The Effects of Prenatal Alcohol Exposure on Cognitive Functioning

Bachelor's Thesis Clinical Health Psychology

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Abstract

Alcohol can have numerous disadvantageous effects on the fetus. These effects together form a spectrum named fetal alcohol spectrum disorders (FASD) and contain structural anomalies and neurocognitive and behavioral disabilities. Fetal alcohol syndrome (FAS) is the most clinically recognized form of FASD (Manning and Hoyme, 2007). Wacha and Obrzut (2007) conclude that infants with FAS or prenatal alcohol exposure (PAE) experience difficulties in areas of cognitive functioning including language, visual-spatial functioning, nonverbal learning, attention, and memory. In adulthood mental health problems are the most demonstrated problems of FAS (Lemoine et al., 2003). In this thesis we are going to find out more about some of these cognitive effects of prenatal alcohol exposure by carrying out a literature review.

Keywords alcohol, attention, central nervous system (CNS), cognition, development, fetal alcohol syndrome (FAS), prenatal alcohol exposure (PAE), pregnancy

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Introduction

Over the past 15 years the drinking habits among women of child-bearing age and pregnant women have changed little (Caetano, Ramisetty-Mikler, Floyd and McGrath, 2006). One study showed that nearly 45% of women consumed alcohol during the 3 months before they found they were pregnant (Floyd, Decoufle and Hungerford, 1999, as cited by Caetano et al., 2006.

It is known that heavy alcohol consumption during pregnancy has a serious risk to the exposed fetus (Caetano et al., 2006). However, experiments in animals show that even lesser amounts of alcohol may also have harmful effects on the fetus (Hanson, Streissguth and Smith, 1978). So the question is what amount is significantly dangerous?

According to Jacobson and Jacobson (1994) consuming 5 or more alcoholic drinks on one occasion increases the risk for women and their children. On the other hand, Barr and Streissguth (2001) suggest that 3 or more drinks in a day and daily or almost daily drinking, increases the risk for fetal alcohol spectrum disorders (FASD) like fetal alcohol syndrome (FAS), which is the most clinically recognized form of FASD compared to other fetal alcohol disorders within this spectrum.

There are many criteria for risk, but there are no data on what is a safe level of drinking during pregnancy (Gunzerath et al., 2004, as cited by Caetano, Ramisetty-Mikler and Mcgrath, 2006). Consequently, many women of child-bearing age who are light drinkers are at risk for giving birth to babies with no identifiable dysmorphology, but who could have significant cognitive and behavioral control problems (Caetano et al., 2006).

Prenatal alcohol exposure can affect several developmental processes, especially for the fetal growth and morphogenesis (Hanson, Streissguth and Smith, 1978). While drinking during any period of pregnancy could be harmful to the fetus, various reports underestimate the period around conception and the first trimester of pregnancy when the central nervous system (CNS) develops and is most vulnerable to damage (Coles, 1994; Day et al., 1993, as cited by Caetano et al., 2006).

Naimi and colleagues (2003) state that maternal demographic factors play a significant role in understanding maternal alcohol consumption during pregnancy and engaging in preconceptional binge drinking. Naimi et al. note that most of women who drink during pregnancy are from socioeconomically disadvantageous groups and have little or no access to health care services. Factors like a younger age, being unmarried and having an unintended pregnancy are also correlated with maternal alcohol consumption habits during pregnancy.

Higher rates of preconceptional binge drinking have been reported among women with unintended pregnancy compared with women with intended pregnancy. Women who were white, unmarried, smokers or had experienced violence are more likely to engage in preconceptional binge drinking. They are also more likely to consume alcohol, binge drink, and smoke during pregnancy.

Negative feelings and emotions about oneself, wrong opinions about the effects of different alcoholic beverages (Kaskutas, 2000, as cited by Caetano, Ramisetty-Mikler and Mcgrath, 2006) and lower rates of prenatal health care in the first trimester of pregnancy (Ventura et al., 2001, as cited by as cited by Caetano, Ramisetty-Mikler and Mcgrath, 2006) reinforce drinking during pregnancy too.

The purpose of this thesis is exploring the effects of prenatal alcohol exposure on cognitive functioning. However, the research field of fetal alcohol spectrum disorders is broad. Many research is done to study the effects of prenatal alcohol exposure on many aspects of life. In this thesis we take a few subjects to find out more about these effects by carrying out a literature review. At first we are going to define FAS. Next we explore the effects of prenatal alcohol usage on CNS and other parts of the body and appearance. Further we are going to find out what the effects of prenatal alcohol exposure are on cognitive functioning (intelligence, language, attention and motor abilities) and executive functioning. Finally we are going to focus on mental health problems and psychopathology caused by or correlated with maternal prenatal alcohol consumption.

1. Fetal alcohol syndrome

1.1 Definition of fetal alcohol syndrome

The fetal alcohol syndrome (FAS) was first described in 1968 by Lemoine and colleagues and named by Smith and Lyon Jones in 1973 (Streissguth, 1993, as cited by Larkby and Day, 1997). FAS is an extreme clinical diagnose applied to prenatal alcohol exposed infants.

Children with FAS exhibit deficits in growth and physical dysmorphology such as deformity of facial structure (Larkby and Day, 1997) and anomalies in brain structure like microcephaly which delay social and motor performance related to mental age, intellectual disability and neonatal problems including irritability and feeding difficulties (O'Leary, 2004).

In FAS we distinguish "primary disabilities" and "secondary disabilities". By primary disabilities we mean functional difficulties due to CNS damage that occur in the uterus during fetal development. We talk about secondary disabilities when the prenatal brain damage caused by the primary disabilities is undetected and behavioral problems arising from it are not understood. For example, impaired dendrites of the hippocampus may be associated with learning problems (Abel, Jacobson and Sherwin, 1983). Secondary disabilities arise when an individual gets older and often emerge when primary disabilities lead to maladjustment to the expectations of the environment (Streissguth et al., 1996; Streissguth and O'Malley, 1997). One of these problems can be alcohol or drugs problems among individuals of twelve years and older (Streissguth et al., 1996)

1.2 Diagnosis

Generally the diagnosis of FAS is made when infants are aged 2 years and older (Burd, Cotsonas-Hassler and Martsolf, 2003, as cited by Wacha and Obrzut, 2007). In order to be diagnosed with FAS there must be evidence that there was maternal alcohol usage during pregnancy (O'Leary, 2004) and Sokol and Clarren (1989) state that an infant must have symptoms in the following three categories: (1) growth deficiency in both the prenatal and postnatal periods, (2) abnormalities in facial and skull structure, including small eye openings (short palpebral fissures), alterations in nose and forehead structure, an absent or a too long groove between the upper lip and nose (philtrum), a thin upper lip, a flattened midface, and underdevelopment of the upper or lower jaw, and (3) CNS deficits like mental retardation and behavioral problems.

Sampson et al. (1997) state that at least 9.1 per 1000 births are diagnosed with FAS or prenatal alcohol exposure (PAE). Larkby and Day (1997) state that the CNS deficits have the most significant effect on overall development. Larkby and Day also explicate that the diagnosis of FAS is complicated because the characteristics associated with FAS change when an individual matures. They state the following:

> "Before age 2, CNS dysfunction is difficult to assess, and the classic facial abnormalities may not be clearly evident. At older ages, growth deficits are offset by the adolescent growth spurt as well as normal changes in facial length and width associated with maturation. Because of these changes, growth deficits and facial features become less apparent after puberty, and without prepubertal photographs and reliable growth records, FAS may be difficult to diagnose in adolescents or adults." (p.193)

1.3 Unknown and confirmed exposure

The diagnosis of FAS is often overlooked because it is not a visible birth defect. There is no particular test to make the diagnosis sure and often, mothers are not asked about their drinking behavior during pregnancy. Consequently, undiagnosed FAS can result in hidden CNS abnormalities and disabilities (Streissguth, Barr, Kogan and Bookstein, 1996, as cited by Larkby and Day, 1997).

A fetus develops in a sequential process with multiple stages. To examine the effects of alcohol on the development of the prenatally exposed child, we should take factors like timing, dose and patterns of alcohol exposure into account. This is because morphologic abnormalities, growth and CNS deficits occur at different points during the development of the embryo. For example, most morphologic abnormalities are a consequence of alcohol exposure in early pregnancy. On the other hand, there is a risk for CNS deficits throughout pregnancy (Larkby and Day, 1997). Altogether Larkby and Day conclude the following:

> "Offspring who are exposed to alcohol throughout pregnancy will not have the same outcome as offspring who are exposed only during early pregnancy or only at specific times during pregnancy. Identifying the nature of the relationships between prenatal alcohol exposure and outcome is also important for research and clinical reasons." (p.194)

When a fetus is exposed to a toxin the effect may have a direct relationship with the amount of exposure. With a direct relationship we mean a linear relationship, in which there is no "safe" level of drinking during pregnancy because even a small amount of alcohol can have

an effect. On the other hand, an exposure may be only problematic when it reaches above a certain level. We call this a “threshold relationship”. This relationship implies that we can assume that a “safe” level of alcohol consumption during pregnancy exists. Data from studies demonstrate that the relationship between alcohol exposure and outcome depends on the type of outcome under consideration (Larkby and Day, 1997). Studies with animals (Schenker et al., 1990, as cited by Larkby and Day, 1997) and humans (Sampson et al. 1989; Goldschmidt et al. 1996, as cited by Larkby and Day, 1997) support a threshold relationship between prenatal alcohol exposure and CNS development. On the other hand, data on physical growth indicate that the effect of gestational exposure to alcohol is linear and therefore, no “safe” level of consumption exists (Day et al., 1994, as cited by Larkby and Day, 1994).

2. Physical development

2.1 Structural Effects on CNS

Structural imaging studies have found several differences between the brains of individuals with FAS or PAE and individuals who were not exposed to alcohol during their fetal development. Children with FAS exhibit structural changes in various brain regions like the basal ganglia, corpus callosum, cerebellum, and hippocampus (Mattson, Schoenfeld and Riley, 2001, as cited by Wacha and Obrzut, 2007).

The basal ganglia is a group of nerve cell clusters, including the putamen, caudate nucleus, and globus pallidus. The basal ganglia controls motor abilities and executive functions. The corpus callosum is a large bundle of nerve fibers connected to the two hemispheres of the brain. It makes communication between the two hemispheres possible. The cerebellum is a structure at the base of the brain and is involved in the control of muscle tone, balance and sensori-motor coordination. The hippocampus is a structure in the temporal lobe that plays a role in learning and memory (Mattson, Schoenfeld and Riley, 2001, as cited by Wacha and Obrzut, 2007).

As shown in MRI studies, infants with FAS have a decrease in the overall size of the brain. This may be related to structural changes in the cerebellum, basal ganglia, hippocampus, and corpus callosum caused by alcohol exposure (Roebuck, Mattson and Riley, 1999). For example, Mattson and colleagues (2001, as cited by Wacha and Obrzut, 2007) found that the overall size of the cerebellum of individuals with FAS is disproportionately reduced compared with the overall size of their brain. The authors also found a disproportional reduced size of the basal ganglia. This reduction was not uniform and the caudate nucleus showed the strongest decrease in size as was shown in MRI studies. Subsequently, the hippocampus in individuals with FAS show volume asymmetries. The volume of the hippocampus in the left temporal lobe was smaller than the one in the right temporal lobe. Finally Roebuck and colleagues (1999) found that the corpus callosum is also reduced in size in FAS patients. The splenium and isthmus are the back part of the corpus callosum and the genu is its most frontal area and these areas are disproportionately smaller in size. According to Roebuck et al. the abnormalities and structural differences related to the volume of the corpus callosum of FAS patients ranges from thinning to complete agenesis. Besides, the corpus callosum of individuals with FAS exhibits a higher rate of agenesis.

The structural changes in the brains of patients with FAS result in several deficits of behavior. For example, prenatal alcohol exposure can affect learning. Coordination and

balance are also affected. Further, changes in basal ganglia may result in deficits in the ability to shift between tasks, inhibition of inappropriate behavior and spatial memory. Damage to the corpus callosum is related to deficits in attention, reading, learning, verbal memory, and executive and psychosocial functions. Finally changes to hippocampus have been linked to deficits in spatial memory and other memory functions (Mattson, Schoenfeld and Riley, 2001, as cited by Wacha and Obrzut, 2007).

2.2 Neurophysiological effects on CNS

According to Wacha and Obrzut (2007) there are negative significant effects of prenatal alcohol exposure on the neurophysiology of the brain. Two studies conducted by Kaneko et al. (1996a; 1996b, as cited by Wacha and Obrzut, 2007) measured the electrical brain activity of adolescents with FAS with EEG. Kaneko and colleagues found that the alpha rhytms of these individuals showed a decrease in power or strength. This is a prominent form of neuroactivity when a person is in a relaxed state. These results suggest immature brain activity. Besides, both studies with EEG analyses of adolescents with FAS found that the P300 spikes which are the brain's electrical response to specific sensory stimuli and reflect the cognitive aspects of the processing information, occur with a delay in the parietal cortex. This finding indicates the possibility that children with FAS have information processing difficulties and impaired functioning of the midbrain dopamine (DA) system.

One study conducted by Dubois et al. (2004, as cited by Wacha and Obrzut, 2007) examined the effects of binge drinking on the neurophysiology of the brain. These researchers looked at the impact of binge alcohol exposure on postsynaptic amonobutyric acid type A receptors (GABAARs) in synapses which are still in growth. They found that binge alcohol exposure directly inhibits immature postsynaptic GABAARs and that this situation obstructs the "developmental program responsible for maturation of inhibitory GABAergic synapses on septal neurons. "(p. 220). Dubois et al. explicate that these deficits in neurotransmission can lead to learning and memory problems in individual with FAS or PAE.

2.3 Variation in CNS abnormalities

Steinhausen and Spohr (1987) state that in FAS, CNS abnormalities vary from person to person. For example, some persons exhibit microcephaly, fine or gross motor deficits, attentional deficits, or cognitive impairments, while others with FAS show none of the above symptoms at all.

According to Streissguth (1993, as cited by Larkby and Day, 1997) there are two factors related to the individual differences in the manifestation of CNS abnormalities, namely: the prenatal alcohol exposure itself (dose, timing, pattern of exposure) and individual differences (genetic variables). Carmichael-Olson et al. (1998) explain that generally, greater prenatal alcohol exposure results in more severe physical problems, at the same time lower levels of exposure (0.5–1 oz alcohol per day) manifest as behavioral problems and problems with adaptive functioning. They call this the dose-response relationship. Besides Carmichael-Olson et al. (1997) explicate that prenatal alcohol exposure can also cause CNS abnormalities without any visible physical signs.

2.4 Growth

As noted in the previous chapter, individuals with FAS exhibit growth deficits and morphologic abnormalities. One study by Streissguth et.al (1991, as cited by Larkby and Day, 1997) gives an overview of the long-term effects of prenatal alcohol exposure. The aim of the research was to study the adolescent and adult manifestations of FAS and prenatal alcohol effects and therefore they examined 61 subjects. They found that the subjects were small in stature and in head circumference at adolescence and adulthood. They also showed many abnormal facial features, although these characteristics were not as visible as they had been at younger age. According to Streissguth and colleagues infants with FAS are small for their age. In the previous chapter we saw that this is one of the criteria for the diagnosis of FAS, although we should not forget that growth deficits are also characteristic among children who do not fulfill the criteria for FAS, but who were exposed to alcohol during their fetal development.

When prenatal alcohol exposure is greater, growth deficits are more pronounced, this shows a linear relationship. Yet we should consider that postnatal environment and maternal demographic factors such as a younger age, unintended pregnancies and lower socioeconomic status affect this relationship (Naimi et al., 2003). In fact, these effects aggravate the effects of prenatal alcohol exposure, because these factors play a significant role in understanding maternal alcohol consumption during pregnancy (Larkby and Day, 1997).

2.5 Facial dysmorphology

Klingenberg et al. (2010) define “directional asymmetry” as systematic differences between the left and right sides of the body. For example, researchers have found asymmetry

of internal organs and the subtle asymmetry of the human brain (Toga and Thompson, 2003, as cited by Klingenberg et al., 2010). These asymmetric differences are widespread in the human population (Klingenberg et al., 2010).

Although subtle facial directional asymmetry is found in healthy individuals (DeLeon, 2007; Ercan et al., 2008; Schaefer et al., 2006, as cited by Klingenberg et al., 2010), more pronounced and stronger directional asymmetry is associated with a disruption of normal craniofacial development (Bock and Bowman, 2006, as cited by Klingenberg et al., 2010), deformational plagiocephaly or craniosynostosis (Netherway et al., 2006, as cited by Klingenberg et al., 2010).

Although there has been little attention paid to the effects of prenatal alcohol exposure on facial asymmetry, it is now known that prenatal alcohol exposure can lead to facial dysmorphology and this is an important criterion for the diagnosis of FAS. Modern techniques of geometric morphometrics have confirmed that prenatal alcohol exposure has significant effects on facial shape. These sensitive morphometric methods are specifically developed to measure asymmetry of shape. Using these methods, Klingenberg and colleagues detected subtle, but statistically significant directional asymmetry in the face. They concluded that this asymmetry is not the same for individuals who were not prenatally exposed to alcohol (Klingenberg et al., 2010).

In one International study, Klingenberg and colleagues (2010) assessed 168 participants from different countries. Each participant was examined using a complete standardized, uniform assessment as described by Jones et al. (2006, as cited by Klingenberg et al., 2010). These researchers used a standard classification system which was based on features and growth deficiency to classify the features of the participants into three groups. The first group included participants diagnosed with FAS. These individuals were prenatally exposed to alcohol. The second group was the control group. In this group neither of the participants was diagnosed with FAS or exposed to alcohol during their fetal development. The third group was labeled as “deferred” and included individuals who were prenatally exposed to alcohol, but who had not received the diagnosis of FAS. This deferred group was excluded from this study, because the aim of this study was to determine if there is a difference between the facial asymmetry of individuals with FAS and the control group.

Klingenberg and colleagues captured two frontal and two lateral left and right facial images of the participants. They used geometric morphometric analyses to measure the facial asymmetries. According to Dryden and Mardia (1998, as cited by Klingenberg et al., 2010) this technique provides information about an object, based on the definition of its shape.

Geometric morphometric analyses make it possible to study the association of facial asymmetry with brain-related functions as well as with neuropsychological and behavioral deficits (Mattson et al.,1998; McGee et al., 2008, as cited by Klingenberg et.al. 2010). In their study, Klingenberg et al. found a significant directional asymmetry in both FAS group and control group and this finding confirms the most published analyses (Ercan et al., 2008; Kimmerle and Jantz, 2005; McIntyre and Mossey, 2002; Shaner et al., 2000, as cited by Klingenberg et al., 2010). Klingenberg et al. state that the direction of midline landmarks was shifted to the right, on the other hand, the direction of the eyes was shifted to the left. They also found that the eye and the frontotemporale were displaced anteriorly to the right side and posteriorly to the left side. They explicate that these features were more accentuated for the FAS group compared with the control group.

3. Cognitive functioning

Cognitive abilities are functional properties that are inferred from behavior (Abikoff et al., 1987, as cited by Lezak, Howieson and Loring, 2004). Questions about cognitive functions are phrased in terms of "what" or "how much" (Burgess et al. 1998; Goldberg, 2001; Lezak, 1982a; Ogden, 1996, as cited by Lezak et al., 2004). Cognitive deficits involve specific functions or functional areas. The four major classes of cognitive functions are: receptive functions, memory and learning, thinking, and expressive functions (Lezak et al., 2004).

3.1 Intelligence

"IQ" is a derived score from test batteries which are designed to measure a hypothetical general ability, named intelligence. An IQ score is a composite score an individual has obtained from different test items. These composite scores are often good predictors of an individual's academic performance (Anastasi and Urbina, 1997; Daniel, 1997, as cited by Lezak et al., 2004).

Deterioration of general intellectual functioning is one of the most devastating effects of FAS or PAE (Wacha and Obrzut, 2007). In one study Connor et al. (2000, as cited by Wacha and Obrzut, 2007) found low average IQ scores in adult men diagnosed with FAS or PAE. These subjects had mean FSIQ scores of 80 and 84. Another study by Kaemingk and Paquette (1999, as cited by Wacha and Obrzut, 2007) found also below average IQ scores, but this time in children with FAS or PAE. These IQ scores were 1-2 or sometimes more standard deviations below the mean with a range of 40 to 83. However, Kerns et al. (1997, as cited by Wacha and Obrzut, 2007) suggest that we should not forget that there are also individuals with FAS who have average or above average intellectual abilities. So according to them, assuming that all persons with FAS have low to below average intelligence is not correct.

Children with FAS or PAE experience difficulties in cognitive functioning such as language, visual-spatial functioning, nonverbal learning, attention, and memory (Wacha and Obrzut, 2007). Kerns et al. (1997, as cited by Wacha and Obrzut, 1997) conducted a study with non-retarded young adults diagnosed with FAS to investigate these cognitive difficulties. They classified the participants in two groups based on their mean IQ score. For this purpose they used the Wechsler Intelligence Scale for Children-Revised (WISC-R) and the Wechsler Adult Intelligence Scale-Revised (WAIS-R) to measure intelligence. The first group included individuals with an average IQ of 97 (range=90–118) and the second group contained

participants with a below average IQ of 75 (range=70–86). After classifying the participants, the Wide Range Achievement Test-Revised (WRAT-R) was used to assess academic performance together with several neuropsychological tests to measure attention, memory or new learning, nonverbal capacity for divergent thinking, cognitive flexibility and planning as indicators of executive functioning. The results showed that both FAS groups demonstrated impairments in complex attention, which requires higher levels of mental control. Both groups also had learning, planning and organization difficulties. However, the average IQ group had an average academic achievement and had no deficits in basic attention and arousal. The below average IQ group showed more severe neuropsychological deficits, but had an average score on tasks which measure basic sustained attention.

3.2 Activity and Attention

Prenatal alcohol exposure can lead to hyperactivity and attentional deficits (Mattson and Riley, 1998). Children with FAS are usually described as hyperactive and irritable (Hanson, Jones and Smith, as cited by Mattson and Riley, 1998). In one study caretakers reported that these children are "always on the go" and "never sit" (Streissguth, Herman and Smith, 1978, as cited by Mattson and Riley, 1998).

Naturalistic observations of alcohol exposed infants found an increased "non-alert state". This means that these infants spend more time with eyes open without any form of attention for the surroundings (Landesman-Dwyer, Keller and Streissguth, 1978, as cited by Mattson and Riley, 1998). The deficits in attention in infants with FAS appear to continue through childhood and include deficits in investing, organizing, maintaining attention and have increased impulsive responses (Nanson and Hiscock, 1990). Adolescents and adults with FAS who suffer from attention deficit disorder, make errors in tests in which focusing is measured (Talland Letter Cancellation Test), encoding (WISC-R Digit Span) and shifting (Wisconsin Card Sorting Test (WCST) (Carmichael-Olson et al., 1998). Attentional deficits are also found in non-FAS children who were exposed to alcohol during their fetal development (Landesman-Dwye, Ragozin and Little, 1981, as cited by Mattson and Riley, 1998).

In one study by Streissguth and colleagues (1984, as cited by Mattson and Riley, 1998) in which four-year-old children of social drinking mothers were observed and compared with the control group, these children had poorer attention spans. Another study by Streissguth et al. (1994, as cited by Mattson and Riley, 1998) also tested four-year-old

prenatal alcohol exposed infants using the Continues Performance Task, which is a psychological test that measures sustained and selective attention. Streissguth et al. found an increase in errors of omission, commission and a decrease in the ratio of correct to total responses. This same cohort demonstrated at age 7 an increase in reaction time and errors of commission and vigilance. Deficits in sustained attention associated with prenatal alcohol exposure were also supported by Brown et al. (1991, as cited by Mattson and Riley, 1998). At age 14 attentional deficits were found again using the WISC-R Arithmetic subtest, which measures attention (Sattler, 1992, as cited by Mattson and Riley, 1998). In addition, it is important to note that in this study the general level of activity did not differ from the control group which contained infants who were not prenatally exposed to alcohol. This outcome means according to Streissguth et al. that hyperactivity did not play a significant role in the attentional problems of these children in this sample.

Besides, it is important to note that not all studies found deficits in attention (Mattson and Riley, 1998). Fried, Wattkinson and Grey (1992, as cited by Mattson and Riley, 1998) found no relationship between alcohol exposure and attention with six-year-old infants. They even found a decrease in impulsive responses. According to them these results can be explained by the fact that in their cohort the alcohol exposure levels were very low. Boyd et al. (1991, as cited by Mattson and Riley, 1998) found the same non-significant results. In their study they did not find any effect of prenatal alcohol exposure on sustained attention in preschool children of alcoholic mothers. Boyd and colleagues explain that in their study the alcohol exposure levels were still low, but higher than the study of Fried and colleagues.

3.3 Language

Several case reports report speech and language disturbances caused by prenatal alcohol exposure (Mattson and Riley, 1998). Abel (1990, as cited by Mattson and Riley, 1998) found 53 cases of speech delay or impediment in a sample of 550 individuals diagnosed with FAS. He also found receptive and expressive language deficits and articulation disorders. Other researchers found symptoms varying from complete lack of intelligible speech (Tsukahara and Kajii, 1988, as cited by Mattson and Riley, 1998) to mild dysarthria (Marcus, 1987, as cited by Mattson and Riley, 1998) or lisping (Koranyi and Csiky, 1978, as cited by Mattson and Riley, 1998). Deficits in speech and language functioning are equally found in group studies of language functioning in children with FAS (Autti-Ramö et al., 1992 ; Steinhausen, Nestler and Spohr, 1982, as cited by Mattson and Riley, 1998). The reported deficits include word comprehension (LaDue, Streissguth and Randels, 1992; Conry, 1990;

Gray and Streissguth, 1990; Mattson et al., 1996, as cited by Mattson and Riley, 1998) and articulation (Becker, Warr-Leeper and Leeper, 1990, as cited by Mattson and Riley, 1998). On tests of verbal fluency, infants with FAS exhibit impairments in letter fluency even though category fluency is less affected (Kodituwakku et al., 1993; Mattson, 1994, as cited by Mattson and Riley, 1998).

Prospective studies of children exposed to various amounts of alcohol report various findings (Mattson and Riley, 1998). Some studies with children and infants exposed to low levels of alcohol found a decrease in language comprehension in 13-month-old (Gusella and Fried, 1984, as cited by Mattson and Riley, 1998), 2-year-old (Fried and Wattkinson, 1988, as cited by Mattson and Riley, 1998) and 3-year-old children. A report from the Seattle prospective study showed a dose-response relationship between maternal alcohol use and word attack performance at age 14 (Streissguth et al., 1994, as cited by Mattson and Riley, 1998). Word Attack is a subtest of Woodcock Reading Mastery Tests and measures reading ability and pronunciation while subjects read non-words (Mattson and Riley, 1998).

Besides, it is also important to note that there were studies which did not find any significant results at all. For example, a study with children with FAS reported relatively intact language development compared with the control group (Ernheart et al., 1995, as cited by Mattson and Riley, 1998). Another study with alcohol-exposed children at 1, 2 or 3 years of age found no effect on expressive or receptive language skills (Greene et al., 1990, as cited by Mattson and Riley, 1998) and like the study of Gusella and Fried described earlier, this group was equally exposed to low levels of alcohol (Mattson and Riley, 1998).

To sum up, infants with FAS appear to exhibit deficits in speech and language, and these similar deficits are found in some groups of prospective studies with alcohol exposed children (Mattson and Riley, 1998).

3.4 Motor abilities

Prenatal alcohol exposure does not only affect cognitive functions but also the developing motor system (Mattson and Riley, 1998). Children of chronic alcoholic mothers exhibit delayed motor development and fine-motor dysfunction (Jones, Smith, Ulleland and Streissguth, 1973, as cited by Mattson and Riley, 1998).

One study reported a nonspecific dyscoordinated motor pattern, hemiplegia, ataxia, and an increase in cerebral palsy in children of alcohol abusing women (Olegard et al., 1980, as cited by Mattson and Riley, 1998). Other studies also noted delayed motor development in infants and children exposed to alcohol prenatally (Streissguth et al., 1980; Jacobson et al.,

1993; Autti-Ramo and Granstrom, 1991, as cited by Mattson and Riley, 1998) and fine- and gross-motor dysfunctions were found in children of alcoholic mothers (Kyllerman et al., 1985, as cited by Mattson and Riley, 1998)and social drinkers (Barr, Streissguth, Darby and Sampson, 1990, as cited by Mattson and Riley, 1998).

Marcus (1987, as cited by Mattson and Riley, 1998) found axial ataxia and kinetic tremor in children with FAS. He also reported deficits in motor speed/precision, finger tapping speed and grip strength.

Animal studies have also shown motor dysfunction caused by prenatal alcohol exposure (Mattson and Riley, 1998). Studies with prenatal alcohol exposed rats have found gait disturbances (Hannigan and Riley, 1989, as cited by Mattson and Riley, 1998), delays in reflex development (Lee, Haddad and Rabe, 1980, as cited by Mattson and Riley, 1998) and poor balance (Meyer, Kotch and Riley, 1990, as cited by Mattson and Riley,1998).

4.Executive functioning

Executive functions enable a person to engage in independent, purposive, self-serving behavior. When executive functions are impaired an individual can no longer care for himself/herself, perform useful work independently or maintain social relationships, regardless of how well their cognitive capacities are. Executive functioning asks questions like how or whether a person does something. Compared with cognitive functions, executive functions show up more globally and affect all aspects of behavior. Because executive functioning differs from cognitive functioning in many ways, we discuss this subject in a separate chapter (Burgess et al. 1998; Goldberg, 2001; Lezak, 1982a; Ogden, 1996, as cited by Lezak et al., *2004).*

4.1 Definition of executive functioning

Funahashi (2001) defines executive function as: 'a product of the co-ordinated operation of various processes to accomplish a particular goal in a flexible manner'. Executive functions are functions involved in complex cognitions, like solving new problems, changing behavior when new information is given, generating strategies or sequencing complex actions Elliott (2003). Elliott clarifies this term more extensively: "This flexible co-ordination of sub-processes to achieve a specific goal is the responsibility of executive control systems. When these systems break down, behavior becomes poorly controlled, disjointed and disinhibited. Co-ordination, control and goal-orientation are, therefore, at the heart of the concept of executive function." (p. 50)

According to Kodituwakku et al. (2001) executive functioning refers to effortful actions that involve various abilities, like holding and manipulating information (working memory) and focusing on one task at a time (inhibiting task-irrelevant habitual responses). Kodituwakku and colleagues divide executive functions into two categories. The first category is "cognition-based actions", in which researchers use a variety of cognitive tests which measure problem solving, conceptual set shifting and rapid generation of verbal or nonverbal responses. Subsequently, the second category is called emotion-related (Rolls et al. as cited in The effects of prenatal alcohol exposure on executive functioning), or affective (Dias et al., 1996, as cited by Kodituwakku, Kalberg and May, 2001) executive functioning. This category is based on rewards and punishments (positive and negative reinforcement) which were used in the past in similar situations. To measure emotion-related executive

functioning we can use tests which assess the ability to modify behavior in response to changing reinforcement situations (Kodituwakku et al., 2001).

4.2 Brain regions

Brain regions involved in executive functions can be identified by determining whether patients with damage in specific brain areas show impaired performance on tasks assessing executive functions. This is regardless of whether that damage is alcohol related. Both cognition-based executive functioning and emotion-related functioning are controlled by different brain areas (Kodituwakku et al., 2001). For example, Damasio (1994, as cited by Kodituwakku, 2001) reported that patients with damage in the orbitofrontal cortex performed poorly on an emotion-related decision-making task but completed the WCST, which assesses cognition-based executive funtioning. Similarly, Rolls and colleagues found that patients with orbitofrontal damage were impaired in the Visual Discrimination Reversal Test, which assesses emotion-related executive functioning, yet exhibited normal performance on cognition-based executive functioning tasks (Rolls, Hornak and McGrath, 1994, as cited by Kodituwakku, 2001)

Moreover, both Damasio and Rolls et al. found that the performance of patients with orbitofrontal damage on these emotion-related tasks was associated with the patients' social and other behavioral problems. This means that these patients with greater impairment on those tasks exhibited greater social and other problems.

4.3 The effects of prenatal alcohol exposure on executive functioning

Various research areas come with evidences that individuals who have been prenatally exposed to alcohol, may perform not so well on relatively complex and novel tasks. These tasks are usually designed to measure executive functioning (Kodituwakku et al., 2001).

Kodituwakku et al. (1995, as cited by Kodituwakku, 2001) state that people with FAS and alcohol exposed people without FAS, exhibit executive dysfunctions to the same degree. In their study they used a test called the Progressive Planning Test to assess planning skills in alcohol exposed children with or without FAS. In this test, the participants must move three or four colored beads that are arranged in a specific order in some position on three stakes to create a series goal positions. These series of problems were of increasing difficulty. The first set of problems (level 1 planning) were simple, with straightforward solutions that did not strain the working memory, however, the solutions in the second and third level required greater mental manipulation. For example, reversing the order of the beads before all beads

could be moved to the goal position. The subject must organize a series of steps to solve the problems. Looking at the results, they concluded that prenatal alcohol exposure was associated with deficiencies in planning skills because the alcohol-exposed children had difficulty in solving the more difficult problems that involved mental manipulation.

In another study, Mattson et al. (1999) found deficiencies in the planning skills of alcohol-exposed infants using the California Tower Test. These infants also violated test rules more often than the control group. The Cognitive Estimation Test examines planning skills and is usually challenging for patients with prefrontal cortical damage Kodituwakku et al (2001). Kopera-Frye Dehaene and Streissguth (1996, as cited by Kodituwakku, 2001).used this test for assessing planning skills in alcohol exposed adolescents and adults and found that these subjects tended to give unrealistic responses on this test. These responses were similar to those of patients with prefrontal damage.

Fluid intelligence tests measure a person's ability to solve new problems quickly and accurately. This sort of tests measures the ability to hold and manipulate information in the working memory (Kodituwakku et al., 2001). Alcohol exposed infants have more difficulty with fluid intelligence tests than with crystallized intelligence tests which require established knowledge (Kodituwakku, May, Clericuzio and Weers, 2001, as cited by Kodituwakku et al., 2001).

At last, Mattson and colleagues (1999), reported deficient performance of alcohol exposed children on a measure of response inhibition called the California Stroop Test. Though, further investigation is needed.

5. Psychopathology

5.1 Depression

According to Larkby and Day (1997), there is a direct relationship between prenatal alcohol exposure and child depressive symptoms. Prenatal alcohol-exposed children between 3 and 16 years showed higher rates of depressive symptoms compared with control children of the same age (Roebuck, Mattson and Riley, 1999).

It is found that there are sex differences in the prevalence of depression, these differences are also found in FASD populations. Like in the healthy population, (50 %) higher depression rates and (50%) higher anxiety rates were found in women compared to men (40% and 0%) among the FASD population (Famy and Streissguth, 1998, as cited by Hellemans, Verma ,Yoon , Yu and Weinberg , 2008).

When Steinhausen and Spohr (1998) assessed children diagnosed with FAS during preschool age, early school age (6 to 12 years) and late school age (> 13 years), they found that 63% of these infants had at least one psychiatric abnormality. It is important to note that mental retardation is not related to the increased risk for depression. This is because the relation between prenatal alcohol exposure and depression also occurs in children (O'Connor et al., 2002) and adults (Famy and Streissguth, 1998, as cited by Hellemans et al., 2008) with normal intelligence.

However, there are also environmental factors such as maternal death, living with an alcoholic parent, maternal mood, child abuse and neglect, removal from the home by authorities, repetitive periods of foster care and other transient home placements, and being raised by adoptive or foster families, which are related to prenatal alcohol exposure and can have a significant contribution to the increased rates of depression (Hellemans et al., 2008).

Specifying maternal mood for example, in one study with prenatal alcohol exposed girls between 4 and 6 years, maternal depression was associated with high levels of negative affect and the highest scores on child measure of depressive symptoms (O'Connor and Kasari, 2000; O'Connor and Paley, 2006, as cited by Hellemans et al., 2008).

O'Connor and Paley (2006, as cited by Hellemans et al., 2008) found that when mothers are emotionally less connected to their children, the more those children exhibit higher levels of depressive symptoms.

Taking together, Larkby and Day (1997) assume that environmental factors might play a role when it comes to the effects of prenatal alcohol exposure on child depressive symptoms. But according to them direct effects of alcohol might also mediate this

relationship. These findings also suggest that mental problems like anxiety and depression may also have a neurobiological basis and therefore could be primary rather than secondary disabilities, at least, in some instances.

5.2 Attention deficit and hyperactivity disorder

Attention deficit and hyperactivity disorder (ADHD) is one of the characteristics that is often identified in infants with prenatal alcohol exposure. Some clinicians even see this as the primary diagnostic sign in preschool and older children and prescribe often stimulant drugs to children with FAS who show behaviors in coherence with ADHD. There is even a suggestion of an association between ADHD and a genetic predisposition to alcoholism (Coles et al., 1997).

Nanson and Hiscock (1990) compared 20 children with FAS or PAE with 20 children with a diagnosis of ADHD and 20 normal controls using three tasks which focused on different components of attention. They measured behavior by parent checklists and cognition with Wechsler Intelligence Scale for Children-Revised (WISC-R) and computerized attention-demanding tasks. Three attention-demanding tasks were used, namely: vigilance tasks which require maintenance of attention, tasks demanding inhibition of impulsive responding and tasks involving reinforcement seeking.

Nanson and Hiscock indicate that FAS or PAE children and those with ADHD were very similar in parental ratings. Children who were exposed to alcohol had, compared to those with ADHD, more problems with computerized tasks involving attention.

On the other hand, children with ADHD were more impulsive in their responses. The IQ scores were also different. Children with FAS or PAE had an intellectual range (IQ, 70-85) and those with ADHD scored an average range (IQ, 85-115) (Nanson and Hiscock, 1990). Subsequently there were also differences in the speed of responding. Those infants with FAS showed a worser performance, compared with children with ADHD and controls (Nanson and Hiscock, 1990).

Although ADHD is often described as an effect of prenatal alcohol exposure (Coles et al., 1997), it is important to note that in some cases infants with FAS exhibit behaviors in coherence with ADHD even when there is no neurologically evidence for ADHD. So it is important to be careful when classifying an infant or child in ADHD (Nanson and Hiscock, 1990).

6. Conclusions and discussion

The aim of this thesis was to find out more about the effects of prenatal alcohol exposure on cognitive functioning. Based on various studies, reports and theories of researchers in this discipline, we came to several conclusions and found some shortcomings.

We found that fetal alcohol spectrum disorders like FAS are completely preventable and non-genetic and can cause CNS deficits like neuropsychological impairment and affect the neurophysiologic programming of the brain (Wacha and Obrzut, 2007). Impairments in physical development like facial dysmorphology and growth retardation are also likely in this target group.

Mental health problems like depression and ADHD are often diagnosed in prenatally exposed individuals. Though, we should not forget that there is a variation in exhibited symptoms among individuals diagnosed with a disorder within FASD, since every individual has his unique set of symptoms.

Besides, there is no specific limit for a safe amount of alcohol consummation during pregnancy. Therefore, even light drinking women can deliver children with CNS abnormalities and disabilities. It is also concerning that many women who are not aware of pregnancy, keep consuming alcohol on regular or occasional basis. In many cases, mothers are not asked about their drinking behavior during pregnancy. So we should direct our attention to the drinking habits of not only the heavy drinking women, but to women in general (Caetano et al., 2006). Therefore it is better not to drink at all during pregnancy (NIAAA, 2002, as cited by Caetano et al., 2006).

On the other hand, we noticed also some shortcomings. We took a look at maternal demographic factors that increase drinking during pregnancy. But conception is a two way process, so what is the influence of paternal drinking habits? For example, according to Abel (2004) about 75% of children with FAS have biological fathers who are heavy drinkers or alcoholics. Therefore, it is possible that some of the anomalies of the teratogenic effects of maternal drinking may be due to or are exacerbated by paternal drinking. For instance, paternal alcohol consumption has been associated with decreases in birth weight and increases in ventricular septal defects. Even though there are many other symptoms caused or correlated with paternal alcohol consumption, it is not possible to mention them all in this part.

Another point of discussion is that in this thesis we only paid attention to the effects of FAS and PAE as disorders of FASD. Nevertheless, the FASD is very broad and includes also subtypes such as Partial Fetal Alcohol Syndrome (PFAS), Alcohol-Related Neurodevelopmental Disorder (ARND) and Alcohol-Related Birth Defects (ARBD) with

their own specific symptoms and diagnosis criteria. So it is important to know more about FASD from the perspective of these disorders.

Studies in this thesis only reported maternal alcohol consumption during pregnancy. However they did not mention the possible effects of other substance usage in combination with alcohol. For example, taking maternal demographic factors like young maternal age, low socioeconomic status and negative feelings and emotions about oneself into account, it is quite possible that these mothers also use and abuse (recreational) drugs in combination with alcohol, because these factors might reinforce substance usage. So it is important to find out what these implications are for the exposed fetus.

Some studies noted that the diagnosis of FAS is often overlooked because the symptoms are not visible at birth and therefore FAS is often diagnosed at age 2. The question is what if FAS is diagnosed earlier, for example at birth? What are the consequences? Can we prevent or even cure the implications these individuals develop and have to deal with when they mature? Can we guarantee these individuals a better quality of life then? Further investigation is needed to develop better instruments and techniques to diagnose FAS at birth. It is also important to find out if an early diagnosis of FAS has positive effects at all.

Finally, it is notable to find out how it is possible that the drinking habits nowadays among pregnant women has changed compared with pregnant women of past generations in Western countries. Is there talk of some sort of trend? What factors determine this increase in drinking behavior? And speaking of countries, can we generalize this drinking behavior to pregnant women from other non-Western countries? For example, Middle-Eastern countries in which alcohol consumption are forbidden because of Islamic or Judaism religious beliefs. How about the occurrence of FASD in those countries? The studies mentioned in this thesis did not give an answer to these questions. Further international and socio-cultural studies are needed to find out more about FASD in non-Western countries like the Middle-East.

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