The development of executive function in children exposed to alcohol *in utero*: An exploratory study

BY

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ABSTRACT

Children who have been exposed to alcohol *in utero* have well documented deficits in executive function. However, previous research in the field has not situated the executive deficits displayed by these children within a developmental framework. The present study endeavoured to address this shortcoming by investigating the development of executive function in children exposed to alcohol *in utero*, through the use of 10 subtests from the NEPSY that assess attention and executive function. It was hypothesised that the executive abilities of children would mature with age. In addition, it was hypothesised that children who were exposed to alcohol *in utero* would display deficits in executive function and that these deficits would become more pronounced with age. The study made use of cross-sectional design that compared the performance of younger children (6- to 7-year-olds) with that of older children (12- to 13-year-olds) on various measures of executive function. Within this, it made use of a natural experimental design, with children exposed to alcohol *in utero* as the experimental group and non-exposed children as the control group. Participants were recruited from a school and a clinic in two towns in the Western Cape. Twenty children with confirmed *in utero* exposure to alcohol took part in the study. Twenty non-exposed volunteers constituted the control group. These two groups were each divided equally into two age groups: 6- to 7-year-olds and 12- to 13-year-olds. The Health Professions Council of South Africa's regulations with regard to research was adhered to. Two-way factorial analysis of variance (ANOVA) was utilised for each subtest of the NEPSY to investigate the main effects of age group (6- to 7-year-olds and 12- to 13-year-olds) and exposure (exposed and non-exposed) as well as any interaction effects. Significant interaction effects were evident on the Tower subtest, the Auditory Attention task, the Auditory Response Set task and the accuracy score of the Visual Attention subtest of the NEPSY. In concordance with previous research in the field, the executive abilities of children were found to improve with age. Incidental findings suggested that the executive abilities of children exposed to alcohol *in utero* may develop at a slower rate than those of non-exposed children. Furthermore, the findings of the present study suggest that children exposed to alcohol *in utero* present with deficits in executive function which dissipates with age. The findings are discussed in terms of theories of recovery of function after brain damage.

DECLARATION

I declare that *The development of executive function in children exposed to alcohol in utero: An exploratory study* is my own work, that it has not been submitted before for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged as complete references

Tania Badenhorst
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Signed: . . . . . .

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CONTENTS

Chapter 1: Introduction

1.1. The effects of *in utero* exposure to alcohol

Although the detrimental effects of maternal ingestion of alcohol during pregnancy are well documented, the neuropsychological consequences of *in utero* exposure to alcohol are still poorly understood (Rasmussen, 2005). A general lowering of intelligence, in addition to deficits in specific cognitive abilities such as language, motor function, learning, memory, and visuo-spatial functions have been noted in the literature (Korkman, Kettunen, & Autti-Rämö, 2003; Mattson, Riley, Delis, Stern, & Jones, 1996; Mattson, Riley, Gramling, Delis, & Jones, 1997; Mattson, Schoenfeld, & Riley, 2001; Stratton, Howe, & Battaglia, 1996; Streissguth, Barr, & Sampson, 1990). In recent years, impairment in executive function following prenatal exposure to alcohol has garnered particular interest, with studies indicating impairment to various aspects of executive function in children who were exposed to alcohol *in utero* (Carmichael Olson, Feldman, Streissguth, Sampson, & Bookstein 1998; Kodituwakku, Handmaker, Cutler, Weathersby, & Handmaker, 1995; Mattson, Goodman, Caine, Delis, & Riley, 1999; Noland, Singer, Arendt, Minnes, Short, & Bearer, 2003; Schonfeld, Mattson, Lang, Delis, & Riley, 2001; Streisguth, Barr, & Sampson, 1990).

Executive function is an umbrella term used to describe those cognitive processes responsible for purposeful, goal-directed activity (Anderson, 2002). These processes (discussed in detail below) play an important role in cognitive function, behaviour, emotional control and social interaction (Anderson, 2002; Anderson, Bechara, Damasio, Tranel, & Damasio, 1999). A growing body of neurodevelopmental research indicates that executive function develops throughout

childhood and adolescence (Stuss, 1992; Anderson, 2002). Despite this, very little is known about the development of executive function in children exposed to alcohol *in utero* (Rasmussen, 2005). The purpose of the present study was to address this shortcoming by investigating the development of executive function in two groups of children, a group of 6- to 7-year-olds and a group of 12- to 13-year-olds, with confirmed exposure to alcohol *in utero*.

1.2. Diagnosis and classification

In its most severe form, *in utero* exposure to alcohol causes foetal alcohol syndrome (FAS), which is defined by four criteria: maternal drinking during pregnancy, pre-and/or postnatal growth deficiency, a distinctive pattern of craniofacial anomalies, and central nervous system (CNS) dysfunction (Stratton, Howe, & Battaglia, 1996). Given that the effects of *in utero* exposure to alcohol vary depending on the dose and exposure, a distinction is made between FAS and "foetal alcohol effects" (FAE). The latter term is applied to children with some, but not all, of the characteristics of FAS (Welch-Carre, 2005). In 1996 the American Institute of Medicine created a 5-category classification system for individuals exposed to alcohol *in utero*. This classification system added the terms: partial FAS (PFAS), alcohol-related birth defects (ARBD), and alcohol-related neurodevelopmental disorder (ARND) to describe children with different levels of deficits or disabilities linked to prenatal alcohol exposure (Welch-Carre, 2005). The term foetal alcohol spectrum disorder (FASD) is an umbrella term used to describe the full range of outcomes observed among individuals who were exposed to alcohol *in utero*. For the purpose of the present study, the term FASD will be used in general to refer to individuals

exposed to alcohol *in utero*. The term FAS will only be used in those cases where the criteria for this particular diagnosis have been met.

1.3. Epidemiology

In the United States, the rate of FAS is estimated to range from 0.33 per 1000 (Abel & Sokol, 1991) to 2.2 per 1000 (Abel & Sokol, 1987). The average for the developed world is estimated at 0.97 per 1000 (Abel, 1995). Recent South African studies, making use of active case ascertainment found very high rates of FAS in schools in the Western Cape (May et al., 2000; Viljoen et al., 2005). These studies have respectively documented rates of 18 – 141 times (May et al., 2000) and 33-148 times (Viljoen et al., 2005) greater than in the United States.

Although both these studies focused on a specific community in the Western Cape, making it difficult to generalise their findings to the rest of the country, they do seem to indicate a high prevalence of FAS in South Africa in general, and in the Western Cape in particular (Viljoen et al., 2005). This is a grave source of concern given that FAS is the most common preventable cause of intellectual disability (Rasmussen, 2005).

Research shows that low socio-economic status (SES); fewer social resources (such as education, income and spirituality); as well as having a husband or partner who drinks, are the most important cofactors that combine with heavy episodic drinking to produce FAS (May et al., 2000; May et al., 2005; Viljoen et al., 2005). These factors point to significant psychosocial dysfunction in the families and wider community of children with FASD.

1.4. A biopsychosocial understanding of the impact of *in utero* alcohol exposure

In addition to psychosocial difficulties, individuals exposed to alcohol *in utero* often suffer from behavioural and cognitive deficits due to pathological changes to the brain (Riley, McGee, & Sowell, 2004). In the neuropsychological literature, a distinction is often made between primary and secondary disabilities. In the case of individuals exposed to alcohol *in utero*, primary disabilities refer to the cognitive and behavioural deficits that can directly be attributed to alcohol exposure, such as intellectual disability, executive dysfunction and other neuropsychological deficits (Welch-Carre, 2005). Secondary disabilities refer to the long-term behavioural consequences associated with FASD. These consequences include mental health problems, going to jail, inappropriate sexual behaviour and substance abuse (Welch-Carre, 2005). Executive dysfunction and its behavioural, emotional and social ramifications may in part account for some of the "secondary disabilities" commonly observed in children with FASD (Koditwakku, May, Clericuzio, & Weers, 2001).

In the neuropsychological literature, interaction between the direct effects of brain damage and psychosocial factors are seen to influence the prognosis of children who have sustained cerebral damage (Anderson, Northam, Hendy, & Wrenall, 2001). Thus there is an urgent need to not only understand the psychosocial context of FASD, but also to expand our neuropsychological understanding of the cognitive deficits associated with it.

By investigating the development of executive function in children exposed to alcohol *in utero* the present study will contribute to this effort. This study specifically drew its sample from communities in the Western Cape, since studies have shown that this area has an extraordinary high rate of FAS when compared to the rest of the

world (May et al., 2000; Viljoen et al., 2005). Long-term, it is hoped that a better understanding of the neuropsychological consequences of *in utero* alcohol exposure will aid the development of appropriate intervention strategies, such as the cognitive-behavioural approach to teaching executive thinking strategies to children with disorders of executive function suggested by Marlowe (2000). This could in turn possibly prevent the manifestation of some of the "secondary disabilities" discussed above.

Chapter 2: Literature review

2.1. Prenatal and postnatal cerebral development

In utero exposure to alcohol leads to neurobehavioral deficits, related to central nervous system dysfunction (Riley, McGee, & Sowell, 2004). Although a full review of the literature on pre- and postnatal cerebral development is beyond the scope of this study, a number of aspects of CNS development are relevant to understand the cognitive and behavioural consequences of *in utero* exposure to alcohol. Knowledge of the biological processes and timing of brain maturation not only allows us to predict the consequences of pre- and postnatal insult, but also allows for the identification of parallels between specific stages of brain development and associated cognitive processes (Anderson et al., 2001b), in this case specifically those associated with executive function.

2.1.1. Prenatal cerebral development

Prenatal cerebral development is primarily concerned with structural formation and is thought to be largely genetically determined (Anderson et al., 2001b; Toga, Thompson, & Sowell, in press). The development of the CNS commences early in gestation, around day 40 of embryonic life, and continues into adulthood (Anderson et al., 2001b). The fertilised cell experiences rapid cell division which results in the formation of the embryonic disc, which in turn is made up of three layers which later form specific organic systems within the human body (Nowakowski, 1993). The nervous system emerges via a process of neurolation from the outer layer of the embryonic disk, which folds into itself and forms the neural tube (Nowakowski, 1993). Cell generation within the neural tube occurs via mitosis or division, and cells

then migrate to predetermined locations within the nervous system (Nowakowski, 1993). Once neurons have migrated, they begin the process of differentiation via the development of cell bodes, dendritic and axonal growth and formation of synaptic connections (Anderson et al., 2001b; Toga et al., in press). During this stage cells become members of specialised systems and, as connections among neurons become established, they begin to function. In addition, redundant neurons are eliminated through a process of selective cell death. This process of differentiation continues postnatally, with some processes, such as the myelination of axons, only reaching completion in the second decade of life (Anderson et al., 2001b; Toga et al., in press).

A variety of aetiological factors could cause disruptions to prenatal development. These include biological factors, such a genetic mutations, trauma, and infections, as well as environmental factors, such as poor maternal nutrition, lead or radiation exposure and maternal alcohol or drug use (Anderson et al., 2001b).

Alcohol is a potent teratogen which causes cell death by both necrosis and apoptosis in the developing foetus and embryo (Goodlett & Horn, 2001; Welch-Carre, 2005). In addition, alcohol interferes with normal CNS development in a variety of other ways: by causing oxidative stress, by affecting the binding of growth factors in the CNS, by adversely affecting glial cells, which guide the migration of neurons in the brain, and by affecting the development of neurotransmitter systems such as serotonin and glutamate (Goodlett & Horn, 2001; Welch-Carre, 2005).

Initially it was believed that damage to the immature brain would yield a better prognosis than equivalent damage in adults, since there is some evidence that the cognitive functions subsumed by damaged brain tissue have the capacity to transfer to other, healthy, areas of the brain (Duchowny et al., 1996; Rasmussen & Milner, 1977). This position, called the 'plasticity' theory, argues that functional organisation

is less established in the immature brain than in the mature brain, leading to a greater capacity for recovery of function after insult (Anderson et al., 2001b). However, the notion of transfer of function is currently under debate since the extent to which it occurs seems to vary depending on the timing (i.e. pre-, postnatal) and nature (i.e. focal, generalised) of insult (Anderson et al., 2001b).

'Early vulnerability' theorists have argued that early brain insults, particularly those that occur prenatally or within the first year of life are particularly detrimental to the development of cognitive functions (Anderson et al., 2001b). This hypothesis is supported by findings that transfer of function does not occur in cases where brain damage was sustained that early in development (Duchowny et al., 1996; Riva & Cazzaniga, 1986). Early vulnerability theorists contend that even if transfer of function occurs after cerebral insult, such reorganisation of function would lead to 'overcrowding' in healthy areas of the brain, thus leading to a general depression of all abilities (Anderson et al., 2001b).

Autopsy and neuroimaging studies have shown that *in utero* exposure to alcohol leads to a variety of neuroanatomical changes in both animals and humans (Chen, Maier, Parnell, & West, 2003). For the purpose of the present study, only the literature pertaining to humans will be reviewed. Although the human autopsy data is limited, several studies have shown that *in utero* alcohol exposure has a damaging effect on the structural organisation of the brain (Mattson & Riley, 1996). Thus these studies have found widespread CNS disorganization, including microcephaly, corpus callosum, basal ganglia, and cerebellar anomalies, and neuroglial heterotopias following *in utero* exposure to alcohol (Clarren, Sumi, Streissguth, & Smith, 1978; Coulter, Leech, Schaefer, Scheithauer, & Brumback, 1993; Ferrer & Galofre, 1987; Jones & Smith, 1973). These findings suggested such variable, widespread and

diffuse damage that some researchers concluded that the localization of brain damage due to *in utero* exposure to alcohol may be impossible (Riley et al., 2004).

However, it is important to note that those who survive *in utero* exposure to alcohol are probably less severely affected than those who succumb (and subsequently come to autopsy) (Riley et al., 2004). Moreover, neuropsychological studies (discussed below) indicate that individuals with FASD suffer from common types of behavioural and cognitive deficits, thus suggesting similar pathological changes to the brain (Riley et al., 2004).

Modern neuroimaging studies, making use of structural magnetic resonance imaging (MRI), have shown that specific brain structures are disproportionately affected by prenatal alcohol exposure (Riley et al., 2004). Thus these studies not only indicate an overall reduction in brain size (Johnson, Swayze, Sato, & Andreasen 1996; Riikonen, Salonen, Partanen, & Verho, 1999; Robin & Zachai, 1994; Swayze et al., 1997), but also a reduction in cerebellar volume (Autti-Rämö et al., 2002; Mattson, Riley, Delis, Stern, & Jones, 1996; Sowell et al., 1996), thinning and agenesis of the corpus callosum (Autti-Rämö et al., 2002; Clark, Li, Conry, Conry, & Loock, 2000; Riikonen et al., 1999; Riley et al., 1995; Swayze et al., 1997), small hippocampi (Autti-Rämö et al., 2002), as well as a reduction in the overall size of the basal ganglia (Mattson et al., 1992), particularly the caudate nucleus (Archibald et al., 2001) following intrauterine alcohol exposure.

The latter finding, indicating structural changes of the basal ganglia, specifically the caudate nucleus, is also supported by the functional neuroimaging data. Clark et al. (2000) made use of positron emission tomography (PET) to assess the brain activity of adolescents and adults with FAS. Their results showed reduced metabolic activity in the caudate nucleus and thalamus when the subjects were at rest.

These findings are especially relevant given the striking deficits in executive function observed in individuals with FASD (discussed in detail below). The basal ganglia have rich neural connections to the frontal lobes of the brain, which are traditionally seen as mediating executive functions (Eslinger & Grattan, 1993). Research has shown that both circumscribed basal ganglia pathology and focal damage to the frontal lobes causes similar deficits in cognitive flexibility (an important aspect of executive function) (Eslinger & Grattan, 1993). Accordingly, reduction in the size and metabolic activity of the caudate nucleus due to *in utero* alcohol exposure may account for some of the executive deficits observed in individuals with FASD (Mattson, Schoenfeld, & Riley, 2001).

Kodituwakku, Kalberg and May (2001) have remarked on the lack of evidence for structural changes to the prefrontal cortex per se, the area of the brain most often implicated in executive function. They hypothesised that structural abnormalities to the basal ganglia, reduced white matter volume (Archibald et al., 2001) and abnormalities in the corpus collosum (Autti-Rämö et al., 2002; Clark et al., 2000; Riikonen et al., 1999; Riley et al., 1995; Swayze et al., 1997) may cause abnormal connectivity among brain regions, thus leading to executive dysfunction (Kodituwakku et al., 2001a). However, a recent structural MRI study has demonstrated highly significant decreased brain surface in the ventral aspects of the frontal lobes, particularly in the left hemisphere (Sowell et al., 2002). These structural changes to the prefrontal cortex (Sowell et al., 2002) in conjunction with abnormal cortico-cortical or cortico-subcortical functional connectivity (Koditwakku et al., 2001a) may account for the executive deficits observed in individuals with FASD.

MRI studies suggest that brain growth continues to be adversely affected long after *in utero* insult due to alcohol exposure (Sowell et al., 2001). Prenatal structural changes to the brain therefore appear to affect the maturational processes of the brain which continues postnatally. This will in turn affect the development of cognitive abilities (Stuss, 1992).

Although there have been no neuropsychological studies to date examining the development of executive function in children exposed to alcohol *in utero,* available data suggests that individuals with FASD present with significant executive deficits, and that these deficits persist into adulthood (Conner, Sampson, Bookstein, Barr, & Streissguth, 2000; Kerns, Don, Mateer, & Streissguth, 1997; Malisza et al., 2005). Although limited, the available neurological and neuropsychological evidence fits well with early vulnerability theories which postulate that early brain damage will lead to the emergence of mounting deficits as cognitive functions mature throughout childhood and adolescence (Anderson et al., 2001b). It was therefore hypothesised that children exposed to alcohol *in utero* will display delays in the development of executive function which will become more prominent with age.

2.1.2. Post-natal cerebral development

The brain quadruples in size from birth to adulthood. This increase in size is not due to a proliferation in neurons, since the full complement of neurons is established prenatally (Anderson et al., 2001b). Instead, the increase in size reflects ongoing elaboration within the CNS, primarily due to three processes: dendritic arborisation, synaptogenesis and myelination (Anderson et al., 2001b; Toga et al., in press). This process of growth and specialisation is driven by a precise genetic programme,

although it is important to note that environmental influences play an important part in its modification (Toga et al., in press).

Histological studies suggest that the time-course for these processes vary greatly by brain region (Toga et al., in press). Interestingly, the frontal regions of the brain, which are associated with executive function, are the last to mature (Anderson et al., 2001b; Toga et al., in press). Electroencephalogram (EEG) and neuroimaging studies have found similar results. EEG studies have shown growth spurts in frontal lobe intracortical connections in the post-natal period (Thatcher, 1992). MRI studies have shown prominent age-related changes in grey matter, white matter and cerebrospinal fluid volume during childhood. These changes appear to reflect ongoing maturation and remodelling of the CNS (Geidd et al., 1999; Reiss, Abrams, Singer, Ross, & Denckla, 1996). Both cross-sectional (e.g. Reiss et al., 1996) and longitudinal MRI studies (e.g. Geidd et al., 1999) suggest that post-natal cerebral development is largely hierarchical in nature, with tertiary association areas (including the prefrontal cortex) only reaching maturation in puberty.

A number of researchers and theorists have remarked on the striking similarities between the stages of brain maturation discussed above and stages of cognitive development (Case, 1992; Hudspeth & Pribram, 1990; Segalowitz & Rose-Krasnor, 1992; Stuss, 1992). Models of cognitive development, such as Piaget's (1963) theory of cognitive development, strongly support the idea of a hierarchical development of cognitive functions. According to this theory, cognitive development progresses in four sequential stages: the Sensorimotor stage (birth to 2 years), the Preoperational stage (age 2 to 6 years), the Concrete Operational stage (age 7 to 11 years) and the Formal Operational stage (age 12 to adulthood) (Piaget, 1963). Although Piaget (1963) did not make specific reference to neural substrates in his theory, it is

interesting to note that the timing of transitions in the cognitive stages he proposed have been found to coincide quite closely with growth spurts in the CNS (Hudspeth & Pribram; Thatcher, 1992).

Contemporary developmental theorists have argued that cognitive abilities do not undergo a fixed progression across all domains of cognitive functioning simultaneously (Anderson et al. 2001b), as suggested by Piaget (1963). Instead, modern studies seem to indicate that different aspects of cognitive function have different, albeit inter-related, developmental time-frames (Anderson et al., 2001b).

In the model proposed by Stuss (1992) cognitive abilities are conceptualised as being hierarchical in nature with three levels of monitoring or 'feedback-feedforward' systems. According to this model, neuropsychological information at the lowest level is sensory/perceptual. This information is domain- or module-specific and is mainly processed by posterior parts of the brain (Stuss & Benson, 1986; Stuss, 1992). These processes are virtually automatic and provide the basis of daily ongoing behaviour (Stuss, 1992).

The second level is executive control and refers to the supervisory or executive functions associated with the frontal lobes (Stuss & Benson, 1986; Stuss, 1992). Input for this level is primarily derived from the information elaborated on by the sensory/perceptual level and thus depend on the reciprocal connections between the frontal lobes, posterior areas and limbic structures (Stuss, 1992).

The third and highest level is consciousness, "the ability to be aware of oneself and the relation of self to the environment" (Stuss, 1992, p. 12). At this level, inputs are primarily abstract mental representations that are integrated by prefrontal cortex. It is therefore postulated that the prefrontal cortex "attends, integrates, formulates,

executes, monitors, modifies, and judges all nervous system activities" (Stuss & Benson, 1986, p. 248).

This model of cognitive abilities fits well with the findings of studies investigating the biological maturation of the brain (reviewed above), which indicate that development is largely hierarchical in nature, with tertiary association areas (including the prefrontal cortex) only reaching maturation in puberty. In addition, the neuropsychological data (reviewed below) indicate that the development of executive functions is largely hierarchical in nature (Anderson, 2002).

The apparently parallel developmental sequences in brain maturation and executive abilities may indicate that these two processes are somehow interrelated (Stuss, 1992). Stuss's (1992) hierarchical feedback-feedforward model fits well with both the biological and neuropsychological data, since the differential timing in the development of specific functions seem to relate to the hierarchical order of the schema. Moreover, since his model ties the three proposed levels to different areas of the brain, it implies that biological maturation, as well as the timing of such maturation is critically important (Stuss, 1992). Damage to the brain, or delays in its maturation, could therefore account for specific developmental problems (Stuss, 1992), including those observed in children with FASD.

2.2. A developmental model for executive function

Neuropsychological theories often take a 'localisationist' approach (Luria, 1973) which ascribes specific cognitive and behavioural functions to specific cortical regions (Anderson et al., 2001b). These theories are often based on studies investigating the pattern of cognitive deficits associated with lesions to specific areas of the brain in adults (Luria, 1973). It is not clear how applicable these theories are

in a developmental context (Anderson et al., 2001b). As mentioned above, theorists such as Stuss (1992) are starting to develop neuropsychological models which would allow for a better understanding of the consequences of brain damage in the developing brain.

The following section focuses on discussing theoretical models of executive function, linking such models to the developmental context. In addition, studies investigating the development of executive function in children and adolescents are reviewed. Finally, some of the psychosocial influences on the development of executive function are considered.

2.2.1. Conceptualising executive function

Modern theories of executive function conceptualise it as "multiple process related systems, that are inter-related, inter-dependent and function together as an integrated supervisor or control system" (Anderson, 2002, pp. 72-73). In the model proposed by Alexander and Stuss (2000) and Anderson (2002), executive function is seen as being made up of four discrete executive domains namely: (i) attentional control: selective attention, sustained attention, and inhibition; (ii) information processing: fluency, efficiency, and speed of output; (iii) cognitive flexibility: attentional shift, self-monitoring, working memory; and (iv) goal setting: initiating planning, problem solving.

Damage to the prefrontal cortex of the brain often gives rise to specific cognitive deficits such as poor impulse control, difficulty in monitoring behaviour, poor planning and organisational abilities, difficulties in generating and implementing problem solving strategies, perseveration, poor utilisation of feedback, and reduced

working memory (Anderson, 2002; Anderson et al., 2001b; Fuster, 1989; Grattan & Eslinger, 1991; Stuss & Benson, 1986). In other words, impairment to those functions that constitute the construct executive functions. This has led to a tendency in the literature to use the terms frontal lobe functions interchangeably with executive functions (Marlowe, 2000). This is problematic, since it limits the way in which executive function is defined and investigated (Marlowe, 2000).

The neural systems that underpin executive functions are numerous, complex and inter-related (Stuss & Benson, 1986). The prefrontal cortex itself is usually divided into three cortical surfaces: dorsolateral, orbital, and medial, and there is some evidence of differential involvement of each of these structures in some cognitive functions (Luria, 1966/1980; Stuss & Benson, 1986). In addition, both efferent and afferent connections link the prefrontal cortex with almost all other cortical structures, including the brain stem, occipital, temporal, and parietal lobes, as well as with limbic and subcortical structures (Stuss & Benson, 1986). Executive dysfunction may therefore occur not only as a consequence of prefrontal pathology per se, but also due to network disconnections, such as white matter damage or lesions to other areas of the brain (Alexander & Stuss, 2000; Eslinger & Grattan, 1993).

Making the distinction between executive functions and frontal functions is particularly important in a developmental context, since "the development of 'frontal functions' may relate not only to anatomical/biochemical maturation of the frontal lobes but also to the integrative demands of tasks on multiple brain regions" (Stuss, 1992, p. 9). This implies that even though the frontal lobes, and the prefrontal cortex in particular, may play a vital role in mediating executive function, the integrity of the whole brain is necessary for efficient executive function (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001).

2.2.2. The development of executive function in children

Initially it was believed that executive functions only emerged functionally in the second decade of life when the frontal lobes reached maturity (Anderson, 2002). However, a growing body of neuropsychological research suggest sequential changes in executive abilities from as early as age 12 months (Diamond, 1985; Diamond & Doar, 1989; Epsy, Kaufmann, McDiarmid, & Glisky, 1999).

A number of researchers have made use of the classic AB task developed by Piaget (1954) to investigate the development of executive function in infants (Diamond, 1985: Diamond & Doar, 1989: Epsy et al., 1999). In this task, the infant observes as a toy is hidden in one of two identical wells, location A. After a brief delay the infant is allowed to reach for the toy in location A over several trials. The contingency is then reversed, with the toy being hidden at location B. Infants younger than 12 months tend to search for the reward at location A, whereas older infants are able to correctly retrieve the reward at location B (Diamond, 1985; Diamond & Doar, 1989; Epsy et al., 1999). According to Piaget (1954), the cognitive mechanism of faulty object permanence underlies the poor performance of younger infants, in that infants younger than 12 months are unable to mentally represent the object independently of the motoric act of retrieval on the previous trial. However, modern researchers have argued that young infants' inability to successfully complete this task may reflect the immaturity of the prefrontal cortex at this age, and that successful completion of this task depends on whether executive abilities, particularly working memory and the ability to inhibit a previously learned response, have become 'on-line' (Diamond, 1985; Epsy et al., 1999)

This renewed interest in the AB task as a measure of the early manifestations of executive behaviour in infants was largely prompted by similarities between the AB

task and the delayed response task from the animal neuroscience paradigm (Epsy et al., 1999). Research findings indicating similar perseverative error patterns on the AB task and the delayed response task in frontally ablated adult monkeys and intact 7- to 12-month-old human infants, led to the hypothesis that frontal lobe maturation underlies the developmental changes in AB performance observed during late infancy (Epsy et al., 1999). This hypothesis is supported by findings that 7- to 12-month-old infants who are able to successfully complete the AB task show increased frontal brain electrical activity as well as increased anterior to posterior EEG coherence when compared to their peers who are not able to complete the task successfully (Bell & Fox, 1992).

Developmental and normative studies indicate that significant gains are made in various aspects of executive function during early and middle childhood with most executive abilities being established by adolescence (Stuss, 1992; Anderson, 2002). However, it is important to note that this sequence of development is not necessarily linear in nature, and that the development of at least some executive functions occurs in spurts (Anderson, 2002). In addition, research indicates that components of executive function may demonstrate different developmental trajectories (Anderson, 2002).

Luciana and Nelson (1998) investigated the functional emergence of executive abilities in a sample of 181 four- to eight-year-olds through the use of the Cambridge Neuropsychological Test Automated Battery (CANTAB). Their results indicated age-related improvements in task performance on all measures of executive function and working memory. Four-year-olds performed worse than 5- to 7-year-olds on all tasks, including tasks that assess the ability to respond quickly to sensory stimuli. This led these researchers to hypothesise that 4-year-olds' poor performance on tests

of complex problem solving ability and working memory may be related to immaturity within the sensori-motor circuitry. Thus their findings suggested that cortico-cortical and coritco-striatial circuitry is no yet completely organised in 4-year-old children. This may be because of immaturity in specific structures, or because the interconnections between these structures are not fully established yet (Luciana & Nelson, 1998). These findings highlight the fact that efficient performance on tests of executive function depend on the maturity of the whole brain (Stuss, 1992).

In terms of older children, age 5- to 7-years, Luciana and Nelson (1998) demonstrated efficient performance on a spatial working memory task and measure of complex problem solving ability, which could possibly be attributed to a growth spurt during this period of development. However, it is important to note that 5- to 7-year-olds performance on these measures of executive function appeared to be critically mediated by task difficulty. Thus children in these age groups performed at adult levels on the easier items of the tasks, while their performance broke down on the more difficult items (Luciana & Nelson, 1998). It therefore appears that when task demands increase, the performance of 5- to 7-year olds deteriorates, perhaps because of the multiplicity of functions the prefrontal cortex is called upon to perform (Luciana & Nelson, 1998). Similar findings were obtained for 8-year-olds who performed more like adults on all measures, although their performance broke down on tasks that required the integration of various aspects of executive function simultaneously (Luciana & Nelson, 1998).

In a second study making use of the CANTAB, De Luca et al. (2003) demonstrated varied developmental trajectories for different components of executive function in a sample of 194 participants ranging from age 8 to age 64 years. Their findings indicated that adult levels of attentional set-shifting ability are obtained by

age 8, whilst functional increments occur in working memory capacity up to the age of 15-19 years and in the strategic planning and organisation of goal directed behaviour up to the age 20-29 years (De Luca et al., 2003). Moreover, their findings suggested that fluctuations in performance on measures of strategic planning and organisation of goal directed behaviour occurred between the ages of 11 and 14 years (De Luca et al., 2003). They hypothesised that the efficiency of executive function improves with age as cortico-cortical connections develop in late adolescence. This maturation allows these cognitive processes to become more comprehensive and flexible in adulthood. The variability of performance during adolescence can therefore be understood as reflecting the increased capacity in neuronal circuitry during this stage of development, although the adolescent is still unable to effectively implement these new found skills (De Luca et al., 2003).

This conclusion is supported by previous studies. Anderson, Anderson and Garth (2001) demonstrated age-related variation in strategy formation on the Rey Complex Figure Test, a complex drawing task which taps executive functions such as planning and organisation skills, in a sample of 376 children between age 7 years 0 months and 13 year 11 months. Their results indicated that older children, between the ages of 12- to 13-years made use of fragmented strategies more often than younger children, leading these researchers to conclude that organisation skills may not be consolidated until middle to late adolescence.

Klenberg, Korkman and Lahti-Nuuttilla (2001) demonstrated sequential changes in attention and executive function in a sample of 400 3- to 12-year-old Finnish children. Their findings suggest accelerated maturation of executive abilities during early and middle childhood. Similarly to the present study, these researchers made use of various subtests of the NEPSY and found evidence of developmental changes

in even the youngest age groups, children aged 3 to 5 years (Klenberg et al., 2001). Consistent with the findings of Luciana and Nelson (1998) and De Luca et al. (2003), their findings indicated that different aspects of executive function display different developmental trajectories. Thus their results showed that motor inhibition and impulse control as tested by the Statue subtest reached mature levels by age 6 (Klenberg et al, 2001). On a more complex test of inhibition, the Knock and Tap subtest, the level of 12-year-olds was reached by age 7 (Klenberg et al, 2001). While a levelling off of performance, indicative of relative maturity, was reached on a test measuring strategic planning (the Tower subtest) by age 8 (Klenberg et al, 2001). Relative maturity was reached in subtests of focussed attention by age 10; with only minor improvements noted after this age (Klenberg et al, 2001). Finally, performance on tests of fluency, such as the Design Fluency subtest and Phonemic Fluency subtest, which place demands on the executive functions of initiation and strategy, did not show a levelling off in even the oldest age groups. This led Klenberg et al. (2001) to conclude that these aspects of executive function most probably continue to develop into late adolescence. However, these findings were not corroborated by Anderson et al. (2001a) who demonstrated a relatively flat developmental trajectory from early to late adolescence on a test of verbal fluency. These researchers found that while attentional control and processing speed gradually increased during adolescence, age trends were less evident on measures of cognitive flexibility and fluency (Anderson et al., 2001a).

Integrating these findings is problematic, especially given that different measures of executive function was utilised in different studies. Nonetheless, some broad conclusions can be drawn. The findings of developmental and normative studies suggest that attentional control emerges in infancy (Diamond, 1985; Diamond &

Doar, 1989; Epsy et al., 1999) and is relatively well developed by age 10 (Klenberg et al., 2001), although more gradual improvements have also been noted during adolescence (Anderson et al., 2001b). In contrast, other aspects of executive function such as cognitive flexibility, goal setting, and information processing appear to experience a critical period of development between the ages of 7 and 9 years and only to achieve relative maturity by age 12 (De Luca et al., 2003; Klenberg et al., 2001; Luciana & Nelson, 1998).

This complicates our understanding of executive function in children tremendously and implies that executive dysfunction due to brain damage may have different behavioural and cognitive manifestations depending on the developmental age of the child (Anderson, 2002). Although executive deficits following *in utero* exposure are well documented, previous studies have not situated their findings in developmental framework (Rasmussen, 2005). The present study aimed to address this shortcoming in the literature.

2.2.3. Psychosocial influences on the development of executive function

Psychosocial factors are known to have an impact on the development of cognitive functions (Anderson et al., 2001b). A number of psychosocial factors, such as the quality of the mother-child relationship, amount of stimulation available to the child, and access to health and educational resources may have an impact on development (Anderson et al., 2001b). Thus, for example, it is well known that children from disadvantaged communities are more highly represented at the lower end of the IQ distribution (Anderson et al., 2001b).

The impact of psychosocial factors on the development of executive function has previously been studied by Ardila, Rosselli, Matute and Guajardo (2005). These researchers examined the relationship between parents' education level and the type of school the child attended (private or public school) and children's performance on tests of executive function. Their findings indicated a significant correlation between parents' level of education and most measures of executive functioning. In addition, children attending private schools were found to perform significantly better than children attending public schools on almost all tests of executive function (Ardila et al., 2005).

In their study, Klenberg et al. (2001) found that parent level of education was connected to a better performance on tests of visual and verbal fluency, and to a lesser extent, to performance on tests of planning and strategy, but not to performance on tests of inhibition or attention. They hypothesised that the development of some executive functions, particularly planning and fluency may be related to environmental factors, such as the amount of stimulation the child receives at home. Other aspects of executive function, such as attention and inhibition, which matures earlier, may depend more strongly on neural maturation (Klenberg et al., 2001). However, it should be kept in mind that biological factors may play a role in the level of education parents' obtain, since this may also be an expression of genetic tendencies (Klenberg et al., 2001).

It is especially important to keep the influence of psychosocial factors in mind when studying the cognitive function of children exposed to alcohol *in utero*. These children are often exposed to significant psychosocial stressors, such as low SES having parents that abuse alcohol, and frequent changes in living circumstances due to fostering or adoption (May et al., 2005; Viljoen et al., 2005) These psychosocial

stressors may have a profound impact on the development of executive function in this population.

2.3. The effect of *in utero* exposure to alcohol on executive function

In utero exposure to alcohol leads to a range of neurocognitive impairments, the severity of which is related to the quantity and duration of exposure (Korkman, Kettunen, & Autti-Rämö, 2003), and therefore the extent of structural damage to the brain (Riley et al, 2004). As mentioned above, studies have demonstrated that a variety of cognitive domains, such as language, motor function, learning, memory, and visuo-spatial abilities are adversely affected by *in utero* exposure to alcohol (Korkman et al., 2003; Mattson et al., 1996; Mattson et al., 1997; Mattson et al., 2001; Stratton et al., 1996; Streissguth et al., 1991). In addition, many studies have found marked impairments in the domain of attention and executive function (Carmichael Olson et al., 1998; Kodituwakku et al., 1995; Mattson et al., 1999; Noland et al., 2003; Schonfeld et al., 2001; Streisguth et al., 1990).

The sheer diversity of cognitive impairments noted in the literature seem to suggest that *in utero* exposure to alcohol causes relatively generalised cognitive impairment (Korkman et al., 2003). The question therefore arises whether a focus on specific cognitive impairments, in this case executive function, is warranted? However, as will be discussed in detail below, studies have demonstrated that a general lowering of IQ scores does not fully explain specific cognitive deficits (Carmichael Olson et al., 1998; Conner et al., 2000; Kerns et al., 1997). This suggests that certain cognitive functions may be especially sensitive to the effects of *in utero* exposure to alcohol (Korkman et al., 2003). In addition, it is important to note that even though executive function may not be *more* affected than other cognitive

domains (Korkman et al., 2003), deficits in executive function may account for many of the behavioural features commonly observed in children with FASD (Koditwakku, Kalberg, & May, 2001). This underlines the importance for more research to be conducted on the executive abilities of individuals who were exposed to alcohol *in utero*. We now turn to a review of the literature pertaining to this area of research.

2.3.1. FASD and executive dysfunction

Studies have demonstrated that individuals exposed to alcohol *in utero* exhibit deficits on a number of aspects of executive function, such as cognitive flexibility (Mattson et al., 1999), inhibition (Mattson et al., 1999; Noland et al., 2003), planning and the use of strategy (Kodituwakku et al., 1995; Mattson et al., 1999), verbal reasoning (Mattson et al., 1999), set shifting (Kodituwakku et al., 1995), verbal and non-verbal fluency (Schonfeld et al., 2001), and working memory (Carmichael Olson et al., 1998; Kodituwakku et al., 1995; Malisza et al., 2005; Streissguth et al., 1990). Deficits in attention are often seen as one of the most salient features of FASD (Coles, 2001; Lee, Mattson & Riley, 2004), and its presence in children exposed to alcohol *in utero* is well established (Coles, Platzman, Raskin-Hood, Brown, Falek, & Smith, 1997; Kodituwakku, May, Clericuzio, & Weers, 2001; Mattson, Calarco, & Lang, 2006; Streissguth et al., 1994).

The attentional deficits present in children with FASD have often been equated with those present in children with Attention Deficit Hyperactivity Disorder (ADHD) (American Psychiatric Association [APA], 2000) since clinical descriptions of FAS and its spectrum often cite ADHD as one of its clinical manifestations (Coles, 2001). However, studies suggest that these two groups of children have unique attentional profiles (Coles et al., 1997).

As mentioned above, attentional control is considered to be an important sub-domain of executive function (Alexander & Stuss, 2000; Anderson 2002). In a model of attention proposed by Mirsky, Anthony, Duncan, Ahern and Kellam (1991), attention is subdivided into four sub-factors. These factors are: *focus,* which refers to the ability to selectively attend to appropriate information; *sustain,* which refers to the ability to maintain focussed vigilance in perceiving a signal; *encode* refers to the ability to maintain information in working memory while performing a cognitive process that involves that information; and *shift,* which refers to the ability to shift attention from one task to another and involves executive functions such as cognitive flexibility (Mirsky et al., 1991).

There is some disagreement in the literature as to which aspects of attention are impaired in individuals with FASD. Some studies have demonstrated that focussed attention is particularly impaired in children with FASD (Mattson et al., 2006), whilst others demonstrated selective deficits in these children's ability to shift attention (Coles et al., 1997; Kodituwakku et al., 2001) and encode new information (Coles et al., 1997). Nonetheless, attentional abilities appear to be one of the core cognitive functions which are impaired in children with FASD, with some studies demonstrating that the presence of these deficits can be used to distinguish children exposed to alcohol *in utero* from non-exposed children with a high degree of accuracy (Lee et al., 2004).

Deficits in executive function have been demonstrated in children as young as 4 years of age (Noland et al., 2003), although the bulk of the research has focused on school-aged children and adolescents with FASD (Carmichael Olson et al., 1998; Kodituwakku et al., 1995; Mattson et al., 1999; Schonfeld et al., 2001). In addition, these deficits have been shown to extend into adulthood (Conner et al., 2000; Kerns et

al., 1997; Malisza et al., 2005). However, limited evidence exists regarding the longitudinal course of these deficits. In one of the few longitudinal studies, Streissguth et al. (1999) demonstrated that deficits in executive function (particularly deficits in attention and inhibition) are present prior to age 7 and persist into adolescence. However, it is important to note, that unlike the present study, Streissguth et al. (1999) made use of different measures of attention and executive function at different developmental ages, making it difficult to establish whether these deficits improve, deteriorate, or remain static with age.

A number of studies suggest that children exposed to alcohol *in utero* present with similar neuropsychological deficits, irrespective of whether or not they meet the diagnostic criteria for FAS (Mattson et al., 1999; Schonfeld et al., 2001). Mattson et al. (1999) made use of the Delis-Kaplan Executive Function Scale to evaluate the executive function of 18 children (aged eight to 15 years) with heavy *in utero* alcohol exposure, with and without a diagnosis of FAS, and compared them with non-exposed controls. They found specific impairments within the domains of planning, inhibition, abstract thinking and cognitive flexibility in both alcohol-exposed groups. In most cases, with the exception of the switching condition of the Stroop test, the two alcohol exposed groups did not differ significantly from each other. Similar results were found by Schonfeld et al. (2001) who compared 18 children with heavy *in utero* alcohol exposure with and without FAS to non-exposed controls on the design and verbal fluency measures from the Delis-Kaplan Executive Function System. Their results indicated that compared to control participants, children with heavy prenatal alcohol exposure displayed deficits in both verbal and non-verbal fluency. No significant differences were found between alcohol-exposed children with and without the facial features of FAS (Schonfeld et al., 2001). Executive function therefore

appears to be adversely affected even in those cases where no facial dysmorphology is present (Mattson et al., 1999; Schonfeld et al., 2001).

Research has shown that cells in the CNS have a lower threshold for alcohol, and that these cells may therefore experience more rapid cell death than other cells in the embryo (Dunty et al, 2001). This may explain why some individuals present with significant CNS dysfunction despite normal facial characteristics (Welch-Carre, 2005).

In addition, it is important to note that there is a highly specific window period in gestation, roughly around the first trimester, during which alcohol exposure must occur to produce the characteristic facial features of FAS (Rasmussen, 2005). The facial features of FAS can therefore not be used as an indicator of the severity of the damage caused by *in utero* exposure to alcohol (Connor et al., 2000). We now turn to a more detailed exploration of the possible contributing factors to the striking deficits in executive function observed in individuals with FASD.

2.3.2. The relationship between executive function and concomitant skills

Theoretical models of executive function (discussed above) generally conceptualise executive function as involving the integration of basic cognitive processes such as motor activity, sensation, perception, and memory (Stuss, 1992). Executive abilities are therefore seen as being dependent on intact basic cognitive processes (Stuss, 1992). In children exposed to alcohol *in utero*, basic cognitive processes are often impaired (Korkman et al., 2003; Mattson et al., 2001; Mattson et al., 1997; Mattson et al., 1996; Stratton et al., 1996; Streissguth et al., 1991). These deficits may in part account for the executive deficits observed in individuals with FASD. Although this hypothesis has not been tested directly, it is supported by a

study conducted by Korkman et al. (2003) who performed a comprehensive assessment of the neuropsychological functioning of 27 children between the age of 12 and 14 years with FAS or FAE. Compared to non-exposed control participants, children who were exposed to alcohol *in utero* performed poorly on the attention and executive function, language, visuomotor function, and memory subtests of the NEPSY. Although impaired, attention and executive function were not found to be disproportionally affected in comparison to other domains of cognitive functioning (Korkman et al., 2003).

However, it is important to note that although deficits in basic cognitive processes may to some extent account for the executive deficits observed in children with FASD, research has shown that these deficits are not simply due to impairment in basic skills. Thus Mattson et al. (1999), for example, have shown that exposed children's performance on the interference and set-shifting tasks of the Stroop test was impaired even after deficits in component skills were considered.

Another concomitant factor that needs to be kept in mind when evaluating the executive function of children with FASD is general intelligence. It is well established that *in utero* exposure to alcohol lowers general intelligence (Mattson et al., 1997; Streissguth et al., 1991). There appears to be a complex overlap between general intelligence and executive function (Conner et al., 2000). Thus Performance IQ, which places an emphasis on fluid intelligence and timed tasks, may be more closely related to executive function than Verbal IQ, which emphasises crystallised intelligence (Connor et al., 2000). The effects of general intelligence on the executive abilities of individuals with FASD have been evaluated by a number of studies. Both Mattson et al. (1999) and Schonfeld et al. (2001) considered general intellectual ability as a potential contributing factor to the executive deficits displayed

by children who were exposed to alcohol *in utero*. However, neither of these studies found a significant relationship between full-scale IQ and their primary executive function measures (Mattson et al., 1999; Schonfeld et al., 2001).

Kerns et al. (1997) investigated the executive function abilities of 16 adults who met the diagnostic criteria for FAS, but were not intellectually disabled. Participants were divided into two groups, an average to above average IQ group and a borderline to low average IQ group. Participants in both groups were found to display deficits in attention and executive function. The severity of these deficits was greater than would have been predicted on the basis of IQ alone (Kerns et al., 1997).

Carmichael Olson et al. (1998) examined the neuropsychological functioning, intelligence and adaptive functioning of 9 adolescents who met the diagnostic criteria of FAS, but were not intellectually disabled, and compared them with a group of 52 non-exposed or minimally exposed children with a similar range of IQ scores. Their results indicated that adolescents with FAS displayed a variety of neuropsychological deficits, including deficits in executive function. In addition, the performance of the participants with FAS could not be fully explained by a general lowering of IQ (Carmichael Olson et al., 1998).

Connor et al. (2001) investigated two possible pathways for impaired executive function in 30 adult men with FAS or FAE; indirectly, through the mediation of IQ, and directly, irrespective of IQ. Their results indicated that the performance of individuals exposed to alcohol *in utero* was lower than predicted on the basis of the participant's IQ score on a number of executive function measures. The executive function scores which appeared to be directly affected by *in utero* exposure to alcohol included scores on the Wisconsin Card Sorting Test (WCST), performance scores on the Stroop task, scores on the Trail Making Test, performance on Ruff's Figural

Fluency Test (RFF), and performance on Consonant Trigrams Test (CTT). These tests assess the ability to shift set, maintain complex attention, perform visuo-spatially mediated tasks, and the ability to maintain and manipulate information in working memory (Connor et al, 2000). *In utero* exposure to alcohol therefore appears to have a direct effect on these aspects of executive function. In contrast, it was found that participants' performance on the Controlled Oral Word Association Test (COWAT), error scores on the Stroop, error scores on the Trail Making Test, perseveration scores on the California Verbal Learning Test (CVLT) and RFF, and Cognitive Estimation scores could be wholly explained by deficits in IQ (Connor et al., 2000). Thus the executive function test scores that appeared to be mediated by IQ were mostly error scores. This led Conner et al. (2000) to conclude that although executive abilities are affected by depressed IQ, alcohol seems to have a direct effect on at least some aspects of executive function above and beyond those expected, given alcohol-related impairments to general intelligence.

These findings are analogous to the well known phenomenon that the adaptive behaviour of individuals with FASD (as measured by tests such as the Vineland Adaptive Behaviour Scale) are often more impaired than is predicted by their IQ scores (Conner et al., 2000). The reasons for these deficits in adaptive behaviour and its link with executive impairments are explored in more detail below.

2.3.3. Socio-emotional functioning and FASD

In utero exposure to alcohol is associated with impaired socio-emotional functioning (Jacobson & Jacobson, 2002). A number of studies have investigated the adaptive and emotional functioning of children with FASD (Carmichael Olson, Feldman, & Streissguth, 1992; Thomas, Kelly, Mattson, & Riley, 1998; Whaley,

Connor, & Gunderson, 2001). Carmichael Olson et al. (1992) administered the Vineland Adaptive Behaviour Scale (VABS), a measure of social skills and emotional maturity to the caregivers of 9 adolescents and 5 adults with FAS. Substantial deficits were noted in the socialisation domain, which assesses interpersonal skills and the ability to conform to social conventions. While the VABS scores in the two other domains, communication and daily living skills, were roughly in keeping with the participants' IQ scores, their interpersonal skills were much lower than expected based on IQ (Carmicheal Olson et al., 1992). Thomas et al. (1998) compared 15 children with FAS with 15 normal control subjects and 15 control children matched for verbal IQ on the social skills domain of the VABS. Children with FAS obtained significantly lower scores than IQ-matched control subjects, especially on the interpersonal skills sub-domain of the socialisation domain of the VABS. In addition, it was found that children with FAS displayed a discrepancy between their chronological age and age-equivalent VABS score which increased with age (Thomas et al., 1998). Taken together, these results suggest that the social deficits displayed by children who were exposed to alcohol *in utero* are beyond what can be explained by low IQ. Thus their social development may be arrested and not simply delayed (Thomas et al., 1998).

Whaley at al. (2001) explored the social and adaptive functioning of 33 children exposed to alcohol *in utero* in comparison to a control group of 33 non-exposed children with psychiatric problems. Their results indicated that although young children displayed deficits in adaptive functioning as measured by the VABS, their adaptive abilities did not differ significantly from non-exposed children. This suggests that although deficits in adaptive functioning are clearly evident in children exposed to alcohol *in utero*, these deficits are not unique to this group (Whaley et al., 2001).

However, as they became older, children who were exposed to alcohol displayed a more rapid decline in socialisation behaviour in comparison to the non-exposed clinical sample (Whaley et al., 2001). Deficits in socialisation behaviour therefore appear to become a more salient feature of *in utero* exposure to alcohol as children become older (Whaley et al., 2001).

Koditwakku (2007) has hypothesised that the social deficits of children with FASD become more pronounced in adolescence due to the greater complexity of social demands at this age. Effective social interactions require the coordination of a wide range of cognitive skills, such as comprehending the pragmatics of language, reading body language, and understanding facial and vocal affective expressions. The sheer complexity of these cognitive demands may lead to a breakdown in these children's ability to negotiate social interactions successfully (Koditwakku, 2007).

Analogous with studies investigating executive function in children with FASD (Mattson et al., 1999; Schonfeld et al., 2001), children who meet the diagnostic criteria for FAS do not appear to differ significantly from those with ARND (Whaley et al., 2001) in terms of the extent of their deficits in adaptive behaviour. This suggests that deficits in adaptive behaviour are not limited to what is generally seen as the most severe outcome of *in utero* alcohol exposure.

One possible explanation for findings indicating deficits in the adaptive behaviour of children with FASD, is the presence of executive dysfunction in this population. The behaviour of children with impairment in executive function may range from apathetic and unmotivated to impulsive and argumentative (Anderson, 2002). Children who suffer from executive dysfunction often show a lack of insight and intuition; a disregard for social rules and conventions; impairment in the acquisition of moral rules; and inflexibility and rigidity as demonstrated by a

resistance to change and a failure to learn from mistakes (Anderson, 2002; Anderson et al., 1999). These aspects of executive function, termed 'emotion-related', or 'hot' executive function (Rasmussen, 2005), have also been found to be impaired in children exposed to alcohol *in utero* (Koditwakku, May, Clericuzio, & Weers, 2001).

Koditwakku et al. (2001b) compared the performance 20 children and adolescents (age 7-19) who were exposed to alcohol *in utero* with that of 20 control subjects on two emotional-related learning tasks (visual discrimination reversal and extinction of reward-response associations), a conceptual set-shifting task (WCST), a test of intellectual ability (Raven Standard Progressive Matrices), and two behavioural measures (the Personal Behaviour Checklist and the Children's Executive Functioning Scale). Their results demonstrated that children who were exposed to alcohol exhibited deficits in both conceptual and emotional set-shifting. In addition, children who were exposed to alcohol exhibited significantly more behavioural problems than control participants as measured by the two parent-rated behavioural questionnaires. Interestingly, the study also found that one measure of cognition based executive function and two measures of emotion-related executive function were reliable predictors of the extent of behavioural problems exhibited by participants (Koditwakku et al., 2001b). This suggests that deficits in executive function may to some extent account for the behavioural and social problems, in other words the "secondary disabilities", commonly observed in individuals with FASD (Koditwakku et al., 2001b).

However, it should be kept in mind that children with FASD are often exposed to significant social stressors and that deficits in cognitive function alone cannot account for their behavioural and social problems. Studies have shown that the severity of emotional and behavioural deficits exhibited by children with FASD are related to the

stability of their home environment (Streissguth et al., 2004), their socio-economic status (Mattson & Riley, 2000), and their parents' level of education (Charmichael Olson et al., 1997). Generally, the emotional and social problems of this population are understood to result from a complex interplay between CNS damage and its associated cognitive deficits, genetic factors, and adverse postnatal experiences (Kodituwakku, 2007). By investigating the executive deficits associated with *in utero* exposure to alcohol, the present study hopes to assist in developing a better understanding of at least one of these contributing factors.

2.3.4. Summary

A fairly large body of research has demonstrated that individuals with FASD exhibit deficits on various aspects of executive function. These deficits have been noted in children as young as 4 years (Noland et al., 2003) and appear to extend into adulthood (Malisza et al., 2005; Conner et al., 2000; Kerns et al., 1997). In individuals exposed to alcohol *in utero*, deficits in executive function appear to occur even in those cases where no facial dysmorphology is present (Mattson et al., 1999; Schonfeld et al., 2001). This suggests that executive dysfunction due to *in utero* alcohol exposure is not limited to the FAS per se. In addition, alcohol appears to have a direct effect on executive function that is not solely attributable to deficits in IQ (Kerns et al., 1997; Carmichael Olson et al., 1998; Mattson et al., 1999; Connor et al. 2000; Schonfeld et al., 2001). Deficits in executive function appear to contribute to the behavioural and social deficits exhibited by individuals exposed to alcohol *in utero* (Koditwakku et al., 2001a).

Thus it appears that a fairly comprehensive profile for executive function in individuals exposed to alcohol *in utero* is starting to emerge. However, more

research is needed, as past research has been flawed in a number of ways (see Rasmussen, 2005, for review). One of the main shortcomings of previous research investigating the executive function of children with FASD is that most of the studies made use of very large age ranges (usually from about eight to 18) and did not make age-related comparisons (Rasmussen, 2005). This is problematic since, as discussed above, research shows that executive function develops throughout childhood and adolescence (Anderson, 2002; Stuss, 1992), and some of the behaviours and lack of cognitive abilities discussed above can therefore not be seen as 'deficits' in the context of the young child or infant (Anderson, 2002). By investigating the extent to which children exposed to alcohol *in utero* display different levels of executive abilities depending on their age, the present study aims to address a major shortcoming in the literature. A better understanding of how executive function develops in children exposed to alcohol *in utero* will aid in the development of a neurodevelopmental profile, which will be able to predict the cognitive and behavioural manifestations of FASD depending on the age of the child. Such a neurodevelopmental profile will thus allow for the accurate diagnosis of FAS and its spectrum at different developmental ages (Malisza et al., 2005). The majority of studies investigating the development of executive function in children have focussed on children from age 6- to 12-years (Anderson et al., 2001). In line with this, the present study focussed on two age groups: younger children (aged 6- to 7-years) and older children (aged 12- to 13- years).

Chapter 3: Research Method

3.1. Aims and hypotheses

The overall aim of the present study was to investigate the development of executive function in children exposed to alcohol *in utero*. It was hypothesised that, in concordance with previous studies in the field, children exposed to alcohol *in utero* (exposed children) would perform poorly in comparison to children who were not exposed (non-exposed) children on tests of executive function at both age 6- to 7-years and at age 12- to 13-years. Given the large body of research (reviewed above) indicating continual maturation of executive function throughout childhood, it was hypothesised that older children (12- to 13-year-olds) would perform better on tests of executive function than younger children (6- to 7-year-olds) irrespective of whether or not they were exposed to alcohol. Furthermore, it was hypothesised that exposed children would exhibit developmental delays in executive function which would become more pronounced with age. Thus we expected that the difference in executive abilities between non-exposed children and exposed children would be less evident in the case of younger children (6- to 7-year-olds) than in the case of older children (12- to 13- year-olds).

3.2. Sample

Participants were recruited from a school in the Overberg region and a clinic in Westcoast/Winelands region of the Western Cape. Both recruitment sites were situated in relatively small towns. Gatekeepers at the two sites were specifically asked to select children in the two age groups: 6- to 7-year-olds and 12- to 13-year-olds. These gatekeepers were provided with information on FAS, including

photographs of the facial characteristics associated with it, prior to the identification of potential participants. In the case of the school, the learner support teacher was asked to identify children who may possibly have been exposed to alcohol *in utero* based on a record of poor school performance, obvious dysmorphic features, and small physical size. In the case of the clinic, the sister in charge was asked to identify potential participants based on clinic records noting the use of alcohol during pregnancy, the presence of dysmorphic features, growth retardation or CNS abnormalities. The parents or guardians of children who were suspected of being exposed to alcohol *in utero* were approached and asked to participate in the study. The T-ACE, a screening tool designed to detect risk drinking during pregnancy (Sokol, Martier, & Ager, 1989), was administered to the parents of these children. In seven cases the child was found to be in foster care, usually with a grandmother or other close relative. In these cases the foster parent was asked to complete the T-ACE and thus to confirm that the biological mother engaged in risk drinking during pregnancy. In cases of unknown alcohol exposure, i.e. in those cases where neither the presence nor the absence of exposure could be confirmed, the potential participant was excluded from the study.

Given that prenatal exposure to alcohol has been found to affect executive function both directly, irrespective of IQ, and indirectly, through the mediation of IQ (Conner et al., 2000), the possible mediating effects of IQ were controlled for. The intellectual functioning of potential participants were assessed using the Junior South African Intellectual Scales (JSAIS) or the Senior South African Intellectual Scales - Revised (SSAIS-R), depending on their age. Initially, the intention was to exclude children with an IQ <70 or >130 in line with previous research on executive function in children with FASD (e.g. Lee et al., 2004). However, after recruiting a number of

participants with confirmed *in utero* exposure to alcohol, preliminary analysis of the data indicated that the average IQ was 63.6. A decision was therefore made to lower the cut-off point for exclusion from the study to an IQ of 50 or below. Furthermore, children suffering from psychiatric or neurological disorders (other than FASD) that would interfere with test performance, and those with uncorrected visual or hearing disorders were excluded from the study.

Twenty seven potential participants with suspected exposure to alcohol were identified. The mother of one of these children initially reported that her child was 13 years old, but when her date of birth was verified it was found that she was actually 16. This child was therefore excluded from the study. One child presented with severe global developmental delay and was therefore excluded from the study. The IQ scores of two children were found to be below 50 and they were therefore excluded from the study. One child was reportedly abusing amphetamines and marijuana and was therefore excluded from the study. In one case, maternal ingestion of alcohol during pregnancy could not be confirmed. This child was therefore excluded from the study. One child declined to participate. Twenty children with confirmed *in utero* exposure to alcohol were finally selected and asked to participate in further neuropsychological testing.

Twenty three non-exposed children were similarly identified by gatekeepers at the two sites. Two of these children were found to fall outside the age limits set by study. One of the children was found to suffer Attention Deficit Hyperactivity Disorder (ADHD) treated with psycho-stimulants. This child was therefore excluded from the study. Twenty children with confirmed non-exposure to alcohol were finally selected and asked to participate in further neuropsychological testing. As far as possible, participants in the control group were selected to be similar to those in the

experimental group in terms of sex, handedness, age range, parent level of education, and IQ. All participants spoke Afrikaans as their first language and were from mixed ancestry ('coloured') decent. Although SES was not measured directly, the majority of participants were judged to be from low SES. The participants' parents were generally employed as unskilled (e.g. farm workers, packers in the fishing industry, domestic workers, and street sweepers) and semi-skilled (e.g. builders, electricians, and machine operators) labourers. The demographics of the sample are indicated below (see Table 1). The results of the statistical analysis of the data are reported in chapter 4.

Table 1

Demographic variables of exposed and non-exposed participants

	Exposed		*Non-exposed*	
	6-7 year olds	*12-13 year olds*	*6-7 year olds*	*12-13 year olds*
Number of Participants	10	10	10	10
Sex				
Males	5	5	7	6
Females	5	5	3	4
Handedness				
Right	9	9	9	10
Left	1	1	1	0
Age				
Mean (years)	6.5	12.3	6.5	12.4
(S.D.) (months)	(5.09)	(8.93)	(19.68)	(7.63)
Years of Parent Education				
Mean	5.4	7.5	11.2	7.5
(S.D.)	(2.63)	(4.17)	(2.09)	(2.80)
Full Scale IQ				
Mean	64.6	65.4	78.3	71.9
(S.D.)	(7.44)	(13.23)	(8.06)	(8.95)

For the purpose of the present study, participants did not have to meet the diagnostic criteria for FAS or any of the foetal alcohol spectrum disorders to be included in the study. Nonetheless, all participants – children with confirmed

exposure to alcohol and control participants – were examined by a neurologist blind to their exposure to alcohol *in utero*. Facial abnormalities, physical growth (height and weight), and neurodevelopmental abnormalities (head circumference, neurological hard and soft signs) were noted. The results of the physical examination are tabled below (Table 2). The results of the statistical analysis of the data are reported in chapter 4.

Table 2

Results from the physical examination of exposed and non-exposed participants

	Exposed		*Non-exposed*	
	6-7 year olds	*12-13 year olds*	*6-7 year olds*	*12-13 year olds*
Number of Participants	10	10	10	10
Weight (kg)				
Mean	20. 5	41.3	21.1	49.5
(S.D)	(3.06)	(8.31)	(1.89)	(11.45)
Height (cm)				
Mean	115.7	148.4	123.0	150.2
(S.D.)	(6.88)	(8.46)	(16.15)	(6.32)
Head Circumference (cm)				
Mean	50.2	53.8	52.7	54.2
(S.D)	(2.22)	(2.93)	(1.64)	(1.32)
Dysmorphic features present				
Yes	10	9	0	0
No	0	1	10	10
CNS dysfunction present				
Yes	5	3	0	0
No	5	7	10	10

3.3. Design

The present study made use of cross-sectional design that compared the performance of younger children (6- to 7-year-olds) with older children (12- to 13-year-olds) on various measures of executive function. Within this, it made use of a

natural experimental design, with children exposed to alcohol *in utero* as the experimental group and non-exposed children as the control group.

3.4. Materials

3.4.1. Demographic questionnaire

A demographic questionnaire was developed to document participants' chronological age, home language, and level of education. In addition, the caregiver's marital status, highest level of education, and occupation was documented. All caregivers underwent a semi-structured interview, which explored the birth and early developmental history of the child in order to detect any gross developmental delays. Furthermore, information was obtained regarding the psychiatric history, substance use history, and medical history of the child. Finally, the T-ACE (described in detail below) was administered in order to detect maternal risk drinking during pregnancy. A copy of the interview schedule can be found in appendix A.

3.4.2. The T-ACE

In order to establish *in utero* exposure to alcohol, the presence of maternal risk drinking during pregnancy required confirmation (Stratton et al., 1996). The present study made use of the T-ACE, a screening instrument developed specifically to detect the presence of risk drinking in pregnant women (Sokol et al., 1989). The T-ACE has been tested as a self-administered, independent screening tool embedded in a health-habits survey among 350 ethnically diverse women (Chang et al., 1998). It was found to be highly sensitive in detecting risk drinking among pregnant women in comparison to other screening tools (where *sensitivity* refers to the probability that women who should test positive, did test positive). But was unfortunately less

specific than other tools (i.e. the probability that women who should test negative, did so, was lower than that of other instruments) (Chang et al., 1998). Despite this, the T-ACE has been found to be a helpful and efficient tool for identifying alcohol use among pregnant women (Chang, 2001). For the purpose of the present study the screening tool was adapted slightly in order to *retrospectively* confirm the presence of maternal risk drinking during pregnancy (see appendix A). Retrospective reports of alcohol consumption during pregnancy have been found to be as accurate as prenatal clinic data (Robles & Day, 1990).

3.4.3. Measures of intellectual functioning: The SSAIS-R and the JSAIS

3.4.3.1. The SSAIS-R

The Senior South African Individual Scales – Revised (SSAIS-R) was utilised to assess the general intellectual level of the older age group (12- to 13-year-olds). The SSAIS-R is a point scale (deviation IQ scale) which has been standardised for South African children between the ages of 7 years 0 months and 16 years 11 months with Afrikaans or English as their first language. The validity and reliability of the SSAIS-R is well established (van Eeden, 1992). However, it is important to note that the content of the SSAIS-R is based on Western technological culture. This implies that environmentally disadvantaged children are handicapped in respect of knowledge of and familiarity with the cultural content of the items of the scale. Normative studies of the SSAIS-R suggest that environmental factors, specifically those relating to environmental deprivation, explain part of the variance in performance on the SSAIS-R (van Eeden, 1992). The majority of the children who participated in the present study could possibly be classified as 'environmentally deprived' based on their socio-economic status. Although the SSAIS-R provides norms for environmentally

deprived children, these norms were not utilised, as the JSAIS, which was used to assess the general intellectual functioning of the younger age group (6- to 7-year-olds), does not have comparative norms. Making use of the SSAIS-R norms for environmentally deprived children would have artificially inflated the IQ scores for children in the older age group relative to the IQ scores for children in the younger age group. Nonetheless, it should be conceded that the IQ scores obtained in the present study is probably an underestimation of the children's true general intelligence level. As will be discussed in detail below, this may account in part for findings that children in our sample obtained lower IQ scores than generally noted in the literature.

3.4.3.2. The JSAIS

The Junior South African Individual Scales (JSAIS) was used to assess the general intellectual level of children in the younger age group (6- to 7-year-olds). Like the SSAIS-R, the JSAIS is a point scale (deviation IQ) and not an age scale. It has been standardised for South African children between the ages of 3 years 0 months and 7 years 11 months with Afrikaans or English as their first language. As in the case of the SSAIS-R, the validity and reliability of the JSAIS is well established (Madge, 1981). However, it is important to note that children from rural areas and from a low socioeconomic status were relatively under-represented in the normative sample of the JSAIS (Madge, 1981). Reservations therefore exist regarding the JSAIS's ability to accurately estimate the general intellectual ability of the sample used in the present study. As in the case of the SSAIS-R, the IQ scores obtained by the current sample is most likely an underestimation of their true abilities. Despite these short-comings, the SSAIS-R and the JSAIS were considered to be the best psychometric tests to use to evaluate the intellectual ability of a South African sample.

3.4.4. The NEPSY: A Developmental Neuropsychological Assessment

The majority of tests used to evaluate executive function in children have been developed and validated in adult populations (Anderson, 2002). These tests may not only be of little interest to children, but are also often unable distinguish normal and abnormal performance within a developmental context due to inadequate normative data (Anderson, 2002). Given this, the present study made use of the NEPSY, a neuropsychological assessment tool developed specifically to assess the cognitive development of children between the ages of 3 and 12 years (Korkman, Kirk & Kemp, 1998). The assessment battery is divided into five functional domains, namely: Attention/Executive Function, Language, Visual-Spatial Processing, Sensorimotor Functions, and Memory and Learning (Korkman et al., 1998). The present study made use of 10 subtests from the NEPSY that assess attention and executive function. In some instances, sub-scores of a subtest were used instead of the total score, as the different parts of the subtest have slightly different task requirements. Given that all participants were Afrikaans first language users, the test instructions and all auditory presented material was translated into Afrikaans. The following subtests were used:

a) ***Tower subtest***. This subtest is designed to assess the executive functions of planning, monitoring, self-regulation, and problem solving. The child moves three coloured balls to target positions on three pegs in a prescribed number of moves. There is a time limit, as well as specific rules to which the child must adhere: (a) Only one ball can be moved at a time; (b) a ball cannot be placed on the table or held in any other way while moving another ball, and (c) only a certain number of balls can be placed on each of the different pegs. The score is

the number of correctly achieved target positions (maximum 20 points). In addition, the number of rule violations is calculated as a supplemental score. The presence of many rule violations may be related to difficulty monitoring performance by maintaining the rules in working memory, and to the inability to inhibit impulsive responses (Korkman et al., 1998).

b) ***Part A of the Auditory Attention and Response Set subtest: Auditory Attention.*** This is a continuous performance test designed to measure the child's ability to selectively attend to simple auditory stimuli during a repetitive task. This child hears a list of 180 words on audiotape and is required to respond only to the word "red" by putting a red foam square in a box. The child is required not to respond in any way upon hearing any other word. If the child responds within 1 second, he or she obtains 2 points, and if he or she responds within 2 or 3 seconds, he or she obtains 1 point. The total score of this subtest is the number of Correct Responses – Commission Errors (maximum 60 points) (Korkman et al., 1998).

c) ***Part B of the Auditory Attention and Response Set subtest: Auditory Response Set***. This continuous performance test assesses the ability to shift set, to maintain a complex mental set, and to regulate a response according to matching and contrasting auditory stimuli. It is presented immediately after the Auditory Attention subtest. A new audio-taped series of 180 words is presented. This time, the child is to respond to contrasting stimuli (by putting a yellow square in a box upon hearing the word "red", and a red square upon hearing the word "yellow") as well as holding a novel matching set (putting a blue square in the box

upon hearing the word "blue"). The score is the number of Correct Responses – Commission Errors (maximum 72 points) (Korkman et al., 1998).

d) ***Visual Attention subtest***. This subtest assesses the speed and accuracy with which a child can scan an array and locate a target. The task requires sustained selective attention and the use of strategy in scanning. The subtest consists of two tasks. During the first task the child must search for and locate target pictures (cats) as quickly as possible in a random array. The second task involves locating two target faces as quickly as possible in a random array. The score is an efficiency index (Total Points Earned [= Correct Responses – Commission Errors] ÷ Performance Time). Given that processing speed (as measured by performance time) may have an impact on a child's performance on this test, a supplementary score, Total Correct [= Correct Responses – Commission Errors] was utilised to determine the accuracy with which the child can scan an array and locate a target (Korkman et al., 1998).

e) ***Statue subtest***. This subtest assesses inhibition and motor persistence. The child has to maintain a body position and remain silent, eyes closed for a 75 second period, while the examiner tries to provoke reactions by producing sounds (e.g. by knocking on the table). Errors include: body movement, eye opening and vocalisation. A score of 2 points is awarded for each error-free 5 second intervals. A score of 1 point is awarded for each interval with only one error, while intervals with two or three errors earn a score of 0 points. The total score is the number of points earned across all intervals (maximum 30 points) (Korkman et al., 1998).

f) ***Knock and Tap subtest***. This is a nonverbal task which assesses self-regulation and inhibition of immediate impulses evoked by visual stimuli that conflict with verbal directions. The subtest consists of two tasks. During the first task the child is required to knock on the table when the examiner taps on the table, and to tap when the examiner knocks. During the second task, the child is to tap with the side of the fist when the examiner knocks with the knuckles, to knock when the examiner taps with the side of the fist, and not to respond at all when the examiner taps with the palm. The score is the total number of correct responses (maximum 30 points) (Korkman et al., 1998).

g) ***Design Fluency subtest.*** This visuomotor fluency subtest assesses the child's ability to generate novel designs as quickly as possible. A poor performance on this task may be related to a difficulty in generating ideas and cognitive deficits in conceptualisation and abstract thought. The subtest is composed of two tasks. First the child generates novel designs on a structured array of dots, then on an unstructured array of dots. During both tasks the child is required to connect two or more dots with straight lines. The score is the total number of correct designs produced by the child (maximum score 70 points) (Korkman et al., 1998).

h) ***Verbal Fluency subtest.*** This subtest assesses the child's ability to generate words in semantic and phonemic categories. Although this subtest is included under the Language domain, as opposed to the Attention/Executive Functions Domain of the NEPSY, it probably requires executive functions such as strategy and self-regulation for an efficient performance (Klenberg et al., 2001). It consists of two tasks: a semantic fluency task and a phonemic fluency task.

During the semantic fluency task the child is required to produce as many animal names as possible in one minute and then as many things to eat and drink as possible in one minute. During the phonemic fluency task the child is required to produce as many words as possible beginning with the letter *S* in one minute and then as many words as possible beginning with the letter *B* in one minute. The score is the total number of correct words given in the four categories (Korkman et al., 1998).

The NEPSY has been standardised using 1000 American children, with a hundred children for each year of age between 3 and 12. The average reliability across all age groups was 0.82 for the Attention/Executive Functions domain (Korkman et al., 1998). The applicability of the NEPSY in developing countries has previously been studied in Zambia (Mulenga, Ahonen, & Aro, 2001). Mulenga et al. (2001) tested forty-five school children aged 9 (n = 25) and 11 (n = 20) on several subtests of the NEPSY and scored their performance according to age-equivalent norms for American children. Their results showed that the NEPSY is relatively insensitive to language and cultural influences that often compromise the applicability of Western tests in developing countries (Mulenga et al., 2001). The NEPSY was therefore seen as an ideal instrument to use in the present context.

Although only standardised for children up to the age of 12 years, the NEPSY has previously been used to evaluate the cognitive function of older children (13- to 14-year-olds) who were exposed to alcohol *in utero* (Korkman et al., 2003). During this study Korkman et al. (2003) made use of a control group of 39 non-exposed 13-to 14-year-olds in order to develop preliminary test norms for children in these age groups. However, these norms were not used in the present study since the sample size in the

Korkman et al. (2003) study was small (twenty-two non-exposed 13-year-olds took part), and details regarding the normative data obtained by these researchers were not available. Therefore the present study made use of raw scores, instead of standard scores. In addition, it is important to note that unlike the Mulenga et al. (2001) study, the present study translated test instructions and verbally presented material into the participants' first language (Afrikaans). This may have affected the validity of the results obtained.

3.5. Procedure

Children who were exposed to alcohol *in utero* were selected according to the procedure described above. Parents or guardians were interviewed regarding the birth, developmental, psychiatric and medical histories of their children (see appendix A). Once *in utero* exposure to alcohol was confirmed, the parents or guardians of these children were told what the neuropsychological testing would involve and asked to give informed consent for their children to participate. The children were assessed at the site where they were recruited. A similar recruitment process was followed with the control participants. Testing was carried out in a quiet room over two days. Day 1 comprised of IQ testing, the administration which took approximately 1.5 hours for the younger age groups and 1 hour for the older age groups. Administration of the relevant subtests of the NEPSY on day 2 took about 1 hour for all groups.

3.6. Ethical considerations

The study was conducted with ethical approval from the University of the Western Cape. Ethical approval and consent was obtained from the Western Cape Education Department to recruit potential participants from the school in the Overberg

region of the Western Cape. Ethical approval and consent was also obtained from the Western Cape Department of Health to recruit participants from a clinic in the Westcoast/Winelands region. Informed consent was obtained from the parents or guardians of all participants prior to the administering of any tests or interviews. In addition, consent was obtained from all participants (see appendix B). Participants were free to withdraw from the study at any time, without having to give a reason, and without this affecting any possible future treatment.

The parents or guardians of children with confirmed *in utero* exposure to alcohol were offered psychoeducation on the effects of prenatal exposure to alcohol on development. Many parents reported experiencing significant social and emotional problems themselves. Where necessary, these caretakers were referred to appropriate social or psychological services in their area. All parents were offered feedback regarding their children's performance on intellectual and neuropsychological tests. However, it is important to note that very few parents attended these sessions. In addition, the school psychologist or learner support teacher at the relevant schools were provided with the results of IQ tests to assist in the planning of long-term school placement, after permission to do so had been obtained from the parent or guardian of the child. The confidentiality of participants' test results were protected within the limitations discussed above.

3.7. Analysis

All data was captured on an Excel spread sheet and analyses were performed using Statistica (Version 7). Two-way factorial analysis of covariance (ANCOVA; 2 x 2) were performed using age group (6- to 7-year-olds, 12- to 13-year-olds) and exposure to alcohol *in utero* (exposed, non-exposed) as independent variables and

executive function test scores as dependent variables. Full scale IQ and parent level of education were used as covariates. It was appropriate to control for IQ since some executive abilities have been found to be directly affected by impairments in IQ (Conner et al., 2000). Parent level of education was controlled for since previous studies in the field have shown that children's performance on tests of executive function correlated significantly with parent level of education (Ardila et al., 2005). Whenever either covariate was found to significantly impact on the results, the influence of that covariate was statistically controlled for. When the covariates made no contribution, a two-way analysis of variance (ANOVA; 2 x 2) was run and the statistic was appropriately reported without controlling for either of the covariates. Partial eta squares (η^2) were used to estimate the effect sizes for the univariate tests of significance.

Two-way factorial ANOVAs (or ANCOVAs, depending on the significance of the covariates) were run to determine whether the main effects for exposure to alcohol *in utero* could appropriately be reported across age groups or, in case of an interaction, if each age group needed to be reported separately. Thus the main effects were reported with no further analyses when no interaction was found in a two-way ANCOVA or ANOVA. When an interaction was found in the case of a two-way ANOVA, analysis of the simple main effects were conducted in the form of a series of one-way ANOVAs (while appropriately using the error term from the overall analysis) to determine whether: (1) young exposed children differed significantly from older exposed children, (2) whether young non-exposed children differed significantly from older non-exposed children, (3) whether young exposed children differed significantly from young non-exposed children, and (4) whether older exposed children differed significantly from older non-exposed children in terms of

their performance on the relevant subtest. When an interaction was found in the case of a two-way ANCOVA, a series of one-way ANCOVAs were run to examine the simple main effects. Although this method has the disadvantage of costing degrees of freedom for error, it has the advantage of simplicity and circumvents the need to make uncomfortable assumptions in the adjustment of the error term (Howell, 1997).

Distributions of the data were reviewed prior to statistical analysis to check for violations of test assumptions. Levene's test was used to examine the homogeneity of variance (Howell, 1997). Alpha levels were set at 0.05, although analyses reaching significance were treated with caution in the context of multiple statistical tests performed on the data. A Bonferroni type adjustment was not applied to the testing at this stage to maximise group differences in task performance. This was considered appropriate for an exploratory study interested in a number of possible relationships and interactions.

Chapter 4: Results

4.1. Demographic characteristics

The demographic characteristics of the sample are reported in Table 1.

In order to examine the main effects of age and *in utero* exposure to alcohol as well as any possible interaction effects in terms of chronological age, a two way ANOVA was utilised. As expected, significant age differences were found, with 12- to 13-year-olds (mean = 12.3) being significantly older than 6- to 7-year-olds (mean = 6.5) [$F(1,36) = 1019.9$, $p < 0.01$]. No significant differences were found between exposed and non-exposed children, and no interaction effects were evident.

In order to examine the main effects of age group and *in utero* exposure as well as any possible interaction effects in terms of full scale IQ, a two-way ANOVA was utilised. Significant exposure effects were identified, with non-exposed children obtaining a significantly higher full scale IQ (mean = 75.1) than exposed children (mean = 65.0) [$F(1,36) = 10.87$, $p < 0.01$]. There were no significant differences between younger and older children, and no interaction effects were evident. This indicates that as a group, exposed children had a lower IQ than non-exposed children irrespective of their age.

In order to examine the main effects of age and *in utero* exposure as well as any possible interaction effects in terms of parent level of education, a two-way ANOVA was utilised. A significant interaction effect was found [$F(1,36) = 9.20$, $p < 0.01$]. Analysis of the simple main effects using one-way ANOVAs indicated that for exposed children, there was no significant difference in parent level of education between 6- to 7-year-olds (mean = 5.4) and 12- to 13-year-olds (mean = 7.5) [$F(1,36) = 2.41$, *ns*]. This was not the case for non-exposed children. The parents of 6- to 7-

year-old non-exposed children (mean = 11.2) had significantly more years of education than the parents of the 12- to 13-year-old non-exposed children (mean = 7.5) [$F(1,36) = 7.48$, $p < 0.01$]. Exposed children (mean = 5.4) were found to differ significantly from non-exposed children (mean = 11.2) at age 6- to 7- years. Thus the parents of 6- to 7-year-old non-exposed children had significantly more years of education than the parents of their exposed peers. Similar results were not found for the 12- to 13-year-olds, since exposed children (mean = 4.2) did not differ significantly from non-exposed children (mean = 2.8) at age 12- to 13-years [$F(1,36) = 0.0$, *ns*]. The differences in parent level of education between non-exposed children at age 6- to 7-years and 12- to 13-years and between exposed and non-exposed children at age 6- to 7-years highlight the importance of controlling for parent level of education when examining the performance of these groups on tests of executive function.

In order to determine whether the number of males and females were dependent on whether or not children were exposed to alcohol *in utero*, a chi-square test of contingency was performed. The sex of the participants did not appear to be contingent on exposure [$\chi^2(1) = 0.92$, *ns*]. Fifty percent of all exposed participants and 65% of all non-exposed participants were male. In order to determine whether the number of males and females were dependent on age group, a chi-square test of contingency was performed. The sex of the participants did not appear to be contingent on age group [$\chi^2(1) = 0.10$, *ns*]. Sixty percent of all 6- to 7-year-old participants and 55% of all 12-to 13-year-old participants were male.

In order to determine whether handedness was dependent on whether or not children were exposed to alcohol *in utero*, a chi-square test of contingency was performed. The handedness of the participants did not appear to be contingent on

exposure [$\chi^2(1) = 0.36$, *ns*]. Ninety percent of all exposed participants and 95% of all non-exposed participants were right handed. In order to determine whether handedness was dependent on age group, a chi-square test of contingency was performed. The handedness of the participants did not appear to be contingent on age group [$\chi^2(1) = 0.36$, *ns*]. Ninety percent of all 6- to 7-year-old participants and 95% of all 12- to 13-year-old participants were right handed.

4.2. Diagnostic signs

The results from the physical examination of the sample are reported in Table 2.

In order to examine the main effects of age and *in utero* exposure to alcohol as well as any possible interaction effects in terms of weight, a two-way ANOVA was utilised. As expected, significant age effects were found, with older children (mean = 45.4) weighing significantly more than younger children (mean = 20.8) [$F(1,36) = 113.99$, $p < 0.01$]. Although exposed children (mean = 30.9) weighed slightly less than non-exposed children (mean = 35.3), this difference was not significant [$F(1,36) = 3.63$, *ns*]. No interaction effects were evident. Similar results were found in terms of height. A two-way ANOVA indicated that older children (mean = 149.3) were significantly taller than younger children (mean = 119.4) [$F(1,36) = 85.47$, $p < 0.01$]. No significant difference was found between exposed (mean = 132.1) and non-exposed (mean = 136.6) children in term of height and no interaction effects were evident. When head circumference was examined through a 2-way ANOVA, significant age effects were found, with younger children (mean =51.4) having a smaller head circumference than older children (mean =54.0) [$F(1,36) = 14.80$, $p < 0.01$]. This indicates that 6- to 7-year-olds had a smaller head circumference than 12- to 13-year-olds. In addition, significant exposure effects were found, with exposed

children (mean = 51.9) having a smaller head circumference than non-exposed children (mean = 53.5) [$F(1,36) = 4.85$, $p < 0.05$]. As a group, exposed children were therefore found to have a smaller head circumference than non-exposed children, irrespective of their age. In order to establish whether this difference in head circumference between exposed and non-exposed children was present for both 6- to 7-year-olds and for 12- to 13-year-olds, the simple main effects were examined utilising one-way ANOVAs. The results indicated that exposed children (mean = 50.2) had a significantly smaller head circumference than non-exposed children (mean= 52.7) at age 6- to 7-years [$F(1,36) = 7.22$, $p < 0.05$]. Exposed (mean = 53.8) and non-exposed (mean = 54.2) children did not differ significantly from each other at age 12- to 13-years [$F(1,36) = 0.18$, *ns*]. This indicates that 6- to 7-year-old exposed children had a significantly smaller head circumference relative to their non-exposed peers. This suggests possible CNS dysfunction in 6- to 7-year-old exposed children. Similar results were not found for 12- to 13-year-old exposed children, who were found not to differ significantly from their non-exposed peers.

In order to determine whether dysmorphic facial features were dependent on whether or not children were exposed to alcohol *in utero*, a chi-square test of contingency was performed. The presence of dysmorphic facial features was found to be contingent on exposure [$\chi^2(1) = 16.36$, $p < 0.01$]. In the sample of exposed children, dysmorphic facial features were present in 95% of the children. In order to determine whether the presence of dysmorphic facial features in exposed children were dependent on age group, a chi-square test of contingency was performed. The presence of dysmorphic facial features was found not to be contingent on age [$\chi^2(1) = 1.1$, *ns*]. One hundred percent of 6- to 7-year-old exposed children and 95% of 12- to 13-year-old exposed children presented with dysmorphic facial features.

In order to determine whether the presence of CNS dysfunction was dependent on whether or not children were exposed to alcohol *in utero*, a chi-square test of contingency was performed. The presence of CNS dysfunction was found to be contingent on exposure [$\chi^2(1) = 10.0$, $p < 0.01$]. Forty percent of exposed children presented with CNS dysfunction. In order to determine whether the presence of CNS dysfunction in exposed children was dependent on age group, a chi-square test of contingency was performed. The presence of CNS dysfunction was found not to be contingent on age [χ^2 (1) = .83, *ns*]. Fifty percent of 6- to 7-year-old exposed children and 30% of 12- to 13-year-old exposed children presented with CNS dysfunction.

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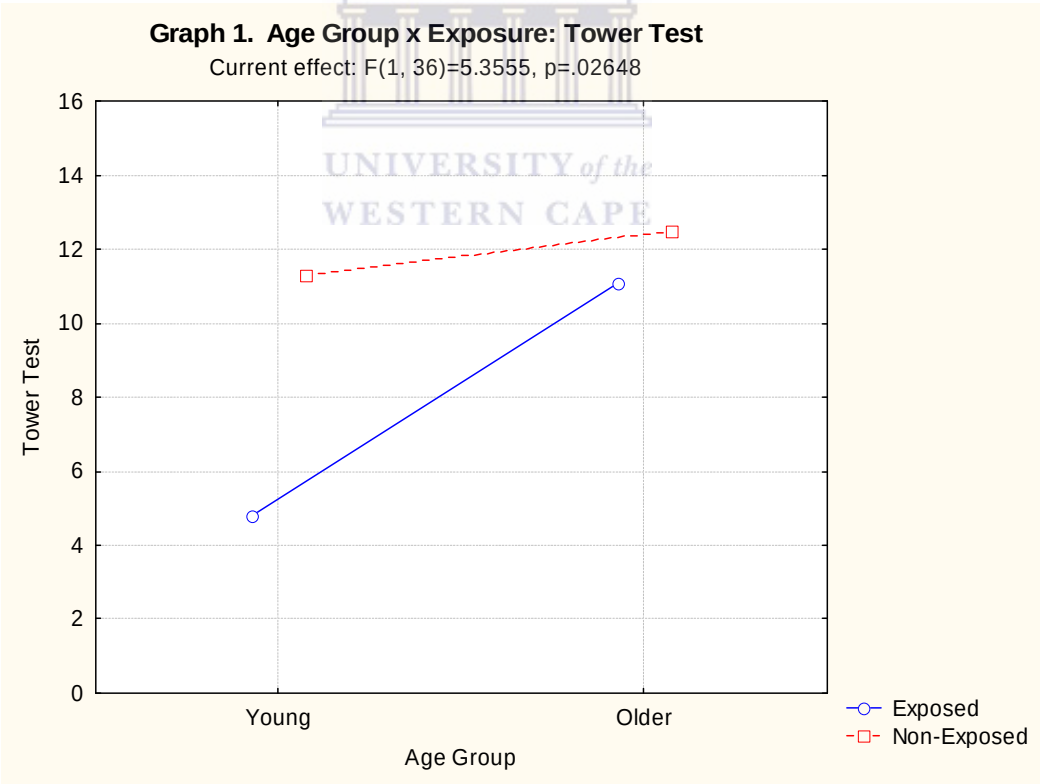
4.3. Development of executive function: age and alcohol exposure effects

Descriptive statistics for the various tests of executive function are indicated in Table 3.

Tower Subtest. Initial two-way analysis of covariance (ANCOVA) indicated that neither full scale IQ nor parent level of education contributed significantly to total test scores on this measure of planning, monitoring, self-regulation, and problem solving. These variables were therefore excluded from the analysis. A two-way ANOVA indicated significant interactions between age and *in utero* exposure to alcohol [$F(1,36) = 5.36$, $p < 0.05$] (see Graph 1 and Table 4). Analysis of the simple main effects using one way ANOVAs indicated that young exposed children (mean = 4.8) differed significantly from older exposed children (mean = 11.1) [$F(1,36) = 16.34$, $p < 0.01$]. This indicates that for children who were exposed to alcohol *in utero*, 12- to 13-year- olds performed significantly better than 6- to 7-year-olds. This result was not replicated in non-exposed children, as no significant differences were

found between 6- to 7-year-old non-exposed children (mean = 11.3) and 12- to 13-year-old non-exposed children (mean = 12.5) on this measure [F(1,36) = 0.59, *ns*]. Thus it appears that non-exposed children's performance on this measure of executive function did not improve significantly with increasing age. A significant difference was found between young exposed children (mean = 4.8) and young non-exposed children (mean = 11.3) [F(1,36) = 17.40, $p < 0.01$]. This suggests that 6- to 7-year-old children who were exposed to alcohol *in utero* displayed significant deficits in planning and problems solving relative to their non-exposed peers. However, similar deficits were not found for the older age group, since 12- to 13-year-old exposed children (mean = 11.1) were not found to differ significantly from their non-exposed peers (mean = 12.5) [F(1,36) = 0.81, *ns*].

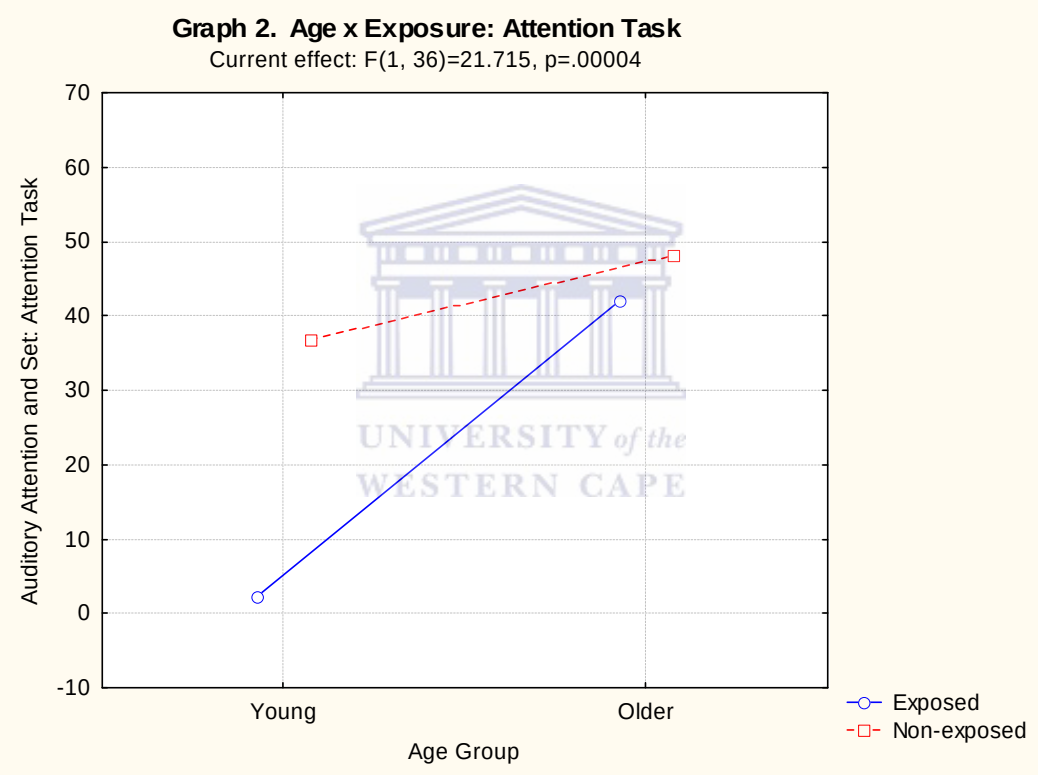


When the number of rule violations made on the Tower Test were examined through ANCOVA, neither covariate was found to contribute significantly to the total

number of rule violations made on this test. Significant age effects were identified through the use of a two-way ANOVA [$F(1,36) = 10.13$, $p < 0.01$] with younger children (mean = 9.7) making significantly more errors than older children (mean = 3.9). This indicates that 6- to 7-year-olds had more difficulty in monitoring their performance by maintaining the rules in working memory, or that they may have struggled to inhibit impulsive responses in comparison to 12- to 13-year-olds. No significant differences were found between exposed and non-exposed children and no interaction effects were evident (see Table 4).

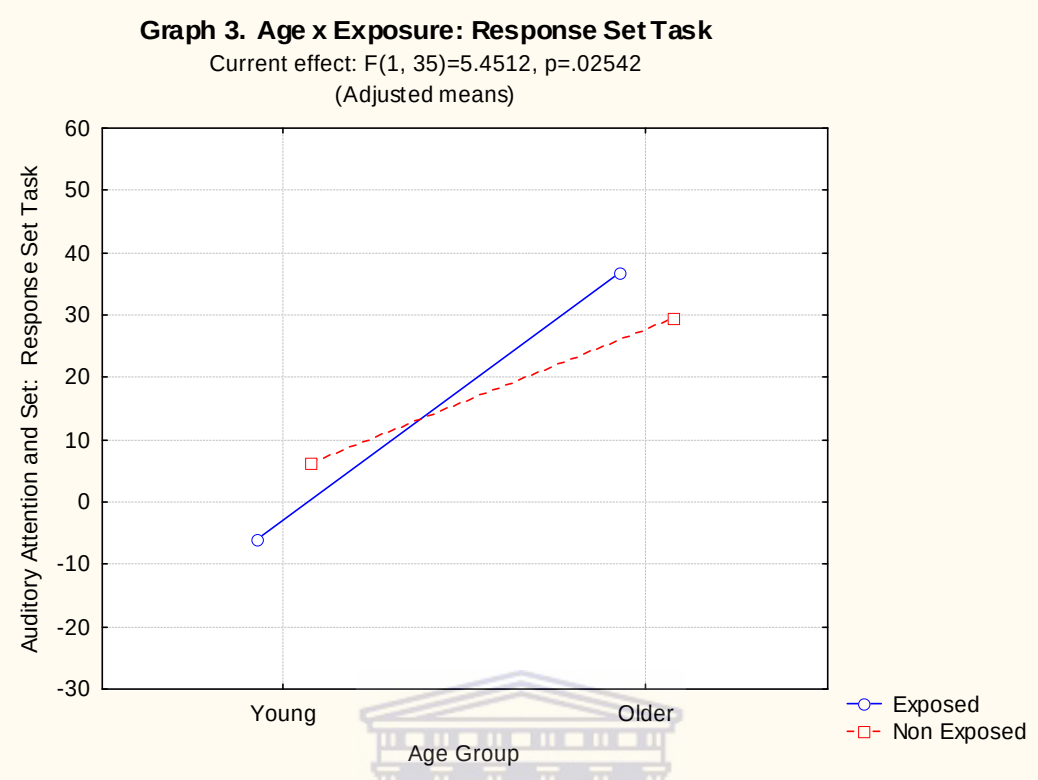
Auditory Attention Task. Initial two-way analysis of covariance (ANCOVA) indicated that neither full scale IQ nor parent level of education contributed significantly to total test scores on this measure of the child's ability to selectively attend to simple auditory stimuli. The two covariates were therefore excluded from further analysis. A two-way ANOVA was utilised to examine the main effects of age and *in utero* exposure as well as any possible interaction effects. A significant interaction effect between age and *in utero* exposure to alcohol was found [$F(1,36) = 21.72$, $p < 0.01$] (see Table 4 and Graph 2). Exploration of the simple main effects using one-way ANOVAs indicated that young exposed children (mean = 2.2) differed significantly from older exposed children (mean = 42.0) [$F(1,36) = 85.29$, $p < 0.01$]. This indicates that 12- to 13-year-old exposed children performed significantly better than 6- to 7-year-old exposed children on this measure of selective attention. Similar results were found for non-exposed children, with 12- to 13-year-old non-exposed children (mean = 48.2) performing significantly better than 6- to 7-year-old non-exposed children (mean = 36.8) [$F(1,36) = 6.99$, $p < 0.05$]. Thus it appears that both exposed and non-exposed children's performance on this measure of executive

function improved significantly with increasing age. A significant difference was found between young exposed children (mean = 2.2) and young non-exposed children (mean = 36.8) [$F(1,36) = 64.46$, $p < 0.01$]. This suggests that 6- to 7-year-old children who were exposed to alcohol *in utero* displayed significant deficits in selective attention. However, similar deficits were not found for the older age group, since 12- to 13-year-old exposed children (mean = 42.0) did not differ significantly from their non-exposed peers (mean = 48.2) [$F(1,36) = 2.07$, *ns*].



Auditory Response Set Task. Initial two-way analysis of covariance (ANCOVA) indicated that only full scale IQ contributed significantly to total test scores on this measure of the child's ability to shift set, to maintain a complex mental set, and to regulate a response according to matching and contrasting auditory stimuli. A two-way ANCOVA was conducted to examine the main effects of age and *in utero* exposure as well as any possible interaction effects while controlling for IQ. A significant interaction effect between age and *in utero* exposure to alcohol was found

[F(1,35) = 5.45, p < 0.01] (see Table 4 and Graph 2). Analysis of the simple main effects using one-way ANCOVAs indicated that young exposed children (adjusted mean = -5.98) differed significant from older exposed children (adjusted mean = 36.70) after controlling for IQ [F(1,17) = 45.09, p < 0.01]. This indicates that 12- to 13-year-old exposed children performed significantly better than 6- to 7-year-old exposed children on this measure of complex auditory attention. Similar results were found for non-exposed children, with 6- to 7-year-old non-exposed children (adjusted mean = 6.28) obtaining significantly lower scores than 12- to 13-year olds (adjusted mean = 29.41). Thus it appears that both exposed and non-exposed children's performance on this measure of executive function improved significantly with increasing age. The performance of young exposed children (adjusted mean = -5.98) did not differ significantly from that of young non-exposed children (adjusted mean = 6.28) [F(1,17) = 2.69, *ns*]. Six- to 7-year-old children who were exposed to alcohol *in utero* therefore did not present with significant deficits on this measure of executive function. Moreover, the performance of older exposed children (adjusted mean = 36.7) did not differ significantly from older non-exposed children (adjusted mean = 29.4) [F(1,17) = 1.07, *ns*], indicating that 12- to 13-year-old exposed children also did not present with significant deficits on this measure of executive function. It is interesting to note that exposed children actually performed slightly better than non-exposed children at age 12- to 13-years on this measure of executive function.



Visual Attention Subtest. The summary score for the Visual Attention subtest of the NEPSY incorporates accuracy and speed components, providing an indication of overall competency. Initial analysis through ANCOVA indicated that neither full scale IQ, nor parent level of education had a significant impact on children's performance on this test. Significant age effects were identified through a two-way ANOVA, with older children (mean = 17.60) performing significantly better than younger children (mean = 6.15) [$F(1,36) = 89.71$, $p < 0.01$]. No differences were found between exposed and non-exposed children on this measure of executive function and no interaction effects were evident. This indicates that, on a measure of visual attention, 12- to 13-year-olds performed significantly better than 6- to 7-year-olds irrespective of diagnosis (see Table 4).

However, when the supplemental Accuracy Score (which excludes the performance speed component of the task) was examined, significant interaction effect between age and *in utero* exposure to alcohol was found [$F(1,36) = 5.50$, $p <$

0.05] (see Graph 4 and Table 4). Analysis of the simple main effects using one-way ANOVAs indicated that in terms of exposed children, 12- to 13-year-olds (mean = 32.7) performed significantly better than 6- to 7-year-olds (mean = 6.1) [$F(1,36) = 41.46$, $p < 0.01$]. Similar results were found for non-exposed children, with 12- to 13-year-olds (mean = 34.6) performing significantly better than 6- to 7-year-olds [$F(1.36) = 9.75$, $p < 0.01$]. This indicates that the performance of both exposed and non-exposed children improved significantly with age on this measure of executive function. Non-exposed children (mean = 21.7) performed significantly better than exposed children (mean = 6.1) at age 6- to 7-years [$F(1.36) = 14.26$, $p < 0.01$]. This indicates that children exposed to alcohol *in utero* presented with significant deficits in terms of their ability to accurately scan an array at age 6- to 7-years of age. However, similar deficits were not found for the older age group, as 12- to 13-year-old exposed children (mean = 32.7) did not differ significantly from their non-exposed peers (mean = 34.6) [$F(1,36) = 0.21$, *ns*].

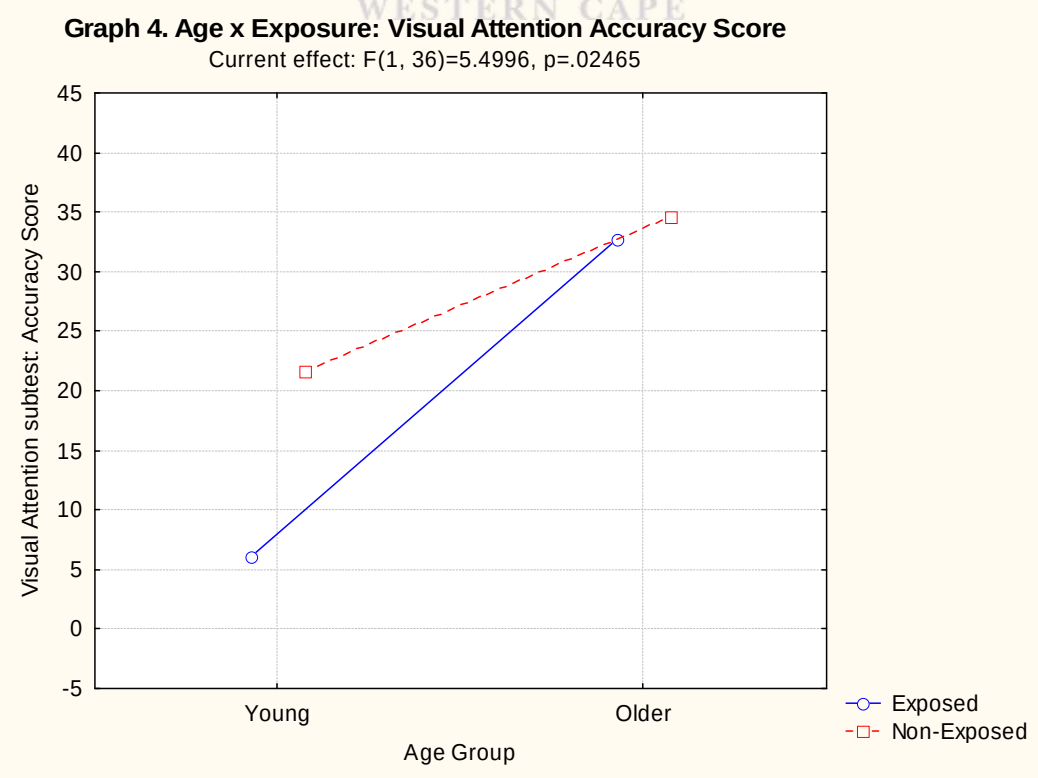


Table 3: Descriptive Statistics for NEPSY subtests

Level of Factor	Level of Factor	N	Tower Test	Tower rule violations	Auditory Attention Task	Auditory Response Set Task	Visual Attention	Visual Attention Accuracy Score	Statue	Knock & Tap	Design Fluency	Verbal Fluency
			Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Total		40	9.93 (4.53)	3.40 (3.26)	32.30 (20.30)	16.60 (21.91)	11.88 (6.96)	23.78 (14.51)	27.05 (4.98)	26.48 (5.33)	10.43 (6.32)	26.55 (12.36)
Young		20	8.05 (5.47)	4.85 (3.50)	19.50 (20.30)	0.90 (15.43)	6.15 (4.16)	13.90 (14.43)	25.35 (6.12)	24.45 (6.91)	5.60 (3.22)	17.40 (8.15)
Older		20	11.80 (2.17)	1.95 (2.28)	45.10 (9.43)	32.30 (15.12)	17.60 (3.62)	33.65 (4.31)	28.75 (2.71)	28.50 (1.36)	15.25 (4.77)	35.70 (8.44)
Exposed		20	7.95 (4.58)	4.30 (3.60)	22.10 (22.21)	12.65 (27.03)	10.90 (7.37)	19.40 (17.60)	25.30 (6.51)	24.80 (6.81)	9.55 (6.69)	23.50 (13.12)
Non-Exposed		20	11.90 (3.58)	2.50 (2.69)	42.50 (11.56)	20.55 (14.90)	12.85 (6.56)	28.15 (9.06)	28.80 (1.44)	28.15 (2.43)	11.30 (5.97)	29.60 (11.05)
Young	**Exposed**	10	4.80 (3.99)	5.70 (3.92)	2.20 (8.55)	-8.90 (11.47)	4.60 (3.66)	6.10 (15.38)	22.60 (7.73)	21.70 (8.63)	4.00 (2.83)	13.40 (6.13)
Young	**Non-Exposed**	10	11.30 (4.88)	4.00 (2.98)	36.80 (11.49)	10.70 (12.54)	7.70 (4.22)	21.70 (8.22)	28.10 (1.60)	27.20 (3.08)	7.20 (2.86)	21.40 (8.18)
Older	**Exposed**	10	11.10 (2.51)	2.90 (2.77)	42.00 (9.40)	34.20 (19.47)	17.20 (3.61)	32.70 (4.90)	28.00 (3.68)	27.90 (1.45)	15.10 (4.25)	33.60 (9.96)
Older	**Non-Exposed**	10	12.50 (1.58)	1.00 (1.15)	48.20 (8.83)	30.40 (9.78)	18.00 (3.77)	34.60 (3.63)	29.50 (0.85)	29.10 (0.99)	15.40 (5.46)	37.80 (6.43)

Note: In cases were IQ or parent level of education was found to be a significant covariate, adjusted means were utilised. These adjusted means are reported in the text.

Table 4: Analysis of Variance for each test of executive function

Test	*Age*		*Exposure*		*Age x Exposure*	
	F	**η²**	**F**	**η²**	**F**	**η²**
Tower Subtest						
Total score	11.58**	0.18	12.85**	0.20	5.36*	0.08
Rule violations	10.13**	0.20	3.90	0.08	0.01	0.00
Auditory Attention and Response Set Subtest						
Auditory Attention Task	70.58**	0.41	44.82**	0.26	21.72**	0.13
Auditory Response Set Task	62.74**	0.57	0.28	0.00	5.45*	0.05
Visual Attention Subtest						
Total Score	89.71**	0.70	2.60	0.02	0.91	0.00
Accuracy Score	45.72**	0.48	8.97**	0.09	5.50*	0.06
Statue Subtest	10.67**	0.18	1.02	0.02	0.01	0.00
Knock and Tap Subtest	7.54**	0.15	5.16*	0.10	2.12	0.40
Design Fluency Subtest	67.28**	0.63	0.07	0.00	0.60	0.01
Verbal Fluency Subtest	68.85**	0.61	1.12	0.01	0.09	0.00

*p < 0.05. **p < 0.01

Statue Subtest. Initial two-way analysis of covariance (ANCOVA) indicated that only parent level of education contributed significantly to total test scores on this measure of inhibition and persistence. A two-way ANCOVA was conducted to examine the main effects of age and *in utero* exposure as well as any possible interaction effects, while controlling for parent level of education. After controlling

for parent level of education, older children (adjusted mean = 29.0) performed significantly better than younger children (adjusted mean = 25.1) on this subtest [$F(1,35) = 10.67$, $p < 0.01$]. No differences were found between exposed (adjusted mean = 26.4) and non-exposed (adjusted mean = 27.7) children on this measure of executive function. No interaction effects were evident. This indicates that, on a measure of inhibition and persistence, 12- to 13-year-olds performed significantly better than 6- to 7-year-olds children irrespective of whether or not they were exposed to alcohol *in utero* (see Table 4).

Knock and Tap Subtest. Initial two-way analysis of covariance (ANCOVA) indicated that neither full scale IQ, nor parent level of education contributed significantly to total test scores on the Knock and Tap subtest, a more complex test of motor inhibition than the Statue subtest. A two-way ANOVA was utilised to examine the main effects of age and *in utero* exposure as well as any possible interaction effects. Significant age effects were identified [$F(1,36) = 7.54$, $p < 0.01$], with older children (mean = 28.50) performing significantly better than younger children (mean = 24.45). This indicates that, on a measure of motor inhibition, 12- to 13-year-olds performed significantly better than 6- to 7-year-olds. Significant differences were found between exposed and non-exposed children [$F(1,36) = 5.16$, $p < 0.05$], with non-exposed children (mean = 28.15) performing significantly better than exposed children (mean = 34.80). This indicates that as a group, non-exposed children performed better than children who were exposed to alcohol *in utero* irrespective of their age (see Table 4). Although no interaction effects were evident, the simple main effects were examined to determine whether differences between 6- to 7-year-olds and 12- to 13-year-olds were significant for both exposed and non-exposed children and

whether the differences between exposed and non-exposed children were significant at both age 6- to 7-years and 12- to 13-years. For exposed children, significant differences were found between 6- to 7-year-olds (mean = 21.7) and 12- to 13-year olds (mean = 27.9) [$F(1,36) = 8.84$, $p < 0.01$]. In contrast, no significant age differences were noted for non-exposed children; 6- to 7-year-olds (mean = 27.2) did not differ from 12- to 13-year olds (mean = 29.1). This indicates that while exposed children displayed increments in this aspect of executive function with age, no such age-related increments were observed for non-exposed children. Significant differences were found between young exposed children (mean = 21.7) and young non-exposed children (mean = 27.2) [$F(1,36) = 6.95$, $p < 0.05$]. This indicates that exposed children displayed deficits on a test of complex inhibition at age 6 – to 7-years. Similar deficits were not found for exposed 12- to 13-year-olds, as exposed children in this age group (mean = 27.9) did not differ significantly from their non-exposed peers (mean = 29.1) [$F(1,36) = 0.33$, *ns*].

Design Fluency Subtest. Initial two-way analysis of covariance (ANCOVA) indicated that only full scale IQ, but not parent level of education contributed significantly to total test scores on this measure of non-verbal fluency. A two-way ANCOVA was utilised to examine the main effects of age and *in utero* exposure as well as any possible interaction effects, while controlling for full scale IQ. When full scale IQ was controlled for, a significant difference between younger (adjusted mean = 5.41) and older (adjusted mean = 15.44) children [$F(1,34) = 67.13$, $p<.01$] was found. No significant differences were found between exposed and non-exposed children on this measure of executive function and no interaction effects were evident. This indicates that, on a non-verbal fluency task, 12- to 13-year-olds performed

significantly better than 6- to 7-year-olds irrespective of whether or not they were exposed to alcohol *in utero* (see Table 4).

Verbal Fluency Subtest. Initial two-way analysis of covariance (ANCOVA) indicated that only full scale IQ, but not parent level of education contributed significantly to total test scores on this measure of verbal fluency. A two-way ANCOVA was utilised to examine the main effects of age and *in utero* exposure as well as any possible interaction effects, while controlling for full scale IQ. Significant age effects were identified [$F(1,35) = 68.85$, $p < 0.01$], with older children (adjusted mean = 36.2) performing significantly better than younger children (adjusted mean = 16.9). No significant differences were found between exposed and non-exposed children and no interaction effects were evident. This indicates that, on a measure of verbal fluency, 12- to 13-year-olds performed significantly better than 6- to 7-year-olds irrespective of whether or not they were exposed to alcohol *in utero* (see Table 4).

4.4. Summary

Statistical analysis revealed various differences between 6- to 7-year-old and 12- to 13-year old children, as well as between children who were exposed to alcohol *in utero* and those who were not. Some of the most important findings are highlighted here.

In terms of the demographic characteristics of the sample, no significant differences were found between exposed and non-exposed children in terms of age. However, exposed and non-exposed children differed significantly in terms of their average IQ, with non-exposed children obtaining a significantly higher IQ than

exposed children. The parental level of education for the group of 6-to 7-year-old non-exposed children was found to be significantly higher than the parental level of education for the group of 6- to 7-year-old exposed children. In addition, 6- to 7-year-old non-exposed children were found to differ significantly from 12- to 13-year-old non-exposed children on this variable. No significant differences were found between exposed and non-exposed children in terms of sex or handedness.

In terms of the diagnostic signs for FAS and its spectrum, exposed and non-exposed children were not found to differ significantly in terms of height and weight. Whilst 6- to 7-year-old exposed children were found to have a significantly smaller head circumference in comparison to their non-exposed peers, similar results were not obtained for 12- to 13-year-olds. The presence of dysmorphic facial features and CNS dysfunction was found to be contingent on *in utero* exposure to alcohol. Six- to 7-year-old exposed children did not differ significantly from 12- to 13-year-old exposed children in terms of the frequency with which they exhibited the facial characteristics of FAS or in terms of the frequency with which CNS dysfunction was detected.

On tests of executive function, significant age effects were identified on all subtests of the NEPSY. Significant exposure effects were noted on the Tower subtest, the Auditory Attention task, the Accuracy Score of the Visual Attention subtest, and the Knock and Tap subtest. Significant interactions between age and exposure were noted on the Tower subtest, the Auditory Attention task, the Auditory Response Set task and the Accuracy Score of the Visual Attention subtest. IQ was found to be a significant covariate on the Auditory Response Set task, the Design Fluency subtest and the Verbal Fluency subtest. Parent level of education was a

significant covariate only on the Statue subtest. These findings are discussed in detail in the next chapter.

Chapter 5: Discussion

5.1. Introduction

The study presented exploratory research on the development of executive function in children exposed to alcohol *in utero*. The data was analysed with respect to age as well as the effects of *in utero* exposure to alcohol. The findings of the present study suggest that executive function matures with age. Incidental findings indicate possible differences in the rate of development of some aspects of executive function in exposed and non-exposed children. In addition, the findings suggest that children exposed to alcohol *in utero* display deficits in executive function which becomes less pronounced as children become older. These findings are discussed in more detail below.

5.2. The development of executive function in children

In concordance with previous research in the field, the findings of the present study suggest that executive function matures with age. Children in the age group 12- to 13-years were found to perform significantly better than 6- to 7-year-olds on measures of auditory and visual attention, inhibition, and verbal and non-verbal fluency, irrespective of whether or not they were exposed to alcohol *in utero*. These findings suggest significant increments in executive abilities with increasing age. Furthermore, incidental findings suggest possible differences in terms of the rate of development of executive abilities in exposed and non-exposed children. While significant age-related increments were noted on the Knock and Tap subtest and the Tower subtest for exposed children, such increments were not evident for non-exposed children. These findings suggest that the performance of non-exposed

children on a measure of inhibition and cognitive flexibility as well as on a measure of planning and strategy reach relative maturity by age 6- to 7-years, whilst the performance of exposed children continues to develop.

In the study by Klenberg et al. (2001), motor inhibition was the first sub-function of executive function to mature; with children in their sample reaching 12-year-old levels of performance at age 6 for the Statue subtest. In the present study, 12- to 13-year-olds were found to perform significantly better on the Statue subtest when compared to 6- to 7-year-olds irrespective of whether or not they were exposed to alcohol *in utero.* These findings suggest that inhibition matured somewhat later in the present sample than in the sample utilised by Klenberg et al. (2001). It is important to note that the present sample was heterogeneous with respect to *in utero* exposure to alcohol. Although no significant differences were detected between exposed and non-exposed children, the presence of children exposed to alcohol *in utero* in the sample may account for findings suggesting a slower rate of development in the present sample in comparison to samples used by other studies.

Other factors that need to be kept in mind when comparing the findings of the present study with those of previous studies are possible social and environmental differences between participants in the present study and participants in other studies investigating the development of executive function. In the present study, parent level of education was used as an indicator of social and environmental differences between exposed and non-exposed children. Interestingly, the findings of the present study indicated that parental level of education was only related to performance on the Statue subtest, as it was not found to be a significant covariate on any of the other measures of executive function. This finding is also inconsistent with those of Klenberg et al. (2001), who found that parents' level of education had a significant

impact on children's performance on the fluency subtests and visual attention subtests of the NEPSY, but not on subtests assessing inhibition and auditory attention. These findings can possibly be ascribed to differences in parent level of education in the present sample in comparison to the sample utilised Klenberg et al. (2001). Klenberg et al. (2001) rated parent level of education using three categories: lower level (4-9 years of primary school, secondary education, vocational school, or all of these); medium level (senior high school or college); and higher level (university education). In the present study, the average level of education of parents in all groups, with the exception of young non-exposed children fell in the lower level, using the categories of Klenberg et al. (2001).

Related to this, is possible differences in the general intelligence of participants in the present sample and those of Klenberg et al. (2001). We know from the literature on FASD that IQ mediates the deficits in executive function displayed by children exposed to alcohol *in utero* to some extent (Connor et al, 2001). Although Klenberg et al. (2001) did not control directly for IQ, they excluded children with learning disorders. This suggests that their sample was most likely of normal intelligence. Other studies investigating the development of executive function in children reported much higher IQ scores than those obtained in the present study. Thus Anderson et al. (2001a), for example, reported average IQ scores ranging from 98.0 for some age groups to 107.7 for other age groups. The findings of the present study indicated that non-exposed children obtained an average IQ of 75.1. According to DSM-IV-TR criteria, these children fall in the borderline range of intellectual functioning (APA, 2000). The average IQ of exposed children was even lower (65.0), which falls in the mild-mental retardation range of intellectual functioning (APA, 2000). As mentioned above, the particularly low IQ scores obtained by

children in the present study can possibly be ascribed to the content of IQ tests, which generally favours Western technological cultures (van Eeden, 1992). However, it also suggests social and environmental differences between participants in the present study and participants in other studies investigating the development of executive function. Social differences, such as the amount of stimulation the child receives, and environmental differences, such as the quality of nutrition the child receives, may have had an impact on children's performance on both tests of general intelligence and tests of executive function, making it difficult to compare the results of the present study with those obtained in previous studies.

Nonetheless, the performance of the present sample on various other tests of executive function was broadly consistent with the findings of previous studies. On the Knock and Tap subtest, a more complex test of inhibition, which also requires the ability to shift flexibly between alternate responses (Korkman et al., 1998), no significant differences were found between non-exposed 6- to 7-year-olds and 12- to 13-year olds. This is consistent with findings by Klenberg et al. (2001) who demonstrated a levelling off in performance, indicative of relative maturity on this subtest by age 7. For exposed children, on the other hand, a significant difference was found between the two age groups, with 12- to 13-year-olds performing significantly better than 6- to 7-year-olds. These findings suggest possible delays in the development of exposed children's ability to inhibit a complex motor response and switch to an alternative response.

Similar findings were obtained on the Tower subtest, a test assessing the child's ability to plan and organise goal directed behaviour. For non-exposed children, no significant differences were found between 6- to 7-year-olds and 12- to 13-year olds. However, 12- to 13-year-old children who were exposed to alcohol *in utero*

performed significantly better on this subtest compared to 6- to 7-year-olds. These findings (discussed in detail below) suggest possible delays in the development of exposed children's ability to plan and organise goal directed behaviour.

The findings for non-exposed children on the Tower subtest are consistent with the findings of Klenberg et al. (2001), who demonstrated mature performance on this subtest of the NEPSY at the age eight. Although it is difficult to compare studies because of differences in the rules, time limits and number of moves required in different versions of the tower test, other studies have found similar results. Thus Luciana and Nelson (1998), for example, found improved problem solving ability on the Tower of London test by age eight. However, these researchers also noted that 8-year-olds did not reach adult levels of performance on the more difficult items of the Tower of London test (Luciana & Nelson, 1998). De Luca et al. (2003) demonstrated age-related increments in performance on the more difficult items of the Tower of London test, with effective problem solving skills being available to the 12-year-old child. However, their results showed that improvements in the strategic planning and organisation of goal directed behaviour continued to occur up to early adulthood. They hypothesised that the efficient goal-directed behaviour of young adults may be related to the achievement and maintenance of maximum short term memory capacity in late adolescence in addition to age – related improvements in working memory (De Luca et al., 2003). Broadly consistent with this, the findings of the present study indicated that 12- to 13-year-old children committed fewer rule violations on the Tower subtest than 6- to 7-year-olds. This finding is most likely due to increased ability to monitor performance by holding the rules in working memory, in addition to increased ability to inhibit impulsive responses in older children (Korkman et al., 1998).

In the study conducted by Klenberg et al. (2001) relative maturity was reached on subtests of visual and auditory attention by age 10. Consistent with this, findings from the present study indicated that 12- to 13-year-old non-exposed children performed better on the Auditory Attention task, the Auditory Response Set task, and the accuracy score of the Visual Attention subtest compared to 6- to 7-year-olds. Similar findings were obtained for children exposed to alcohol *in utero*, although it is important to note that because the present study only had two age groups, important differences in the rate of development between exposed and non-exposed children may have been obscured.

Finally, the findings of the present study suggest that 12- to 13-year-olds performed better than 6- to 7-year-olds on tests of verbal and non-verbal fluency irrespective of *in utero* exposure to alcohol. These findings are consistent with those obtained by Klenberg et al. (2001) who demonstrated that 12-year-old levels was only reached at age 11 for the Phonemic Fluency and Design Fluency subtests. These researchers also noted that there was no evidence for a levelling off in performance even in the oldest age groups, suggesting that this aspect of executive function continues to develop during adolescence (Klenberg et al., 2001). This hypothesis has been questioned by the findings of Anderson et al. (2001a), who demonstrated that adolescents between the age of 11 and 17 years showed slight, but non-significant, increases in total words generated on a verbal fluency task. However, it is important to note that these researchers also noted a variable performance within the 11- to 13-year-old groups (Anderson et al. 2001a), which may account for differences between their findings and those of Klenberg et al. (2001). Klenberg et al. (2001) have suggested that fluency tasks require the integration of a variety of executive abilities, such as the active use of strategy, monitoring, and the evaluation of ongoing

performance. As such, these tasks may represent higher-level cortical functions, and performance on such tasks may vary greatly even in the adult population (Klenberg et al., 2001).

5.3. *In utero* exposure to alcohol and executive dysfunction

Based on previous research in the field, it was hypothesised that the executive abilities of children exposed to alcohol *in utero* would be significantly compromised. As expected, the results of the present study indicated that exposed children, as a group, displayed deficits on various tests of executive function. Thus children exposed to alcohol *in utero* were found to perform poorly in comparison to non-exposed children on the Auditory Attention task of the Auditory Attention and Response Set subtest, the accuracy score of the Visual Attention subtest, the Tower subtest and the Knock and Tap subtest.

Based on the early vulnerability model of recovery of function after brain damage, it was also hypothesised that the deficits in executive function displayed by children exposed to alcohol *in utero* would become more pronounced with age. Surprisingly, deficits in executive function appeared to be present only in 6- to 7-year-old children, whilst 12- to 13-year old children were not found to differ significantly from their non-exposed peers. These findings are discussed in relation to previous studies investigating deficits in executive function following *in utero* alcohol exposure.

Deficits in attention are often considered the hallmark of *in utero* alcohol exposure (Mattson et al., 2006), as impairments in this area of cognitive functioning are often seen as accounting for many of the behavioural characteristics of FASD (Korkman et al., 2003). As mentioned above, models of attention often subdivide

attention into several factors (Mirsky et al., 1991). In addition, a distinction is often made between auditory and visual attention, with studies suggesting that attentional skills in the two modalities may function independently of each other to some extent (Klenberg et al., 2001). Some disagreement exists in the literature as to which aspects of attention are affected in children with FASD (Mattson et al., 2006). In the study conducted by Korkman et al. (2003), children with FASD were found to exhibit significant deficits in auditory attention, with a poor performance on both the Auditory Attention task and the Auditory Response Set task of the NEPSY relative to control participants. These findings correspond to the present ones, with one exception: the present study did not find significant deficits on the Auditory Response Set task.

The Auditory Attention task and the Auditory Response Set task have been shown to measure slightly different aspects of attention (Klenberg et al., 2001). Whilst efficient performance on both subtests require the ability to focus and sustain auditory attention, the Auditory Response Set task also require the ability to shift set and to regulate responses according to matching and contrasting auditory stimuli, which would require encoding (Klenberg et al., 2001). Thus the findings of the present study suggest that children exposed to alcohol *in utero* displayed significant deficits in terms of the ability to focus and sustain auditory attention, but not in terms of the ability to shift set and to regulate responses according to matching and contrasting auditory stimuli. These findings are inconsistent with those of Coles et al. (1997) who demonstrated that children with FASD had more difficulty in shifting attention and encoding new information. However, it is important to note that Coles et al. (1997) were comparing children with FASD with children with ADHD, and that the pattern of attentional deficits they observed in children with FASD may therefore

be relative to other children with severe attentional difficulties. The findings of the present study are consistent with those of Mattson et al. (2006) who demonstrated that children with FASD had particular difficulties on tasks of focussed auditory attention, but not on tasks of encoding and shifting, in comparison to control participants.

In their study, Korkman et al. (2003) did not find significant deficits in the domain of visual attention in children with FASD. Consistent with this, the findings of the present study suggest that children exposed to alcohol *in utero* did not present with significant deficits on the Visual Attention subtest when performance time was taken into account. However, children exposed to alcohol *in utero* were found to perform significantly worse than control participants in terms of their accuracy score on the Visual Attention subtest, which excludes the processing speed component of the task. These findings are consistent with those of Mattson et al. (2006) who also demonstrated lower accuracy levels on a test of visual focussed attention in children with FASD.

In terms of other aspects of executive function, the present study noted deficits on tests measuring the ability to plan and organise goal directed behaviour (Tower subtest) in addition to those measuring the ability to inhibit salient responses (Knock and Tap subtest). Similar results were found by Korkman et al. (2003) who also demonstrated that children with FASD exhibited deficits on the Tower subtest and the Knock and Tap subtest of the NEPSY. These findings are also consistent with findings by Kodituwakku et al. (1995), who demonstrated deficits in planning and problem solving on the Progressive Planning Test in children with FASD.

In their study, Schonfeld et al. (2001) demonstrated deficits in verbal and non-verbal fluency in children between the age of 8 and 15 years of age with FASD. No such deficits were found in the present study. This is consistent with findings by

Korkman et al. (2003), who also did not find deficits in verbal and non-verbal fluency in children with FASD. These discrepant findings can possibly be explained in terms of different age ranges used in the Schonfeld et al. (2001) study and the present study. Studies investigating the development of executive function in normal children suggest that fluency continues to develop into adolescence and even young adulthood (Klenberg et al., 2001), albeit at possibly a slower rate (Anderson et al., 2001a). Thus the findings from Schonfeld et al. (2001) study may reflect age-related changes in executive abilities.

Although the findings of the present study are broadly consistent with previous studies investigating executive function in children with FASD, it is important to note that the alcohol exposed group was heterogeneous with respect to age. A closer look at the data revealed that only 6- to-7-year-old, but not 12- to 13-year-old exposed children exhibited deficits on the Tower subtest, the Knock and Tap subtest, the Auditory Attention task, and the Visual Attention Accuracy score. These findings are more difficult to reconcile with the literature. Although most previous studies have made use of very wide age-ranges making it difficult to compare their results with those of the present study, at least one study has examined the executive function of adolescents (12- to 14-year-olds) with FASD (Korkman et al., 2003). This study clearly demonstrated the presence of deficits in executive function in adolescents with FASD (Korkman et al., 2003).

One possible explanation for these discrepant findings is differences in the level of exposure in our sample of 12- to 13-year-olds and the sample of Korkman et al. (2003). It is interesting to note that Korkman et al. (2003) only found significant impairments in executive function in those children who were exposed to alcohol

throughout pregnancy, as opposed to those children who were exposed only during the first trimester and those only exposed during the first and second trimester.

This raised the question of whether 6- to 7-year-old and 12- to 13-year-old exposed children in the present study differed with respect to the quantity and duration of alcohol exposure, and whether these differences could possibly account for the lack of deficits in the older age group. This hypothesis is supported by findings that 6- to 7-year-old exposed children had a significantly smaller head circumference than their non-exposed peers, whilst similar findings were not obtained for 12- to 13-year-olds. However, findings indicating that 6- to 7-year-olds and 12- to 13-year-olds did not differ with respect to the frequency with which they manifested with the facial characteristics of FAS and the frequency with which they presented with neurological hard and soft signs argues against this. Neither can these findings be attributed to differences in IQ, since there were no significant differences in the IQ scores obtained by 6- to 7-year-old and 12- to 13-year-old exposed children. IQ was also not a significant covariate on any of the tests where deficits were noted for 6- to 7-year olds. When the mean scores obtained by exposed and non-exposed children in the older age group was examined, it was found that 12- to 13-year-old children consistently obtained a lower mean score than their non-exposed peers on all relevant subtests of the NEPSY. These findings suggest that there may have been differences in the performance of exposed and non-exposed children in this age range, but that these differences were difficult to detect due to the small sample size.

Nonetheless, the findings of the present study suggest that the deficits in planning and organisation of goal directed behaviour, inhibition, focused and sustained auditory attention, and accuracy of visual attention present in children exposed to alcohol *in utero* dissipates with age. Interestingly, these findings are

consistent with findings in the animal literature. Studies have demonstrated that rats exposed to alcohol *in utero* typically present with overactivity as pups (see Riley, 1990 for review). However, as the animal matures, this behaviour generally dissipates (Riley, 1990). This has led to the hypothesis that prenatal alcohol exposure leads to developmental delays, with young animals exhibiting less mature behaviour than their non-exposed peers. However, as the animal matures, it catches up with its peers leading to diminishing differences in its behaviour in comparison to that of controls (Riley, 1990). This hypothesis fits well with the findings of the present study suggesting that both exposed and non-exposed children display increasing executive abilities with age, albeit at possibly a different rate. Although tentative, the findings of the present study suggest that at least some aspects of executive function develop more gradually in children exposed to alcohol *in utero* in comparison to that of non-exposed children. This possibly leads to developmental delays which manifests as deficits in younger children. These deficits appear to dissipate as alcohol exposed children grow older and catch up with their non-exposed peers. The implications of these findings in relation to theories of recovery of function after brain damage are discussed in more detail below.

5.4. The development of executive dysfunction in children exposed to alcohol *in utero*

The findings of the present study suggest that exposed and non-exposed children may display somewhat different trajectories in terms of the development of executive function. In the developmental neuropsychological literature, the development of executive function is seen to be dependent on the functional maturity of anterior and posterior cortical, thalamic and striatal structures, as well as the maturation of

interconnections between these structural nodes (Luciana & Nelson, 1998). However, studies have shown that children exposed to alcohol *in utero* present with wide-spread structural changes to cortical and subcortical structures (Archibald et al., 2001; Autti-Rämö et al., 2002), as well as white matter changes (Autti-Rämö et al., 2002; Clark et al., 2000; Mattson et al., 1996; Sowell et al., 1996). These structural changes are likely to have an impact on the efficient functioning of the various cortical and subcortical structures, and would also prevent efficient interconnections between structural areas from forming during postnatal cerebral development. Structural changes to the brain are therefore likely to impede the development of executive function, leading to a slower rate of development in children exposed to alcohol *in utero*.

The findings of the present study also suggest that whilst exposed children exhibit significant deficits in executive and attention abilities at age 6- to 7-years, such deficits are no longer salient at age 12- to 13-years. As mentioned above, these findings are supported by the animal literature, which suggests that the behavioural disturbances present in rats follow *in utero* alcohol exposure dissipates with age (Riley 1990). In a developmental context, impaired executive function following *in utero* exposure to alcohol can therefore possibly be better understood as "delays" rather than "deficits" per se. Such a hypothesis fits well with plasticity theories of recovery of function after brain damage, which posits that the immature brain has a greater capacity for recovery after insult because functional organisation is less established in the immature brain than in the mature brain (Anderson et al., 2001b). In cases of early brain damage, children may therefore be able utilise parallel or alternative routes to develop a specific skill (Anderson et al, 2001b).

However, plasticity theories have been widely criticised as being over-simplistic. Hebb (1949 cited in Anderson et al., 2001b) has argued that plasticity theorists ignore the possibility that damage to the brain will have different consequences depending on the age of insult. Studies of children with prenatal lesions, or children sustaining insults before the first year of life, suggest that these children present with greater impairment to cognitive functions than children sustaining damage later in childhood (Ducowny et al., 1996; Riva & Cassaniga, 1986). Based on studies such as these, proponents of the early vulnerability theory have argued that early brain damage, especially insults occurring prenatally or in the first year of life, are particularly detrimental to the development of cognitive abilities (Anderson et al., 2001b). Such a hypothesis is certainly much more consistent with the findings of previous studies documenting deficits in executive function in adolescents (Klenberg et al., 2001) and adults (Connor et al., 2000; Kerns et al., 1997; Malisza et al., 2005) exposed to alcohol *in utero*.

Riley (1990) has argued that conceptualising the behavioural disturbances exhibited by rat pups as simply an expression of developmental delays may be an oversimplification. Based on studies demonstrating that the behaviour of adult animals exposed to alcohol *in utero* breaks down under stressful conditions, he argues that in addition to developmental delays, these animals suffer from developmental dysfunction (Riley, 1990). He hypothesised that the behavioural disturbances exhibited by *in utero* exposed animals may diminish with age because these animals learn compensatory strategies to deal with their dysfunction (Riley, 1990). However, under stressful conditions these compensatory mechanisms break down, leading to the re-emergence of behaviour disturbances (Riley, 1990).

As discussed above, previous studies have shown that children's performance on tests of executive function are critically mediated by task difficulty (Luciana & Nelson, 1998). The tests of executive function utilised in the present study may not have been demanding enough to elicit deficits in the performance of older children. This concern is highlighted by the fact that the NEPSY has only been standardised and validated for children up to the age of 12 (Korkman et al., 1998). Although this neuropsychological test has been used previously to evaluate the executive function of older children exposed to alcohol *in utero* (Korkman et al., 2003), its applicability in older children is not well established.

In addition, it is important to note that the assessment of executive function is problematic at best (Anderson, 2002). Most tests of executive function are complex, demanding and multi-faceted tasks, which tap executive function as well as more basic cognitive processes (Anderson, 2002). Distinguishing between the influences of these various cognitive processes becomes problematic, especially when only quantitative data is used to interpret performance (Anderson, 2002). Furthermore, it is important to note that the ecological validity of executive function tests have been questioned, because of frequently observed differences between performance on measures of executive function and real life behaviour (Anderson, 2002). The relatively modest ability of executive function tests to predict everyday behaviour (Anderson, 2002) may account for inconsistencies between the findings of the present study suggesting that executive dysfunction following *in utero* exposure becomes less pronounced with age and findings from previous studies, indicating that deficits in the adaptive behaviour of children with FASD become more pronounced with age (Thomas et al., 1998; Whaley et al., 2001). In testing situations, the examiner performs various executive functions for the examinee; by providing a quiet and

structured setting, by giving encouragement, and by planning and initiating activities (Anderson 2002). Similar to animals exposed to alcohol *in utero* (Riley, 1990), children with FASD may develop compensatory strategies to deal with their cognitive deficits. In keeping with the findings of the present study, this may manifest in a more efficient performance on tests of executive function in older children in comparison to younger children. However, when these individuals are exposed to more complex testing procedures or have to cope with the stress created by complex social situation, these compensatory strategies may breakdown.

5.5. Limitations

Given the hypothesis and rationale of the study, it could be argued that a longitudinal design would have improved its methodology. However, the present study was intended to be exploratory in nature. As such, it is hoped that this study's findings will form the basis of future longitudinal work tracking the development of executive function in children exposed to alcohol *in utero* from early childhood to adolescence.

For similar reasons, the sample size of the present study was rather small, with few participants at each age level. Although statistical analysis was able to detect significant differences between exposed and non-exposed children at different age levels, these results need to be interpreted with caution. It is therefore accepted that the results obtained in this study may not be fully generalisable.

Previous studies in the field have found that a significant relationship exists between the duration of alcohol exposure and the severity of neuropsychological deficits (Korkman et al. 2003). A limitation of the present study is that it did not control for the quantity and duration of *in utero* alcohol exposure. Findings

suggesting that 12- to 13-year-olds did not present with significant deficits in executive function may therefore be related to less severe exposure in this age group in comparison to 6- to 7-year-old exposed children. Although it is possible that the younger age group were exposed to more alcohol for a longer period of time, findings indicating that dysmorphic facial features and CNS dysfunction occurred with similar frequency for the 6- to-7-year-olds and 12- to 13-year-olds, suggest that both age groups suffered at least some neurobiological consequences due to maternal alcohol use during pregnancy. Nonetheless, it is important to note that the sample utilised in the present study may not be representative of children with FASD in the general population.

The influence of non-optimal social environment on the development of executive abilities was also not adequately controlled for. As Korkman et al. (2003) pointed out; the inability to control for the influence of non-optimal social background is a problem inherent in all studies investigating the cognitive deficits associated with FASD. Maternal alcohol use has both social and neurobiological consequences. Children with alcoholic mothers frequently lead disrupted lives, characterised by high level of family dysfunction and frequent changes in placement (Korkman et al., 2003) In this sample, seven children who were exposed to alcohol *in utero* were in foster care, usually with an aunt, grandmother or other close relative. The adequacy of these placements was not established. The adequacy of care received by those children still living with their parents was not ascertained either. These psychosocial factors may have had an impact on the development of executive function in this sample.

All participants in the present study spoke Afrikaans as a first language. This necessitated the translation of tests instructions and verbally mediated test material

into Afrikaans. This may have affected the validity of the NEPSY. Previous studies investigating the applicability of the NEPSY in developing countries have shown that the performance of children in developing countries is generally one standard deviation below that of children in developed countries (Mulenga et al., 2001). These findings may be related to language and cultural differences (Mulenga et al., 2001). There is an urgent need for the translation and standardisation of neuropsychological tests such as the NEPSY for South African children.

5.6. Directions for future research

Future research should focus on establishing a comprehensive profile for the development of executive function in children with FASD, since the development of executive function in this population is still poorly understood. Ideally such research should take the form of longitudinal studies, tracking the development of executive function in children exposed to alcohol *in utero* from early childhood to adolescence. Future cross-sectional studies should make use of larger sample sizes. It may also be valuable to include a greater number of age groups. The present study only made use of two age groups, and was therefore unable to establish the age at which different aspects of executive function reached maturity in children exposed to alcohol *in utero* in comparison to non-exposed control participants. Future studies may also want to consider using behavioural inventories, such as the Behavior Rating Inventory of Executive Function [BRIEF] (Gioia, Isquith, Guy, & Kenworthy, 2000) to obtain qualitative information about executive function behaviour at home, school, and in social situations. The information obtained on behavioural inventories such as the BRIEF may be a useful addition to those obtained by standard measures of executive

function, since they allow for a better prediction of child's everyday behaviour (Anderson, 2002).

5.7. Summary

The findings of the present study suggest possible age-related increments in executive abilities from age 6- to 7-years to age 12- to 13-years in both exposed and non-exposed children. To our knowledge, this is the first study reporting such age-related changes in executive abilities in a South African sample. Although limited, the findings of the present study suggest that at least some aspects of executive function may develop at a slower rate in children exposed to alcohol *in utero* in comparison to non-exposed children. It is clear from both the present study and previous research in the field that the executive abilities of children exposed to alcohol *in utero* are significantly compromised. However, the findings of the present study suggest that these deficits may become less pronounced with age. Thus the findings of the present study suggest that children exposed to alcohol *in utero* display delays in the development of executive function which may dissipate with age. These findings are most likely related to the level of task difficulty. Based on previous studies in the field, we can hypothesise that older children may have developed compensatory strategies, which allowed them to perform fairly well on tests of executive function. However, these compensatory strategies are likely to break down under more complex testing situations, as well as real-life situations which place greater demands on the child than the relatively structured situation of one-to-one testing. This hypothesis fits well with the available evidence, indicating that executive deficits in individuals exposed to alcohol persist into adulthood. These findings have important implications for rehabilitative strategies, as they suggest that

children exposed to alcohol will perform relatively well in structured setting, where others function as their supervisory control system.

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Appendix A: Interview schedule

Patient ☐ Participant Nr_____

Control ☐

Name of child:	
Sex:	
Birth Date:	
Age:	
Home Language:	
Grade:	
Nr of Grades repeated, if any:	
Handedness:	
Full Scale IQ:	
Name of Parent:	
Marital Status:	
Occupation:	
Highest Level of Education Attained:	

Birth History and Developmental milestones

Pregnancy_____

Labour_____

Sit_____

Crawl_____

Walk_____

Bladder and Bowl control_____

Psychiatric history of the child (e.g. Depression, ADHD, Anxiety)

_____

_____

_____

_____

History of Alcohol/Drug Use (in the child)

_____

_____

Medical History of the child

_____

_____

_____

_____

T-ACE

Please answer the following questions honestly.

T **Tolerance**: When you were pregnant with your child, how many drinks did it take to make you feel high?

A Did people ever **Annoy** you by criticising your drinking while you were pregnant?

C While you were pregnant, did you ever feel you ought to **cut down** on your drinking?

E **Eye opener**: Did you ever have a drink first thing in the morning to steady your nerves or to get rid of a hangover, while you were pregnant?

Notes

Appendix B: Informed Consent Forms

UNIVERSITY *of the* WESTERN CAPE

DEPARTMENT OF PSYCHOLOGY

Private Bag X 17, Bellville 7535, South Africa, Telephone: (021) 959-2283/2453

Fax: (021) 959-3515 Telex: 52 6661

Parent/Guardian Information Sheet and Consent Form

Title of the Project:

The development of executive function in children exposed to alcohol* in utero*: An exploratory study

Researcher	Tania Badenhorst
Tel:	021 447 8942
e-mail:	harper@ananzi.co.za
Supervisor	Kamal Kamaloodien
Institution	University of the Western Cape
Tel:	021 959 2283

You are invited to participate as a subject in a psychological study. Please read this information sheet carefully and do not hesitate to ask the researcher any questions.

The aim of the study is to explore the cognitive function of children exposed to alcohol before birth. As a participant in the study you will be asked some questions about your child's history. Your child will undergo a physical examination by a doctor. He/she will also undergo psychological testing. We do not expect this study to harm you or your child in any way, but you should tell the researcher immediately if you or your child should become mentally or physically tired or if you or your child experience any distress. The researcher will refer you to appropriate counselling services should this be the case.

It is up to you and your child to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part, you are still free to withdraw from the study **at any time**, **without having to give a reason** and **without this affecting future treatment**. The confidentiality of your child's answers and identity will be protected. However, the results of your child's performance on the psychological tests will be given to psychologists attached to the Education Management and Development Centre (EMDC) attached to your child's school in order to benefit him or her, if you give us permission to do so.

This study forms part of a Masters degree in psychology at the University of the Western Cape. The study is being reviewed by the University of the Western Cape's higher degrees ethics committee. If you have any questions about this study, or concerns about the manner in which the study was conducted or would like to be informed of the results when the study is completed, please feel free to contact the researcher or her supervisor.

MAY YOUR CHILD'S RESULTS BE PASSED ON THE PSYCHOLOGISTS AT THE EMDC? YES/NO

Signed_____ Date_____

NAME OF PARENT (IN BLOCK LETTERS)_____

NAME OF CHILD (IN BLOCK LETTERS)_____

UNIVERSITY *of the* WESTERN CAPE

DEPARTMENT OF PSYCHOLOGY

Private Bag X 17, Bellville 7535, South Africa, Telephone: (021) 959-2283/2453

Fax: (021) 959-3515 Telex: 52 6661

Child Assent Form

Title of the Project:
The development of executive function in children exposed to alcohol* in utero*: An exploratory study

Researcher	Tania Badenhorst
Tel:	021 447 8942
e-mail:	harper@ananzi.co.za
Supervisor	Kamal Kamaloodien
Institution	University of the Western Cape
Tel:	021 959 2283

You are invited to participate as a subject in a psychological study. Please read this information sheet carefully and do not hesitate to ask the researcher any questions.

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It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part, you are still free to withdraw from the study **at any time**, **without having to give a reason** and **without this affecting future treatment**. The confidentiality of your answers and identity will be protected.

Signed_____ Date_____

NAME OF CHILD (IN BLOCK LETTERS)_____