gottfredson & Deary, 2004). A large caveat to these correlations however, is that the effects appear to diminish in countries with lower GDP, and in collectivist cultures as opposed to individualistic cultures (Sternberg, Grigorenko, & Bundy, 2001; Stolarski, Jasielska, & Zajenkowski, 2015). This is likely due, at least in part, to the use of IQ tests and similar assessments in educational and vocational systems within western countries. If the system we use to evaluate individuals is biased to favour people with high IQ scores, then those people will tend to do well within that system, gain higher qualifications, earn more money, and even receive a higher standard of healthcare in countries where those services are not free at the point of use. Nonetheless, IQ tests are useful for predicting life outcomes, at least in high-income, western countries.

Individuals with FASD tend to have below-average IQ scores, and deficits in intelligence were among the first cognitive issues to be described in the FASD literature (e.g. Jones & Smith, 1975; Streissguth, Barr, Martin, & Herman, 1980). Further studies have supported these early findings in children (Mattson, Riley, Gramling, Delis, & Jones, 1997), adolescents (Howell, Lynch, Platzman, Smith, & Coles, 2005) and adults (Streissguth et al., 1991), indicating that the effect is a lasting deficit rather than a delay. Studies of low to moderate alcohol exposure on intelligence have produced mixed results. Some children prenatally exposed to moderate levels of alcohol appear to have lower IQ scores as a result, whereas others remain unaffected, and at least some of this variation appears to be due to genetic differences (Lewis et al., 2012). Intellectual deficits associated with PAE are often not severe enough to meet criteria for intellectual disability (i.e. IQ < 70), but the average estimated IQ of individuals with heavy PAE and a diagnosis of FAS is around 70. For those on the wider spectrum, without dysmorphic features, the average estimated score is around 80 (Mattson, Crocker, & Nguyen, 2011). Studies that have reported differences between verbal and non-verbal

intelligence in children with FASD have yielded inconsistent results, with some finding higher verbal scores and others finding higher non-verbal scores (Mattson & Riley, 1998). Kodituwakku (2007) suggests these differences could be due to level or timing of alcohol exposure or environmental factors. One aim of the present study will therefore be to assess the impact of childhood trauma on IQ subscales in children with PAE.

Some studies have identified deficits in intelligence in individuals with a history of trauma, but the effect may not be as severe as the effect of PAE. The Romanian orphan studies (Sonuga-Barke et al., 2017) found that severe early neglect beyond six months of age was associated with mean estimated IQ scores of around 80. Other studies have focused on neglect, and there is some evidence that neglect is associated with more cognitive deficits than other forms of trauma (Hildyard & Wolfe, 2002). It can be difficult to delineate the effects of different types of trauma, especially since they often occur together (Dong et al., 2004) but one study of young children (Pears, Kim, & Fisher, 2008) found that neglect and/or physical abuse was predictive of more severe cognitive deficits, including low IQ scores, compared to other forms of trauma. Like the results seen in the FASD literature, differences have been reported between verbal and non-verbal IQ scores in individuals with a history of trauma, but the direction is inconsistent. Tomoda et al (2011) found that adults with a history of childhood psychological abuse had lower non-verbal than verbal IQ scores, and McCurry et al (1998) found a history of sexual abuse was associated with reduced non-verbal IQ scores. Conversely, Leslie et al (2005) found more cases of significant delay in the verbal intelligence scores of children with a history of trauma, compared to non-verbal scores.

6.1.2 Executive function

Executive function describes the range of effortful, conscious cognitive processes that enable humans and some animals to navigate the world by: applying learned knowledge to solve problems; inhibiting some autonomic or habitual responses; and controlling behaviour in order to affect plans for the future (Suchy, 2009). EF is associated with the prefrontal cortex (PFC; Miller & Cohen, 2001), although other brain areas are involved, and parts of the PFC are associated with particular aspects of EF – for example, the dorsolateral PFC is associated with working memory (Suchy, 2009). Although an individual's EF scores will tend to correlate with their scores on measures of intelligence (Brydges, Reid, Fox, & Anderson, 2012; Salthouse, 2005), clinical studies have shown that individuals with significant EF deficits can have IQ scores in the normal range (Friedman et al., 2006). This shows that although the two constructs are closely related, they represent distinct aspects of neurological functioning and require specialised methods of assessment (Friedman et al., 2006). Like intelligence or IQ score, the results of an EF assessment are useful for predicting certain educational or life outcomes, although not to the same extent. As mentioned above, EF scores

correlate with intelligence, but also reasoning skills (Richland & Burchinal, 2013), reading and comprehension (Christopher et al., 2012), mathematics abilities (Mazzocco & Kover, 2007), academic achievement, and social functioning (Miller, & Hinshaw, 2010). Amongst older adults, EF scores are related to walking ability (Ble et al., 2005) gait (Yogev-Seligmann, Hausdorff, & Giladi, 2008), and daily living skills (Cahn-Weiner, Boyle, & Malloy, 2002), and amongst patients with Parkinson's disease, lower EF scores predict onset of dementia (Levy et al., 2002).

EF deficit is considered a core characteristic of FASD, and forms part of the diagnostic assessment criteria under the Canadian system (Chudley et al., 2005), 4-digit code (Astley, 2004), CDC (Centres for Disease Control; Bertrand, Floyd, & Weber, 2005), and the proposed criteria for ND-PAE in the DSM (Kable et al., 2016). As is the case for intelligence, EF scores in children with FASD tend to be worse in those with the dysmorphic features of FAS (Khoury, Milligan, & Girard, 2015), and rather than representing a delay, deficits have been shown to persist into adulthood (Rasmussen & Bisanz, 2009). EF has several components, and these can overlap and differ depending on which measure of EF is used. A widely used scale - the Behaviour Rating Inventory of Executive Function (BRIEF; Gioia, Guy, Isquith, & Kenworthy, 1996) - has eight subscales: inhibitory control; shifting (between tasks); emotional control; initiation (of tasks); working memory; planning and organising; organisation of materials; and monitoring (of one's own performance; Gioia, Isquith, Guy, & Kenworthy, 2000). Miyake et al. (2000) used factor analysis to develop a model of EF that describes the range of functions in terms of three broad components – inhibitory control, working memory, and shifting. The full range of executive functions appear to be affected by PAE (Rasmussen, 2005), and all studies of EF in children with FASD have each assessed at least one of the three components set out by Miyake et al (see Khoury, Milligan, & Girard, 2015 for a review).

In children with a history of trauma, EF impairments are also common. As part of the Romanian orphan studies, Colvert et al (2008) found children adopted following early severe deprivation performed worse on a measure of inhibitory control than adopted children with no history of deprivation. A similar study, the Bucharest Early Intervention Project, found children with early deprivation had deficits in attention and working memory compared to non-institutional controls (Bos, Fox, Zeanah, & Nelson, 2009). DePrince, Weinzierl, and Combs (2009) found that children with a history of abuse and/or witnessing domestic violence had lower scores on an EF battery that included measures of working memory, inhibitory control, processing speed, attention and interference control, compared with non-exposed controls and children who had other types of traumatic experiences such as car crashes. Dissociation – a state of sensory disconnect sometimes used as a coping mechanism by trauma victims – was implicated in the study and suggested as a mechanism for reduced EF abilities in those children who were abused. Beers and De Bellis (2002)

found children with post-traumatic stress disorder following abuse performed more poorly than healthy controls in measures of inhibitory control, attention, and interference control. Studies have also shown a lasting effect of trauma on EF: adolescents with histories of trauma had deficiencies in working memory, inhibitory control and fluency compared with controls (Kirke-Smith, Henry & Messer, 2014); and women with histories of childhood sexual abuse were more susceptible to distraction during a working memory task compared to non-exposed controls and women exposed to other trauma (Cromheeke, Herpoel, & Mueller, 2014).

6.1.3 Aims and hypotheses

To summarise, intelligence and executive function are important and well-studied cognitive domains, which tend to correlate positively with one another, and are predictive of many important educational, vocational, social and health outcomes. Individuals with FASD or a history of trauma have each been found to have deficits in intelligence and EF compared with typically developing populations. These deficits appear in childhood and persist into adulthood. Children with FASD or a history of trauma may have differences between verbal and non-verbal IQ scores, but the direction of these differences has been inconsistent. To date, only one study has been published on the impact of a dual exposure of PAE and trauma on intelligence. Henry et al (2007) found children with both exposures had lower overall, verbal and non-verbal IQ scores than children with trauma only, but they did not compare children with both exposures and children with PAE only. No study has assessed the impact of dual exposure on EF.

The systematic review (chapter 3; Price et al., 2017) and clinical audit data (Mukherjee et al., 2019) suggest that children with a dual exposure of PAE and trauma are functionally similar to children with just PAE. It is therefore expected that children in this study with both exposures will have similar intelligence and EF scores as children with just PAE. The study also features a control group of typically developing children, who are expected to achieve higher scores than both PAE groups.

The alternative hypotheses for this study are as follows:

- Children with both PAE and a history of trauma will have lower EF scores than children with just PAE
- Children with both PAE and a history of trauma will have lower IQ scores than children with just PAE
- Children with PAE, with or without a history of trauma, will have lower EF scores than typically developing children
- Children with PAE, with or without a history of trauma, will have below-average IQ scores

- There will be a difference between verbal and non-verbal IQ scores in children with PAE, with or without trauma

6.2 Methods

6.2.1 Design

The study was a between-subjects quasi-experiment, where participants were assigned to one of three groups based on the presence or absence of prenatal alcohol exposure and trauma. With the exception of the control group, the participants in this study were a sub-sample of the children whose carers completed the online survey described in chapter five. The ACE questionnaire was therefore the tool that was used to assess trauma (since that data had already been collected). In order to separate participants into groups determined by their exposure to trauma, the first five ACE questions, which relate to maltreatment (abuse and/or neglect) were used. Regardless of their ACE score, if participants had any reported history of abuse or neglect, they were assigned to the maltreatment group. The three groups were:

- PAE without history of maltreatment (PAE)
- PAE with a history of maltreatment (PAE-M)
- Non-exposed, typically developing controls (control).

The University was able to purchase a well-validated, standardised, commercially available measure of IQ (see section [6.2.3](#) for details of all measures), but funding was not available for a standardised measure of EF. The EF measures used were well-cited and considered valid but did not contain normative data. The control group was therefore recruited to provide typical EF scores, but not typical IQ scores. In order to determine that the control participants represented typically developing children, IQ, empathy and behavioural difficulties were also assessed for this group.

6.2.2 Participants

Participants with PAE were from the same group that were recruited through Facebook support groups as described in chapter five. Control participants were recruited through advertisements around the University campus. The parents and carers of all participants in this study also completed the survey described in chapter five. Since participants and their parents or carers were required to visit the university, only residents of the UK were included. A £10 contribution to travel expenses was provided for each visit, and it was anticipated that only families from the Greater Manchester area would volunteer. In fact, volunteers came from across the UK, and some families travelled hundreds of miles at their own expense to take part.

Children aged 8-14 years with FASD or suspected FASD were recruited for the study, alongside a control group of typically developing children of the same age range. Since up to half of all UK pregnancies are estimated to be exposed to some alcohol (Popova, Lange, Probst, Gmel & Rehm, 2017), and since minimal PAE is not usually predictive of significant cognitive or behavioural deficits (e.g. Robinson et al., 2010), control participants were recruited if their mothers had consumed no alcohol or a minimal amount of less than two 2 small drinks per week (e.g. Ware et al., 2012). Three out of the 15 control participants' mothers reported that they had consumed some alcohol during their pregnancy, but less than two small drinks per week. About half of the children with FASD also had a history of maltreatment, so it was not necessary to separately recruit two PAE groups. Table 6.1 shows the sample characteristics by group. Between November 2016 and March 2018, 44 children took part in the study. Low intellectual functioning can confound performance in EF tasks (Danielsson, Henry, Messer, & Rönnerberg, 2012); therefore two children with FASD who had an IQ score < 70 were excluded from the analysis, as is typically done (e.g. Schonfeld, Paley, Frankel, & O'Connor, 2006). Data from two further participants did not record properly, leaving data from 40 participants in the final analysis. There were 13 children in the PAE group, 12 in the PAE-M group, and 15 in the control group. There were 18 girls and 22 boys in the full sample, and the mean age was 10.43 years ($SD=1.99$). A one-way between-groups ANOVA showed that the age of participants across the three groups was statistically similar, $F(2, 37) = .16, p = .86$, and a Pearson's Chi-square test found the distribution of boys and girls was similar across the three groups, $\chi^2 = 3.49, p = .18$. All the control participants lived with their biological parents, and all but one of the children in the two PAE groups were adopted. One child in the PAE-M group lived with foster carers, and their social worker's permission was sought prior to recruitment. Across the two PAE groups, 13 children had a diagnosis on the foetal alcohol spectrum, whereas 12 had prenatal exposure to alcohol and suspected but undiagnosed FASD. Parents also answered questions regarding prenatal exposure to drugs and tobacco, but due to high levels of uncertainty and low levels of non-exposure in the PAE groups, the impact of these exposures could not be reliably assessed.

6.2.3 Measures

Intelligence

Often used in studies of intelligence in children is the Wechsler Intelligence Scale for Children (WISC; Watkins, Wilson, Kotz, Carbone, & Babula, 2006). This comprehensive, long-form measure provides a full-scale IQ for children aged 6-17, across verbal comprehension, perceptual reasoning, working memory, and processing speed (Watkins et al, 2006). The WISC is specific to children, and although other tests within the Wechsler range are designed for younger children and

Table 6.1: Sample characteristics

	PAE	PAE-M	Control
<i>n</i>	13	12	15
Sex			
Male	9 (69.2%)	4 (33.3%)	9 (60%)
Female	4 (30.8%)	8 (66.7%)	6 (40%)
Living arrangement			
Lives with birth family	0 (0%)	0 (0%)	15 (100%)
Adopted	13 (100%)	11 (91.7%)	0 (0%)
Fostered	0 (0%)	1 (8.3%)	0 (0%)
FASD diagnosis			
No diagnosis	4 (30.8%)	8 (66.7%)	15 (100%)
FAS	2 (15.4%)	2 (16%)	0 (0%)
pFAS	1 (7.7%)	0 (0%)	0 (0%)
ARND	2 (15.4%)	1 (8.3%)	0 (0%)
FASD with dysmorphic features	3 (23.1%)	1 (8.3%)	0 (0%)
FASD without dysmorphic features	1 (7.7%)	0 (0%)	0 (0%)
Ethnicity			
White British	6 (46.2%)	8 (66.7%)	13 (86.7%)
Mixed race white and Caribbean	3 (23.1%)	3 (25%)	1 (6.7%)
Mixed race white and Asian	2 (15.4%)	1 (8.3%)	0 (0%)
White gypsy or Irish traveller	1 (7.7%)	0 (0%)	0 (0%)
African	0 (0%)	0 (0%)	1 (6.7%)
Prefer not to say	1 (7.7%)	0 (0%)	0 (0%)

adults, some tests such as the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 2011), the Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 2004), and the Wide Range Intelligence Test (WRIT; Glutting, Adams, & Sheslow, 2000) are applicable to broader age ranges. These brief tests contain fewer subscales than the WISC and other full-scale measures, but can be

administered more quickly whilst providing reliable estimates of verbal, non-verbal and general intelligence (Kaufman & Kaufman, 2001). Due to the high quality of brief measures, and to prevent discouraging potential participants with longer visits, it was decided that a brief measure would be used for the present study. Contenders were the K-BIT, WASI and WRIT. Each of these highly similar measures is well-cited, validated and reliable. The K-BIT is based upon three subtests and takes around 20 minutes to complete, whereas the WASI and WRIT are based upon four subtests and take around 30 minutes. When compared with one another, the WASI was found to be slightly more useful than the K-BIT for determining distinct cognitive functions (Hays, Reas, & Shaw, 2002), but little difference was found between WASI and WRIT (Canivez, Konold, Collins, & Wilson, 2009). With little to choose between the two, the WRIT was selected ahead of the WASI based on cost. The WRIT takes approximately 30 minutes to administer, and is formed of four tasks: matrices, diamonds, analogies and vocabulary. It provides measures of verbal and non-verbal intelligence, as well as an overall intelligence (IQ) score.

Executive functioning

Measures of EF in children tend to fall into one of two categories: caregiver-report psychometric inventories such as the Behaviour Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy & Kenworthy, 2000); and cognitive procedures such as the Stroop task (Stroop, 1935) or trial making task which generate a score based on accuracy, mistakes or completion time (Anderson et al, 2002). These two approaches are associated with certain limitations: parent-report measures are subjective and may be susceptible bias due to parent frustration (Gross, Deling, Wozniak & Boys, 2015); whereas cognitive tasks lack ecological validity, and may not provide a measure of children's day-to-day functioning (Gross et al., 2015). Objective and subjective measures of EF have been found to have only a weak relationship with each other (Anderson, Anderson, Northam, Jacobs, & Mikiewicz, 2002) which, without any reliable benchmark, highlights the need for multiple methods to be used in order to produce a rounded picture of EF in children. The UK National FASD clinic uses the BRIEF in its assessment of patients with suspected FASD, and data from those patients will be analysed separately. In order to make a novel contribution to the field, it was therefore decided that cognitive measures of EF would be preferable here.

Computer-based versions of traditional EF procedures allow the researcher to precisely detect time taken by the participant to complete the task, and reliably record number of mistakes. Two computer-based versions of traditional cognitive EF procedures that measure two key components of EF - inhibitory control and working memory - were identified which were suitable for children and available online free of charge. Furthermore, these particular versions are based on graphics and do not feature words on screen as part of the procedure, which excludes language

deficiency as a confounding variable. Both were available on the widely-used E-Prime behavioural task platform which can be run on University of Salford computers.

Both EF tasks were completed at desktop computers and run on the E-Prime platform. For inhibitory control, a version of the traditional Go/No-go task was acquired, which was based on the whack-a-mole fairground game and developed by Sarah Getz and the Sackler Institute for Developmental Psychobiology (see screenshot in [appendix 4](#)). The 'go' stimulus was a cartoon mole in various outfits, and the 'no-go' stimulus was an aubergine. Participants were encouraged to "Whack the mole (by pressing space), to stop him digging up the garden, but not to whack the aubergine" (the game instructions actually used the word 'eggplant', but this was translated by the researcher). If the participant responded to the no-go stimulus, an error feedback of "Whoops" immediately flashed on screen. The task consisted of four runs of 53 trials, with an average of 42 go trials, resulting in an average of 12 no-go trials per run. Stimulus duration was 1500 milliseconds, with an interval of 5000 milliseconds.

For working memory, a version of the traditional Tower of Hanoi task (ToH), developed by Paul de Groot (VU Amsterdam, the Netherlands) was conducted (see screenshots in [appendix 5](#)). The task consists of three pins, containing a number of disks of varying size. The object of the game is to move the pins around, one at a time, to match a target picture on-screen, without placing a larger disk on top of a smaller disk. There was a total of ten trials, which increased in difficulty. To avoid trial and error tactics, participants were instructed to think about their moves before executing. If a participant made a mistake, the trial began again from the beginning.

Caregiver-report measures

Parents and carers provided information on prenatal exposures, placement history, diagnoses, and living arrangements, as well as the parent-report measures of empathy (GEM), behaviour (SDQ), and trauma (ACE) via an online survey (the same survey that was used in the previous study – see [appendix 2](#)). The first five questions of the ACE questionnaire pertain to maltreatment (physical, psychological or sexual abuse, and physical or emotional neglect). Participants with FASD were assigned to the PAE-M group if their caregivers responded with at least one 'yes' response to any of those questions. Control participants were required to have a score of zero for maltreatment but were not required to have an ACE score of zero.

6.2.4 Procedure and ethics

Ethical approval for the study was granted by the University of Salford Health Research Ethical Approval Panel. The lead researcher (the only researcher to have contact with participants and families) provided an enhanced Disclosure and Barring Service (DBS) certificate as a background

and criminal record check. Recruitment of participants with PAE was conducted by advertising on Facebook support groups and at physical FASD support groups in North-West England. Contact was made with the now defunct FASD Trust, whose representative for the North of England was able to help with recruitment locally. Control participants were recruited with posters displayed on the university campus. At first contact, parents or carers were sent a link to the online survey and were provided with a unique code to ensure anonymity. Trauma was assessed using the online survey completed in advance by the caregiver, which prevented the need to discuss that subject in the presence of the child. Following survey completion, parents and children were invited into the university for the lab study. The single session took about one hour for a family with one participating child, although some participants were siblings of each other. Each additional participating child roughly doubled the duration of the visit. A relaxed, informal atmosphere and rapport between researcher, caregiver and participant was cultivated. Families were met, usually outside the building, and escorted in before being shown the testing rooms. Caregivers and participants were informed of their right to anonymity, right to withdraw, and were allowed to take as many breaks as they needed. Caregivers were given full study information online and signed their consent at the university (see [appendix 6](#) for information and consent form). Children were given a simplified information sheet with pictures, and the study was described to them at the university. Children also provided written consent to take part on an age and ability appropriate consent form (see [appendix 7](#) for children's information and consent form). Drinks and snacks were provided before the participant and researcher began the intelligence and EF tasks. The WRIT was completed at a small table in a developmental psychology lab designed for children. Researcher and participant sat opposite each other, and completed the four games of the WRIT, usually with at least one caregiver watching from an adjacent sofa. Caregivers were invited to stay in the testing room with their child at all times, although some took other children into a waiting area. If more than one participant was present, those waiting were asked to stay in the waiting area to avoid exposing them to their siblings' answers. Breaks were allowed throughout, and the two EF tasks took place in a separate room, where a desktop computer was set up to run the two tasks. Caregivers were also invited into this room to watch. All participants completed the Tower of Hanoi task first, and were fitted with a brain-imaging headset, which recorded brain activity during this task. The brain imaging study will be described in chapter 7. Following the Tower of Hanoi task, the brain imaging headset was removed, and participants completed Go/no-go, which was the final task of the session. The order of the tasks was consistent to prevent fatigue from interfering with the brain imaging study. Caregivers were given a £10 contribution toward their travel expenses, made possible by a £300 research grant from the Psychology Postgraduate Affairs Group (PsyPAG), and approximately £150

of university funds. Each child was also given a small gift to acknowledge their efforts. The study was designed specifically for children, many of whom had learning, behavioural or emotional difficulties, or short attention spans. The visit was therefore kept as brief as possible, and every effort was made to ensure our participants and their families were happy and comfortable. None of the participants requested to discontinue the session or expressed any complaints, and many reported that the experience was enjoyable.

6.2.5 Analysis

WRIT tests, and caregivers' responses to the ACE, GEM and SDQ, were scored by the researcher according to the author's instructions. Participants' performance data for Go/no-go and Tower of Hanoi were recorded automatically by the E-Prime software. The dependent variable for inhibitory control was number of errors of commission in Go/no-go – meaning the number of times the participant erroneously responded to the no-go stimulus. This is the standard measure of inhibitory control in Go/no-go tasks (e.g. Boggio et al., 2007; Brocki & Bohlin, 2004; Hoaken, Shaughnessy & Pihl, 2003). The dependent variable for Tower of Hanoi was the total number of errors made, meaning the total number of times the participant made an incorrect move and was forced to restart that trial (e.g. Salthouse, Atkinson & Berish, 2003; Sorel & Pennequin, 2008; Zook, Davalos, DeLosh, & Davis, 2004).

The differences of interest to this study are those associated with the exposures of a) prenatal alcohol, and b) postnatal maltreatment, so group membership serves as a proxy for the presence or absence of those exposures. The primary outcomes of interest were intelligence (measured as IQ score) and the two EF scales – inhibitory control (measured as number of errors in Go/no-go) and working memory (measured as number of errors in Tower of Hanoi). Using number of errors as a dependent variable means that that interpretation of the variable becomes counter-intuitive – higher scores indicate poorer performance.

Four different types of statistical analysis were applied to the data. Paired t-tests were used to measure any differences between verbal and non-verbal intelligence scores within each group. To assess between-group differences in the related outcomes of overall, verbal and non-verbal IQ scores, multivariate analysis of variance (MANOVA) was used. Analysis of variance (ANOVA) was used to assess between-group differences in both EF subscales (inhibitory control and working memory), empathy, and behavioural difficulties. Finally, multiple regression analysis was used to develop models to predict inhibitory control and working memory performance based on age, intelligence, PAE and maltreatment.

6.3 Results

6.3.1 Verbal, non-verbal and overall IQ scores

The WRIT scores for each participant were calculated and are presented in table 6.2 by group. Both the PAE and the PAE-M groups' mean scores on all scales were within the normal range (85-115). The mean scores of the control group were in the high-average range on all scales (115-130).

Table 6.2 Overall, verbal and non-verbal IQ scores by group

	PAE (n=13)		PAE-M (n=12)		Control (n=15)	
	M	SD	M	SD	M	SD
Verbal IQ	98.92	11.64	101.50	11.25	116.33	8.58
Non-verbal IQ	96.62	15.31	97.50	14.81	116.07	16.37
Overall IQ	97.38	13.10	99.50	11.94	118.73	12.58

Within-group differences in IQ sub-scales

In order to assess any differences between verbal and non-verbal IQ scores within each group, a series of dependent t-tests was conducted. Within the PAE group, PAE-M group, and the control group, no differences were found between verbal and non-verbal IQ scores (all p 's >.05).

Between-group differences in IQ scales

In order to test the hypotheses that participants' verbal and non-verbal IQ scores would be affected by exposure (maltreatment and/or PAE), a one-way multivariate analysis of variance (MANOVA) was performed. Box's test of equality of covariance matrices found that between groups covariance matrices were equal (Box's $M = 4.05$, $p = .71$). The one-way MANOVA revealed a significant multivariate main effect for exposure, Wilks' $\lambda = .59$, $F(4, 72) = 5.47$, $p = .001$, $\eta_p^2 = .23$, which demonstrates a significant between-group difference in verbal and non-verbal IQ scores.

Fisher's least significant difference (LSD) post-hoc tests were used to assess mean differences between scores on each of the IQ scales by group. Table 6.3 shows that no significant differences were found between the PAE group and the PAE-M group on either of the IQ scales, but participants in the control group had significantly higher scores on both scales compared with both other groups. These results demonstrate a significant effect of PAE, but no further effect of maltreatment, on IQ nor either of its subscales.

Table 6.3: Fisher's LSD results for IQ scale differences by group

IQ scale	(I) group	(J) group	Mean difference	SE
Verbal	PAE	PAE-M	-2.58	4.19
		Control	-17.41*	3.96
	PAE-M	PAE	2.58	4.19
		Control	-14.83*	4.05
	Control	PAE	17.41*	3.96
		PAE-M	14.83*	4.05
Non-verbal	PAE	PAE-M	-.88	6.23
		Control	-19.45*	5.90
	PAE-M	PAE	.88	6.23
		Control	-18.57*	6.03
	Control	PAE	19.45*	5.90
		PAE-M	18.57*	6.03

* $p < .001$

6.3.2 Executive function, empathy, and behaviour scores

The effects of exposure (maltreatment and/or PAE) on: a) number of errors made in the Go/no-go (inhibitory control) task and b) number of errors made in the Tower of Hanoi (working memory) task were examined using one-way between-subjects ANOVAs. It was expected that participants in the PAE-M group would make the most errors (indicating poorest performance) in Go/no-go and Tower of Hanoi, followed by the PAE group, and finally the controls. However, there was no significant difference between groups in number of errors made on either the Go/no-go task or the Tower of Hanoi task, indicating no significant effect of either exposure on inhibitory control or working memory.

Due to the lack of difference between the three groups in either EF measure, scores from the GEM and SDQ were also analysed using ANOVA. The first hypothesis was that the control group would have the highest GEM scores (indicating high levels of empathy), followed by both PAE groups (chapter five showed no effect of trauma on GEM score). The second hypothesis was that the PAE-M group would have the highest SDQ scores (indicating most severe behavioural difficulties), followed by the PAE group, and finally the controls (chapter five showed a small but significant effect of trauma on SDQ score). There was a significant difference in the GEM scores of the three groups $F(2, 37) = 14.45, p < .001, \eta_p^2 = .44$. Tukey's HSD revealed that non-exposed controls had higher GEM scores than participants in the PAE-only group ($p < .001$) and PAE-M group ($p = .006$). There was no difference in the GEM scores of participants in the PAE and PAE-M groups ($p = .19$). There was also a significant difference in the SDQ scores of the three groups $F(2, 37) = 39.90, p < .001, \eta_p^2 = .68$.

Tukey's HSD revealed that non-exposed controls had lower SDQ scores than participants in the PAE and PAE-M groups (both p 's < .001). There was no difference in the SDQ scores of participants in the PAE and PAE-M groups ($p = .78$). These results indicate a significant effect of PAE, but no further effect of maltreatment on empathy or behavioural difficulties. Table 6.4 shows the ANOVA results for both measures of EF, GEM and SDQ.

Table 6.4 Mean (SD) of EF, GEM and SDQ scores with ANOVA results by group

	PAE (n=13)	PAE-M (n=12)	Control (n=15)	F	df	η_p^2
Go/no-go errors	5.69 (5.82)	7.58 (5.8)	5.40 (4.31)	.62	2, 37	.03
ToH errors	9.15 (4.78)	7.92 (3.97)	6.27 (3.69)	1.71	2, 37	.09
GEM	-22.15 (43.17)	3.75 (45.74)	50.20 (14.86)	14.45*	2, 37	.44
SDQ	23.38 (6.33)	25.00 (7.53)	6.80 (10.33)	39.90*	2, 37	.68

* $p < .001$

6.3.4 Multiple regression

Inhibitory control

A stepwise multiple linear regression analysis was calculated to predict number of errors in the Go/no-go task based on age of participant, PAE, maltreatment and overall IQ score. A significant regression equation was found $F(1,38) = 10.12, p = .003$, with an R^2 value of .21. PAE, maltreatment and IQ were excluded in the stepwise analysis, and age was the only significant predictor of Go/no-go errors. Participants' predicted number of errors in the Go/no-go task is equal to $18.93 - 1.23$ (age), where age is measured in years. Participants' number of errors in the Go/no-go task decreased by 1.23 for each additional year of age.

Working memory

A second stepwise multiple linear regression analysis was calculated to predict number of errors in the Tower of Hanoi task based on age of participant, PAE, maltreatment and overall IQ score. A significant regression equation was found $F(2,37) = 5.52, p = .008$, with an R^2 value of .23. PAE and maltreatment were excluded in the stepwise analysis, but age and IQ were significant predictors of Tower of Hanoi errors. Participants' predicted number of errors in the Tower of Hanoi task is equal to $27.52 - .12$ (IQ) - $.72$ (age), where IQ is measured in points and age is measured in years. Participants' number of errors in the Tower of Hanoi task decreased by .12 for each additional IQ point, and by .72 for each additional year of age.

6.4 Discussion

The study described in this chapter assessed the impact of a dual exposure of prenatal alcohol and trauma on intelligence and executive function, compared to PAE only and neither exposure, in children aged 8-14 years. Each exposure had previously been shown to predict poorer function in both domains, and one previous study (Henry et al., 2007) found dual exposure was associated with further damage compared to trauma alone, although the systematic review and clinical audit showed little difference between children with PAE and trauma and those with only PAE. This study tested the hypothesis that dual exposure would be associated with further damage than just PAE in terms of both EF and IQ. The hypotheses were not supported, and the results of the study were in keeping with the pattern seen in other studies, where children with both exposures are functionally similar to children with only PAE. Children in this study with both exposures had similar intelligence and EF compared to children with PAE only. Furthermore, intelligence in all children with PAE in this study (regardless of trauma) was within the average population range (85-115), and the EF scores of all PAE participants was similar to the scores of the typically developing control group. One issue with the control group in this study is that their mean IQ score was in the high average range (115-130), making this group non-representative, and a poor control group for the EF measures, which were not standardised. Therefore, there are no available normative or control data for the EF measures used in this study. Since the mean IQ score of the control group was above average, it is likely that their EF scores were also above average. If so, this means the EF scores of the PAE participants was also above average, making them an unusual sample and potentially not representative of the FASD population.

Since previous studies have shown differences between verbal and non-verbal IQ scores in individuals with either PAE or trauma, and since the direction of these differences has been inconsistent, the secondary hypothesis of this study was that there would be a difference between the verbal and non-verbal IQ scores of the PAE-only group, and of the PAE+maltreatment group. Neither hypothesis was supported. In each group, there was no difference between verbal and non-verbal IQ scores. Kodituwakku (2007) suggested differences in specific intellectual abilities in children with FASD could be explained by level of alcohol exposure or environmental factors. This study did not find evidence that environmental maltreatment has an impact on either verbal or non-verbal intellectual ability in children with FASD.

The finding that trauma was not associated with increased difficulties in children with PAE was contrary to the experimental hypothesis, but these results are consistent with the emerging pattern of evidence. The systematic review (chapter 3; Price et al., 2017), clinical audit data (Mukherjee et al., 2019), and the study described in chapter 5, showed weak or no correlations and small or no differences in cognitive and behavioural outcomes in children with dual exposure

compared with PAE alone. The studies that took the opposite perspective, (Henry et al, 2007; Hyter, 2012) ‘added’ PAE to the model containing trauma as opposed to ‘adding’ trauma to the model containing PAE – and tended to show stronger effects, suggesting that PAE is responsible for more of the damage seen in individuals with a dual exposure. The finding here that trauma did not make these outcomes any worse fits in with the previous studies and strengthens the suggestion that trauma is the less damaging of the two exposures.

However, the finding that children in this study with PAE had IQ scores in the average population range (85-115), and especially that they had average or high scores for executive functioning, is more surprising. This contradicts the vast majority of previous research and, at worst, questions the reliability of these results. Since the PAE participants of this study did not have deficits in EF compared with controls, this suggests either a) that these participants were not representative of the wider FASD population, or b) that the EF measures used in this study were not sensitive enough to capture the differences between children with and without PAE. However, not all EF studies in children with FASD have yielded significant differences. Burden et al (2009) measured inhibitory control in children diagnosed with FASD versus healthy controls. There was no difference in EF performance between the two groups, but the study also observed brain activity using electroencephalography (EEG). Although children in the FASD group were able to inhibit their responses as well as the controls, their level of brain activity was higher, which suggests those children had to expend more cognitive energy to achieve the same level of performance. Similarly, Diwadkar et al (2013) measured verbal working memory in children a) diagnosed with FAS/pFAS, b) with histories of heavy PAE without physical signs of FAS, and c) healthy controls. Again, there was no difference in verbal working memory between the three groups, but the participants’ brain activity was recorded using functional magnetic resonance imaging (fMRI). The brain imaging results showed that control participants had activity mostly in their left inferior frontal gyrus (an area strongly associated with language), whereas the two PAE groups showed a more widely spread pattern of activity across their frontal and parietal regions, again suggesting a more effortful pattern of activity for this task compared with typically developing controls. In the present study, activity in the prefrontal cortex was recorded using functional near infra-red spectroscopy (fNIRS), and it is possible that the PAE participants exhibited different patterns of brain activity than controls. Chapter 7 will describe the brain imaging study.

Due to the lack of observed difference between the three groups in this study, two measures used in the previous study were carried out for this sub-sample. All participants’ caregivers completed the online survey, which included the Griffith Empathy Measure (GEM) and the Strengths and Difficulties Questionnaire (SDQ). As expected, both measures showed significant differences

between the PAE participants and the control participants, with moderate (GEM) or strong (SDQ) effect sizes. However, there was also no difference in GEM or SDQ score between the PAE and PAE-M groups. This is consistent with the results of chapter 5 and demonstrates that there are some domains where the PAE participants of this study are distinct from the control participants. One way to look at these results would be to say that the social, emotional and behavioural attributes of the PAE participants were significantly different from controls, whereas the cognitive attributes of the PAE participants were similar to control and normative data. Moreover, this pattern is identical when trauma is added to PAE.

The main finding of this study is that, in this sample at least, trauma is not associated with reduced cognitive function in children with PAE. This information is useful to clinicians and those who design interventions for individuals with FASD. Clinicians who diagnose children with FASD can benefit from these results in two ways. First, if we know that the cognitive deficits in children with PAE are more likely to have been caused by their prenatal rather than postnatal exposure, trauma can be ruled out as a contributing factor, making a diagnosis more reliable. Neglect is specifically mentioned in the DSM-V (APA, 2013) proposed criteria for ND-PAE. Clinicians diagnosing the disorder need to be aware that environmental neglect may account for some of the symptoms of ND-PAE. The findings of this study do not rule out neglect as a potential cause of cognitive deficit in children with PAE, not least because this study did not isolate the variable of neglect from maltreatment. This is, however, a first step towards a fuller understanding of the relationship between abuse, neglect, PAE and cognitive deficit in children. Further studies will be required to separate the impact of neglect and abuse within individuals with PAE. The second advantage of these results for clinicians, other healthcare providers, and researchers or practitioners developing interventions, is that they will be in a better position to advise patients and caregivers of what to expect of the developmental trajectory of children with FASD, and design interventions based on this knowledge. Although evidence is only now emerging, caregivers of children with FASD who also have a history of trauma can be informed that the evidence currently suggests that their child will not suffer any further cognitive difficulties compared to non-maltreated children with FASD.

The study had several limitations. The sample was self-selecting, and therefore may not be representative of the wider population of children/families with FASD. For example, those families whose children have a higher level of need may have less time to complete surveys. As stated above, the control group was not representative because their mean IQ was in the high average range. This may be because most of the control participants were recruited through advertising at the university campus, and most were the children of staff and students of the university. A measure of socioeconomic status (SES) was not used in this study. If the control group had been purposively

recruited to represent a wider range of SES, their cognitive abilities may have been closer to the average range (Hanscombe et al., 2012). This is also the case for the PAE groups, which may not have been representative. Caregivers responded to advertisements and were unpaid volunteers (except for a small donation to their expenses). Families with lower SES, other commitments, or whose children had more severe cognitive and behavioural problems may have been less likely to volunteer. In addition, the PAE group were not required to be diagnosed. Since only a small minority of children with FASD are diagnosed in the UK (Morleo et al., 2011), this was a necessary limitation of the study. If possible, future studies should attempt to recruit diagnosed participants from a variety of backgrounds.

The measures of executive function used in this study may not have been sensitive enough to capture the differences between experimental and control groups. Khoury, Milligan and Girard (2015) reviewed EF studies in children with FASD, grouped according to the Miyake et al (2000) tripartite model, where EF is described in terms of three core components: working memory, inhibitory control, and shifting. The review found that in the domains of working memory and inhibitory control, the differences between FASD and control groups had moderate effect sizes, but in shifting, the effect sizes were large. A measure of cognitive shifting, such as the Wisconsin Card Sorting Task (WCST; Heaton, 1993) would have been a useful addition to this study, and further studies should include a measure of all three of the Miyake components. Another issue here is that the two EF measures chosen for this study did not have normative data available, leaving the scores out of context. With a more representative control group this would have been less of an issue, but normative data would have provided a more reliable benchmark.

The study was not able to provide a measure of the dose, pattern or timing of alcohol exposure in pregnancy. This is unrealistic in a small observational study, but where possible it is imperative that these details are taken into account. The wide variation of presentation seen in patients with FASD is in large part due to the level of alcohol exposure (O'Leary et al., 2010). Further to this, the present study was unable to account for exposure to other drugs and tobacco. Caregivers were asked about these other exposures, but there were high levels of uncertainty. A larger study, with groups of children exposed and non-exposed to alcohol, specific other drugs, tobacco and trauma would be necessary to investigate this interaction. Finally, the study did not recruit a group of children with trauma and not PAE. A four-way comparison of children with PAE, trauma, both, and neither exposure would be a very useful next step in this area of research because it would enable the interaction of both exposures to be assessed. Since this is an issue that affects all the studies in this thesis, it is further discussed in Chapter nine.

6.4.1 Conclusion

The study found no evidence of any impact of trauma on intelligence or executive function in children with prenatal alcohol exposure. It was found that verbal, non-verbal and overall IQ scores of children with PAE were not different from normative data, and EF scores in children with PAE were not different from the scores of a small, locally recruited, typically developing control group. There was also no difference between the verbal and non-verbal IQ scores in any group. The PAE participants had low empathy and high levels of behavioural difficulties compared with healthy controls, but trauma did not make these outcomes any worse. These findings may be useful to healthcare professionals, who can advise caregivers of children with both exposures about the expected cognitive development of their children, and researchers or practitioners designing interventions for children with both exposures. Despite some important limitations, this study provides the first evidence of the impact of trauma on IQ and executive functioning in children with FASD.

Chapter 7: The impact of trauma on prefrontal cortical blood oxygenation during a working memory task in children with prenatal alcohol exposure.

7.1 Introduction

The literature overview in chapter two describes the findings of brain imaging studies in individuals with PAE, and others with a history of trauma. Structural neuroimaging studies show global changes such as reduced total volume in both populations, and local differences in a similar pattern across both populations in the prefrontal cortex, corpus callosum and in parts of the limbic system such as the hippocampus. Functional neuroimaging studies have shown differences in brain activity in both populations (when compared to healthy functioning) across the same regions, although particular attention has been paid to the prefrontal cortex (Coles & Li, 2011; Hart & Rubia, 2012). The systematic review in chapter three (also Price et al, 2017) found that no published study had investigated the impact of a dual exposure of PAE and trauma on brain structure or functioning. In the theoretical framework of this thesis (chapter 4), a pathway of damage from both exposures is set out, starting from exposure, through neurology, cognition and behaviour, ultimately resulting in an effect on other people. The studies described in chapters five and six deal with cognition and behaviour, and the study described in chapter eight deals with the impact on other people. This chapter describes a study that used functional neuroimaging to compare brain activity in children with a) PAE, b) PAE and trauma, and c) typically developing children.

The study described in chapter six assessed intelligence and executive functioning in three groups of children with a) prenatal alcohol exposure (PAE), b) PAE and a history of trauma, and c) typically developing children. No difference was found between children with both exposures and children with only PAE on either outcome. This was contrary to the experimental hypothesis but fits with the emerging pattern of this thesis: that a history of trauma makes little difference to, at least some, cognitive and behavioural outcomes in children with PAE. However, there was also no difference found between those with PAE (with or without trauma) and typically developing controls. This was more surprising, especially since executive functioning (EF) is considered a central deficit of FASD (Kable et al., 2016), and since the same sample of children had clear difficulties in social and behavioural functioning, as shown by their scores on the GEM (empathy) and SDQ (behavioural difficulties) inventories.

Some studies have shown that children with PAE can exhibit similar EF task performance to controls, whilst their brain imaging data shows differences in neurological activation during those

tasks (e.g. Burden et al., 2009; Diwadkar et al., 2013). These findings suggest that, although the same goals can be reached by children with PAE, they may take a more effortful route, employing a wider volume of brain area, and expending more cognitive energy to do so. If extended to real-world tasks, this relative depletion of cognitive energy could lead to fatigue or frustration, and this could explain some of the emotional and behavioural disturbances seen in children with FASD. Similarly, studies comparing individuals with a history of traumatic childhood experiences and non-exposed controls have shown differing patterns of brain activation during EF tasks in which task performance was similar (e.g. Carrion, Garrett, Menon, Weems, & Reiss, 2008; Mueller et al., 2010). The overview of literature in chapter two shows that EF abilities tend to be inferior in persons with PAE or a history of trauma compared to non-exposed individuals, but the studies described above (Burden et al., 2009; Diwadkar et al., 2013) demonstrate that, where no difference in performance is identified, it is valuable to assess neurological activity, which may still reveal between-group differences. No published study has investigated the dual impact of prenatal alcohol and postnatal trauma on neurological activity. Given the between-group similarity in EF task performance in chapter 6, and the findings of the studies presented in this paragraph, it is important to investigate the brain activity of the three groups of children who completed the EF tasks in the previous chapter.

Three groups of children took part in the study: a) PAE, b) PAE with trauma, and c) typically developing children. The hypotheses of this study were that there will be between-groups differences in PFC activation during the cognitive task: both between PAE (both groups) and controls, and between the PAE group and the PAE with trauma group.

7.2 Methods

7.2.1 Brain imaging technologies

The Tower of Hanoi (ToH) task, which was completed by all participants in the study described in chapter 6, is a commonly-used measure of executive functioning, and specifically of working memory (Ozonoff & Strayer, 2001), although studies have shown that inhibitory control and fluid intelligence also contribute significantly to ToH performance (Welsh, Satterlee-Cartmell, & Stine, 1999; Zook, Davalos, DeLosh, & Davis, 2004). Nevertheless, the ToH task is strongly associated with activity in the prefrontal cortex (PFC), which is the brain area most strongly associated with executive functioning (Kane & Engle, 2002). In order to investigate task-related activity in the PFC, a brain imaging technology may be chosen from several potential options. The following two paragraphs will discuss some of these options, and how one was chosen above others.

Technologies that have been used in the assessment of task-related brain activity in children have included positron emission tomography (e.g. Müller et al., 1998; Moteki et al., 2014),

electroencephalography (e.g. Groen et al., 2008; Hillman, Buck, Themanson, Pontifex, & Castelli, 2009), functional magnetic resonance imaging (e.g. Carrion et al., 2008; Fryer, Tapert, et al., 2007), and functional near infra-red spectroscopy (e.g. Weber, Lütschg, & Fahnenstich, 2005; Yasumura et al., 2012). Each of these technologies can provide a real-time measure of brain activity, but each has its own limitations. Positron Emission Tomography (PET), which was employed more frequently before the arrival of other technologies, requires the injection of a radionuclide tracer, usually either ^{18}F -labelled fluorodeoxyglucose (^{18}FDG) or more recently ^{15}O -labelled water (H_2^{15}O) into the bloodstream of the participant. This causes positively charged subatomic particles called positrons to be released in a predictable pattern, which can be interpreted to show the distribution of the tracer as a measure of the pattern of brain activity in the participant (Crosson et al., 2010). This must be supervised by a radiochemist, requires the presence of a small particle accelerator, and the number of scans per participant is limited to prevent overexposure to radiation (Crosson et al., 2010). The temporal resolution of PET is also slower than other methods, meaning that brain activity is measured and described in terms of blocks of activity, which last around 40 seconds (Crosson et al., 2010), which may not be useful for assessing task-related brain activity. Electroencephalography (EEG) uses a more direct measure of brain activity – the electrical current generated by neuronal electrical activity (action potentials), which is detected by electrodes placed on the scalp. In order to investigate task-related brain activity, event-related potentials (ERP) can be measured using EEG, which provide a temporal resolution superior to that of PET, with details relevant to within milliseconds. However, its spatial resolution is less accurate, providing data on brain areas relevant on a scale of centimetres rather than millimetres (Crosson et al., 2010). Functional Magnetic Resonance Imaging (fMRI) is a system that uses a powerful magnet to plot the distribution of deoxygenated haemoglobin in the brain, which is indicative of brain activity. The spatial resolution of fMRI is superior to EEG, and its temporal resolution is superior to PET, with the added advantage of not requiring the exposure of the participant to radiation. fMRI data can be clearly visualised within a structural MRI image of the participant's brain, allowing for precise anatomical location (Crosson et al., 2010). However, fMRI requires the participant to lie down and keep still in a small space inside a noisy machine, which can be difficult especially for individuals who have issues with hyperactivity or anxiety. This can lead to stress effects on brain activity as well as movement artefacts in the data (Boas, Elwell, Ferrari, & Taga, 2014).

Recently, a technology has become available which is portable, inexpensive and non-invasive, with temporal resolution in milliseconds and spatial resolution in millimetres. Functional Near Infra-Red Spectroscopy (fNIRS) provides a measure of brain activity by emitting light at the near infra-red spectrum into the brain via a wearable cap or headband. Light at this wavelength travels

through biological tissue including bone, and into the brain (Boas et al., 2014). Here, it is absorbed in predictable and distinct ways by both oxygenated (HBO) and deoxygenated (HBR) haemoglobin, whilst the remainder is scattered. This effect follows the Beer-Lambert law¹, which allows the pattern of cortical blood flow, as a proxy for brain activity, to be calculated (Ferrari & Quaresima, 2012). The ability of fNIRS to provide a measure of HBO and HBR represents an improvement over fMRI, which provides only a single measure of blood oxygenation (Crosson et al., 2010). The advantage of including both measures is that the pattern of oxygen delivery to brain tissue can be presented – HBO delivers its oxygen content to cells that require it, while HBR represents the oxygen-depleted blood returning from its delivery (Fantini, 2014). Moreover, and of particular relevance for the present study, an fNIRS head cap or band is wearable, allowing the participant to sit, stand, or move around to some extent, without causing movement artefacts in the data. Children with FASD, who may have issues with hyperactivity or sensitivity to loud noises, would be able to complete tasks while wearing the fNIRS headset, where they may not be able to complete tasks while lying still inside the small cavity of a noisy fMRI scanner. A limitation of fNIRS is that near infra-red light only penetrates into the outer region of the brain – the cerebral cortex, and not subcortical regions (Crosson et al., 2010). It is therefore not useful for studies of the limbic system or other sub-cortical areas.

fNIRS has been used in studies of executive functioning in children with neurodevelopmental disorders including ADHD (e.g. Pan et al., 2015; Weber et al., 2005) and Autism (Xiao et al., 2012; Yasumura et al., 2012), but to date, only one published study has used fNIRS in an EF study of children with FASD, and this appears to be the only published study using fNIRS in a sample of participants with FASD. Kable and Coles (2017) used fNIRS to measure HBO and HBR in the pre-frontal cortex (PFC) during a task that elicits emotional arousal (with both rewarding and frustrating conditions) in three groups of children with a) heavy PAE and neurodevelopmental impairment, b) neurodevelopmental impairment without PAE, and c) typically developing controls. Task performance was similar across the three groups, but distinct patterns of PFC activation were identified for the three groups, including reduced activation in the medial PFC during the rewarding condition. The relevance of this to the present study is that fNIRS has now been shown to differentiate children with PAE from typically developing children, and from those with other neurodevelopmental impairments. Children with FASD may have distinct patterns of brain activity related to some tasks, which could lead to improvements in diagnosis, and aid the understanding of

¹ The transmission of light through a solution is a logarithmic function of the density or concentration of the absorbing molecules in the solution. The intensity of the transmitted light is also a function of the pathlength of light through the solution and the specific extinction coefficient for the material at a given wavelength (Wahr, Tremper, Samra, & Delpy, 1996, pp 407).

the relationship between the PAE-damaged brain and cognitive or behavioural difficulties in children with FASD (Kable & Coles, 2017). fNIRS also appears have been used in only one published study into the effects of childhood trauma. Nakao et al (2013) found a negative correlation between score on the Childhood Abuse and Trauma Scale (CATS; Sanders & Becker-Lausen, 1995) and activity in the medial PFC in 22 Japanese university students. Taken together, the results of these studies suggest that fNIRS should be able to distinguish the brain activity of children with PAE or trauma from typically developing children.

7.2.2 Design

The study was a between-groups quasi-experiment, with two independent variables. Participants were divided into groups according to the presence or absence of prenatal alcohol exposure and postnatal trauma. Participants were grouped specifically by the presence of maltreatment (abuse and/or neglect) as determined by their caregivers' responses to the ACE questionnaire. The groups are therefore named PAE, PAE-M, and control.

7.2.3 Participants

All of the 40 participants described in chapter six also took part in this study. However, in several cases the fNIRS data did not record properly. Since data analysis was conducted several weeks after data collection, it was not possible to make further attempts to collect missing data. Data are reported here from 23 participants: eight from the control group, eight from the PAE-M group, and seven from the PAE group. A Kruskal-Wallis test showed that the age of participants across the three groups was not statistically different, $H(2)=2.05$, $p = .36$, and a Pearson's Chi-square test found the spread of boys and girls was similar across the three groups, $\chi^2(2)=1.93$, $p=.38$.

All PAE participants lived with adoptive parents, and all control participants lived with their biological parents. Four out of the seven PAE-only participants had a diagnosis on the foetal alcohol spectrum, as well as two of the eight PAE+maltreatment participants. Fisher's exact tests showed no significant relationship between group membership and diagnosis, $p=.19$, nor between group membership and ethnicity, $p=.09$. Sample characteristics are shown in table 7.1.

7.2.4 Materials and procedure

In left-handed or ambidextrous persons, some brain functions usually associated with one brain hemisphere in particular (e.g. language in the left hemisphere) can be more strongly associated with the opposite hemisphere (Guadalupe et al., 2014). In order to reduce the risk of neurophysiological differences confounding results, many neurological studies only include right-handed participants (e.g. Anwar et al., 2016; Zhao et al., 2016). However, since left-handed people

Table 7.1: Descriptive statistics for sex, living arrangement, EHI, diagnosis, and ethnicity by group

	PAE	PAE-M	Control
n	7	8	8
Sex			
Male	5	3	5
Female	2	5	3
Median age (IQR)	11 (4)	11 (3)	8.5 (4)
Living arrangement			
Lives with birth family	0	0	8
Adopted	7	8	0
FASD diagnosis			
No diagnosis	3	6	8
FAS	2	1	0
ARND	1	1	0
FASD without dysmorphic features	1	0	0
Ethnicity			
White British	2	5	7
Mixed race white and Caribbean	3	2	0
Mixed race white and Asian	1	1	0
White gypsy or Irish traveller	1	0	0
African	0	0	1

make up approximately 10% of the population, it has been suggested that their exclusion may be impeding the results of neurological research (Willems, Van der Haegen, Fisher, & Francks, 2014). In order not to exclude left-handed and ambidextrous participants in this limited sample, the Edinburgh Handedness Inventory – Short Form (EHI-SF; Veale, 2014) was used to provide a handedness score for each participant. The EHI-SF lists four activities (writing, throwing, toothbrushing, and eating with a spoon) to which participants indicate which hand they use and how often. This generates a handedness score of between -100 and 100 where negative numbers

indicate left-handedness. A Kruskal-Wallis test showed no difference between groups, $H(2)=.14, p=.93$.

In order to collect fNIRS data, a 16-channel fNIRS headset (BIOPAC Systems Inc., U.S.A.) was attached to each participant's forehead immediately prior to task performance. The headset consists of a flexible pad with four light emitting diodes (LEDs) as light sources and ten photodiodes as detectors facing inward, strategically located at positions on the participant's forehead to collect data from the lateral and medial PFC. Refracted light from each of the four LEDs is detected by its four adjacent detectors, which gives a total of 16 channels of blood oxygenation data. The headset was fastened to the head using Velcro straps, and a scarf was wrapped around to prevent ambient light from interfering with the sensors. fNIRS does not provide an absolute measure of brain activity, rather it compares task activity to baseline, which is recorded prior to the task. Participants were asked to fixate on a cross in the centre of their computer screen while 15 seconds of baseline data was collected by the fNIRS equipment. After this, the participants completed the Tower of Hanoi task described in the previous chapter. This task was always conducted first (before the Go/No-go task) to prevent fatigue from affecting fNIRS data. Since some fNIRS participants have reported the fNIRS headset feeling uncomfortable (e.g. Kaiser et al., 2014), and since the study was designed with the participants' comfort paramount, only the (considerably shorter) Tower of Hanoi game was used during fNIRS data collection. Cognitive Optical Brain Imaging (COBI; Ayaz et al., 2011) was used to encode light data during task performance, and FNIRSoft (Ayaz, Izzetoglu, Shewokis, & Onaral, 2010) was used to process this encoded data into numerical data. Finally, SPSS was used to analyse the numerical data.

7.2.5 Analysis

The 16 channels of light data were divided into three brain areas (as in Kable & Coles, 2017): the leftmost four channels provided data for the left lateral PFC, the centre eight channels provided data for the medial PFC, and the rightmost four channels provided data for the right lateral PFC. Both HBO and HBR data were coded for each of the three brain areas of each participant. The outcome variables of interest were therefore the mean difference between baseline and task HBO and HBR for each of the three brain areas and a global score each for HBO and HBR, by group. Therefore there were eight dependent variables (right lateral HBO, medial HBO, left lateral HBO, global HBO, right lateral HBR, medial HBR, left lateral HBR, and global HBR) from which to determine any patterns of brain activation across the three groups.

7.3 Results

7.3.1 Data screening

Data were screened for parametric assumptions. A series of Shapiro-Wilk tests showed that data for global HBO, medial HBO, and right lateral HBR were not normally distributed, and a Levene's test showed that the data for left lateral HBR did not have homogeneous variances. Therefore all brain activity data were analysed using non-parametric Kruskal-Wallis tests.

7.3.1 fNIRS data

Across all three groups there were task-related increases in HBO compared to baseline in all three brain areas, demonstrating a relative increase in neuronal activity (see figure 7.1). The PAE group also showed an overall increase in HBR, indicating increased activity, whereas the PAE-M and control groups showed an overall decrease in HBR, indicating a reduction in activity (see figure 7.2). These differences were not significant however, since Kruskal-Wallis tests showed no significant difference in activation in any brain area between the three groups (see table 7.2). Change in HBO and HBR are presented in micromolars (mm).

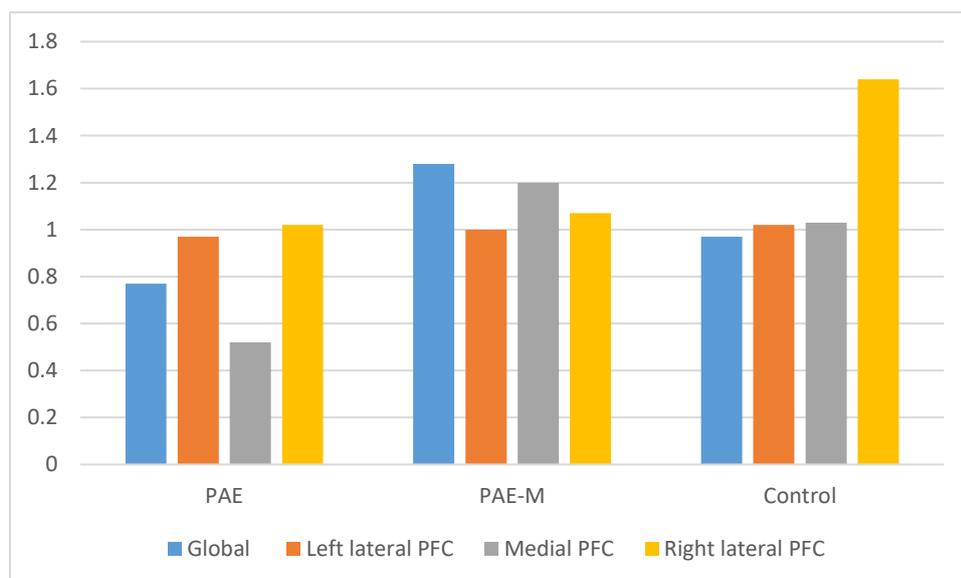


Figure 7.1 Median change in HBO (mm) by group and brain area

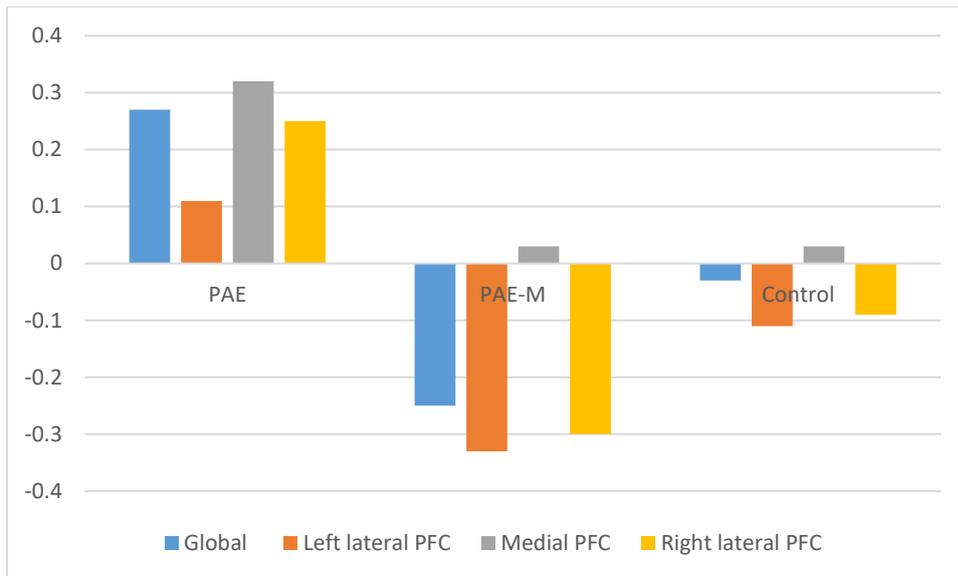


Figure 7.2 Median change in HBR (mm) by group and brain area

7.4 Discussion

The aim of this study was to assess the effect of childhood trauma and PAE on activity in the prefrontal cortex in three groups of children: a) PAE with trauma, b) PAE without trauma, and c) typically developing controls, using functional near infra-red spectroscopy. Only one previous study had used fNIRS in a sample of children with PAE (Kable & Coles, 2017), and only one study had used fNIRS to measure brain activity linked to childhood trauma (Nakao et al., 2013). Both previous studies showed significant differences compared to controls. The present study found that both HBO and HBR activity were similar across all three groups in terms of the full PFC, as well as both lateral and medial sections.

The finding that there was no difference in brain activity between children with PAE with and without trauma fits with the other results of the thesis: that there appears to be little or no difference in neurological, cognitive and behavioural functioning in children with both PAE and traumatic experiences, compared to those with only PAE. However, as was the case in chapter six, no difference was found between the typically developing controls and those with PAE (with or without trauma). These findings contradict previously published brain-imaging studies in FASD. A recent systematic review (Donald et al., 2015) of fMRI studies in children with PAE found that no published study has yet delivered a null difference in brain activity in children with PAE compared to controls. While these studies used fMRI rather than fNIRS, the pattern was nonetheless surprising. Thus there is no difference detected in the comparison where there was a strong expectation that there should be a difference.

Table 7.2: Median and interquartile range of change in HBO and HBR (mm) for each brain area across groups

		PAE	PAE-M	Control	Test statistic
HBO					
	Global	Med=.77, IQR=.92	Med=1.28, IQR=.91	Med=.97, IQR=1.02	H=.87, $p=.65$
	Left lateral	Med=.97, IQR=1.02	Med=1.00, IQR=.85	Med=1.02, IQR=1.76	H=.05, $p=.98$
	Medial	Med=.52, IQR=.67	Med=1.20, IQR=1.32	Med=1.03, IQR=.70	H=1.45, $p=.49$
	Right lateral	Med=1.02, IQR=1.37	Med=1.07, IQR=.99	Med=1.42, IQR=1.18	H=.81, $p=.66$
HBR					
	Global	Med=.27, IQR=1.90	Med=-.25, IQR=.65	Med=-.03, IQR=1.23	H=.96, $p=.62$
	Left lateral	Med=.11, IQR=2.50	Med=-.33, IQR=.62	Med=-.11, IQR=1.49	H=.76, $p=.68$
	Medial	Med=.32, IQR1.27	Med=-.03, IQR=.85	Med=-.03, IQR=1.07	H=.02, $p=.99$
	Right lateral	Med=.25, IQR=2.05	Med=-.30, IQR=.37	Med=-.09, IQR=1.37	H=2.53, $p=.28$

The key hypothesis of interest for this chapter was that there would be a difference in brain activity between PAE and PAE with trauma. Given that there was no difference where we would have expected a difference (between PAE and controls), the reliability of the findings when looking at the hypothesis of interest could be called into doubt.

The three groups of children used in this study were shown to have clear differences in social, emotional and behavioural functioning, as demonstrated by their respective scores on the GEM and SDQ inventories (see chapter 6). The differences associated with trauma were non-significant for both empathy and behavioural difficulties, but the two groups of children with PAE had very low empathy and very high levels of behavioural difficulties, whilst the typically developing children's scores were in the normal range on both measures. This reassures that the two groups (PAE and non-PAE) were representative of their populations. The specific lack of neurological difference identified in this study may be characterised as a reflection of the cognitive performance in the previous study; the three groups of children were able to perform at similar levels in the cognitive tasks, so it is not surprising that their brain activity data are also similar. However, the lack of neurological and cognitive difference overall requires some explanation.

The executive functioning tasks used here were not designed to measure emotional, or 'hot' executive functioning. The one previous study using fNIRS in children with FASD (Kable and Coles, 2017) did use an emotionally salient task, and found a difference between FASD and control groups. Little research has been conducted on the difference between emotional (hot) and cognitive (cold) executive functioning in children with FASD; one may or may not be more impaired than the other,

but hot EF performance has been shown to be independent of cold EF performance in children with FASD (Kodituwakku, Kalberg, & May, 2001; Kully-Martens, Treit, Pei, & Rasmussen, 2013). More research is required, but it is possible that the null results of the present study (in terms of the lack of a PAE effect) may be partly due to the task not addressing the problematic emotional side of executive functioning. In terms of the lack of a trauma effect, this appears more likely to be reliable, given the lack of cognitive differences seen so far in this thesis (chapters 3, 5, and 6), but further studies are a priority. Further studies should seek to improve on the following limitations, which were present in this study.

The cognitive task, Tower of Hanoi, is primarily a measure of working memory. Although planning and inhibitory control are also important factors in determining success (Welsh, Satterlee-Cartmell, & Stine, 1999), more tasks should be used to measure other executive functions, especially cognitive shifting which may be more impaired in persons with FASD (Khoury, Milligan, & Girard, 2015). Tasks should be included that test both cognitive (cold) and emotional (hot) EF. In this study, blood oxygenation data were recorded from the prefrontal cortex only. This is the area most strongly associated with EF, but there is evidence that differences in brain activity during EF tasks can be seen in other areas of the cortex such as the parietal lobes (e.g. Astley et al., 2009). Similarly, sub-cortical regions such as the thalamus may exhibit differences (e.g Meintjes et al., 2010). fNIRS headsets are available that record data from across the cortex, but fNIRS is not capable of measuring activity in deeper areas. fMRI could solve this problem, but since that technique requires participants to lie inside a machine and keep still, hyperactivity and anxiety may prevent data recording from some participants. The participants in this study were self-selecting, and measures of PAE and trauma were self-reported by carers, with no diagnosis required (many participants were not diagnosed). There were no measures of dose, pattern or timing of PAE, nor severity of trauma. Finally, the groups in this study were small, even by neuroscience standards; further studies should aim for numbers that are consistent with those in the literature, with at least 15-20 participants per group (Donald et al., 2015, for a review).

In conclusion, this study found that the presence of childhood trauma in children with prenatal alcohol exposure was not associated with any differences in brain activity in the prefrontal cortex during an executive functioning task compared to a control group of typically developing children. The lack of relationship between trauma and functioning in children with FASD is consistent with the other results of this thesis: for example, in chapter five there was no impact of trauma on empathy and a weak relationship between trauma and behavioural difficulties; in chapter six there was no impact of trauma on intelligence or executive functioning. The finding that prenatal alcohol exposure was not associated with any differences in brain activity compared to typically developing

children raises questions that further studies will need to address. Nonetheless, this study is a milestone as it provides the first known evidence of the impact of PAE and trauma on brain functioning.

Chapter 8: The experiences of adoptive parents of children with FASD with and without a history of trauma

8.1 Introduction

This chapter describes a qualitative investigation into the experiences of adoptive parents of children with FASD, some of whom also had a history of trauma. The thesis framework in chapter 4 (figure 4.1) shows the four levels at which this thesis aims to investigate the impact of traumatic experiences on children with FASD: within the child at the neurological, cognitive, and behavioural levels; and beyond the child in terms of the impact of children's difficulties on other people, especially their parents or carers. Chapters 5, 6 and 7 supported previous research by finding that children with FASD have significant social, emotional and behavioural difficulties, although the presence of traumatic experiences seemed to make little difference to the severity of those problems. In this final study, the focus moves away from the child, and on to how those difficulties impact the people who live in proximity to them. By interviewing families whose children did not experience trauma, as well as those who did, the aim was to describe the experiences of families whose children had both exposures, within the context of children with FASD generally.

Previous studies have shown that people who care for children with FASD have high levels of associated stress (Bobbitt et al., 2016), which can even be at higher levels than carers of children with other developmental disorders such as autism spectrum disorder (Watson, Coons, & Hayes, 2013). Carers of children with FASD have reported that their children's cognitive and behavioural problems are difficult to manage (Green et al., 2014; Paley, O'Connor, Frankel, & Marquardt, 2006), which is consistent with studies of other developmental conditions (Hastings, 2002). Carers of children with FASD also tend to report feeling isolated and lacking support from adoption or fostering agencies and feeling frustrated at a lack of knowledge and understanding among professionals (Brown & Bednar, 2004; Mukherjee, Wray, Commers, Hollins, & Curfs, 2013).

Parents or carers of children with a history of traumatic experiences may also experience stress related to their children's emotional and behavioural difficulties. Studies have focussed on the relationship between adoptive parents and their children, who often present with conduct problems or conduct disorders, which can result from internalising difficulties including low self-esteem, powerlessness, fear, and anxiety (Smith, Howard, & Monroe, 2000). Judge (2003) found that parents who adopted neglected children from Eastern European institutions reported no more stress than parents from a normative sample, but that more severe behavioural difficulties in children predicted higher levels of stress in parents. Adoption can be a difficult experience in and of itself, since it

represents a break, or potentially multiple breaks, in attachment. Adoptive parents must instigate a new attachment relationship with children who may have experienced trauma with previous attachment figures, which can impede the development of the new relationship (Carnes-Holt, 2012). Many interventions are available for families affected by attachment and trauma issues, such as Child Parent Relationship Therapy (Carnes-Holt, 2012) and Attachment Based Family Therapy (Diamond, Russon, & Levy, 2016), which tend to focus on the attachment relationship between the traumatised child and the adoptive parent.

No published research has explicitly described the experiences of parents of children with both FASD and a history of traumatic experiences. The systematic review (chapter 3) and the parent questionnaire (chapter 5) showed that behavioural problems may be somewhat more severe in children with both exposures, compared to children with FASD only. Koponen et al. (2013; reviewed in chapter 3) used content analysis to describe the social and emotional difficulties of children with FASD, some of whom had been fostered at birth, while others had stayed for some time in a chaotic or abusive environment. The children who had stayed longer in their original homes experienced more traumatic experiences and displayed a wider range of social and emotional difficulties than the children who were taken into care at a younger age.

Studies into the impact of children's behavioural difficulties on parents and carers have tended to overlook the effect on other family members, such as siblings. Families of children with developmental disorders can expend large amounts of time and energy to care for their child, while their typically developing siblings may receive less attention and be expected to take on extra responsibilities at home, potentially leading to a disrupted childhood and feelings of resentment (McGinty, Worthington, & Dennison, 2008; Naylor & Prescott, 2004). Such feelings can last well into adulthood, when siblings may be expected to take over the care of their siblings following their parents declining health or death (Davys, Mitchell & Haigh, 2010, 2016). Grandparents, aunts, uncles and other extended family members can also be affected by the difficulties of children with developmental disorders including FASD (Olson, Oti, Gelo, & Beck, 2009). Changes in family structure and dynamics as the result of caring for a child with behavioural difficulties can lead to grief or denial in extended family members, who may withdraw themselves from the situation, although in many cases these family members provide extra support (McGinty et al., 2008).

The studies cited above, as well as the wider literature review in chapter 2, indicate that children with FASD or a history of traumatic experiences tend to have difficulties with behavioural, social and emotional development, and that these issues can cause stress in the people who care for them. However, no study has assessed the impact of exposure to both prenatal alcohol and

postnatal trauma on children's carers. The present study aims to describe the experiences of family members of children with FASD and a history of traumatic experiences. It consists of a series of semi-structured interviews with adoptive parents, and aims to explore issues around children's past and present emotional, social and behavioural difficulties, with a focus on how those issues affect family life, not just for parents but also for siblings and other family members.

8.2 Method

8.2.1 Design

The study was a qualitative investigation of the experiences of 12 adoptive families of children with FASD, about half of whom also have a history of traumatic experiences (8 children with just PAE, 9 with both exposures). Semi-structured interviews were conducted and audio-recorded with 12 families and thematic analysis, as described by Braun and Clarke (2006) was applied. Thematic analysis is a method of organising written or spoken data to identify patterns or themes. It is a versatile approach to analysis of qualitative data, where the ontological and epistemological assumptions of the researcher allow a number of decisions to be made, leading to a number of possible variants of thematic analysis. Braun and Clarke (2006) describe how the researcher can choose to generate themes at the semantic or latent levels. The semantic level is where participants' speech or writing is taken at face value, without trying to look beyond what is explicitly presented. The latent level is where the researcher seeks to read between the lines and interpret underlying meaning from the speech or writing in a dataset. Similarly, the thematic analyst may approach research with either an essentialist or a constructionist paradigm. Under the essentialist approach, the language used by participants is assumed to be an accurate portrayal of their lived experience. This is similar to the positivist approach used in many quantitative studies, where the ontological assumption is that there is an objective reality to be researched, and the epistemological assumption is that the researcher can, at least potentially, accurately measure and describe this reality. Subjectivity is inherent in qualitative research, since the individual researcher is part of the process and the tools used are less accurate than in hypothesis testing, but an essentialist approach at least acknowledges that there is a lived experience that can be accurately described. Under the constructionist approach, emphasis is placed on social context and cultural determinants of meaning and experience. Thematic analysis would seek to use the dataset to describe the constructs around the participants, rather than their individual and internal experiences. Finally, the thematic researcher can choose between a theoretical or inductive approach to analysis. A theoretical approach would identify themes according to a framework, with themes included or excluded according to pre-existing criteria. An inductive approach would allow any themes to emerge from the data according to their merit as themes (Braun and Clarke, 2006).

The aim of the present study is to identify the actual experiences of the participants, to determine their children's characteristics and behaviour, and the effect that these issues have on family members. The study is inductive in nature, meaning that no hypothesis is tested, but instead open questions are asked, and participants provide their answers, which are used to generate theory. Because the study is designed to elicit factual experiences, characteristics and feelings, it is conducted within an essentialist paradigm and themes are identified at the semantic level. Descriptions of experiences are assumed to be real and true, while deeper cultural, opaque or unspoken meanings are not considered. Within this literal approach, the study is exploratory. As the first of its kind, no theoretical framework is used, but themes are allowed to emerge from the dataset according to their own merit.

8.2.2 Participants

The adoptive parents of the children who took part in the studies described in chapters six and seven were routinely asked if they would be willing to take part in an audio-recorded interview about the experience of caring for a child with FASD. Interviews were conducted until saturation of themes was attained, which was after interview number 12. Thematic saturation is however subjective, and it may be possible to continue with interviews and identify new themes indefinitely (Varpio, Ajjawi, Monrouxe, O'brien, & Rees, 2017). In this case, a judgement was made by the researcher to cease recruitment when the experiences that participants were reporting appeared to fit well into themes that had already been identified.

The characteristics of the 12 families and the children they care for are shown in table 8.1. All interviewees were adoptive parents to at least one child with PAE. Some families also had their own biological children, none of whom had FASD. Four families had children with FASD and a history of trauma, seven had children with FASD only, and one family had one child of each category. The mother of the family was always present, and the father was present in seven interviews. One interview was with the mother and her grown up biological daughter. All were residents of North-West England, Yorkshire, or the West Midlands. Of the children with PAE who were discussed, there were 17 in total, eight male and nine female, with an age range of 8-13 ($M=10.24$, $SD=1.77$). All children were assigned pseudonyms to protect their identity.

8.2.3 Materials

The interview schedule (see [appendix 8](#)) was designed to generate descriptions of the experience of raising a child with FASD. The opening questions were kept quite simple in order to ease the interviewee(s) into a conversation and establish rapport, for example "How long has your son/daughter lived with you?" Questions were asked about children's social, emotional and

Table 8.1: Interview participant characteristics

Interview number	Number of children discussed	Interviewees	Child's pseudonym	Child's age at interview	Child's gender	PAE/trauma
1	1	Mother and Sister	Kieran	11	Male	PAE only
2	1	Mother and Father	Robert	8	Male	PAE only
3	1	Mother and Father	Katie	9	Female	PAE only
4	2	Mother	Adam	12	Male	Both
			Alice	8	Female	Both
5	2	Mother and Father	Hannah	12	Female	Both
			Nicky	9	Male	Both
6	1	Mother and Father	Talia	8	Female	PAE only
7	1	Mother	Jordan	13	Male	PAE only
8	3	Mother and Father	Amy	12	Female	Both
			Ailsa	11	Female	Both
			Lexi	9	Female	Both
9	1	Mother	Lydia	11	Female	PAE only
10	2	Mother	Ryan	9	Male	Both
			Kyle	8	Male	PAE only
11	1	Mother and Father	Christopher	11	Male	PAE only
12	1	Mother and Father	Julia	13	Female	Both

PAE: Prenatal alcohol exposure

behavioural functioning, for example “Can you tell me about their behaviour at home?”. Follow-up questions were asked about how these issues had affected the parents, and about how they had affected any other family members. The interviews were semi-structured, and the interview schedule was used as a guide only. Interviewees were encouraged to talk about any issues that they felt were important. The final questions of the survey were designed to elicit descriptions of positive experiences; this was to ensure that the dataset was not biased by a negative interview schedule, and to leave interviewees in a positive mood as much as possible.

8.2.4 Procedure

All interviews took place in participants' own homes. This was for their convenience, but also to promote a relaxed atmosphere, and because of context effects on memory – people tend to recall experiences more accurately in the physical environment in which they occurred (Davies, 1986). Participants were given written information and signed a consent sheet (see [appendix 10](#)) The interviewees were already known to the researcher, having participated with their children in a previous study. The interviews were conducted in living rooms or at kitchen or dining tables, and not in the presence of any children. Interviews were recorded on a digital dictaphone and tended to last just over an hour. The first six recordings were transcribed by the researcher, but time constraints necessitated the use of a professional transcribing service for the final six.

8.2.5 Ethical considerations

The content of the interviews was sensitive and potentially upsetting. The children that were being discussed were vulnerable and may have been removed from the care of their biological parents by order of the state. For these reasons, the emotional state of the interviewees and issues around anonymity and data protection were paramount. Interviewees were provided with full written study information before being asked for their written, informed consent to take part. Any personal details including names and addresses were kept separate from interview transcripts and write-ups including this chapter. Parents are not mentioned by name, only by their interview number and relationship to the child being discussed (e.g. Mother). Other identifiable information such as town names and local business are left out or replaced with generic names (e.g. 'local city'). All children have been assigned pseudonyms. Interview recordings were deleted from the dictaphone, stored electronically on a password-protected University network, and will be deleted after three years. Consent forms were stored in a locked filing cabinet in a locked office at the university.

Participants were informed that some potentially upsetting questions would be asked. They were informed that they were under no pressure to respond, and that they were entitled to take a break or discontinue the interview at any time. Following the interviews, each family was provided with a debrief sheet that contained contact details of charities that offer support with issues around adoption, trauma and FASD. The study was approved by the University of Salford Health Research Ethics panel (HSR1617110 see [appendix 9](#)).

8.2.5 Analysis

The transcribed interviews were analysed using thematic analysis, as described by Braun and Clarke (2006). The process began with a familiarisation of the data. The initial stages of this were

conducting and transcribing the interviews, but also reading and re-reading the transcripts as well as making notes of possible themes. Next, passages of dialogue were condensed into codes – brief summaries that capture the essence of what was said. Codes were generated from the 12 transcripts, which were then grouped together to form themes. The sorting of codes into themes was an iterative process; some initial themes were changed or split, and multiple themes were incorporated into broader themes until the themes formed an accurate summary of the content of the dataset, as determined by the researcher. Themes were categorised into themes and sub-themes in a hierarchical structure with two overarching themes emerging. Once the hierarchy of themes was established, the analysis was undertaken with reference to the original transcripts for quotes.

8.3 Results

The interviewees were highly motivated, and the interview schedule was never used exactly as designed. Instead, parents elaborated on their experiences with little need for guidance or structure from the researcher. The study was designed to elicit descriptions of the interviewees' children, their particular set of behavioural, social or emotional difficulties, and the impact that those difficulties might be having on family life. Parents did provide many rich descriptions on this topic, but every family also described their difficulties with service providers such as educators, medical professionals, adoption agents and social workers. Thematic analysis identified ten broad themes, each with between zero and five sub-themes, and which are described here in terms of two overarching themes: The Child, and The System. Table 8.2 shows the hierarchy of themes. In reality, the child, their family, and the system of service providers are not separate from one another but form a complex structural arrangement where the actions or needs of one will both determine and result from change in the others. However, for the sake of thematic analysis, this hierarchy appeared to offer the most useful structure to arrange the themes that emerged from the 12 interviews.

Domain 1: The Child

All interviewees talked about their children with FASD. The questions that were asked were mostly negative (e.g. describe any behavioural problems your child has), but positive aspects were also sought, and parents described many positive experiences or strengths of their children. Interviewees described how their children were a source of stress or daily difficulties; this was not always due to their children's behavioural difficulties, but also how the child and their condition interact with society. For example, parents found that having a child with FASD prevented them

Table 8.2 Hierarchy of themes from interviews

Overarching themes	Themes	Sub-themes
The Child	Child with FASD as a source of change or stress in the family	The child that nobody wanted Children’s problems were difficult to manage Child prevents normal family or social life Having to parent in a different way Worrying about children’s future
	Children as a risk to themselves or others	Indiscriminate friendliness Children easily led or suggestable Poor social skills as a risk of danger Aggressive child as a risk to others
	School as a source of stress for the child	Holding it together at school, letting it out at home
	Some approaches were effective	Having other adults around to help Structure, hard work and a positive attitude
	Child as a source of pride	Skills and abilities Rewarding moments
The system	A disjointed system	
	Service providers as a liability or source of stress	Lack of FASD knowledge among service providers Inappropriate or insufficient services offered
	Lack of FASD information or training for adopters	Information about FASD downplayed or not provided by service providers Lack of training or preparation provided for FASD
	Having to fight for services	Needing support, but not getting it Struggling to get a diagnosis Struggling to get an EHCP
	Getting access to services was positive	

from leading a typical social life. Interviewees tended to describe the school system as problematic, and that schools and teachers were not set up to deal effectively with their children. This was a

source of stress for the child, which in turn was a cause of stress for parents. Parents worried that their children with FASD were at risk of harm due to their social or behavioural difficulties and were especially worried about the future as their children became more independent. There were also positive aspects however; parents recounted happy memories of their children achieving milestones or showing improvements at home or school, and these experiences were rewarding. Parents also explained that some things had been helpful in dealing with their children, especially the presence of other adults such as grown-up children, or a structured home life with clear boundaries and extra-curricular activities.

Theme 1: Child with FASD as a cause of change or stress for family

Children were generally seen as difficult to manage due to their conditions. All families contributed to this theme, and children with additional histories of trauma were also described as having challenging behaviours or needs due to their prenatal alcohol exposure. Five sub-themes contributed to this theme. Many parents reported that they had initially been foster carers but ended up adopting when no other families agreed to adopt. Children's behavioural difficulties were a source of stress to parents, and in some cases, children's behaviour seen as a barrier to a normal family or social life. Parents were worried about their children's futures and reported having to change the way they parent because normal practices were unsuitable for their children.

Sub-theme 1: The child that nobody wanted

Eight of the interviewees had been foster carers for their children initially, but the placements had lasted longer than expected when prospective adopters turned the children down. Potential adopters were put off by the children's developmental delays or behavioural difficulties, and in some cases the adoption agencies tried dozens of families with no success - a process that could go on for years.

"...his profile had been seen by 150 different applicants...they'd read it and turned him down" (Interview 2- PAE²).

*"...they'd been looking for eighteen months for adopters and nobody would take her. She was the child that nobody wanted really, that nobody could cope with."
(Interview 12 - both).*

Prospective adopters were seen as being unable to cope with these children's disabilities or having unrealistic standards in terms of the children's current and future functioning. One family described

² For each quote, the child or children being discussed are indicated as 'PAE' (child has PAE without trauma) or 'both' (PAE and trauma).

how they were part of the vetting process for adopters, and between themselves and the adoption agents, were dissatisfied with the attitudes of the prospective families.

“...he went up for adoption at age four, and the people that they’d picked out to match with him, because he had problems with food, and didn’t sleep at all, they said they couldn’t cope...” (Interview 1 - PAE).

“...the families that they thought could match to Talia were all wanting to know about her future. They were asking the wrong questions, will she be able to do this, but she’ll never be able to do this.” (Interview 6 PAE).

In some cases, there seemed to be nowhere for the children to go. One adoption agent stated that a sibling pair were at risk of being separated, which the foster family felt was unacceptable. At this point they altered their plans and adopted both of their foster children.

“The fostering agency said, we’re gonna have to split them up because they’re unadoptable... but we stepped in and said, we’ll take both” (Interview 5 - both).

The overall feeling was that these children were different – even from other looked after children. All the interviewees, whether or not their child had also had traumatic experiences, gave this impression in some way. Children with FASD were seen as unusually difficult to manage and this was enough to discourage potential adopters. Those parents who fostered first found themselves in a situation where a vulnerable child whom they knew and loved was in need of a family and seemed unable to find one. At this point adoption was seen as the right thing, perhaps the only thing, to do.

Sub-theme 2: Children’s problems were difficult to manage

Parents talked about many of their children’s difficulties. Their behavioural problems were described as unrelenting, which could be exhausting. One parent talked in depth about how her son was persistently argumentative and belligerent.

“...from the moment he gets up, it’s like he wants a fight...it’s all the time, cos it’s the arguments and the talking at you...he’s constant... Groundhog Day every morning.” (Interview 1 - PAE)

Some children were described as violent or aggressive, which was upsetting. One parent talked about having to pull her daughter away from play areas when she attacked other children. This was stressful and embarrassing for the mother but was also a stressful event for the daughter.

“I’ve had to bring her home from many, many soft plays, because she’d get into a ball pool and start attacking another child, and I’d have to run in and grab her and take her home, and they were very stressful for me, but they were very, very stressful for her.” (Interview 3 - PAE)

Daily living issues like sleeping and eating were seen as particularly problematic. One parent talked about the struggle of mealtimes.

“Mealtimes are always a problem, cos he’s got a really poor, picky appetite... he’ll find any excuse to get out of his chair and, you know, do something else, you have to constantly bring him back to the table” (Interview 2 - PAE)

Most of all, children were described as being difficult at night. Recalling their early years, children had sleep disturbances or would not sleep without the parent present. As they got older, some children slept very little. This was described as a very stressful problem because it would lead to sleep deprivation for the parents.

“Sleeping was always an issue...when he was little I used to have to lie next to his cot and hold his hand.” (Interview 7 - PAE)

“And then try and get her to bed, God that’s something else. It can go on for hours and hours. Sometimes it’s gone on that late, I’ve gone in my room, she comes in puts my light on, then won’t let me go to sleep. (Interview 9 - PAE)

These issues are examples of some of the difficulties that parents had dealing with their children, but there were several others. Some were mentioned often and have been given their own themes, such as the issue of children’s behaviours as risks to themselves or others, which are described later in this section. The experiences described above highlight some of the less dangerous, but nonetheless stressful experiences that were described throughout the interviews. Occasionally these were issues that would sound familiar to any parent, such as having to remind and nag children to brush their teeth or wash or hurry up to get ready for school; but the impression was that these everyday issues were especially difficult for these families.

Sub-theme 3: Child prevents ‘normal’ family or social life

Some interviewees talked about the impact that caring for their child had on their social lives. At first, one family described how the period of probationary placement prior to adoption had an impact on their social lives. They were legally unable to hire a childminder during this time.

“Socialising was difficult...when you adopt them, they're placed with you and you can't apply to legally adopt them for three months... which means that you can't have babysitters. You can't leave them with anybody, so that whole time we just had no social lives whatsoever, we just didn't go out.” (Interview 8 - both)

Parents tended not to mention going out with friends, but some parents regretted not being able to see their own family members. This was difficult for one parent, whose own siblings, nephews and nieces lived in Ireland. Their daughter's behavioural and social difficulties meant trips to stay with relatives were so difficult that they had to stop going.

“...and it really did hurt, the fact that we couldn't have that social mingling with other people... and it wasn't just friends, it was also family, you know, she does have cousins, a cousin of the same age as her in Ireland, but she can't cope with her.” (Interview 3 - PAE)

One mother described how her daughter would play very roughly with the mother's biological grandson. She would treat him like a doll, picking him up, which made the boy and his mother reluctant to visit. The girl could not be dissuaded from this behaviour even with CAMHS (Child and Adolescent Mental Health Services) support, and the mother described how this was leading to a breakdown in her relationship with her grandson.

“She's not hurt any of them, but I see when she starts throwing, they know it's time to go. So, I don't get to have my other grandkids very often.” (Interview 9 - PAE)

However, many parents did describe the advantage of having grown-up children or other adults around to help look after their children, and this theme is described in sub-theme 11. Where parents described the impact of their children on socialising, it was as much the child's own missing relationships with extended family that was regretted, as the parents' relationships.

Sub-theme 4: Having to parent in a different way

Most of the interviewees described having to use different parenting methods to deal with their children. Some had previously raised their own biological children and were able to compare 'normal' parenting with 'FASD' parenting.

“...normal parenting we're probably quite good at, because we've had lots of experience! But with Robert it's like a whole different ball game... but you've got to parent in a different way.” (Interview 2 - PAE)

“Parenting a child with FASD is not your normal parenting, it turns everything on its head.” (Interview 1 - PAE)

One mother discussed her daughter’s poor social skills and how she spent long periods of time training her with role-play. She would be the other child, and ask her daughter to imagine what she could say to her school friends

“We’d do role playing over and over again. I would pretend to be somebody, a friend of hers, and I would go, ‘Hi’, and she would have to look at me and go, ‘Hi, how are you?’. So, that was ... yeah, that was a lot of work we did with her.”
(Interview 8 - both)

Many of the parents made the link between parenting tactics and their children’s understanding of consequences. Across the interviews, children were described as being unable to learn from mistakes, punishments or rewards. If they did something wrong and were reprimanded, they would never seem to learn not to repeat that behaviour. Similarly, positive reinforcement was seen as ineffective, and especially when there was a delay between the behaviour and the consequence.

“They started her on a sticker chart at school, and we said ‘It won’t work. It doesn’t work with them. You have to praise them in the moment, or they’ll forget...she won’t remember in ten minutes time. When she comes home with a headteacher’s sticker, what she got it for, ‘I don’t know, I went up to the front and she gave me it.’” (Interview 6 - PAE)

Many parents described their methods, especially the use of firm boundaries and structure, in a positive way, and this is discussed in sub-theme 12. However, one family regretted having to become strict parents. They viewed themselves as liberal, easy-going parents, but were unable to fulfil this ambition because of the structure and discipline that were required with their children.

“So, we turned from very easy going, mild, on the hippy scale about half way up the hippy scale, very relaxed parents, to becoming fascist dictators overnight, it was horrible. And we became these really... and still are.” (Interview 8 - both)

The impression parents gave in this theme is that their children with FASD do not operate or respond like typically developing children. Parenting typically developing children may involve some kind of rewarding or punishing of behaviour but due to a lack of understanding of consequences and poor learning or planning abilities, these strategies did not seem to be working with these children.

Caregivers have to suppress their instinctive methods and learn a new way of parenting, which is tailored to the needs and limits of their children.

Sub-theme 5: Worrying about the children's future

Interviewees were worried about what kinds of lives their children would lead in the future, especially when they become more independent and do not have parents with them at all times to control their behaviour, and further into the future when they may be living independently or after their parents have died.

"We're forty years older than him so he could still be a young adult struggling with this when we're not around." (Interview 7 - PAE)

"I have absolutely no idea if he'll be able to have a job and keep a flat and sort out his money and pay his bills, and stuff like that." (Interview 11 - PAE)

Many of the parents were concerned that their child's carefree, suggestible or hedonistic nature would lead them to experimenting with drugs and alcohol, and that this would lead to further inhibition of risky behaviours, or addictions.

"We have lots of discussions about drink, and drugs, and what people would say if they offered you anything, because I know that they act differently with drink"
(Interview 1 - PAE)

Yeah, I'm really worried. She will have problems. She is a hedonist, she will do whatever feels good, so if she ever gets hold of any drugs, we're done for."
(Interview 8 - both)

In some cases parents feared their sons might end up in prison, or that their daughters would have an unplanned pregnancy.

"We want him to be with us but as I said to him today, if he carries on the path that he's going at the moment the one place he'll be heading is prison."
(Interview 7 - PAE)

"I could just imagine Lydia like, this sounds horrible, sleeping around, getting pregnant and then, obviously, I'm left to deal with another one because she isn't capable of looking after it." (Interview 9 - PAE)

The children described here were seen as uninhibited, reckless and hedonistic. Parents feared that these characteristics could lead their children into dangerous situations. Their lack of planning and

self-control was seen as something that was currently problematic but could become disastrous if and when these children become independent young adults. Adolescents with FASD were seen as not being ready to explore the world unsupervised. There are too many difficulties for which they will be unprepared, and temptations that they may not be able to resist. At the age of 18 they will be expected to adhere to the rules of adult society and will be punished for noncompliance despite their stunted cognitive or emotional age.

Theme 2: Children as a risk to themselves or others

Children tended to be viewed as a potential risk to themselves or others, or as unable to avoid risky situations. They were seen as susceptible to manipulation due to a trusting or suggestible nature or were at risk of becoming isolated from or targeted by peers due to poor social communication skills. Some children had an aggressive nature, lacked empathy and did not play well with others, especially children their own age, or were rough with younger children or animals.

Sub-theme 6: Indiscriminate friendliness

Some parents described how their child was not wary of strangers as a typically developing child would be. This was not necessarily a dangerous behaviour whilst under supervision but was worrying. Parents were aware of the potential danger and feared that their child could be easily led away by a stranger. One parent attributed this to a possible attachment disorder.

“She’s still very vulnerable, even now I’m still convinced she’d go off with anyone, if someone had a dog, you know, that old thing...” (Interview 3 - PAE)

“Yeah, and we’re pretty sure she has an attachment disorder, because whenever we go anywhere, she will quite happily find somebody and then go and sit with their parents and stay with them.” (Interview 8 - both)

Children were seen as easy prey for abusive or predatory adults due to their social difficulties. One parent attributed these social difficulties to attachment issues caused by their history of trauma. However, other parents whose children had no history of trauma reported very similar patterns of behaviour. It would appear that in this sample, these social difficulties were as apparent in children with and without histories of trauma.

Sub-theme 7: Children easily led or suggestible

Children were also seen as easily led by other children. Typically developing peers were able to take advantage of their compliant, suggestible nature and easily persuade them into dangerous situations.

“They [peers] can be misleading toward him, like, run over there, or go and jump on that, and he’ll do it, ‘cause he’s got no sense of danger or fear, he doesn’t understand any of that” (Interview 5 - both)

Peers sometimes took advantage of these children by asking for things such as money, which the children were happy to provide.

“She is vulnerable. One time she asked for money, because someone asked her to bring some money in for them at school, and she was going to do it, just because they asked.” (Interview 6 - PAE)

Parents suspected that their child would be persuaded to commit criminal acts by others in a peer group, to commit the act themselves so that their peers could avoid the blame.

“I just think she’ll get taken advantage of a lot as well. If somebody wanted something done, they’re like oh let’s set fire to that man’s bin Lydia, she’d probably do it, to stay in that crowd.” (interview 9 - PAE)

Parents described these childhood issues, some of which were potentially dangerous, but parents were also mindful of these issues in the future, when their child would be more independent. Parents worried that their children would be used by other, more manipulative adolescents or young adults, to commit crimes on their behalf and end up getting hurt or being arrested.

Sub-theme 8: Poor social skills as a risk of danger

Some parents described how their children’s poor social communication skills or poor empathy could get them into disagreements, arguments or fights with their peers. Violence could be instigated by the child or their peers but was usually put down to either a failure of communication or understanding, or as a backlash for irritating behaviour.

“Nobody understood what she wanted. Her peers didn’t understand anything, and so she would get very frustrated and spit at them, bite, kick...” (Interview 8 - both)

“He takes things too far, he doesn’t know when to kind of switch off. So, if someone says, ‘stop doing that Christopher, no I’ve had enough now, stop’, and then it’ll get to the point where someone will just thump him.” (interview 11 - PAE)

These incidents or potential future incidents were seen in light of their children's difficulties. Blame was neither directed at the child nor their peers, but the reason for these issues was put down to the difference between the child with FASD and their peers. Typically developing children might expect their friends to be capable of empathy to a similar extent as themselves and become annoyed when that child shows apparent disregard for social rules.

Sub-theme 9: Aggressive child as a risk to others

Many interviewees discussed aggressive tendencies in their children. This could be verbal, but was more commonly physical aggression, which could be directed toward friends, peers, other children or adults. Often this aggression was described as impulsive or spontaneous rather than premeditated. Aggression against other children was described as a hindrance to a normal life.

"She was very aggressive with other children, you know, a child would walk past, and she'd just run up and scratch them... and we found it very hard to take her anywhere, because she would attack other children." (Interview 3 - PAE)

Most of the descriptions of aggression were incidents that had happened at home. Younger children exhibited spontaneous aggression toward their siblings, but parents also worried that siblings would be upset or traumatised by witnessing aggression directed toward their parents.

"Lexi perforated Alexa's eardrum because she just whacked her with a towel, for absolutely no reason. I mean, there was ... she just felt like it." (Interview 8 - both)

"I think she [younger sister] has suffered from secondary trauma to a certain extent. I mean she's bound to. It's not natural listening to your brother swearing at your parents all the time. That's not a normal situation to be in." (Interview 7 - PAE)

Parents also described violence toward themselves. This was sometimes from younger children who did not pose a physical threat, but also from older, stronger children who could cause some serious damage. In one case, this was accompanied by verbal abuse.

"I've had bruises, lots of bruises. Like I say, she's kicked me that hard, just in the right places, it's like I've just gone down and then I've sat there, and I've cried and nothing, 'What you crying for baby?'" (Interview 9 - PAE)

Aggression was seen as a symptom of the difficulties that some of these children have, and parents were somewhat resigned to it. As children, especially males, became older and bigger, there was an increasing worry of how to handle the situation if they could no longer physically restrain their child.

Like many of the issues described by parents in this wider theme, this is one where the behaviour of younger children is difficult and upsetting, but of older children is potentially very dangerous and could have criminal justice implications.

Theme 3: School as a source of stress for the child

Going to school was difficult for many of these children. In particular, parents described the school environment as overstimulating – their children did not cope well with the noise levels, high number of other children, social and academic demands, and pressure from teachers to behave in a certain way.

*“And mainstream school was, and I can clearly see now, was just way too overwhelming, on every level, on a sensory level ... the work is just too fast paced”
(Interview 4 - both)*

“...he had problems going into school and coming out of school, cos, he hated all the people outside the door, and the noise and the rush.” (Interview 2 - PAE)

This mix of stressors often led to meltdowns in school, where teachers who were unfamiliar with FASD did their best to restrain or isolate the child, which resulted in further distress. Parents noted a lack of understanding from teachers of their children’s particular needs and abilities.

“He did have mega, mega meltdowns, and it’s easy to forget, but I would just hear over the phone the teacher shouting at him and he’d be screaming, and he’d be under the head teacher’s desk. They’d have to physically lift him right up to about year five, physically lift him out of a class and put him somewhere. It was horrendous, but it was lack of understanding.” (Interview 11 - PAE)

In one case, a child threatened to self-harm or attempt suicide due to school stressors. His parent described how this was partly down to exams, but also due to his school trousers that were causing sensory problems. He felt unable to explain this to teachers and suffered in silence at school until he couldn’t take any more.

“...and when it came to his SATs his anxiety got even worse, and he threatened to throw himself out the window or down the stairs, so eventually we wrote a letter to the head mistress, explaining why he can’t wear his trousers, cos they hurt so much, but he’d never told them before.” (Interview 1 - PAE)

School was stressful for many of these children and for many reasons, but the impression given by the parents was that this was largely down to overstimulation. In some children, this was manifested

by meltdowns or other behavioural problems in school. More often however, parents described how their child would let their feelings 'build up' in school and 'burst out' upon returning to the safer environment of home.

Sub-theme 10: Holding it together at school, letting it out at home

Parents described their children almost as Jekyll and Hyde characters; well-behaved at school and very difficult at home. Often children would be ready for a meltdown as soon as they stepped through the door and this was a regular occurrence for many families.

"...but when she comes home from school, all hell breaks loose. We call it the witching hour, when you've held it in all day at school and then you come here and it's like, boof!" (Interview 9 - PAE)

"He wasn't having meltdowns in school, he was having them as soon as he got home, and he's not good at expressing his feelings or what's going on." (Interview 4 - both)

This caused further stress because teachers often did not see the difficult side of these children, so when other service providers such as doctors contacted teachers for a description of that child to aid with an assessment or diagnosis, the teachers' reports would often contradict parent reports, and this could prevent an accurate assessment.

"They don't see anything wrong with him at school, cos he won't show them what he's like." (Interview 1 - PAE)

"The school haven't really... because they haven't seen it, 'cause he holds it in at school, they haven't really taken on board, maybe, that it takes us about an hour in the morning to get him from the kitchen table out the back door..." (Interview 2 - PAE)

One parent described how his daughter needed to do this and he was happy to let it happen.

"They just want to flop, which is fine, and you do let them. 'I spent all day doing as I'm told and now I'm tired'. And she knows she has this safe, secure place here, so she can kick off with us, you know, things happen, if she does have a row with someone at school, it's later on that it'll come out, with us, which is what it should be" (Interview 3 - PAE)

Home was described as a safe place, not just by this parent, where these children could safely vent or express their emotions, sometimes violently. School was described as a major source of frustration, sensory overload or other stress. The difference between school and home environments caused a major change in the emotional state and behaviour these children, and this was a daily event. Some parents described moving children into a better-equipped school as helpful – this will be discussed later under the sub-theme ‘Getting access to services was positive’.

Theme 4: Some approaches were effective

Although the focus of the interviews was primarily negative by design, all families reported some positive aspects of caring for their children when prompted. These included parents’ positive reflections on the character of their children, as well as some effective approaches to parenting or strategies for dealing with difficult behaviour. Some parents were grateful that they had their own adult children or other relatives or friends nearby to help look after their children, especially for short periods of respite. Some parents also described strategies that they felt had been helpful in raising children with learning or behavioural difficulties, and these were associated with hard work, a positive attitude and structure at home.

Sub-theme 11: Having other adults around to help

Families talked about having, or not having, other adults around to act as babysitters. Where older children were still at home they often helped to care for their younger siblings and some had taken on a somewhat caring role even as children themselves. As well as helping their parents or taking their younger siblings for a short time, some typically developing siblings played a major role in their care and development.

“They’ve [older siblings] helped out over the years, the older two...they helped Nicky learn to walk. They were just constantly showing him what to do, you know, like, they’d help out with anything with them, homework, anything, they’ve had patience with them, although they know their behaviour can be really bad.”

(Interview 5 - both)

One single parent relied heavily on her older biological daughters.

“They [older biological children] all helped, they all did their part, so it took that many more adults to look after him when he was little...just one person on their own, I don’t think they would have managed.” (Interview 1 - PAE)

The children discussed in these interviews were described as having a level of needs that were difficult for one or two parents to meet, and other carers were necessary. Caring for these children

was seen as a full-time, high-energy job and some kind of assistance was considered crucial, even if this was short occasional breaks.

Sub-theme 12: Structure, hard work, and a positive attitude

Some of the families felt strongly that a life of routine and structure, with clear boundaries was highly beneficial for these children. Similarly, one-to-one attention from an adult, either in school or at home, was enjoyable for the child and conducive to progress.

“He is very impulsive, but his new teacher supervises him closely. There are boundaries and he’s thriving at the moment in her class but, as soon as he goes to playtime where there’s a lack of supervision, he gets into trouble.” (Interview 10 - both)

“We know with Katie, if we sit down and do some colouring in or anything, she loves that one-to-one with an adult, and with her teachers, or TAs, when she has that one-to-one she loves it.” (Interview 3 - PAE)

Some families talked about extra-curricular activities out of school such as clubs or music lessons. Some of these children seemed to thrive with this level of structure, and hard work on the part of the parent led to hard work and success on the part of the child.

“We had a rule that she can do any club she wants, and we’ll pay for it happily, but she has to do it for a whole year...and because it was piano, she had to practice every day. I sat with her every time she practiced... so we worked really intensively. And she realised, ‘Oh, I’m good at this’, and it really was the first thing, ever, that she was good at.” (Interview 8 - both)

When describing the hard work they had put in, some parents had a sense of pride and achievement at their children’s development, especially when their child had surpassed the predictions of professionals. In at least one case, a poor prognosis in part led to a positive and determined attitude in the parents, whose child exceeded expectations by some distance.

“I think she will achieve things that probably no-one will ever have dreamt ...the social workers who knew her, when they saw her again, they didn’t think it was the same child.” (Interview 12 - both)

“The doctors said to us he’d never walk, now he’s riding a bike! We were in the car coming back from the hospital, and we were just like “No, I’m not having that, we’re gonna try and show him the right way to go” (Interview 5 - both)

As has been the case in other themes, these children were seen as requiring a different style of parenting. These children needed high levels of structure; they needed a reliable routine at home to help them to achieve their daily living tasks, but this highly structured approach could also allow them to achieve success in different areas. This included behaviour in public places, academic achievement at school, extracurricular activities such as playing musical instruments, or surpassing the developmental predictions of doctors, especially in terms of motor skills. In some cases, these skills were beyond the expectations even of typically developing children.

Theme 5: Child as a source of pride

Following from the previous theme, parents also described several of their children's characteristics or achievements that were rewarding or a source of pride. Parents described some special skills or abilities that their children had, or progress that they had made. Some rewarding moments were simple things, which parents were able to reflect upon during the interviews.

Sub-theme 13: Skills and abilities

Some children had a high level of knowledge about specific or obscure subjects. Something had peaked their interest and they had been able to pay a great deal of attention to these topics, learning and storing a surprising amount of information.

"If it's something that he's interested in, like he did the Titanic. How many people were on board, how it went down, who survived, he'll tell you the whole lot if he's really interested" (Interview 1 - PAE)

"Yeah Hoovers. She can take one to pieces, she knows what's the best wattage, which is the best Hoover, what's the lightest... but doesn't like cleaning her room!" (Interview 5 - both)

Some of the children had developed impressive abilities, especially playing musical instruments.

"She's quite brilliant at music. From never having heard classical music, she started keyboard at seven years old, French horn at eight, and she's now thirteen and she's doing her Grade seven for both instruments." (Interview 8 - both)

Despite their social difficulties, some parents described how their children showed empathy toward animals or were caring and nurturing of younger children.

"If there's any little kids around, he tries to make them laugh, and if they're crying he wants to get involved and stop them being upset. He's great with kids." (Interview 1 - PAE)

“...and little things like, seeing that the cat’s got nothing, and picking him up and giving him, whatever, you know, occasional empathy.” (Interview 6 - PAE)

These children had many positive characteristics and impressive talents which parents were keen to discuss. In particular, the impression was that these were children whose cognitive and behavioural abilities were generally poor, but in some areas their abilities were far above average. Despite difficulties with focus and paying attention, they were able to devote significant resources to one or two specific areas and reach a high standard.

Sub-theme 14: Rewarding moments

Parents described many rewarding moments with their children. Often these were little things like seeing the child enjoying a sense of achievement at school sports day. One mother who had also described a very difficult time with her daughter talked about going out together at weekends, and how she enjoys her daughter’s company despite the difficulties they have had.

“She loves walking the canals... we’ll sit on a bench and have a picnic and she’s interested in how the water goes down and stuff like that. She likes museums... I always find something to do at the weekend, whereas, if I didn’t have her, I think I’d be stuck in.” (interview 9 - PAE)

Other parents were also keen to point out that, despite the negative experiences they had described, they were happy to be caring for their children.

“He’s quirky, he’s funny, when he’s not on a meltdown, which isn’t all the time, he’s a lovely person to be around... he’s a great kid.” (Interview 2 - PAE)

“But, on a positive note, we wouldn’t do without the girls. I mean, they are amazing, they really are quite amazing, and lovely and we wouldn’t do without them. We don’t regret for a second that we’ve adopted them.” (Interview 8 - both)

Parents also described how rewarding it was to witness a transformation in their children. This was in terms of their development of cognitive or academic skills, confidence, or other abilities. However, in the case of one child with profound learning difficulties, it was her whole personality that transformed during her middle to late childhood in their care – she came to them as a ‘nobody’ but became a colourful individual.

“There's a book called Mr Nobody, and it describes somebody who's not really there, he's a sort of non-person, and he goes to live with Mr Happy, and Mr Happy looks after him, and he gradually starts to get some colours and become a person, and it felt like that.” (Interview 12 - both)

Overall, parents reported several problems and difficulties with their children, and with their relationship with their children. But in a series of interviews that was designed to explore mostly negatives, there were about as many positive descriptions of children as there were negative ones. These children were seen as fundamentally different from typically developing children, with a range of difficulties that required a different approach altogether from their previous typically developing biological children, or even from other adopted or foster children. Parents described high levels of stress and talked about the importance of having short breaks if possible, even for a few minutes, or having someone else around to share the workload. These children seemed to have a general level of cognitive, social or motor ability that was diminished compared to their peers, but with a small number of highly developed special skills or talents. Caring for these children was rewarding, especially in terms of seeing a development of character or abilities, and their level of development was often beyond what had been predicted at a younger age.

Domain 2: The System

All families talked in some way about their relationship with service providers such as schools, social services, adoption agencies, local authorities and medical professionals. These service providers were mostly discussed in a negative way but there were some services or individuals that were praised. Some parents were highly critical of particular service providers or individuals, or the relationship (or lack of a relationship) between different service providers. Mostly, the problems and negative experiences were due to a lack of understanding of the needs of children with FASD on the part of the service providers, or the withholding of information about FASD from adopting or fostering families.

Theme 6: A disjointed system

When describing the system of educational, social, and medical service provision, many parents remarked on a lack of cohesion or poor communication between different services or departments. One experience that some families described was being passed from one service to another, sometimes all the way back to the first provider with no action having been taken.

“...and the paediatrician also referred us to CAMHS [Child and Adolescent Mental Health Services], so we went to CAMHS, and all they did was hand me a leaflet for post-adoption support, which we'd already been to.” (Interview 3 - PAE)

“We've gone everywhere, that's the point, everybody tries to pass the buck on. I mean, they literally sent us around ... we eventually got assigned our own social worker, and she sent us back to the GP” (Interview 8 - both)

Parents discussed how there was a disconnect between different service providers. After having explained their child's needs to one provider, the next provider often had no knowledge of this, which could be irritating and time-consuming, but could also mean services that were needed were not provided.

“Well I thought that primary school had told high school [about child's needs], but it wasn't really passed on, so I arranged to see the SENCO in the summer and they hadn't a clue.” (Interview 11 - PAE)

Parents described an unhelpful attitude from some service providers, who were reluctant or unable to offer help because that service was the responsibility of another service provider. This led to delays or lack of services. On at least one occasion there was disagreement between service providers on whose responsibility it was to deal with a situation.

“They were both out here in one meeting, a representative from the local authority and a representative from CAMHS, and I was [describing child's report of sexual abuse in birth family] and they sat here and argued with each other as to who was responsible for it, and neither of them did anything.” (Interview 4 - both)

Parents wanted, expected or needed a cohesive system that was designed to help with their child's needs. Instead, they reported falling through gaps in service provision, or having to take part in several appointments with different providers over extended periods of time in order to get access to services, or in many cases still not receive services. This was especially the case with health service provision, or with organisations that deal with adoption or fostering such as local authorities, social services and adoption agencies.

Theme 7: Service providers as a liability or a source of stress

There was a general impression that healthcare or social service providers were ineffective at dealing with these children's problems. A lack of training or understanding of the needs of children with FASD seemed to be a major reason for this. Some services seemed to be set up to deal with trauma and attachment issues in adopted children, and when faced with a neurodevelopmental disorder of which they had little training, tended to recommend interventions that may have been inappropriate.

Sub-theme 15: Lack of FASD knowledge among service providers

Many families described how service providers were unknowledgeable about FASD. Teachers, social workers, and even medical professionals were unfamiliar, did not have appropriate training, and were not able to provide suitable services for the needs of children with FASD.

“CAMHS don’t know nothing about foetal alcohol syndrome. So, they basically can only basically treat Lydia for the ADHD and they haven’t got no ideas how to help me.” (Interview 9 - PAE)

Some parents described feeling blamed by professionals for their children’s difficulties. Medical professionals and social workers saw a child making little progress or behaving worse at home than in school and appeared to attribute these issues to parenting practices rather than neurodevelopmental issues.

“...and I think that social services, who kept on pointing the finger at me and telling me that I had to go on parenting courses, and they’re like “Well, he can hold it together at school, so why can’t he hold it together in your house?” I found that was really hard.” (Interview 1 - PAE)

Sub-theme 16: Inappropriate or insufficient services offered

When services were offered, they were typically designed for other conditions such as ADHD, or for the effects of trauma or attachment problems. Trauma or attachment interventions were offered to children without a history of trauma as well as those with a history of trauma. Parents of children with PAE without a history of trauma were frustrated and bewildered that these kinds of therapies were being offered to a child with a brain-based condition. They were seen as ineffective and in many cases counter-productive.

“They wanted to take him away for a weekend, in school time, so he’d be in school for a week, then there for the weekend, so he’s holding it together all week, then all weekend, and as soon as he gets back he’s gonna throw an almighty tantrum and not go to school the next week.” (interview 1 - PAE)

“But she [psychiatrist] basically sent him away with a worry box. ‘Write down your worries Jordan and put it in a box. Excuse my French he said, ‘I’m not doing that fucking shit’ and threw it away. So, no the worry box didn’t help.” (Interview 7 - PAE)

Service providers were seen as inadequately trained to deal with families affected by FASD. In some cases, their training seemed to lead them to suspect trauma or attachment problems, even in children who were adopted at birth with no history of trauma. They offered therapies accordingly, which were often ineffective. This 'misdiagnosis' also led to some parents feeling blamed for their child's lack of improvement, which only served to compound their stress.

Theme 8: Lack of FASD information or training for adopters

Following from the previous theme, which referred to a lack of training or awareness of FASD among professionals, parents also described a lack of information or training when they first adopted their children. This left them unprepared, and in many cases, let down by the adoption agencies and other professionals.

Sub-theme 17: Information about FASD downplayed or not provided by service providers

When first adopting or fostering their children, most parents discussed a lack of information about prenatal alcohol exposure or FASD. Prenatal drug exposure and attachment problems were explained, and training was provided, but the issue of alcohol seems to have been largely overlooked. Parents were aware that children with prenatal drug exposure or postnatal exposure to trauma tend to make better progress during childhood than children prenatally exposed to alcohol.

"No, they didn't mention alcohol, all they mentioned is drugs, so he was withdrawing from drugs... and that's basically all they said, and ...oh he'll be ok"
(Interview 1 - PAE)

"You get given a, sort of, profile, a few pages of, a profile of the child, and the background and everything, not one mention of alcohol! The focus from the social worker was drugs, and Hepatitis C... and we said, fine, that didn't matter to us."
(Interview 3 - PAE)

Some parents suspected the information was deliberately downplayed or hidden in order to secure a placement.

"...and everybody at the support groups are reporting the same things, about lack of information, not only lack of information but the deliberate hiding of information..." (Interview 4 - both)

"We said we categorically don't want [to adopt] an alcohol damaged child but we'll handle a drug damaged child because the brain is plastic and can rewire"

with our help. So, it was kind of played down, the alcohol thing... But now his notes seem to say foetal alcohol and drug damage, so we think we were duped. I think she's just glossed over things because she wanted to get a nice tick."

(Interview 11 - PAE)

Parents felt let down and lied to by the adoption system. The feeling here was not so much that the adoption agents and social workers were unaware of issues around FASD, but that they were concerned about the difficulty of securing placements for these children (see sub-theme 1: The child that nobody wanted). Based on the testimony of these families, it appears that professionals with responsibility for fostering and adoption are well aware of the difficulties faced by families of children with FASD and are keeping this information from prospective adopters in order to secure a placement.

Sub-theme 18: Lack of training or preparation provided for FASD

Parents described how they were offered training and information and were sent on courses to learn about adoption, trauma, attachment, ADHD and other relevant issues for prospective adopters, but here was no training on FASD. All of these families were eventually able to educate themselves, often with little help from officials.

"But we had not been trained in FASD. Pre-adoption, all the courses were about attachment, neglect, children who come from a neglectful and violent background... fine, good training, but they didn't talk about FASD!" (Interview 3 -

PAE)

"We know now they've got FASD, ADHD and all that, but we didn't know any of that, we started from scratch without the support of social services. We just did all our own research." (Interview 5 - both)

Parents described how things could have been different if they had known about prenatal alcohol exposure or FASD from the beginning. They would have been better able to predict the development of their children and would have the opportunity to put strategies in place for dealing with their difficulties.

"I've paid a fortune to go on all sorts of, you know, adoption courses and FASD things, but if we knew that when he was two and three then we would have been more understanding and we could have put things in place earlier." (Interview 11

- PAE)

“We wouldn’t have changed our minds either [about adopting], but what [FASD training] would have changed is how we started up... it would have been putting support in place, and trying to understand, ‘cause you completely think it’s your own parenting, don’t you?” (Interview 3 - PAE)

Again, families felt let down by service providers over their lack of FASD training. The training that they did receive, on ADHD, attachment, and other issues, was useful and appreciated. Families who had children with those issues were able to use their knowledge to good effect. The feeling was that early knowledge about FASD would also have been very helpful, but the lack of training, combined with a lack of acknowledgement of FASD on the part of officials, left parents doubting their own abilities as parents, which was upsetting and stressful.

Theme 9: Having to fight for services

Many families discussed their relationship with service providers in terms of a struggle or fight. These families were all adoptive, and many had previously been foster carers to their children. The impression they had been given was that adoptive parents were eligible for some support from adoption agencies, local authorities or social services, but this was often not forthcoming. This was particularly true in the case of an FASD diagnosis or an Education Health and Care Plan (EHCP) – a legal contract that sets out a child’s needs and what service providers such as schools must do in order to meet those needs.

Sub-theme 19: Needing support, but not getting it

Parents described how they wanted or needed certain services for their children. They asked for these things but were often denied or made to wait indefinitely. In some cases parents considered these services to be of an urgent nature.

“We have actually asked for some anger management from Post Adoption, but that was two years ago and we’re still waiting.” (Interview 2 - PAE)

When services were provided, this was often only after having to make a considerable effort. Some parents described needing services but were denied due to some criteria being unmet. Sometimes this demonstrated a lack of understanding of FASD among professionals.

“I’ve fought for one-to-one, but because she’s intelligent, they won’t give it to her, but she’s in trouble every single day.” (Interview 5 - both)

Some families felt they had been disregarded by officials who had given the impression that they would be supported.

“This was one of the promises, ‘You will not be alone’. Yeah, you are so alone... as soon as you’ve adopted them that’s it, they just don’t give a damn. They [adoption support agency] didn’t do anything.” (Interview 8 - both)

There was an overall feeling here again that families had been let down by professionals. The reason for this was not necessarily attributed to a lack of willingness on the part of service providers, yet families felt that some organisations had failed to keep their promises. Parents talked about being in a battle, not only at home working to deal with the issues around their children but fighting against a system that seemed to be set up not to provide them with assistance. Fighting a battle on two fronts with no support was exhausting.

Sub-theme 20: Struggling to get a diagnosis

One particular struggle that parents had was trying to have their children assessed and diagnosed on the foetal alcohol spectrum. One barrier to this was the unavailability of the birth mother’s antenatal records, which may have contained written evidence of alcohol consumption during pregnancy. Diagnosis is usually not possible without such a record.

“The GP told me that basically those notes belong to the birth mother and not us. Well, we’re raising him and living with the bloody consequences of what they did, it just seems so unfair.” (Interview 11 - PAE)

Again, when describing the process of trying to get a diagnosis, parents described going round in circles – being passed from one service to another without making progress toward their goal.

“I had years of attempting to get him diagnosed with [FASD], and just going round to all the different professionals, repeating all this information, and not getting anywhere.” (Interview 4 - both)

Parents were aware that the other services they were struggling to access were largely dependent on a formal diagnosis.

“It was quite frustrating, because we were aware that she was an FASD child, we knew what kinds of problems she was going to have, but there was no formal diagnosis. And until you’ve got a formal diagnosis there’s no machinery that’s going to come into place to offer support.” (Interview 6 - PAE)

There was an impression that some professionals were reluctant to diagnose or even acknowledge FASD. Conversations with social and medical service providers demonstrated a lack of understanding about FASD and a lack of understanding that a diagnosis and the support that this can induce can improve the prognosis of children with FASD.

You almost feel, when you talk to some of these people, that there's a wilful disbelief of the existence of FASD. They'll only accept it if they can see the facial features." (Interview 6 - PAE)

Sub-theme 20: Struggling to get an EHCP

Several families talked about wanting an EHCP. This was typically in order to improve or allow access to special educational resources or strategies at school to help the child cope with their academic and social demands. The gatekeepers of EHCP access were the local authorities, who were described as reluctant to provide funding. Parents described some of the things that an EHCP would do for their child, and these were often very simple interventions that could help to reduce their child's daily stress at school:

"It would be written in that somebody needs to do these things, like for example somebody needs to meet her in the morning and bring her in to school, somebody needs to take her out at break and bring her back in, those are the things that'll be written in the EHCP." (Interview 6 - PAE)

As with diagnosis, the long wait for an EHCP was described as wasted years and missed opportunities for intervention. Parents were aware of the benefits of earlier interventions for these children and felt more frustrated with each passing week or month that their children were struggling unnecessarily.

"It's a battle to get the EHCP... and it goes to appeal, and they're waiting again, but in the meantime, the kids' key developmental years are flying past! You know, six years it took me to get Adam diagnosed, you know, he's not gonna get those years back (Interview 4 - both)

The reason for delay or refusal to grant an EHCP was sometimes described as being due to a lack of local authority funding. EHCPs were sometimes not granted despite an overwhelming case in favour of them. Evidence and testimony from multiple medical sources were not enough to convince a local authority to provide funding.

“Despite the fact that we’ve sent a copy of Dr Mukherjee’s [UK National FASD Clinic] letter, an occupational therapy report saying that Jordan has visual processing difficulties, a result of an executive functioning questionnaire that shows Jordan has executive functioning difficulties, details of all the therapies he’s had so far, we’ve still been refused an application to assess for EHCP.”

(Interview 7 - PAE)

In terms of diagnosis or EHCP, the process was still described as a fight or struggle against a system that was not designed to help, but rather to hinder progress. Every step of the way, parents described feeling alone and frustrated when their expectation was that the system should be on their side. Moreover, these processes were merely means to ends. What these parents really wanted was quite simple: someone to meet their intimidated and overwhelmed child at the school gate and walk into school with them; time with a teaching assistant in the classroom; access to a therapist who might be able to help with feelings of anger in an aggressive teenager. A lack of training or resources often prevented even the first steps toward these goals and parents often felt like they had an impossible task.

Theme 10: Getting access to services was positive

Despite the many negative experiences these families had when dealing with service providers, most parents described at least one positive experience, effective organisation or helpful individual that enabled them to access appropriate services or help in some way with the difficulties they were facing. Some families were able to access diagnostic assessment or an EHCP. Some schools or other organisations did have FASD training or were keen to learn how best to meet the needs of these children, regardless of a legal obligation. Upon seeing a diagnosis or EHCP, some organisations became much more helpful.

“She has one-to-one support now [in school] for 25 hours [per week] which is unheard of. They don’t give her more than one instruction at a time, otherwise she can’t follow it through.” (Interview 3 - PAE)

“From the day he came out [from mainstream into special school] and he started those half days, the meltdowns went, and they’ve never come back, because from then on his needs have been getting met.” (Interview 4 - both)

Where children had other diagnoses or a history of trauma, the therapy or other interventions they received for those issues was described as helpful, appropriate and effective.

“So, [therapist] did all the nurturing stuff with Adam, which was great, ‘cause that’s for the attachment part, which he’s also been diagnosed with.” (Interview 4 - both)

One family described their experience of finally getting a diagnosis of FASD. The attitude of previously dismissive school staff changed dramatically, and their daughter’s experience of school and her life at home improved as a result.

“She wouldn’t be in school now if we didn’t have that diagnosis, I’m sure. Because we got it on the Saturday, we took the diagnosis into school on the Monday, and the school did a 360 on us, and they found out within the day what they could actually do to help us, where before, they’d been saying it was all us. That day, from that diagnosis, it changed that child’s life.” (Interview 6 - PAE).

8.4 Discussion

This study represents the final stage of the theoretical framework shown in chapter four (figure 4.1). Chapters five, six and seven showed that the impact of childhood trauma on the cognitive and behavioural functioning of children with FASD may be very subtle. The study described in this chapter was designed to explore the impact of cognitive and behavioural difficulties on the families of individuals with a dual exposure of PAE and trauma. By interviewing caregivers of children with just PAE as well as some with both exposures, the study sought to explore any thematic differences between the families of those two categories of child. Further to this, the study was designed not just to describe the experiences of parents and caregivers, but also the impact on other family members such as siblings and extended family.

There were many challenges reported in association with these children, although there were also many positives. Although the interviews were designed to explore difficulties associated with behavioural or emotional difficulties in their children, all 12 families also described dealing with service providers, which was largely a stressful experience and the impression given was that this was more stressful than dealing with their children. There was little difference between the experiences of families of children with dual exposure and families of children with FASD only, and families of both categories of children contributed to all themes. The main difference was that parents of children with a history of trauma were grateful for services such as therapy, which was designed to deal with trauma and attachment issues. Children without a history of trauma were also offered these services however, and their parents felt bemused at being directed towards

interventions that were unhelpful, and frustrated at the lack of appropriate interventions for a brain-based condition.

When discussing siblings and other family members, there were isolated examples of the stress or suffering of siblings due to a child with FASD. One girl's eardrum was pierced in a fight (interview 8), and two mothers (interviews 4 and 7) described how they had to protect their younger daughters from the aggressive behaviour of their sons. Other than this, parents described their typically developing, older, biological children as having a positive impact on their younger, adopted child with FASD. Older children would help care for their younger siblings, and grown-up children would look after their younger siblings to provide respite for their parents. Other adults, including friends, would also help with childcare, and this was seen as highly valuable.

When describing the adoption or fostering process, parents described how other prospective adopters had turned their children down. Children with FASD were seen as more difficult to manage with a worse prognosis than children with prenatal drug exposure or trauma, and people were reluctant to adopt a child with FASD. Adoption agencies and social services appeared to be aware of this and may have downplayed or hidden information in order to secure a placement. Many of the parents in this sample who did adopt a child with FASD were not told about prenatal alcohol exposure or the full extent of its effects. This was frustrating because the opportunity was missed to have sought diagnoses and interventions or set up strategies earlier that would have been advantageous to both the parents and children with FASD. Their children may have suffered to a greater extent than necessary because of this and their outcomes may be more adverse due to later diagnosis and implementation of interventions. Previous studies and evidence from this thesis have shown that earlier diagnosis in children with FASD is associated with reduced behavioural difficulties (see chapter 5), social difficulties (Alex & Feldmann, 2012), and reduced risk of a range of adverse life outcomes (Streissguth et al, 2004). Social workers and any other professionals involved in the placements of looked after children should be given FASD-specific training. With the knowledge that children with FASD can make improvements with early recognition and appropriate support they should be able to provide realistic and helpful advice to caregivers, which will improve the developmental trajectory of the child and reduce stress in the carers.

The children discussed in these interviews had a wide range of social and behavioural difficulties which were a cause of stress for their families, including parents and siblings, and for themselves. Some were aggressive or suffered from meltdowns, many were seen as easily led and an easy target for bullies, criminal gangs or adult predators. Parents worried about their children becoming independent as adolescents or adults and not being able to effectively navigate the adult

world. These kinds of concerns have been documented previously: the challenges of dealing with behavioural difficulties has been shown to predict levels of stress in caregivers (Bobbitt et al., 2016); children and adults with FASD have been described as highly suggestible and easily victimised by others, leading to criminal justice involvement (Greenspan & Driscoll, 2016); and adults with FASD living independently have been found to have high levels of problems with employment and victimisation including high levels of sexual abuse (Freunscht & Feldmann, 2011). The concerns of parents in this sample reflect reality and their children would likely benefit from some kind of social support during adulthood.

Most of the children described here attended mainstream school, and this was described as overwhelming for some, and could be cause of meltdowns. The school environment was overstimulating, but children were ill-equipped to express their discomfort or emotions, causing violent outbursts in the home after school. This pattern of behaviour was stressful for families but also led teachers to underestimate the behavioural problems of these children, which may have influenced assessments. When children received extra support such as one-to-one classroom time with a teaching assistant or were transferred to a special school, this was described as highly effective and in one case meltdowns ceased in a child who previously had them regularly. Getting access to an Education Health and Care Plan (EHCP) and/or receiving an FASD diagnosis was something that many of these parents felt their child needed in order to get access to special educational or mental health services. When diagnoses or EHCPs were accessed, these were seen as highly valuable and often led to effective educational interventions. Specifically designed support for children with FASD in school has been recommended previously; schools can help to prevent secondary disabilities in children with FASD by supporting them to utilise their strengths (Millar et al., 2017). Despite their difficulties, many of the children in this sample had specific skills and abilities that were beyond their typically developing peers. Research, practice and interventions for FASD have tended to focus on weaknesses, but many individuals with FASD have impressive talents that would make a useful focus of strategies in education and elsewhere (Harriman, 2007). School-based or other interventions for children with FASD should include opportunities for individual children to focus on and utilise their strengths and talents instead of focussing on their limitations.

Some of the parents in this sample were highly critical of local authorities, social services, schools and healthcare services. These organisations were seen as disjointed and lacking understanding of FASD. Inappropriate services were offered, and parents sometimes felt blamed for their children's difficulties. Dealing with service providers was described in terms of a battle. Similar descriptions have been found previously in UK focus groups of parents of children with FASD (Mukherjee, Wray, Commers, Hollins, & Curfs, 2013). Parents in the focus groups reported receiving

a lack of information from social workers about FASD, a lack of knowledge among professionals, having to fight for services, feeling blamed for their children's difficulties, becoming socially isolated, and feeling worried about their children's future. Every one of the themes identified by these focus groups (Mukherjee et al., 2013), which themselves reflected findings from similar studies in other countries (Brown and Bednar, 2003; Brown, Sigvaldason and Bednar, 2005; Caley, Winkelman and Mariano, 2009; Gardner, 2000; Gelo and O'Malley, 2003) was replicated in the present study. Children with FASD in the UK and abroad have been reported as difficult to manage but dealing with professionals may in fact be the greater source of stress for caregivers. Professionals in the UK who are likely to come into contact with individuals or families affected by FASD should receive specific training as a matter of urgency.

Finally, parents also described many positive experiences. Parents enjoying spending time with their children, who were often caring and empathic, funny, talented, and a source of pride. Watching them develop and reach milestones was rewarding; their children often had talents although witnessing simple accomplishments was equally or more enjoyable. Some service providers did a good job and were well-equipped or willing to learn how to do the best for these children. Some individual healthcare professionals were praised, but more often it was educators who were described positively. When children had a history of trauma or another diagnosed condition such as ADHD, these were dealt with effectively with therapies or other interventions delivered to the child, or with specific training provided to parents before or shortly after adoption. Similar descriptions of the rewarding aspects of parenting a child with FASD, such as witnessing growth and accomplishments, and feeling appreciated, have been described in the FASD literature (Brown, Rodger, George, St Arnault, & Sintzel, 2008) as well as in studies of other conditions, such as learning disabilities (Hastings & Taunt, 2002). The authors of that study noted that reports typically focus on the negative aspects and challenges of caring for children with disabilities, whereas rewarding experiences may be overlooked. The willingness of many educators to help children with FASD to maximise their potential in school is encouraging for potential interventions. Similarly, bespoke interventions for trauma or ADHD that worked well serve as a model for FASD interventions. Educational interventions or parent training should be specifically designed for the developmental profile of FASD.

8.4.1 Limitations and reflexivity

The findings of this study should be interpreted with a certain amount of caution. As a small ($n=12$ interviews) qualitative study, it was designed to offer an initial exploration of an issue that had not previously been assessed by any published study – the impact of a dual exposure of PAE and trauma on the families of the exposed individual. With no current theory on this specific research

question, this study was inductive in its approach. It began with no preconceptions and sought to collect data with which to generate theory. Further studies are therefore needed to validate the claims made here, and if possible, to test hypotheses generated by these inductive findings. For example, parents in this study reported the presence of other adults such as grown-up children in the home was very helpful. A quantitative study could assess the relative stress in families of children with FASD that do and do not have other adults around to help.

The participants in this study formed a self-selecting sample. Caregivers responded to advertisements or invitations to take part in a previous study (the online survey described in chapter 5 and/or the lab studies described in chapters 6 and 7). They were therefore potentially not representative of the wider population of carers of children with FASD (with or without trauma) and may in fact represent a specific category of caregivers who are well aware of the issues around FASD, and crucially, how to deal with them. Since the majority of people with FASD in the UK are undiagnosed (Morleo et al., 2011), and given the apparent reluctance (described in this chapter) of social workers and other professionals to provide information to adopters about FASD, it may well be the case that the majority of carers of children with FASD in the UK do not know their child has FASD. The carers in this study were members of online and/or physical support groups and had done a considerable amount of their own research into such things as prognosis, presentation and how best to deal with a child with FASD. Therefore, this sample of carers have had the opportunity to put strategies in place, while others (perhaps the majority) may be facing different problems, not least the problem of not knowing what is wrong with their child.

The reliance on participant report in qualitative studies such as this, can be affected by social or cognitive biases. For example, participants may sometimes wish to appear socially desirable by representing themselves in a positive way that may downplay or disregard some negative or embarrassing experiences (Van de Mortel, 2008). Similarly, participants may want (whether consciously or unconsciously) to please the researchers by providing responses or behaviours that are expected (Nichols, & Maner, 2008). Having met and got to know the participants, I suspect that they would not be significantly affected by such issues. I found that the families were highly motivated and typically had thought very carefully about the issues discussed in the interviews and were ready and keen to tell their own story. In many cases, I did not have to ask many questions, and instead the interviewees described their experiences at length and in detail. They were all too aware of the lack of attention paid to FASD research and knew the value of sharing their stories honestly and frankly. On a similar note, my own biases may have affected the study or this report. Having been involved in the field of FASD research now for nearly four years and having met several affected individuals and family members, I feel emotionally involved in the movement to raise

awareness of FASD and the difficulties faced by families. Although I have tried to remain impartial as researcher, it is possible that my feelings have influenced the write-up of this report. My choice of words or decisions on which aspects to emphasise could have been affected by my desire to make the issue of FASD more prominent in the research literature. Such biases are an unavoidable part of qualitative research; however this aspect of the study provides a rich and detailed understanding of the impact of FASD upon the lives of children and their families which may not be apparent within the findings of a more quantitative approach.

8.4.2 Conclusions

This study set out to explore difficulties and challenges in the families of children with FASD and a history of trauma. Based on previously published studies and the earlier chapters of this thesis it was expected that behavioural and social problems would be similar across this sample of children, regardless of exposure to trauma, and that parents and other family members would report feeling stressed as a result. To some extent this was the case, but parents gave the impression that dealing with the system of schools, social services, healthcare services and local authorities was their biggest stressor. These organisations should be a source of support, but parents described their relationship with them in terms of a battle. One of the main reasons for this appears to be a lack of training and understanding of FASD among professionals, and this reflects other studies in the literature. Similarly, there was a lack of training and information available to parents, which, if delivered in the early stages or prior to placements, could have moderated some of the difficulties seen in these children. Social workers, medical professionals, teachers, other professionals, and especially parents require bespoke, FASD-specific training and interventions, which should aim to incorporate classroom changes and support, develop social skills, and allow children to focus on their individual strengths and abilities. Further studies are needed to support the findings of this initial, exploratory study.

Chapter 9: General discussion

9.1: Introduction to discussion

This thesis was designed to investigate differences associated with a history of traumatic childhood experiences in children with FASD, in terms of neurocognitive and behavioural functioning, and the impact of this on the families of affected individuals. Prenatal alcohol exposure can lead to foetal alcohol spectrum disorder, which is thought to affect around 1% of the world population, but in countries where alcohol use is prevalent, the rates of FASD are higher than this. In the UK, the prevalence of FASD has been estimated at 3.24% by meta-analysis (Lange et al., 2017) and between 6% and 17% based on modelling of cohort data (McQuire et al., 2018). More reliable data from an active case ascertainment study, where cases of FASD are actively sought from a population sample, are not currently available. One such study is currently being planned in Greater Manchester however, and should produce the most accurate estimate yet of FASD prevalence in the UK.

Individuals prenatally exposed to alcohol tend to present with difficulties in intelligence, learning and memory, motor skills, attention, speech and language, executive functioning, adaptive functioning and social communication, as well as a wide range of behavioural difficulties (Mattson, Bernes & Doyle, 2019). The long-term effects of traumatic childhood experiences, such as neglect and abuse, can be similar to those seen in FASD, with a range of behavioural, social and emotional difficulties, as well as cognitive deficits especially in the case of children who were neglected (Hildyard and Wolfe, 2002). The similarity between the effects of trauma and the effects of PAE on cognitive and behavioural functioning, and their high level of comorbidity (Coggins et al., 2007) were behind the rationale for this thesis. It is necessary for clinicians and others who work with affected individuals to be able to delineate the effects of each exposure, and to be able to predict, to some extent, the developmental trajectory of patients with PAE with and without a history of trauma. Furthermore, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; APA, 2013) requires studies to investigate the relationship between trauma (specifically neglect) and PAE in order to develop the criteria for their proposed diagnosis of Neurobehavioural Disorder associated with Prenatal Alcohol Exposure (ND-PAE).

In the first stage of the thesis, a systematic literature review of all previously published studies into the dual exposure of prenatal alcohol and postnatal trauma was conducted and published (Price et al., 2017; [appendix 1](#) Chapter 3). Later, an audit of data from the UK National FASD clinic was published, which assessed the impact of neglect on neurodevelopmental outcomes in patients with FASD (Mukherjee et al., 2019). These two publications provided some evidence that

children with a dual exposure of PAE and trauma appear to be more similar to children with just PAE than they are to children with just trauma. In other words, the impact of trauma on the presentation of children with PAE may be subtle and PAE may be a better explanation than trauma for the deficits seen in individuals with both exposures. However, the extent of the evidence at this stage was still lacking. Some major gaps identified in the literature were addressed by this thesis, which contains four novel studies into the neurocognitive and behavioural impact of dual exposure, and the effect of behavioural difficulties on caregivers and other family members. The thesis has contributed a deeper understanding of the differences in functioning associated with prenatal alcohol exposure (PAE) alone and when combined with trauma.

The thesis employed a causal modelling framework (see figure 9.1 below) to structure and plan the four novel studies. Each exposure separately (as detailed in chapter 2) is capable of affecting neurological structures and functioning, which can lead to cognitive and behavioural difficulties, which in turn can cause stress to other individuals, such as caregivers. The general hypothesis that was tested by the thesis was that, where both exposures are present, this chain of neurological, cognitive, behavioural and interpersonal deficits and difficulties would be more likely and/or more severe at each stage. Broadly, and consistent with the extant literature, the thesis found no differences between groups of children with single and dual exposure, and only weak relationships between severity of trauma and some emotional and behavioural difficulties. The following section will detail the main findings of the thesis chapter-by-chapter and provide an overall summary. This will be followed by discussions of the implications of these findings for practice and policy, methodological limitations of the thesis, further required research, and finally an overall conclusion.

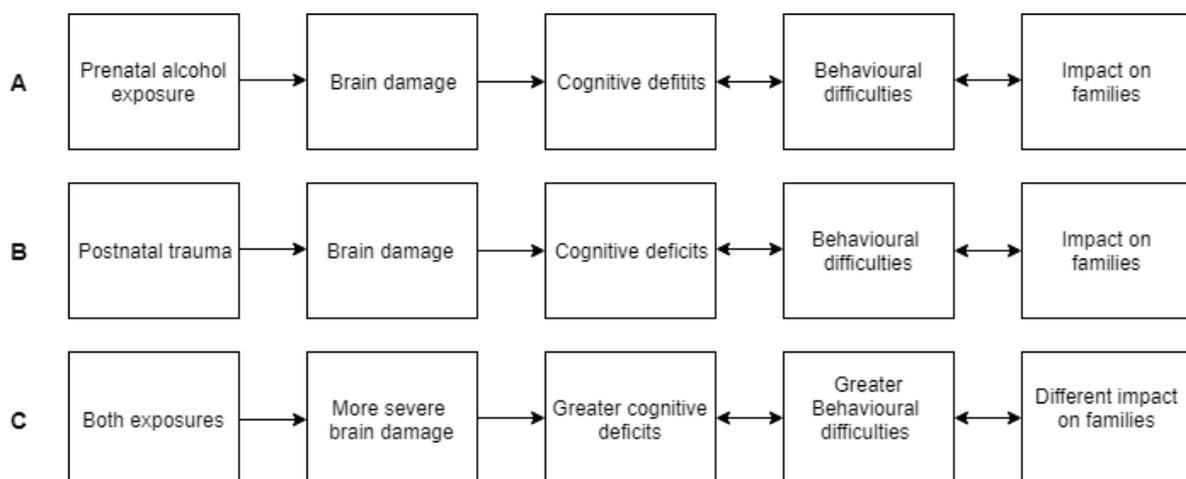


Figure 9.1 Causal modelling framework of PAE and trauma

9.2 Summary of main findings

9.2.1 Systematic review

Chapter three describes the systematic review, which identified five articles that investigated a dual exposure of prenatal alcohol and postnatal trauma. Children with both exposures tended to have moderate to severe deficits in speech, language and social communication, developmental delay and a range of behavioural difficulties. There was substantial comorbidity between PAE and trauma of between 58% and 95%, although samples were clinical or purposively recruited. Children with PAE and trauma were more likely to exhibit delays or deficits in language, attention, memory and intelligence, and were more likely to exhibit hyperactivity, impulsivity, oppositional behaviour and social difficulties compared to children with trauma but not PAE. Conversely, children with both exposures were more likely to exhibit attachment and behavioural problems compared to children with PAE alone. Time spent in a nurturing and stable home was negatively correlated with cognitive and behavioural problems in children, and with drug use, school exclusion and trouble with the law in adults. Overall the review showed that children with dual exposure are more similar to children with just PAE than they are to children with just trauma. This suggested that, in children with both exposures, behavioural, and especially cognitive deficits may be better explained by PAE than by trauma. However, several gaps remained in the literature. No study had investigated the dual exposure of PAE and trauma on executive functioning or brain activity. No study had assessed the impact of trauma on IQ or empathy in children with PAE. Only one small study had assessed the impact of trauma on behavioural difficulties in children with PAE. No study had assessed the impact of behavioural difficulties associated with PAE and trauma on family members of the exposed individual. The following studies were designed to address these gaps.

9.2.2 Caregiver-report survey of ACEs, empathy and behavioural difficulties

Chapter five describes an online caregiver report survey that aimed to assess trauma, empathy and behavioural difficulties in children with PAE, and investigate relationships between level of trauma and severity of outcomes. The survey was a composite of three previously published and validated questionnaires: The Adverse Childhood Experiences questionnaire, the Griffith Empathy Measure, and the Strengths and Difficulties Questionnaire. Carers of 245 children with diagnosed or suspected FASD, mostly residents of the USA, Canada and the UK reported on their children aged 4-16. Across the full sample, children had considerably lower empathy scores than children in the general population. They had higher levels of behavioural difficulties than the general population including peer problems, hyperactivity, emotional problems, conduct problems and anti-social behaviour. They had higher levels of adverse childhood experiences than the general

population including psychological abuse, neglect and household dysfunction. Levels of physical and sexual abuse were not higher than general population figures, although these may be underestimates due to uncertainty among respondents. Children with FASD had high levels of comorbid diagnoses including ADHD, intellectual disability, anxiety disorder, attachment disorder, oppositional defiant disorder, autism spectrum disorder, post-traumatic stress disorder and depressive disorder. No significant correlation was identified between ACE score and empathy. There was a weak positive correlation between age at diagnosis and peer problems and a very weak positive correlation between age at diagnosis and conduct problems. Children with FASD and a history of maltreatment were more likely to be diagnosed with PTSD or attachment disorder than children with FASD without history of maltreatment. Overall, the results of the survey show little to no effect of trauma on the presentation of children with dual exposure. The main difference was that children with dual exposure had a slight tendency to exhibit more conduct problems and were more likely to be diagnosed with PTSD or attachment disorder than those with PAE alone.

9.2.3 Cognitive study of intelligence and executive functioning

Chapter six describes a smaller study, which aimed to assess intelligence and executive functioning in groups of children with a) PAE with trauma, b) PAE without trauma, and c) typically developing control children. Families who had completed the survey who lived close to the Greater Manchester area were invited in to the University of Salford for the cognitive assessments. Thirteen children with PAE only, 12 with dual exposure and 15 typically developing control children completed a brief IQ test and two executive functioning computer tasks. The IQ test provided scores on verbal, non-verbal and overall IQ, and the two executive functioning tasks assessed working memory and inhibitory control. Children with PAE in this sample had mean verbal, non-verbal and overall IQ scores in the normal range and working memory and inhibitory control scores similar to the control group regardless of trauma. No differences were found between children with dual exposure, children with only PAE in terms of their intelligence or executive functioning. The executive functioning scores of both PAE groups were also similar to the scores of the control group.

9.2.4 Neuroimaging study of task-related prefrontal cortex activity

Chapter seven describes a study that compared brain activity between children with dual exposure and only PAE. During their visit to the University for the intelligence and executive functioning assessments (described above), all children in that study also had their brain activity monitored whilst they completed the working memory tasks. Functional near infra-red spectroscopy was used to measure blood oxygenation in the prefrontal cortex (PFC), where activity would be expected during tasks that require executive functioning. The pattern of task-related neural activity

was statistically similar across both PAE groups, as well as the control group, indicating no impact of PAE or trauma on brain activity in the PFC during this task.

9.2.5 Qualitative study of caregiver and family experiences

Chapter eight describes a series of interviews conducted with some of the carers whose children took part in the cognitive studies. This qualitative study was designed to explore the final stage of the causal framework – the impact of cognitive and behavioural difficulties on other people, especially parents and siblings. Since chronologically this study followed the quantitative studies, by the time of the interviews there was evidence that children with dual exposure had similar presentations to children with PAE only. Parents of children from both groups were interviewed and all 12 families contributed to all themes, providing further support for the null hypothesis (no difference between groups), albeit in an inductive study with no hypothesis testing. Family members described the challenges of dealing with their children, whose cognitive and behavioural problems were described as stressful. This however was set in an overall context of high stress levels generated because service providers were not able to provide appropriate support for children with FASD due to a lack of training and understanding, a lack of diagnostic services, and sometimes a sceptical or dismissive attitude towards FASD. Many parents represented this relationship in terms of a battle or struggle, which was demoralising. Services or interventions that were available had been designed for children with conditions such as ADHD, or life events such as trauma or attachment problems. Where children had those needs these services were useful, but children without those needs were also offered the same services, which left parents frustrated. Parents did also discuss many positives, especially when describing their relationship with their children, but some service providers, especially schools, were keen to make an effort and this was gratefully received. Overall, the study found parents were in need of assistance, however there was either a lack of services or those that were available were not designed for FASD.

Taking the whole thesis together, on this evidence, the overall findings were that the behavioural profile of children with PAE is affected very little by a history of trauma, and the cognitive profile is not affected at all. There are several caveats to this in terms of methodological limitations and studies yet to be conducted and these issues will be discussed in the next section but taken together with the parent reports of inappropriate services being offered, an interesting overall finding does emerge. Children who have a history of prenatal alcohol exposure and postnatal trauma in the UK appear currently to be receiving services designed for trauma and attachment issues. Given the emerging evidence that their profile seems to be more similar to children with PAE only and less like the profile of children with trauma only, they would probably benefit more from

services designed specifically for FASD. Such services appear to be currently unavailable in the UK, even for children with FASD in absence of trauma.

9.2.6 Summary of novel findings of the thesis

This thesis contributes to the literature by, first of all, synthesising the available evidence on the dual impact of PAE and trauma. The literature review suggests that children with both exposures may be more similar to those with just PAE than those with just trauma, but that the evidence is scarce. Secondly, the thesis provides the first evidence of the impact of dual impact of PAE and trauma on: working memory, inhibitory control, verbal, non-verbal and overall IQ, empathy, and brain activity, and adds to the evidence on behavioural difficulties. It provides the first evidence on the prevalence of adverse childhood experiences in children with PAE and contains the first study of the impact of PAE and trauma, via the affected individual, on family members. The thesis also provides support for previous studies which have shown that caregivers of children with PAE in the UK feel frustrated and let down by services that are not designed to help them.

9.3 Implications

9.3.1 Implications for research and practice

The main overall finding of the thesis, that children with PAE and a history of trauma appear to have comparable cognitive and behavioural functioning as those with PAE but without a history of trauma, was contrary to the experimental hypotheses but was not completely unexpected. The systematic review found some differences in behavioural problems but no difference in cognitive functioning between children with both exposures versus those with only PAE. Dinkler et al (2017) used a large cohort of Swedish twins to assess the impact of childhood maltreatment of symptoms of neurodevelopmental disorders such as Autism and ADHD. Children in their sample who were maltreated did have a greater number of neurodevelopmental symptoms, but the twin analysis revealed that genetic and (non-traumatic) environmental factors explained more of the variance in outcome than childhood maltreatment. Similarly, the audit of clinical data from the UK National FASD Clinic (Mukherjee et al., 2019) found no more neurodevelopmental symptoms or diagnoses in individuals with FASD and neglect, than in children with FASD without neglect.

The available literature on the effects of traumatic experiences in children or adults with PAE is still scarce, but this thesis demonstrates an emerging pattern of subtle differences in behaviour and no apparent difference in neurocognitive function. The mechanisms that might explain this pattern were not investigated by this thesis, but one finding from the survey (chapter 5) presents a potential explanation. Children living in North America (the USA or Canada), who had a higher number of adverse childhood experiences, also had a slight tendency toward more severe

behavioural difficulties, whereas there was no such relationship in the British children.. The reason for this disparity could possibly be due to better recognition, diagnosis and support for FASD in North America compared to the UK. Earlier recognition, diagnosis and support for FASD is associated with improved outcomes (Chapter 5 of this thesis; Streissguth et al., 2004). In countries where FASD services are more readily available, the symptoms of other issues may be more distinct. The current available data are mostly European (Chapter 5 of this thesis; Koponen et al., 2009; Mukherjee et al., 2019) and show little effect of trauma on functioning in individuals with FASD, but the North American data in this thesis do show some relationship between ACE score and behavioural functioning. Only one North American study has assessed trauma in FASD and found no effect on speech and language ability (Coggins et al., 2007). No published study using North American participants has yet assessed the impact of trauma on behavioural functioning in children with FASD. If indeed, data became available that showed this effect, it would strengthen the rationale for studies to test the hypothesis that a lack of support for FASD in European countries is obfuscating the developmental impact of trauma in that population.

The main implication of these findings for policy and practice is that children with FASD and a history of trauma should be treated primarily as children with FASD, since prenatal exposure to alcohol appears to better explain their presentation. From the parent reports in the interview study, it seems that many health and social services in the UK are better equipped to deal with trauma and attachment issues in children than they are to deal with the challenges associated with FASD. The literature overview (chapter 2) shows the similarities between the effects of PAE and trauma, but they are not identical. Crucially, their harm is caused in different ways, and this should be reflected in the services that these individuals receive. Interventions for children who have been maltreated tend to focus on internal and environmental safety, self-regulation, dissociation, interpersonal relationships, self-narratives, dealing with reminders of traumatic events, intimacy and self-esteem (Cook et al., 2017, for a review). Such therapies also deal with behavioural and cognitive functioning and may be useful to some extent in children with FASD, especially if those children also have a history of trauma. However, their focus is one that may not be ideal for children whose deficits are caused by a congenital brain injury.

These results also have implications of the future of diagnosis in FASD. The DSM-5 criteria for ND-PAE suggests neglect as an exposure to be ruled out when diagnosing. If a patient has a history of PAE, neglect, and meets other diagnostic criteria for ND-PAE (such as cognitive and behavioural deficits), the presence of neglect would currently bring a diagnosis of ND-PAE into doubt, because the neglect can also explain the cognitive and behavioural difficulties. The studies in this thesis, including those identified by the systematic review, investigated the impact of trauma,

maltreatment, or adverse childhood experiences on the cognitive and behavioural functioning of children with PAE, and found that those exposures made little difference to presentation. The audit of clinical data (Mukherjee et al., 2019) also specifically compared children with FASD with and without neglect in terms of neurodevelopmental features, and also found that neglect was not associated with more severe outcomes. Taken together, this body of research finds very poor evidence that the presence of neglect or abuse in a patient history should be considered a better explanation of behavioural, and especially cognitive, deficits in individuals with PAE. In fact, prenatal alcohol exposure should be ruled out where patients are suspected of developmental damage caused by neglect or other childhood trauma. This brings into question the methods used by several studies of the impact of childhood trauma on cognitive and behavioural functioning – those that did not also test for PAE may have missed a better explanation for their patients' or participants' developmental problems. This includes every study ever conducted on the long-term effects of childhood trauma, with the exception of those included in the systematic review (Price et al., 2017) or wider thesis.

9.3.2 Implications for interventions

Some evidence-based interventions have been specifically designed for children and adults with FASD. A recent systematic review (Reid et al., 2015) identified 32 published interventions trialled on individuals with FASD. Results were mixed, but studies that focussed on specific areas of dysfunction in children such as verbal or mathematical abilities and executive functions tended to achieve positive results (Kerns, MacSween, Vander-Wekken, & Gruppuso, 2010; Nash et al., 2015). Some interventions were able to improve social skills in children with FASD (e.g. Keil et al., 2010). Other studies aimed to improve skills and knowledge among caregivers, to decrease their stress levels and improve child outcomes (Bertrand et al., 2009). These studies provided promising results, but long-term outcomes were not measured. Overall, interventions designed for FASD were found to be of mixed quality and the authors of the review concluded that more high-quality interventions needed to be developed, especially that took a holistic, rather than domain-specific approach to improving outcomes in individuals with FASD. In the UK, there is currently no legislation or national strategy to guide diagnostic or treatment services for FASD, and previous studies as well as this thesis (chapter 8) have shown a lack of knowledge among healthcare professionals (Mukherjee, 2019; Mukherjee et al., 2015). By demonstrating the homogeneity among children with FASD with and without a history of trauma, this thesis adds support to the argument that children with FASD require services tailored to that particular profile and not for the profile of patients with a history of trauma, despite comorbidity. A project is currently underway at the University of Salford, which

should produce an effective, evidence-based parenting programme specifically designed for the needs of families affected by FASD.

9.4 Limitations

The methodological limitations of each of the studies within this thesis are discussed in their respective chapters. However, some general issues with the design of the thesis, caveats to potential conclusions, and remaining gaps in the literature will now be addressed. One of the biggest problems with the design of this thesis is the lack of participants who have a history of trauma but not prenatal alcohol exposure. A four-group, 2x2 design where participants had either PAE, trauma, both, or neither would have enabled the interaction between those exposures to be assessed. The scores of a 'just trauma' group would have enabled the studies to assess the relative impacts of each exposure separately and determine which, in this sample, was associated with more severe outcomes. The recruitment of such a group was attempted, but due to practical difficulties (detailed in section 4.3) this was unfortunately not achieved

The participants with FASD and a history of trauma who were recruited in the studies reported here were living in stable, nurturing homes with their loving adoptive parents and had been for several years. This kind of environment is known to reduce the impact of traumatic experiences (Harden, 2004; WHO, 2009), which could help to explain the apparent lack of an impact of trauma on the functioning of those children. This also leaves the question of what differences might be seen in children who are not living in nurturing environments. Perhaps children with FASD who remain in abusive or neglectful homes, or who live with non-abusive but uncaring adults do exhibit a difference in functioning associated with trauma. Koponen et al (2009) showed that children in their sample who had been removed from abusive or neglectful environments sooner, tended to exhibit fewer behavioural difficulties. The children who participated in the studies of this thesis may represent the part of the population who were able to avoid the more harmful, long-term effects of trauma. Children still living in such environments would be unlikely to take part in these studies, which relied on caregiver engagement.

The participants with FASD in these studies were aged 4-16 years (survey) and 8-14 years (lab and interview studies). The findings of this thesis therefore tell us about outcomes in children and younger adolescents, but not older adolescents or adults. Since the effects of childhood trauma differ from the short to long term (Anda et al., 2006; Mulvihill, 2005) some of the effects of trauma may not have fully emerged by this age. This thesis therefore falls short of assessing the impact of childhood trauma in individuals with FASD by ignoring adolescent and adult development. No

published study has yet assessed the impact of childhood trauma on cognitive or behavioural functioning in adults with FASD.

There is now some evidence of the combined impact of PAE and trauma on speech and language, intelligence, executive functioning, behavioural difficulties, attention, empathy, memory, Autism symptoms, ADHD symptoms, social communication, sensory processing, and adaptive behaviour. However, there are several areas of functioning that have not yet been assessed. The list of cognitive and behavioural domains that have been shown to be impacted by either PAE or trauma, have not yet all been investigated in terms of the dual impact of both exposures. Candidates for assessment include the stress response, cognitive shifting, dissociation, attachment, self-esteem, criminality, addictions and other longer-term life outcomes in adults.

The use of exposures such as PAE and trauma in this thesis are quite broad and lead to a study population that may be heterogeneous. Neglect in childhood may have more of an impact on cognitive functioning than abuse in childhood (Hildyard and Wolfe, 2002), but in these studies they are grouped together. Similarly, individuals with PAE can have a highly varied presentation due to dose, pattern and timing of alcohol exposure, and maternal factors (O’Leary et al., 2010). The reason for using trauma or maltreatment instead of abuse or neglect specifically was due to the designs of the studies in the systematic review, all of which used the same broader definitions. Now that more evidence is available, as demonstrated by the results of this thesis, on the impact of trauma and maltreatment in children with PAE, future studies should aim to use the more specific exposures of abuse or neglect, and ideally the different categories of physical, psychological and sexual abuse, and physical and emotional neglect to assess their respective outcomes.

Many of the participants in this thesis were undiagnosed, and the caregiver’s opinion was used to fulfil inclusion criteria. Levels of FASD diagnosis in the UK are thought to be very low (Morleo et al., 2011), so this is a difficulty that is inherent in FASD research. Studies that are able to identify dose, pattern and timing of alcohol exposure would be valuable but reliable assessment may be difficult. Diagnosis of FASD is required to improve the reliability of these types of studies – this is yet another important reason for increasing the diagnostic capacity for FASD in the UK.

9.5 Further research

Based on the findings and limitations of this thesis, the following suggestions for further research are presented. Studies should no longer assess either the impact of trauma within PAE, or PAE within trauma, but should recruit participants with both exposures, participants with each exposure, and participants with neither exposure. Whilst mindful of the practical constraints, studies

should aim to include measures of the severity of childhood trauma and the dose, pattern and timing of PAE. Variables known to moderate the impact of trauma, such as the presence of a trustworthy adult (Werner, 1993) should also be included. Studies should be conducted into the longer-term effects of PAE and trauma in older adolescents and adults. Studies should seek to replicate findings in the domains that have already been covered but should also assess the impact of dual exposure on the stress response, cognitive shifting, dissociation, attachment, adaptive functioning, self-esteem, criminality and addictions. Studies assessing dual exposure should separate the effects of neglect, abuse, and other traumatic childhood experiences on all outcomes.

9.6 General conclusions

The current available evidence contained in this thesis suggests a subtle impact of traumatic childhood experiences on behavioural functioning – largely in terms of conduct problems – in children aged 4-16 years with FASD or suspected FASD in the United States and Canada. This effect is not seen in children living in the UK. There is currently no evidence of an impact of traumatic childhood experiences on empathy, brain activity, intelligence or executive functioning in children aged 4-16 years with FASD or suspected FASD in any country. Caregivers of children with FASD or suspected FASD in the UK have reported feeling frustrated at the lack of training and knowledge of FASD among service providers, and the lack of appropriate services for their children. Clinicians should be aware that children with a dual exposure of PAE and trauma may benefit more from services designed for FASD than issues related to traumatic experiences. For diagnosis of patients with suspected FASD, there is poor evidence that neglect and abuse are better explanations for cognitive or behavioural dysfunction than PAE. However, the current evidence is still lacking in quality and scope. Studies are needed to further investigate the impact of specific types of trauma in children and adults with FASD in a range of domains. Given the very high estimated prevalence of FASD, evidence-based interventions need to be designed specifically for children and families affected by FASD and these need to be made widely available along with diagnostic and other services to reduce the long-term adverse outcomes of PAE.

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Appendix 1: Systematic review

Price, A., Cook, P. A., Norgate, S., & Mukherjee, R. (2017). Prenatal alcohol exposure and traumatic childhood experiences: A systematic review. Neuroscience & Biobehavioral Reviews, 80, 89-98

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.

Keywords: Systematic review, prenatal alcohol exposure, FASD, trauma, maltreatment.

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Highlights

- Reviewed impacts of Prenatal Alcohol Exposure and trauma (e.g. abuse and neglect)
- There are high levels of comorbidity but a lack of studies that address both exposures
- Dual exposure was associated with increased cognitive and behavioural impairment
- The spectrum of effects and diagnostic criteria of PAE were not fully accounted for
- Longitudinal studies on PAE and trauma needed to strengthen evidence of causality

1. Introduction

Prenatal alcohol exposure (PAE) can lead to a range of neurodevelopmental disorders collectively known as Foetal 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 foetus, where it can disrupt healthy growth across the body, including in the brain (Goodlett, Horn, & Zhou, 2005). The type and scale of foetal 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 foetal vulnerability factors (Mattson, Schoenfeld, & Riley, 2001; Ungerer, Knezovich, & Ramsay, 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 & 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, Stevens, Nash, Koren & Rovet, 2009; Kingdon, Cardoso & McGrath, 2015). These deficits can lead to a diagnosis of one or more of a range of disorders within the foetal 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 foetal 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 & Horn, 2001; Guerri, Bazinet & Riley, 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, Weinberg & Kobor, 2017). These and other mechanisms can lead to improper growth of the corpus callosum, hippocampus, basal ganglia, 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, Desrocher, & Moore, 2011) speech and language (O'Keeffe, Greene, & Kearney, 2014), executive

functioning (Kingdon, Cardoso & McGrath, 2015), social cognition, emotional processing (Greenbaum, Stevens, Nash, Koren & Rovet, 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, Putney, Furniss & Kahane, 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, adrenocorticotrophic hormone (ACTH) and cortisol from the sympathetic nervous system, pituitary gland, and adrenal glands respectively (Neigh, Gillespie, & Nemeroff, 2009). Prolonged or frequent activation of this system during infancy is associated

with immune and endocrine system dysfunction, and neurodevelopmental delay in adults (Neigh, Gillespie, & Nemeroff, 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, Mayberg, Mletzko, Nemeroff, & Pruessner, 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, Bakermans-Kranenburg, Alink, & IJzendoorn, 2015). Studies into FASD prevalence rely on detection of CNS damage, and significant misdiagnosis is suspected (e.g. Chasnoff, Wells, & King, 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, Lange, Probst, Gmel, & Rehm, 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, Sliwowska, Verma, & Weinberg, 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, Sloan & Black-Pond, 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, Liberati, Tetzlaff, & Altman, 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, foetal alcohol and prenatal exposure were searched for alongside terms relating to trauma such as abuse, maltreatment and neglect (see appendix 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, 2,369 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 (figure 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, Timler and Olswang (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, Sloane and Black-Pond (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, Kalland and Autti-Rämö (2009) and Koponen,

Kalland, Autti-Rämö, Laamanen and Suominen (2013) use ‘traumatic experiences’, which as well as abuse and neglect, includes drug abuse by parents, witnessing violence, death of parents, criminal behaviour of 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 foetal 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.

INSERT FIGURE 1 ABOUT HERE

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%.

INSERT TABLE 1 ABOUT HERE

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 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.

INSERT TABLE 2 ABOUT HERE

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 ($n = 113$; $p < .001$), and that 50% of children with just trauma showed moderate to major delays in expressive language, compared to 72% of children with both exposures ($p = .001$). Hyter (2012) reports that children with both exposures ($n = 34$) were more likely to show deficits in phonological awareness (Cohen's $d = .12$, $p = .003$), semantics ($d = .31$, $p = .004$), syntax ($d = .47$, $p = .015$), and comprehension ($d = .31$, $p = .018$) 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 ($d = .31$, $p = .007$), nonverbal intelligence ($d = .22$, $p = .04$), and in the composite score ($d = .42$, $p = .01$) 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 ($r = .47$, $p < .01$) 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 ($n = 113$; $p = .004$; 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%; $p = .005$).

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 to 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 ($d = .26, p = .04$), social problems ($d = .35, p = .02$), ADHD index ($d = .47, p = .004$), restless/impulsive ($d = .40, p = .01$), global index ($d = .46, p = .02$), DSM-IV criteria for inattention ($d = .50, p = .004$), DSM-IV criteria for hyperactivity/impulsivity ($d = .33, p = .03$), and DSM-IV total ($d = .27, p = .005$) 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 ($d = .40, p = .006$), ADHD index ($d = .36, p = .02$), restlessness/impulsivity ($d = .38, p = .03$), DSM-IV criteria for inattention ($d = .27, p = .009$), and DSM-IV total ($d = .46, p = .01$). 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%, $p < .01$). 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 ($r = .43, p < .05$),

age at placement into their present foster family ($r = .34, p < .05$), and number of traumatic experiences ($r = .45, p < .01$), 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 ($r = .39, p < .05$) and bullying behaviour towards other children ($r = .37, p < .05$).

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, $p<.001$), DSE (OR=4.67, $p<.001$), TWL (OR=2.69, $p=.01$), and ADP (OR=4.10, $p=.001$). Fewer years per household by age 18 increased the risk of CNF (OR=7.35, $p=.001$). Having been the victim of sexual or physical assault or domestic violence increased the risk of ISB (OR=3.37, $p<.001$) and ADP (OR=2.56, $p<.05$). 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; above). 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; above). 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; above). 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 dysmorphism 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, Loomis & Booth, 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, Telle, & Votruba, 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 1: Search terms

“fetal alcohol” OR “foetal alcohol” OR “fetal-alcohol” OR “foetal-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

Appendix 2: Tables and figures

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

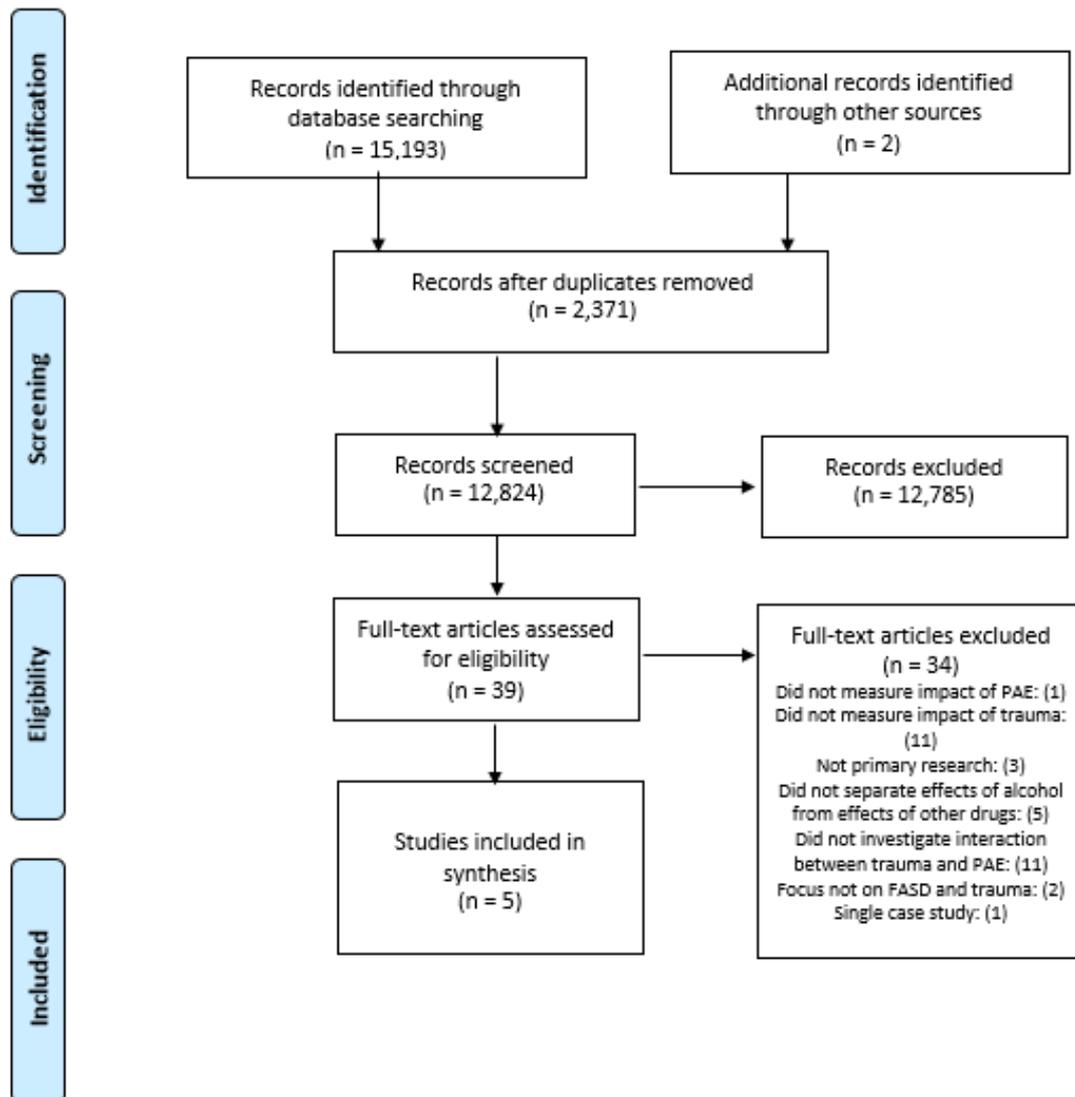
Study	Aims	Groups	FASD diagnostic criteria	Diagnoses of participants	Evidence of prenatal exposure	Method of evaluation	Robustness of evidence
Coggins et al., 2007	To assess the levels of environmental risk, language performance, and narrative discourse data within a clinical database of school-age children with foetal 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.

Study	Aims	Groups	FASD diagnostic criteria	Diagnoses of participants	Evidence of prenatal exposure	Method of evaluation	Robustness of evidence
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: Foetal Alcohol Syndrome (FAS), partial Foetal 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 Foetal Alcohol Syndrome (FAS) and Foetal Alcohol Effects (FAE) as well as the category of no diagnosis (NDs).

Figure 1: Flow diagram showing selection procedure



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Questionnaire

Section One – Information sheet and consent form

Please only complete this questionnaire if you are the parent or guardian of a child aged 4 – 16, who was exposed to alcohol before he/she was born.

Title of study

The impact of fetal alcohol spectrum disorders (FASD) and traumatic childhood experiences on social and behavioural development in children.

Invitation paragraph

We would like to invite you to take part in a research study. Before you decide whether to take part you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Ask questions if anything you read is not clear or would like more information. Take time to decide whether or not to take part.

The study

This questionnaire has been designed to measure social and behavioural factors relating to FASD and traumatic childhood experiences. The information you provide about your child will be analysed along with information from other participants, to see whether trauma is associated with issues such as empathy and behaviour in children with FASD.

The following questionnaire will first collect some personal details relating to your child's diagnoses, history, and education. Following this, there will be a series of questions about your child's ability to understand the thoughts and behaviours of other people, and finally a section on your child's behavioural and social strengths and difficulties.

IMPORTANT: There is one section of the questionnaire, concerning any traumatic experiences that your child may have suffered in the past, which you may find upsetting. You will be asked some very personal questions about neglect and emotional, physical and sexual abuse, so please think carefully about whether you would like to proceed. We would not have included this section if it was not vital to the research, but please remember that you are under no obligation to complete the questionnaire. You can take a break and come back to the questionnaire later, and if you are a couple, you may complete the questionnaire together or have your partner complete some sections if this helps. After that section of the questionnaire, there will be no further questions of this nature. Please also remember that the information you provide will remain completely anonymous and confidential in accordance with strict research practices set out by the British Psychological Society.

What will happen if I decide to take part?

Your participation in the study involves completing an online questionnaire. Once you have read this information page, you will be asked to consent to being involved in a research study. After this, the questionnaire will take the form of 4 sections: Personal details, your child's history of traumatic experiences (if any), your child's ability to understand the thoughts and behaviours of other people, and finally your child's social and behavioural strengths and difficulties. The majority of the questions are yes or no answers, or require you to answer on a scale – e.g. from 1 (strongly disagree)

to 5 (strongly agree). The whole questionnaire should take no longer than about 20 minutes to complete, although you may take breaks and come back to it later.

Possible disadvantages

As mentioned above, there is a risk that one section of the questionnaire will be upsetting or distressing, especially if your child has a history of traumatic experiences. The nature of the research means that we are particularly interested in the impact of trauma, and for this reason these types of questions unfortunately could not be avoided. You are reminded that you may discontinue the questionnaire at any point, or take a break and come back later. Furthermore, if you would prefer not to complete the questionnaire at all, you may leave now. We still appreciate your time and effort. If you are feeling distressed and would like to talk to someone, there are some charity run helplines available:

United Kingdom

FASD Trust Helpline: 01608 811599 <http://www.fasdtrust.co.uk/>

NOFAS UK Helpline: 020 8458 5951 <http://www.nofas-uk.org/>

USA

Minnesota Organisation on Fetal Alcohol Syndrome

<http://www.mofas.org/>

Helpline: (Toll-Free) 1-866-90-MOFAS (66327)

Canada

Motherisk Helpline (1-877-327-4636)

<http://www.motherisk.org/FAR/>

Possible advantages

Many people suspect that children with FASD are negatively affected by traumatic childhood experiences, and that this will further impact their mental, social and behavioural abilities. However, very little research has been conducted in order to provide evidence of this. The data that you and others provide in this questionnaire will be analysed and the results will be written up for publication in a scientific journal. This new knowledge can lead to more accurate information for adoptive and foster parents in terms of the kinds of issues that can be expected in their children, and how to deal with them. Furthermore, this information can be used to help teachers to improve special educational arrangements for children with FASD and a history of trauma.

Where do I go if I have a problem?

If you have any issues concerning the study, you may contact the lead researcher Alan Price at: a.d.price1@edu.salford.ac.uk

If you would rather contact someone other than the lead researcher, you can contact research supervisor Professor Penny Cook at: p.a.cook@salford.ac.uk

Confidentiality

The data that we record from the questionnaire will only be identified by a unique code, and not your name or any other personal details. Your unique code will be linked to your details only in one electronic document, which will be safely stored on a password protected computer only accessible to the research team. Your data will be used as part of an analysis, which may be published in scientific journals and presented at academic conferences, but your data will always remain anonymous. All data will be securely stored for a minimum of three years to allow for external verification or further research purposes. All data will be destroyed after this time.

Right to withdraw

You may postpone or withdraw from the study at any time and for any reason. You may also have your data removed from the study up to one month after coming completing the questionnaire.

What happens to the results?

Once we have collected questionnaires from all our participants, the data will be compiled and analysed. The results of the analysis will be written up as part of an academic paper, which may be published in a scientific journal. We may also present the findings in the form of a talk or poster at academic conferences, so that the scientific community can benefit from this new information. If you would like a copy of the results, please contact the lead researcher who will be happy to provide them and discuss them with you.

Who is organising or funding the research?

The study is being undertaken as part of a PhD project, and is funded by the University of Salford.

Further information

If you would like any more information, please contact the lead researcher Alan Price at a.d.price1@edu.salford.ac.uk

Consent form

- I confirm that I have read and understood the information sheet for the above study and what my contribution will be Yes No
- I have been given the opportunity to ask questions (face to face, via telephone, or by e-mail) Yes No
- I understand that my participation is voluntary and that I can withdraw from the research at any time **without giving any reason** Yes No
- I understand how the researcher will use my responses, who will see them and how the data will be stored. Yes No
- **I agree to take part in the above study** Yes No

Name of participant

Date

Memorable word

Please provide a memorable word or phrase. Since this questionnaire is completely anonymous, we will use this to identify your responses in the event that you would like your data to be removed from the study.

.....

Participant code

If you have signed up to the lab study at the University of Salford, please give your unique participant code here, so that we can link your information to your child's data from the second part of the study.

.....

Demographics

How would you describe your child's ethnicity? Free answer

How would you describe your ethnicity? Free answer

Which country do you live in?

What is your child's gender? (male, female, other – if other please state)

What age is your child now? (in years and months)

If your child is adopted, what age was he/she first came to live with you? (years, months...n/a)

How did your child come to live with you? (Adopted, fostered, biological other – give details)

Was your child prenatally exposed to alcohol by his/her birth mother drinking during pregnancy? Please say how you were made aware of this.

Was your child prenatally exposed to any other drugs by his/her birth mother drinking during pregnancy? Please give details, and say how you were made aware of this.

Does your child have a diagnosis on the fetal alcohol spectrum? (FAS, pFAS, ARBD, ARND) At what age did he/she receive this diagnosis?

Does your child have any other diagnosed mental or developmental disorders? Please give details

Does your child have any physical illnesses or disabilities? Please give details

Is your child in:

- a) mainstream school, mainstream class with no special assistance
- b) mainstream school, mainstream class with special assistance
- c) mainstream school, special educational needs class
- d) special educational needs school
- e) home-schooled
- f) other, please give details

If you would like to make any extra comments, please do so here:

Griffith Empathy Measure

For each statement, please indicate the extent to which you agree or disagree by checking the box next to the appropriate point on the line. (9-point Likert scale from -4 strongly disagree to +4 strongly agree)

It makes my child sad to see another child who can't find anyone to play with.

My child treats dogs and cats as though they have feelings like people.

My child reacts badly when he/she sees people kiss and hug in public.

My child feels sorry for another child who is upset.

My child becomes sad when other children around him/her are sad.

My child doesn't understand why other people cry out of happiness.

My child gets upset when he/she sees another child being punished for being naughty.

My child seems to react to the moods of people around him/her.

My child gets upset when another person is acting upset.

My child likes to watch other people open presents, even when he/she doesn't get one themselves.

Seeing another child who is crying makes my child cry or get upset.

My child gets upset when he/she sees another child being hurt.

When I get sad my child doesn't seem to notice.

Seeing another child laugh makes my child laugh.

Sad movies or TV shows make my child sad.

My child becomes nervous when other children around him/her are nervous.

It's hard for my child to understand why someone else gets upset.

My child gets upset when he/she sees an animal being hurt.

My child feels sad for other people who are physically disabled (e.g., in a wheelchair).

My child rarely understands why other people cry.

My child would eat the last cookie in the cookie jar, even when he/she knows that someone else wants it.

My child acts happy when another person is acting happy.

My child can continue to feel okay even if people around are upset.

If you would like to make any extra comments, please do so here:

Strengths and difficulties questionnaire

Please indicate how true you consider each statement to be in relation to your child during the last 6 months. Responses: Not true, somewhat true, certainly true.

- Considerate of other people's feelings
- Restless, overactive, cannot stay still for long
- Often complains of headaches, stomach-aches or sickness
- Shares readily with other children (treats, toys, pencils etc.)
- Often has temper tantrums or hot tempers
- Rather solitary, tends to play alone
- Generally obedient, usually does what adults request
- Many worries, often seems worried
- Helpful if someone is hurt, upset or feeling ill
- Constantly fidgeting or squirming
- Has at least one good friend
- Often fights with other children or bullies them
- Often unhappy, down-hearted or tearful
- Generally liked by other children
- Easily distracted, concentration wanders
- Nervous or clingy in new situations, easily loses confidence
- Kind to younger children
- Often lies or cheats
- Picked on or bullied by other children
- Often volunteers to help others (parents, teachers, other children)
- Thinks things out before acting
- Steals from home, school or elsewhere
- Gets on better with adults than with other children
- Many fears, easily scared
- Sees tasks through to the end, good attention span

If you would like to make any extra comments, please do so here:

Adverse Childhood Experiences (ACE) questionnaire

The following 10 questions are concerned with traumatic events that your child may have experienced. Please remember that you are under no obligation to continue and to take a break if you feel distressed.

If your child is adopted/fostered:

Please answer this section to the best of your knowledge what your child's life was like before they came to live with you.

If your child is your own biological child or if you adopted your child at birth:

Please answer this section to the best of your knowledge what your child's life has been like so far.

Psychological abuse

1. Did a parent or other adult in the household **often**

Swear at them, insult them, put them down, or humiliate them?

OR

Act in a way that made them afraid that they might be physically hurt?

Yes No Unsure

Physical abuse

2. Did a parent or other adult in the household **often**

Push, grab, slap, or throw something at them?

OR

Ever hit them so hard that they had marks or were injured?

Yes No Unsure

Sexual abuse

3. Did an adult or person at least 5 years older than them **ever**

Touch or fondle them or have them touch the other person's body in a sexual way?

OR

Try to or actually have oral, anal, or vaginal sex with them?

Yes No Unsure

Emotional neglect

4. Did they **often** feel that:

No one in their family loved them or thought you were important or special?

OR

Their family didn't look out for each other, feel close to each other, or support each other?

Yes No Unsure

Physical neglect

5. Did they **often** not have enough to eat, had to wear dirty clothes, and had no one to protect them?

OR

Were their parents **often** too drunk or high to take care of them or take them to the doctor if they needed it?

Yes No Unsure

Divorce

6. Did their parents ever separate or divorce?

Yes No Unsure

Violence against mother

7. Was their mother or stepmother:

Often pushed, grabbed, slapped, or had something thrown at her?

OR

Sometimes or **often** kicked, bitten, hit with a fist, or hit with something hard?

OR

Ever repeatedly hit over at least a few minutes or threatened with a gun or knife?

Yes No Unsure

Family member with drug or alcohol misuse

8. Did they live with anyone who was a problem drinker or alcoholic or who used street drugs?

Yes No Unsure

Family member with mental health issues

9. Was a household member depressed or mentally ill or did a household member attempt suicide?

Yes No Unsure

Imprisonment

10. Did a household member go to prison?

Yes No Unsure

If you would like to make any extra comments, please do so here:

Section 6 – Debrief and thankyou

You have now reached the end of the survey. Thank you very much for your time and effort.

This survey was designed to measure social and behavioural effects of traumatic experiences on children who were prenatally exposed to alcohol. The information provided about your child will be grouped based on whether he/she suffered significant trauma in infancy and early childhood. We will then be able to measure what kind of impact maltreatment has on the social and behavioural development of children prenatally exposed to alcohol. This information is very important, as it can be used to develop more appropriate and effective educational strategies which can improve the educational attainment and quality of life of young people with these issues. We would like to remind you that you are entitled to have your data removed from the study, by emailing the lead researcher Alan Price at a.d.price1@edu.salford.ac.uk and quoting the memorable word you provided in section 1. Again, from the whole research team, thank you very much for your time.

Alan Price and colleagues

University of Salford

Manchester, England

If you are feeling distressed and would like to talk to someone, there are some charity run helplines available:

United Kingdom

FASD Trust Helpline: 01608 811599 <http://www.fasdtrust.co.uk/>

NOFAS UK Helpline: 020 8458 5951 <http://www.nofas-uk.org/>

USA

Minnesota Organisation on Fetal Alcohol Syndrome

<http://www.mofas.org/>

Helpline: (Toll-Free) 1-866-90-MOFAS (66327)

Canada

Motherisk Helpline (1-877-327-4636)

<http://www.motherisk.org/FAR/>

Appendix 3: Ethical approval notification

University of
Salford
MANCHESTER

Research, Innovation and Academic
Engagement Ethical Approval Panel

Research Centres Support Team
00.3 Joule House
University of Salford
MS 4WT

T +44(0)161 295 2280

www.salford.ac.uk/

6 September 2016

Dear Alan,

RE: ETHICS APPLICATION HSCR16/82 – The impact of traumatic childhood experiences on cognitive and behavioural development in children with fetal alcohol spectrum disorder.

Based on the information you provided, I am pleased to inform you that application HSCR16-82 has been approved.

If there are any changes to the project and/ or its methodology, please inform the Panel as soon as possible by contacting Health-ResearchEthics@salford.ac.uk

Yours sincerely,

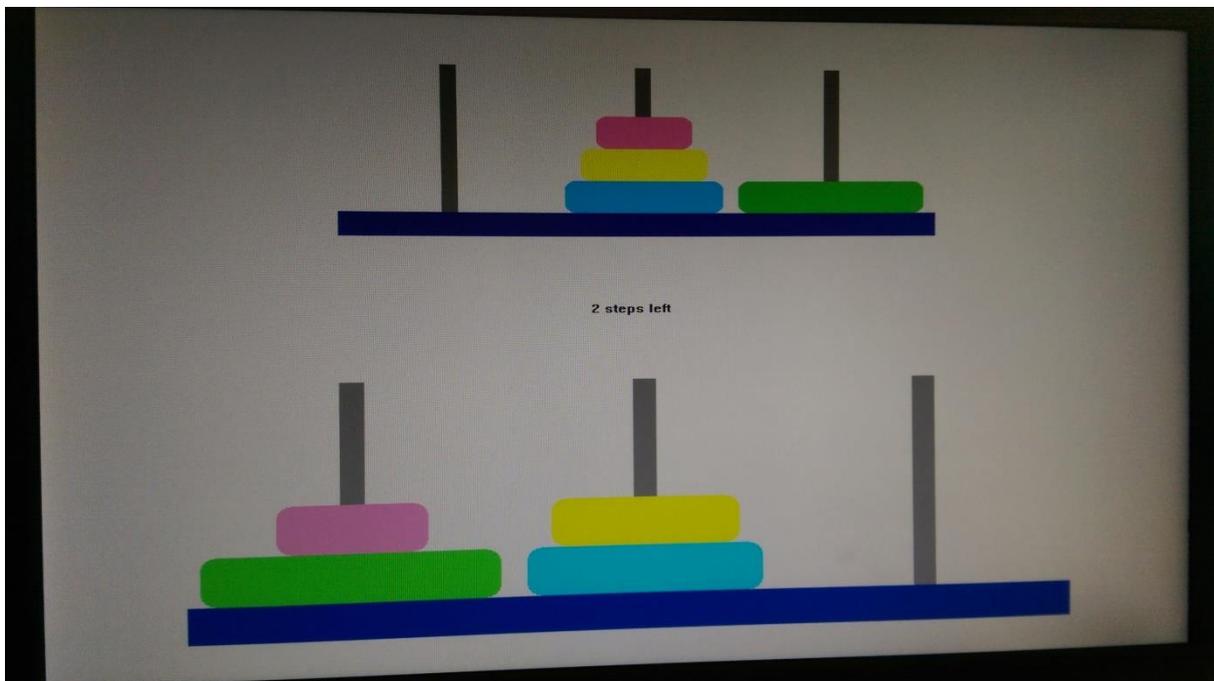


Sue McAndrew
Chair of the Research Ethics Panel

Appendix 4: Go/No-go screenshot



Appendix 5: Tower of Hanoi screenshot



Appendix 6: Parents information and consent for lab study

Participant information sheet – Lab study

Title of study

Cognitive and neurological issues related to fetal alcohol spectrum disorders and early childhood maltreatment.

Invitation paragraph

We would like to invite you to take part in a research study. Before you decide whether to take part, you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Ask questions if anything you read is not clear or would like more information. Take time to decide whether or not to take part.

The study

This study has been designed in order to measure mental difficulties in children with FASD, and how these difficulties are affected by early childhood maltreatment. The information you have provided about your child's history will be analysed alongside his or her scores in a series of computer based tasks, to see whether maltreatment is associated with mental difficulties in children with FASD. We also want to know whether a system called functional near infra-red spectroscopy (fNIRS) can be used to accurately measure brain activity in children with FASD. This is a harmless process which uses infra-red light to detect activity in the brain. It is often used in research with children but has not been used so far in children with FASD. We would like to stress that this technology is completely safe, and only uses light waves that we are all exposed to on a daily basis.

The tasks are designed to measure your child's executive functioning. Executive functions are mental processes such as planning and decision making. Your child has been invited to take part in this study because he or she fits the age group of 8-14 years, is not looked after by his or her biological parents, and was prenatally exposed to alcohol. You and your child are under no obligation to take part in the study, and you may withdraw and have your data removed at any time.

What will happen if we decide to take part?

You and your child will be invited into the University of Salford, where the lead researcher Alan Price will meet you and show you to the lab – which is just a quiet room in the psychology department with two computers at a desk. You will be asked to sign a form to say that you consent to your child participating in the study. It is important that your child is happy to participate, but you may consent on their behalf. Following this, your child will be invited to sit at a desktop computer, and will be fitted with the fNIRS headset like the one in this picture.



Once the headset is on, your child will take part in a series of three tasks, which are presented as computer games. These games will measure your child's executive functioning, and have been specially designed for children. Each game should take no longer than 15 minutes, and your child will be allowed a break after each game if they wish.

After the third game, the study will be over. You will be paid £10 to compensate for your travel expenses. During the study, if you or your child would like to take a break, postpone the research, or withdraw from the research, you may do so at any time without giving any reason. You will still be paid travel expenses.

Possible disadvantages

Possible disadvantages to participating include:

That you will have to take time out of your day to travel to the University of Salford, however you will be compensated for your travel expenses with £10. The total time spent at the university should not exceed two hours.

That your child may become irritated or bored whilst playing the games. We have tried to avoid this by making the tasks as agreeable as possible to children, and by keeping them as short as possible, as well as allowing breaks in between.

That your child may find the fNIRS headset uncomfortable. We do not expect this to be an issue, but must regard it as a possibility. We will be using the more comfortable of the two fNIRS headsets we have available, and many similar research studies have been conducted in this way.

Possible advantages

An advantage of participating is that we will be able to tell you your child's score on the three executive functioning tasks, and give you some indication of how these compare to the wider population. It is important to note however that this information does not constitute any kind of diagnosis and does not substitute for examination by a registered psychiatrist.

A further advantage relates to the benefit to the wider population. The data collected in this study will be analysed and used to advance the limited knowledge of how maltreatment affects the development of children with FASD. Research such as this can lead to more accurate information for adoptive and foster parents in terms of the kinds of issues that can be expected, and how to deal with them. Furthermore, this information can be used to help teachers to improve special educational arrangements for children with FASD and a history of maltreatment.

Where do I go if I have a problem?

If you have any issues concerning the study, you may contact the lead researcher Alan Price at: a.d.price1@edu.salford.ac.uk

If you have any complaints, or would rather contact someone other than the lead researcher, you can contact research supervisor Professor Penny Cook at: p.a.cook@salford.ac.uk

Confidentiality

The data that we record during the study, from fNIRS and the computer tasks, will only be identified by a unique code, and not your name or any other personal details. Your unique code will be linked to your details only in one electronic document, which will be safely stored on a password protected computer only accessible to the research team. Your data will be used as part of an analysis, which

may be published in scientific journals and presented at academic conferences, but your data will always remain anonymous. All data will be securely stored for a minimum of three years to allow for external verification or further research purposes. All data will be destroyed after this time.

Right to withdraw

You may postpone or withdraw from the study at any time and for any reason. You may also have your data removed from the study up to one month after coming into the lab.

What happens to the results?

Once we have collected data from all our participants, the scores from the computer tasks and brain activity data will be compiled and analysed. The results of the analysis will be written up as part of an academic paper, which may be published in a scientific journal. We may also present the findings in the form of a talk or poster at academic conferences, so that the scientific community can benefit from this new information. If you would like a copy of the results, please contact the lead researcher who will be happy to provide them and discuss them with you.

Who is organising or funding the research?

The study is being undertaken as part of a PhD project, and is funded by the University of Salford.

Further information

If you would like any more information, please contact the lead researcher Alan Price at a.d.price1@edu.salford.ac.uk

Parent / Guardian Consent Form

Title of Project: The impact fetal alcohol spectrum disorder (FASD) and traumatic childhood experiences on mental processing in children.

Name of Researcher: Alan Price

Please circle

- I confirm that I have read and understood the information sheet for the above study and what my contribution will be. Yes No
- I have been given the opportunity to ask questions (face to face, via telephone and e-mail) Yes No
- I understand that my child/children's participation is voluntary and that we can withdraw from the research at any time without giving any reason Yes No
- I understand how the researcher will use my child/children's responses, who will see them and how the data will be stored. Yes No
- I give permission for my child/children to take part in the above study Yes No
- I am happy to be contacted with information about further research studies Yes No

Name of parent/guardian

Signature

Date

Name(s) of child/children

.....

Appendix 7: Children's information and consent for lab study

Research study information for young person

Thank you for coming here today. We would like to learn about how children your age think and make decisions. First we will play some games with words and pictures at the table like this:



These games should take about 30 minutes, and afterwards you can have a quick break if you like.

Next, we will play two games on the computer: the mole game and the tower game. Before you play the tower game, we will fit you with a special headset that tells us what your brain is doing. These games will take about 10 minutes each and you can take a break in between if you like.



When you have finished the second computer game, the session will be finished and you can leave. You can stop or take a break any time you like.

If you are happy to carry on, please fill in the form on the next page.

Research Consent Form for Young Person (Lab study)

Please circle

- I understand what will happen today Yes No
- I understand that I can stop or take a break at any time Yes No
- I am happy to take part in the study Yes No

Name

Date of birth

Appendix 8: Interview schedule

1. How long have they lived with you?
 - a) How old were they then?
 - b) And did you adopt them straight away, or foster first?
2. Can you tell me about the process of adoption/fostering?
3. What were you told about FASD and how they might be affected?
4. (Unless children were adopted/fostered at birth) What were you told about their lives before they came to live with you?
 - a) (If traumatic) What were you told about how this kind of trauma might affect them?
5. When they first came to live with you, what were the first few days and weeks like?
6. How would you describe their behaviour since then?
 - a) How does this affect you?
 - b) Does it affect other family members?

Prompts

- does the child display the following types of behaviour?
- does not differentiate between familiar and unfamiliar persons
- takes responsibility for tasks which should be carried out by adults
- self-endangering behaviour
- attention or concentration problems

7. How would you describe their ability to cope with everyday things like getting ready for school, mealtimes, playing?
 - a) Does this affect you or other family members?
 - l) How?
8. How are they socially with other children?
 - a) How does this affect you?
9. How would you describe their emotions – for example, are they often anxious or depressed?
 - a) How does that affect you?
 - b) Does it affect other family members?
 - l) How?

Prompts

How does the child behave when he/she is

- frightened or troubled
 - has hurt him-/herself
 - when parents have been away from home for a while
10. What situations have been the hardest?
 - a) How has this affected you personally?
 - b) Has it affected your relationships with partners, friends etc.?
 - l) How?
 - c) Has it affected other siblings or other family members?
 - l) How?
 11. What kinds of things are they best at?
 12. What have you enjoyed the most?
 13. Is there anything you would like to add that we have not covered?

Appendix 9: Qualitative study ethical approval



Research, Innovation and Academic
Engagement Ethical Approval Panel

Research Centres Support Team
00.3 Joule House
University of Salford
M5 4WT

T +44(0)161 295 2280

www.salford.ac.uk/

22 May 2017

Dear Alan,

RE: ETHICS APPLICATION–HSR1617-110–‘Cognitive and behavioural difficulties in children with foetal alcohol spectrum disorder and a history of traumatic experiences: A qualitative investigation into the impact on families.’

Based on the information you provided I am pleased to inform you that application HSR1617-110 has been approved.

If there are any changes to the project and/or its methodology, then please inform the Panel as soon as possible by contacting Health-ResearchEthics@salford.ac.uk

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Sue McAndrew'.

Sue McAndrew
Chair of the Research Ethics Panel

Appendix 10: Qualitative study information and consent



Information sheet Version 2: 9th May 2017

Title of study

Cognitive and behavioural difficulties in children with FASD and a history of traumatic experiences: A qualitative investigation into the impact on families

Invitation paragraph

We would like to invite you to take part in a research study. Before you decide whether to take part, you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Ask questions if anything you read is not clear or would like more information. Take time to decide whether or not to take part.

The study

This study has been designed to investigate behavioural, social and emotional strengths and difficulties in adopted children aged 8-14 with foetal alcohol spectrum disorder (FASD). We are especially interested in the impact that any difficulties can have on family members, and what the impacts are in children who also suffered traumatic childhood experiences such as abuse or neglect before they were adopted. We would like to speak to people whose children have not had traumatic experiences as well, so that we can explore a range of experience.

The information you provide about your child will be analysed along with information given by other adoptive parents, and we will try to identify any recurring themes and patterns. We hope that this kind of information can help health and educational professionals to deliver more effective interventions and strategies to help young people with FASD and their families.

You have been invited to take part in this study because you have adopted a child/children who have FASD and fit the age group of 8-14 years. You may have taken part in a previous study on FASD at University of Salford and at the time you indicated that you might be interested in being contacted with further opportunities to take part in research. You are under no obligation to take part in the study, and you may withdraw and have your data removed at any time.

What will happen if we decide to take part?

Your participation in the study involves you, and your partner if you have one, taking part in a single tape-recorded interview with the lead researcher Alan Price, who you met in the previous study. Alan will arrange to meet you in a suitable location. This can be in your own home or you can come back into the university where we can arrange a quiet room for the interview. Unfortunately, we cannot provide travel expenses for this study. If we conduct the interview in your own home, you may wish to think about whether you want your children to be in the room during the interview. If you have a partner, they are welcome to join in the interview.

The interview will focus on your child/children's behavioural, social and emotional strengths and difficulties, and we may also discuss any traumatic events that your child may have experienced before they came to live with you. These kinds of issues can be upsetting, so please think carefully about whether you would like to proceed. Please remember that you are under no obligation to volunteer for the study. During the interview, you can take a break whenever you feel like it, or we can discontinue the interview if you do not want to carry on.

Possible disadvantages

Possible disadvantages to participating include:

That you will have to take time out of your day to take part in the interview. The interview can take place in your own home, and we do not expect it to last more than about an hour.

That the interview may include questions about traumatic experiences your child may have suffered in the past. You are under no obligation to answer any questions that you do not wish to answer.

Possible advantages

Although there is no direct advantage, we hope that you can benefit from the opportunity to reflect on your child's development. The data collected in this study will be analysed and used to advance the limited knowledge of how families are affected by any behavioural, emotional and social strengths and difficulties in children with FASD. Research such as this can lead to more accurate information for adoptive and foster parents in terms of the kinds of issues that can be expected, and how to deal with them. Furthermore, this information can be used to help health and educational professionals to improve interventions and strategies for children with FASD and their families.

Where do I go if I have a problem?

If you have any issues concerning the study, you may contact the lead researcher Alan Price at: a.d.price1@edu.salford.ac.uk

If you would rather contact someone other than the lead researcher, you can contact research supervisor Professor Penny Cook at: p.a.cook@salford.ac.uk / +44 (0) 161 295 2804

If you would like to contact someone outside the research team, you can contact the associate director of research Dr Jo Cresswell at: j.e.cresswell@salford.ac.uk / +44 (0) 161 295 6355 / Research & Enterprise Division, Room 208, Joule House, University of Salford, Salford, M5 4WT

Confidentiality

The data that we record during the study will only be identified by your interview number and/or initials. This is to ensure that all research participants and their children remain anonymous. For example, if you say during the interview that "*...we have found that Jane is forgetful*", we may use this quote in the write-up of the study in order to reinforce the finding that parents reported forgetfulness in their children:

Interview #4: "...we have found that J is forgetful".

We will never use your own names or your children's names, or any other information which could be used to identify you or your children, in any write-up of any research.

Your interview number will only be linked to your name and email address on a password-protected computer accessible only to the research team.

With your permission, an anonymised version of the dataset will be stored indefinitely at the University and may be used in future research on this topic.

Right to withdraw

You may postpone or withdraw from the interview at any time and for any reason. You may also withdraw from the study and have your data removed up to one month after the interview. If you wish to do this after the interview, please email the lead researcher at a.d.price1@edu.salford.ac.uk.

What happens to the results?

Once we have held interviews with all our participants, the recordings of the interviews will be transcribed by the lead researcher and one other member of the research team. We will analyse the transcripts to identify any recurring themes or patterns. We will then produce a written report of our findings which may be published in an academic journal. We may also present the findings at academic conferences. The findings will be presented as part of the lead researcher's PhD thesis. All data will be strictly anonymous. If you would like to see the report, please ask the lead researcher, who will be happy to send you a copy and discuss it with you.

Who is organising or funding the research?

The study is being undertaken as part of a PhD project, and is funded by the University of Salford.

Further information

If you would like any more information, please contact the lead researcher Alan Price at a.d.price1@edu.salford.ac.uk

Participant Consent Form

Title of study: Behavioural, emotional and social strengths and difficulties in adopted children aged 8-14 with fetal alcohol spectrum disorders and a history of traumatic experiences, and their impact on families: A qualitative study.

Name of Researcher: Alan Price

Please circle

- I confirm that I have read and understood the information sheet for the above study and what my contribution will be. Yes No

- I have been given the opportunity to ask questions (face to face, via telephone and e-mail) Yes No

- I understand that my participation is voluntary and that I may withdraw from the study at any time without giving any reason Yes No

- I understand how the researcher will use my responses, who will see them and how the data will be stored. Yes No

- I am happy to take part in the above study Yes No

Print name
.....

Sign
.....

Date
.....