PSYCHOLOGICAL FUNCTIONING IN CHILDREN WITH LOW BIRTH WEIGHT

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PSYCHOLOGICAL FUNCTIONING IN CHILDREN WITH LOW BIRTH WEIGHT

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DECLARATION

I, Anna Cornelia Haycock, declare that the thesis hereby submitted to the University of Limpopo as fulfilment for the degree of Doctor of Philosophy in Clinical Psychology, has not previously been submitted by me for a degree at any other university, that it is my own work in design and execution, and that all the material contained therein has been duly acknowledged.

Signature ..... A Haycock .....

Date ..... 2008-06-27 .....

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LIST OF ABBREVIATIONS

ADD	Attention Deficit Disorder
ADHD	Attention-Deficit/Hyperactivity Disorder
ADHD-C	ADHD combined type
ADHD-HI	ADHD predominantly hyperactive-impulsive type
ADHD-PI	ADHD predominantly inattentive type
AIDS	Acquired Immuno-Defiency Syndrome
ANOVA	Analysis of Variance
AGA	Appropriate for gestational age
BAS	Behavioural activation system
BIS	Behavioural inhibition system
CD	Conduct Disorder
CLD	Chronic lung disease
CNS	Central nervous system
CPM	Coloured progressive matrices
CRH	Corticotropin-releasing hormone
CSF	Cerebrospinal fluid
DBD	Disruptive Behaviour Disorder
DCD	Developmental Coordination Disorder
DHA	Docosohexanoic acid
DNA	Deoxyribonucleic acid
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision
EF	Executive functions
ELBW	Extremely low birth weight
FAS	Foetal Alcohol Syndrome
GABA	Gamma-aminobutyric acid
GAD	Generalised Anxiety Disorder
HGV	Head-circumference growth velocity
HIV	Human immuno-deficiency virus
HPA	Hypothalamic-pituitary-adrenal

ICH	Intracranial haemorrhage
IUGR	Intrauterine growth restriction
IVH	Intraventricular haemorrhage
IQ	Intelligence quotient
LBW	Low birth weight
MDD	Major Depressive Disorder
MRC	Medical Research Council
MRI	Magnetic resonance imaging
NBW	Normal birth weight
OAD	Overanxious Disorder
ODD	Oppositional Defiant Disorder
PL/VE	Parenchymal lesions and/or ventricular enlargements
PPIP	Perinatal Problem Identification Programme
PVL	Periventricular leukomalacia
ROCF	Rey-Osterrieth Complex Figure
SAD	Separation Anxiety Disorder
SES	Socio-economic status
SGA	Small for gestational age
SSAIS-R	Senior South African Individual Scale – Revised
VLBW	Very low birth weight

ABSTRACT

Low-birth-weight/premature children seem to be vulnerable to psychiatric, neuropsychological and other deficiencies. Limited research is available in the South African context about these ever-increasing phenomena. The aim of this study was to investigate the magnitude and characteristics of internalising (Separation Anxiety, Overanxious and Major Depressive Disorders) and externalising symptoms (Attention-Deficit/Hyperactivity, Oppositional Defiant and Conduct Disorders) among low-birth-weight children in comparison with normal-birth-weight children, as well as to establish neuropsychological deficiencies (motor, visual-spatial, memory and executive functioning) between the birth weight groups, analysed as a function of gender and age. The sample (158 children) was selected from nine urban mainstream primary schools in the Tshwane North and South districts by means of stratified random sampling. Low-birth-weight children (weighing below 2 000 g) (N=79) were matched with normal-birth-weight children (above 3 000 g) (N=79) according to age, gender, language and socio-economic status. The neuropsychological test battery and self-reporting questionnaire were individually administered to the sample at the selected schools during school hours. Teachers and parents of selected participants were requested to complete a rating scale. As expected, low birth weight is associated with a tendency towards increased internalising and externalising psychological symptoms, as well as poorer neuropsychological functioning. This was particularly significant in the domains of internalising symptoms (depression), externalising symptoms (hyperactivity/impulsiveness, inattention, Oppositional Defiant Disorder and Conduct Disorder) and neuropsychological impairments (motor, visual-spatial/visual-motor, memory and executive functioning). The neuropsychological impairments observed in this study among the LBW children probably increase the risk of subsequent externalising (conduct and oppositional behavioural problems) and internalising (depressive) psychological symptoms. These impairments are possibly exacerbated by inattention and hyperactivity/impulsiveness. Reciprocal interaction seems to take place between the psychological symptoms and neuropsychological functions. Only a few gender differences were observed. Neuropsychological deficits were observed both in the 6 to 9 and 10 to 13 age groups, indicating deficient resolution of impairments with increasing age. Increased pre-, peri- and postnatal complications in the low-birth-weight group may predispose these children biologically to neuropsychological deficiencies and subsequent internalising/externalising symptoms. These impairments most probably affect academic, emotional, social and other significant areas of functioning, increasing public health cost.

CONCEPTUAL CLARIFICATION OF TERMS

Abruptio placentae: Abruptio placentae refers to bleeding from a normally situated placenta causing its complete or partial detachment from the uterine wall after the 24th week of gestation. It is often associated with hypertension and pre-eclampsia.

Anaemia: Anaemia is a condition in which there is reduced delivery of oxygen to the tissue. Anaemia is not a disease but a symptom of any of a number of different disorders. It can be caused by factors such as poor diet, blood loss, congenital defects of haemoglobin, exposure to industrial poisons, diseases of the bone marrow, or any other disorder that upsets the balance between blood loss through bleeding or destruction of blood cells and production of blood cells.

Auto-immune disease: Auto-immune disease is one of a number of otherwise unrelated disorders caused by inflammation and destruction of tissue by the body's own antibodies (auto-antibodies).

Bicornate: Bicornate refers to having two processes or projections.

Cardiovascular: Cardiovascular relates to the heart and the blood vessels or the circulation.

Cerebral palsy: Cerebral palsy is a nonspecific term used to describe a persistent qualitative motor disorder caused by nonprogressive damage to the brain. Although manifested primarily in motor dysfunction, the disorder also may involve sensory deficits and impairment of the intellect. Most cases are diagnosed before the age of three. However, prior to age eight or nine, function lost by damage to one part of the brain can be taken over by another part of the

brain. Hence, many people consider that brain damage occurring at any time prior to this age can lead to cerebral palsy.

Developmental Coordination Disorders (DCD): DCD is a disorder with marked impairment in the development of motor coordination, which cannot be attributed to a general medical condition or mental retardation

Erythroblastosis: Erythroblastosis is the presence in the blood of the nucleated precursors of the red blood cells (erythroblasts). This may occur when there is an increase in the rate of red cell production.

Gastrointestinal: Gastrointestinal is a term relating to the stomach and intestines.

Haematology: Haematology refers to the science dealing with the morphology of blood and blood-forming tissues, and with their physiology and pathology.

Hydrops: Hydrops is an abnormal accumulation of fluid in body tissue or cavities.

Iatrogenic: Iatrogenic is a term describing a condition that has resulted from treatment, as either an unforeseen or inevitable side-effect.

Inanition: Inanition is a condition of exhaustion caused by lack of nutrients in the blood. This may arise through starvation, malnutrition, or intestinal disease.

Intrauterine growth restriction (IUGR): IUGR is the condition resulting in the birth of a baby whose birth weight is abnormally low in relation to its gestational age (i.e. small for dates). Causes include maternal disease (e.g. infection, malnutrition, high blood pressure, smoking and alcoholism), poor socio-economic conditions, multiple pregnancies (e.g. twins) and foetal disease. It may be associated with preterm birth.

Intraventricular haemorrhage: Intraventricular haemorrhage is the extravasation of blood into the ventricular system of the brain.

In vitro fertilisation: In vitro fertilisation is the fertilisation of an ovum outside the body, the resultant zygote being incubated to the blastocyst stage and then implanted in the uterus.

Low birth weight: Babies born with low birth weight (less than 2 500 g) are born either pre-term (less than 37 completed weeks of gestation) or small for gestational age (SGA – less than 10th percentile for gestational age) or both.

Morbidity: Morbidity is the state of being diseased. Morbidity is also referred to as the ratio of sick to well in a community.

Mortality: The incidence of death in the population in a given period.

Obstetrics: Obstetrics refers to the branch of medical science concerned with the care of women during pregnancy, childbirth, and the period of about six weeks following the birth, when the reproductive organs are recovering.

Perinatal: During the period just preceding, during or just following childbirth.

Placenta: The placenta is an organ within the uterus by means of which the embryo is attached to the wall of the uterus. Its primary function is to provide the embryo with nourishment, eliminate its waste, and exchange respiratory gases. This is accomplished by the close proximity of the maternal and foetal blood systems in the placenta.

Placenta previa: Placenta previa is a placenta situated wholly or partially in the lower and noncontractile part of the uterus. When this becomes elongated and stretched during the last few weeks of pregnancy, and the cervix becomes stretched either before or during labour, placental separation and haemorrhage will occur.

Pre-eclampsia (pregnancy-induced hypertension): Pre-eclampsia is defined as high blood pressure (greater than 140/90 mmHg) developing during pregnancy in a woman whose blood pressure was previously normal. It is often accompanied by excessive fluid retention and less often by the presence of protein in the urine.

Premature birth: Premature birth refers to the birth of a baby weighing less than 2 500 g. Usually this is indicative of preterm birth but it can also be caused by IUGR. Birth weights of less than 500 g are almost invariably incompatible with life.

Preterm birth: Preterm birth occurs when a baby is born before 37 weeks (259 days) of gestation (calculated from the first day of the mother's last menstrual period). Birth at less than 23 weeks is at present incompatible with life.

Renal: Renal relates to or affects the kidneys.

Seizure: Seizure is defined as the sudden attack or recurrence of a disease; a convulsion or attack of epilepsy. Convulsions are a series of involuntary contractions of the voluntary muscles. Convulsive seizures are symptomatic of some neurologic disorders; they are not in themselves a disease entity.

Sequelae: Sequelae are any disorders or pathological conditions that result from a preceding disease or accident.

Teratogen: Teratogen refers to any substance, agent or process that induces the formation of developmental abnormalities in a foetus. Known teratogens include drugs such as alcohol, infections such as German measles and also irradiation with X-rays and other ionising radiation.

Chapter 1

GENERAL INTRODUCTION AND BACKGROUND

1.1 Introduction and background to study

The future welfare of all levels of low-birth-weight (LBW) or premature infants has stimulated research for several decades (Breslau & Chilcoat, 2000; Chapieski & Evankovich, 1997; Lawson & Ruff, 2004). The improved survival of LBW infants (Aylward, 2002; Jobe, 2001; Valkama, Pääkkö, Vainionpää, Lanning, Ilkko & Koivisto, 2000; Vohr, Wright, Dusick, Mele, Verter, Steichen et al., 2000) owing to improved techniques of newborn intensive care (Gross, Mettelman, Dye & Slagle, 2001), even those with birth weights lower than 1 000 g, compelled researchers to investigate the later development of these children, in order to optimise their chances of leading a healthy, productive life (Breslau & Chilcoat, 2000; Campbell, 2001a; Subramanian, 2002). According to Wolke (1998) premature birth is one of the most challenging and costly public health problems.

Cherkes-Julkowski (1998) states that preterm children are at increased risk of developmental difficulties due to a central nervous system (CNS) that is not fully organised at the time of birth for sustaining itself in the extra-uterine environment. LBW children seem to be vulnerable to neurodevelopmental disturbances due to prenatal complications and neonatal risk factors (Breslau, Brown, DelDotto, Kumar, Ezhuthachan, Andreski et al., 1996a; Sommerfelt, Troland, Ellertsen & Markestad, 1996). According to Bhutta, Cleves, Casey, Cradock and Anand (2002) preterm neonates are at higher risk of postnatal complications, such as intraventricular haemorrhage (IVH) or chronic lung disease (CLD). They are consequently subjected to painful procedures and maternal separation for prolonged periods. Bhutta et al. (2002) further postulate that these factors can promote or

precipitate neuronal cell death in the immature brain, as shown by experimental evidence from animal models. Thus, increasing numbers of extremely immature and sick infants with a high risk of cerebral problems now have a chance to survive and could contribute to the total number of children with behavioural difficulties (Hille, den Ouden, Saigal, Wolke, Lambert, Whitaker et al., 2001).

Harrison (2002) describes specific types of neurodevelopmental morbidities in LBW cohorts, for example social problems, lower attention, cognitive delays (such as lower intelligence quotient [IQ]), needing remedial assistance, speech and language disorders, persistent neuro-motor abnormalities and perceptual problems. Greater rates of behavioural problems are generally associated with decreasing birth weights (Berk, 2006; Harrison, 2002). Berk (2006) postulates that frequent illness, inattention, overactivity, language delays, low intelligence, deficits in school learning, as well as emotional and behavioural problems, are some of the difficulties that persist throughout childhood and adolescence and into adulthood. Adults also show lower occupational success and income (Breslau, Johnson & Lucia, 2001; Reiss, Kesler, Vohr, Duncan, Katz, Pajot et al., 2004).

Chapieski and Evankovich (1997) report that preterm children are particularly vulnerable to psychiatric disturbances. Ten percent of a sample of premature children exhibited an emotional disturbance severe enough to interfere with their development and to make them difficult to manage. Elgen, Sommerfelt and Markestad (2002) document that 27% of LBW children compared to 9% of normal-birth-weight (NBW) children were diagnosed with a psychiatric disorder. Botting, Powls, Cooke and Marlow (1997) note increased vulnerability to emotional and behavioural problems among very-low-birth-weight (VLBW) children, even into early adolescence.

1.2 Objective of the study

This research proposes to study the externalising and internalising psychological disorders associated with LBW, as well as neuropsychological functioning among current primary school children born with LBW. Similarities and differences between birth weight, gender and age groups will be determined pertaining to the focus areas mentioned.

1.3 Significance of the study

Limited research on LBW and its outcomes is available in the South African context. Challenges in South Africa, such as poverty (Campbell, 2001a) and high human immuno-deficiency virus (HIV)/acquired immuno-deficiency syndrome (AIDS) infection rates (The Medical Research Council [MRC] Unit for Maternal and Infant Health Care Strategies, Perinatal Problem Identification Programme [PPIP] Users & the National Department of Health, 2001), are considered significant risks in enhancing the prevalence of LBW/prematurity. These risk factors will probably have an adversely impact on child development and prognosis, with significant cost implications and burdening of public health services.

International movements, such as the Scottish Low Birthweight Study Group, set standards for longitudinal studies (Breslau et al., 1996a). Such movements investigating the sequelae of LBW in South Africans are of paramount importance in developing prevention and intervention strategies.

Moreover, internationally the short-term and longer-term outcomes of LBW children are not improving, though survival rates are increasing (Jobe, 2001). A disproportionate amount of educational resources, behavioural and psychological therapy is used, especially by the extremely-low-birth weight (ELBW) population (Saigal, Stoskopf, Streiner & Burrows, 2001).

It is therefore essential to determine if there is a relationship between LBW, externalising and internalising psychological problems and neuropsychological impairments, as well as to clarify the nature, significance, aetiology and consequences of such a possible relationship. Determination of functioning and needs in specific areas (behavioural, emotional and neuropsychological) will enable professionals and significant others to develop relevant treatment strategies in order to optimise long-term outcomes. Attempts should be made to identify predictors of behavioural difficulties and consequent possible areas where interventions might reduce the extent of an adverse outcome in preterm children (Hoff, Hansen, Munck & Mortensen, 2004). Moreover, new research data indicate that behavioural problems in premature children may worsen with age, though data seem to be inconsistent (Harrison, 1996).

Awareness of psychiatric and neurological outcomes in VLBW children among teachers, parents and the children themselves is of increased importance in combating long-term impairments (Botting et al., 1997). Awareness will enable parents to adjust their expectations and demands to the child's abilities (Hoff et al., 2004).

Intervention programmes based on research findings should aim at continuous monitoring of development, including identification, diagnosis and treatment of problem areas. These programmes should focus on preventing possible pathological symptoms from reaching a full diagnostic level. Early identification of LBW children at risk of behavioural and other problems, and tailoring early intervention to address behavioural competence is of paramount importance in developing prevention programmes (Olness, 2003; Saigal et al., 2001; Saylor, Boyce & Price, 2003).

Insufficient knowledge exists about the possible long-term psychiatric outcomes of VLBW (Botting et al., 1997). Bregman (1998) emphasises that further research on LBW is essential in order to determine the academic functioning and educational needs of children born with LBW, as well as determining other treatments (such as medical, behavioural and educational techniques). It is hoped that national and international research will enable all parties involved to optimise the outcomes of LBW children, where necessary, given the fact that the number of LBW children is increasing.

Powerful evidence exists that most psychiatric disorders originate early in life. The risk of adult-onset disorders is often increased by childhood adversities. Disorders experienced in early years often recur in adulthood. The World Health Organisation has emphasised that psychiatric disorders that have their origins in childhood are a major contributor to the 'global burden of disease.' Primary and secondary prevention in child and adolescent mental health is of the utmost importance (Costello, Egger & Angold, 2005).

This investigation will contribute to a data base in order to identify problem areas, their frequency, nature and severity, determine tendencies, predictors, the course of psychopathology from childhood to adolescence and beyond, cultural determinations and appropriate interventions from a South African perspective. Patterns of disability seem to change over time, implying continuous updating of research findings (Saigal, Pinelli, Hoult, Kim & Boyle, 2003b). All LBW children, including low-risk populations, should be included in follow-up programmes for early detection of deficits and treatment before school entry (Pietz, Peter, Graf, Rauterberg-Ruland, Rupp, Sontheimer et al., 2004).

1.4 Delineation of the study

An array of possible outcomes of interest exists: medical/physiological, neurological, cognitive, academic, neuropsychological, motor, social competency and emotional/behavioural (Aylward, 2002). According to Wolke (1998) four domains have been considered in the psychological development of preterm children: cognitive development (e.g. memory), behavioural and emotional status (ranging from individual differences such as temperament to behavioural problems such as hyperactivity), social functioning (the ability to form and maintain social relationships and to reflect on these relationships, including self-concept), and school adaptation and failure. Cognitive development (particularly neuropsychological functioning), as well as behavioural and emotional status, will be the focus of this study, as indicated below.

Chapter two focuses on the definition of LBW in accordance with the different degrees or populations or levels of LBW. The incidence of LBW will then be referred to. Correlation between risk factors relating to LBW and causes of LBW will be elaborated on, with specific reference to intrauterine growth restriction (small for gestational age [SGA]) and prematurity. Reference to outcomes of LBW in the neonatal stage will be summarised, for short-term outcomes will not be the focus of this study. The aim of the chapter is to explore the consequences of LBW regarding cognitive, developmental, neurological, physiological and behavioural functioning, including its risk factors. Available findings on gender and age differences will also be indicated.

Chapter three focuses on a discussion of internalising psychological disorders, particularly anxiety (Separation Anxiety Disorder [SAD] and Overanxious Disorder [OAD]) and Major Depressive Disorder (MDD). The aim of this chapter is to explore particular aspects of anxiety and depression in LBW children (where data are available), namely the

symptoms, prevalence, comorbidity, age of onset, gender differences and aetiological factors. The neurobiological structures involved in anxiety and depression in LBW children will be referred to.

Chapter four provides a brief description of the symptoms, prevalence, gender differences, comorbidity, aetiology and consequences pertaining to externalising psychological disorders, specifically Attention-Deficit/Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD). The incidence of ADHD, ODD and CD in LBW children will be explored. This chapter focuses particularly on the neurobiological structures involved in LBW children with ADHD, ODD and CD symptomatology.

Chapter five reflects on available research on the neuropsychological deficits in LBW children pertaining to prevalence, implications, gender differences and aetiology. This chapter also attempts to explore the nature of neurobiologically based impairments in fine motor skills, visual-spatial, memory and executive functions (EF). Gender differences will be reflected.

Chapter six is directed at a discussion of problem formulation and hypotheses.

Chapter seven focuses on the methodology of data collection.

Chapter eight reports on the results of the study.

In chapter nine the results, limitations of the study and suggestions for future research will be discussed.

Chapter 2

LOW BIRTH WEIGHT

2.1 Introduction

Various researchers confirm the increasing number of LBW infants as a result of improved medical interventions (Aylward, 2002; Jobe, 2001; Vohr et al., 2000; Whitaker, van Rossem, Feldman, Schonfeld, Pinto-Martin, Tore et al., 1997). Premature birth is also associated with stressful procedures and environmental conditions (Perlman, 2001). These children tend to be at higher risk of medical conditions and brain injury (Bhutta et al., 2002; Sola, Wen, Hamrick & Ferriero, 2005). Consequent increased risk of cognitive (Isaacs, Lucas, Chong, Wood, Johnson, Marshall et al., 2000), behavioural (Saigal et al., 2001), psychiatric (Elgen et al., 2002) and other problems has been noted by numerous investigators. Preventative strategies are therefore essential to reduce risk and aetiological factors, particularly in South Africa as a developing country confronted with challenges such as low socio-economic status (SES) and high HIV infection rates.

LBW will be defined in this chapter in accordance with the different degrees or levels of LBW. The incidence of LBW in the South African context will then be referred to. Correlation between risk factors relating to LBW and causes of LBW will further be elaborated on with specific reference to intrauterine growth restriction (IUGR) or SGA and prematurity. Reference to outcomes of LBW in the neonatal stage will be summarised, for short-term outcomes will not be the focus of this study. The main aim of the chapter is to familiarise the reader with the consequences of LBW in various domains (cognitive, developmental, neurological and physiologicall). Available findings on gender differences will be indicated.

2.2 Definition of low birth weight

LBW infants, according to the descriptions of Avery, Fletcher and MacDonald (1999) and Behrman, Kliegman and Jenson (2000), constitute the following populations:

- Appropriately grown premature infants, delivered prior to 37 weeks' completed gestation, who weigh 2 500 g or less.
- Full-term infants, born at or after 37 completed weeks' gestation who weigh 2 500 g or less. These infants are SGA, that is, they display IUGR. Papageorgiou and Bardin (1999) state that infants with IUGR are smaller than normal at any gestational age. According to Taeusch and Ballard (1998) SGA is usually defined as birth weight below the 10th percentile; at term this may vary from 2 500 g to 2 750 g. Sohl and Moore (1998) further state that at times the terms SGA and IUGR do not necessarily reflect identical clinical situations. Some perfectly normal, constitutionally small babies are below the 10th percentile for gestational age at birth, whereas some babies born above the 10th percentile exhibit growth restriction.
- Infants born both prematurely and SGA.

LBW infants form a heterogeneous group, perhaps needing separate types of medical treatment and intervention and facing different developmental outcomes (Bukatko & Daehler, 2001). According to Behrman et al. (2000) prematurity and IUGR are associated with increased neonatal morbidity and mortality.

Campbell (2001a), as well as Breslau, Chilcoat, Johnson, Andreski and Lucia (2000), define various levels of LBW as follows:

- LBW – birth weight between 1 500 g and 2 500 g
- VLBW – birth weight between 1 000 g and 1 500 g
- ELBW – less than 1 000 g.

Very preterm is defined as birth before 33 weeks (Nosarti, Al-Asady, Frangou, Stewart, Rifkin & Murray, 2002) or birth at 30 weeks or less (Marlow, 2004). Extremely preterm birth refers to a gestational age before 26 weeks (Marlow, 2004), 28 weeks (Hoff et al., 2004) or 29 weeks (Nadeau, Boivin, Tessier, Lefebvre & Robaey, 2001).

2.3 Incidence

The number of LBW infants seems to continue growing as a result of improved techniques of newborn intensive care (Aylward, 2002; Taylor, Klein, Minich & Hack, 2000a; Whitaker et al., 1997), such as increased use of antenatal steroids, more aggressive approaches to delivery room resuscitation and surfactant replacement (Aylward, 2002). Behrman et al. (2000) state that during 1997, 7.5% of live-born neonates in the United States weighed less than 2 500 g. Approximately 30% of LBW infants in the United States have IUGR and are born after 37 weeks. In developing countries, approximately 70% of LBW infants have IUGR. According to Sohl and Moore (1998) 4% to 8% of all infants born in developed countries have IUGR. March of Dimes (2003) reports that more than 60% of LBW babies are preterm.

Dr. A. Dhansay of the MRC of South Africa (2006, personal communication) states that there is no national coordinated register of LBW or birth weight in South Africa. No one-stop centre is available, providing complete statistics on LBW/prematurity. Pattinson, Woods, Greenfield and Velaphi (2005) found that the LBW rates for live-born infants weighing 1 000 g or more in 102 sentinel sites within the public health service in South Africa from October 1999 to September 2003 were 15.1%, 15.5% and 11.4% in metropolitan, cities and towns, and rural sites respectively. Data on live-born infants weighing 500 g to 999 g were excluded, as the reliability of this information was

questionable. Data were obtained only from public hospitals and clinics willing to participate in the project. In 2001 the average LBW rate was 17.8% (The MRC Unit for Maternal and Infant Health Care Strategies et al., 2001). Data from private institutions were also excluded.

LBW rate was considered an indicator of the SES and health of the community in general. LBW rates for births in developed countries is around 7%, whereas in developing countries it is two to three times higher (around 15%) (The MRC Unit for Maternal and Infant Health Care Strategies et al., 2001).

2.4 Risk factors

There seems to be correlation in the literature between risk factors and causes of LBW. Various causes of LBW will be elaborated on in Section 2.5. Risk factors related to LBW are many and complex (Breslau et al., 1996a; Campbell, 2001a), and include the following:

- Environmental (for example working conditions, violence towards women, prenatal care, poverty) (Breslau et al., 1996a; Campbell, 2001a), housing (for example lead paint, safety, crowding and pollution) (National Institute of Health, 1999)
- Behavioural (for example smoking, nutrition, alcohol and substance use, physical activity) (Breslau et al., 1996a; Campbell, 2001a)
- Social (for example stress, lack of social support) (Breslau et al., 1996a; Campbell, 2001a)
- Biological (for example pregnancy under 20 or over 40 years) (Breslau et al., 1996a; Campbell, 2001a)
- Previous premature birth (Breslau et al., 1996a; Campbell, 2001a)
- Maternal illness, such as HIV (The MRC unit for Maternal and Infant Heath Care Strategies et al., 2001), genital or urinary tract infections, hypertension and diabetes mellitus

- Multiple gestations (Vohr et al., 2000): this has become more common because of treatment for infertility
- Low maternal weight gain and low pre-pregnancy weight (National Institute of Health, 1999).

2.5 Aetiology

It is difficult to separate factors associated with prematurity from those associated with IUGR. A positive correlation exists between both premature birth and IUGR and low SES (Behrman et al., 2000; Kilbride, Thorstad & Daily, 2004). Families of low SES have a relatively high incidence of maternal under-nutrition, anaemia, illness, inadequate prenatal care, drug addiction, obstetric complications and maternal histories of reproductive inefficiency (Behrman et al., 2000). The degree to which genetic versus environmental factors influence the variance in birth weight among various populations is difficult to determine (Behrman et al., 2000).

2.5.1 Aetiology of intrauterine growth restriction

According to Sohl and Moore (1998) and Papageorgiou and Bardin (1999) growth restriction can be classified into asymmetric or symmetric growth restriction.

Asymmetric growth restriction (usually IUGR occurring late in pregnancy) refers to a decrease in weight, but length and head size are not restricted.

In symmetric growth restriction all indices are decreased, affecting both brain and body.

This division is apparently an oversimplification. Mixed patterns of abnormal growth are often noted (Sohl & Moore, 1998).

Symmetric IUGR usually has an earlier onset and is associated with diseases that affect foetal cell numbers. These diseases refer to conditions with chromosomal, genetic, malformation, teratogenic, infectious or severe maternal hypertensive aetiologies. Asymmetric IUGR usually has a late onset and is associated with poor maternal nutrition or exacerbation of maternal vascular disease (such as pre-eclampsia, chronic hypertension) (Behrman et al., 2000). Thus, factors intrinsic to the foetus cause symmetric growth restriction, whereas external factors are associated with asymmetric growth (Papageorgiou & Bardin, 1999). The causes of IUGR can be grouped into intrinsic and extrinsic types (Sohl & Moore, 1998), which are summarised in Table 2.1.

Table 2.1 Foetal growth restriction (Sohl & Moore, 1998 p. 92 adapted)

Intrinsic causes
Constitutional (for example parents of small stature)
Genetic (especially trisomy 18, 13 syndromes)
Toxic: alcohol, nicotine, virus, epanutin, warfarin
Infectious: TORCH (toxoplasmosis, other infections, rubella, cytomegalovirus infection, herpes simplex), syphilis, malaria
Teratogenic: radiation, drugs
Extrinsic causes
Decreased maternal nutrient delivery
Maternal cardiac disease
High altitude
Maternal anaemia (for example sickle cell disease)
Maternal starvation/inanition
Placental dysfunction
Hypertensive disease
Auto-immune disease (for example lupus)
Placental infection (for example syphilis)
Reduced placental area (multifoetal gestation, placental infarction)

2.5.1.1 Constitutional influences on growth

The genetic contribution to birth weight is approximately 40%, whereas environmental factors contribute 60%. Small mothers are more likely to produce small babies. Maternal influences on foetal growth are greater than paternal ones. During childhood and young adulthood maternal and paternal influences are more even (Sohl & Moore, 1998).

2.5.1.2 Race

According to Klaus and Fanaroff (2001) studies in the United States have demonstrated a significantly higher rate of LBW in African Americans when compared with their white contemporaries. Perinatal and neonatal mortality rates remain much greater in the black population. The origins of this problem remain unclear. Breslau et al. (1996a) report that social class and membership of a racial minority are strongly associated with biologic determinants of LBW. The National Institute of Health (1999) notes that these disparities remain even when adverse economic and social conditions are controlled.

2.5.1.3 Genetic and developmental influences

The influence of chromosomes on foetal growth is significant (Sohl & Moore, 1998). Males at term weigh 150 g to 200 g more than females. Infants born with trisomy 13 or 18 are often severely and symmetrically growth restricted. Syndromes that cause multiple genital abnormalities, massive congenital malformations and foetal cardiac anomalies are associated with IUGR (Sohl & Moore, 1998).

2.5.1.4 Congenital infection

Infections occurring at a critical time in foetal development can cause enough disruption of foetal cells to result in IUGR. Intrauterine infections usually have more severe consequences when they occur early in gestation. Most of the agents associated with the

TORCH syndrome cause IUGR (Sohl & Moore, 1998). It is not entirely clear whether a HIV-caused embryopathy involving IUGR exists. The MRC Unit for Maternal and Infant Health Care Strategies et al. (2001) however found that a pregnant woman who is HIV-infected has a twice greater risk of preterm labour. Bacterial infections, with the exception of syphilis, have not been associated with IUGR (Sohl & Moore, 1998). The National Institute of Health (1999) also refers to genital tract and oral microbial infections and inflammation as causes of LBW.

2.5.1.5 Smoking

In developed countries, smoking is the single most important contributor to LBW (Klaus & Fanaroff, 2001). Rates of IUGR in smokers are 3 to 4.5 times higher than in non-smokers, with average birth weights decreasing by 70 g to 400 g. These adverse effects are particularly pronounced in babies born to older women. However, the mean duration of gestation is not affected by maternal smoking (American Heart Association, 2002). The effects of maternal smoking during pregnancy seem to be dose-related (American Heart Association, 2002). Paternal smoking was associated with a decline in infant birth weight of 112 g. Whitaker et al. (1997) note that postnatal maternal smoking might also play a role.

Whitaker et al. (1997) state that nicotine alters the receptors in the basal ganglia of the foetal brain. According to Ernst, Moolchan and Robinson (2001) prenatal exposure to nicotine may lead to dysregulation in neurodevelopment. This may indicate a higher risk of psychiatric problems, including substance abuse.

A variety of other recreational drugs, including alcohol, cannabis, cocaine and amphetamines, have also been associated with adverse foetal effects. With the exception of Foetal Alcohol Syndrome, the effect of these drugs is not as well established or as pervasive

as that of tobacco (Klaus & Fanaroff, 2001). Foetal Alcohol Syndrome is associated with LBW (Mash & Wolfe, 2002). Certain prescription drugs, anticonvulsants in particular, can result in foetal growth restriction and specific malformation syndromes. Even consumption of coffee may pose a risk (Klaus & Fanaroff, 2001).

2.5.1.6 Maternal disease states

Maternal vascular disease, for example chronic hypertension, pregnancy-induced hypertension, severe diabetes with vasculophathy and chronic renal disease, has been associated with poor foetal growth. The common thread in all these diseases is vascular pathology that reduces uteroplacental perfusion (Sohl & Moore, 1998). Klaus and Fanaroff (2001) emphasise that pre-eclampsia is not only a contributor to foetal growth restriction, but is also the factor that carries the most unfavourable prognosis in terms of severity of growth deficit. Maternal hypertension (Sohl & Moore, 1998) unaccompanied by underlying vascular or renal disease is unlikely to be associated with IUGR. Maternal medical complications that compromise delivery of oxygen to the foetus are associated with IUGR. Severe maternal anaemia, such as that associated with sickle cell disease, is also linked with IUGR. Up to 30% of infants born to women with sickle cell disease weigh less than 2 500 g at birth (Sohl & Moore, 1998).

2.5.1.7 Altitude

A two- to three-fold greater rate of LBW is observed at altitudes higher than 2 000 m than at sea level (Klaus & Fanaroff, 2001).

2.5.1.8 Maternal nutritional states

Some research evidence demonstrates the potential benefits of nutritional intervention in the mother who was poorly nourished before pregnancy, but not in women who were

well-nourished before pregnancy (Klaus & Fanaroff, 2001). Larroque, Bertrais, Czernichow and Leger (2001) state that under-nutrition during vulnerable periods of brain development may have long-term effects on brain development that can affect learning and memory. The highest numbers of infants who are underweight at birth are born to poverty-stricken women (Berk, 2006). Poor nutrition (Breslau et al., 2001; Goyen, Veddovi & Lui, 2003; Wynn & Wynn, 1997), deprivation of oxygen (Goyen et al., 2003) and infection (Breslau et al., 2001; Wynn & Wynn, 1997) are significant risk factors of LBW/IUGR.

2.5.1.9 Prior obstetric and family history

Women younger than 15 years of age or older than 45 years of age who have a history of miscarriages or unexplained stillbirths after 20 weeks' gestation, or have had prior preterm deliveries, are at increased risk of delivering a growth-restricted baby (Klaus & Fanaroff, 2001). Those aged 35 and older are at a 20% to 40% increased risk of LBW and preterm delivery (Tough, Newburn-Cook, Johnston, Svenson, Rose & Belik, 2002).

Familial factors appear to play a role in the birth weight of babies. Mothers of LBW infants were frequently LBW infants themselves (Klaus & Fanaroff, 2001).

2.5.1.10 Obstetric factors

Multiple pregnancies are associated with IUGR. Up to 25% of twins are born with IUGR. Placental crowding in some of the foetuses probably contributes to higher rates of IUGR in higher order gestations (Berk, 2006). Vohr, Wright, Dusick, Perritt, Poole and Tyson (2004) confirm that increased short-term and long-term morbidities are associated with higher order multiples. Tough et al. (2002) found that almost 45% of the observed increase in the delivery of infants weighing less than 1 250 g and 50% of the increase in

delivery before 35 weeks (which is partly related to multiple births) were accounted for by in vitro fertilisation.

2.5.1.11 Placental contributions

There are placental pathologic correlates of known causes of IUGR (intrauterine infections, chromosomal anomalies, hypertensive disorders) and gross placental and cord abnormalities (for example extensive infarction and abnormal cord insertions), which are likely to result in restricted foetal growth (Klaus & Fanaroff, 2001).

Sohl and Moore (1998) summarise the various influences on foetal birth weight in Table 2.2:

Table 2.2 Factors affecting foetal weight at birth (Sohl & Moore, 1998 p. 91)

Factor	**Comment**
Gender	Males weigh more than females
Race	White babies at term weigh more than black babies
Constitutional factors	As a rough general rule, small parents produce small babies and large parents produce large babies; maternal constitutional factors have a greater influence on foetal growth than paternal factors
Multiple gestation	Singletons are larger than twins, which are larger than triplets, and so forth
Maternal disease states and maternal placental infarction	Diseases include obesity, diabetes, hypertension, infections and substance abuse, among others

IUGR is commonly associated with conditions that are also related to preterm delivery. Therefore, IUGR is an increasingly common finding among infants born at earlier gestational ages (Papageorgiou & Bardin, 1999). Thus, IUGR often occurs with a variety of maternal conditions that are associated with preterm delivery, for example very young or advanced maternal age, low maternal prepregnancy weight, poor maternal weight gain, maternal illness, lower SES status, race, pre-eclampsia, diabetes, intrauterine infections and substance abuse (Papageorgiou & Bardin, 1999).

2.5.2 Aetiology of prematurity

Behrman et al. (2000) state that premature birth of infants whose LBW is appropriate for their preterm gestational age is associated with medical conditions in which there is inability of the uterus to retain the foetus, interference with the course of the pregnancy, premature separation of the placenta or an undetermined stimulus to effective uterine contractions before term (Table 2.3).

Table 2.3 Identifiable causes of premature birth (Behrman et al., 2000 p.477)

Foetal
Foetal distress
Multiple gestation
Erythroblastosis
Non-immune hydrops
Placental
Placental dysfunction
Placenta previa
Abruptio placentae
Uterine
Bicornate uterus
Incompetent cervix (premature dilation)
Maternal
Pre-eclampsia
Chronic medical illness (e.g. cyanotic heart disease, renal disease)
Infection (e.g. group B streptococcus, urinary tract infection, bacterial vaginosis)
Drug abuse (e.g. cocaine)
Other
Premature rupture of membranes
Polyhydramnios
Iatrogenic

Overt or symptomatic bacterial infection of the amniotic fluid and membranes (such as group B streptococci) may initiate preterm labour. Bacterial products may induce premature uterine contractions or a local inflammatory response with focal membrane rupture (Behrman et al., 2000).

2.6 Expected consequences of low birth weight

Though neonatal outcomes will not be the focus of this study, relevant aspects will be addressed briefly before general longer-term outcomes are discussed.

2.6.1 Neonatal outcomes

Most LBW infants go on to lead normal lives, despite many obstacles they face to develop healthily. About half of them have no disabilities (Berk, 2006).

However, all very premature babies are developmentally behind normal babies of the same age for the first 6 to 9 months. Most have caught up by 12 to 18 months. Many premature babies show disturbances of reflexes, posture and muscle tone in the early months, which usually resolve by 12 to 18 months without specific treatment (Campbell, 2001b). VLBW infants however may not catch up, especially in the presence of chronic sequelae (for example mental retardation, seizures, sensory impairment), insufficient nutritional intake or an inadequate caretaking environment (Bregman, 1998). Whereas some children grow out of neurodevelopmental problems, infants with a birth weight of less than 1 000 g frequently experience behavioural problems, learning difficulties and school failure (Jobe, 2001). SGA infants tend to have more serious problems than premature infants (Berk, 2006).

Preterm neonates are at increased risk of postnatal complications (Bhutta et al., 2002). The following neonatal problems are associated with premature infants:

- Respiratory (Marlow, 2004), for example respiratory distress syndrome (Breslau & Chilcoat, 2000), CLD (also known as bronchopulmonary dysplasia) (Bhutta et al., 2002; York & DeVoe, 2002), congenital pneumonia and apnoea (Behrman et al., 2000)
- Cardiovascular, for example bradycardia, hypotension and hypertension (Behrman et al., 2000)
- Haematologic, for example organ haemorrhage (Behrman et al., 2000)
- Gastrointestinal, for example poor gastrointestinal function (Behrman et al., 2000)

- Metabolic-endocrine, for example hypocalcemia (Behrman et al., 2000; Bhutta et al., 2002)
- CNS, for example IVH (Bhutta et al., 2002), hypotonia, deafness, seizures and retinopathy of prematurity (Behrman et al., 2000)
- Renal, for example hyponatremia (Behrman et al., 2000)
- Visual (Aylward, 2002; Behrman et al., 2000; Bregman, 1998; Marlow, 2004) and hearing impairments (Aylward, 2002; Behrman et al., 2000; Hack, Wilson-Costello, Friedman, Taylor, Schluchter & Fanaroff, 2000; Vohr et al., 2000; York & DeVoe, 2002)
- Other, for example infections (Behrman et al., 2000).

According to Chapieski and Evankovich (1997) some of the above-mentioned neonatal problems may have long-lasting effects on the CNS, as indicated in Table 2.4. The length of neonatal intensive care unit stay was the second most important variable predicting premature children's use of early intervention programmes, as well as neurological damage predicting long-term risk (Lindeke, Stanley, Else & Mills, 2002).

In the case of VLBW infants, approximately 50% to 60% will have normal outcomes and 40% to 50% will have some degree of impairment ranging from mild-moderate outcomes (20% to 30%) to severe ones (approximately 20%). Researchers note that birth weight alone does not identify poor outcome, but rather associated risk factors for poor outcome, such as intracranial haemorrhage (ICH) or periventricular leukomalacia (PVL), CLD and social risk (Piecuch & Leonard, 1997).

Preterm and different levels of LBW infants appear to be biologically more susceptible to perinatal morbidity and mortality, and often show long-term impairments in the following domains: neurological (Dewey, Crawford, Creighton & Sauve, 1999; Hack et al., 2000; Nadeau et al., 2001; Perlman, 2001; Pietz et al., 2004; Reiss et al., 2004; Saigal et al., 2001;

Sajaniemi, Hakamies-Blomqvist, Katainen & von Wendt, 2001; Tully, Arseneault, Caspi, Moffitt & Morgan, 2004; Vohr et al., 2000), neurodevelopmental (Huddy, Johnson & Hope, 2001; Indredavik, Vik, Heyerdahl, Kulseng, Fayers & Brubakk, 2004), neurosensory (Huddy et al., 2001; Taylor, Klein, Minich & Hack, 2000b), cognitive (Bhutta et al., 2002; Breslau & Chilcoat, 2000; Breslau et al., 1996a; Dieterich, Hebert, Landry, Swank & Smith, 2004; Indredavik et al., 2004; Lawson & Ruff, 2004; Peterson, Vohr, Kane, Whalen, Schneider, Katz et al., 2002; Richards, Hardy, Kuh & Wadsworth, 2001; Saigal et al., 2001; Sajaniemi et al., 2001; Taylor et al., 2000b; Tully et al., 2004), educational or learning (Huddy et al., 2001; Sajaniemi et al., 2001); psychiatric (Indredavik et al., 2004), behavioural (Breslau & Chilcoat, 2000; Breslau et al., 1996a; Huddy et al., 2001; Peterson et al., 2002; Potgieter, Vervisch & Lagae, 2003; Sajaniemi et al., 2001; Taylor et al., 2000a; Tully et al., 2004), and adaptive functioning (Taylor et al., 2000a), including developmental disabilities (de Haan, Bauer, Georgieff & Nelson, 2000; Dieterich et al., 2004; Hack et al., 2000; Kilbride et al., 2004; Lui, Sun, Neiderhiser, Uchiyama & Okawa., 2001; Nadeau et al., 2001; Reiss et al., 2004; Saigal et al., 2001; Sajaniemi et al., 2001; Stoelhorst, Rijken, Martens, Zwieter, Feenstra, Zinderman et al., 2003; Vohr et al., 2000). According to Saigal et al. (2003b) the pattern of disabilities changes over time as new concerns (such as learning difficulties, behavioural problems and growth deficits) surface after resolution of earlier neurodevelopmental difficulties.

There appears to be a gradient effect of LBW and gestational age on development, with the smallest and youngest having the highest incidence of impairment (Aylward, 2002; Lou, 1996; Piecuch & Leonard, 1997; Pietz et al., 2004; Potgieter et al., 2003; Vohr et al., 2000), such as behavioural and learning problems (Potgieter et al., 2003). Developmental, neurosensory and functional morbidities increased with decreasing birth weight (Vohr et al., 2000). This gradient effect will be reflected in the various domains below, as research

findings sometimes appear to be inconsistent. Various researchers indicated that as birth weight decreased, the magnitude of behavioural, social, attention and language problems increased (Klebanov & Brooks-Gunn, 1994), including cognition and neurodevelopment (Vohr et al., 2000). Children with these problems place increasing demands on school systems and often require multidisciplinary coordination of intervention (Aylward, 2002).

A discussion of the long-term sequelae of LBW will follow. Specific implications regarding internalising, externalising and neuropsychological functioning (motor, visual-spatial, memory and EF) will be reflected in Chapters 3, 4 and 5 respectively.

2.6.2 Educational/cognitive difficulties

Tideman (2000) found that preterm children without major disabilities, who show satisfactory development up to their early school years and who have access to adequate support, should not be expected to experience subsequent developmental cognitive deviations.

However, being born prematurely and very small entails a major risk of developing cognitive difficulties in childhood (Isaacs et al., 2000), as indicated in Table 2.4. Each year in the United States 25% to 50% of survivors display cognitive and behavioural deficits (Sola et al., 2005). Even children born preterm that did not experience medical complications during the perinatal period may still be at risk of cognitive deficits (Curtis, Lindeke, Georgieff & Nelson, 2002).

A high proportion of school failure was observed in ELBW teenagers (Saigal, Hoult, Kim, Pinelli & Boyle, 2003a), children after very preterm birth (Marlow, 2004), LBW children (Pietz et al., 2004; Pinto-Martin, Whitaker, Feldman, Cnaan, Zhao, Rosen-Bloch et al., 2004; Tully et al., 2004), VLBW primary school children (Nadeau et al., 2001; Rickards,

Kelly, Doyle & Callanan, 2001; Wolke, 1998) and extremely preterm or ELBW children (Kilbride et al., 2004). Those born prematurely (Gross et al., 2001; Peterson et al., 2002), SGA (O'Keeffe, O'Callaghan, Williams, Najman & Bor, 2003; Sohl & Moore, 1998) and with VLBW (Sajaniemi et al., 2001) seem to have significantly lower IQ scores and/or greater educational difficulties than NBW children. More frequent grade retention was also observed in LBW children (Pinto-Martin et al., 2004). Even those LBW children who did not fail a grade are still rated by teachers as having more problems than NBW children, which suggests that even without being identified by the school as having problems, they may be at risk of future academic, behavioural and social problems (Klebanov & Brooks-Gunn, 1994).

Special education: LBW children (Bhutta et al., 2002; Pinto-Martin et al., 2004), ELBW children (Aylward, 2002; Kilbride et al., 2004; Saigal et al., 2001; Vohr et al., 2000), VLBW (Aylward, 2002; Rickards et al., 2001; Taylor et al., 2000a) and children with IUGR (Frisk, Amsel & Whyte, 2002) were significantly more likely to require special education or remedial education. Special education placement followed a birth weight gradient (Pinto-Martin et al., 2004). Despite an overall mean IQ of 90 (range 50 to 141) at a mean age of 10 years, 64% of these children had been or at the time were in special school educational programmes (Saigal et al., 2001). Making use of special education services was more common among males (Pinto-Martin et al., 2004).

Learning problems: A higher prevalence of learning problems was observed in children born prematurely (Abernethy, Klafkowski, Foulder-Hughes & Cooke, 2003; Aylward, 2002; Huddy et al., 2001; Isaacs et al., 2000; O'Keeffe et al., 2003; Peterson et al., 2002; Potgieter et al., 2003), children born with VLBW (Astbury, Orgill & Bajuk 1987; Botting et al., 1997; Bregman, 1998; Huddy et al., 2001; Isaacs et al., 2000; Taylor et al.,

2000a; Ulvund, Smith & Lindemann, 2001; York & DeVoe, 2002), ELBW (Aylward, 2002; Saigal et al., 2001) and who experienced IUGR (Frisk et al., 2002). Learning problems in reading, spelling, mathematics or writing were identified in ELBW children, independent of IQ scores (Aylward, 2002). According to Elgen, Sommerfelt and Ellertsen (2003) two thirds of LBW children with learning disabilities could be identified at 5 years of age when using the criteria of low verbal IQ and motor problems. Marlow (2004) postulates that most learning difficulties appear to be related to low overall IQ. Bregman (1998) further states that deficits in early information-processing skills are consistent with findings of deficits in academic performance, often resulting in a specific learning problem.

Difficulties with reading and mathematics: Cognitive deficits are difficult to detect and often appear when reading comprehension and mathematical reasoning are expected (Lindeke et al., 2002). Preterm/LBW children had significantly lower scores in tests of numeracy skills (Isaacs et al., 2000; Olness, 2003; Sajaniemi et al., 2001), mathematics (McGrath, Sullivan, Lester & Oh, 2000; Olness, 2003; Papageorgiou & Bardin, 1999; Rickards et al., 2001), reasoning and numerical operations (Olness, 2003; Rickards et al., 2001), as well as arithmetic skills among VLBW children (Rickards et al., 2001). Reading (Frisk et al., 2002; Papageorgiou & Bardin, 1999; Rickards et al., 2001) and mathematic achievement scores were the lowest for the preterm groups classified as neurologically suspect or abnormal (McGrath et al., 2000). Mathematics achievement followed a birth weight gradient regardless of educational placement (Pinto-Martin et al., 2004). Deficits in spatial ability attributed to the hippocampus may underlie difficulties with mathematics, because of the spatial component involved in numerical skills (Isaacs et al., 2000). Breslau et al. (2001) state that LBW has greater effects on mathematics than on reading. Mathematics is more strongly related to non-verbal processing, including visual-perceptual and motor

functions. LBW children tend to show greater impairments in these areas. This finding is consistent with evidence that early neurological insults are more closely related to deficits in visual than in verbal abilities.

According to Richards et al. (2001) birth weight is associated with education. Those with higher birth weight are more likely to achieve higher qualifications. This effect is accounted for partly by cognitive function at age 8.

Assessment: Frisk et al. (2002) suggest that neuropsychological assessment of SGA children prior to 8 years of age may reflect a potentially false picture of cognitive integrity and fail to reveal important cognitive impairments occurring at later ages. Other studies however concluded that impairments in cognitive function at age 3 appear to be an important factor in identifying children with VLBW who may show deficits in neuropsychological functioning at school age (Dewey et al., 1999). De Haan et al. (2000) note that testing children during the second year of life is important, because this is a transitional period when a shift in level of function occurs and thus may be a particularly sensitive time for detecting differences in developmental trajectories. Marlow (2004) also postulates that at age 2 most serious neurological and sensory disabilities are likely to be identified. Some studies have found that deficits in cognitive abilities and learning are relatively stable over time, while others suggest progressively greater impairments with age (Taylor et al., 2000a). Various problems often become apparent at school age because of larger demands on differential abilities (Wolke, 1998). Kesler, Ment, Vohr, Pajot, Schneider, Katz et al. (2004) however mention that certain cognitive abilities improve over time, possibly by adolescence. This association between LBW and cognitive outcomes does not appear to decrease with age (Tully et al., 2004). Research findings of Breslau et al. (2001) imply that most of the differences between LBW and NBW academic achievements at age

11 could be eliminated by reducing differences in cognitive abilities at age 6. Therefore, interventions to improve academic performance of LBW children should focus on the preschool years.

2.6.2.1 Risk factors of cognitive impairments

Neurosensory impairment: As can be expected, most children with major neurosensory impairments have subaverage cognitive development. However, developmental outcomes are poor even for those without major neurosensory impairments (Greenbaum & Auerbach, 1992; Hack et al., 2000; Stathis, O'Callaghan, Harvey & Rogers, 1999).

SES: Lower IQ was generally associated with SES (Kilbride et al., 2004; Sohl & Moore, 1998) or gender (Sohl & Moore, 1998). Huddy et al. (2001) however found no association between low social class and maternal education with poor school performance.

Brain abnormalities: A decline in verbal and full-scale IQ ratings was observed for SGA children (Frisk et al., 2002) who had experienced brain growth compromised *in utero*, whether or not they also experienced suboptimal brain development after birth. LBW was related to enduring IQ deficits due to suboptimal development *in utero* or vulnerability to postnatal disease and associated suboptimal brain development in infancy (Saigal et al., 2001). Lower intellectual abilities correlated with brain anomalies (Anderson, Doyle & the Victorian Infant Collaborative Study Group, 2004), such as decreased volumes of cortical areas in preterm children (Hoff et al., 2004). Abernethy et al. (2003) note in their study of preterm children that IQ relates to brain size and cortical grey matter volume, which may be impaired independently of previous white matter injury such as PVL. Regional grey matter was strongly associated with the global IQ of adolescents born preterm (Giménez, Junqué, Narberhaus, Caldú, Salgado-Pineda, Bargalló et al., 2004). Previous studies found that preterm children

tend to have smaller brains, less cortical complexity and often delayed myelination (Abernethy et al., 2003). A positive correlation among cortical and corpus callosum volume and IQ was found in children born preterm, including between cerebellar volume and intelligence (Curtis et al., 2002). Abernethy, Cooke and Foulder-Hughes (2004) found in their study of preterms that IQ correlated with right and left caudate volume and poorer development of the caudate relative to the rest of the brain, independent of other lesions. Significant associations were identified between the caudate and hippocampal volumes and intelligence (Abernethy et al., 2003).

According to Espy (2004), cognitive functions may be subserved by more diffuse brain areas in school-age children. SGA children with motor problems more often appear to have neuropsychological deficits than SGA children without motor problems.

Hypoxic-ischaemic brain damage and IVH, secondary to perinatal asphyxia, may result in neurological and intellectual dysfunction (Zappitelli, Pinto & Grizenko, 2001). Huddy et al. (2001) observed an association between poor outcome at school and respiratory illness. According to Goyen et al. (2003) CLD and social risk factors are associated with poorer cognitive outcome.

Head circumference: ELBW and VLBW children tend to have a smaller head circumference (Abernethy, Palaniappan & Cooke, 2002; Kilbride et al., 2004) and small stature (Abernethy et al., 2002), which have been associated with lower developmental performance (Abernethy et al., 2002; Kilbride et al., 2004). Birth weight is strongly related to head circumference, which is closely associated with brain size and subsequent childhood cognitive function (Richards et al., 2001). Frisk et al. (2002) found that SGA children who experienced brain growth compromise prior to birth due to IUGR, as well as during the first 9

months post-term, had the worst outcomes on various measures, e.g. lower verbal and non-verbal IQ, phonological awareness, visual-motor integration, problem-solving and literacy. Inadequate head growth *in utero* appears to be the critical factor affecting the expression of these impairments. Good to excellent catch-up brain growth after birth did not guarantee normal cognitive and academic outcome (Frisk et al., 2002). Cooke and Abernethy (1999) however did not observe an association between brain measurements and school performance among the VLBW group.

Perinatal variables: Gross et al. (2001) observed that perinatal complications had little correlation with school achievement at 10 years of age. Perinatal variables were related to physical impairment, sensory impairment, as well as profound and trainable mental handicap; socio-demographic influences were associated with emotional handicap and speech/language impairment. Both biomedical and environmental risks were related to educable mental handicap and specific learning impairment (Aylward, 2002). Cooke and Abernethy (1999) concluded that the school-related difficulties experienced by VLBW children are unlikely to be the result of perinatal brain injury, but may be attributable to the effects of poor postnatal growth.

Nutrition: Abnormal brain development after perinatal injury or postnatal nutritional deficits is responsible for cognitive deficits in preterm children (Abernethy et al., 2004). Greater emphasis on nutritional and environmental requirements of VLBW infants in the newborn period might reduce the impact of premature birth on later learning and behavioural problems (Abernethy et al., 2002; Abernethy et al., 2004). Foetal under-nutrition at critical periods can result in neurodevelopmental impairments such as reducing cellular growth, IQ and learning performance. Abnormal nutrition and metabolic functioning, as well as environmental stresses, may disrupt rapid brain development (especially in those with PVL)

(Inder, Wells, Mogridge, Spencer & Volpe, 2003). Mild malnutrition lasting one year or more has been associated with cognitive impairment in the general population of children (Olness, 2003). Isaacs et al. (2000) note that substantial differences in IQ occurred at age 7 to 8 years, depending on nutritional intervention shortly after birth. According to Abernethy et al. (2004) and Cooke and Abernethy (1999) brain growth is most rapid at the time of term, and the period between birth and term is one of relative malnutrition for many preterm infants. Adequate nutrition at this time may be of particular importance in limiting the development of key cerebral structures (Abernethy et al., 2004), including improvement of growth and school performance (Cooke & Abernethy, 1999).

Gradient effect of birth weight: In general, the risk of neurodevelopmental and intellectual problems is higher as birth weight and gestational age decrease (Aylward, 2002; Behrman et al., 2000; Klaus & Fanaroff, 2001; Tully et al., 2004). The significant correlation between lower birth weight and gestational age, and decreased cognitive test scores, highlight the developmental vulnerability of the immature brain (Bhutta et al., 2002). Some researchers postulate that only children born with ELBW experience increasing school difficulties, while others observe increased risk in all levels of LBW (Lindeke et al., 2002; Pietz et al., 2004). Elgen et al. (2003) found no differences in cognitive functions between children weighing less than 1 500 g at birth and those weighing between 1 500 and 2 000 g. The risk of morbidity depends on the aetiology, but babies for whom no diagnosis is made still have a higher risk of future problems than babies within the normal weight range (Campbell, 2001b).

Table 2.4 Adverse neurocognitive outcomes after very preterm birth (Marlow, 2004)

Early outcomes (to 2 years)	School age outcomes
Low developmental scores	Cognitive impairment
Cerebral palsy	Motor impairment (clumsiness)
Blindness	Visual-spatial/perceptual problems
Deafness	ADHD
Transient dystonia	Psychiatric symptoms
Feeding difficulty	Ocular impairments
Delayed language skills	Poor auditory discrimination
	Special educational needs

2.6.3 Abnormal neurological development

Curtis et al. (2002) note that 55% of the magnetic resonance imaging (MRI) scans of 14-to-15-year-olds born preterm were rated as abnormal. However, no ultrasonography abnormalities were observed in 80.5% of LBW children, though ultrasonography is not completely sensitive to milder forms of white matter injury that would lead to an under-estimation of the effects of parenchymal lesions and/or ventricular enlargements (PL/VE) (Whitaker et al., 1997). Perlman (2001) notes that cognitive and behavioural problems occur equally commonly in the presence or absence of neuroimaging abnormalities.

Neuropsychological deficits were observed in children with LBW in the following areas: language (Aylward, 2002; Breslau et al., 2001; Dewey et al., 1999; Huddy et al., 2001; Papageorgiou & Bardin, 1999; Pinto-Martin et al., 2004), memory, visual-motor and motor skills (Dewey et al., 1999), as well as mental retardation (Aylward, 2002; Bregman, 1998; Pietz et al., 2004; Pinto-Martin et al., 2004), epilepsy and cerebral palsy (Aylward, 2002; Pietz et al., 2004), extra pyramidal movement disorders (Pietz et al., 2004), and spatial orientation (Rickards et al., 2001). Arzoumanian, Mirmiran, Barnes, Woolley, Ariagno, Moseley et al.

(2003) note that preterm infants are at high risk of neurological insults, which may include visual, auditory, cognitive, behavioural and motor abnormalities and cerebral palsy.

2.6.3.1 Factors affecting brain development

Various researchers suggest that long-term problems (particularly during middle childhood [Peterson et al., 2002]), including cognitive and behavioural problems, may be a consequence of cerebral damage in the neonatal period (Reiss et al., 2004; Tully et al., 2004). A high incidence of cerebral abnormality was observed (Curtis et al., 2002; Inder et al., 2003). Preterm birth and the complicated postnatal course disrupt many cellular and subcellular mechanisms, as well as the genetically programmed brain genesis (Sola et al., 2005).

Increased neurodevelopmental morbidity was associated with CLD (Stoelhorst et al., 2003; Vohr et al., 2000), extensive IVH (Stoelhorst et al., 2003; Vohr et al., 2000), including PVL, steroids for CLD, necrotising enterocolitis and male gender (Vohr et al., 2000). Dieterich et al. (2004) and Stoelhorst et al. (2003) also mention that children born preterm are at increased risk of developmental delays owing to the fact that they are more likely to be born into poverty or low SES.

Various factors are thought to affect the development of the premature brain, including gestational age, hypoxia, infection, congenital malformation and genetic abnormality (Childs, Ramenghi, Cornette, Tanner, Arthur, Martinez et al., 2001). Other factors, including cerebral hypoperfusion, chronic hypoxia, poor cerebral autoregulation and free radical production, can lead to necrosis, cystic formation and gliosis of white matter surrounding the ventricles (Sola et al., 2005). Many clinical factors (e.g. CLD, recurrent apnoea and bradycardia, transient hypothyroxemia of prematurity, hyperbilirubinaemia, nutritional deficiencies, glucocorticoid exposure), as well as stressful environmental conditions in hospital, multiple medication,

infant-provider interaction, constant noise and bright light, may act in combination to influence the developing brain, even in the absence of haemorrhage and/or ischaemia (Perlman, 2001), as indicated in Figure 2.1. These clinical factors and environmental conditions affect vulnerable brain areas, most commonly the subplate neurons, basal ganglia, thalamus and hippocampus. Perlman (2001) notes that the developing brain of the premature infant is vulnerable to injury secondary to other factors, including periventricular white matter haemorrhage and/or ischaemia, disruption of one or more of the organisational events in brain development, a transient developmental overexpression of glutamatergic receptors within basal ganglia and vulnerability of the hippocampus to hypoxia-ischaemia. Glutamate recognition sites are widely distributed in the human foetal brain within the caudate, globus pallidus, putamen, subthalamic nuclei and hippocampal formation, which is distinct from the distribution observed in adult brain tissue (Perlman, 2001).

Figure 2.1 Interaction between medical and environmental risk factors and vulnerable brain regions (Perlman, 2001)

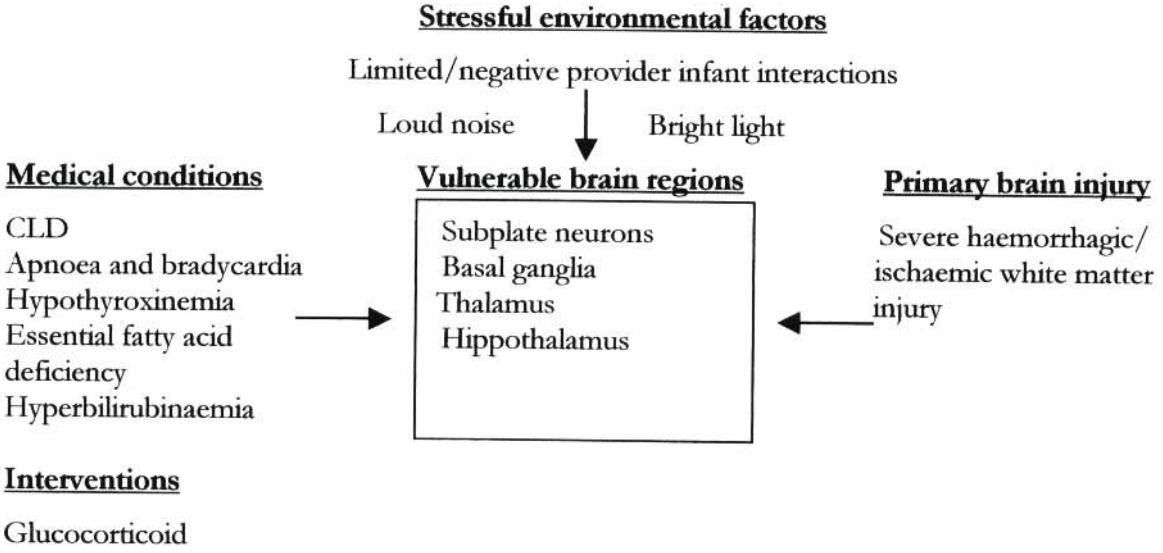


Figure 2.1 illustrates how clinical factors and stressful environmental conditions associated with prematurity may act in combination to influence the developing brain.

Preterm infants also seem to be vulnerable to neurodevelopmental impairments due to neurological injuries. According to Vollmer, Roth, Baudin, Stewart, Neville and Wyatt (2003) the subplate zone of the developing brain has its peak between 22 and 34 weeks of gestation. Injuries to the transient foetal subplate zone, containing "waiting" axons and neurons, result in the disruption of processes that are essential for normal brain organisation.

Structural differences in brain tissue, as well as a reduction in the number of brain cells, have been noted in infants who experienced significant undernourishment after birth (Frisk et al., 2002). Even subtle changes in the diets of VLBW infants can have dramatic effects on later growth and outcome. Prenatal nutrition may contribute to compromised development (de Haan et al., 2000). The demands for neural growth are high during the third trimester. The placenta is the unique source of docosohexanoic acid (DHA) (a polyunsaturated fatty acid), which is important for proper development of grey matter and synaptic membranes. Infants born prematurely who are not fed human milk, which contains DHA, may be predisposed to altered development of brain structures (de Haan et al., 2000). Most neurodevelopmental impairments are likely to be the consequence of brain damage during the perinatal period (Vollmer et al., 2003).

Severity of illness in preterm neonates, their physiological instability and exposure to adverse experiences may have a persisting impact on brain development (Bhutta et al., 2002). Various neonatal diseases, for example IVH and respiratory distress syndrome, predict short-term outcomes and two-year outcomes. The more diagnoses an infant has and the more severe those diagnoses, the more likely it is that the infant will have adverse long-term outcomes (Jobe, 2001). Gross et al. (2001) conclude that neonatal medical risk factors become less critical over time as environmental influences begin to play a more dominant role in cognitive outcome. Abernethy et al. (2002) postulate that abnormalities in brain structure

(observed by MRI) do not necessarily imply current aetiological significance, and may result from early environmental and/or genetic influences or physical insults.

2.6.3.2 Abnormalities in brain developmental processes and anatomy

Very preterm births occur at a time when the foetus should be growing rapidly, with all the body systems maturing rapidly and the brain developing at its fastest (Marlow, 2004). Preterm birth is associated with long-term abnormalities in brain development, including regionally specific disturbances in brain structure and function (Peterson et al., 2002). Premature-related anatomic abnormalities in brain development are prominent in premotor, sensori-motor and parieto-occipital cortices (Peterson et al., 2002). Deficits in frontal lobe functions have been identified (Giménez et al., 2004).

In the absence of genetic, infectious and metabolic causes, long-term neurological deficits are primarily due to major IVH and echolucent PVL (Verma, Tejani, Klein, Reale, Beneck, Figueroa et al., 1997). IVH and PVL were found to be preceded by acute fluctuations in cerebral blood flow in the preterm foetus and neonate where autoregulation is impaired (Verma et al., 1997). The presence of PL/VE significantly increased the risk of any psychiatric disorder (specifically ADHD but not ODD) and subnormal IQ (Breslau et al., 2000), while germinal matrix haemorrhage or IVH did not affect the risk of psychiatric outcome (Whitaker et al., 1997). Significant differences in IQ between children with lesions detected by MRI and those with normal scans were also not identified. It however is possible that brain plasticity (the capacity to recover from injury or insult) in the neonate may enable children to compensate for initial brain damage (Curtis et al., 2002; Lindeke et al., 2002). Childs et al. (2001) also mention that it is not clear whether all aspects of brain development are equally affected by a particular neurological insult. The development of neurobehavioural problems in VLBW infants without haemorrhage and/or ischaemia remains unclear, but may be partly

attributable to a lasting disturbance in one or more of the organisational events in brain development and/or injury to the basal ganglia or hippocampus (Perlman, 2001).

Genetically programmed, spatially and temporally organised cascades of events occur during the early stages of brain development (Nadeau et al., 2001). According to Charmandari, Kino, Souvatzoglou and Chrousos (2003) the developing brain undergoes rapid growth and is characterised by high turnover of neuronal connections during the prenatal and early postnatal stages. These processes and brain plasticity slow down during childhood and puberty and plateau in young adulthood. Negative prenatal and perinatal events associated with premature birth may disrupt this sequence and lead to developmental impairments, including cerebral palsy and mental retardation (Nadeau et al., 2001). Hormonal action in early life, and to a much more limited extent later, can have effects that last for long periods of time, often for the entire life of the individual (Charmandari et al., 2003). It appears to be still unclear whether extrauterine life provides increasing stimulus for brain development (if optimal), or whether brain maturation takes place at the same rate as *in utero* development (Childs et al., 2001).

Although neuronal migration is complete by 20 weeks' gestation, extensive development occurs in the foetal brain during the last trimester, including myelination of white matter, glial cell migration and the development of a complex gyral pattern (Childs et al., 2001). Major developmental events occur in VLBW infants during hospitalisation, including the establishment and differentiation of subplate neurons, proper alignment, orientation and layering of cortical neurons, elaboration of dendrites and axons, formation of synapses, cell death, selective elimination of neuronal processes and synapses, and the proliferation and differentiation of glial cells (Perlman, 2001).

The brain between 6 months post conception and 1 year of age undergoes a marked transformation from a relatively primitive structure into a complex, integrated organ (Georgieff & Innis, 2005). Significant neurodevelopmental processes at this time include the onset of myelination, organisation of neurotransmitter systems, dendritic arborisation and selective pruning, and synaptogenesis, particularly in the visual system and the hippocampus. The composition of the cerebral white matter undergoes rapid changes in the first year of life, including myelination (Abernethy et al., 2003). Defects in postnatal myelination are possibly due to injury to axons and oligodendrocyte progenitors after perinatal infections or ischaemia, effects of drugs such as corticosteroids or nutritional deficiencies (Abernethy et al., 2003). Thus, disorganised cortical development, possibly involving disrupted or delayed synaptic pruning and neural migration or other mechanisms responsible for plasticity, appears to be associated with preterm birth (Kesler et al., 2004).

Frontal lobes: The SGA group with abnormal head growth seems to be at increased risk of altered frontal lobe functioning (Frisk et al., 2002). Individual brain regions are most vulnerable to the adverse effects of IUGR, under-nutrition, or damage during periods of rapid glial proliferation and differentiation, including periods of rapid myelination. The frontal lobes develop slowly in relation to other brain regions, with myelination reaching peak velocity in the first year of life, and full synaptic density in the prefrontal area being attained only between 2 and 3 years of age. Frisk et al. (2002) postulate that prolonged brain growth compromise experienced by the abnormal SGA group may impede frontal lobe development, resulting in impairments on tests measuring frontal lobe functions. They also mention that it is important to note that the frontal lobes are not homogeneous, in terms of function and structure. The cognitive abilities mediated by the frontal lobes do not mature at the same rate. Early neurological insults experienced by children born preterm may slow down the normative

developmental process in the prefrontal cortex during the first 8 to 10 years (Curtis et al., 2002). By adolescence these children may to some extent overcome the developmental lag by normal brain maturation mechanisms.

Iron and essential fatty acids have an impact on the above-mentioned developmental processes at multiple levels, which may have lasting effects in preterm infants inadequately nourished with these nutrients (Georgieff & Innis, 2005). Iron deficiency may affect multiple developmental brain processes e.g. myelination, monoamine metabolism, energy metabolism and hippocampal dendritic growth. Essential fatty acids and iron, which are both crucial to normal CNS development, are commonly deficient in the preterm infant. Newborn brain iron status is affected by several common pathologic conditions during gestation, such as IUGR and premature delivery. Premature birth places the developing brain at risk of iron deficiency and iron overload (Georgieff & Innis, 2005).

White and grey matter: Neonatal risk factors were significantly correlated with both grey and white matter proportions, although the results indicated stronger correlations in girls than boys (Reiss et al., 2004). Grey matter proportion was strongly correlated with cognitive outcome (Abernethy et al., 2004) at both 4.5 and 8 years in preterm girls, but not in preterm boys (Reiss et al., 2004). Lower birth weight and maternal education, as well as the presence of IVH and reduced subcortical grey matter volume, may increase the risk of neuroanatomic abnormality (Kesler et al., 2004).

According to Nagy, Westerberg, Skare, Andersson, Lilja, Flodmark et al. (2003) it appears that during the period between birth and term, the development of fibre organisation or myelination of preterm children does not keep up with the intrauterine development of infants born at term. Oades (2005) notes that by the age of 5 years (in the general population)

the child's brain is filled with far more neurons (grey matter) that make far more connections than in the adult brain. Irregularities may occur from the first to the second decade of life, when the process of reducing grey matter for efficiency and establishing the right pattern of neuronal connections occurs (Oades, 2005).

Both grey (Abernethy et al., 2004; Giménez et al., 2004; Nosarti et al., 2002; Reiss et al., 2004) and white matter (Arzoumanian et al., 2003; Inder et al., 2003; Nagy et al., 2003; Reiss et al., 2004) volumes were significantly reduced relative to controls, including decreased grey/white matter differentiation (Kesler et al., 2004). According to Inder et al. (2003) grey matter abnormality was characterised by marked enlargement of the subarachnoid space and immature gyral development. Enlarged parietal and frontal grey matter, as well as reduced temporal and subcortical grey volumes in preterm children compared to controls, was observed (Kesler et al., 2004). IVH was associated with reduced subcortical grey matter (Kesler et al., 2004). Early brain insults involving white matter tend to impair later myelinations and development of grey matter structures, as well as alterations in the volume of cortical grey matter (Inder et al., 2003). Grey matter and white matter volumes increase dramatically during the third trimester (Anderson et al., 2004; Nosarti et al., 2002), which makes the brain development of preterm infants vulnerable, even in the absence of acute brain insults (such as PVL and IVH) (Anderson et al., 2004).

The CNS lesions of most significant importance to prognosis in childhood and adulthood involve the white matter (York & DeVoe, 2002). Alterations in cerebral white matter structure were common in VLBW infants, with closely related abnormalities in gyral development (Inder et al., 2003). IVH and ventriculomegaly are powerful predictors of white matter damage in the first few weeks of life (Nosarti et al., 2002). Nosarti et al. (2002) suggest that only the most premature individuals may suffer from white matter injury, which is

commonly known to be the main cause of neonatal mortality and long-term neurological impairment in very preterm infants. Nagy et al. (2003) observed disturbances in the white matter of children born preterm that were still detectible at the age of 11 years. A high incidence of minor cerebral white matter injury occurs in preterm survivors (O'Brien, Roth, Steward, Rifkin, Rushe & Wyatt, 2004) and VLBW infants (Inder et al., 2003), which may alter or delay normal developmental maturation of processing abilities (O'Brien et al., 2004), such as motor and cognitive difficulties (Inder et al., 2003). White matter abnormality was related to major risk factors such as hypotension and perinatal infection (Inder et al., 2003). Reiss et al. (2004) observed that white matter volumes were significantly reduced only in boys born preterm compared to age-matched healthy control males. One or more processes underlying white matter development (e.g. myelination, axonal growth and glial proliferation) may be particularly affected by premature birth, especially in those with the lowest birth weights.

Brain volume: Decreases in whole brain volume were observed in the preterm (Cooke & Abernethy, 1999) and very preterm group (Nosarti et al., 2002). Prematurity appears to affect brain development, resulting in long-term structural abnormalities. These abnormalities include smaller volumes of the cortex (Anderson et al., 2004; Giménez et al., 2004; Nosarti et al., 2002), sensori-motor cortex (Kesler et al., 2004), basal ganglia (Abernethy et al., 2002; Anderson et al., 2004; Giménez et al., 2004; Kesler et al., 2004; Nosarti et al., 2002), amygdala (Anderson et al., 2004; Giménez et al., 2004; Kesler et al., 2004; Nosarti et al., 2002), hippocampus (Abernethy et al., 2002; Anderson et al., 2004; Curtis et al., 2002; Giménez et al., 2004; Kesler et al., 2004; Nosarti et al., 2002), cerebellum (Abernethy et al., 2004; Curtis et al., 2002; Giménez et al., 2004; Kesler et al., 2004), corpus callosum (Anderson et al., 2004; Cooke & Abernethy, 1999; Curtis et al., 2002; Giménez et al., 2004; Kesler et al., 2004; Nagy et al., 2003), decreased cortical surface area and complexity (Kesler et al., 2004), as well as an increase

in the size of the lateral ventricles in comparison with term control subjects (Anderson et al., 2004; Nagy et al., 2003; Nosarti et al., 2002). A thinner corpus callosum was observed at ages 8 and 15 years in preterm children (Nagy et al., 2003). Ventricular enlargement (Curtis et al., 2002; Kesler et al., 2004; Nosarti et al., 2002) may result from impairment of cerebrospinal fluid (CSF) flow, or absorption or white matter damage (Nosarti et al., 2002).

Hippocampus: Stress in older individuals may result in changes in the growth of the hippocampus, possibly due to the effect of high catecholamine concentrations of brain growth (Abernethy et al., 2002). The hippocampus (and also the basal ganglia according to Abernethy et al. [2004]) is susceptible to damage in preterm/VLBW infants owing to a variety of hypoxic (Abernethy et al., 2004; Isaacs et al., 2000; Perlman, 2001), metabolic (Abernethy et al., 2004; Isaacs et al., 2000; Perlman, 2001), and nutritional insults (Abernethy et al., 2004; Isaacs et al., 2000), infections (Abernethy et al., 2004), hypoglycaemia and hypothyroidism (Abernethy et al., 2004), including medication and/or stress (Perlman, 2001). Giménez et al. (2004) observed significant left hippocampal and bilateral thalamic reductions in children born preterm. Abernethy et al. (2004) did not observe significant smaller hippocampal volumes in children born preterm at age 7.

Other brain areas: According to Perlman (2001) the basal ganglia, more specifically the corpus striatum, play a central role in the feedback loop that modulates cerebral cortical function. The cerebral cortex is the grey matter that covers the surface of the brain, while the striatum refers to a large mass of subcortical grey matter deep in the cerebral cortex (Wickens, 2005). Many of the brain's higher functions, such as perception, cognition, and language, have been attributed to the cerebral cortex (Wickens, 2005). The cerebral cortex appears to be the seat of human intelligence (Berk, 2006). The striatum is involved in many aspects of behaviour, including but not limited to movement, and extending to higher functions such as

thought, language, learning and sequencing or the serial organisation of complex behaviour (Wickens, 2005). Striatal injury produces abnormalities of both motor and cognitive function in sick premature infants (Perlman, 2001). The corpus callosum appears to be the main white matter gateway between the two hemispheres (Rademaker, Lam, van Haastert, Uiterwaal, Lieftink, Groenendaal et al., 2004).

Neurological soft signs: According to Breslau et al. (2000) LBW was associated with a two-fold increased risk of neurological soft signs, which increased the risk of subnormal IQ, learning disorders (especially Reading Disorder), externalising and internalising problems. They also observed a gradient relationship between levels of LBW and soft signs. Males were more likely than females to display soft signs (Breslau et al., 2000). Subnormal IQ and learning disorders however have multiple causes.

2.6.3.3 Prognosis/implications

Kesler et al. (2004) note that the inconsistency regarding birth weight and neurodevelopment across studies may suggest a complex combination of factors contributing to neurodevelopment in preterm children. It is difficult to predict if any abnormal neurological signs remaining after the first year of life will persist (Brandt, Sticker, Höcky & Lentze, 2000). It is dangerous to regard transient neurological anomalies as predictive of future disorders of neuropsychic development. They conclude in their longitudinal study into adulthood that abnormal neurological signs may improve or even disappear. An essential factor is early and high-energy feeding of SGA infants in order to enable catch-up growth of head circumference, thus preventing adverse consequences of malnutrition. All SGA children with complete catch-up growth of head circumference with abnormal neurological signs beyond the first year became normal by the age of 17 (Brandt et al., 2000). Aylward (2002) notes that it is extremely difficult to determine early on whether a child is continuing recovery

or 'catch-up' from the negative effects of extremely low gestational age/birth weight, or whether the problem is the emergence of the true magnitude of a more permanent handicap. This complexity is due to continued cortical development, as well as increased demands for performance in different areas.

Curtis et al. (2002) note inconsistent findings on the association between brain structural abnormalities (detected by MRI) and neurological outcome. Nosarti et al. (2002) postulate that individuals born prematurely continue to show irregularities (increases in size of lateral ventricles and decreases of the white matter) in brain development into adolescence. Deficits in academic areas (Breslau et al., 2001), such as vocabulary, spelling and mathematics, may occur throughout childhood and adolescence. Brandt et al. (2000) also found that 16% of preterm infants labelled as normal at expected date of delivery and not normal later on, had abnormal neurological signs at adult age.

2.6.4 Physiological impairment/medical conditions

Pharmacological treatment often includes antenatal and postnatal steroids and indomethacin (Hack et al., 2000), including dexamethasone (Inder et al., 2003). Corticosteriods are considered when the infant continues to require assisted ventilation with a high oxygen requirement beyond 10 days of age (York & DeVoe, 2002). Vohr et al. (2000) observed that increased neurodevelopmental morbidity was associated with various factors, including steroids for CLD. Marlow (2004) states that the early use of steroids, particularly in long courses, is associated with neurodisability, such as impairment of gyral development (Inder et al., 2003). The exact mechanisms by which postnatal steroids affect neurodevelopment are unclear (Vohr et al., 2000).

CLD is a significant predictor of poor outcomes (Hack et al., 2000; Vohr et al., 2000). Other factors contributing to these poor outcomes include periods of hypoxia, hypotension, as well as the detrimental effects of poor growth and prolonged hospitalisation (Hack et al., 2000). According to Aylward (2002) ELBW infants with lung disease have an increased likelihood of bronchopulmonary dysplasia, which increases the risk of reactive airway disease or asthma. Related restrictions in their ability to engage in the usual childhood activities and slower physical growth would interfere with socio-emotional development and later school development (Aylward, 2002). Mild to moderate cognitive delays have been associated with CLD or high social risk (Piecuch & Leonard, 1997).

Birth weight is associated with insulin-like growth factors (Richards et al., 2001). Three key risk factors for LBW, namely poor nutrition, smoking and alcohol misuse, influence brain glucose concentrations or the function of insulin-like growth factors. ELBW and VLBW children were reported to have a higher prevalence of poor physical growth, ill health and re-hospitalisations during mid-childhood compared with their peers (Saigal et al., 2001), including lower attainment of growth parameters of weight and height (Saigal et al., 2001; York & DeVoe, 2002).

Saigal et al. (2001) postulate that the majority of limitations (e.g. developmental delay, clumsiness, learning difficulties, emotional and visual problems) were attributable to chronic conditions, mainly neurosensory impairments.

There is a high risk of cerebral palsy (Hack et al., 2000; Marlow, 2004; Vohr et al., 2000; York & DeVoe, 2002) with an increasing degree of birth weight deficit (Goyen et al., 2003). Approximately 10% of preterm survivors show signs of cerebral palsy (Sola et al., 2005). Hypoxic-ischaemic brain events and haemorrhages in the perinatal period seem to be the most

significant aetiological factors in cerebral palsy in prematurely born children (Valkama et al., 2000). According to Abernethy et al. (2003) the major disability rates in children born preterm are caused mostly by cerebral palsy and hearing and visual disabilities. The frequency of cerebral palsy, seizure disorders and other neurological problems increases, especially in the case of VLBW or ELBW (Bhutta et al., 2002; Bukatko & Daehler, 2001; Stathis et al., 1999). Neonatal white matter damage may be associated with cerebral palsy (Nadeau et al., 2001).

A consistent link between LBW (or rather complex factors associated with LBW) and heart disease, stroke and diabetes was observed in middle adulthood (Berk, 2006). The increased cardiovascular and diabetes risks were attributed to early physiological adaptation, particularly of the hypothalamic-pituitary-adrenal (HPA) axis, to intra-uterine nutritional deficiencies (Patton, Coffey, Carlin, Olsson & Morley, 2004). Some hypothesise that a poorly nourished foetus diverts large amounts of blood to the brain, causing organs in the abdomen, such as the liver and kidney (involved in controlling cholesterol and blood pressure), to be undersized (Berk, 2006). This results in heightened future risk of heart disease and stroke. Diabetes may be related to inadequate prenatal nutrition that may permanently impair functioning of the pancreas, causing glucose intolerance to rise as the person ages. Others postulate that the malfunctioning placentas of some expectant mothers permit high levels of stress hormones to reach the foetus. These hormones retard foetal growth, increase foetal blood pressure and promote hyperglycaemia (excess blood sugar), predisposing the developing individual to later disease. Prenatally growth-stunted babies often gain excessive weight in childhood, once they have access to plentiful food. The excess weight usually persists, increasing the risk of diabetes in midlife (Berk, 2006).

2.7 Gender differences

Preterm males appear to experience increased neurodevelopmental-cognitive deficits compared with preterm females (Aylward, 2002; Reiss et al., 2004). Males have more behavioural problems and higher rates of disability, such as a two-fold increase in IQ < 85 and use of special education/remedial assistance (Aylward, 2002). Boys are more likely to have problems with reading, language (spelling and writing) and mathematics (Aylward, 2002; Papageorgiou & Bardin, 1999), including speech difficulties (Papageorgiou & Bardin, 1999).

Female children are also superior in areas of speech, language and personal skills (Hindmarsh, O'Callaghan, Mohay & Rogers, 2000; Papageorgiou & Bardin, 1999). Girls may be protected by hormones or more X-chromosomes against the consequences of premature birth (Papageorgiou & Bardin, 1999). Although VLBW girls did not differ significantly from full-term-birth-weight girls, suggestive trends in the same direction as the boys may indicate that there is an increased risk of behavioural problems in both genders but that these sequelae become evident at an earlier age in boys than in girls (Papageorgiou & Bardin, 1999).

Boys are more vulnerable to the effects of pre- and perinatal insult, including the effects of LBW, which may relate to slower brain maturation in males (Martel, Lucia, Nigg & Breslau, 2007). Male ELBW and premature infants are at greater risk of perinatal brain injury and later neurological and cognitive impairment and learning difficulties. The neurological development of preterm boys aged 2 to 4 is more vulnerable than that of preterm girls, which places them at multi-causal risk of later cognitive disabilities if their behavioural development also contributes to their suboptimal cognitive development (Sajaniemi et al., 2001). Sauver, Katusic, Barbaresi, Colligan and Jacobsen (2001) mention that elevated foetal testosterone levels are responsible for the increased number of school problems observed in boys in the general population. Reuters (2004) reports in *Beeld*, a local newspaper, that premature boys tend to have a smaller

brain than premature girls, owing to reduced white and grey matter, especially in the areas controlling reading, language, emotion and behaviour. Male gender has been found to be a predictor of disability in infants below 28 weeks' gestation (Vohr et al., 2000). Hack et al. (2000) postulate that the effect of gender is partly associated with the greater severity of illness in male infants.

Boys are more likely than girls to have any disruptive disorder, ADHD, ODD, Obsessive-Compulsive Disorder and Nocturnal Enuresis (Whitaker et al., 1997). Mental retardation, ADHD, learning disabilities and autism were significantly more prevalent among VLBW boys (Reiss et al., 2004). Simonoff, Picles, Meyer, Silberg, Maes, Loeber et al. (1997) found that among twins the rate of any emotional disorder increases significantly with age and is higher in girls. The rate of any behavioural disorder also increased with age, but is significantly higher in boys (Simonoff et al., 1997).

2.8 Environment

The post discharge environment can reduce or compensate for neonatal risk in LBW children. Social and environmental factors (such as poverty/income, parental race, education and marital status) have an impact on outcome (Breslau et al., 2001; Greenbaum & Auerbach, 1992; Gross et al., 2001; Jobe, 2001; Vohr et al., 2000). Maternal education (Aylward, 2002; Kesler et al., 2004; Vohr et al., 2000) and white race (Vohr et al., 2000) are considered protecting factors against disability, particularly cognitive functioning. Low SES at birth has been associated with a significant increase in school failure and need for special education at 9 years of age (Gross et al., 2001), including behaviour problems (Chapieski & Evankovich, 1997). Environmental risk factors such as poverty and parental expectation appear to have a negative impact on term and preterm children's cognitive, social and language outcome

(Dieterich et al., 2004). Language appears to be particularly susceptible to negative environmental influences (Aylward, 2002).

High levels of maternal warmth protected LBW children from poor behavioural outcomes, but not from lower IQ scores. Cerebral damage during the neonatal period sometimes results in cognitive difficulties that are neither exacerbated nor reduced by maternal attitudes or emotions (Tully et al., 2004).

Kilbride et al. (2004) and Tully et al. (2004) note that it is important to assess whether any environmental factors (e.g. family risk and protective factors) exacerbate or reduce the effect of biological risk status in LBW children on development. Environmental factors appear to be responsible for more variation in cognitive development than biological factors, especially in the absence of major neurological impairments and with increasing age. Individuals react differently to similar environmental influences. The impact of the environment is mediated by behavioural differences (Sajaniemi et al., 2001). According to Marlow (2004) social factors and the quality of the home environment can compensate for perinatal and neonatal disadvantage and predict catch-up in cognitive and behavioural development in larger LBW and preterm infants. Biological factors however remain the best predictors of cognitive and behavioural outcome into school age (Marlow, 2004). According to Aylward (2002) biological influences will determine whether or not a deficit will occur, but the environment will influence the magnitude of the deficit, unless the biological insult is extreme. Various degrees of CNS insults reduce the ability to take advantage of environmental offers.

2.9 Conclusion

The increasing numbers of LBW/premature children are at higher risk of deficits in virtually all domains owing to increased risk of more pre-, peri- and postnatal complications, medical conditions, brain injury with subsequent stressful medical procedures and the hospital environment. These risk factors enhance impaired neurological, physiological, cognitive, behavioural, psychiatric, emotional and social development with implications for gender and age. The post-discharge environment can reduce or compensate for the sequelae of LBW.

Chapter 3

INTERNALISING PSYCHOLOGICAL DISORDERS

3.1 Introduction

A relationship between LBW and internalising psychological problems has been indicated in previous studies (Chapieski & Evankovich, 1997; Hack, Youngstrom, Cartar, Schluchter, Taylor, Flannery et al., 2005; Nadeau et al., 2001). Others however observed no differences in ratings of internalising symptoms (Breslau & Chilcoat, 2000; Hille et al., 2001; Rickards et al., 2001; Saigal et al., 2003b) or reported inconsistent findings (Aylward, 2002).

Approximately 25% to 30% of preterm children are affected by psychiatric disorders at adolescence (Perlman, 2001). According to Indredavik et al. (2004) psychiatric problems affected the overall functioning of both VLBW and SGA adolescents, even though widespread emotional or behavioural symptoms did not always reach the diagnostic level of a psychiatric disorder.

Premature delivery is associated with various challenges. Many clinical factors (e.g. CLD, nutritional deficiencies), as well as stressful environmental conditions in hospital, multiple medication and infant-provider interaction, may act in combination to make an impact on the developing brain (Perlman, 2001). Neurodevelopmental delays tend to increase the risk of internalising symptoms (Breslau et al., 2000; Lui et al., 2001). Other associated impairments, such as cognitive problems (see Section 2.6.2), may also enhance internalising symptoms. These short-term and long-term consequences of LBW may also influence the parent-child relationship, enhancing emotional problems during childhood. A high prevalence of externalising disorders and neuropsychological impairments is reflected in Chapters 4 and 5

respectively. Internalising disorders often occur comorbidly with externalising disorders and neuropsychological deficiencies. Therefore, a higher incidence of internalising (SAD, OAD and MDD) psychological disorders in children born with LBW than in children with NBW was hypothesised in this study.

A discussion of the internalising psychological disorders, particularly anxiety (SAD and OAD) and MDD, will be the focus of this chapter. Relevant aspects of OAD, SAD and MDD will be briefly explored, namely the symptoms, prevalence, comorbidity, age of onset, gender differences and aetiological factors. The neurobiological structures involved in anxiety and depression in LBW children will be addressed.

Limited information is available on the relationship between psychiatric disorders (pertaining to SAD, OAD and MDD) and LBW. Researchers reported inconsistent findings in children, irrespective of birth weight. Available findings on children born with LBW and those from the general population will be reflected. Findings regarding anxiety from the general population that are generalised to LBW children raise the opportunity for further investigation.

3.2 Internalising psychological disorders

It can be concluded from literature that the term internalising psychological disorders refers to psychological symptoms that are projected inwards. These symptoms seem to be less visible in nature (for example a knot in the stomach) and therefore often go unnoticed and untreated. Internalising psychological disorders refers to emotional disorders, specifically anxiety and mood disorders (Mash & Wolfe, 2002).

Cultural variation should be considered in the expression and evaluation of internalising disorders. In some cultures anxiety is expressed predominantly through somatic symptoms

and in others through cognitive symptoms (American Psychiatric Association, 2000). Hack et al. (2005) found that black participants tended to inhibit emotions. Social context and social cognition play a role in how emotions are expressed. Cultural influences are an important aspect that should be considered in the interpretation of results, since a multicultural sample from 10 language groups was selected for this study.

The anxiety and depression scales of the "Terry" picture questionnaire were used to establish the symptoms of anxiety (SAD and OAD) and depression (see Appendix M).

3.3 Anxiety

According to Barlow and Durand (2002) anxiety refers to a mood-state characterised by marked negative affect, bodily symptoms of tension and apprehension about the future. The types of anxiety disorders experienced during childhood are similar to those of adulthood, namely SAD, Generalised Anxiety Disorder (GAD), Specific Phobia, Social Phobia, Obsessive-Compulsive Disorder, Panic Disorder, Panic Disorder with Agoraphobia, Posttraumatic Stress Disorder and Acute Stress Disorder (Mash & Wolfe, 2002). SAD and OAD (GAD) among LBW children will be the focus of this study.

Indredavik et al. (2004) found the prevalence of anxiety disorders to be 8% to 10% in LBW and VLBW 6-to-12-year-old children. LBW and consequent generally delayed developmental milestones were significantly associated with increased risk of behavioural and emotional problems such as somatic complaints, anxiety and social problems (Lui et al., 2001). Other studies also confirmed increased anxiety in VLBW children at 12 years of age (Hoff et al., 2004). Children in general who experienced sleeping difficulties had significantly increased odds of anxiety or depression based on mothers' reports, but not teachers' reports. Sleeping difficulties however were not associated with LBW children (Johnson, Chilcoat & Breslau,

2000). Some research studies did not find an association between LBW and childhood anxiety disorders (Breslau et al., 1996a; Klebanov & Brooks-Gunn, 1994).

The above-mentioned findings indicate a developmental tendency of increased anxiety symptoms in older children. Age differences in the expression of specific childhood fears and anxiety symptoms should therefore be considered (Weems & Costa, 2005). Specific symptom predominance in a sample from the general population was as follows: separation anxiety appeared to be predominant in children aged 6 to 9 years, death and danger fears in children aged 10 to 13 years, and social anxiety symptoms as well as failure and criticism fears in youths aged 14 to 17 years. Only modest evidence reflected symptoms of generalised anxiety as a dominant expression of anxiety in children aged 10 to 13 years (Weems & Costa, 2005).

Anxiety disorders seem to have an earlier age of onset than major depression. Temperamental factors may play a relatively greater role in early onset anxiety than the environment (Levitan, Rector, Sheldon & Goering 2003).

Anxiety and depression tend to develop in late childhood and early adolescence (Johnson et al., 2000; Mash & Wolfe, 2002), because older children have more time to develop problems (Hirshfeld-Becker, Biederman, Faraone, Robin, Friedman, Rosenthal et al., 2004). Other studies indicate that early problem behaviour has been linked clearly to later psychopathology (Weiss & St. Jonn Seed, 2002).

SAD developmentally precedes OAD. Symptoms of separation anxiety seem to decrease with school grade level (Weems & Costa, 2005). OAD seems to increase with age (Simonoff et al., 1997).

3.3.1 Separation Anxiety Disorder

Few studies have been conducted on the relationship between LBW and SAD. Available findings, together with relevant literature from the general population, will be reflected.

SAD can be defined as excessive and developmentally inappropriate anxiety about separation from home or from those to whom a person is attached (American Psychiatric Association, 2000; Sadock & Sadock, 2003).

3.3.1.1 Symptoms

Three or more of the following symptoms must last for at least 4 weeks, beginning before 18 years of age, and must cause significant distress or impairment in important areas of life (American Psychiatric Association, 2000; Sadock & Sadock, 2003):

- Recurrent excessive distress when separation from home or major attachment figures occurs or is anticipated
- Persistent and excessive worry about losing important attachment figures, or about possible harm befalling them
- Persistent and excessive worry that an untoward event will lead to separation from an important attachment figure (for example, getting lost)
- Persistent reluctance or refusal to go to school or elsewhere because of fear of separation
- Persistent and excessive fearfulness or reluctance to be alone or without important attachment figures at home or without significant adults in another setting
- Persistent reluctance or refusal to go to sleep without being near an important attachment figure or to sleep away from home
- Repeated nightmares involving the theme of separation

- Repeated complaints of physical symptoms (such as headaches, stomach aches, nausea or vomiting) when separation from important attachment figures occurs or is anticipated.

SAD and depression in children overlap, and some professionals view SAD as a feature of a depressive disorder (Sadock & Sadock, 2003).

3.3.1.2 Prevalence

The prevalence of certain SAD symptoms varies as a function of age. For example, worry that something would happen to their loved ones was the prominent symptom among the youngest children. Excessive distress upon being separated was significant in the middle age groups and physical complaints on school days were characteristic of separation anxiety in adolescents (Barlow & Durand, 2002).

SAD appears to be the most common anxiety disorder of childhood, occurring in about 10% of children (Mash & Wolfe, 2002). The prevalence rate in children and adolescents was 2% to 5.4% for SAD (Toren, Sadeh, Wolmer, Eldar, Koren, Weizman et al., 2000). SAD appears to decrease in prevalence from childhood through adolescence (American Psychiatric Association, 2000; Simonoff et al., 1997). Prevalence rates for SAD among LBW children were not indicated in the literature listed.

3.3.1.3 Comorbidity

Most children with SAD appear to have another anxiety disorder, most commonly GAD (Last, Strauss & Francis, 1987b; Mash & Wolfe, 2002). Specific phobia was also found to coexist with SAD, which occurs in about one third of all referred cases of SAD (Sadock & Sadock, 2003). According to Mash and Wolfe (2002) about one third of children with SAD may over time become increasingly withdrawn, apathetic and depressed. Comorbidity tendencies for SAD in the LBW group were not identified in this literature survey.

3.3.1.4 Gender differences

Symptoms of SAD have been reported to occur equally in boys and girls (American Psychiatric Association, 2000; Mash & Wolfe, 2002; Sadock & Sadock, 2003). Research found that more children with SAD were female, prepubertal and from lower socio-economic backgrounds (Last, Francis, Hersen, Kazdin & Strauss, 1987a). Mash and Wolfe (2002) note that when gender differences are found in the general population, they tend to favour girls. The rates of SAD are higher in females with the ADHD inattentive subtype (Levy, Hay, Bennett & McStephen, 2005). The consulted literature did not refer to gender findings regarding SAD in LBW children.

3.3.1.5 Aetiology

Neurobiological structures, parental psychiatric illness and pregnancy complications are some of the aetiological factors in SAD.

3.3.1.5.1 Neurobiological structures

PL/VE, in LBW children of normal intelligence, independently increased the risk of separation anxiety (Whitaker et al., 1997). The effects of PL/VE on separation anxiety at age 6 years may suggest an effect of perinatal ischaemic injury on brain maturational events that occur at this age, in particular maturation of the striatum (caudate and putamen) of the basal ganglia. Maturation of the striatum, which supposedly plays an important role in the improvement of behavioural inhibition that normally occurs in middle childhood, appears to be deficient in anxiety disorders. It is possible that PL/VE increases the risk of disorders during puberty (characterised by cortical maturation and synaptic pruning) that typically have a later onset and in which abnormalities of cortical-basal ganglionic circuits have been implicated (Whitaker et al., 1997). The basal ganglia and other significant areas in the brain are vulnerable to brain injury, stressful environmental factors during hospitalisation and medical conditions

associated with premature birth/LBW (see Section 2.6.3) (Perlman, 2001). Thus, PL/VE appears to be a significant risk factor in the development of OAD and SAD, probably independently of LBW.

3.3.1.5.2 Parental psychiatric illness

Genetic factors partially explain the aetiology of SAD. Biological children of adults with anxiety disorders are prone to suffer from SAD in childhood. Parents diagnosed with Panic Disorder with Agoraphobia appear to have an increased risk of having a child with SAD (Sadock & Sadock, 2003). Both parental panic disorders and major depression, individually or comorbidly, were associated with increased risk of SAD and multiple (two or more) anxiety disorders in children (Biederman, Faraone, Hirshfeld-Becker, Friedman, Robin & Rosenbaum, 2001). Other studies confirm that SAD is more common in first-degree biological relatives than in the general population and is more frequent in children of mothers with Panic Disorder (American Psychiatric Association, 2000). A history of parental mental illness, together with elevated levels of anxiety in parents due to their infant's medical condition, may contribute to increased anxiety in their child (Chapieski & Evankovich, 1997). "Anxiety-enhancing" parenting appears to contribute to this co-occurrence of parental and child anxiety, in addition to a genetic predisposition (Bögels & Siqueland, 2006; Hack et al., 2005). Thus, a biological vulnerability to anxiety disorders is attributed to neurological insults associated with preterm birth, as well as a genetic predisposition to parents' mental illness.

3.3.1.5.3 Pregnancy complications

Childhood anxiety disorders associated most often with pregnancy complications were SAD and agoraphobia, disorders assumed to be associated with parental overprotection (Hirshfeld-Becker et al., 2004).

Research in the general population indicates that SAD tends to occur after a child has experienced major stress (Mash & Wolfe, 2002). As previously stated, brain injuries (see Section 2.6.3) and pregnancy complications may have an adverse impact on neurodevelopmental processes of the foetus (as indicated in Section 3.3.1.5.5), which contribute to a biological predisposition to psychiatric disorders. These complications may also result in increased maternal anxiety levels, with consequent neurophysiological effects on the developing foetus. Overanxiousness may also be a psychological consequence of parental insecurity and anxiety in raising a preterm child (Hoff et al., 2004).

3.3.2 Overanxious Disorder

Before the publication of the DSM-IV (Diagnostic and Statistical Manual, fourth edition), OAD was the appropriate diagnosis in the case of children displaying excessive worry (American Psychiatric Association, 2000). This diagnosis was changed to GAD, because of concerns that criteria for OAD were vague and non-specific, as well as symptoms that overlapped with those of other disorders (Wiener & Dulcan, 2004). Regarding GAD, only one of the six symptomatic (somatic) criteria is required, in addition to excessive worries. The criteria for childhood OAD and GAD are apparently similar, though findings supporting the generalisations from OAD to juvenile GAD are inconsistent (Foley, Rutter, Angold, Pickles, Maes, Silberg et al., 2005).

An overlap between the criteria for GAD and depression may lead to worry and nervous tension being mistaken for sadness or irritability (Foley et al., 2005). GAD is often over-diagnosed in children, because the worry that is better explained by another anxiety disorder is mistaken for GAD (American Psychiatric Association, 2000).

3.3.2.1 Symptoms

The diagnostic criteria for OAD (Foley et al., 2005) require at least four of the following symptoms:

- Excessive or unrealistic worry about future events
- Excessive or unrealistic concern about the appropriateness of past behaviour
- Excessive or unrealistic concern about competence in one or more areas, for example sport, academic, social
- Somatic complaints, such as headaches or stomach aches, for which no physical basis can be determined
- Marked self-consciousness
- Excessive need for reassurance about a variety of concerns
- Marked feelings of tension or inability to relax.

The diagnostic criteria for GAD (American Psychiatric Association, 2000) include excessive anxiety and worry about a number of events or activities that a person finds difficult to control. The anxiety and worry are associated with three or more of the following six symptoms (with at least some symptoms present more often than not for the past 6 months and only one item being required in children):

- Restlessness or feeling keyed up or on edge
- Being easily fatigued
- Difficulty concentrating or mind going blank
- Irritability
- Muscle tension
- Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep).

GAD in children and adolescents is also often characterised by anxiety and worries involving issues such as punctuality or catastrophic events (e.g. earthquakes or nuclear wars). Children with the disorder tend to be overly conforming, perfectionist and unsure of themselves and to seek approval and require excessive reassurance about their performance and their other worries (American Psychiatric Association, 2000).

3.3.2.2 Prevalence

Anxiety disorders constitute one of the most prevalent mental health problems in children from all birth weight levels (Mifsud & Rapee, 2005). GAD (Mash & Wolfe, 2002) and OAD (Toren et al., 2000) were evident in 3% to 6% of children from the general population. Overanxiousness was observed in 4% of adolescents included in an epidemiological survey among general practitioners (Mathet, Martin-Guehl, Maurice-Tison & Bouvard, 2003). Eight percent of VLBW children compared to 1% of peers (Botting et al., 1997) were diagnosed with GAD. Group status (particularly ELBW) was a significant predictor of OAD (Saigal et al., 2003b). No evidence could be found in existing literature on the prevalence of OAD, in particular for LBW children.

3.3.2.3 Comorbidity

Mash and Wolfe (2002) note that children with GAD present with a high rate of other anxiety disorders and depression. Children and adolescents diagnosed with GAD with comorbid depression had significantly more anxiety symptoms than patients without depression. Those with comorbid depression experienced more severe functional impairment (Masi, Favilla, Mucci & Millepiedi, 2000).

Children with anxiety continue to be at increased risk of substance abuse and CD (but not other disorders), as well as increased use of long-term psychiatric and medical services

(Weissman, Wolk, Wickramaratne, Goldstein, Adams, Greenwald et al., 1999). Co-occuring SAD and ADHD are most frequently observed in younger children (Mash & Wolfe, 2002). The rate of GAD is higher for females with the ADHD combined subtype (Levy et al., 2005).

High levels of anxiety in children were reported to be associated with significantly more task-inhibiting thoughts, negative evaluations and difficulties in shifting attention from internal to external stimuli. Furthermore, anxiety disorders in children and adolescents may be associated with lowered linguistic abilities, attention, cognitive flexibility and short-term memory or working memory, such as vocabulary, reading comprehension, mathematics and problem-solving (Toren et al., 2000). Another study however found that children with social phobia or GAD did not differ from normal controls regarding attentional performance or memory functions (Günther, Holtkamp, Jolles, Herpertz-Dahlmann & Konrad, 2004).

Oosterlaan (1996) found no support for the notion that anxiety disorders were associated with enhanced levels of motor inhibition or inhibitory processes underlying motor inhibition in the normal population, due to a hypothetically overactive behavioural inhibition system (BIS). However, a strong tendency to response inhibition was found to predict later anxiety disorders (Oosterlaan, 1996).

Comorbid conditions in LBW children with anxiety disorders/symptoms were not indicated in the literature consulted.

3.3.2.4 Gender differences

The disorder appears to be equally common in boys and girls of the general population, with perhaps a slightly higher prevalence in older adolescent females (Mash & Wolfe, 2002). Generalised anxiety was found to be more common in girls (7%) than in boys (2%) of the VLBW group (Botting et al., 1997; Simonoff et al., 1997). Female adolescents who

experienced poverty in the first five years of life had increased symptoms of anxiety, according to maternal reports (Mifsud & Rapee, 2005). Levy et al. (2005) found that internalising disorders are more common in females, particularly SAD.

3.3.2.5 Aetiology

The aetiology of OAD can be viewed from a multi-dimensional approach. Existing research on the aetiology of OAD in LBW children however seems to be insufficient and needs further investigation.

3.3.2.5.1 Neurobiological structures

OAD was more prevalent in the LBW cohort with PL/VE compared with the group with no abnormalities (Whitaker et al., 1997). A number of pregnancy complications were found to be associated with OAD in the child (Hirshfeld-Becker et al., 2004). As previously stated under Section 2.6.3, brain injuries and pregnancy complications may have an adverse impact on neurodevelopmental processes of the foetus, which contribute to a biological predisposition to psychiatric disorders. These complications may also result in increased maternal anxiety levels, with consequent neurophysiological effects on the developing foetus. Overanxiousness may also be a psychological consequence of parental insecurity and anxiety in raising a preterm child (Hoff et al., 2004).

Although no convincing data prove that benzodiazepine receptors are abnormal in patients with GAD, some adult studies have focused on the occipital lobe, which has the highest concentrations of benzodiazepine receptors in the brain. The basal ganglia, limbic system and frontal cortex have been hypothesised to be involved in GAD in adults. An abnormal serotonergic, norepinephrine, glutamate and cholecystokinin system was also suggested (Sadock & Sadock, 2003). This finding needs further investigation in LBW children,

since various brain areas (Section 2.6.3 refers) appear to be vulnerable to neurological insults and subsequent increased risk of psychiatric problems.

Neurological soft signs, as reflected in Section 2.6.3, were associated with an excess of internalising problems in both LBW and NBW children (Breslau et al., 2000). Soft signs at age 7 predicted anxiety-withdrawal symptoms at age 17. There seems to be a connection with disorders involving the basal ganglia, i.e. mood and anxiety disorders. A relationship was also determined between parenchymal lesion or ventricular enlargement in the neonatal period and anxiety disorders at age 6. The possibility of an effect of perinatal ischaemic injury on brain maturation is suggested, particularly in the striatum of the basal ganglia (Breslau et al., 2000). Except for the association between periventricular leukomalacia and anxiety at age 6 years, specific neonatal risk factors have not been found to be predictive of anxiety, depression or overall internalising symptoms in VLBW children (Hack et al., 2005). The basal ganglia is one of the multiple brain areas in LBW infants vulnerable to injury, as indicated in Section 2.6.3 (Abernethy et al., 2002; Anderson et al., 2004).

During pregnancy the placenta seems to be a source of a regulatory factor, corticotropin-releasing hormone (CRH) that can interact with both the maternal and foetal pituitary-adrenal axes to initiate a number of endocrine events that determine the timing of delivery (Hobel, Dunkel-Schetter, Roesch, Castro & Arora, 1999). Maternal stress is associated with elevated maternal levels of CRH and activation of the placental-adrenal axis before preterm delivery. Those who had preterm delivery had significantly higher plasma CRH levels than their control subjects at all three gestational ages (18 to 20 weeks, 28 to 30 weeks and 35 to 36 weeks), especially during the second trimester. Changes in CRH between 18 to 20 weeks' gestation and 28 to 30 weeks' gestation are associated with maternal age and stress level at 18 to 20 weeks' gestation. This association between placental CRH level and the foetal pituitary-adrenal

axis could be an attempt by the maternal-foetal-placental unit to bring about early foetal maturation to increase the chances of survival in case the foetus is delivered early. Thus, maternal stress is associated with increased maternal levels of CRH and activation of the placental-adrenal axis before preterm delivery (Hobel et al., 1999), which consequently have an impact on the developing foetus.

Several possibilities exist to explain how pregnancy complications mediate anxiety in children (Hirshfeld-Becker et al., 2004). Biological mechanisms might include the effect of hypoxia or of stress hormones on the development of the foetal brain. Maternal anxiety during pregnancy is associated with a restriction of blood flow to the foetus or a change in foetal blood distribution. High levels of stress may result in increased plasma norepinephrine. Animal studies have indicated that infusion of norepinephrine can decrease uterine blood flow and reduce oxygen to the foetus, as can induced stress. In humans catecholamines may also be released as a result of maternal anxiety, which may cause uterine vasoconstriction. Maternal infection and high blood pressure may result in foetal anoxia, which may affect brain development and consequent increasing vulnerability to psychiatric disorders (Hirshfeld-Becker et al., 2004). Stress hormones cross the placenta and may affect the foetus directly. Repeated elevations in glucocorticoids can influence the stress circuitry in the developing infant's brain. Stress may lead to changes such as a reduction in cortisol receptors, increased and prolonged HPA axis and catecholamine responses to stress, reduction in sustained attention and increased fearful behaviour. In addition, environmental stressors together with a genetic predisposition to be prone to anxiety, may increase the likelihood of an anxiety disorder developing (Hirshfeld-Becker et al., 2004). Other researchers are of the opinion that the relationship between brain dysfunction and manifest anxiety in childhood may be non-specific (Toren et al., 2000).

3.3.2.5.2 Parental mental illness

Women with a history of psychiatric illness, substance use or both diagnoses were at significantly higher risk of delivering VLBW, LBW and preterm infants even when adjusted for the effects of known socio-demographic and medical risk factors (Kelly, Russo, Holt, Danielsen, Zatzick, Walker et al., 2002). According to this finding a large number of LBW children seem to be genetically predisposed to psychiatric illness.

Recent findings confirmed that parental Panic Disorder selectively increased the risk of anxiety disorders in their children (Biederman, Petty, Faraone, Hirshfeld-Becker, Henin, Pollack et al., 2005). Moreover, an overlap of up to 80% between parental and child anxiety disorders has been identified (Bögels & Siqueland, 2006). Elevated levels of anxiety in parents due to their infant's medical condition may contribute to increased anxiety in their child (Chapieski & Evankovich, 1997). "Anxiety-enhancing" parenting appears to contribute to this co-occurrence of parental and child anxiety, in addition to a genetic predisposition (Bögels & Siqueland, 2006; Hack et al., 2005).

Hack et al. (2005) note a genetic vulnerability and/or reporting bias with projection of anxious thoughts onto their children. A maternal history of any psychiatric disorder has been associated with apparent over-reporting of psychiatric and behavioural problems in their children (Johnson et al., 2000).

3.3.2.5.3 Parenting style

An overprotective parenting style was not found to be more common in parents of preterm children than in parents of children born at term (Hoff et al., 2004). Another study however postulates that overprotective parental behaviour might develop and lead to differences in parental perception of the child's behaviour and consequent inadequate socio-

emotional behavioural adjustment in the child (Hille et al., 2001). Overprotective and critical parenting can result from parental anxiety disorder or be caused by children's anxiety disorder or by both child and parental anxiety (Bögels & Siqueland, 2006).

Limited or negative interaction between LBW infants and caretakers during hospitalisation, as indicated in Section 2.6.3, may disrupt the bonding process between parents and infants (Perlman, 2001). Emotional and behavioural problems may be a psychological consequence of parental insecurity and anxiety in raising a preterm child (Hoff et al., 2004).

3.3.2.5.4 Family environment

Research suggests that internalising problems of withdrawal, depression and anxiety strongly correlates with adverse family environment variables, such as insecure attachment and economic disadvantage (Weiss & St. Jonn Seed, 2002). Poverty increases the incidence of behavioural and emotional disorders (Chapieski & Evankovich, 1997), such as anxiety and depression (Weiss & St. Jonn Seed, 2002). Social disadvantage in general contributes to an increased risk of child psychopathology (Breslau et al., 1996a). Dieterich et al. (2004) and Stoelhorst et al. (2003) mention that children born preterm are at increased risk of developmental delays because they are more likely to be born into poverty or low SES. Indredavik et al. (2004) however found an association between VLBW and psychiatric problems that could not be explained by SES or parents' mental health.

The family environment is more influential in LBW children's risk of developing emotional or behavioural problems than either initial medical complications or their emerging cognitive and social competence at age 1. Accumulating research indicates that prenatal risk factors are not as critical as environmental influences in predicting behavioural and emotional outcomes (Weiss & St. Jonn Seed, 2002). The families of origin of children with anxiety

disorders were found to be less sociable, more enmeshed, more disengaged and more conflictual and to experience more marital discord (Bögels & Siqueland, 2006). See Section 2.7 for a detailed discussion of environmental influences.

3.3.2.5.5 Pregnancy complications

The number of pregnancy complications predicted various childhood anxiety disorders independently of parental diagnosis (Hirshfeld-Becker et al., 2004). Pregnancy complications included heavy bleeding requiring bed-rest, hypertension or excessive fluid retention, illness requiring medical attention and serious family problems. Childhood anxiety disorders were not associated with maternal smoking during pregnancy or complications at the time of birth. These results were most consistent when parents had Panic Disorder, with or without MDD. These results suggest that pregnancy factors may partially mediate associations between parental Panic Disorder and childhood anxiety (Hirshfeld-Becker et al., 2004). Pregnancy complications may have an adverse impact on the neurodevelopmental processes of the foetus (as indicated in Section 2.6.3), which contributes to a biological predisposition to psychiatric disorders. These complications may also result in increased maternal anxiety levels, with consequent neurophysiological effects on the developing foetus and long-term implications for the parent-child relationship.

3.3.2.5.6 Other aetiological factors

Individuals with GAD tend to pay selective attention to negative details in the environment, by distortions in information processing and by an overly negative view of the person's own ability to cope (Sadock & Sadock, 2003). Increased risk of cognitive, social, behavioural and emotional problems, as well as lower self-esteem (see Section 2.6), may contribute to more anxiety symptoms. It is highly possible that other sequelae of VLBW, such as motor deficits, lower IQ scores, educational impairments, shorter stature and poorer social

skills, may enhance anxiety. However, this possible relationship between affective disorders, IQ and motor skills at age 12 was not confirmed (Botting et al., 1997).

3.4 Depression

The essential feature of MDD is a period of depressed or irritable mood and/or loss of interest or pleasure in nearly all activities (American Psychiatric Association, 2000). MDD, Dysthymic Disorder and Bipolar Disorder (emerging during adolescence) are the main types of mood disorders (Barlow & Durand, 2002; Mash & Wolfe, 2002). MDD will be the focus of this study.

3.4.1 Major Depressive Disorder in children

Mood disorders are apparently similar in children and in adults (Barlow & Durand, 2002). The DSM-IV-TR (Diagnostic and Statistical Manual, fourth edition, text revision) therefore does not refer to "childhood" mood disorders, unlike anxiety disorders. According to Mash and Wolfe (2002) there are some differences between children and adults in the expression of depressive symptoms. Depressed appearance, separation anxiety, phobias, somatic complaints and behavioural problems seem to occur more frequently in younger than older individuals.

3.4.1.1 Symptoms

The DSM-IV-TR defines MDD as the presence of five or more (American Psychiatric Association, 2000) of the following symptoms that have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either depressed mood or loss of interest or pleasure:

- Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). In children and adolescents, it can be irritable mood.
- Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
- Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. In children, failure to make expected weight gains must be considered.
- Insomnia or hypersomnia nearly every day
- Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
- Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
- Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

Hopelessness/helplessness, lack of energy/tiredness, hypersomnia, weight loss, suicidality, substance abuse, as well as less comorbid SAD and ADHD are more characteristic of depressed adolescents compared with children (Yorbik, Birmaher, Axelson, Williamson & Ryan, 2004).

The expression of depressive symptoms however changes with age. Children younger than 3 years of age might manifest depression by their facial expression, as well as by their

eating, sleeping and play behaviour, which is quite different from that of children between the ages of 9 and 12. Children obviously gradually exhibit an adult presentation of MDD with increasing age (Barlow & Durand, 2002).

Clinicians should be aware of the following symptoms in order to diagnose depression during childhood: failure to make expected weight gains, daily insomnia or hypersomnia, psychomotor agitation or retardation, daily fatigue or loss of energy, feelings of worthlessness or inappropriate guilt, diminished ability to think or concentrate and recurrent thoughts of death. Adults seem to have more problems with sleep and appetite than do depressed children and adolescents (Sadock & Sadock, 2003).

3.4.1.2 Prevalence

ELBW adolescents presented with significantly higher scores on the depression subscale when compared with their NBW cohort, based on parental reports (Saigal et al., 2003b). Another study also found a substantially higher rate of depressive disorder among premature and LBW adolescents. Even after adjustment for potential confounders such as parental education, parental separation, maternal age at birth, maternal smoking in pregnancy, serious illness in the first year of life and parental depressive disorder, the odds for depressive disorder were elevated more than 11-fold in adolescents born prematurely or with LBW (Patton et al., 2004). Group status (particularly ELBW) was a significant predictor for depression (Saigal et al., 2003a). A tendency towards increased depressive symptoms in VLBW children at 12 years of age was also reported, though differences in meeting the full diagnostic criteria for a major depressive episode was not significant (Botting et al., 1997). Shyness and withdrawn behaviour were significant in LBW children (Aylward, 2002). Indredavik et al. (2004) did not find an increased prevalence of depression among 10-to-14-year-old VLBW adolescents.

Dysthymic Disorder appears to be more common than MDD among school-age children, which carries a high likelihood that MDD will develop at some point after one year of Dystymic Disorder. Dysthymic Disorder is however less common than MDD in adolescents, as in adults (Barlow & Durand, 2002; Sadock & Sadock, 2003).

3.4.1.3 Comorbidity

Childhood onset MDD accounted for a disproportionately high percentage of depression in adults with two or more comorbid Axis 1 disorders, such as Social and Simple Phobias, Alcohol Abuse/Dependence, Panic, Generalised Anxiety, Obsessive Compulsive and Somatoform Disorders (Alpert, Fava, Uebelacker, Nierenberg, Pava, Worthington et al., 1999). Children with prepubertal-onset MDD in adulthood have a high risk of suicide attempts, bipolar disorders, substance abuse and CD (Weissman et al., 1999).

Anxiety disorders were found to be more commonly comorbid with Dystymic Disorder, especially separation anxiety in children and GAD in adolescents. Comorbid externalising disorders presented less frequently (Masi, Favilla, Mucci, Poli & Romano, 2001). Comorbid CD was observed in 16% to 23% of children with depressive disorders. CD developed in most cases as a complication of depression and persisted after the depression remitted. Comorbid CD did not affect depressive symptom presentation, was similarly distributed among boys and girls, and did not affect recovery. CD at any time was associated with an increased rate of long-term functional problems (Kovacs, Paulauskas, Gatsonis & Richards, 1988). CD and/or ADHD often co-occur with depression (Barlow & Durand, 2002).

Childhood depression was found to be associated with memory impairment, particularly verbal memory, but not with attention deficit (Günther et al., 2004). Cognitive dysfunctions including attention, EF, memory and psychomotor slowing were identified in adults with

major depression (Constant, Adam, Gillain, Seron, Bruyer & Seghers, 2005). Motor milestones were delayed in children with affective disturbances, who also ran a greater risk of speech defects between the ages of 6 and 15 years, decreased psychomotor alertness and an excess of twitching and grimacing motor behaviours in adolescence (van Os, Jones, Lewis, Wadsworth & Murray, 1997). Sensitive/isolated behaviours were best explained by neuro-motor delays (Nadeau et al., 2001). School performance of depressed children is affected by a combination of difficulty in concentration, slowed thinking, lack of interest and motivation, fatigue, sleepiness, depressive ruminations and preoccupations. Depression during childhood may be misdiagnosed as a learning disorder. Secondary learning problems are corrected after a child's recovery from the depressive order (Sadock & Sadock, 2003).

Literature consulted did not indicate comorbid disorders for depression in the LBW cohort.

3.4.1.4 Age of onset

Mood disorders tend to increase with increasing age (Berk, 2006; Sadock & Sadock, 2003). The peak risk period for the onset of depression is middle to late adolescence (Gale & Martyn, 2004). Children seem to show fewer symptoms of depression than adolescents, though the symptomatic profile is comparable (Masi et al., 2001). Mood disorders with an early onset tend to be chronic (Sadock & Sadock, 2003). There is conclusive evidence that depressive disorders occur less frequently in children than in adults but rise dramatically in adolescence (Barlow & Durand, 2002). Cortical maturation and synaptic pruning, increasing the risk of psychiatric illness, accompany puberty. It is assumed that similar tendencies regarding age will be observed among LBW children, since these observations in the general population have not been investigated in the LBW cohort.

Dysthymic Disorder in children has an average age of onset that is several years earlier than the age of onset of MDD (Sadock & Sadock, 2003). Dysthymic Disorder is characterised by chronic, less severe depressive symptoms that have been present for many years without discrete major depressive episodes, that may not be easily distinguished from the person's usual functioning (American Psychiatric Association, 2000).

3.4.1.5 Gender differences

Depression among 12-year-old VLBW boys and girls did not differ significantly (Botting et al., 1997). Another study confirmed insignificant differences in depressive symptoms between male and female children aged 7 to 18 years (Masi et al., 2001). Findings on gender differences however are inconclusive. Gale and Martyn (2004) also found that women whose birth weight were low or at the lower end of the normal range had an increased risk of depression at age 26 years. Berk (2006) confirms that in the general population adolescent girls are twice as likely as boys to report persistent depressive symptoms. Female gender and low educational test scores at ages 8, 11 and 15 years were risk factors for childhood affective disturbances (van Os et al., 1997).

Men with LBW were more likely to be psychologically distressed at age 16 years and to report a history of depression at age 26 years (Gale & Martyn, 2004). Foetal under-nutrition seems to predispose men to depression in late adult life, which suggests a neurodevelopmental aetiology of depression (Thompson, Syddall, Rodin, Osmond & Barker, 2001).

Children, especially boys, seem to have the tendency to become aggressive and even destructive during depressive episodes (Barlow & Durand, 2002). Childhood depression is consequently sometimes misdiagnosed as hyperactivity or CD. Increased suicidality was more

significant in depressed female adolescents than in depressed male adolescents (Yorbik et al., 2004).

Female adolescents who experienced poverty in the first 5 years of life had increased symptoms of depression, according to maternal reports (Mifsud & Rapee, 2005). As in adults, MDD occurs more frequently in female adolescents than in males, although this is not the case in more mild depression (Barlow & Durand, 2002).

3.4.1.6 Aetiology

Parent and teacher reports revealed that LBW and consequent general delayed developmental milestones were significantly associated with increased risk of behavioural and emotional problems among 6-to-16-year-olds (e.g. being withdrawn, somatic complaints, social problems, thought problems, depression and aggressive symptoms) (Lui et al., 2001).

3.4.1.6.1 Neurobiological structures

LBW has been linked to later cardiovascular and diabetes risks due to early physiological adaptation, particularly of the HPA axis, to intra-uterine nutritional deficiencies (Patton et al., 2004). The HPA and hypothalamo-pituitary-gonadal axes have also been implicated in early depression. Both are affected by LBW. Thus, a tendency of premature or LBW children to have high circulating glucocorticoids may imply early acquired and persisting neurophysiological vulnerability. Such vulnerability might lower the threshold for depressive and anxiety symptoms that eventually lead to a more negative appraisal and heightened vulnerability to life events (Patton et al., 2004).

MRI scans of children with mood disorders showed a decrease in frontal lobe volume and an increase in ventricular volume. These findings are consistent with MRI results in depressed adults, namely selective loss of frontal lobe cells and frontal lobe serotonin. The

frontal lobes appear to have multiple connections with the basal ganglia and the limbic system and are believed to be involved in the neuropathology of depressive symptoms (Sadock & Sadock, 2003). Significant deficits in frontal lobe functions have been identified in LBW children in Section 2.6.3 (Curtis et al., 2002; Frisk et al., 2002; Giménez et al., 2004).

The 5-HT transporter sites (central serotonin systems) may be increased in the frontal and cingulate cortices of patients with major depression. Other studies found a reduction in 5-HT transporter binding sites in the brainstem and the thalamus-hypothalamus region. Most radioactivity concentrates in the basal ganglia, thalamus and midbrain and those cortical regions have demonstrated low binding values (Reivich, Amsterdam, Brunswick & Shiue, 2004). The basal ganglia, thalamus and hypothalamus are vulnerable brain regions in LBW children (see Section 2.6.3) (Perlman, 2001).

According to Hack et al. (2005) stress during critical phases of human development, together with a genetic disposition, may lower an individual's threshold for developing depression and anxiety later in life. Charmandari et al. (2003) confirm that stress activates the central and peripheral components of the stress system, particularly the HPA axis and the arousal (sympathetic) system. Severe and/or prolonged stress has an adverse impact on the developing brain, which may result in hyperactivity/hyperreactivity of the stress system, with consequent amygdala hyperfunction (fear reaction), decreased activity of the hippocampus (defective glucocorticoid-negative feedback, cognition), and the mesocorticolimbic dopaminergic system (dysthymia, novelty-seeking, addictive behaviours), hyperactivation of the HPA axis (hypercortisolism), suppression of reproductive, growth, thyroid and immune functions, and changes in pain perception. These changes in the brain may be accompanied by abnormal childhood, adolescent and adult behaviours, including excessive fear, addictive behaviours, dysthymia and/or depression. Thus, inappropriate responsiveness of the stress

system may impair growth and development and may account for various endocrine, metabolic, autoimmune and psychiatric disorders (Charmandari et al., 2003). The genetic vulnerability of the individual, exposure to adverse environmental factors and the timing of stressful event(s) influence the development and severity of these mentioned conditions, given that prenatal life, infancy, childhood and adolescence are critical periods characterised by increased vulnerability to stressors (Charmandari et al., 2003).

Adverse environmental exposures *in utero* influence both size at birth and the set point of the HPA axis (Gale & Martyn, 2004; Thompson et al., 2001). Exposure to various prenatal stressors results in lower birth weight, with raised basal or stress-induced glucocorticoid secretion and with increased CRH activity, as shown in animal models (Gale & Martyn, 2004). These physiological characteristics are similar to those seen in people with depression, which suggests that gestational stress at a critical time during foetal neurodevelopment may increase susceptibility to affective illness (Gale & Martyn, 2004).

Early brain development may be affected by foetal genotype, maternal physiology and placental function through nutritional and hormonal mechanisms. Perinatal stress and suboptimal nutrition in the early weeks *ex utero* also play a role in those born prematurely (Patton et al., 2004). Under-nutrition and slow growth of male foetuses *in utero* predispose them to become depressed in adulthood (Thompson et al., 2001). The female foetus grows more slowly than the male and is less vulnerable at critical periods of development. Prepubertal children diagnosed with depression also secrete significantly more growth hormone during sleep than normal children and those with non-depressed mental disorders. These children also secrete significantly less growth hormone in response to insulin-induced hypoglycaemia than non-depressed patients (Sadock & Sadock, 2003).

The HPA axis and growth hormone axis are possible underlying mechanisms explaining the relation between *in utero* under-nutrition and late life depression in males. Concerning the HPA axis, small male infants have increased urinary adrenal androgen and glucocorticoid metabolite excretion at age 9 and higher fasting cortisol concentrations as adults. Increased plasma cortisol level is the most consistently demonstrated biological abnormality in depressive disorder (Thompson et al., 2001). *In utero* under-nutrition is one of the multiple significant risk factors in the development of LBW (Campbell, 2001a). Berk (2006) postulates that the malfunctioning placenta of some expectant mothers permits high levels of stress hormones to reach the foetus, predisposing the developing individual to later disease. According to the growth hormone axis the median 24-hour plasma growth hormone concentrations are related to weight at 1 year. Control of growth hormone secretion is known to be disturbed in depression. Thyroid function may also be set during foetal growth and infant feeding. Reduced plasma thyrotropin levels coupled with impaired response to thyrotropin-releasing hormone are linked with depression (Thompson et al., 2001).

It is possible that PL/VE increases the risk of disorders during puberty (characterised by cortical maturation and synaptic pruning) that typically have a later onset and in which abnormalities of cortical-basal ganglionic circuits have been implicated, such as mood disorders (Whitaker et al., 1997). PL/VE is considered a significant risk factor for psychiatric disorders in LBW children (Breslau et al., 2000; Whitaker et al., 1997).

The hippocampus, which is one of the regions of the brain injured in preterm infants, has been associated with depression in adulthood; Section 2.6.3 refers (Hack et al, 2005).

3.4.1.6.2 Neuropsychological impact of parental depression

Parental MDD increased the risk of Unipolar and Bipolar Mood Disorders and Disruptive Behaviour Disorders (DBD) in children (Biederman et al., 2001; Biederman et al., 2005), as well as anxiety disorder (Biederman et al., 2001). Biederman et al. (2005) suggest a syndromatic overlap and familial co-aggregation between disruptive behaviour and depressive disorders. Most findings indicate that children with the most severe episodes of MDD show much evidence of dense and deep familial aggregation for MDD (Sadock & Sadock, 2003). Hack et al. (2005) note a genetic vulnerability and/or reporting bias with projection of depressive thought onto their children.

Maternal stress and depression directly affect neuroendocrine parameters, uterine blood flow, contractility and other physiological responses that might play a role in preterm labour, newborn neurobehavioural functions and other adverse pregnancy outcomes (Kelly et al., 2002).

Women with a history of psychiatric illness, substance use or both diagnoses had a significantly higher risk of delivering VLBW, LBW and preterm infants even when adjusted for the effects of known socio-demographic and medical risk factors (Section 3.3.1.5.2) (Kelly et al., 2002). Recurrent parental MDD and co-parent alcohol abuse were strong identified risk factors for offspring MDD (Sadock & Sadock, 2003; Warner, Mufson & Weissman, 1995). One explanation for this tendency might be that the 'gestational stress' of maternal depression causes permanent changes in the HPA settings. It could also be due to the postnatal effects of exposure to negative maternal affect, cognitions and behaviour, as well as to the stress of living with a depressed mother (Gale & Martyn, 2004). Dysregulation in the HPA axis linked with high cortisol levels has been associated with depressive symptoms in adults and adolescents. Memory dysfunctions in depressed children may be explained by the effects of cortisol

hypersecretion on cognitive neuroendocrine functioning. Continuous exposure of the brain to abnormal cortisol levels during development may contribute to the worsening of functioning in a range of cognitive domains from childhood to adulthood (Günther et al., 2004). Inconsistent data regarding cortisol hypersecretion appear to exist (Sadock & Sadock, 2003).

3.4.1.6.3 Parent-child attachment

The question was raised by various researchers whether disrupting the bonding process between mother and infant during the first six months could partly lead to a vulnerability to psychiatric symptoms in later life (Botting et al., 1997). Poor maternal bonding during childhood did not appear to be a mechanism for the association between premature adolescents and depressive disorder. Heightened sensitivity to social adversity, such as negative life events, is suggested as a role in depressive disorder in this specific group (Patton et al., 2004).

3.4.1.6.4 Other aetiological/risk factors

Six-year motor impairment was the only predictor of depression at 12 years when taking variables such as motor impairment, full-scale IQ at age 6, birth weight status and perinatal variables into consideration (Botting et al., 1997).

The following significant risk factors were identified when examining the relation between birth weight and psychological distress or depression: SES, maternal depression, separation from the mother for over a month in the first five years of life, teenage or high parity mothers, mother smoking during pregnancy, no father figure at the time of birth, father in a manual occupation, parental marital disruption and experience of local authority care (Gale & Martyn, 2004). Another study confirmed that a high level of depressive symptoms was

associated with a 100 g to 150 g lower infant birth weight among lower income women with less education (Kelly et al., 2002).

Perinatal insults and motor skills deficits, caretaker instability, criminality, psychopathology in the family of origin, as well as behavioural and socio-emotional problems were significant indicators during early childhood (irrespective of birth weight) of juvenile-onset depression (Jaffee, Moffitt, Caspi, Fombonne, Poulton & Martin, 2002).

The quality of the family environment, family dysfunction, maternal mood, birth weight, intelligence, grade level and reading comprehension were significant predictors of anxiety and/or depression among VLBW children (Hack et al., 2005). Moreover, VLBW was a significant predictor of parent-reported internalising symptoms, only among white subjects whose mothers had high levels of psychological distress.

Infants with intrauterine growth failure usually have accelerated rates of growth after birth. Such catch-up growth may have an ameliorating effect on internalising symptoms (Hack et al., 2005).

3.5 Conclusion

According to available research there seems to be an association between LBW and internalising psychological disorders (pertaining to OAD, SAD and MDD), though inconsistencies are indicated.

In spite of insufficient research findings on the association mentioned, it can be concluded that interplay between multiple factors increases the neurobiological and psychological vulnerability of LBW children to internalising symptoms. Gestational age, pre-, peri- and postnatal complications, medical conditions, a stressful hospital environment, family

environment, parental style, impairments in other domains and numerous other factors associated with LBW/prematurity are in reciprocal interaction.

Chapter 4

EXTERNALISING PSYCHOLOGICAL DISORDERS

4.1 Introduction

The discussion of internalising psychological problems leads to the next variable, externalising psychological problems. More externalising symptoms among children with LBW have been indicated (Breslau & Chilcoat, 2000; Grunau, Whitfield & Fay, 2004; Nadeau et al., 2001). Others mention that no differences were observed in ratings of externalising problem behaviours (Rickards et al., 2001; Saigal et al., 2003b). Bhutta et al. (2002) propose that the biological and environmental insults associated with preterm birth may promote some anatomical differences, since developing neurons are more vulnerable to cell death during the perinatal period. Behavioural, ADHD and other problems surface as a result of the mediating effect of both neuro-motor and cognitive deficits (e.g. EF), which develop as sequelae of prematurity (Aylward, 2002). Thus, prematurity often results in specific deficits in cognitive/neuro-motor function, contributing to behavioural, socio-emotional and other problems.

The DBD rating scale (see Appendix G) was used for assessment of the presence and degree of externalising psychological symptoms according to the DSM-IV symptoms for ADHD subtypes (inattention, hyperactivity and impulsivity, full ADHD scale), ODD and CD.

The aim of this chapter is to reflect available research on the relation between LBW and externalising psychological disorders and to explore the nature of this hypothesised relationship. The following relevant aspects pertaining to ADHD, ODD and CD will be addressed: symptoms, prevalence, gender differences, comorbid disorders and aetiological factors.

4.2 Externalising psychological disorders

Externalising refers to symptoms initially internal or "inside" that become represented, projected or manifested in the external world (Plug, Louw, Gouws & Meyer, 1997). Externalising psychological disorders refer to behavioural disorders, specifically ADHD and conduct problems (Mash & Wolfe, 2002).

4.3 Attention-Deficit/Hyperactivity Disorder

According to Tannock (2005) ADHD is a major public health concern because of its increased risk of additional and serious psychopathology in adulthood, including its detrimental effects on the individual's educational, social and occupational attainments. ADHD, which is among the most common childhood psychiatric disorders (Luman, Oosterlaan & Sergeant, 2005; Newcorn, Spencer, Biederman, Milton & Michelson, 2005), causes severe impairments at home and school (Asherson, Kuntsi & Taylor, 2005; Heptinstall & Taylor, 2002; Johansen, Aase, Meyer & Sagvolden, 2002; Plug et al., 1997; Sauver, Barbaresi, Katusic, Colligan, Weaver & Jacobsen, 2004). ADHD is regarded as a neurodevelopmental disorder, as it tends to be chronic (Schachar, Crosbie, Barr, Ornstein, Kennedy, Malone et al., 2005) and involves a significant disturbance in the acquisition of basis skills, due to neurobiological factors (Asherson et al., 2005; Heptinstall & Taylor, 2002).

4.3.1 Symptoms

DSM-IV refers to three subtypes of the disorder, namely: ADHD predominantly inattentive type (ADHD-PI), ADHD predominantly hyperactive-impulsive type (ADHD-HI) and ADHD combined type (ADHD-C) (American Psychiatric Association, 2000). The most common characteristics of children with ADHD are listed by Sadock and Sadock (2003) in order of frequency: hyperactivity, perceptual-motor impairment, emotional lability,

general coordination deficit, attention deficit, impulsiveness, memory and thinking deficits, specific learning disabilities, speech and hearing deficits, and equivocal neurological signs.

Intra-individual variability of behaviour or moment-to-moment fluctuation in task performance is another feature of ADHD (Aase, Meyer & Sagvolden, 2006; Aase & Sagvolden, 2005; Castellanos, Sonuga-Barke, Scheres, Di, Hyde & Walters, 2005; Russell, Oades, Tannock, Killeen, Auerbach, Johansen et al., 2006), referring to short-term fluctuations in the performance of an individual. These behavioural and performance fluctuations are displayed over multiple time scales within seconds, hours or days. Intra-individual variability however is not unique to ADHD, but is also found in other disorders, such as Traumatic Brain Injury, Schizophrenia and Narcolepsy. It is a strong predictor of success, suggesting that poor performance on control tasks, inhibition versions of continuous performance test and stop-signal tasks may reflect problems in response variability rather than poor inhibitory control per se (Russell et al., 2006).

The main clinical symptoms of ADHD are outlined as follow:

4.3.1.1 Attention deficit

According to the DSM-IV-TR six or more of the symptoms of inattention must be present and must have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental level (American Psychiatric Association, 2000):

- Fails to give close attention to details
- Has difficulty sustaining attention
- Does not seem to listen
- Does not follow through on instructions
- Experiences difficulty organising tasks or activities

- Avoids tasks requiring sustained mental effort
- Loses things necessary for tasks
- Is easily distracted
- Is forgetful in daily activities.

Attention deficit seems to be characterised by slow retrieval and information processing, low levels of alertness and mild problems with memory/orientation (sluggishness, drowsiness, daydreaming) (McBurnett, Pfiffner & Frick, 2001). Martel et al. (2007) also mention a relation between inattention/hyperactivity at age 6 and low arousal, slower motor speed and poorer fine motor control. Böhm, Smedler and Forssberg (2004) note that impaired impulse control, working memory and other EF are considered intrinsic to Attention Deficit Disorders (ADD). Many researchers regard attention as an EF (Jeyaseelan, O'Callaghan, Neulinger, Shum & Burns, 2006). Johansen et al. (2002) are of the opinion that the ADHD-PI subtype may have a different aetiology from the ADHD-HI subtype.

Sustaining and focusing attention depend on inhibitory skills (Lawson & Ruff, 2004). Various aspects of self-regulation are involved in attention, for example inhibition. Attention and inhibition are important aspects to perform cognitive tasks and problem-solving. Learning and memory are dependent on attention (Lawson & Ruff, 2004). According to Hernandez, Sauerwein, Jambaqué, de Guise, Lussier, Lortie et al. (2003) attention control develops progressively between the ages of 8 and 12 years in relation to the maturation of the frontal lobes.

York and DeVoe (2002) noted that the presentation of ADHD might differ among premature babies. Premature infants with ADHD have more significant attention problems, but less hyperactivity.

4.3.1.2 Hyperactivity/impulsiveness

The DSM-IV-TR refers to six or more symptoms of hyperactivity/impulsiveness, which have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental level (American Psychiatric Association, 2000):

- Fidgets with hands or feet or squirms in seat
- Leaves seat in classroom inappropriately
- Runs about or climbs excessively
- Has difficulty playing quietly
- Is "on the go" or "driven by a motor"
- Talks excessively
- Blurts out answers before questions are completed
- Has difficulty awaiting turn
- Interrupts or intrudes on others.

Impulsiveness can be defined as a response that is executed with insufficient forethought, planning or control, and is therefore inaccurate or maladaptive (Solanto, Abikoff, Sonuga-Barke, Schachar, Logan, Wigal et al., 2001). According to Aase (2005) impulsiveness is increasingly seen as the main symptom of ADHD, leading to inattention, hyperactivity and variability of all behaviour. Impulsive behaviour was also conceptualised as arising from a response inhibition deficit (Oosterlaan, 1996). Inhibition can be defined as the ability to withhold or interrupt a motor response. Response inhibition overlaps with several other aspects, such as delay of gratification, impulsiveness, response modulation, self-control or self-regulation and delay aversion (Oosterlaan, 1996).

Johansen et al. (2002) argue that impulsiveness has both a motor and a cognitive component. "Motor impulsiveness" can be defined as bursts of responses with short inter-response times. This behaviour seems to emerge in children with ADHD. "Cognitive impulsiveness" implies that private events (such as thoughts and plans) are dealt with for short sequences of time with rapid shifts, which results in problems with generating and following plans, difficulty with organising own behaviour, forgetfulness and inefficient use of time. Solanto et al. (2001) confirm that impulsiveness may be differentially expressed in the motor, cognitive, social and emotional domains.

Tucha and Lange (2001) state that children with ADHD have poor motor coordination and perceptual-motor skills. Kalff, Hendriksen, Kroes, Vles, Steyaert, Feron et al. (2002) have identified impairments in working memory, visual-motor ability, EF (especially inhibitory control), deficient motivation and difficulties with serial information processing. Working memory is a core causal cognitive process behind the behaviour problems in children with ADHD (Böhm et al., 2004; Wilens, Biederman, Brown, Tanguay, Monuteaux, Blake et al., 2002), which leads to disorganised behaviour, redirection of attention to other stimuli and eventually hyperactivity or impulsiveness (Böhm et al., 2004). Motor coordination, memory, EF and other neuropsychological functions are discussed in Chapter 5.

4.3.1.3 Impaired executive functions

Dysregulation of EF is assumed to be intrinsic to ADD (Böhm et al., 2004) or ADHD (Heptinstall & Taylor, 2002; Max, Manes, Robertson, Mathews, Fox & Lancaster, 2005; Rosenthal, Riccio, Gsanger & Jarratt, 2006). Oosterlaan (1996) notes that poor response inhibition may be part of a general impairment in EF. Barkley (2006) states that impaired self-control and behavioural inhibition (Boonstra, Oosterlaan, Sergeant & Buitelaar, 2005) or response inhibition (Oosterlaan, 1996) are the central deficits in ADHD, particularly

diminished responsivity to conditioned stimuli on which punishment is contingent (Olson, 2002). Response inhibition depends on both response execution and inhibitory processes. Inability to delay gratification may also be explained by poor response inhibition (Sonuga-Barke, Williams, Hall & Saxton, 1996).

Poor response inhibition in ADHD is part of a more pervasive impairment in cognitive functioning, rather than a deficit restricted to the power of response inhibition (Oosterlaan, 1996). This deficit in inhibition causes difficulties with various EF such as working memory, self-regulation and motor control (Boonstra et al., 2005). Oosterlaan (1996) postulates that deficits in response inhibition, response execution and response re-engagement may all arise from a deficit in the regulation of activation, which in turn impairs motor processing. However, children with ADHD often manifest motivational problems that appear to be deficits in inhibitory control (Olson, 2002). Geurts, Verté, Oosterlaan, Roeyers and Sergeant (2005) did not find deficits in children with ADHD on working memory, planning and cognitive flexibility, in contrast with Oosterlaan, Scheres and Sergeant (2005), who observed deficits in planning and working memory. Oosterlaan et al. (2005) note that EF deficits in ADHD may be a risk factor for the maintenance of ADHD in later development, and possibly for the development of other DBDs, including ODD and CD. Oosterlaan (1996) mentions uncertainty about whether impairments in response inhibition and EF represent a stable deficit or a maturational lag in development.

Russell et al. (2006) postulate that intra-individual variability may account for a substantial proportion of the variance in performance of EF tasks such that poor tasks performance may not reflect impaired EF per se, but rather an admixture of poor neurobiological regulation of the external physiological environment of rapidly firing neurons

as well as slowed processing speed arising from inadequately myelinated neurons, particularly those involved in working memory.

Boonstra et al. (2005) emphasise that though there is clear evidence of EF impairments in ADHD children, the specificity of EF deficits for ADHD is questioned. Deficits in response inhibition processes or motor inhibition did not appear to be exclusively related to ADHD, but also characterised under-contolled or externalising childhood behaviour (particularly CD) (Oosterlaan, 1996). Many other childhood disorders (such as ODD and CD) are also associated with deficits in EF. Boonstra et al. (2005) also indicate a relation between EF and IQ. Controlling for IQ might remove some of the variance that is related to ADHD. Therefore, researchers should report EF results with and without controlling for overall IQ performance.

4.3.1.4 Working memory

ADHD also includes deficits in working memory contributing to difficulties with disinhibition (Rosenthal et al., 2006). According to Rapport, Chung, Shore and Isaacs (2001) failure of working memory not only leads to disorganised behaviour, but also motivates children to redirect their attention to other stimuli in the environment. This phenomenon is described as *stimulation seeking.* The inability to maintain working memory representations leads to behaviour that increases the rate at which input is delivered to working memory so as to compensate for the rapid rate at which representations fade. Consequently, the rate at which stimulation impinges on working memory increases. Redirection of attention can be alternatively conceptualised as a form of escape from monotonous or high task demand conditions that is observed by others as hyperactivity and impulsiveness (Rapport et al., 2001).

According to Botting et al. (1997) it is possible that the combination of ADHD, motor impairments and poor mathematical ability seen in some VLBW children may indicate a deficit in mechanisms that may link these abilities, such as visual-spatial or working memory impairment.

A more detailed discussion on working memory in children born with LBW follows in Section 5.4.

4.3.2 Prevalence

Various studies estimate that between 2% and 9.5% of all school-aged children worldwide have ADHD (Barkley, 2006; Meyer & Sagvolden, 2006b). The disorder occurs in about 5.5% of children in the Limpopo Province of South Africa (Meyer, Eilertsen, Sundet, Tshifularo & Sagvolden, 2004).

However, cultural influences may have an impact on the diagnosis of the disorder (Jensen, Mrazek, Knapp, Steinberg, Pfeffer, Schowalter et al., 1997). There might be slight geographical variations in the percentage of children diagnosed with ADHD (Alarcon, Westmeyer, Foulks & Ruiz, 1999; Meyer, 1998; Meyer & Sagvolden 2006a; Taylor, 1998).

Little is known about ADHD on the African continent. Research among the different ethnic groups of the Limpopo Province of South Africa indicates that ADHD is the most prevalent childhood disorder also in South Africa and that the prevalence rates for ADHD subtypes are similar to Western rates for both genders in all ethnic groups (Meyer et al., 2004), which suggest the same neurobiological processes probably caused by genetic factors expressed independently of cultural differences (Meyer, 2005). Meyer (2005) however did find that cultural differences affect the performance on neuropsychological measures.

According to Lou (1996) ADHD is among the most common causes of behavioural disturbance in schools. Sufferers constitute one of the largest groups of patients in the clientele of child psychiatrists and child neurologists.

4.3.3 Incidence of Attention-Deficit/Hyperactivity Disorder in low-birth-weight children

The meta-analysis performed by Bhutta et al. (2002) shows that children born preterm have a 2.64-fold risk of developing ADHD, as well as frequently manifesting externalising or internalising behaviour at school age.

LBW and/or preterm infants appear to be at risk of hyperactivity (Klebanov & Brooks-Gunn, 1994; Peterson et al., 2002). Most research studies confirm that there is a significant relationship between LBW/prematurity and ADHD (Aylward, 2002; Bhutta et al., 2002; Breslau, Chilcoat, DelDotto, Andreski & Brown, 1996b; Breslau et al., 2000; Harrison, 1996; Hoff et al., 2004; Huddy et al., 2001; Marlow, 2004; Mick, Biederman, Prince, Fischer & Faraone, 2002; Olness, 2003; Saigal et al., 2001; Saigal et al., 2003a; Saigal et al., 2003b; Szatmari, Saigal, Rosenbaum, Campbell & King, 1990; Ulvund et al., 2001; Winders & Burns, 2001). Breslau and Chilcoat (2000) note that this higher incidence was accounted for in large part by a history of maternal smoking in pregnancy. Moreover, prenatal exposure to smoking signalled an increase in externalising problems regardless of LBW status (Breslau & Chilcoat, 2000).

Botting et al. (1997) state that the prevalence of ADHD in the 12-year-old VLBW group was 22% in comparison to 6% in the control group. Whitaker et al. (1997) found that 22% of the 6-year-old LBW sample had at least one psychiatric disorder, the most common being ADHD (15.6%). Ulvund et al. (2001) report a 27% prevalence of ADHD in 8-to-9-year-old VLBW children. According to Barlow and Lewandowski (2000) preterm children are four to

six times more likely than the national estimates of 3% to 5% of the general population to be diagnosed with ADHD. LBW appears to be an independent risk factor for ADHD (Lawson & Ruff, 2004).

Significant attention deficits were observed by various researchers (Aylward, 2002; Bhutta et al., 2002; Haycock, 2004; Indredavik et al., 2004; Jeyaseelan et al., 2006; Klebanov & Brooks-Gunn, 1994; Lawson & Ruff, 2004; Lui et al., 2001; Nadeau et al., 2001; Peterson et al., 2002; Rickards et al., 2001; Sajaniemi et al., 2001; Saylor et al., 2003; Tideman, 2000). However, the minority of VLBW adolescents with attention deficits satisfied the diagnostic criteria (Breslau & Chilcoat, 2000; Indredavik et al., 2004). Significant attention problems were observed in the LBW group from the urban disadvantaged community, but not in the suburban middle class community (Breslau & Chilcoat, 2000).

Impulsiveness was also reported as one of the frequently reported behavioural problems among preterms (Sajaniemi et al., 2001). Difficulty with concentration has been found most consistently in follow-up studies of VLBW children (Wolke, 1998). Teacher reports of inattentive behaviours were strongly influenced by the difficulty premature children have in concentrating, maintaining auditory information in working memory and reusing it in an orderly fashion (Nadeau et al., 2001).

Chapieski and Evankovich (1997) report more inconsistent findings of studies, which have included children with birth weights above 1 500 g. Huddy et al. (2001) confirm that studies investigating rates of hyperactivity in LBW infants are inconsistent. However, Breslau and Chilcoat (2000) indicate that the increased prevalence of psychiatric problems also applies to LBW children with a birth weight of more than 1 500 g. Behavioural and attention problems were more common in infants weighing less than 750 g at birth (Avery et al., 1999).

Szatmari et al. (1990) report that 16% of children between 500 and 1 000 g birth weight had attention deficiencies with hyperactivity, compared with 6.9% of controls. Problems with inattention and hyperactivity were evident even in those with higher LBW (Lawson & Ruff, 2004; Olness, 2003).

Anderson et al. (2004) found that ELBW/very preterm children were no more impulsive than their NBW counterparts. Stathis et al. (1999) report no difference in the prevalence of ADHD between controls and children with ELBW, small head circumference or those with changes in head-circumference growth velocity (HGV) during the first year. Cooke and Abernethy (1999) did not identify significant differences in frequency of ADHD between VLBW children with MRI lesions and those with normal scans. Zappitelli et al. (2001) and Sommerfelt et al. (1996) mention no association between LBW and ADHD. They observed that the VLBW children with ADHD did not differ from the term-born children with ADHD, including no differences between VLBW children without ADHD and children born at normal term. Indredavik et al. (2004) also identify only a low prevalence of ADHD in VLBW adolescents. Pregnancy and labour characteristics, LBW and twin births were not associated with ADHD (Sauver et al., 2004). Sato, Aotani, Hattori and Funato (2004) found that high positive rates on a minor neurological signs test did not show a significant difference between the VLBW and NBW groups regarding behavioural problems. Scores on the minor neurological signs test however were a significant predictor for criteria of ADHD.

Differences in attention control problems between SGA and non-SGA children in adolescence were only modest (O'Keeffe et al., 2003). Elgen, Lundervold and Sommerfelt (2004) indicated no specific identifiable attentional dysfunctions in the LBW group, as well as continued uncertainty about the nature of the reported impaired attention among LBW

children. Prematurity did not induce specific attentional brain dysfunction or maturation delays in stimulus-processing during cognitive tasks (Potgieter et al., 2003).

Harrison (1996) emphasises that some premature children have symptoms of ADHD that do not reach the full diagnosis. Ideally a behaviour continuum should be referred to rather than an absolute diagnosis (Harrison, 1996; Kalff et al., 2002). Auerbach (2005) conceptualises ADHD as falling on a continuum of temperamental characteristics, also reflecting neurodevelopmental immaturity.

Reports on the prevalence of ADHD vary because of differences in study design, inclusion criteria, assessment age and methodology (Indredavik et al., 2004; Torrioli, Frisone, Bonvini, Luciano, Pasca, Lepori et al., 2000; Zappitelli et al., 2001). For example, Tully et al. (2004) found that birth weight did not significantly predict teachers' rating of ADHD, but significantly predicted parent reports. The role of LBW in ADHD seems to remain unclear (Zappitelli et al., 2001).

4.3.4 Gender differences

Recent evaluations suggest male-to-female ratios of 3:1 or 2:1 in community samples (Barkley, 2006; Böhm et al., 2004; Meyer & Sagvolden, 2006b; Sauver et al., 2004; Stein, 2002; Swanson, 2003), raising the possibility that affected females are different in some ways (Heptinstall & Taylor, 2002). Increasing interest has developed in gender differences in ADHD, both in terms of the practical concerns regarding treatment and in terms of finding answers to the aetiology of the disorder, which could account for the gender differences (Heptinstall & Taylor, 2002). The disorder is more common in boys than in girls (Heptinstall & Taylor, 2002; Johansen et al., 2002; Sauver et al., 2001), but during adolescence and young adulthood relatively more females are affected (Heptinstall & Taylor, 2002; Johansen et al.,

2002). According to Heptinstall and Taylor (2002) the prevalence rate for ADHD among boys declines by nearly 20% per year between the ages of 10 and 20, while the prevalence among girls remains relatively constant. Indredavik et al. (2004) note that the male predominance described in children with ADHD was not found in the VLBW adolescent group. Hoff et al. (2004) also did not find significant gender differences after controlling for differences in IQ.

Mercugliano (1999) states that the prominent decreases in the metabolism of female adolescents could suggest either that females have a more rapid rate of developing an "adult ADHD brain activity pattern" or that they have relatively more severe ADHD. Girls with ADHD may have greater intellectual impairment, more comorbid internalising disorders, less comorbid externalising disorder and lower rates of hyperactivity than boys with ADHD (Martel et al., 2007).

Boys are generally more frequently afflicted with neurodevelopmental disorders than girls (Heptinstall & Taylor, 2002). One possibility is that girls appear to be more mature than boys at all developmental stages. Boys are one year behind girls in maturity at the time of starting school and this widens to two years at puberty. Prenatal and birth complications, infectious disease and neurodevelopmental abnormalities occur more frequently in boys. There is agreement that affected girls develop a more severe form of the disorder. Because girls mature faster, they will acquire a relatively greater degree of divergence from their norm and will therefore be affected more severely than boys (Heptinstall & Taylor, 2002). Another possibility is that girls have a higher threshold, which implies that girls tend to be more seriously affected; they have a higher genetic loading and have more affected relatives (Heptinstall & Taylor, 2002). Girls may be protected by factors (e.g. hormones such as oestrogen), which keep them from developing ADHD and buffering them from some of the impact of risks associated with LBW (Martel et al., 2007). Boys born at LBW may be more

likely than girls to display neuropsychological deficits and ADHD due to foetal testosterone that slows the lateralisation of the left hemisphere of the brain, increasing their vulnerability to prenatal injury, LBW and neuropsychological problems (Martel et al., 2007).

Girls seem to have the tendency to be diagnosed with ADHD later, with more symptoms of the inattentive subtype and cognitive problems and fewer symptoms of ODD, CD or aggressive/impulsive behaviour (Cantwell, 1996; Swanson, 2003). Girls were found to be at greater risk of later cognitive and behavioural problems, including concentration difficulties. However, Heptinstall and Taylor (2002) report that girls of all ages had fewer attention problems and less hyperactivity than same-age boys on parent and teacher rating scales, but ADHD girls showed more inattentive behaviour during testing than ADHD boys. Accardo and Blondis (2001) are of the opinion that non-hyperactive girls with attentional disorders remain an under-diagnosed and untreated group.

According to Abikoff, Jensen, Arnold, Hoza, Hechtman, Pollack et al. (2002) girls with ADHD had relatively higher rates of verbal aggression to children, when compared to a comparison group of girls. They further observed that boys with ADHD engaged in more rule-breaking and externalising behaviour than girls with ADHD. However, girls with ADHD should exhibit fewer externalising, observable forms of behaviour than do boys with ADHD, just as normal girls should also exhibit fewer than normal boys. Crijnen, Achenbach and Verhulst (1997), as well as Heptinstall and Taylor (2002), confirm that across all cultures boys tend to have more externalising problems and girls more internalising problems. Therefore boys are more frequently referred for treatment (Heptinstall & Taylor, 2002).

Generalisation of research findings should however be done with caution. Hunt, Paguin and Payton (2001) state that although hyperactivity is more frequent in boys, distractibility and disorganisation can also be a major problem in girls.

Chapieski and Evankovich (1997) report inconsistencies between studies investigating the relation between LBW, ADHD and gender. It appears that there is some indication that males may be at higher risk, in spite of insufficient research on gender differences (Chapieski & Evankovich, 1997; Whitaker et al., 1997). Sajaniemi et al. (2001) note that behavioural problems such as attention deficit, impulsiveness and general externalising problems are more common in preterm boys than in preterm girls. Breslau and Chilcoat (2000) observed a trend towards a greater LBW effect on attention problems in males in the urban setting and on externalising problems in males in both urban and suburban settings. The excess in problems associated with LBW was twice as large in males as in females (Breslau & Chilcoat, 2000).

O'Keeffe et al. (2003) mention that girls with more severe growth restriction are at increased risk of attentional difficulties. Inhibition and impulse control mature earlier in girls in the normal population, but this lead will disappear after the age of 6 years. It seems that VLBW children also follow the ordinary pattern of female superiority, but at a slightly slower pace. This may indicate that gender differences in cognition develop independently of preterm birth.

Sauver et al. (2004) mention that low maternal and paternal education levels increased the risk of ADHD in boys more than in girls.

4.3.5 Comorbid disorders

Accardo (1999) and Fischer, Barkley, Smallish and Fletcher (2002) state that the presence of ADHD should be considered as a marker for other psychiatric and developmental

conditions, as indicated in Table 4.1. Early attentional difficulties in VLBW infants may be associated with subsequent psychopathology and academic difficulties at adolescence (Saigal et al., 2003a). Levy et al. (2005) found that children with the combined subtype showed more comorbid symptoms, indicating a strong relationship between high rates of externalising symptoms and high rates of internalising symptoms. ADHD-C subtype did not increase the risk of anxiety disorders (Sanders, Arduca, Karamitsios, Boots & Vance, 2005). Moreover, ADHD-C subtype was associated with CD and decreased verbal and fullscale IQ. Hyperactive behaviour reported by parents was mediated by a global intellectual delay rather than by specific intellectual components (Nadeau et al., 2001). GAD, followed by SAD, was the most common disorder in the ADHD-C subtype and Dystymic Disorder group (Sanders et al., 2005). Breslau et al. (1996a) further state that ADHD in LBW did not differ from ADHD in NBW children with respect to associated comorbidity. About 50% of LBW as well as NBW children with ADHD met criteria for at least one additional disorder.

According to Johansen et al. (2002) children with ADHD-PI subtype tend to be more socially withdrawn, experience greater academic problems and develop comorbid anxiety or other mood disorders. However, early hyperactive-impulsive behaviour is associated more closely with externalising problems such as aggression, oppositional behaviour, adolescent delinquency and substance abuse (Johansen et al., 2002).

According to Leslie (2002) the symptoms associated with ADHD interfere with normal developmental milestones of childhood and adolescence. Table 4.1 represents the prevalence of selected comorbid conditions in children with ADHD.

Table 4.1 Prevalence of selected coexisting conditions in children with ADHD (Stein, 2002)

Coexisting condition	**Estimated prevalence (%)**
ODD	35.2
CD	25.7
Anxiety disorder	25.8
Depressive disorder	18.2

Accardo (1999) states that a comprehensive medical assessment assists in confirming the diagnosis of ADHD or identifies other conditions that mimic it (see Table 4.2). Various chronic diseases and neurological conditions produce a picture of inattention, but with a range of other signs and symptoms (Accardo, 1999; Cantwell, 1996).

Table 4.2 Conditions that are associated with ADHD or mimic it (Accardo, 1999)

Medical disorder	**Developmental disorders**
Chronic diseases	Communication disorders
Hearing impairment	Learning disability
Sleep disorders	Mental retardation
Neurological disorders	**Psychiatric disorders**
Brain injury	Mood disorders
Tic Disorder	Obsessive/Compulsive Disorder
Seizure Disorder	Conduct disorders
Genetic/endocrine/metabolic disorders	
Syndromes:	
Fragile X	
Foetal Alcohol Syndrome	
Thyroid disease	

Edwards, Schulz and Long (1995) confirm that diagnosing ADHD is complicated by the possibility that some other primary problem is producing the ADHD symptoms. There is a variety of psychiatric, developmental, medical and environmental conditions that can either mimic ADHD symptoms or coexist with ADHD. Oppositional and conduct disorders frequently co-occur with ADHD and it can be difficult to determine whether one or two conditions are present (Edwards et al., 1995). Children with ADHD who also have other comorbid conditions have more negative outcomes when compared with children who have ADHD only (Hechtman, 1999).

Comorbid conditions seem to be encountered much more rarely in younger children. They tend to become important during the transition to adolescence, especially in teenagers who have not been diagnosed or adequately treated previously (Accardo, 1999).

The most prevalent comorbid conditions, as indicated in Table 4.2, are discussed separately under the respective headings: ODD (Section 4.7), CD (Section 4.8), as well as anxiety and depression in Chapter 3.

It is important to note that the rate of ADHD and comorbid depression and anxiety ranges from 20% to 40%, depending on the sample and diagnostic criteria (Accardo, 1999; Hechtman, 1999; Spencer, Biederman & Wilens, 1999). The rates of anxiety disorders were much higher among children with ADHD in the normal population (Chavira, Stein, Bailey & Stein, 2004). Wilens et al. (2002) found that ODD and MDD were the most common comorbid disorders in both preschool and school age children in the general population. According to Cantwell (1996) internalising problems, such as anxiety and mood disorders, may be under-reported by parents or teachers, because externalising forms of behaviour are more

observable. Hack et al. (2005) confirm that childhood depression may co-occur or precede externalising symptoms.

The following common comorbid disorders will be discussed:

4.3.5.1 Specific learning disability

Section 2.6.2 indicates that learning problems are prevalent in LBW children. The association between ADHD, LBW and learning problems is not reflected in research findings consulted.

Klebanov and Brooks-Gunn (1994) question whether attention and hyperactivity problems are due to language and learning deficits rather than an ADD per se. According to Accardo (1999) day-to-day variations in academic performance are more suggestive of ADHD than of learning disabilities. Hyperactivity was significantly more associated with placement in special education among LBW 9-year-olds (Pinto-Martin et al., 2004).

Taylor, Sergeant, Doepfner, Gunning, Overmeyer, Mobius et al. (1998) and Tannock (2005) report delayed language milestones, problems with expressive language and reading disabilities in hyperactive children. Language abilities (due to possible cerebellar dysfunction) also place heavy demands on other cognitive functions, such as working memory, organisation and attention (Tannock, 2005). Aylward (2002) and Sajaniemi et al. (2001) note that the more complex verbal language processes, which are critical in social and academic endeavours, have been found to be deficient in preterm infants.

Impaired performance with respect to motor planning and EF may not be attributed completely to ADHD but may also partly be caused by learning disabilities (Kalff et al., 2002). Children with ADHD and reading disability were impaired in various domains, including EF. Impairments in reading/language and mathematics (see Section 2.6.2), as well as in motor,

visual-spatial, memory and executive functioning (see Chapter 5), are associated with LBW. Thus, future research should also focus on learning disabilities in addition to ADHD in order to ascertain whether neuro-cognitive differences between groups are accounted for by ADHD or by learning disabilities (Kalff et al., 2002).

4.3.5.2 Immature motor coordination

There is a strong relationship between ADHD and Developmental Coordination Disorder (DCD), dyscoordination, motor-perceptual dysfunction (Gillberg & Kadesjö, 2000). Meyer and Sagvolden (2006b) also identified this association between motor problems (motor control, accuracy and speed) and ADHD in South African children from the general population, particularly in the younger group with ADHD-combined symptoms. Poor motor control seems to predict worse outcomes for children with ADHD (Martel et al., 2007). Marked clumsiness or weak motor coordination may represent an aetiologically distinct subgroup of children with ADHD, relating to subtle pre- or perinatal insult, especially in view of strong findings linking poor motor control with LBW (Martel et al., 2007). Weaknesses in right brain functions, such as mathematics and grapho-motor skills, are common in children with ADHD (Accardo, 1999; Taylor et al., 1998).

According to Gillberg and Kadesjö (2000) ADHD children do not seem to have impaired input processing, but dysfunctional motor output. Timing, pacing and preparation to act are all deficient. Consequently, ADHD may primarily be a failure in intention, inhibition and capacity to delay responding (Blondis, 1999; Gillberg & Kadesjö, 2000). Children with ADHD usually outgrow clumsiness, while it is not the case if the ADHD child also has a comorbid DCD (Blondis, 1999). Gillberg and Kadesjö (2000) state that clumsiness and poor motor coordination are considered to be clear markers of neurological dysfunction.

Impaired motor functioning is an area of significant concern in LBW children (see Section 5.2.1) (Blondis, 1999; Huddy et al., 2001; Marlow, 2004; Nadeau et al., 2001; O'Brein et al., 2003; Rickards et al., 2001). Haycock (2004) also observed significant motor impairment in a South African LBW cohort. The relation between LBW, ADHD and motor functioning needs further exploration internationally and locally.

4.3.6 Aetiology

Various factors are in reciprocal interaction (Martel et al., 2007; Rapport et al., 2001). According to Hunt et al. (2001) the CNS regulates attention, arousal, activity and affect by means of neurotransmitters, which are influenced by genetic factors. Asherson et al. (2005) suggest that the dopamine D4 and D5 receptors, the dopamine transporter (DAT1) and other deoxyribonucleic acid (DNA) changes occur more frequently in children with ADHD. These genetic factors might be influenced by environmental factors (Asherson et al., 2005; Edwards et al., 1995; Mercugliano, 1999). Dopamine is released in response to rewarding events, and is required for certain types of learning (Wickens, 2005). Three main groups of environmental risk factors have been identified in the development of ADHD: Prenatal and perinatal events (e.g. prematurity, LBW, pregnancy and/or birth complications and mother's use of alcohol or tobacco during pregnancy) (Asherson et al., 2005; Zappitelli et al., 2001), parental and family factors (e.g. neglect, inconsistent parenting, family conflict and institutional rearing), and neurobiological risks (e.g. head trauma and exposure to lead) (Asherson et al., 2005).

The risk of either a diagnosis or symptoms of ADHD in premature children increases as birth weight decreases (Botting et al., 1997; Chapieski & Evankovich, 1997). However, Elgen et al. (2002) found that behavioural problems and psychiatric disorders were as common in children born with a birth weight of less than 1 500 g as in children born with a birth weight of between 1 500 and 2 000 g.

The relationship between LBW and ADHD seems to vary by level of IQ (Breslau et al., 2000; Kalff et al., 2002). LBW children with an IQ below 80 show the highest rate of ADHD. Those with an IQ between 80 and 99 exhibit an intermediate rate. LBW/preterm children with an IQ in the normal range were not more likely than NBW/term children to be diagnosed with ADHD (Breslau et al., 1996b; Hoff et al., 2004). Hoff et al. (2004) however found that hyperactive behaviour persisted in the extremely preterm (gestational age < 28 weeks) or ELBW group, even when differences in intellectual development and parental sensitivity were controlled.

According to Aylward (2002) behavioural, ADHD and other problem areas surface as a result of the mediating effect of both neuro-motor and cognitive deficits (e.g. EF), which develop as sequelae of prematurity. Thus, prematurity often results in specific deficits in cognitive/neuro-motor function, contributing to behavioural, socio-emotional and other problems. Neuro-motor deficits often cause the older VLBW child to be more cautious in peer interactions and result in peer rejection, cognitive problems (disruptions in EF, memory or global intelligence), which are more strongly associated with deficits in attention and hyperactivity (Aylward, 2002).

4.3.6.1 Genetic influences

ADHD seems to run in families. Hunt et al. (2001) and Mercugliano (1999) state that studies of twins, siblings and adopted children reflect a significantly higher incidence of ADHD in biological relatives of patients compared with the general population. According to Barkley (2006) and Mercugliano (1999) the child of an adult with childhood-onset ADHD has a more than 50% chance of having ADHD. Barkley (2006) stipulates that heredity appears to play the largest role in the occurrence of ADHD. Parents of children with ADHD are more likely to have a history of numerous problems, such as antisocial behaviour, alcoholism and

learning disabilities (Accardo, 1999; Edwards et al., 1995), as well as depression and marital problems (Heptinstall & Taylor, 2002). Impairments on some neuropsychological measures, including those that rely on processing speed, mathematics and aspects of EF, may indicate a familial vulnerability to ADHD (Doyle, Biederman, Seidman, Reske-Nielsen & Faraone, 2005). As indicated in Section 3.3.1.5.2, women with a history of psychiatric illness, substance use or both diagnoses had a significantly higher risk of delivering VLBW, LBW and preterm infants even when adjusted for the effects of known socio-demographic and medical risk factors (Kelly et al., 2002). Thus, a large number of LBW children seem to be geneticically predisposed to psychiatric illness.

4.3.6.2 Neurochemistry of Attention-Deficit/Hyperactivity Disorder

Genetic studies focus on the chromosomes that regulate neurotransmitter production, release, reuptake and receptor sensitivity (Hunt et al., 2001). Alterations in dopaminergic (Cantwell, 1996; Lou, 1996; Mercugliano, 1999; Russell, 2005; Sagvolden, 2005; Swanson, Sergeant, Taylor, Sonuga-Barke, Jensen & Cantwell, 1998; Wickens, 2005) and noradrenergic functions (Cantwell, 1996; Lou, 1996; Mercugliano, 1999; Russell, 2005; Swanson et al., 1998) appear to be central in the symptoms of ADHD. Symptoms of ADHD are treated most effectively by medication (stimulants) that influences these neurotransmitters (Cantwell, 1996; Lou, 1996; Mercugliano, 1999; Swanson et al., 1998). A dysfunctioning dopamine system in ADHD children results in difficulty in integrating the consequences of their past actions into the organisation of their future actions, suggesting impairment of the adaptive sequencing capabilities of the corticostriatal system (Wickens, 2005).

Collaborative brain systems were suggested to modulate behaviour, namely the behavioural activation system (BAS) and the BIS (Luman et al., 2005; Oosterlaan, 1996). BAS involves the dopaminergic pathway, nucleus accumbens and ventral striatum (Lou, 1996),

which initiate approach behaviour and active avoidance, and are activated by conditions of reward. BIS is located in the septo-hippocampal system, which is activated by conditions of punishment and non-reward, and interrupts continuing or anticipated motor behaviour. An under-active BIS appears to characterise ADHD, whereas an overactive BIS underlies anxiety disorders (Oosterlaan, 1996).

Sagvolden (2005) postulates that the dynamic developmental behavioural theory is based on the hypotheses that altered dopaminergic function plays a crucial role by failing to modulate non-dopaminergic (primarily glutamate and gamma-aminobutyric acid [GABA]) signal transmission appropriately. Behavioural characteristics of ADHD may result from impaired dopamine transmission in the cortico-strato-thalamo-cortical circuits (Hoff et al., 2004; Lou, 1996; Russell, 2005; Sagvolden, 2005). An imbalance between increased noradrenergic and decreased dopaminergic regulation of neural circuits that involve the prefrontal cortex may be responsible for aspects of ADHD behaviour (Russell, 2005; Sagvolden, 2005). According to Barkley (2006) and Sagvolden (2005) dopamine is secreted by neurons, as indicated in Figure 4.1, in specific parts of the brain in order to inhibit or enhance the activity of other neurons, particularly those involved in emotion and behaviour (Barkley, 2006).

Figure 4.1 A dopamine synapse (Sagvolden, 2005)

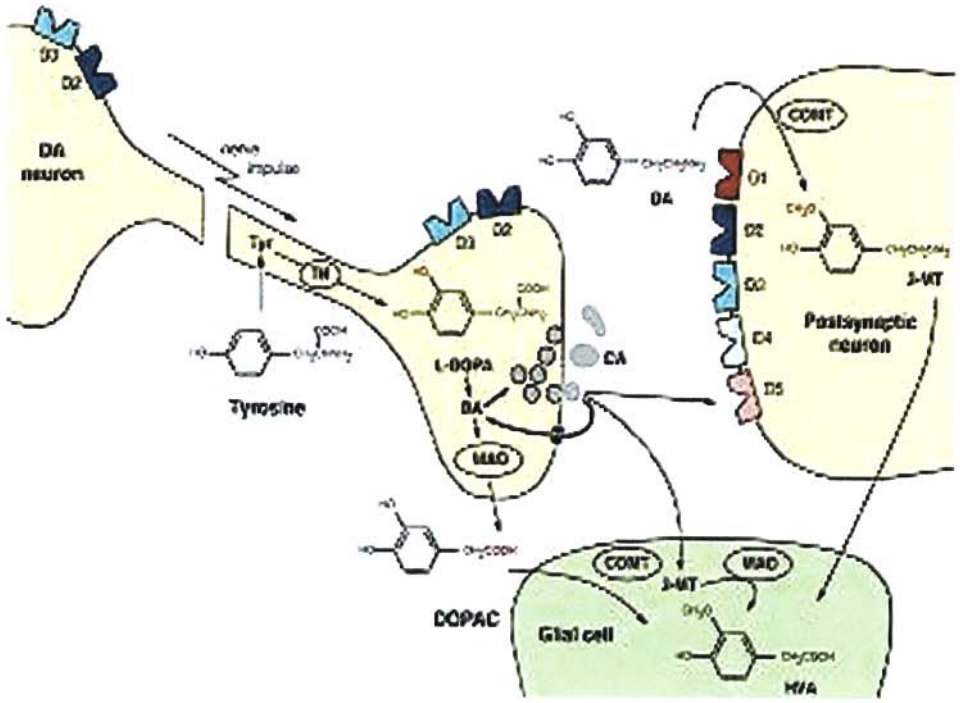


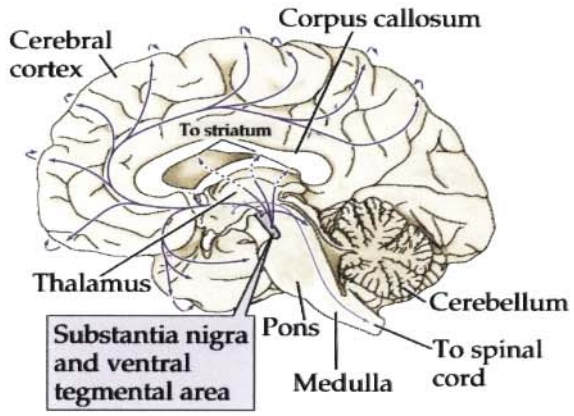
Figure 4.1 indicates the neuronal secretion of dopamine in order to inhibit or enhance the activity of other neurons.

Johansen et al. (2002) confirm that ADHD symptoms may to a large extent be caused by a dysfunctioning dopamine system (see Figure 4.2), particularly in the right prefrontal cortex and striatum (Wickens, 2005; Zappitelli et al., 2001).

A dysfunctioning meso-limbo-cortical dopamine branch (see Figure 4.3) will produce altered reinforcement and extinction processes that cause deficient sustained attention, hyperactivity, increased behavioural variability and impulsiveness (Hunt et al., 2001; Johansen et al., 2002; Sagvolden, 2005), including poor behavioural planning (poor EF) (Sagvolden, 2005) and attention (Russell, 2005). Luman et al. (2005) and Solanto et al. (2001) confirm that children with ADHD have reduced sensitivity to reinforcement. As a result, more immediate, frequent or intense rewards are needed to maintain appropriate performance and behaviour,

such as sustained attention. The mesolimbic dopamine system seems to be involved in reward and reinforcement processes (Johansen, 2005). A dysfunctioning nigro-striatal dopamine branch (see Figure 4.3) will contribute to poor motor control (Hunt et al., 2001; Johansen et al., 2002; Russell, 2005; Sagvolden, 2005), including deficient non-declarative habit learning and memory (Russell, 2005; Sagvolden, 2005). These impairments will contribute to apparent developmental delay, clumsiness, neurological 'soft signs' and a 'failure to inhibit' responses appropriate to demands (Russell, 2005; Sagvolden, 2005).

Figure 4.2 Dopamine pathways (Purves, Augustine, Fitzpatrick, Katz, Lamantia & McNamara, 2001)



Pathways of the dopamine system are reflected in Figure 4.2.

Dopamine dysfunctioning will probably be mainly genetically determined. However, non-genetic factors such as drugs of abuse and environmental toxins may also contribute to the regional differences found in the prevalence of ADHD (Sagvolden & Sergeant, 1998).

A deficit in dopamine is related to an increased binding capacity of the dopamine transporter. This implies that synaptic dopamine is cleared more rapidly in ADHD individuals in the striatum where reuptake via dopamine transporters is the most important means of

removing dopamine from the synapse (relative to prefrontal cortex, where synaptic dopamine activity is primarily decreased by diffusion and uptake by noradrenaline [norepinephrine] transporters). The question still remains whether increases in striatal dopamine transporter density represent the primary neurochemical deficit or a secondary overcompensation (Castellanos & Swanson, 2002). According to Lou (1996) the striatum is the cerebral structure with the richest endowment of dopaminergic synapses, which is coherent with the finding of striatal dysfunction as an anatomical basis of ADHD (Lou, 1996; Zappitelli et al., 2001).

Figure 4.3 A neurobiological model of ADHD (Johansen et al., 2002)

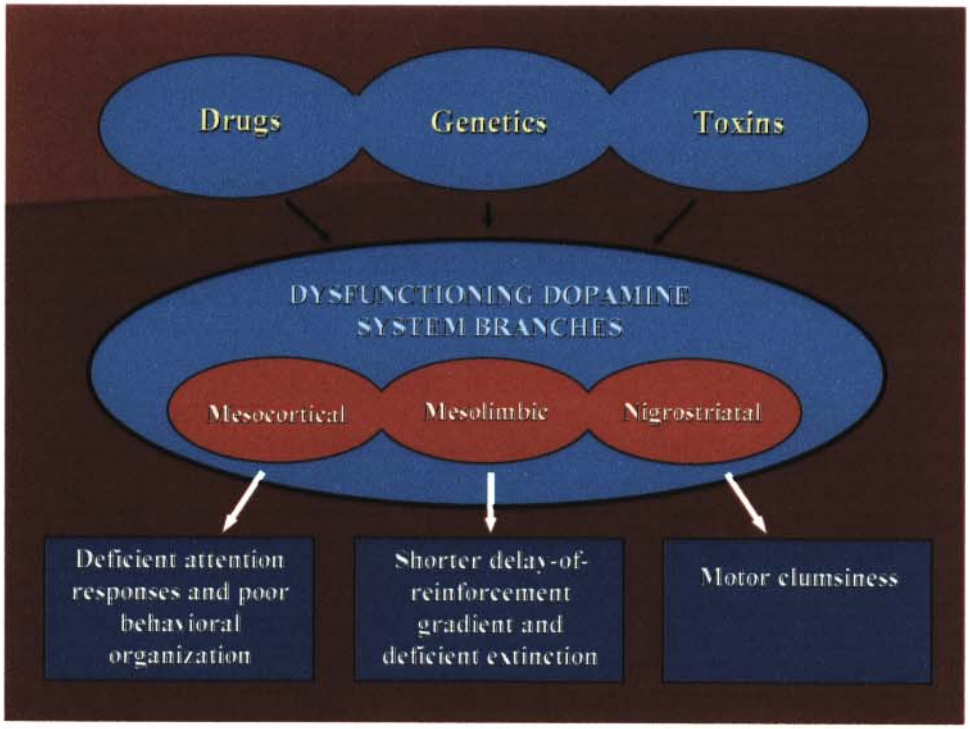


Figure 4.3 illustrates how a dysfunctioning dopamine system contributes to symptoms of ADHD.

Different abnormalities might exist in two dopamine regions: under-activity in a cortical region (anterior cingulate) that results in cognitive deficits and over-activity in a sub-cortical region (caudate nucleus) that results in motor excesses. Similarly different abnormalities may

exist in two noradrenergic regions: under-activity in the cortex (dorsolateral prefrontal) resulting in primary memory deficits and over-activity in a sub-cortical system causing over-arousal (Castellanos & Swanson, 2002). The pulvinar nucleus is a region of the thalamus that is related to attentional functions and projects to the occipital region (Giménez et al., 2004).

The principal finding regarding ADHD is heightened activity of genes that regulate norepinephrine, concurrent with diminished activity of genes that regulate dopamine and serotonin. Thus, no one gene or neurobiological abnormality in isolation can account for ADHD disorders (Cantwell, 1996; Hunt et al., 2001; Johansen et al., 2002; Sadock & Sadock, 2003). Whalen (2001) also emphasises that asymmetry and other structural brain differences vary among children with ADHD.

4.3.6.3 Anatomical differences in the brain

Alterations in frontal cortical and basal ganglia information processing may be central to the symptoms of ADHD (Böhm et al. 2004; Mercugliano, 1999). Barkley (2006), Castellanos and Swanson (2002), and Swanson et al. (1998) confirm reduced size of the frontal lobes and basal ganglia, as well as of the cerebellum (specifically the posterior inferior cerebellar vermis), which is consistent with the notion that the relevant brain areas are hypofunctioning. Inadequate activity in the prefrontal cortex of individuals with ADHD during attentional tasks is suggested (Hernandez et al., 2003; Hunt et al., 2001; Olness, 2003). The parietal and particularly the frontal cortex were also associated with selective and/or focused attention, and with control of attention (Fan, McCandliss, Sommer, Raz & Posner, 2002; de Fockert, Rees, Frith & Lavie, 2004; Olness, 2003). Research of Kalff et al. (2002) also suggests that the maturation of prefrontal structures in children at risk of ADHD at a later age lags behind that of children of the same age without ADHD. Restricted blood flow and activity in frontal areas in ADHD children are reported, which increase after administration of medication

(Grodzinsky & Diamond, 1992; Sadock & Sadock, 2003). Zappitelli et al. (2001) state that a dysfunction of the dopamine systems in the prefrontal cortex is regarded as the accepted neurochemical hypotheses behind the pathophysiology of ADHD. Hypoperfusion (poor blood flow) has been found in the striatum. The striatum is also a component of the executive attention network (Max et al., 2005). Structural and functional changes have been identified in the prefrontal cortex, striatum and cerebellum, including increased dopamine transporter density in the striatum (Asherson et al., 2005). According to Max et al. (2005) the prefrontal corticostriatopallidal pathways appear to subserve Posner's executive attention network, which is constituted by frontal mesial structures including the cingulated, supplementary motor area, prefrontal region and basal ganglia. Other studies however only found IVH grades 3 and 4 to be significant predictors of ADHD in extremely preterm children (Hoff et al., 2004). Accardo (1999) views ADHD as a neurological disorder itself. The mentioned neurological areas (frontal lobe, basal ganglia, cerebellum and striatum) involved in ADHD were also identified as vulnerable sites in children with LBW (see Section 2.6.3.1).

Inattention was best predicted by sequential problems, which depended on the child's capacity to sustain attention, to maintain auditory information in the working memory, to keep in mind temporal sequence (number questions, word memory, numerical memory subtest), and to recall the sequence in the same order for the latter two items (Nadeau et al., 2001). This factor relies on the components of working memory: The capacity to handle information is primarily prefrontal cortex-mediated, while processes necessary for working memory storage are primarily posteriorly mediated. The prefrontal cortex mediates the response-inhibition that allows working memory manipulation, as well as the ability to plan a sequence of action (to recall a list of words). This is also connected with the basal ganglia, and would fall within the

realm of EF (Nadeau et al., 2001). Thus, specific aspects of working memory can explain inattentive behaviour.

According to Sadock and Sadock (2003) major growth spurts normally occur in the human brain at several ages: 3 to10 months, 2 to 4 years, 6 to 8 years, 10 to 12 years, and 14 to16 years. A maturational delay in the sequence sometimes manifests itself and results in ADHD symptoms, which appear to normalise by about age 5.

4.3.6.4 Biological structures involved in low-birth-weight children with Attention-Deficit/Hyperactivity Disorder

A pattern of hyperactive behaviour was observed in the early 1900s when brain damage was expected, including factors such as birth injury or mild anoxia. This observation led to the concept of minimal brain damage/dysfunction, characterised by impairments in control of attention, impulse, motor function, perception, conceptualisation, language and memory, linked to deviations in the function of the CNS (Asherson et al., 2005).

According to Cherkes-Julkowski (1998) preterm children are at increased risk of developmental difficulties because the CNS is not fully organised at the time of birth for sustaining itself in the extra-uterine environment. Prematurity places a child at risk of failure to achieve the self-regulation required for autonomic function. Preterm children are also at risk of dysregulation of attention and arousal. Cherkes-Julkowski (1998) further postulates that attention regulation reflects the regulation of the CNS to a great extent. Children with a compromised CNS have difficulty regulating internal arousal well enough, in order to tolerate environmental stimulation. They tend to allocate arousal/attention resources to internal-state regulation rather than to the external stimulus field. These problems with attention have been found in almost all groups of premature children with disabilities at school age (Cherkes-Julkowski, 1998). Impairments in the development of the self-regulation of attention may

explain deficits in the acquisition of cognitive skills as well as other deficits (Winders & Burns, 2001). Specific variables may directly, indirectly or in both ways influence mechanisms and processes underlying the development of attention in LBW children.

Harrison (1996) confirms that children with birth weights below 1 000 g have specific biologically based problems of attention. Michelsson (1986) documents that prenatal insults and neonatal risk factors have an additive effect on the origin of neurodevelopmental disturbances. Relative immaturity of the cerebellum and the prefrontal cortex of ELBW infants may enhance vulnerability to injury or delayed development from prematurity and its associated complications, with the risk of attentional problems (Jeyaseelan et al., 2006).

Whitaker et al. (1997) state that PL/VE increases the risk of normal intelligent children of contracting any disorder, ADHD and separation anxiety, irrespective of gender or social advantage. Perinatal white matter lesions are correlated with ventricular enlargement and with ischaemic/infarctive lesions of the basal ganglia, brainstem and cerebellum. Cortical development might be adversely affected in preterms by germinal matrix haemorrhage/IVH and ischaemic white matter injury because of their effects on late migration, organisation and myelination. In spite of inconsistent results, white matter injury (PL/VE) seems to increase the risk of some psychiatric disorders at age 6 years in LBW children significantly, especially for ADHD (Hille et al., 2001; Saigal et al., 2003b; Whitaker et al., 1997). Thus, elevated rates of ADHD in LBW children do not seem to be caused by birth weight or gestational age independently, but by higher rates of PL/VE (Whitaker et al., 1997). Social advantage did not protect children with PL/VE from increased risk of psychiatric disorder (Whitaker et al., 1997). Krageloh-Mann, Toft, Lunding, Andresen, Pryds and Lou (1999) report that low oxygen delivery to the brain was found in 63% of children born preterm, in contrast to 12.5% in those with normal MRI, which indicates neonatal hypoxia-ischaemia as a significant factor.

MRI abnormalities were mainly periventricular lesions, especially PVL. Symptoms of ADHD were related to these mild MRI abnormalities. Premature infants are particularly prone to developing ADHD, owing to repeated hypoxic-ischaemic events with modest systemic circulatory failure. The striatum is vulnerable in these repeated hypoxic-ischaemic events, which may explain attention deficit (Lou, 1996). Whitaker et al. (1997) confirm that maturation of the striatum, which plays an important role in the improvement of behavioural inhibition that normally occurs in middle childhood, is deficient in ADHD. According to Lou (1996) the striatum has a significant role in intracerebral communication, receiving direct information from almost the entire neocortex, making the striatum vulnerable in repeated incidents of asphyxia with even modest systemic circulatory failure. These incidents occur commonly in premature infants.

Post-mortem studies demonstrated that ischaemic/infarctive white matter lesions were associated with ischaemic/infarctive lesions of the basal ganglia, as well as hypoperfusion (poor blood circulation). These findings are confirmed by structural and functional brain imaging studies of children with ADHD, which have found abnormalities in the basal ganglia, specifically the corpus striatum (caudate and putamen). The striatum receives dopaminergic input (the neurotransmitter mainly involved in ADHD) from the substantia nigra. Alterations of the dopaminergic system have been associated with ischaemic brain injury in human neonates. The striatal dopaminergic system seems to be more vulnerable to ischaemic injury than other striatal neurotransmitter systems. As these children undergo puberty, which is accompanied by cortical maturation and synaptic pruning, it is possible that PL/VE will increase the risk of disorders that typically have a later onset and in which abnormalities of cortical-basal ganglionic circuits have been implicated. However, this last statement needs further investigation (Whitaker et al., 1997).

White matter disturbances were related to attention deficits (Böhm et al., 2004) and increased risk of ADHD (Saigal et al., 2003b). Preterm birth in children with attentional impairments is associated with a regionally specific white matter disturbance within the internal capsules and posterior corpus callosum (Böhm et al., 2004; Nagy et al., 2003). These disturbances reflect impairment of myelination (Nagy et al., 2003) and interrupted axonal connectivity, which is essential for the development of integrated neural circuits involved in neural functioning (Böhm et al., 2004).

Harrison (1996) notes that the metabolic activity and blood flow patterns of children with suboptimal gestational or perinatal conditions showed hypoperfusion in the frontal lobe and symmetrically throughout both hemispheres of the brain. This finding is consistent with an aetiological role for early hypoxic-ischaemic lesions (for example PVL).

According to Stathis et al. (1999) the first two years of life is a critical stage for normal head growth and brain development. Cortical glial cell multiplication, myelination and growth of the neocerebellum are problems often associated with reduced head size during this critical period. Stathis et al. (1999) further postulate that a small head circumference or a fall in the rate of head growth during the first two years of life, particularly the first four months after birth, has been associated with long-term disability. IUGR and a small head size at 8 months in infants below 1 500 g at birth were predictors of cognitive dysfunction, poor academic achievement and behavioural problems at 8 years. However, HGV seems to be a poor predictor of future learning problems after 8 months of age. No association was found between head circumference or HGV and ADHD (Stathis et al., 1999).

Bhutta et al. (2002) document that 8-year-old children born preterm showed disproportionately smaller volumes of the sensori-motor cortex, other cortical areas, the

corpus callosum, amygdala, hippocampus (Abernethy et al., 2004; Bhutta et al., 2002) and basal ganglia. These smaller volumes were associated with significantly lower cognitive scores, an increased incidence of ADHD and other behavioural disorders. Nadeau et al. (2001) suggest that subplate neuron damage is associated with intellectual and attentional deficit. Bhutta et al. (2002) propose that the biological and environmental insults associated with preterm birth may promote some of these anatomical differences, since developing neurons are more vulnerable to cell death during the perinatal period. Adolescents born preterm and with attention deficit or low IQ showed reduced volumes of the caudate nuclei and the hippocampus (Abernethy et al., 2002; Marlow, 2004). The caudate nuclei receive inputs from the cortical regions involved in EF and attentional tasks. Their relative size within the brain, and between right and left nuclei, changes with maturation. This process may be interrupted by a variety of insults (Abernethy et al., 2002).

Lui et al. (2001) note that abnormal prenatal and perinatal brain development were suggested as the mechanisms in hyperactivity. Stathis et al. (1999) confirm that ADHD in ELBW children has also been associated with structural and functional changes in the developing brain. Bhutta et al. (2002) emphasise that physiological instability and exposure to early adverse experiences may have a persistent impact on brain development leading to negative cognitive and behavioural outcomes. According to Abernethy et al. (2002) attention deficit in children born with VLBW does not correlate with conventional markers of perinatal brain injury, but may be related to global brain growth and the development of key structures (such as the caudate nuclei and hippocampal formations). Other researchers postulate that perinatal brain injury may involve the white matter, which can affect long-term neurologic and cognitive development, including difficulties with attention (Nagy et al., 2003). These long-

term effects are either a result of the inability to repair the original lesions (e.g. PVL) or caused by a disruption of maturational processes.

Potgieter et al. (2003) conclude that reported poor attention in preterm children with ADHD cannot be explained by a simple maturational delay in the development of attention and inhibition mechanisms. In their study of event-related potentials during attention tasks they could not demonstrate a specific brain dysfunction in children born prematurely that could explain the higher incidence of ADHD in prematurely born children (Potgieter et al., 2003).

Neurological soft signs were associated with attention and externalising problems only in the LBW group. This excess in externalising problems was observed only at age 6 (Breslau et al., 2000). The higher prevalence of soft signs in LBW children and the wider range of psychiatric problems raise the possibility of suboptimal brain maturation due to perinatal complications (Breslau et al., 2000).

Oosterlaan et al. (2005) postulate that a developmental lag would imply that ADHD is associated with a delay in brain maturation (such as the frontal cortex and its subcortical connections), whereas a permanent impairment would suggest a neurological deficit that remains stable across development.

Breslau and Chilcoat (2000) conclude that the LBW-attention problems association in the urban community suggests interaction between biologic vulnerability associated with premature birth and environmental risk associated with social disadvantage.

4.3.6.5 Environmental factors

In the presence of a genetic predisposition to ADHD, environmental factors may enhance its expression (Jensen et al., 1997; Mercugliano, 1999; Taylor et al., 1998).

Environmental factors are also known to cause ADHD. These include the effects of foetal exposure to alcohol and benzodiazepines, as well as other adverse factors in pregnancy, such as pre-eclamptic toxaemia, maternal smoking, low foetal heart rate during labour and small head circumference at birth (Taylor et al., 1998; Taylor, Sandberg, Thorley & Giles, 1991). The mentioned environmental risk factors in ADHD (alcohol, drugs, smoking and pre-eclamptic toxaemia) are also significant risk factors in LBW (see Sections 2.4 to 2.6). Small head circumferences often occur in LBW children (Abernethy et al., 2002; Kilbride et al., 2004). Toxins, such as lead, alcohol, cigarette smoke or other drugs, appear to be capable of contributing to ADHD (Mercugliano, 1999). Zappitelli et al. (2001) state that maternal cigarette smoking leads to foetal hypoxia and nicotine causes disturbances to the dopaminergic system in the brain. Heavy alcohol use during pregnancy has been linked to Foetal Alcohol Syndrome (FAS), a condition that can lead to LBW, intellectual impairment and certain physical defects (Cantwell, 1996; Johansen et al., 2002). Many children born with FAS show much the same hyperactivity, inattention and impulsiveness as children with ADHD. Drugs such as cocaine (including the smokeable form known as crack) seem to affect the normal development of brain receptors.

According to Mercugliano (1999) suboptimal parenting skills and particular parenting characteristics have not been shown to cause ADHD. However, specific kinds of parent-child interaction are believed to be helpful or harmful to symptom expression. In a study of the effects of medication on parent-child interaction, it was found that medication that was effective for disruptive behaviour led to more positive mother-child interaction. This indicates that negative maternal behaviour was the result rather than the cause of the child's difficult behaviour (Mercugliano, 1999). However, Edwards et al. (1995) state that it is unclear whether observed family dysfunction is caused by having a child with ADHD, or whether the child's

misbehaviour is caused by parental and/or family dysfunction. Auerbach (2005) notes that non-optimal parent-child interaction and family adversity (e.g. marital stress, parental psychopathology) are associated with ADHD. Family adversity at age 5 predicted inattentive behaviours at age 7 years (Nadeau et al., 2001). Hoff et al. (2004) and Tully et al. (2004) found in their study with prematurely born 5-year-old children that sensitive parenting was associated with less externalising and less hyperactive behaviour. Oosterlaan (1996) notes that an environment that does not foster the inhibition of inappropriate responding could facilitate response inhibition deficits.

The minority of children are detectably affected by food additives and allergenic whole foods. However, results of studies on iron deficiency and supplementation, deficiencies in essential fatty acids, zinc and other minerals, and the relationship of behaviour to the relative dietary content of protein and carbohydrate suggest that further research in this area is indicated (Cantwell, 1996; Mercugliano, 1999). The National Institute of Mental Health (1996) emphasises that ADHD is usually not caused by too much television, food allergies, excess sugar, poor home life or poor schools.

According to Swanson et al. (1998) foetal distress due to environmental factors may damage striatal neurons and affect the development of the frontal lobe and basal ganglia neural networks.

The role of environmental factors in the expression of ADHD symptoms in premature children is unclear. However, available data indicate that ADHD symptomatology in premature children is associated with adverse social conditions such as lack of parental involvement, negative maternal attitude and lower SES (Chapieski & Evankovich, 1997). Low SES (often measured by parental education and subsequent parenting style and family

functioning) is considered a significant predictor of ADHD in the normal population (Sauver et al., 2004). Tripp (2005) found that lower SES was associated with increased perceptions of externalising child behaviour. Breslau et al. (1996a) report interaction between social class and VLBW in connection with hyperactivity and motor-visual coordination. Bhutta et al. (2002) confirm inconsistencies regarding the effect of SES on neurodevelopmental outcomes of preterms. However, a study of preterms found that family factors were stronger predictors of school performance than were perinatal complications (Gross et al., 2001). Cherkes-Julkowski (1998) also confirms that caretakers who can help their at-risk infants to self-regulate attention and arousal often have infants who achieve adequate CNS organisation and consequent richer opportunities to learn.

Robson and Pederson (1997) and Sato et al. (2004) found that attention problems were predicted by temperament, environment and the interaction between developmental status and quality of home environment. Children viewed as having a more difficult temperament in infancy continued to have more behaviour problems at school age (Saylor et al., 2003).

4.4 Oppositional Defiant Disorder

More externalising problems among children with LBW have been noted (Breslau & Chilcoat, 2000; Nadeau et al., 2001), which include a mix of impulsive, overactive, aggressive and delinquent acts (Mash & Wolfe, 2002).

4.4.1 Symptoms

ODD is considered as developmentally inappropriate negativistic, hostile and defiant behaviour lasting for at least six months and causing clinically significant impairment in social, academic or occupational functioning (American Psychiatric Association, 2000; Dick, Viken, Kaprio, Pulkkinen & Rose, 2005), including the following symptoms:

- Often losing temper
- Often arguing with adults
- Often actively defying adults or refusing to comply with their requests or rules
- Often deliberately annoying people
- Blaming others for his/her mistakes
- Often being touchy or easily annoyed by others
- Often being angry or resentful
- Often being spiteful or vindictive.

Symptoms usually emerge before the age of 8 years (American Psychiatric Association, 2000). Symptoms of behavioural impulsiveness or inhibition and social cognition are linked to DBDs (Burke, Loeber & Birmaher, 2002).

4.4.2 Prevalence

Various studies indicated a relationship between LBW and ADHD, but not with ODD or CD (Breslau et al., 1996b; Burke et al., 2002; Zappitelli et al., 2001). This association may be mediated by intellectual and neuro-motor delays associated with prematurity (Burke et al., 2002). According to Breslau et al. (1996a) ODD was the most common comorbid disorder in both LBW and NBW children with ADHD. Approximately 40% to 60% of children with ADHD, irrespective of birth weight, are comorbid for ODD. Wilens et al. (2002) also found that ODD and major depression were the most common comorbid disorders in both preschool and school age children in the general population.

4.4.3 Gender differences

The disorder appears to be more prevalent in males than in females in the general population before puberty (American Psychiatric Association, 2000; Mash & Wolfe, 2002), but

insignificant gender differences were observed after puberty (American Psychiatric Association, 2000). Males may display more confrontational behaviour and persistent symptoms than females (American Psychiatric Association, 2000). Levy et al. (2005) also found higher rates of ODD and CD in males, indicating that externalising disorders are more common in males. The relation between LBW, ODD and gender were not indicated in this literature survey.

4.4.4 Comorbidity

Comorbid ODD is often a precursor of CD, which is a more serious disorder with significant long-term consequences (Burke et al., 2002; Dick et al., 2005; Hechtman, 1999).

Kalff et al. (2002) also report that the performance of children with comorbid ADHD and ODD or CD is significantly impaired on tasks measuring EF, working memory and visual-motor ability compared to children with pure ODD/CD. Deficits in reading, IQ, academic performance and neuropsychological functioning have been linked to DBDs, though confounding factors such as comorbid ADHD, early psychosocial factors and gender differences should be considered (Burke et al., 2002). Comorbid disorders for ODD in the LBW cohort were not reflected in the literature consulted.

4.4.5 Aetiology

ODD appears to be more common when at least one parent has a history of a mood disorder, ODD, CD, ADHD, Antisocial Personality Disorder or Substance Dependence (American Psychiatric Association, 2000). Parental MDD increases the risk of DBDs in children (Biederman et al., 2001; Biederman et al., 2005). As indicated in Section 3.3.1.5.2, women with a history of psychiatric illness, substance use or both diagnoses had a significantly higher risk of delivering VLBW, LBW and preterm infants, even when adjusted for the effects

of known socio-demographic and medical risk factors (Kelly et al., 2002). Thus, a large number of LBW children seem to be geneticically predisposed to ODD.

Marital discord and inconsistent or neglectful child-rearing practices predispose children to oppositional behaviour (American Psychiatric Association, 2000). Ford, Racusin, Daviss, Ellis, Thomas, Rogers et al. (1999) found that ODD was associated with a history of victimisation trauma, independent of age, gender, parent education, family psychopathology, parent-child relationship, child internalising psychopathology and social competence. Hechtman (1999) determined that the ADHD children who were also comorbid for ODD had more negative mother-child interaction, more home conflicts, and greater maternal psychological distress, as well as a poor prognosis (Newcorn et al., 2005). Sixty percent of the ADHD group, but only 11% of the controls met criteria for comorbid ODD in adolescence.

Childrearing practices, such as degree of involvement, parent-child conflict management and monitoring, as well as harsh and inconsistent discipline, have been significant in children with disruptive or delinquent behaviour (Burke et al., 2002). Punitive discipline by parents was considered a common risk factor among children with oppositional, aggressive, hyperactive and internalising behaviour (Burke et al., 2002).

Social and economic risk factors, such as unemployment, neighbourhood violence, family poverty, childhood aggression, low SES and duration of poverty are associated with antisocial behaviour (Burke et al., 2002). Dieterich et al. (2004) and Stoelhorst et al. (2003) mention that children born preterm are more likely to be born into poverty or low SES (Section 2.5).

ODD was not related to PL/VE (Whitaker et al., 1997).

Lower levels of cortisol were associated with ODD, as well as both early onset and persistent aggression in sons of fathers with a childhood history of CD (Burke et al., 2002). A genetic deviation of the dopamine D2 receptor has been identified in a significant proportion of adolescents diagnosed as pathologically violent (Mash & Wolfe, 2002).

Other sequelae of VLBW may enhance more oppositional behaviour, such as motor deficits, lower IQ scores, educational impairment, shorter stature and poorer social skills (Botting et al., 1997).

4.5 Conduct Disorder

CD can be defined as the violation of the basic rights of others or major age-appropriate societal norms or rules (American Psychiatric Association, 2000).

4.5.1 Symptoms

The first significant symptoms usually emerge from middle childhood through middle adolescence (American Psychiatric Association, 2000; Dick et al., 2005).

Symptoms fall into the following main groupings: aggression to people and animals, destruction of property, deceitfulness or theft and serious violations of rules (American Psychiatric Association, 2000).

According to Dick et al. (2005) ADHD with CD may represent a more severe form of ADHD, while ADHD with ODD represents an intermediate phenotype between ADHD with CD and ADHD alone.

Oosterlaan et al. (2005) found that executive dysfunction is associated with ADHD, but not ODD or CD, specifically working memory. The effect of ADHD on EF was independent of the presence or absence of ODD or CD. Oosterlaan (1996) determined that CD children

were equally impaired in response and motor inhibition. Though executive dysfunction was also associated with CD, the majority of studies failed to find evidence for frontal lobe deficits (Oosterlaan, 1996). Mash and Wolfe (2002) note deficits in neuropsychological functioning, such as EF similar to ADHD and lower verbal IQ.

4.5.2 Developmental presentation

Symptoms of CD vary with age as the child develops increased physical strength, cognitive abilities and sexual maturity. The severity of symptoms usually increases with age. Behaviours such as lying or shoplifting tend to emerge first, whereas others (for example burglary and rape) emerge progressively later (American Psychiatric Association, 2000). Literature consulted did not refer to these developmental aspects in LBW children.

4.5.3 Prevalence

Most studies have not found an increased risk of anti-social behaviour among the premature group (York & DeVoe, 2002; Zappitelli et al., 2001) or CD among children born prematurely (Chapieski & Evankovich, 1997), or among VLBW adolescents (Indredavik et al., 2004) and mid-childhood (Saigal et al., 2003b), as long as the effects of adverse environmental conditions are controlled (Chapieski & Evankovich, 1997). Marlow (2004) notes that ADD in VLBW teenagers is more often associated with internalising symptoms of anxiety and depression than with CD. Aylward (2002) however is of the opinion that CD occurs more frequently in LBW children than in NBW peers. Lui et al. (2001) also observed markedly higher rates of delinquent behaviour in children with LBW and delayed development.

4.5.4 Gender differences

CD is more common in males (American Psychiatric Association, 2000; Levy et al., 2005; Mash & Wolfe, 2002), especially the childhood-onset type (American Psychiatric

Association, 2000). According to Mash and Wolfe (2002) the gender disparity increases through middle childhood and decreases or disappears completely by about age 15 years. Boys however remain more prone to violence throughout their lifespan (Mash & Wolfe, 2002). CD in males is more frequently characterised by fighting, stealing, vandalism, confrontational aggression and school discipline problems, whereas females exhibit more lying, truancy, running away, non-confrontational behaviour, substance abuse and prostitution. A previous study of school-age children born under 1 500 g identified an increased incidence of CD among males (Chapieski & Evankovich, 1997).

Burke et al. (2002) note that girls with CD, compared to boys with CD, report more daily stress, higher levels of emotion-focused coping, fewer active coping strategies and a higher frequency of self-harm. Family disruption is a significant risk factor for externalising problems in girls, but not boys (Burke et al., 2002).

4.5.5 Comorbidity

According to Mash and Wolfe (2002) about 30% to 50% of children with ADHD (in the general population) eventually develop CD. Substance abuse was mostly linked to CD, later antisocial behaviour, arrest and continuation of ADHD symptomatology (Hechtman, 1999). According to Chilcoat and Breslau (1999) children with a high level of externalising problems had a high risk of drug use (and vice versa), regardless of ADHD status. Thus, risk of early drug use in children with ADHD seems to depend on the level of externalising problems.

Mash and Wolfe (2002) mention a strong link between learning problems and antisocial behaviour, specifically school failure, academic underachievement in language and reading, as well as executive dysfunctioning. LBW children are at risk of these learning problems mentioned (Section 2.6.2) and executive dysfunctioning (Section 5.5) with subsequent possible

antisocial behaviour. ADHD however is a crucial mediating factor. Subtle language deficits may lead to reading and communication difficulties, which in turn may increase antisocial behaviour in elementary school (Mash & Wolfe, 2002).

According to Accardo (1999) many of the behavioural symptoms interpreted as consistent with CD and ODD are frequently simply reflections of undiagnosed and untreated ADHD. However, hyperactive behaviour in primary school children is considered to be a risk factor for the development of CD (Taylor et al., 1998).

4.5.6 Aetiology

4.5.6.1 Parental mental illness

Children are at increased risk of developing CD in the presence of biological parents with Schizophrenia, or a history of ADHD or CD (American Psychiatric Association, 2000), including Alcohol/Substance Dependence, mood disorders and Antisocial Personality Disorder (American Psychiatric Association, 2000; Burke et al., 2002). Biologically based traits, such as a difficult temperament or impulsiveness, may predispose children to develop aggressive and antisocial behaviour (Mash & Wolfe, 2002). As indicated in Section 3.3.1.5.2, women with a history of psychiatric illness, substance use or both diagnoses had a significantly higher risk of delivering VLBW, LBW and preterm infants even when adjusted for the effects of known socio-demographic and medical risk factors (Kelly et al., 2002). Thus, a large number of LBW children seem to be geneticically predisposed to CD.

4.5.6.2 Birth and pregnancy complications

Pregnancy (Burke et al., 2002) and birth complications (Burke et al., 2002; Mash & Wolfe, 2002) were also associated with the development of behaviour problems. LBW is often associated with pre-, peri- and postnatal complications, as reflected in Section 2.6.2.

Neurological soft signs at age 7 did not predict conduct problems at age 17 (Breslau et al., 2000).

4.5.6.3 Genetic influences

Dick et al. (2005) found that the comorbidity among CD, ADHD and ODD is primarily explained by shared genetic influences. This finding does not suggest that all these externalising disorders result from exactly the same genetic factors, as each also reflects some unique genetic influences. Some genes are general risk factors that increase the risk of externalising disorders. Other genetic factors contribute to symptoms specific to the individual disorder. Thus, ADHD, ODD and CD are not simply alternative manifestations of the same underlying genetic predisposition (Dick et al., 2005). Mash and Wolfe (2002) note that ADHD is usually associated with cognitive and neurodevelopmental difficulties, whereas CD is more often related to family adversity, parental psychopathology and social disadvantage.

4.5.6.4 Neurological factors

Mash and Wolfe (2002) note that a possible genetic deviation associated with alterations in the reward pathways of the brain has been linked to conduct problems and impulsiveness, involving a variant form of the dopamine D2 receptor gene. They further state that antisocial patterns of behaviour result from an overactive BAS and an under-active BIS, which are determined by a genetic predisposition. Consequently, children with conduct problems show heightened sensitivity to reward (consistent with an overactive BAS). They fail to respond to punishment and continue to respond under conditions of no reward, typical of an under-active BIS (Mash & Wolfe, 2002).

In the general population frontal lobe functioning, including decreased glucose metabolism, is associated with violence (Burke et al., 2002). Frontal lobe damage is indicated in aggression, especially orbitofrontal damage with impulsive aggression. Frontal lobe aggression is characterised by provocations to aggression and patterned aggressive responses, while temporal lobe aggression is characterised by responding to minimal provocation and without premeditation. Impaired functioning in the amygdala is associated with deficits in the interpretation of social cues, such as facial expression. A connection between the amygdala and prefrontal cortical regions aids in the suppression of negative emotion (Burke et al., 2002). These mentioned brain regions are referred to as vulnerable in LBW children (see Section 2.6.2)

Barlow and Durand (2002) note that abnormally low levels of cortical arousal are the primary cause of antisocial and risk-taking behaviours, which is consistent with the under-arousal hypothesis. Individuals seek stimulation in order to boost their chronically low levels. A general population-based sample of 15-year-olds indicated that lower skin conductance activity, lower heart rate during rest periods and more slow-frequency brain wave activity (all indicative of low arousal) predicted adult anti-social behaviour (Barlow & Durand, 2002).

Moreover, various neurotransmitters may be associated with the development of DBDs (Burke et al., 2002). A reduction in the turnover of serotonin is associated with aggression and other aspects of DBDs, especially in males. Serotonin however is also linked to mood disorders, impulsive behaviour, particular brain regions and other neurotransmitters. The link between serotonin and aggression reflects a more complex relationship between neuroanatomical and neurochemical interconnections, executive brain functions and behavioural dysregulation. Testosterone was also indicated in aggression, including early onset

aggression (Burke et al., 2002). Mash and Wolfe (2002) however mention that testosterone levels were more correlated with reactive than with unprovoked forms of aggression.

In general, conduct problems are associated with conditions that often accompany low SES (e.g. family adversity and stress, economic hardship, limited employment opportunities or residence in high-risk urban neighbourhoods) (Mash & Wolfe, 2002). Verbal IQ was consistently lower than performance IQ in children with conduct problems. As mentioned in Section 2.5, children born preterm are more likely to be born into poverty or low SES (Dieterich et al., 2004; Stoelhorst et al., 2003). Verbal deficits may increase the child's vulnerability to the effects of a hostile family environment (Mash & Wolfe, 2002). Family problems are among the strongest and most consistent correlates of antisocial behaviour, including general family disturbances (e.g. parental psychopathology and family instability) and/or specific disturbances in parenting practices and family functioning (Mash & Wolfe, 2002; Sadock & Sadock, 2003). Limited or negative interaction between LBW infants and caretakers during hospitalisation, as mentioned in Sections 2.6.3 and 3.3.1.5.3, may disrupt the bonding process between parents and infants (Perlman, 2001). Emotional and behavioural problems may be a psychological consequence of parental insecurity and anxiety in raising a preterm child (Hoff et al., 2004).

4.5.6.5 Other factors

Botting et al. (1997) note that ELBW children with hyperactivity were not developing antisocial behaviour or CD as frequently as matched peers who had also been recognised as hyperactive. This might imply a different aetiology or development of attention deficit in ELBW infants to that of NBW babies. The lower incidence of comorbid antisocial behaviour may also indicate that VLBW children may present with a "purer" form of ADHD than that found in the general population, for whom social factors may be more important (Botting et

al., 1997; Huddy et al., 2001) with a dominating neurological cause (Indredavik et al., 2004). Max et al. (2005) note that inattention may be more closely related to cognitive dysfunction than is the hyperactive/impulsive symptom dimension.

Burke et al. (2002) mention that maternal smoking during pregnancy predicted CD in boys.

4.6 Implications

The group with both hyperactivity and CD continued to have ADHD symptoms, aggressiveness, non-compliance, antisocial behaviour and alcohol use at follow-up. Adolescents with ADHD who were comorbid for CD indulged in more cigarette and cannabis use (but not alcohol) and experienced more school expulsions and suspensions (Hechtman, 1999). Hyperactive individuals had significantly higher juvenile (46% versus 11%) and adult (21% versus 7%) arrest rates. Conduct problems in childhood and serious antisocial behaviour in adolescence are considered to be significant risk factors for becoming an adult offender. The authors concluded that children with both hyperactivity and CD problems are at increased risk of later criminality (Dick et al., 2005; Fischer et al., 2002; Hechtman, 1999; Olson, 2002; Spencer et al., 1999). ADHD teenagers with more pronounced comorbid ODD and CD symptoms seem to be at highest risk of defiant driving skills or habits and negative driving-related outcomes (Abikoff et al., 2002).

Mash and Wolfe (2002) summarise the aetiology of antisocial behaviour in Table 4.3

Table 4.3 Causal influences of early-onset antisocial behaviour (Mash & Wolfe, 2002, p 156)

Biological/constitutional	Developmental	Family/environment
Male gender	Disruptions in attachment	Marital discord
Genetic risk	Early-stage social-cognitive deficits and distortions (reactive aggression type)	Discordant parent-child interactions
Neuropsychological deficits	Later-stage social-cognitive pattern (proactive aggression subtype)	Child abuse
Lowered verbal IQ and verbal deficits		Low SES
Lowered arousal and reactivity		Poor neighbourhood
ADHD		

4.7 Conclusion

LBW children seem to be at significant risk of externalising disorders (ADHD, ODD and CD). Evidence is strongest for the prevalence of ADHD. Inconsistent findings were indicated for ADHD, ODD and CD.

Biological (e.g. genetics, neurological insults and dysfunctioning), developmental and environmental (e.g. suboptimal parenting, SES) risk factors associated with prematurity/LBW may promote vulnerability to externalising psychological symptoms. Problem areas that develop as sequelae of LBW may be in reciprocal interaction, enhancing the expression of behavioural disorders.

ADHD is a debilitating neurological disorder and considered to be a marker for other psychiatric and developmental conditions. Children experiencing externalising disorders seem to be at risk of negative long-term consequences (e.g. lower cognitive functioning, anti-social behaviour).

NEUROPSYCHOLOGICAL FUNCTIONING OF LOW BIRTH WEIGHT CHILDREN

5.1 Introduction

The main focus of this study is to investigate the internalising (see Chapter 3) and externalising (Chapter 4) psychological disorders associated with LBW, as well as neuropsychological functioning among current primary school children born with LBW.

The neuropsychological sequelae of LBW have been investigated by numerous researchers, reporting neurological (Dewey et al., 1999; Hack et al., 2000; Nadeau et al., 2001; Perlman, 2001; Pietz et al., 2004; Reiss et al., 2004; Saigal et al., 2001; Sajaniemi et al., 2001; Tully et al., 2004; Vohr et al., 2000), neurodevelopmental (Huddy et al., 2001; Indredavik et al., 2004), neurosensory (Huddy et al., 2001; Taylor et al., 2000b), cognitive (Bhutta et al., 2002; Breslau & Chilcoat, 2000; Breslau et al., 1996a; Dieterich et al., 2004; Indredavik et al., 2004; Lawson & Ruff, 2004; Peterson et al., 2002; Richards et al., 2001; Saigal et al., 2001; Sajaniemi et al., 2001; Taylor et al., 2000a; Tully et al., 2004), educational or learning (Huddy et al., 2001; Sajaniemi et al., 2001); psychiatric (Indredavik et al., 2004), behavioural (Breslau & Chilcoat, 2000; Breslau et al., 1996a; Huddy et al., 2001; Peterson et al., 2002; Potgieter et al., 2003; Sajaniemi et al., 2001; Taylor et al., 2000a; Tully et al., 2004) and other impairments.

These global impairments may be explained by reciprocal multiple aetiological factors associated with preterm birth or growth restriction. Neuropsychological impairments occur partially as a result of the sequelae of medical complications often associated with preterm birth, such as hypoxia, IVH and respiratory distress syndrome that directly or indirectly compromise the CNS (Curtis et al., 2002). Thus, many clinical factors (e.g. CLD), as well as

stressful environmental conditions in hospital, multiple medication, infant-provider interaction, constant noise and bright light, may act in combination to make an impact on the developing brain, even in the absence of haemorrhage and/or ischaemia (Perlman, 2001). These clinical factors and environmental conditions affect vulnerable brain areas (Perlman, 2001) - see Section 2.6.3.

Neurological abnormalities are considered to be the primary cause of cognitive deficits in preterm children, although the exact nature of the association between such abnormalities and specific cognitive impairments in children born preterm is not well established (Curtis et al., 2002).

Accumulating evidence indicates that children born preterm have identifiable brain abnormalities (as indicated under Section 2.6.3). Cognitive tasks measured by neuropsychological tests were used in this study, similar to the investigation by Espy (2004), to understand the nature of brain function in children born with LBW. Anderson et al. (2004) also emphasise that identifying the nature of cognitive deficits associated with premature birth will provide some indication of the neural systems compromised.

Longitudinal investigations of the impact of LBW on functioning on different levels indicated contradictory findings on prognosis. O'Brien et al. (2004) found deterioration in neurodevelopmental functioning, including cognitive and neurological measures, in preterm children between the ages of 8 and 15 years. A proportion of children with previously normal functioning had mild impairments at 15 years, such as lower full-scale IQ. De Haan et al. (2000) note that by the second year of life even low-risk preterm infants cannot be assumed to have 'caught up' with term children in all aspects of cognitive development. Rickards et al. (2001) found that the VLBW children continued at age 14 years to lag behind in cognitive

development, just as they did at 2.5 and 8 years. Pietz et al. (2004) note that children who were apparently neurologically normal during infancy and preschool years, showed significant neuropsychological and behavioural deficits at school age. Aylward (2002) also confirms the worsening outcome of ELBW and VLBW children as they become older, due to possible underlying cognitive deficiencies to meet increasing, higher-level demands. Brandt et al. (2000) postulate that abnormal neurological signs were observed mainly during the first year and that these abnormalities reappeared when new abilities developed. They concluded that all the SGA children in their study with complete catch-up growth of head circumference with abnormal neurological signs beyond the first year became normal by the age of 17 years. Tideman (2000) also found that group differences at age 4 were no longer observed at 9 years of age, including no overall significant differences between preterm and term children at 19 years of age. According to Curtis et al. (2002) the period from middle childhood to the beginning of adolescence is characterised by continued protracted maturation of the prefrontal cortex, with myelination of the frontal cortex continuing into early adulthood, as well as continued development of synapse neurotransmitter systems into adolescence. Thus, ongoing neuropsychological review throughout middle childhood is essential (Anderson et al., 2004).

According to Böhm et al. (2004) there are five domains evaluating basic function, according to the tradition of Luria: attention, impulse control and organisation, language functions, sensori-motor functions, visual-spatial functions and memory. All these functions mentioned, except language (due to time constraints), were investigated in this study. Additionally, internalising, externalising and neuropsychological problems have an adverse impact on the family system. The neuropsychological tests administered for measurement of the specific functions will be indicated under the respective discussions.

5.2 Motor dysfunctioning

According to Dewey et al. (1999) motor and visual-motor problems may be particular areas of vulnerability, especially for children with VLBW. Visual- and perceptual-motor problems may be interrelated disorders (Torrioli et al., 2000).

Kilbride et al. (2004) mention that psychomotor disabilities were most pronounced in infants with the lowest birth weight, which suggests a gradient effect of prematurity on outcome. Children born with birth weights of below 750 g were found to be at higher risk of perceptual-motor difficulties than those weighing above 750 g.

The Grooved Pegboard (see Appendix N) and Rey-Osterrieth Complex Figure (ROCF) Test (Appendix O) were used for measurement of fine motor functioning. The Grooved Pegboard measures motor control (Lezak, Howieson & Loring, 2004), particularly complex fine motor coordination (Meyer & Sagvolden, 2006b), and psychomotor speed (Elgen et al., 2003; Meyer & Sagvolden, 2006b). Visual-motor integration (Frisk et al., 2002) and perceptual-motor functions (Bosson, Holland, & Barrow, 2002; Caffarra, Vezzadini, Dieci, Zonato & Venneri, 2002) were assessed with the ROCF Test.

5.2.1 Prevalence

Deficient neuro-motor/psychomotor abilities were reported among 2-year-old premature children (Stoelhorst et al., 2003), ELBW premature infants at school age (Blondis, 1999; Cuddihy, Anderson, Wells & Darlow, 1999; Marlow, 2004), 6-year-old LBW children (Whitaker et al., 1997), 31% of 7-year-olds born between 32 and 35 weeks' gestation (Huddy et al., 2001), extremely preterm/VLBW children (Jeyaseelan et al., 2006; Nadeau et al., 2001), 8-year-old children (Rickards et al., 2001) with birth weights below 2 000 g (O'Brein et al., 2003),

and among VLBW children (Dewey et al., 1999; Klebanov & Brooks-Gunn, 1994; Taylor et al., 2000a).

Visual/perceptual-motor skills: Visual-motor integration skills were one of the compromised developmental areas among VLBW children (Dieterich et al., 2004; Hemgren & Persson, 2004). Even in the absence of neonatal brain disorders, VLBW preschool children had significantly lower scores in perceptual-motor abilities (Torrioli et al., 2000) and motor abilities (Burns, O'Callaghan, McDonell & Rogers, 2004). Even in VLBW children who were developing normally at age 3, motor and visual-motor deficits were significant at school age (Aylward, 2002; Dewey et al., 1999).

Gross and fine motor skills: Aylward (2002) notes that former VLBW and ELBW children with normal IQ have problems with fine and gross motor functioning, with fine motor problems as high as 71% in ELBW children. Very preterm children with good co-ordination had significantly more deviations in gross and fine motor performance at age 3 than their term counterparts (Hemgren & Persson, 2004). Transient abnormal neurologic signs (e.g. fine and gross movements, tone, reflexes and excitability) and a reduced recovery rate were more significant in the SGA group, with normal outcome at 2 years (Brandt et al., 2000). Haycock (2004) also observed significantly affected fine motor skills in primary school children born with LBW.

DCD: Hemgren and Persson (2004) mention various previous studies indicating deficits in neuro-motor competence or psychomotor development in VLBW children, which are often labelled as 'clumsiness' or DCD. Holsti, Grunau and Whitfield (2002) found that 51% of the ELBW children they studied met criteria for DCD, which can be defined as difficulties with movement and spatial organisation.

Transient dystonia: Transient dystonia, also referred to as faulty muscle power regulation, has been identified among approximately one third of the preterm population in early infancy (Cameron, Maehle & Reid, 2005). It is suggested that transient dystonia has a non-neurological aetiology, with a predominance of hyperextension of the trunk and extensor tone of the lower limbs. It has been linked to motor difficulties in early infancy and motor performance at school age (Cameron et al., 2005).

Significant motor impairments were not indicated in all investigations. Term SGA preschoolers and 6-year-olds differed little from their appropriate for gestational age (AGA) peers regarding neuropsychological profile and neuro-motor outcome (Sommerfelt, Sonnander, Skranes, Andersson, Ahlsten, Ellertsen et al., 2002).

Developmental changes in motor development are largely qualitative from 2 to 4 years (Hemgren & Persson, 2004). O'Brien et al. (2004) found a significant improvement in motor skills in VLBW children without major neurodevelopmental impairment from 6 to 8 years. No further changes at 12 to 13 years were observed, but neuro-motor impairments occurred in 51% of the cohort instead.

Lee, Chow, Ma, Ho and Shek (2004) report significantly lower scores in VLBW children, who were monitored for three years up to the age of 5 to 7 years. Early intervention did not facilitate developmental catch-up of motor performance delay. O'Brien et al. (2004) note that it is not clear if the decrease in neurodevelopmental outcome from 8 to 15 years is due to a genuine deterioration in neurocognitive function or to the expression of pre-existing cerebral pathology in an increasingly complex environment.

5.2.2 Implications

Liebhardt, Sontheimer and Linderkamp (2000) mentioned that impaired copying of geometrical figures was significantly related to later reading problems. Visual-motor problems have an impact on mathematics (Aylward, 2002), written language (Aylward, 2002; Dewey et al., 1999) and reading problems (Aylward, 2002). Deficits in spatial ability, attributed to the hippocampus, may underlie difficulties with mathematics, because of the spatial component involved in numerical skills (Isaacs et al., 2000). Breslau et al. (2001) state that mathematics is more strongly related to non-verbal processing, including visual-perceptual and motor functions. Reading also involves visual-spatial components (Lezak et al., 2004). Children with fine motor or fine and gross motor problems are vulnerable to poorer reading and arithmetic skills, compared to children with only gross motor difficulties (Holsti et al., 2002). Development occurs according to a sequence from basic concept formation, visual-perceptual skills, visual-motor integration to cognitive development. Motor skills develop from gross, diffuse activities to fine movements (Berk, 2006). Thus, well-developed fine motor skills are the gateway to higher cognitive development. Visual-spatial problems, poor mathematic ability, attention deficit, low IQ, visual problems and poor social skills often co-occur with minor motor impairment, which suggests a cortical developmental problem (Abernethy et al., 2003). Thus, visual- and perceptual-motor skills may be interrelated functions (Torrioli et al., 2000), subscribed by overlapping neural networks.

Motor difficulties in ELBW infants at 2 years were associated with later clinical measures of attention and cognitive deficits (Jeyaseelan et al., 2006). Disruption of shared or independent neurological pathways between the cerebellum and prefrontal cortex may result in abnormal development and functioning of both motor and attention abilities.

Holsti et al. (2002) note that children who were labelled as clumsy in elementary school continued to experience motor difficulties at ages 15 to 17 years. They are also more prone to behavioural problems and high-risk behaviour, including suicide, drug use, bullying and poor concentration, as well as a higher risk of psychiatric disorders.

Poor postnatal growth was associated with poorer motor and cognitive outcome at school age. Early psychomotor retardation was considered an important predictor of later mental retardation (Pietz et al., 2004). In a previous study delayed walking was a good marker for morbidity by age 3 years.

Pietz et al. (2004) also mention that problems of language and visual-motor functioning in the preschool years of children born preterm seem to be precursors of later learning disabilities. Poor motor skills in the LBW cohort were markers of later learning difficulties and problems with school activities (Cooke & Abernethy, 1999; Huddy et al., 2001). Burns et al. (2004) postulate that minor neurological, motor and coordination problems are the major predictors of school failure. Elgen et al. (2003) found that motor problems and low verbal IQ at 5 years of age in LBW children each doubled the risk of experiencing a school problem at 11 years of age. Even children with minimal movement problems functioned on a lower cognitive level. Dewey et al. (1999) showed that intellectual and memory deficiencies were consistently associated with poor visual-motor production. Thus, motor and cognitive development are fundamentally related processes, which may be explained by the involvement of the striatum and neocerebellum in many cognitive processes (Burns et al., 2004). Perlman (2001) confirms abnormalities in both motor and cognitive functions in sick premature infants, produced by striatal injury.

Thus, fine motor and visual/perceptual-motor skills investigated in this study play a significant role in academic skills such as mathematics, language, reading, writing and learning.

It is important to note that some areas of development, such as motor and neurological function, show lags (early delays but with subsequent catch-up), while others such as cognitive and expressive language, may represent deficits (early delays that reflect persistent problems) (Aylward, 2002).

5.2.3 Gender differences

DCD seems to be more common in boys of the full-term population. No differences were observed in the rates of DCD between ELBW boys and girls (Holsti et al., 2002). Lee et al. (2004) only determined a significant difference between female VLBW children, aged 5 to 7 years old, and their NBW counterparts, possibly because the VLBW female survivors had lower birth weights and were more premature than the VLBW male survivors.

Sajaniemi et al. (2001) mention that preterm boys tend to be neurologically more vulnerable and have more visual-motor problems than preterm girls. Preterm boys may have a twofold risk of developmental problems. Consistently however no significant gender differences in visual-motor abilities were observed, though girls tended to have better results (Liebhardt et al., 2000).

5.2.4 Aetiology

Abernethy et al. (2003) found a high prevalence of minor motor impairment and lower IQ in preterm children, even in the absence of major neurodevelopmental sequelae at primary school age. Other studies in contrast found that VLBW preschool children born at higher medical risk had difficulty with motor and neurological development (Dieterich et al., 2004).

5.2.4.1 Brain injury

VLBW children are at major risk of severe motor, perceptual, cognitive and behavioural disorders due to frequent perinatal brain damage (Torrioli et al., 2000). Lui et al. (2001) also note that abnormal prenatal and perinatal brain development was suggested as the mechanisms in subtle visual-motor abilities. Perinatal insults to the brain, such as ventricular haemorrhages, prolonged oxygen therapy, abrupt changes in arterial blood pressure and hypoxic-ischaemic encephalopathy may underlie deficient neuro-motor control (Brandt et al., 2000). Haemorrhagic parenchymal infarction, cystic PVL (Abernethy et al., 2003; Maalouf, Duggan, Counsell, Rutherford, Cowan, Azzopardi et al., 2001) and most commonly diffuse non-cystic white injury increase the risk of developing motor, cognitive and other impairments (Maalouf et al., 2001). Localised insults to periventricular and subcortical white matter were also observed in other studies (Taylor et al., 2000a). Cooke and Abernethy (1999) however found that PVL occurred with equal frequency in 8-year-old premature children with minor motor dysfunction and in those considered to be clinically normal.

Bleeding in the germinal matrix extends to the subependymal, ventricular or parenchymal regions, in the last case most commonly having an adverse impact on motor development. IVH may coexist with a terminal vein obstruction and lead to asymmetric white matter damage. An extensive lesion of this kind can result in motor deficits (Valkama et al., 2000).

Valkama et al. (2000) state that ventricular enlargement often occurs after large-scale IVH, but especially when the posterior horn is involved, it has been found to be associated with end-stage PVL in VLBW infants. Wide CSF spaces occur owing to poor resorption of fluid after haemorrhage or to brain atrophy. Preterm infants may have wider CSF spaces without significant consequences, such as cerebral palsy. However, gross and fine motor

impairments were observed in another study of non-disabled VLBW children who had gliosis, ventricular dilatation and/or cortical atrophy at the age of 6 years (Valkama et al., 2000).

Sola et al. (2005) note that 25% of infants with a birth weight of 500 g to 750 g, and more than 10% of those weighing 750 g to 1 000 g develop severe IVH, which is associated with a high mortality rate, major motor deficits and cognitive delay. Other studies confirmed that grades 3 and 4 IVH have been shown to result in a significantly higher rate of motor problems compared with gestational age- and birth weight-matched controls within 3 and 7 days of life (Verma et al., 1997).

A correlation between minor motor impairment and IQ and visible lesions on the MRI scans (e.g. PVL, ventricular dilation, thinning of the posterior part of the corpus callosum) was observed (Abernethy et al., 2003). These changes may imply gross loss, atrophy, or gliosis of periventricular white matter after the perinatal period. Different types of lesions have different outcomes. Cooke and Abernethy (1999) did not identify significant differences in motor clumsiness between VLBW children with MRI lesions and those with normal scans.

5.2.4.2 Brain volume

Rademaker et al. (2004) found a clear relation between motor performance (including visual-motor integration) and the size and shape of the corpus callossum (total midsagittal cross area as well as middle and posterior area, except for the frontal area) at the age of 7 or 8 years, with a birth weight of below 1 500 g or birth before 32 weeks. This finding relates with volumetric studies where the volume of the white matter was found to be smaller in preterm children. Haemorrhagic or ischaemic focal infarction was the most common aetiology of reduction of the size of the corpus callosum (Rademaker et al., 2004). Cooke and Abernethy (1999) did observe a smaller corpus callosum in the preterm infants, but it did not relate to

motor or learning problems. Previous studies found that the cortical volumes of preterm children were smaller in the sensori-motor and premotor cortical regions, as well as in the basal ganglia and corpus callosum (Nagy et al., 2003).

Minor motor impairment was significantly associated only with total brain volume and was more common in children with evidence of thinning of the posterior corpus callosum, though most children with minor motor impairment have a normal corpus callosum (Abernethy et al., 2004). Curtis et al. (2002) however postulate that decreased brain volume per se may not severely impair neurocognitive development, possibly because of compensatory mechanisms such as increased density of synapses, re-wiring of connecting circuits and maximising of the efficiency of neural wiring in the reduced cortical substrate. Rademaker et al. (2004) note a normal increase in the volume of the corpus callosum during childhood. An examination is usually performed at the age of 2, when myelination is more or less completed and changes in the corpus callosum are already present. Cerebral lesions were associated with lower IQ and more minor motor impairment at 7 years of age (Abernethy et al., 2004). Motor clumsiness has been ascribed by some researchers to maturational delay, but by others to early cerebral injury (Cooke & Abernethy, 1999). The preterm group particularly demonstrated differences in the temporal lobes and deep cerebral (peri-striatal) regions. The white matter tracts within these areas play important roles in behaviours such as sensori-motor function, attention, emotion, reading and language (Reiss et al., 2004).

5.2.4.3 Delayed neural maturation

Hemgren and Persson (2004) attribute a delay in neural maturation to deficient motor development in very preterm children at age 3.

Valkama et al. (2000) note that delayed myelination provides useful information for predicting poor motor outcome in studies of full-term and preterm infants after the age of 1 month. Delayed myelination may be expected during complicated perinatal courses, which involve a disturbance in the circulation and nutrition (haemorrhage, ischaemia or infarction) in areas where active myelination processes occur. Premature infants are subjected to oxidative stress from various sources and to nutritional deficiencies, which may potentially lead to cerebellar damage (Cuddihy et al., 1999). Preterm infants with optimal nutrition seem to reach normal myelination at term age (Valkama et al., 2000).

5.2.4.4 Head growth

Frisk et al. (2002) mention that SGA children whose head growth slowed significantly prior to 26 weeks' gestational age obtained lower perceptual-motor scores at 4 years of age. Visual-motor integration skills can however develop to normal levels, provided that adequate postnatal head growth occurs. Frisk et al. (2002) concluded that both the gestational age at onset and the duration of the brain growth compromise are critical determinants of whether perceptual-motor impairments, particularly visual-motor integration difficulties, will be observed. According to Cuddihy et al. (1999) poor cerebellar growth may be related to deficits in visual-motor integration and clumsiness. Other studies reported no association between brain measurements and motor clumsiness in VLBW children at ages 12 to 13 years (Torrioli et al., 2000).

5.2.4.5 Postnatal treatment

Delayed mental and psychomotor outcome were associated with postnatal dexamethasone treatment of infants with respiratory problems (Stoelhorst et al., 2003).

5.2.4.6 Disease

Approximately 30% of very preterm infants suffer from CLD. CLD per se seems to have an unfavourable effect on the psychomotor performance, such as hand and eye coordination, perception and intelligence of 3-year-olds who were born very preterm (Katz-Salamon, Gerner, Jonsson & Lagercrantz, 2000). CLD predisposes VLBW infants to neurological sequelae, compared to those without CLD. Katz-Salamon et al. (2000) further postulate that the impaired development of infants with CLD can rather be linked to IVH and/or PVL than to lung disease per se. Early motor developmental delay or impairment may be indicative of a central or peripheral neurological disease (Lui et al., 2001).

5.2.4.7 Environment

According to Dewey et al. (1999) biological risk factors (for example LBW, early gestational age, respiratory distress syndrome) are more likely to be associated with motor and perceptual difficulties, whereas social factors (for example mother's education, family SES) are rather associated with language, overall cognitive and behavioural functions. Medical risk factors (e.g. lower gestational age) and neurological abnormalities were associated with delayed mental and/or psychomotor outcome (Stoelhorst et al., 2003). They also note that social factors become more important as children grow older. Liebhardt et al. (2000) postulate that the influence of social factors on the cognitive and neurological outcome of VLBW children increases with age, whereas the impact of peri- and neonatal factors diminishes. In contrast, subtle motor changes were related to biological injury and were not significantly influenced by SES (Kilbride et al., 2004).

5.2.4.8 Nutrition

Intrauterine under-nutrition, undetectable lesions and socio-economic factors may be responsible for functional impairments, such as lower perceptual-motor abilities (Torrioli et al., 2000).

Georgieff and Innis (2005) note that early iron deficiency (in rats) had significant effects on the developing dopaminergic system, particularly in the basal ganglia, which subserves memory and motor function. A decade ago the functions of the basal ganglia and cerebellum were restricted to motor control (Ravizza & Ivry, 2001). The output from both structures project to the prefrontal cortex. The basal ganglia and cerebellum however have been implicated in non-motor aspects of cognition as well (Ravizza & Ivry, 2001). Thus, identifying restricted brain regions subserving specific functions should be done with caution, as these regions appear to be interconnected.

5.3 Visual-spatial dysfunctioning

According to Liebhardt et al. (2000) visual-spatial problems were identified as the primary deficit experienced by preterm children. VLBW children seem to have a central deficit in processing different stimuli at the same time, such as is required in visual-motor integration or logical reasoning (Wolke, 1998).

The ROCF Test (Appendix O) was used to measure visual-spatial functioning (see Section 7.4.6).

5.3.1 Prevalence

Aylward (2002) notes that VLBW and ELBW children with normal IQ have problems with spatial and visual-motor skills. These deficits include copying, perceptual matching, spatial processing, finger-tapping, pegboard performance, visual memory, visual-sequential

memory, visual-perceptual and visual-motor integration. The lower the birth weight, the greater the likelihood of these problems (Aylward, 2002; Dewey et al., 1999).

Visual-spatial deficits were observed in SGA children at age 5 years (Sommerfelt et al., 2002) and ELBW children, even after controlling for IQ (Taylor et al., 2000a). Vicare, Caravale, Carlesimo, Casadei and Allemand (2004) also confirm difficulty in visual-spatial processing among preterm, LBW preschool children (3 to 4 years) without evident brain disorders and normal cognitive functioning. Rickards et al. (2001) observed deficits in visual processing, visual memory and visual-perceptual organisation at age 8 and 14 years in LBW children. Visual-spatial/-perceptual impairments in LBW and VLBW children at school age have also been noted in other studies (Elgen et al., 2003; Klebanov & Brooks-Gunn, 1994; Taylor et al., 2000a). Difficulties in spatial organisation and mental flexibility were indicated to increase as birth weight decreased (Anderson et al., 2004).

5.3.2 Implications

Bellinger, Bernstein, Kirkwood, Rappaport and Newburger (2003) found that a deficit in mathematics is a frequent comorbid condition among those with visual-spatial impairments. Dewey et al. (1999) note that VLBW children with perceptual problems are more likely to have problems in cognition, reading and behaviour, to have shorter gestation, and to have more frequently shown a brain lesion shortly after birth.

5.3.3 Gender differences

Males appear to have an advantage in visual-spatial tasks (Hindmarsh et al., 2000; Taylor et al., 2000a). On the contrary, Sajaniemi et al. (2001) observe that preterm boys tend to have more visual-perceptual problems than preterm girls.

5.3.4 Aetiology

5.3.4.1 Pre-, peri- and postnatal development

Lui et al. (2001) note that abnormal prenatal and perinatal brain development have been suggested as the mechanisms in visual-perceptual deficits. Breslau et al. (1996b) and Hille et al. (2001) state that brain injury, as well as abnormal brain development during the prenatal and perinatal stages, have been suggested as the mechanisms in subtle visual-motor and visual-perceptual deficits, as well as hyperactivity in preterm children. According to Taylor et al. (2000a) tests of perceptual-motor abilities are more sensitive to the effects of IVH and hydrocephalus in preterm children than are other neuropsychological measures. Localised insults to periventricular and subcortical white matter were observed (Taylor et al., 2000a). Morphometric studies demonstrated abnormalities in the right ventral extrastriate cortex and left parietal lobe of VLBW children with visual-spatial and calculation deficits respectively (Kesler et al., 2004). Dewey et al. (1999) mention that VLBW children with perceptual problems tend to have more frequently shown a brain lesion shortly after birth.

5.3.4.2 Neurological factors

According to Isaacs et al. (2000) it is possible that a deficit in spatial ability among 13-year-old VLBW children can be attributed to the hippocampus, which may underlie difficulties with mathematics, owing to the spatial component in numerics. Compromised visual processing in children born preterm may be due to differences in the timing of development of the dorsal (spatial) visual pathway and ventral (form) visual pathway (de Haan et al., 2000). The pulvinar nucleus is a region of the thalamus that is related to visual-spatial functions and projects to the occipital region (Giménez et al., 2004).

Caffarra et al. (2002) state that patients with posterior brain lesions (for example parietal-occipital) have difficulties with spatial organisation of the ROCF drawing, while patients with

anterior lesions (mainly in the frontal lobe) show impairment in their strategic approach to reproduction.

5.3.4.3 Environment

Aylward (2002) notes that visual-motor integrative and visual-perceptual problems are not related to social class or other environmental influences, but are associated with biological risk. Maalouf et al. (2001) mention that very preterm infants without definite cranial ultrasound abnormalities are at risk of deficits in the cognitive, visual-spatial and visual-motor domains.

5.4 Memory dysfunctioning

Immediate verbal recall, working memory, as well as immediate and delayed visual-spatial memory, were investigated in this study.

Working memory is described as the process of temporarily storing information in memory, including the ability to manipulate the stored information (Boonstra et al., 2005; Donohoe, Corvin & Robertson, 2005; Golob & Starr, 2004). This process is essential in more sophisticated capabilities such as reasoning, planning and language comprehension. Working memory comprises encoding, maintenance and retrieval phases.

The memory for digits (forward and backward) subtests of the Senior South African Individual Scale – Revised (SSAIS-R) (Appendix P) were used for auditory short-term memory and working memory respectively (Section 7.4.7). The ROCF Test (Appendix O) tapped working memory, immediate and delayed recall, as well as visual-spatial memory (Section 7.4.6).

5.4.1 Prevalence

Aylward (2002) notes that former VLBW and ELBW children with normal IQ have problems with memory. VLBW children free of sensori-neural impairments experienced significant memory problems (Dewey et al., 1999). Impairments of everyday memory were identified in adolescents born prematurely (Abernethy et al., 2004; Isaacs et al., 2000) and 13-year-old VLBW children (Isaacs et al., 2000).

Curtis et al. (2002) report previous findings of school age preterm children demonstrating deficits on behavioural measures of immediate and delayed memory, memory of spatial sequence, recognition memory, non-verbal memory span and spatial working memory. Taylor et al. (2000b) found significant differences in verbal memory, delayed recall and inaccurate recall between the below 750 g group and the term-born controls. Memory impairments were less evident in the 750 g to 1 499 g group than in the children below 750 g. The high-risk children obtained lower scores on delayed recall and made more recall errors than the low-risk children.

Suboptimal working memory skills were significant in premature children, regardless of their degree of prematurity (Lindeke et al., 2002). Spatial working memory impairments have been observed in children born prematurely (Anderson et al., 2004). Preterm children had a shorter spatial memory span length and committed more forgetting errors on a spatial working memory task when initially assessed (Curtis et al., 2002). Vicare et al. (2004) note difficulty in spatial working memory among preterm, LBW preschool children (3-4 years) without evident brain disorders and normal cognitive functioning.

5.4.2 Implications

Memory impairment is considered one of the most important cognitive deficits, because in the immature brain it may be responsible for learning disabilities at school (Geva, Eshel, Leitner, Fattal-Valevski & Harel, 2006; Giménez et al., 2004). According to Klingberg, Forssberg and Westerberg (2002) the amount of information kept in working memory increases throughout childhood and early adulthood, which is essential for the development of a wide range of cognitive skills (e.g. reading and logical reasoning). Isaacs et al. (2000) mention that lack of attention or even disobedience may be linked to or coexist with a specific memory deficit.

The literature consulted did not indicate findings on gender differences.

5.4.3 Aetiology

The hippocampus appears to play a significant role in learning and memory (Curtis et al., 2002; de Haan et al., 2000; Nosarti et al., 2002; Olness; 2003; Taylor et al., 2000b). Abernethy et al. (2004) report discrepancies regarding the role of the hippocampus in memory. Smaller hippocampal volume was the best predictor of everyday memory (Olness, 2003), episodic memory deficits (Curtis et al., 2002) and memory impairment (Isaacs et al., 2000) in adolescents with a history of prematurity (Abernethy et al., 2004; Isaacs et al., 2000; Perlman, 2001) and VLBW (Isaacs et al., 2000). Giménez et al. (2004) suggest that left hippocampal grey matter atrophy in adolescents born prematurely may be responsible for memory impairment (verbal memory impairment), which may be related to learning disabilities. Reduction of the hippocampi (probably caused by hypoxic-ischaemic damage) may have accounted for some of the memory deficits observed in preterm children, i.e anterograde amnesia (Nosarti et al., 2002). The hippocampus appears to be particularly vulnerable to adverse perinatal events (such as hypoxia-ischaemia, hypoglycaemia and iron deficiency) and

neuronal loss as a result of interruptions in the supply of oxygen and glucose, which may result in memory deficits in children born preterm (Curtis et al., 2002).

The possibility was also raised that impaired memory performance may be a reflection of additional abnormalities that may be present elsewhere in the brain, such as the prefrontal cortex or frontal lobes (de Fockert et al., 2004), which are known to play a significant role in episodic memory (Isaacs et al., 2000). Short-term memory deficit may reflect an executive short-term memory deficit characteristic of the anterior hippocampal-prefrontal network. Damage to the amygdala was also associated with memory impairments (Curtis et al., 2002). Improvement in memory performance in older preterm children may indicate that there is no behavioural evidence indicating obvious hippocampal or prefrontal damage. These findings suggest evidence of neural plasticity, which refers to the process by which compensatory neural events, brought about either by endogenous, genetically driven mechanisms or through environmental experience, facilitate change or reorganisation in the neural substrate (Curtis et al., 2002).

Cooke and Abernethy (1999) mention that the corpus callosum is vulnerable in sick VLBW infants. It is often the site of cystic leucomalacia or atrophy, particularly posteriorly. The role of the corpus callosum may relate to interhemispheric function and coordination, sharing learning and memory.

Children with ELBW are vulnerable to insult in periventricular brain structures and the projections of these structures to the frontal lobe. VLBW children are susceptible to damage to the germinal matrix, with consequent adversities for myelinisation and abnormal cortical development (Taylor et al., 2000b). Memory problems in children with such pervasive brain insults may be associated with generalised cognitive impairment, while children with localised

periventricular lesions are at risk of selective deficits. Early hydrocephalus, alcohol exposure and hypoxia-ischaemia affect the same structures (Taylor et al., 2000b).

According to Taylor et al. (2000b) memory tests are more sensitive to the effects of IVH and hydrocephalus in preterm children than are other neuropsychological measures. De Haan et al. (2000) found that the medical evidence did not indicate that preterm infants sustained neural damage perinatally. Compromised development of experience-dependent memory circuits may rather be caused by environmental deprivation of the unique needs of the child born preterm (de Haan et al., 2000). Curtis et al. (2002) however found no association between SES and memory functions.

5.4.3.1 Working memory

Curtis et al. (2002) state that episodic and working memory functions rely to a large extent on the interconnection between the prefrontal cortex, caudate nucleus and hippocampus. Curtis et al. (2002) further postulate that neurobiological risk may have a wide impact on discrete networks in the prefrontal cortex, producing continued deficits in spatial working memory.

Auditory cortical areas are involved in a network that supports working memory for auditory information. Posterior parietal lobe activation specifically increases as a function of verbal working memory load (Golob & Starr, 2004).

It has been hypothesised that changes in working memory capacity correlate in time with several neuronal developmental processes, including a decrease in synaptic density, axonal elimination, changes in global cerebral metabolism, myelination and changes in catecholamine receptor structure and density (Klingberg et al., 2002). The cortex in the superior frontal sulcus and intraparietal sulcus indicated a positive correlation between age and working

memory-related brain activity. A positive correlation between working memory capacity and working memory activity was identified in the left superior frontal and left intraparietal areas, which indicate an increase in working memory capacity with age (Klingberg et al., 2002).

Several age-related processes coincide with the increase in working memory capacity. The inferior parietal cortex is among the last brain regions to myelinate (Klingberg et al., 2002). The interaction between brain activity and age can also be explained by synaptic and axonal pruning. An overproduction of connections and synapses occur in early life, with consequent pruning of the connections that are not used. Although the number of synapses decreases, the connections related to working memory would be more active during the performance of working memory tasks. Activities in the frontal and parietal areas may be affected by developmental changes outside these areas (Klingberg et al., 2002).

5.4.3.2 Spatial memory

Curtis et al. (2002) found the number and extent of medical complications at birth were negatively correlated with spatial memory span, planning and spatial recognition memory. Gestational age was of primary importance in predicting spatial memory span, while neurobiological risk was vital in the prediction of spatial working memory. The amount of neurobiological risk experienced during the neonatal stage, particularly the presence of factors that influence brain blood flow and oxygenation, contributes to the prediction of spatial working memory errors (Curtis et al., 2002). The atypical experience of the preterm child has an impact on the development of explicit memory skills (de Haan et al., 2000).

5.4.3.3 Visual-spatial working memory

"Voluntary control" of top-down attention has been found to activate the identical superior frontal site as in visual-spatial working memory or working memory tasks. Thus, top-

down attention and working memory could be overlapping concepts, with overlaps in the underlying brain activity, namely the inferior and intraparietal cortex, which is often correlated with areas in the superior and middle frontal gyri (Klingberg et al., 2002).

Studies of visual-spatial working memory also reported activation of the cortex lining the superior frontal sulcus, extending anteriorly from the intersection of the superior frontal sulcus and precentral sulcus (Klingberg et al., 2002). Spatial working memory tasks (relying on response inhibition, working memory and planning, in addition to explicit memory), are primarily mediated by the dorsal and ventral regions of the prefrontal cortex (Curtis et al., 2002). Spatial memory span appears to be mediated by the right ventrolateral prefrontal cortex and its reciprocal connections with subcortical regions. Curtis et al. (2002) emphasise several risk factors that may contribute to memory deficits in low-risk preterm children including nutrition, early physical environment and differences in the development of sleep-wake cycles. These factors may contribute to inadequate development of grey matter and synaptic interconnections within neural networks, subserving memory for spatial sequences. The dramatic increase in synaptogenesis and the accompanying increase in synaptic density during the perinatal period (shortly before and after birth) may be specifically disrupted as a result of preterm birth, regardless of any medical complications. Deviations from the environment may affect or impair this process.

5.4.3.4 Immediate memory

The correlation between aspects of short-term memory and hippocampal size was not confirmed. The hippocampus, which is involved in various functions (such as memory), is vulnerable to changes in volume associated with stress and other insults (Abernethy et al., 2002). Isaacs et al. (2000) confirm that problems in attention in preterm children may coexist with and contribute to impaired performance in immediate recall. Taylor et al. (2000b) report

that delayed recall is poorer in children with a birth weight below 1 000 g with IVH than in children of similar birth weight without IVH.

Memory impairments were observed in children with bilateral hippocampal pathology related to neonatal hypoxia-ischaemia. These children did however score relatively well on tests of immediate memory (Taylor et al., 2000b). Distinctions between brain systems that subserve memory formation and memory storage are essential in formulating a basis for memory impairment (Taylor et al., 2000b). The medial temporal lobe and medial thalamic structures are more essential in declarative memory, whereas the neocortex is involved in retention of learned information. Regions of the frontal lobe (such as the ventromedial frontal cortex) either work in concert with the medial temporal lobe and medial thalamus in memory storage, or assist in directing the encoding and retrieval process. Thus, VLBW children's learning deficits and delayed recall are ascribed to damage to the medial temporal lobe and diencephalon. Deficient EF due to damage of the frontal-striatal circuits (Olness, 2003; Taylor et al., 2000b) may contribute further to slow learning rates and may also account for problems in retrieval and recall errors (Taylor et al., 2000b). Though the thalamus forms part of the neural memory circuitry in memory functions, this finding was not confirmed in a study with adolescents born prematurely, though bilateral thalamic reductions were observed (Giménez et al., 2004).

5.5 Executive dysfunctioning

In this investigation executive functioning is one of the neuropsychological functions hypothesised to be compromised in LBW, owing to a strong biological vulnerability associated with LBW (see Section 5.5.3). Executive functioning includes an array of functions essential for effective scholastic performance, social adjustment and responsible, self-serving adult

conduct (Lezak et al., 2004). Though EF includes functions investigated separately (such as attention, working memory, motor control and EF associated with visual-spatial skills), numerous other constructs are measured with EF tasks (such as cognitive flexibility, decision-making) indicated in the definition of EF. Assessment of EF is also included in view of its association with externalising disorders, particularly ADHD (as discussed in Section 4.3.1.3).

EF are defined as a complex system of functions including or dependent on interference control, non-verbal and verbal working memory, planning, reconstitution (Anderson et al., 2004; Böhm et al., 2004; Boonstra et al., 2005; Geurts et al., 2005), response inhibition (Oosterlaan, 1996), decision-making, judgement and cognitive flexibility (Anderson et al., 2004; Boonstra et al., 2005; Cheung, Mitsis & Halperin, 2004; Geurts et al., 2005). Barkley's stage-wise hierarchy in the development of EF (see Tables 5.1 and 5.2) includes non-verbal working memory (emerging during the second year of life), verbal working memory, the internalisation of emotion/motivation and the ability to reconstitute behaviour (Böhm et al., 2004). EF enable an individual to self-regulate, orient towards the future, carry out goal-directed behaviour, inhibit behaviour and time or delay a response (Anderson et al., 2004; Cheung et al., 2004).

Böhm et al. (2004) postulate that EF develop sequentially from simple forms of motor inhibition and impulse control at an early age to more complex functions, such as selective and sustained attention, as well as fluent production of abstract content. These functions strongly correlate with IQ. Curtis et al. (2002) confirm that EF may occur in a stage-like process. Distinct levels of maturation and integration occur at age 6 years, age 10 years and in adolescence, possibly reflecting an extended period of maturation of the prefrontal cortex during the first two decades of life. Deficits in inhibition cause secondary impairments in other EF, which emerge later in development (Oosterlaan, 1996).

According to Blondis, Snow and Accardo (2000) executive processes include higher-level skills such as focused and divided attention, planning abilities, impulse control, mental flexibility and working memory. The EF can be grouped into four mental activities, as reflected in Table 5.1 (Barkley, 2006; Mercugliano, 1999).

Self-control can be defined as the ability to inhibit or delay one's initial motor (and perhaps emotional) responses to an event. Self-control is an essential foundation for the performance of any task. As children grow up, most obtain the ability to engage in mental activities, known as EF, that help them deflect distractions, recall goals and take the steps needed to reach them. For instance, in order to achieve a goal in work or play, people need to be able to remember their aim (use hindsight), prompt themselves about what they need to do to reach that goal (use foresight), keep their emotions reined in and motivate themselves. These functions can only be carried out successfully when a person is able to inhibit interfering thoughts and impulses (Barkley, 2006).

Table 5.1 Executive functioning (Barkley, 2006; Mercugliano, 1999)

1. Working memory, which refers to holding information in the mind while working on a task, even if the original stimulus that provided the information is gone. Such remembering is essential to timeliness and goal-directed behaviour. Working memory provides the means for hindsight, forethought, preparation and the ability to imitate the complex, novel behaviour of others, which are all impaired in individuals with ADHD. 2. Internalisation of self-directed speech: Most children, before the age of six, frequently speak out aloud to themselves, for instance by reminding themselves how to perform a particular task. Such private speech usually disappears by age 10 and evolves into inaudible muttering. Internalised, self-directed speech enables one to reflect to oneself, to follow rules and instructions, to use self-questioning as a form of problem-solving and to construct "meta-rules", which form the basis for understanding the rules for using rules. 3. Control (self-regulation) of emotions, motivation and state of arousal. Such control enables individuals to achieve goals by delaying or altering potentially distracting emotional reactions to a particular event and to generate private emotions and motivation. 4. Reconstitution, which consists of two separate processes: breaking down observed forms of behaviour and combining the parts into new actions not previously learned from experience. Reconstitution involves a great degree of fluency, flexibility and creativity. It enables individuals to propel themselves toward a goal without having to learn all the needed steps by rote. Children with ADHD seem to be less capable of reconstitution than other children.

According to Barkley (2006) loss of behavioural inhibition and self-control leads to various disruptions in brain functioning, as reflected in Table 5.2. Table 5.2 indicates the consequences of specific impaired EF.

Table 5.2 Consequences of impaired executive functioning (Barkley, 2006)

Impaired function	Consequence
Non-verbal working memory	Diminished sense of time. Inability to hold events in mind. Defective hindsight. Defective foresight.
Internalisation of self-directed speech (verbal working memory)	Deficient rule-governed behaviour. Poor self-guidance and self-questioning
Self-regulation of mood, motivation and level of arousal	Displays all emotions publicly; cannot censor them. Diminished self-regulation of drive and motivation.
Reconstitution (ability to break down observed forms of behaviour into component parts that can be recombined into new forms of behaviour in pursuit of a goal)	Limited ability to analyse forms of behaviour and synthesise new forms of behaviour. Inability to solve problems.

The ROCF Test (see Section 7.4.6 and Appendix O), digits forward and backward (Section 7.4.7 and Appendix P), as well as the Stroop Word-Colour Test (Section 7.4.8 and Appendix Q) were used as measures of executive functioning.

5.5.1 Prevalence

Nadeau et al. (2001) note that previous studies found deficits in EF among premature children of ELBW with normal intelligence. Aylward (2002) mentions that former VLBW and ELBW children with normal IQ have problems with EF such as organisation, planning, problem-solving and abstracting. Deficits in impulse control, working memory and other EF (such as mental processing speed and cognitive flexibility) were reported at 5.5 years of age in preterms (Böhm et al., 2004). Anderson et al. (2004) identified difficulties in ELBW/very preterm 8-year-olds on measures of reasoning ability, working memory, planning,

organisational abilities, impulse control, starting activities, generating new ideas, mental flexibility and strategic decision-making. Self-regulation of emotions and behaviour were one of the developmental areas of concern among 8-year-old VLBW children (Dieterich et al., 2004). Problem-solving impairments were also significant among children born preterm (Sajaniemi et al., 2001). A global deficit in EF rather than a specific pattern of executive deficits was observed. Sajaniemi et al. (2001) indicate that birth weight and gestational age correlated weakly with cognitive and behavioural EF measures.

The number of children with IVH and PVL were inadequate to determine the effect of these factors on results. Anderson et al. (2004) confirm that whether executive dysfunction is a primary deficit or secondary to impairments in other domains has to be established and will be resolved only with neuroimaging studies. Improvement in memory and executive impairment in preterm children was observed by Curtis et al. (2002).

5.5.2 Implications

Oosterlaan et al. (2005) postulate that early developmental EF deficits, caused by hereditary and environmental factors, may cause a cascade of other future executive dysfunctions leading to gross EF deficits and severe impairments in planning, execution and goal-directed behaviour. Executive dysfunction among premature children of ELBW with normal intelligence increased the likelihood of learning difficulties at school (Nadeau et al., 2001). Even slight deficits in EF affected educational progress and adaptive functioning, needing neuropsychological assessment and specialist assistance (Sajaniemi et al., 2001).

5.5.3 Aetiology

Böhm et al. (2004) found that general intelligence, gender and visual impairment were significant predictors of EF. Visual impairment may be related to complex neurodevelopmental dynamics in preterm children.

Neural circuits that connect prefrontal cortical regions with an array of more posterior cortical and subcortical brain structures mediate EF, referring to higher order cognitive abilities. These abilities may be carried out by three circuits that originate in the anterior frontal grey matter, involving the dorsolateral prefrontal, lateral orbitofrontal and anterior cingulate portions of the frontal lobe (Cheung et al., 2004). Executive processes are implemented in circuits involving the prefrontal cortex and basal ganglia (Ravizza & Ivry, 2001; Schachar et al., 2005), thalamus (Schachar et al., 2005) and the cerebellum (Ravizza & Ivry, 2001). The frontal lobes seem to mediate the most complex behavioural and cognitive functions, also known as frontal lobe functions or EF (Demakis, 2004). The frontal cortex (de Fockert et al., 2004; Oosterlaan, 1996), specifically the prefrontal cortex (Anderson et al., 2004; Mercugliano, 1999; Nadeau et al., 2001; Olness, 2003; Oosterlaan, 1996; Ravizza & Ivry, 2001; Schachar et al., 2005), and its striatal connections, contains the most essential neuroanatomic substrates for executive functioning (Mercugliano, 1999). Böhm et al. (2004) note the harmful effect of repeated hypoxic-ischaemic events on the striatum, which commonly occur in preterm infants. The striatum is regulated by the dopaminergic system and has a prominent role in the frontal-striatum-thalamic-frontal circuits involved in EF. The frontal lobe function and its connection with the basal ganglia fall within the realm of EF (Nadeau et al., 2001; Ravizza & Ivry, 2001; Schachar et al., 2005).

The frontal cortex is related to control of interference (de Fockert et al., 2004). Corticostriatal circuits, particularly the striatum and prefrontal cortex, play an important role in

planning action and maintaining working memory during tasks (Wickens, 2005). Tasks involving spatial planning and behavioural inhibition seem to activate the parietal cortex bilaterally, as well as the left caudate nucleus and left dorsolateral prefrontal cortex (Curtis et al., 2002). The caudate nuclei receive inputs from the cortical regions involved in EF and attentional tasks (Abernethy et al., 2002; Cooke & Abernethy, 1999). Damage or myelination of either may result in motor dysfunction, attention deficit or learning disability (Cooke & Abernethy, 1999).

Neuropsychological deficits appear not to be caused by focal deficits in cerebral visual pathways, but rather are probable signs of diffuse or widespread, slight brain dysfunction (Sommerfelt et al., 2002). Anderson et al. (2004) confirm that the underlying neural systems for EF are numerous, complex and interrelated, involving prefrontal connections with virtually all other brain regions including the brainstem, occipital, temporal and parietal lobes, as well as the limbic and subcortical regions. Executive dysfunction is not always related to prefrontal pathology directly, but may be associated with network disconnections such as white matter damage or impairment to subcortical or posterior brain regions. Very preterm or ELBW children seem to exhibit general cognitive impairment, including executive dysfunction, which is consistent with neuroimaging studies indicating impaired myelination and reduced volumes of many subcortical and posterior structures (Anderson et al., 2004). The specific site of the physiological or neurochemical dysfunction will determine the particular manifestation of executive control deficit. Recent studies emphasise that a distributed network including both cortical and subcortical structures is involved in EF, instead of overemphasising the prefrontal cortex (Ravizza & Ivry, 2001).

Russell (2005) notes that the mesocortical dopamine system originates in the ventral tegmental area and projects to the cortical areas (prefrontal, parietal and temporal cortex).

These dopamine projections (as indicated in Figure 4.3) modulate circuits that are known to play an important role in a variety of EF, including motor control, behavioural inhibition, behavioural planning, attention and working memory (Russell, 2005).

The problem-solving ability of the SGA group was adversely affected only after prolonged brain growth compromise, for example in children whose brain growth compromise began *in utero* and continued throughout the first year of life (Frisk et al., 2002). The authors further postulate that the deficit in problem-solving ability of the SGA group is a marker of suboptimal development of the frontal lobe, particularly due to prolonged brain growth compromise during a period when this brain region is most vulnerable to perturbation (Frisk et al., 2002).

Curtis et al. (2002) found no association between SES and executive functioning.

5.6 Conclusion

Impaired neuropsychological functioning in LBW children is indicated by previous research. Neuropsychological dysfunctioning in motor, visual-spatial, EF and memory domains may be related to reciprocal multiple aetiological factors associated with preterm birth or growth restriction. Clinical factors (e.g. hypoxia, brain injury, CLD) and stressful environmental conditions may have an impact on the developing brain. Some neuropsychological functions are interrelated, suggesting possible overlapping neural networks. Neuropsychological dysfunctioning plays a pivotal role in cognitive/academic deficits, as well as subsequent externalising and internalising psychological disorders.

Chapter 6

PROBLEM STATEMENT

6.1 Introduction

As previously mentioned, increasing survival rates for the smallest infants imply increasing rates of disability (Winders & Burns, 2001). Premature birth is associated with stressful procedures and environmental conditions (Perlman, 2001). These children tend to be at higher risk of medical conditions and brain injury (Bhutta et al., 2002; Sola et al., 2005), pre- and perinatal insults (Hille et al., 2001), as well as postnatal complications (Bhutta et al., 2002). Vulnerability to developmental difficulties may be ascribed to a CNS that is not fully organised at the time of birth for sustaining itself in the extra-uterine environment (Cherkes-Julkowski, 1998).

Some researchers postulate that in the absence of brain-compromising events, about 80% to 90% of preterm children develop normally (Ohlweiler, da Silva & Rotta, 2002). Though about half of LBW infants have no disabilities (Berk, 2006), increased risk of neurodevelopmental (Huddy et al., 2001; Indredavik et al., 2004), cognitive (Curtis et al., 2002; Dieterich et al., 2004; Isaacs et al., 2000), behavioural (Potgieter et al., 2003; Saigal et al., 2001; Sola et al., 2005), psychiatric (Elgen et al., 2002), social (Dieterich et al., 2004; Indredavik et al., 2004; Rickards et al., 2001; Sajaniemi et al., 2001) and other problems has been noted by numerous investigators.

A mediational model posits that behaviour problems emerge as a result of the mediating effects of both neuro-motor and cognitive delays associated with birth status (prematurity) (Nadeau et al., 2001). According to Indredavik et al. (2004) psychiatric

problems affected the overall functioning of both VLBW and SGA adolescents, even though widespread emotional or behavioural symptoms did not always reach the diagnostic level of a psychiatric disorder. According to the findings mentioned, cognitive, behavioural and emotional development are in reciprocal interaction. This possibility necessitates investigation in the South African context, because of the implications for academic, emotional, social and other important areas of functioning, as well as the economic burden on society.

As stated in Section 1.3, limited, if any, research on LBW and its outcomes is available in the South African context. A high incidence of LBW/prematurity is expected in South Africa, a developing country, characterised by great poverty and high HIV/AIDS rates, factors considered to be significant risks in LBW/prematurity.

The focus of this chapter is on highlighting the purpose of the study as a whole, by addressing the problem statement, aim of the study and the hypotheses.

6.2 The problem: Psychological functioning in children with low birth weight

6.2.1 Problem statement

The main focus of this study is to investigate the internalising and externalising psychological disorders associated with LBW, as well as neuropsychological functioning among current primary school children born with LBW. Similarities and differences between birth weight, gender and age groups will be determined pertaining to the focus areas mentioned.

The first sub-problem: The first phase of the investigation is to determine the prevalence of psychological disorders, including internalising psychological symptoms (particularly SAD, OAD and MDD) and externalising psychological symptoms (referring to

ADHD, ODD and CD) in children with LBW compared to children with NBW, analysed as a function of gender and age.

The second sub-problem: The second phase of the investigation is to determine the differences in neuropsychological functioning between the LBW and NBW groups, analysed as a function of gender and age.

6.2.2 Aim of the study

The main aim of this research study was two-fold, namely

1. to study the magnitude and characteristics of internalising and externalising symptoms among LBW children in comparison with NBW children; and
2. to establish neuropsychological deficiencies (motor, visual-spatial, memory and EF) between LBW and NBW children.

6.2.3 Hypotheses

Primary hypothesis:

There is a higher incidence of psychological disorders and neuropsychological deficits in primary school children born with low birth weight than in children with normal birth weight.

Secondary hypothesis 1:

There is a higher incidence of internalising (Separation Anxiety Disorder, Overanxious Disorder and Major Depressive Disorder) and externalising (Attention-Deficit/Hyperactivity Disorder, Oppositional Defiant Disorder and Conduct Disorder) psychological disorders in children born with low birth weight than in children with normal birth weight.

Secondary hypothesis 2:

There is a higher incidence of neuropsychological deficiencies (motor, visual-spatial, memory and executive functions) in children born with low birth weight than in children with normal birth weight.

A description of the statistical tests employed to accept or reject the hypotheses formulated here will be supplied in the next chapter.

Chapter 7

METHODOLOGY

7.1 Introduction

As mentioned in Chapter 6, the main focus of this study was to investigate the internalising and externalising psychological disorders associated with LBW, as well as neuropsychological functioning among current primary school children born with LBW. Similarities and differences between birth weight, gender and age groups were determined pertaining to the focus areas mentioned. Measurement instruments referred to in this chapter were essential in the assessment of the focus areas mentioned in order to accept or reject hypotheses. The quantity and dimension of internalising and externalising psychological symptoms were measured by means of a self-reporting questionnaire and rating scale respectively. Cognitive tasks (motor, visual-spatial, memory and EF) measured by neuropsychological tests were used in this study, similar to the investigation by Espy (2004), to understand the nature of brain function in children born with LBW. Anderson et al. (2004) also emphasise that identifying the nature of cognitive deficits associated with premature birth will provide some indication of the neural systems that were compromised.

This chapter elaborates on the research design applied, sampling and demographic characteristics of the sample. Descriptive statistics for responses on the biographical data questionnaire (Appendix F) will be summarised in Tables 7.4 to 7.7. The measurement instruments, procedures and methods of analysis will also be referred to. The Cronbach's alpha for each measuring instrument is indicated as determined for this study, indicating the internal consistency and reliability of the instrument.

7.2 Research design

This research investigation focused on the prevalence of the associated internalising and externalising psychological disorders with LBW, as well as neuropsychological functioning by means of participant observation in the form of neuropsychological testing, as well as a questionnaire and rating scale. Scores on neuropsychological tests, questionnaires and rating scales should be able to verify the hypotheses.

A control group of children with NBW was used to determine differences in the prevalence of externalising and internalising symptoms, as well as performance on neuropsychological tests in LBW children and NBW children. A control group is characteristic of an experiment, which refers to quantitative research. This was a quantitative research study, with a quasi-experimental research design, as the subjects cannot be randomly assigned to the conditions of the independent variable, because they already exhibit the variable. Methods used in this study, such as direct observation, questionnaires and rating scales, are also characteristic of quantitative research (de Vos, Strydom, Fouché & Delport, 2002).

7.3 Sample

The Human Sciences Research Council selected a sample of 20 urban, mainstream, English/Afrikaans primary schools in the Tshwane North and South districts (see Appendix A) of the Gauteng Province in South Africa. Stratified random sampling was used to ensure representation of all cultures and socio-economic groups. A minimum of 144 children (72 children in the clinical group and 72 children in the control group) was needed for this study (18 per cell to arrive at a 95% confidence interval) (Clark-Carter, 2004). Schools were approached in the sequence provided in the sample group up to the stage where a sufficient

number of participants (minimum of 144) had been identified. Approval of a request to conduct research was obtained from the Gauteng Department of Education (see Appendix B) as well as the principals of the selected schools (see Appendix C).

Children with a birth weight of below 2 000 g were considered for the clinical group. The control group (consisting of children with a birth weight of above 3 000 g) was matched with the clinical group for age, gender, home language and SES. Only children under the age of 14 years were considered for inclusion in the sample.

The final sample, consisting of 158 children, was selected from nine primary schools in the Tshwane North and South districts.

The gender and age group distribution of the sample is indicated in Table 7.1

Table 7.1 Gender and age group distribution

Group	Age group 6-9	Age group 10-13
LBW males	23	15
LBW females	26	15
NBW males	23	15
NBW females	26	15
All groups	98	60

Figure 7.1 Gender and age group distribution

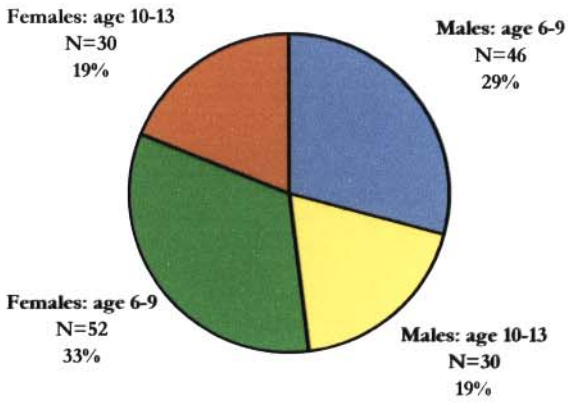


Figure 7.1 reflects the gender and age group distribution of the sample.

Figure 7.2 Language distribution of the sample

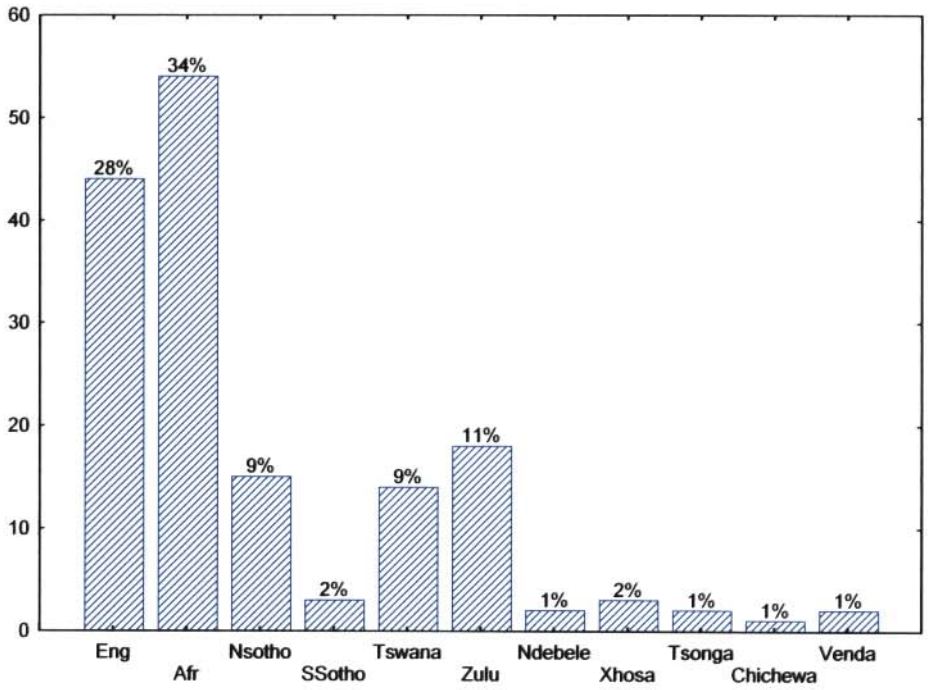


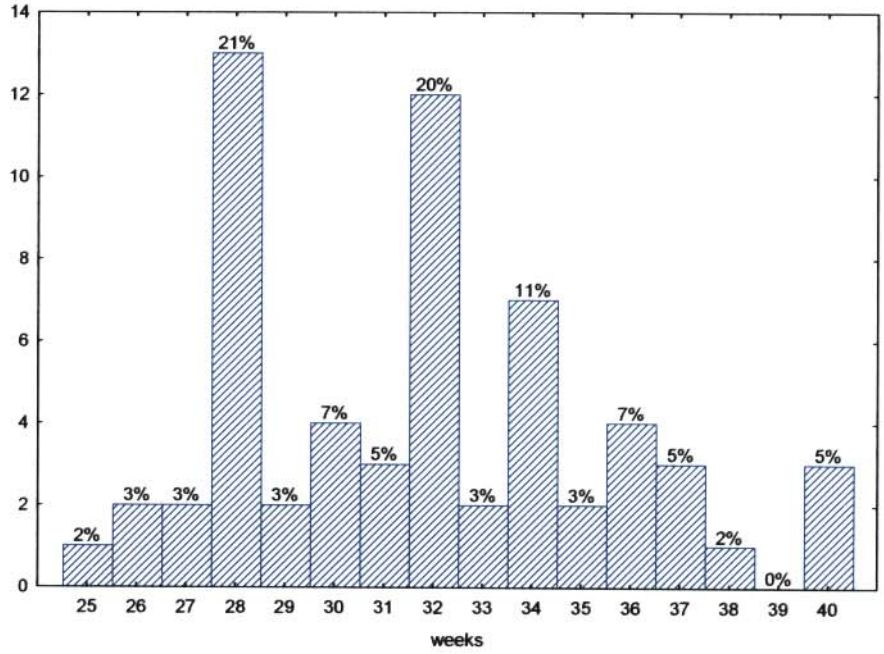
Figure 7.2 illustrates the language distribution of the sample.

Table 7.2 represents the length of pregnancy in weeks of the NBW and LBW group.

Table 7.2 Length of pregnancy in weeks of the LBW and NBW group

Weeks	Frequency	Percentage
25	1	0.633
26	2	1.266
27	3	1.899
28	14	8.861
29	2	1.266
30	4	2.532
31	3	1.899
32	14	8.861
33	2	1.266
34	7	4.430
35	2	1.266
36	7	4.430
37	7	4.430
38	12	7.595
39	9	5.696
40	41	25.949
41	2	1.266
42	1	0.633
43	1	0.633
Missing	24	15.190

Figure 7.3 Length of pregnancy in weeks of LBW participants



The length of pregnancy in weeks of the LBW group is indicated in Figure 7.3.

Thus, 87 % of the LBW respondents were born prematurely, excluding the missing responses. IUGR seemed to occur in 12 % of the LBW group.

Figure 7.4 Length of pregnancy in weeks of NBW participants

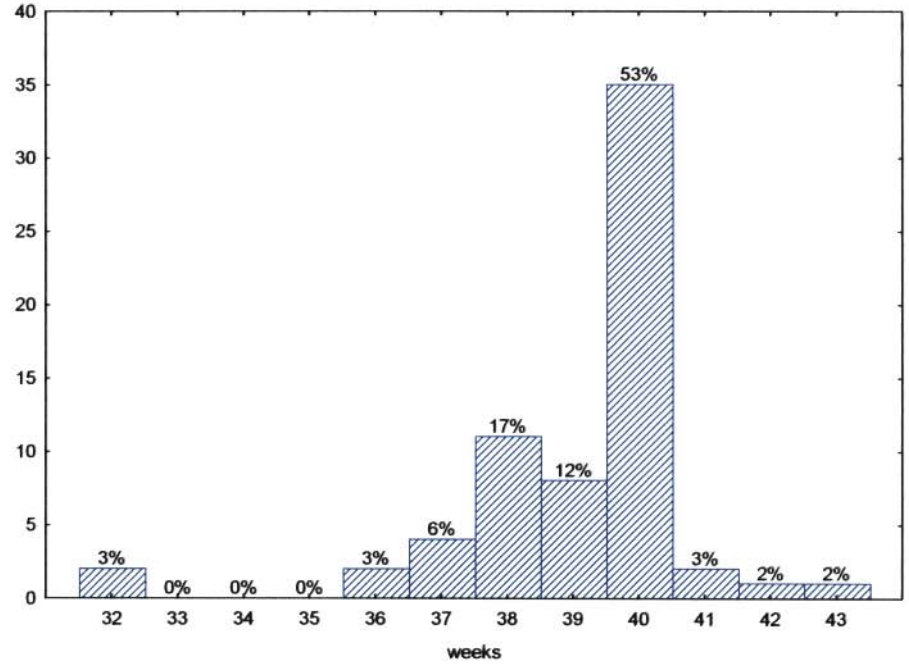


Figure 7.4 illustrates the length of pregnancy in weeks of the NBW group.

Significant differences ($p = 0.00$) between the length of pregnancy in the birth weight groups were observed.

Figure 7.5 Mothers' age at birth of the LBW participants

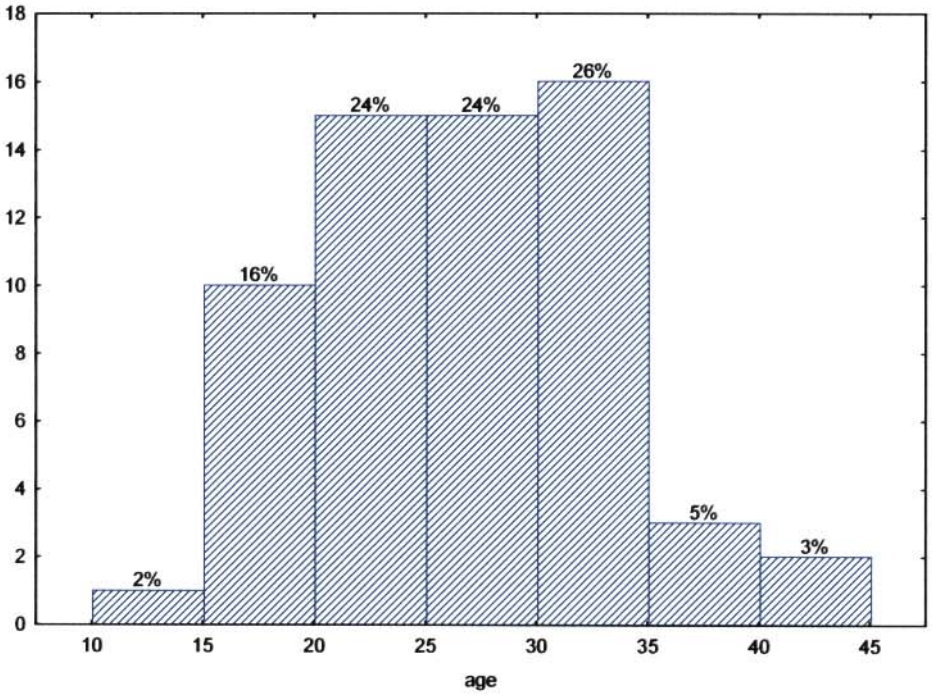


Figure 7.5 reflects the age of the mothers of the LBW respondent when birth occurred.

Figure 7.6 Mothers' age at birth of the NBW participants

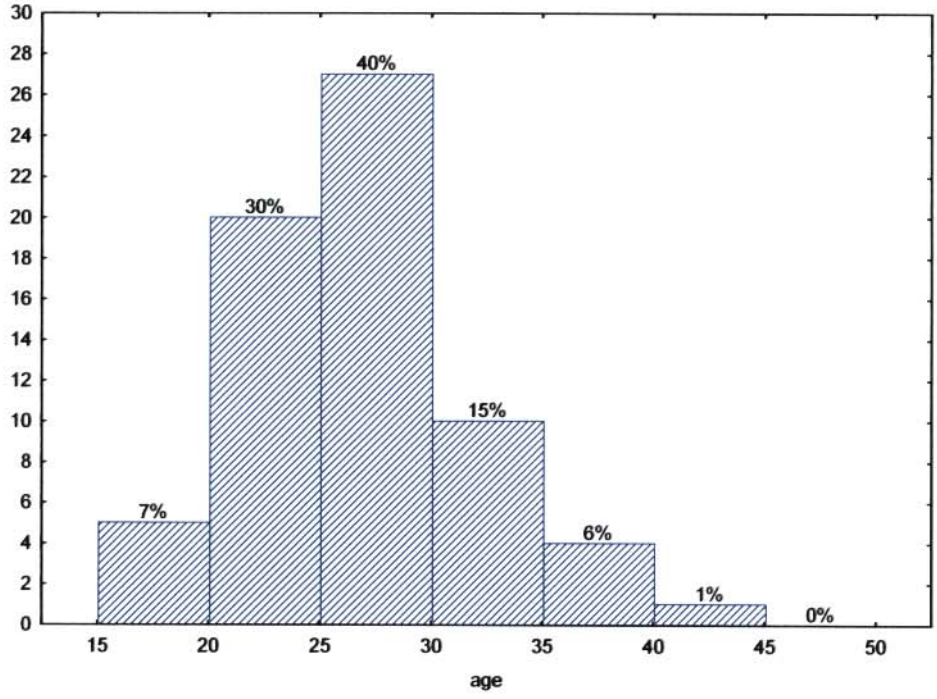
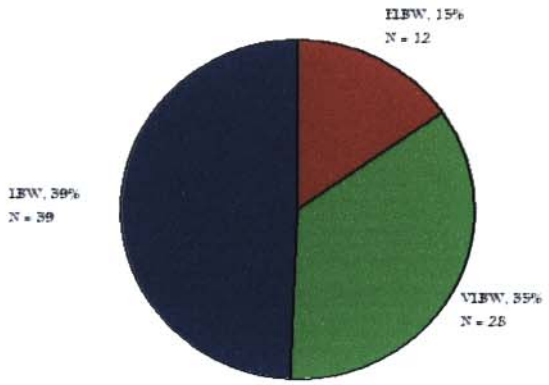


Figure 7.6 indicates the age of the mothers of the NBW respondents when birth occurred.

The comparison between the mothers' age at birth of the various birth weight groups was statistically not significant ($p = 0.725$).

Figure 7.7 Levels of LBW



The representation of the various levels of LBW is illustrated in Figure 7.7

The mean birth weight of the gender and age groups of the LBW and NBW participants is reflected in Table 7.3.

Table 7.3 Mean birth weight and age of birth weight, gender and age groups

Group	Gender	Age group	N	Birth weight Means	Age in months Means
LBW	Male	6-9	23	1491.957 ± 334.951	98.097 ± 11.119
		10-13	15	1369.600 ± 409.937	134.867 ± 13.553
	Female	6-9	26	1530.385 ± 357.709	99.346 ± 12.853
		10-13	15	1460.467 ± 339.498	135.933 ± 10.826
NBW	Male	6-9	23	3463.043 ± 319.502	100.696 ± 11.679
		10-13	15	3624.267 ± 337.392	139.533 ± 10.302
	Female	6-9	26	3535.962 ± 314.789	101.000 ± 11.342
		10-13	15	3462.667 ± 333.969	135.200 ± 13.040

The difference in birth weight between the LBW and NBW group was significant ($p=0.000$), while the difference in age was statistically not significantly ($p = 0.290$).

Table 7.4 gives an overview of the occurrence of specific conditions during pregnancy or delivery (see Appendix F). The results of Tables 7.4 to 7.7 reflect the total responses of the sample group, including those who did not respond at all.

Table 7.4 Occurrence of conditions during pregnancy/delivery – Descriptive statistics for birth weight, gender and age groups

	LBW								NBW							
	Male				Female				Male				Female			
	6-9		10-13		6-9		10-13		6-9		10-13		6-9		10-13	
During pregnancy/ delivery the following occurred:	*N*	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Received proper medical care	17	85	10	91	23	96	14	100	21	91	13	100	21	91	14	100
Followed a well-balanced diet	18	95	10	91	21	91	13	93	18	82	12	92	20	87	14	100
Vaginal bleeding	8	40	5	46	9	38	3	21	3	13	1	8	5	22	0	0
Excessive weight gain (more than 20 kg)	1	5	3	27	5	21	2	14	9	39	2	15	5	22	4	29
Low weight gain by mother	5	28	0	0	11	50	3	21	2	9	1	8	4	18	1	8
Toxaemia	1	6	1	9	1	5	1	7	1	5	0	0	2	9	0	0
Pre-eclampsia	3	16	4	36	5	21	4	29	2	9	0	0	3	14	1	7
Rh factor incompatibility	2	13	0	0	3	15	1	8	1	5	0	0	1	5	11	100
Frequent nausea or vomiting	20	10	2	18	10	42	5	36	3	13	3	23	6	27	3	21
Maternal anaemia	5	25	1	9	2	9	2	14	5	22	0	0	4	18	1	7
Illness or injury	5	26	1	9	4	17	1	7	5	22	0	0	4	18	2	14
Serious illness	4	20	2	18	5	22	1	7	3	13	0	0	2	9	1	8
Took prescription medication	5	29	1	11	6	26	3	21	1	5	0	0	4	18	2	18
Took illegal drugs	2	11	1	9	0	0	0	0	0	0	0	0	1	5	0	0
Used alcoholic beverage	2	10	1	9	3	13	1	7	1	4	2	15	3	14	0	0
Smoked cigarettes	3	15	1	9	0	0	3	21	5	22	0	0	5	23	2	14
Was given medication to ease labour pains	5	26	2	18	4	19	4	31	5	22	3	23	6	29	3	21
Delivery was induced	4	21	2	20	6	26	6	43	5	24	3	23	4	17	6	43
Forceps were used during delivery	1	6	1	9	4	18	1	8	2	9	2	15	2	9	0	0
Had a breech delivery	3	15	2	18	3	14	2	14	1	5	0	0	2	9	0	0
Had a caesarean section delivery	8	40	9	82	15	63	4	29	6	29	5	39	14	61	3	21

The impact of smoking could not be investigated, owing to the small sample size. Only 11% of mothers of children from the LBW group and 16% of mothers of children from the NBW group smoked. Under-reporting by mothers regarding smoking during pregnancy is possible (Breslau & Chilcoat, 2000).

Table 7.5 indicates the occurrence of specific conditions that affected the child during delivery or in the first few days after birth (see Appendix F).

Table 7.5 Conditions affecting the child during delivery or in the first few days after birth – Descriptive statistics for birth weight, gender and age groups

	LBW								**NBW**							
	Male				**Female**				**Male**				**Female**			
	6-9		**10-13**		**6-9**		**10-13**		**6-9**		**10-13**		**6-9**		**10-13**	
During delivery or in the first few days after birth the following occurred:	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Injured during delivery	4	21	1	9	1	4	0	0	0	0	0	0	0	0	0	0
Heart distress during delivery	2	10	2	18	2	8	2	14	2	9	0	0	1	4	0	0
Delivered with cord around neck	1	5	1	9	1	4	2	14	2	9	0	0	2	9	0	0
Had trouble breathing following delivery	7	35	5	50	7	29	7	50	1	4	1	8	2	9	0	0
Needed oxygen	10	50	7	70	11	46	10	71	0	0	1	8	1	4	0	0
Turned blue	1	5	3	30	3	14	4	31	2	9	0	0	1	4	1	7
Was jaundiced, turned yellow	9	47	4	40	11	46	6	43	6	26	8	62	7	30	3	21
Had an infection	2	10	2	18	1	4	3	21	1	4	0	0	1	4	0	0
Had seizures/convulsions	1	5	1	9	2	8	0	0	0	0	0	0	1	4	0	0
Was given medication	7	37	6	55	8	36	8	57	0	0	1	8	1	4	0	0
Born with a defect/abnormality	1	5	1	9	0	0	1	7	0	0	0	0	2	9	1	7
Was in hospital for more than seven days	14	70	8	73	17	71	14	100	1	4	2	15	2	9	0	0

Table 7.6 reflects the health and temperamental characteristics during the first 12 months of the child (see Appendix F).

Table 7.6 Health and temperamental characteristics during the first 12 months of the child – Descriptive statistics for birth weight, gender and age groups

	LBW								NBW							
	Male				Female				Male				Female			
	6-9		10-13		6-9		10-13		6-9		10-13		6-9		10-13	
During the first 12 months the child had the following health and temperamental characteristics:	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Difficult to feed	2	10	7	64	6	25	7	50	4	17	0	0	1	4	1	7
Difficult to put to sleep	4	20	4	36	5	21	5	36	5	22	1	8	2	8	2	14
Colicky	5	26	4	44	3	13	4	31	4	18	0	0	5	22	4	29
Difficult to put on a schedule	4	20	2	18	2	9	5	36	4	17	3	23	1	4	1	7
Alert	16	80	9	82	17	71	11	85	12	55	8	62	17	71	7	50
Cheerful	18	90	9	82	20	83	13	93	19	86	10	77	22	92	13	93
Affectionate	18	90	9	82	22	96	11	85	16	73	12	92	22	92	12	86
Sociable	17	85	9	82	20	83	12	92	18	86	12	92	20	87	14	100
Easy to comfort	18	90	9	82	19	79	11	79	17	77	12	92	19	79	10	71
Difficult to keep busy	3	15	1	9	5	21	2	14	3	14	3	23	1	4	3	21
Overactive, in constant motion	5	26	2	18	6	26	4	29	7	32	2	15	2	9	3	23
Very stubborn, challenging	1	5	2	18	5	21	4	29	5	23	3	23	2	8	0	0

Table 7.7 shows the occurrence of health problems at any time of the child's life (see Appendix F).

Table 7.7 Health problems – Descriptive statistics for birth weight, gender and age groups

	LBW								NBW							
	Male				Female				Male				Female			
	6-9		10-13		6-9		10-13		6-9		10-13		6-9		10-13	
The child experienced the following health problems at some time:	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Asthma	3	15	2	20	4	17	0	0	5	22	1	8	4	17	2	14
Allergies	3	15	2	20	8	33	5	36	9	39	5	39	6	26	5	36
Diabetes, arthritis or other chronic illness	2	10	0	0	1	4	0	0	0	0	2	15	1	4	0	0
Epilepsy or seizures/convulsions	2	11	0	0	3	13	1	7	0	0	0	0	0	0	1	7
Seizures/convulsions due to high fever	3	17	3	30	2	9	1	7	3	13	0	0	0	0	0	0
Heart or blood pressure problems	1	5	0	0	1	5	0	0	2	9	0	0	1	4	0	0
High fever (over 38°C)	7	47	8	80	12	50	6	43	15	65	9	69	13	54	6	43
Head injury with loss of consciousness	0	0	1	10	0	0	1	7	0	0	2	15	0	0	1	7
Lead poisoning	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lengthy hospitalisation	7	35	5	50	10	42	6	46	5	25	2	15	2	8	2	14
Speech or language problems	7	35	4	40	6	25	5	39	6	26	0	0	2	8	2	14
Chronic ear infections	1	5	4	44	6	25	3	21	5	23	3	23	1	4	5	36
Hearing difficulties	0	0	0	0	0	0	1	7	3	13	0	0	0	0	1	7
Eye or vision problems	2	10	5	50	3	13	4	29	3	13	0	0	1	4	1	7
Fine motor/handwriting problems	6	32	5	56	5	21	4	29	7	30	0	0	0	0	0	0
Gross motor difficulties, clumsiness	3	16	2	22	8	33	3	21	4	18	1	8	3	13	0	0
Appetite problems (overeating/under-eating)	6	30	3	33	14	58	5	36	10	46	3	23	8	33	4	31
Sleep problems (falling asleep, staying asleep)	5	25	0	0	4	17	4	29	7	30	3	23	2	8	2	14
Soiling problems	3	15	0	0	2	9	2	14	3	13	0	0	4	17	2	14
Wetting problems	6	32	2	20	5	23	6	43	5	22	0	0	3	13	2	14

The Pearson Chi-Square results for significant results of pre-, peri- and postnatal complications as shown on Tables 7.4 to 7.7 are indicated in Table 7.8.

Table 7.8 Pearson Chi-Square results of pre-, peri- and postnatal complications

Variables	Group	PEARSON CHI-SQUARE							
		Gender		Age		Male		Female	
		Male	Female	6-9	10-13	6-9	10-13	6-9	10-13
Vaginal bleeding	0.001	0.004		0.024	0.008	0.043	0.033		
Excessive weight gain						0.008			
Low weight gain by mother	0.008		0.019	0.006				0.026	
Pre-eclampsia	0.014	0.036			0.007		0.017		
Took prescription medication	0.039	0.014				0.033			
Smoked cigarettes								0.013	
Had a breech delivery	0.029				0.031				
Had caesarean section							0.032		
During delivery or in the first few days after birth the following occurred:									
Injured during delivery	0.009	0.011		0.017		0.021			
Heart distress during delivery					0.031				
Had trouble breathing following delivery	0.000	0.001	0.001	0.002	0.000	0.010	0.022		0.002
Needed oxygen	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.001	0.000
Turned blue	0.029				0.010		0.034		
Had an infection	0.039				0.015				
Was given medication	0.000	0.000	0.000	0.000	0.000	0.002	0.016	0.007	0.001
Was in hospital for more than seven days	0.000	0.000	0.000	0.000	0.000	0.000	0.005	0.000	0.000
During the first 12 months the child had the following health and temperamental characteristics:									
Difficult to feed	0.000		0.002		0.000		0.001	0.041	0.012
Difficult to put to sleep					0.033				
Colicky		0.044					0.008		
Alert	0.024	0.041			0.033				
Very stubborn, challenging			0.022						0.031
The child experienced the following health problems at some time:									
Epilepsy or seizures/convulsions	0.040			0.017					
Seizures/convulsions due to high fever	0.037				0.027		0.034		
Lengthy hospitalisation	0.001		0.001	0.017	0.011			0.008	
Speech or language problems	0.006		0.038		0.007		0.012		
Chronic ear infection								0.041	
Eye or vision problems	0.016				0.002		0.004		
Fine motor/handwriting problems	0.002		0.001		0.000		0.002	0.018	0.031
Gross motor difficulties, clumsiness	0.039		0.018		0.050				
Wetting problems	0.023				0.020				

7.4 Measurement instruments

The following measurement instruments were used in this study:

7.4.1 Biographical Data Questionnaire

The Biographical Data Questionnaire (Barkley & Murphy, 2006) was used to obtain child and family information, as well as developmental and medical history (see Appendix F).

7.4.2 Raven's Coloured Progressive Matrices

The Raven's Coloured Progressive Matrices (CPM) was used as an intellectual screening device (Gregory, 2000) in order to identify subjects with an IQ below 75 (Appendix L refers).

The Raven's Progressive Matrices were developed as a 'culture fair' test of general intellectual inability (Lezak et al., 2004; Meyer & Sagvolden, 2006b; Raven, 2000; Tideman, 2000). The test is more vulnerable to posterior than anterior lesions. The subject is provided with a large design, part of which is missing. Below are six different small pattern-samples, one of which the subject chooses to complete the larger design above. The CPM consists of 36 items, with norms for children and adults over 65. The CPM has satisfactory reliability. It is considered to be a measure of general ability (Tideman, 2000).

7.4.3 Clinic or immunisation cards

Information on respondents with LBW was obtained from their clinic or immunisation cards.

7.4.4 Psychological measurements

The following instruments were used:

7.4.4.1 Internalising psychological disorders

The "Terry", a cartoon-like questionnaire, was designed for evaluation of mental disorders of children aged 6 to 12 years (Bidaut-Russell, Valla, Thomas, Bergeron & Lawson, 1998; Valla, 1997; Valla, Bergeron & Smolla, 2000). It is based on DSM-IV criteria (American Psychiatric Association, 2000). It takes into account the cognitive limitations of children. The questionnaire contains four introductory pages designed to familiarise the child with material and characters and to indicate what he or she is expected to do. It covers the seven mental disorders that occur most frequently: simple phobia (10 drawings), separation anxiety (13 drawings), overanxiety (11 drawings), major depression (19 drawings), hyperactivity with attention deficit (16 drawings), oppositional disorder (13 drawings) and CD (12 drawings). Terry can be a boy or a girl, who is portrayed in a variety of contexts, such as at home, at school and in various interpersonal relationships. The child is asked specific oral questions on the image(s) on a page, which illustrates the target emotion or behaviour. Despite its graphic elements, the "Terry" is not a projective test because it illustrates specific situations that leave little room for interpretation.

The anxiety and depression scales of the "Terry" picture questionnaire were used to establish the symptoms of anxiety (SAD and OAD) and depression (see Appendix M).

The Cronbach's alpha determined for the "Terry" in this study was 0.847, which indicates strong reliability.

7.4.4.2 Externalising psychological disorders

The DBD rating scale (Appendix G refers) was used for assessment of the presence and degree of externalising psychological symptoms according to the DSM-IV symptoms for ADHD subtypes (inattention, hyperactivity and impulsivity, full ADHD scale), ODD and

CD (Bhutta et al., 2002; Geurts at al., 2005; Pelham, Hoza, Pillow, Gnagy, Kipp, Greiner et al., 2002; Pillow, Pelham, Hoza, Molina & Stultz, 1998).

This scale was translated into some of the official languages of South Africa (Afrikaans, Pedi, Venda, Tsonga and Tswana) and norms were established for those population groups (Meyer et al., 2004). There are 18 items on the scale that measure ADHD-related symptoms. Teachers and parents were asked to rate the behaviour on a four-point scale offering the following options: not at all (0); just a little (1); quite often (2); and very much (3).

The total score is added up for ADHD-related symptoms, ODD and CD, and compared to the cut-off point of the 93rd percentile, which has previously been identified as clinically significant (Barkley, 1997; Barkley & Murphy, 2006). A higher score implies more impairment in the child (Geurts et al., 2005; Meyer et al., 2004).

The Cronbach's alpha reliability for the parent and teacher DBD rating scales in this study was indicated as 0.790 and 0.786 respectively, which is considered to be modest.

7.4.5 Neurocognitive measurements

The following measurements were used:

7.4.5.1 Fine motor control (Grooved Pegboard, Rey-Osterrieth Complex Figure Test)

The Grooved Pegboard Test was used for the measurement of deficiencies in the areas supplied by the nigro-striatal dopamine branch (fine motor control) (Lezak et al., 2004). Motor control (Lezak et al., 2004), particularly complex fine motor coordination (Meyer & Sagvolden, 2006b) and psychomotor speed (Elgen et al., 2003; Meyer & Sagvolden, 2006b), were assessed by means of the Grooved Pegboard (see Appendix N). It adds a dimension of complexity not found in other motor tasks, as the pegs must be rotated into position to be

placed successfully. It is also used to evaluate cognitive and motor slowing in LBW children (Bryden & Roy, 2005).

The Grooved Pegboard apparatus consists of a metal board (10 x 10 cm) containing a five-by-five set of slotted holes, angled in different directions. Each of the 25 pegs has a ridge along one side, which requires it to be rotated into position for correct insertion (Lezak et al., 2004). The child is instructed to insert the pegs as fast as possible, completing one row before starting on the next. The test is performed once with each hand, starting with the dominant hand.

The following instruction is given to the child:

> *"You are now going to put each of these pegs into the holes of this board (demonstrate). You may only use one hand. Pick up one peg at a time. Notice that the pegs are not round, neither are the holes in the board. In order to insert it you will have to rotate the peg so that it fits exactly (show two pegs, let the child try the next three, then remove all five pegs from the holes). When I tell you to start, you must start over here (point to the upper left hole if the child is using its right hand and to the upper right hole if the child is using its left hand), fill this upper row, continue on the next, and so on until all the pegs are inserted. Try to be quick, use only your (dominant/ non-dominant) hand."*

A strong reliability of 0.830 was determined by the Cronbach's alpha for the Grooved Pegboard results in this study.

Fine motor control and integration (Frisk et al., 2002) were also measured by the ROCF Test, as discussed in Section 7.4.5.2.

7.4.5.2 Visual-spatial abilities (Rey-Osterrieth Complex Figure Test)

The ROCF (attached Appendix O) was used as a measure of visual-spatial recall and construction (Akshoomoff, Feroleto, Doyle & Stiles, 2002; Caffarra et al., 2002; Frisk et al., 2002; Hernandez et al., 2003; McClure, Treland, Snow, Dickstein, Towbin, Charney et al., 2005); visual-motor integration (Frisk et al., 2002); spatial organisation and strategic decision-making (Anderson et al., 2004; Caffarra et al., 2002); planning and non-verbal memory (Akshoomoff et al., 2002; Bosson et al., 2002); object orientation, organisational, problem-solving strategies, perceptual and motor functions (Bosson et al., 2002; Caffarra et al., 2002); EF (Bosson et al., 2002; Caffarra et al., 2002; Taylor et al., 2000a); attention (Taylor et al., 2000a) and memory (Bosson et al., 2002; Caffarra et al., 2002; Hernandez et al., 2003; Lezak et al., 2004; Taylor et al., 2000b).

Grodzinsky and Diamond (1992) observed impairments in visual-motor planning and organisation in patients with frontal lobe damage. Bosson et al. (2002) postulated that the ROCF might reflect delayed development in the neuronal pathways related to the midbrain and HPA. Akshoomoff et al. (2002) found that early right hemisphere injury leads to persistent difficulty in reorganising and reformulating the spatial structure of a graphic object. Very young children with early unilateral brain injury perform poorly on visual-spatial tasks in comparison with same-age peers, but their performance on these tasks improve with age, regardless of site of injury. However, when they are confronted with more challenging tasks, their characteristic deficit reappears (Akshoomoff et al., 2002).

ADHD males in the general population performed worse on the ROCF and other measures of visual-spatial planning (Grodzinsky & Diamond, 1992).

The ROCF was used for three trials: administration, immediate recall (within three minutes after administration) and delayed recall (approximately 20 minutes after second trial) (Lezak et al., 2004).

The participant is instructed to copy the figure, which has been positioned so that its length runs along the participant's horizontal plane. A plain white sheet of paper is also placed horizontally. The participant is not allowed to rotate either the design or the paper so that rotational errors and difficulties in working with the unrotated material will be clear. Participants are requested to reproduce the design without warning on the recall trails. Time to completion is recorded on all the trials (Lezak et al., 2004).

The Taylor scoring system for the ROCF is followed. The figure is divided into 18 units. A maximum of two scores may be allocated to each unit, according to specific scoring guidelines (Lezak et al., 2004).

The Cronbach's alpha for the ROCF showed strong reliability of 0.904.

7.4.5.3 Memory: short-term verbal, working, non-verbal/ visual-spatial (memory for digits, Rey-Osterrieth Complex Figure Test)

The memory for digits (forward and backward) subtest of the SSAIS-R (van Eeden, 1997) was included in the test battery (see Appendix P). The digits forward task requires the child to repeat each sequence of numbers verbally exactly as it is given orally. Test items become progressively longer, from two to nine digits. Digits backward vary from two to eight digits, which must be repeated in an exactly reversed order.

Digits forward measures are commonly thought of as memory. However, these are related more closely to the efficiency of attention (Anderson et al., 2004, Jeyaseelan et al., 2006; Lezak et al., 2004; Rosenthal et al., 2006). Various researchers used the digits forward subtest

of different versions of the Wechsler Adult Intelligence Scale as a measure of verbal memory, with few EF connotations (Boonstra et al., 2005), including attention capacity (Tideman, 2000) and short-term auditory memory (Elgen et al., 2003; Rosenthal et al., 2006; Tideman, 2000). Digits backward are more of a memory test than digits forward, specifically involving working memory (Anderson et al., 2004, Boonstra et al., 2005; Cheung et al., 2004; Lezak et al., 2004; Rosenthal et al., 2006). Digits backward can be viewed as a predictor of executive functioning (Rosenthal et al., 2006). It involves mental tracking in that both the memory and reversing operations must proceed simultaneously (Lezak et al., 2004).

According to Lezak et al. (2004) digit repetition tasks, forward and backward, tend to be more vulnerable to left hemisphere involvement than to right hemisphere or diffuse damage. Anxiety and stress tend to lower the number of digits recalled (Lezak et al., 2004).

The Cronbach's alpha for the memory for digits in this study was 0.661, which is considered to be modest.

The ROCF Test (see Section 7.4.5.2) measured non-verbal (Akshoomoff et al., 2002; Bosson et al., 2002) or particularly visual-spatial memory.

7.4.5.4 Executive functioning (Stroop Word-Colour Test, Rey-Osterrieth Complex Figure Test, memory for digits)

Though EF includes functions investigated separately (such as attention, working memory, motor control and EF associated with visual-spatial skills), numerous other constructs are measured with EF tasks (such as cognitive flexibility, decision-making) indicated in the definition of EF. EF is defined as a complex system of functions including or dependent on interference control, non-verbal and verbal working memory, planning, reconstitution (Anderson et al., 2004; Böhm et al., 2004; Boonstra et al., 2005; Geurts et al.,

2005), response inhibition (Oosterlaan, 1996), decision-making, judgement and cognitive flexibility (Anderson et al., 2004; Boonstra et al., 2005; Cheung et al., 2004; Geurts et al., 2005). See detailed discussion of executive functioning under Section 5.5.

The Stroop Word-Colour Test (Stroop, 1935) was used as a measure of interference control (Cheung et al., 2004; Oosterlaan et al., 2005), inhibition (Constant et al., 2005; Lezak et al., 2004), EF (Constant et al., 2005; van der Elst, van Boxtel, van Breukelen & Jolles, 2006), cognitive flexibility and control (van der Elst et al., 2006) or the ease with which a person could ignore distracters and make the correct response (Cheung et al., 2004). The interference task of the Stroop Test is one of the most commonly administered measures of frontal lobe or executive functioning and seems to tap different cognitive functions mediated by these brain regions (Demakis, 2004). Various versions of the Stroop task are used to study executive control of attention, particularly resolving conflict among responses, which activates midline frontal areas (anterior cingulate) and the lateral prefrontal cortex (de Fockert, Rees, Frith & Lavie, 2004; Fan et al., 2002).

The test consists of three phases: Reading words ('blue', 'green', 'red' and 'yellow') printed in black, naming the colour of blocks and saying the colour the words are printed in and not reading the word (for example, the word "red" is printed in blue ink). The task requires inhibiting the cognitive impulse to read and pronounce the word, and substituting this impulse with naming the colour of the word. A computerised version of the Stroop (Appendix Q refers) was used (Ormond Software Enterprises, 1998). The increase in time taken to perform phase three compared with the basic phases is referred to as 'the Stroop interference effect' (van der Elst et al., 2006). Thus, latency scores indicate the response time and error scores refer to the response accuracy.

The reliability of the Stroop Word-Colour Test in this study was determined to be 0.592, as indicated by the Cronbach's alpha, which is considered to be modest.

Dimensions of EF were also reflected in results of the ROCF Test (Bosson et al., 2002; Caffarra et al., 2002; Taylor et al., 2000a) (see Section 7.4.5.2), the memory for digits backward (Rosenthal et al., 2006) subtest of the SSAIS-R, as well as only a few EF connotations with the memory for digits forward (Boonstra et al., 2005) (see Section 7.4.7).

7.5 Procedure

Written permission was obtained from the Gauteng Department of Education (Appendix B), as well as verbal approval from the principals of selected schools. Principals of the selected schools were provided with information during a personal visit (attached Appendix C). The Ethics Committee of the University of Limpopo approved the study.

A letter with a return slip (see Appendix D) was distributed to all parents via the selected schools. The purpose of this letter was to introduce the research project, identify LBW and NBW children and obtain written informed consent. A tentative sample was drawn from available return slips. All children with a birth weight of below 2 000 g were included in the clinical group. The control group (consisting of children with a birth weight above 3 000 g) was matched with the clinical group for age, gender, home language and SES. Only children under the age of 14 years were considered for inclusion in the sample.

An IQ below 75, a history of particular physical impairment (such as auditory or visual impairment), neurological trauma, psychosis or other severe psychiatric disorders were used as exclusion criteria in the study. Teachers were therefore requested to identify possible participants' level of global intellectual functioning, based on their observations, as well as possible physical impairment. Teachers' feedback prevented overrepresentation of control

children from a specific intellectual group. The intellectual functioning of those with possible borderline (IQ between 71 and 84) or mild mental retardation (IQ between 55 and 70) were screened with the CPM Test (Appendix L refers). The final sample was selected after feedback from teachers regarding children's estimated intellectual functioning. Attempts were made to stick to the original sample as far as possible. Seven LBW children were excluded from the study owing to lack of suitable controls or lack of confirmation of birth weight below 2 000 g. Finding suitable controls from the same language group complicated the matching process.

Parents were informed of their child's selection (see Appendix E) and requested to complete a Parent DBD rating scale (attached Appendix G), Biographical Data Questionnaire (see Appendix F) and consent form (Appendix H refers). Parents were requested to discontinue non-essential medication in children for at least 24 hours before testing to allow complete neutralisation of its effects. One Teacher DBD rating scale (attached Appendix G) per child was requested from his/her school. Teachers were unaware of birth weight status. A total of 158 (100%) teachers returned their DBD rating scales. One-hundred-and-forty-two parents (89.9%) returned their DBD rating scales and biographical data questionnaires.

The neuropsychological test battery and the "Terry" were administered to the sample at the selected schools during school hours. One-off individual testing, lasting for approximately 60 minutes, was conducted. Test instructions were given according to the preference of the participant (English or Afrikaans). As stated, only English or Afrikaans medium schools were included in the sample. Before the actual neuropsychological testing commenced, the children were introduced to the researcher and the research study and informed about the procedure. Participation was voluntary and therefore individual children's permission was obtained during the introduction stage.

The researcher who conducted the testing was unaware of the children's group affiliation. The researcher was registered with the Health Professions Council of South Africa as a clinical psychologist (community service) and had experience in the administration of psychometric tests.

General feedback to schools (see Appendix I) and individual feedback to parents (see Appendix J) were given after statistical analysis of data.

All expenses were at the cost of the researcher. No compensation fees were paid for participation. Parents of children with significant problems were offered free services rendered by the relevant public sector service provider.

7.6 Method of analysis

Data were analysed by using the statistical computer program STATISTICA 7.1 (StatSoft, 2007) and SPSS (15.0). Analysis of Variance (ANOVA) models were used to investigate possible between-group differences. The results were analysed with 2 x 2 x 2 (group x gender x age) ANOVAs. *Post hoc* tests (Newman-Keuls) were employed to determine within-group differences. Moderate to strong correlations between variables were indicated, as reflected in the table of correlations (see Appendix K).

Chapter 8

RESULTS

8.1 Introduction

The aim of this study was to investigate the magnitude and characteristics of the internalising and externalising psychological symptoms among LBW children in comparison with NBW children, as well as to determine whether LBW children have more neuropsychological impairments than NBW children.

Measurement instruments were used to identify between-group and within-group differences pertaining to birth weight, gender and age on the mentioned focus areas. The "Terry" questionnaire measured internalising symptoms, whereas the parent and teacher DBD rating scales focussed on externalising symptoms. A neuropsychological test battery was administered to assess neuropsychological functions. Fine motor skills were measured with the Grooved Pegboard and ROCF Test, visual-perceptual abilities with the ROCF Test, memory with the memory for digits subtest of the SSAIS-R (forward and backward) and the ROCF Test, as well as various EFs with the Stroop Word-Colour Test, ROCF Test and memory for digits subtest. Significant group differences in psychological symptoms and neuropsychological functions may indicate the nature of possible brain dysfunction in children born with LBW (Anderson et al., 2004; Espy, 2004).

8.2 Results of the study

In order to test the respective hypotheses, results of the above-mentioned psychological symptoms and neuropsychological functions are presented in the following format:

The results for the internalising and externalising psychological symptoms, as well as the neuropsychological functions, are presented separately and include descriptive statistics (in table and graph form), ANOVA results investigating possible between-group differences (groups were divided according to birth weight, gender and age) and the *post hoc* (Newman-Keuls) test to indicate where the differences occur. These results are presented for birth weight, gender and age groups for the questionnaire, rating scales and each test with reference to the specific hypothesis.

8.2.1 Internalising and externalising symptoms

The first phase of the investigation was to determine the prevalence of psychological disorders, including internalising psychological symptoms (referring to SAD, OAD and MDD) and externalising psychological symptoms (particularly ADHD, ODD and CD) in children with LBW compared to children with NBW, as a function of gender and age. The results are illustrated below in Sections 8.2.1.1 and 8.2.1.2.

8.2.1.1 Internalising symptoms

Table 8.1 represents the descriptive statistics for the results on the "Terry" questionnaire for symptoms of SAD, OAD and MDD, for the LBW and NBW groups for the age and gender groups.

Table 8.1 Internalising symptoms - SAD, OAD and MDD
Descriptive statistics for birth weight, gender and age groups

Group	Gender	Age group	N	SAD	OAD	MDD
LBW	Male	6-9	23	4.783 ± 3.302	3.696 ± 2.566	3.609 ± 2.726
		10-13	15	3.533 ± 3.357	4.800 ± 3.783	4.200 ± 5.308
	Female	6-9	26	4.923 ± 2.296	4.615 ± 2.729	3.885 ± 3.128
		10-13	15	4.267 ± 3.218	4.000 ± 2.952	4.600 ± 2.849
NBW	Male	6-9	23	4.217 ± 2.504	3.522 ± 1.880	3.087 ± 2.410
		10-13	15	3.000 ± 3.000	2.933 ± 2.815	2.533 ± 1.885
	Female	6-9	26	4.462 ± 2.874	4.038 ± 2.645	2.808 ± 2.623
		10-13	15	3.533 ± 2.560	3.600 ± 2.558	2.933 ± 2.604

Figure 8.1 Internalising symptoms - SAD, OAD and MDD (age 6 to 9)

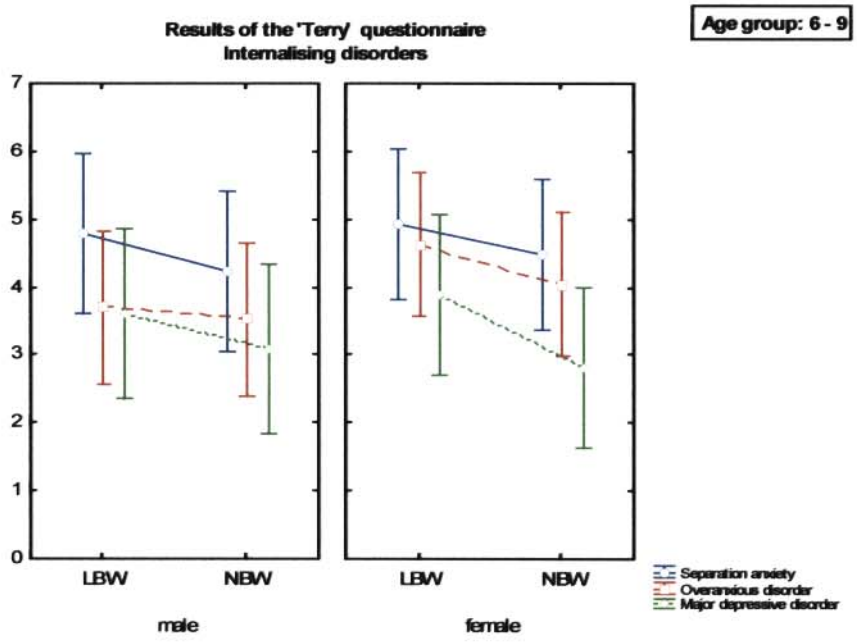
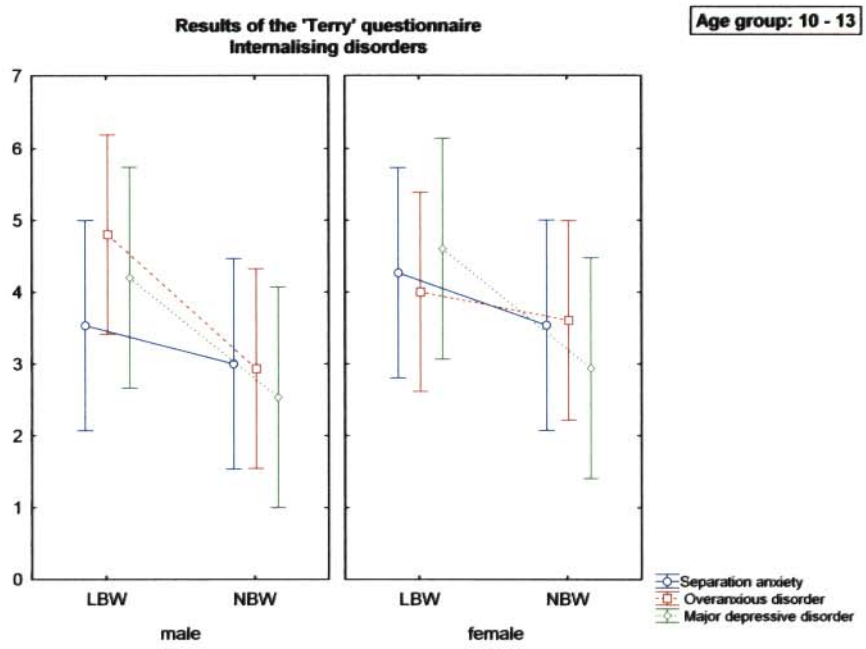


Figure 8.1 illustrates the plot of means for SAD, OAD and MDD scores on the "Terry" questionnaire, for birth weight and gender of the 6 to 9 age group.

Figure 8.2 Internalising symptoms - SAD, OAD and MDD (age 10 to 13)



The plot of means for SAD, OAD and MDD scores on the "Terry" questionnaire, for birth weight and gender of the 10 to 13 age group is illustrated in Figure 8.2.

The results of the ANOVA for SAD, OAD and MDD on the "Terry" questionnaire, for the birth weight, gender and age groups are indicated in Table 8.2.

Table 8.2 ANOVA results for internalising disorders (SAD, OAD and MDD)

Variable	ANOVA						
		SAD		OAD		MDD	
	Df	*F*	*p*	*F*	*p*	*F*	*P*
Group	1, 150	1.482	0.225	2.861	0.093	6.228	0.014*
Gender	1, 150	0.768	0.382	0.534	0.466	0.163	0.687
Age	1, 150	4.624	0.033	0.091	0.763	0.198	0.657
Group x gender	1, 150	0.003	0.959	0.356	0.552	0.079	0.779
Group x age	1, 150	0.016	0.899	0.722	0.397	0.771	0.381
Gender x age	1, 150	0.219	0.640	0.774	0.380	0.165	0.685
Group x gender x age	1, 150	0.026	0.872	1.099	0.296	0.079	0.779

* $p \leq 0.05$

The ANOVA showed statistically significantly more major depressive symptoms in the LBW group than in the NBW counterparts (p=0.014), but not for SAD and OAD. No main or interaction effects of gender or age groups were indicated, therefore the gender and age groups were not analysed separately.

8.2.1.2 Externalising symptoms

Externalising symptoms were assessed by the DBD rating scale. Bias was checked by collecting data from both parents and teachers (Breslau & Chilcoat, 2000). Teachers were assumed to be generally unaware of children's birth weight status.

8.2.1.2.1 Parent rating scale

Table 8.3 gives an overview of the descriptive statistics for the hyperactive/impulsive, inattentive, ODD and CD scores on the parent DBD rating scale, for the LBW and controls, as well as for the gender and age groups.

Table 8.3 Hyperactivity/impulsiveness, inattention, ODD and CD (parent DBD ratings) – Descriptive statistics for birth weight, gender and age groups

Group	Gender	Age group	N	H/I	Inatt	ODD	CD
LBW	Male	6-9	19	7.211 ± 3.966	7.105 ± 4.841	4.842 ± 3.452	1.263 ± 1.485
		10-13	11	5.545 ± 4.719	6.273 ± 5.764	4.273 ± 4.125	0.727 ± 1.009
	Female	6-9	24	7.750 ± 5.343	7.250 ± 5.566	4.958 ± 4.154	1.167 ± 1.308
		10-13	13	4.923 ± 4.499	7.923 ± 6.538	4.692 ± 4.289	1.231 ± 1.536
NBW	Male	6-9	22	6.636 ± 5.720	4.455 ± 3.569	5.455 ± 3.900	1.318 ± 2.255
		10-13	13	4.231 ± 4.086	4.000 ± 4.509	3.308 ± 3.473	0.538 ± 0.660
	Female	6-9	24	3.958 ± 2.216	3.458 ± 3.776	4.000 ± 3.079	0.750 ± 1.482
		10-13	14	3.429 ± 2.377	2.571 ± 2.652	5.000 ± 4.368	0.571 ± 0.938

Figure 8.3 Hyperactivity/impulsiveness, inattention, ODD and CD - Parent DBD ratings (age 6 to 9)

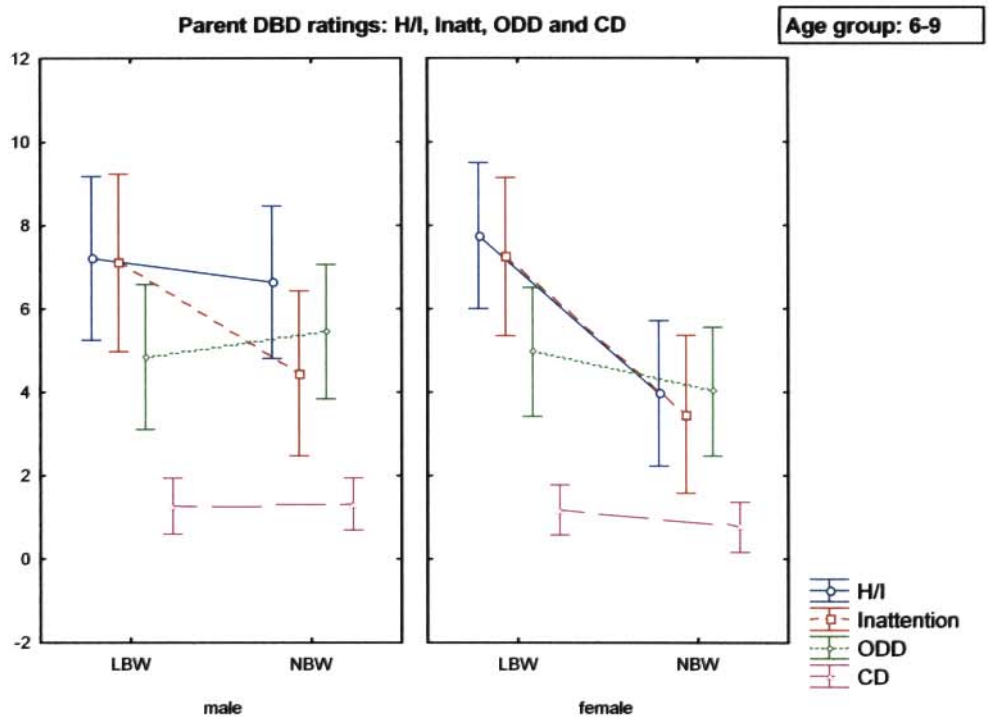
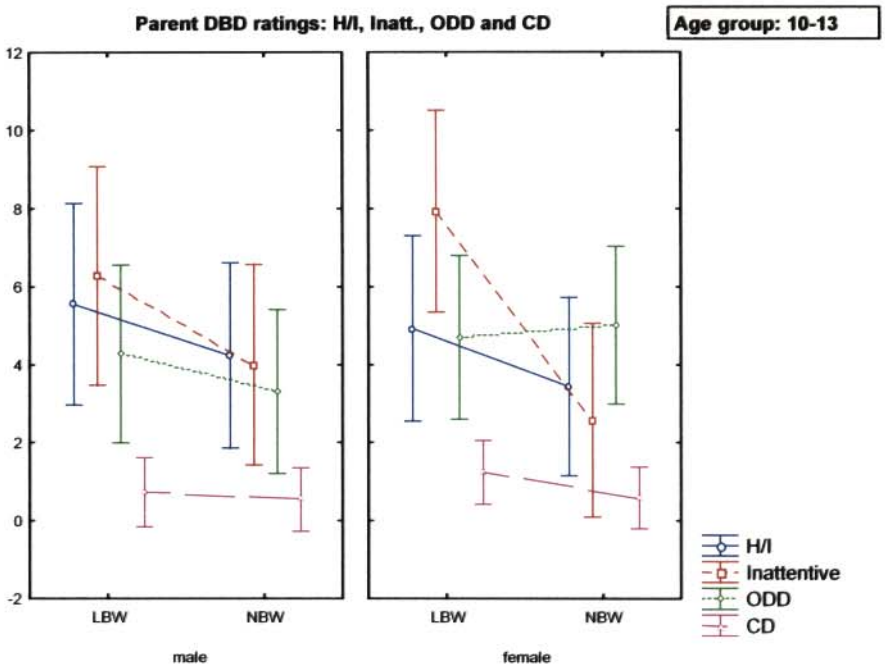


Figure 8.3 illustrates the plot of means for hyperactivity/impulsiveness, inattention, ODD and CD scores on the parent DBD rating scale, for birth weight and gender of the 6 to 9 age group.

Figure 8.4 Hyperactivity/impulsiveness, inattention, ODD and CD - Parent DBD ratings (age 10 to 13)



The plot of means for the hyperactivity/impulsiveness, inattention, ODD and CD scores on the parent DBD rating scale, for birth weight and gender of the 10 to 13 age group, is shown in Figure 8.4.

Table 8.4 reflects the results of the ANOVA for hyperactivity/impulsiveness, inattention, ODD and CD scores on the parent DBD rating scale, for the birth weight, gender and age groups.

Table 8.4 Hyperactivity/impulsiveness, inattention, ODD and CD (parent DBD ratings) – ANOVA results for birth weight, gender and age groups

Variable	ANOVA								
		H/I		Inatt		ODD		CD	
	Df	*F*	*p*	*F*	*p*	*F*	*p*	*F*	*p*
Group	1, 132	5.509	0.020*	18.036	0.000***	0.138	0.711	1.332	0.251
Gender	1, 132	1.359	0.246	0.036	0.850	0.082	0.775	0.015	0.903
Age	1, 132	5.903	0.016*	0.205	0.651	0.539	0.464	1.861	0.175
Group x gender	1, 132	1.235	0.268	1.623	0.205	0.012	0.912	0.808	0.370
Group x age	1, 132	0.259	0.611	0.127	0.722	0.013	0.908	0.215	0.643
Gender x age	1, 132	0.055	0.816	0.105	0.746	1.634	0.203	1.313	0.254
Group x gender x age	1, 132	0.987	0.322	0.342	0.559	1.110	0.294	0.000	1.000

* $p \leq 0.05$; *** $p \leq 0.001$

The ANOVA showed significantly more symptoms of hyperactivity/impulsiveness (p=0.020) and inattention (p=0.000) in the LBW group when compared to NBW participants, but no differences for ODD and CD. In the case of hyperactivity/impulsiveness age had an effect, therefore the age groups were analysed separately. No effect of gender was found, neither main nor interacting, for any of the four scales. Therefore, the gender groups were not analysed separately.

The result of the *post hoc* (Newman-Keuls) test performed on the results of the parent DBD rating scale for the birth weight and age groups is depicted in Table 8.5.

Table 8.5 Hyperactivity/impulsiveness and inattention (parent DBD ratings) – Post hoc (Newman-Keuls) results for birth weight and age groups

DBD scale	H/I	
LBW v NBW	Age 6 to 9	Age 10 to 13
	0.035*	n/s

* $p \leq 0.05$

The *post hoc* test indicated that there were significantly more symptoms of hyperactivity/impulsiveness in the 6 to 9 LBW group when compared to the NBW cohort (p=0.035), whereas no significant difference in symptoms was found for the 10 to 13 group.

8.2.1.2.2 Teacher rating scale

Table 8.6 gives an overview of the descriptive statistics for hyperactive/impulsive, inattentive, ODD and CD scores on the teacher DBD rating scale, for the LBW and controls, as a function of gender and age.

Table 8.6 Hyperactivity/impulsiveness, inattention, ODD and CD (teacher DBD ratings) – Descriptive statistics for birth weight, gender and age groups

Group	Gender	Age group	N	H/I	Inatt	ODD	CD
LBW	Male	6-9	23	4.870 ± 4.948	7.652 ± 7.101	3.652 ± 3.892	1.130 ± 1.546
		10-13	15	6.000 ± 5.593	9.667 ± 6.821	3.933 ± 4.605	1.667 ± 2.742
	Female	6-9	26	3.000 ± 3.888	5.231 ± 5.494	0.615 ± 1.472	1.269 ± 5.869
		10-13	15	1.667 ± 3.016	4.200 ± 5.199	2.800 ± 4.570	0.667 ± 1.113
NBW	Male	6-9	23	3.913 ± 4.481	5.174 ± 5.694	1.957 ± 2.836	0.435 ± 0.788
		10-13	15	2.867 ± 4.406	3.600 ± 4.852	1.133 ± 1.457	0.067 ± 0.258
	Female	6-9	26	1.423 ± 2.043	1.462 ± 4.140	1.000 ± 2.315	0.077 ± 0.272
		10-13	15	1.400 ± 2.923	1.000 ± 3.071	0.800 ± 2.077	0.400 ± 1.298

Figure 8.5 Hyperactivity/impulsiveness, inattention, ODD and CD - Teacher DBD ratings (age 6 to 9)

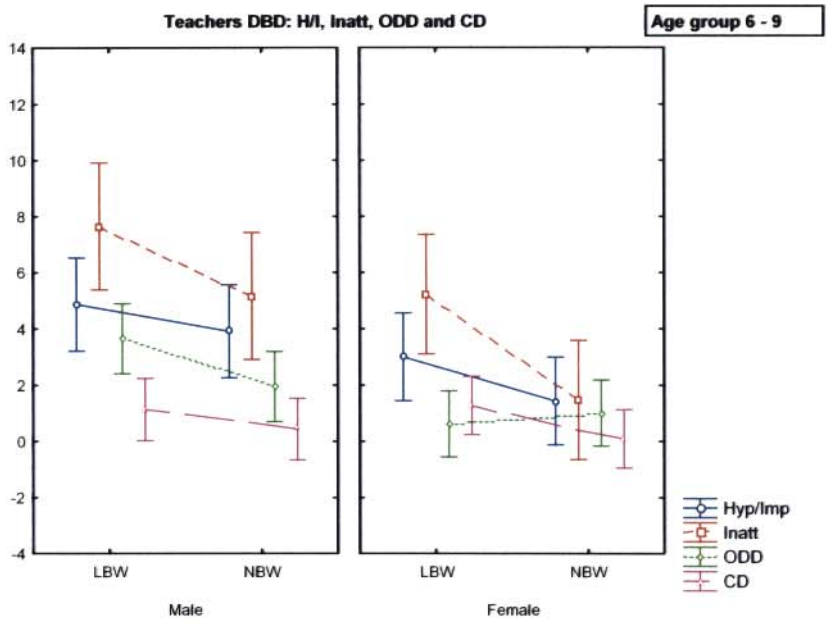
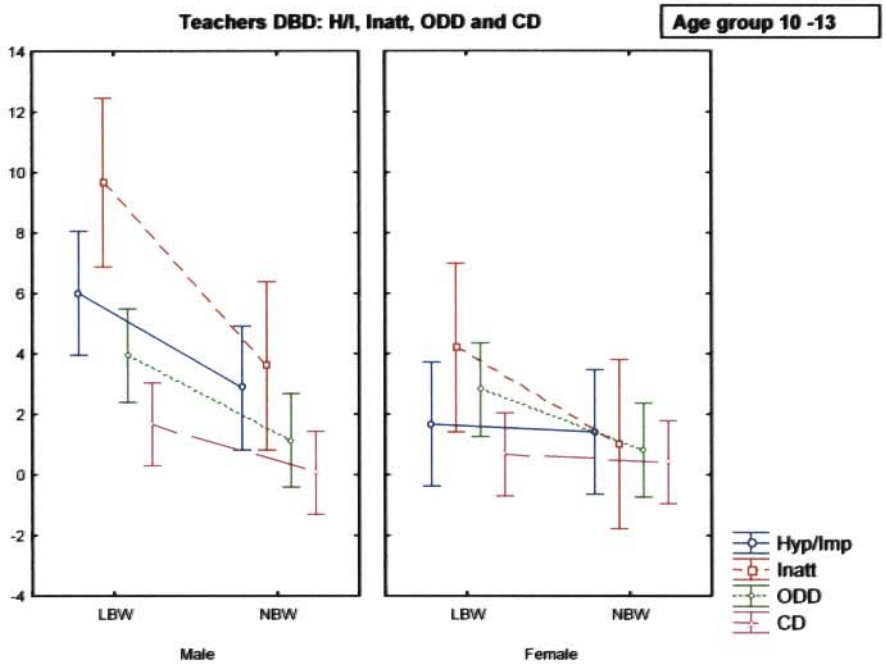


Figure 8.5 illustrates the plot of means for hyperactivity/impulsiveness, inattention, ODD and CD scores on the teacher DBD rating scale, for birth weight and gender of the 6 to 9 age group.

Figure 8.6 Hyperactivity/impulsiveness, inattention, ODD and CD - Teacher DBD ratings (age 10 to 13)



The plot of means for hyperactivity/impulsiveness, inattention, ODD and CD scores on the teacher DBD rating scale, for birth weight and gender of the 10 to 13 age group, is shown in Figure 8.6.

Table 8.7 reflects the results of the ANOVA for hyperactivity/impulsiveness, inattention, ODD and CD scores on the teacher DBD rating scale, for the birth weight, gender and age groups.

Table 8.7 Hyperactivity/impulsiveness, inattention, ODD and CD (teacher DBD ratings) – ANOVA results for birth weight, gender and age groups

Variable	ANOVA								
		H/I		Inatt		ODD		CD	
	Df	*F*	*p*	*F*	*p*	*F*	*p*	*F*	*p*
Group	1, 150	5.070	0.026*	18.647	0.000***	9.443	0.003**	4.563	0.034*
Gender	1, 150	14.863	0.000***	15.623	0.000***	7.538	0.007**	0.254	0.615
Age	1, 150	0.233	0.630	0.086	0.770	0.526	0.469	0.004	0.950
Group x gender	1, 150	0.727	0.395	0.192	0.662	2.098	0.150	0.227	0.635
Group x age	1, 150	0.108	0.743	0.706	0.402	3.078	0.081	0.000	0.990
Gender x age	1, 150	0.299	0.585	0.289	0.591	1.614	0.206	0.065	0.799
Group x gender x age	1, 150	1.751	0.188	1.339	0.249	0.414	0.521	1.084	0.230

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$

The ANOVA indicated significant group differences, with the LBW group rated by teachers with more symptoms of hyperactivity/impulsiveness (p=0.026), inattention (p=0.000), ODD (p=0.003) and CD (p=0.034). A gender effect was shown on the hyperactive/impulsive, inattentive and ODD scales, but not for CD. There was no effect of age for any of the four scales, neither main nor interacting; therefore the *post hoc* analyses were employed for birth weight and gender effects only.

The results of the *post hoc* tests (Newman-Keuls) performed on the hyperactive/impulsive, inattention, ODD and CD scales of the teacher DBD rating scale for the birth weight and gender groups, are demonstrated in Table 8.8.

Table 8.8 Hyperactivity/impulsiveness, inattention and ODD (teacher DBD ratings) – Post hoc (Newman-Keuls) results for birth weight and gender groups

Group	H/I		Inatt		ODD	
LBW V NBW	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
	0.045*	n/s	0.005**	0.011*	0.002**	n/s

* $p \leq 0.05$; * $p \leq 0.01$

The *post hoc* test indicated significantly more hyperactive/impulsive (p=0.045), inattentive (p=0.005) and ODD (p=0.002) symptoms among LBW males when compared to their NBW counterparts. Significantly more inattentive symptoms (p=0.011) were shown in the LBW female group than in the NBW cohort.

8.2.2 Neuropsychological functions

The second phase of the investigation was to determine the neuropsychological functioning, including motor (measured by the Grooved Pegboard and ROCF Test), visual-spatial (ROCF Test), memory (memory for digits subtest and ROCF Test) and executive functioning (Stroop Word-Colour Test, ROCF Test and memory for digits subtest) in children with LBW compared to children with NBW, as a function of gender and age. The results of neuropsychological functions are illustrated below in the respective neuropsychological test results.

8.2.2.1 Fine motor skills (Grooved Pegboard)

The Grooved Pegboard task and ROCF Test were used to measure fine motor skills. The results of the ROCF Test are shown in Section 8.2.2.2.

Table 8.9 illustrates the descriptive statistics for the results of the fine motor skills on the Grooved Pegboard for the LBW group and controls.

Table 8.9 Fine motor skills (Grooved Pegboard) – Descriptive statistics for birth weight, gender and age groups

Group	Gender	Age group	N	Dom hand	N-dom hand
LBW	Male	6-9	23	101.174 ± 19.757	111.739 ± 30.780
		10-13	15	80.200 ± 20.516	84.800 ± 18.237
	Female	6-9	26	105.654 ± 27.629	119.615 ± 29.834
		10-13	15	79.933 ± 16.667	96.200 ± 38.488
NBW	Male	6-9	23	90.348 ± 17.699	94.261 ± 17.700
		10-13	15	65.800 ± 6.085	72.400 ± 8.149
	Female	6-9	26	85.769 ± 18.474	97.539 ± 23.247
		10-13	15	70.600 ± 12.608	76.867 ± 16.071

Figure 8.7 Results of fine motor skills task (Grooved Pegboard) – age 6 to 9

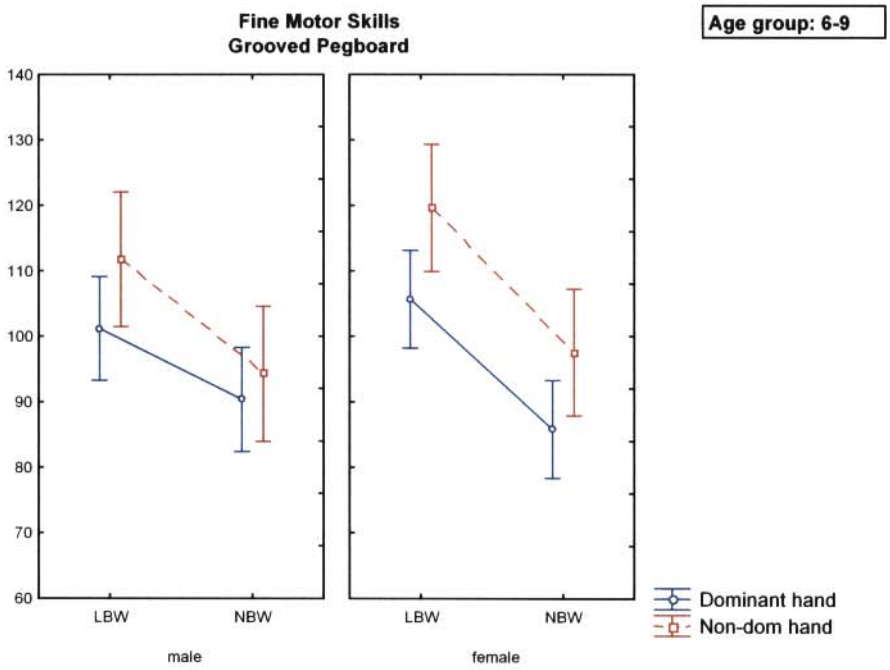
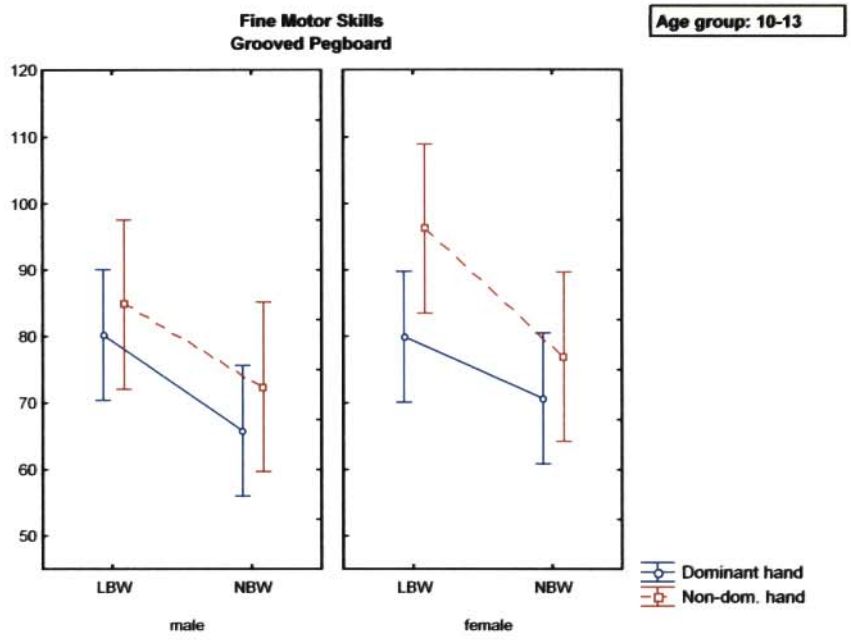


Figure 8.7 shows the plot of means for birth weight and gender of the 6 to 9 age group, for completion time on the Grooved Pegboard.

Figure 8.8 Results of fine motor skills task (Grooved Pegboard) – age 10 to 13



The plot of means for birth weight and gender of the 10 to 13 age group for completion time on the Grooved Pegboard is depicted in Figure 8.8.

The results of the repeated measures ANOVA for the Grooved Pegboard for the birth weight, gender and age groups are reflected in Table 8.10. Repeated measures were employed, since the same function is measured with the dominant and non-dominant hand.

Table 8.10 Fine motor skills (Grooved Pegboard) – repeated measures ANOVA results for birth weight, gender and age groups

Variable	ANOVA		
	Fine motor skills		
	Df	*F*	*p*
Group	1, 150	23.003	0.000***
Gender	1, 150	1.440	0.232
Age	1, 150	46.779	0.000***
Group x gender	1, 150	0.351	0.555
Group x age	1, 150	0.319	0.573
Gender x age	1, 150	0.127	0.722
Group x gender x age	1, 150	0.202	0.654
Dominance	1, 150	32.458	0.000***
Dominance x group	1, 150	1.684	0.196
Dominance x gender	1, 150	3.028	0.084
Dominance x age	1, 150	0.249	0.619
Dominance x group x gender	1, 150	0.338	0.562
Dominance x group x age	1, 150	0.004	0.948
Dominance x gender x age	1, 150	0.000	0.995
Dominance x group x gender x age	1, 150	1.608	0.207

***$p \leq 0.001$

The repeated measures ANOVA showed that the LBW group used significantly more time to complete the Grooved Pegboard tasks than the NBW counterparts (p=0.000). Effects of age and hand dominance were indicated, which were analysed separately. There was no effect of gender, neither main nor interacting, therefore the results were analysed according to birth weight groups and age groups only.

The result of the *post hoc* (Newman-Keuls) test performed on the Grooved Pegboard scores for the birth weight and age groups is demonstrated in Table 8.11.

Table 8.11 Fine motor skills (Grooved Pegboard) – Post hoc (Newman-Keuls) results for birth weight and age groups

Group	Dom hand		Non-dom hand	
	6-9	**10-13**	**6-9**	**10-13**
LBW v NBW	0.013*	0.056	0.000***	0.011*

* $p \leq 0.05$; *** $p \leq 0.001$

For the dominant hand there were significant differences in performance for the 6 to 9 age group only (p=0.013), with the LBW group having the poorer performance, as determined by the *post hoc* (Newman-Keuls) test. A tendency toward significance was shown on the dominant hand in the 10 to 13 group. Both the 6 to 9 (p=0.000) and 10 to 13 (p=0.011) LBW age groups showed poorer performance with the non-dominant hand when compared to the NBW participants.

8.2.2.2 Visual-spatial and motor skills, executive functions and visual-spatial memory (Rey-Osterrieth Complex Figure Test)

Visual-spatial and motor skills, various EFs and visual-spatial memory were assessed with the ROCF Test, as indicated in Section 7.4.5.2. Table 8.12 gives an overview of the results on the ROCF, for the LBW and controls, as a function of gender and age.

Table 8.12 Visual-spatial and motor skills, EF and visual-spatial memory (ROCF) – Descriptive statistics for birth weight, gender and age groups

Group	Gender	Age group	N	Administration	Immediate recall	Delayed recall
LBW	Male	6-9	23	21.565 ± 6.537	14.261 ± 5.988	14.043 ± 6.105
		10-13	15	26.400 ± 4.653	19.067 ± 6.819	18.633 ± 6.942
	Female	6-9	26	23.038 ± 5.217	14.519 ± 6.600	14.423 ± 5.599
		10-13	15	28.467 ± 3.916	20.200 ± 6.894	20.267 ± 7.639
NBW	Male	6-9	23	28.783 ± 4.056	20.891 ± 3.829	20.587 ± 4.083
		10-13	15	31.067 ± 2.815	23.700 ± 5.644	23.733 ± 5.428
	Female	6-9	26	28.865 ± 3.503	20.231 ± 4.522	20.269 ± 4.750
		10-13	15	31.233 ± 3.206	22.867 ± 4.103	22.633 ± 5.111

Figure 8.9 Results of the ROCF task (age 6 to 9)

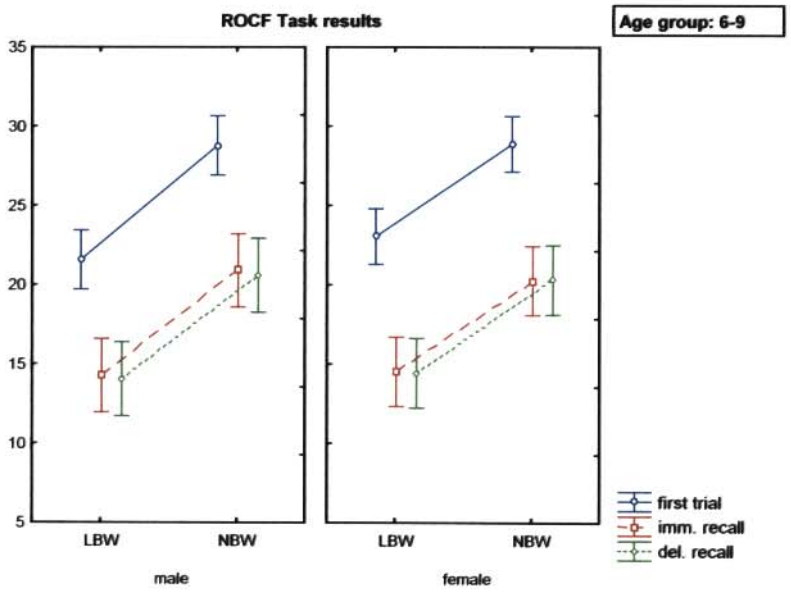
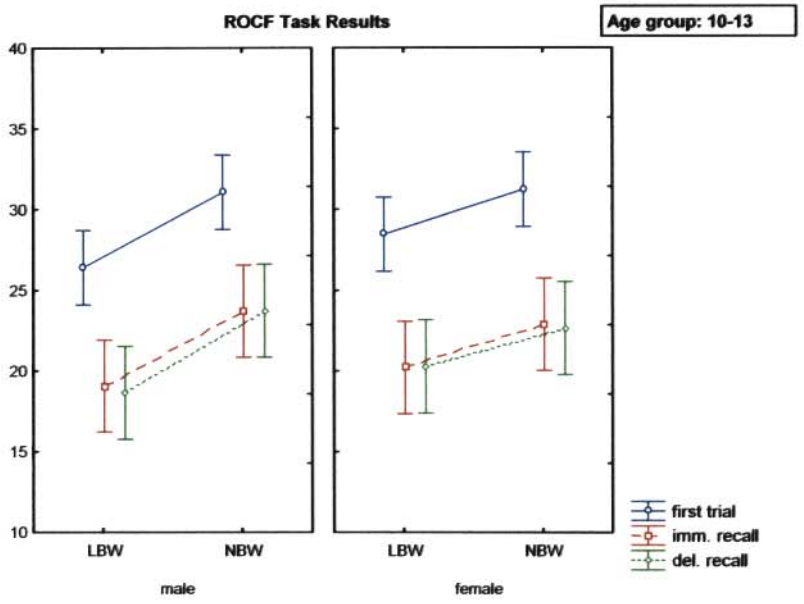


Figure 8.9 illustrates the plot of means for birth weight and gender of the 6 to 9 age group, for scores on the ROCF.

Figure 8.10 Results of the ROCF task (age 10 to 13)



The plot of means for birth weight and gender of the 10 to 13 age group for scores on the ROCF is indicated in Figure 8.10.

Table 8.13 reflects the results of the ANOVA for the ROCF for the birth weight, gender and age groups

Table 8.13 Visual-spatial and motor skills, EF and visual-spatial memory (ROCF) – ANOVA results for birth weight, gender and age groups

Variable	ANOVA						
		First trial		Immediate recall		Delayed recall	
	Df	*F*	*p*	*F*	*p*	*F*	*p*
Group	1, 150	47.712	0.000***	28.539	0.000***	28.590	0.000***
Gender	1, 150	1.634	0.203	0.001	0.978	0.026	0.873
Age	1, 150	25.311	0.000***	18.775	0.000***	18.433	0.000***
Group x gender	1, 150	1.232	0.268	0.616	0.434	0.853	0.357
Group x age	1, 150	3.582	0.060	1.881	0.172	1.757	0.187
Gender x age	1, 150	0.052	0.819	0.036	0.849	0.016	0.899
Group x gender x age	1, 150	0.030	0.863	0.081	0.776	0.301	0.584

*** $p \leq 0.001$

The ANOVA showed significant group differences for the first trial (p=0.000), immediate recall (p=0.000) and delayed recall (p=0.000) of the ROCF Test, with the LBW group having the poorer performance. An age effect was also indicated on all three trials, therefore the age groups were analysed separately. There were no effects of gender, neither main nor interacting, therefore the gender groups were not analysed separately.

The result of the *post hoc* (Newman-Keuls) test performed on the ROCF scores for the birth weight and age groups is demonstrated in Table 8.14.

Table 8.14 Visual-spatial and motor skills, EF and visual-spatial memory (ROCF) – Post hoc (Newman-Keuls) results for birth weight and age groups

Group	First trial		Immediate recall		Delayed recall	
	6-9	**10-13**	**6-9**	**10-13**	**6-9**	**10-13**
LBW v NBW	0.000***	0.001***	0.000***	0.014*	0.000***	0.012*

* $p \leq 0.05$; *** $p \leq 0.001$

The *post hoc* (Newman-Keuls) test showed that the LBW 6 to 9 age group performed significantly poorer than the NBW comparisons on the first trial (p=0.000), immediate recall (p=0.000) and delayed recall (p=0.000) of the ROCF Test. Significant differences for the 10 to 13 age group were also indicated on the first trial (p=0.001), immediate recall (p=0.014) and delayed recall (p=0.012), with the LBW cohort having the poorer performance.

8.2.2.3 Memory: short-term verbal memory and working memory (memory for digits forward and backward)

Short-term verbal and working memory were measured with the memory for digits forward and backward respectively. Working memory was also measured by the ROCF Test (see Section 8.2.2.2).

Table 8.15 gives an overview of the results of the memory for digits subtest (forward and backward), for the LBW and controls, as a function of gender and age.

Table 8.15 Short-term verbal and working memory (digits forward and backward subtest) – Descriptive statistics for birth weight, gender and age groups

Group	Gender	Age group	N	Digits forward	Digits backwards
LBW	Male	6-9	23	6.783 ± 1.506	3.304 ± 1.550
		10-13	15	9.400 ± 1.502	5.000 ± 1.195
	Female	6-9	26	7.923 ± 1.853	3.731 ± 1.511
		10-13	15	7.933 ± 2.492	4.200 ± 1.207
NBW	Male	6-9	23	7.957 ± 1.609	3.696 ± 0.974
		10-13	15	9.467 ± 1.995	5.933 ± 1.534
	Female	6-9	26	8.346 ± 2.058	4.500 ± 1.241
		10-13	15	9.933 ± 1.580	5.000 ± 1.414

Figure 8.11 Memory results (digits forward and backward) - age 6 to 9

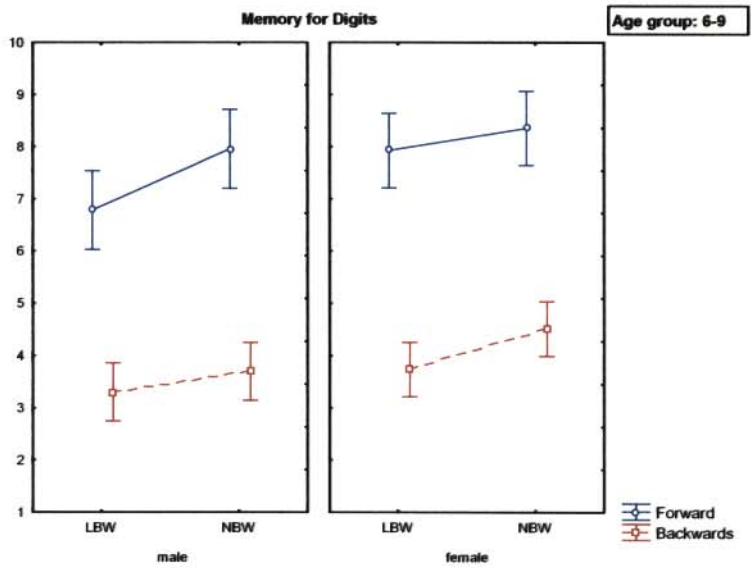
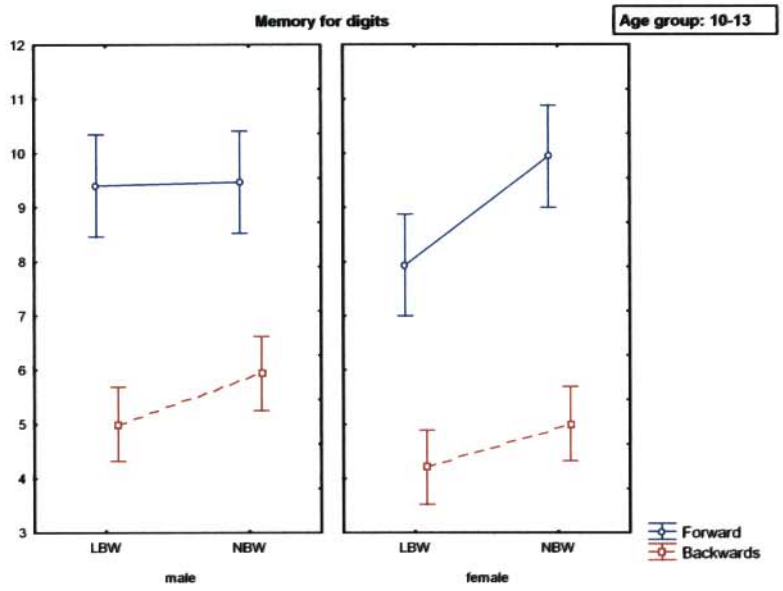


Figure 8.11 illustrates the plot of means for birth weight and gender of the 6 to 9 age group, for scores on the memory for digits subtest.

Figure 8.12 Memory results (digits forward and backward) - age 10 to 13



The plot of means for birth weight and gender of the 10 to 13 age group for scores on the memory for digits subtest is illustrated in Figure 8.12.

Table 8.16 shows the results of the ANOVA for the memory for digits subtest for the birth weight, gender and age groups.

Table 8.16 Memory results – ANOVA results for birth weight, gender and age groups

Variable	ANOVA				
		Digits forward		Digits backward	
	Df	*F*	*p*	*F*	*p*
Group	1, 150	9.209	0.003**	10.779	0.001***
Gender	1, 150	0.193	0.661	0.325	0.569
Age	1, 150	22.487	0.000***	30.935	0.000***
Group x gender	1, 150	0.959	0.329	0.077	0.782
Group x age	1, 150	0.151	0.698	0.422	0.517
Gender x age	1, 150	4.392	0.038*	11.308	0.001***
Group x gender x age	1, 150	4.943	0.028*	0.336	0.563

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$

The ANOVA showed significant group differences for digits forward (p=0.003) and digits backward (p=0.001), with poorer scores for the LBW group than their NBW counterparts. An effect of age was indicated on both digits forward and backward, therefore the age groups were analysed separately. There was an interacting effect of gender on digits forward.

The result of the *post hoc* (Newman-Keuls) test performed on the memory for digits forward and backward scores for the birth weight, gender and age groups, is demonstrated in Table 8.17.

Table 8.17 Memory results – Post hoc (Newman-Keuls) results for birth weight, gender and age groups

Group	Digits forward				Digits backward	
	Male		Female			
LBW v NBW	**6-9**	**10-13**	**6-9**	**10-13**	**6-9**	**10-13**
	n/s	n/s	n/s	0.012*	0.057	0.005**

* $p \leq 0.05$; ** $p \leq 0.01$

The *post hoc* (Newman-Keuls) test indicated that the 10 to 13 females (p=0.012) of the LBW cohort scored significantly lower than the NBW comparison group. For the digits backward there were significant differences in performance for the 10 to 13 group (p=0.005), with the LBW group having the poorer performance. A tendency toward significance was shown on the digits backward in the 6 to 9 group.

8.2.2.4 Executive functioning (Stroop Word-Colour Test)

The Stroop Word-Colour Test, ROCF Test (see Section 8.2.2.2) and memory for digits forward and backward (see Section 8.2.2.3) measured aspects of executive functioning, such as interference control (Stroop, 1935), inhibition (Lezak et al., 2004) and cognitive flexibility (van der Elst et al., 2006). The Stroop Word-Colour Test consists of latency and error scores. Table 8.18 gives an overview of the results on the latency scores of the Stroop Word-Colour Test (latencies: neutral, blocks, interferences and interference difference), for the LBW and controls, as a function of gender and age.

Table 8.18 Executive functioning (Stroop Word-Colour Test: latency scores) – Descriptive statistics for birth weight, gender and age groups

Group	Gender	Age	N	Neutral	Blocks	Interference	Interference diff.
LBW	Male	6-9	23	176.297 ± 159.767	158.517 ± 59.337	259.510 ± 122.584	107.716 ± 102.726
		10-13	15	103.287 ± 70.754	120.927 ± 37.038	210.134 ± 44.634	89.207 ± 32.467
	Female	6-9	26	137.687 ± 113.049	140.930 ± 50.867	242.798 ± 92.067	101.868 ± 62.461
		10-13	15	82.892 ± 32.329	115.025 ± 39.816	234.019 ± 109.565	106.994 ± 45.457
NBW	Male	6-9	23	137.209 ± 79.902	150.387 ± 64.004	231.719 ± 57.393	81.332 ± 57.288
		10-13	15	71.995 ± 30.759	92.305 ± 17.291	158.011 ± 31.780	65.707 ± 25.017
	Female	6-9	26	94.598 ± 26.241	121.083 ± 22.175	209.244 ± 47.303	94.720 ± 60.003
		10-13	15	69.406 ± 11.826	97.916 ± 21.175	179.743 ± 44.543	81.827 ± 31.040

Figure 8.13 Executive functioning - Stroop Word-Colour Test: latency scores (age 6 to 9)

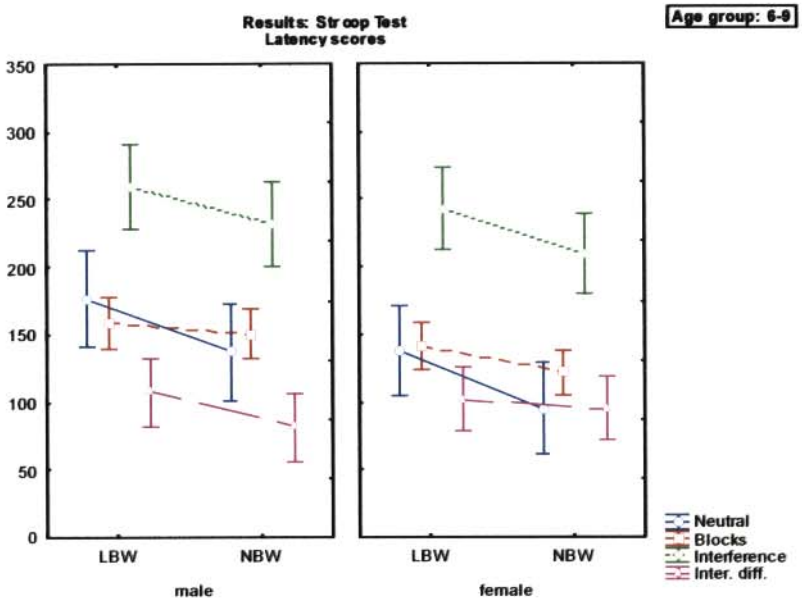
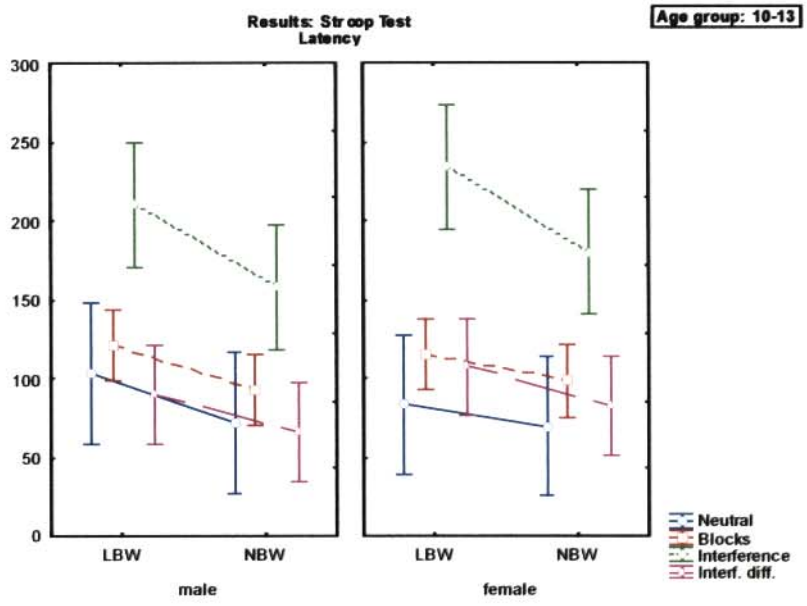


Figure 8.13 illustrates the plot of means for birth weight and gender of the 6 to 9 age group, for executive functioning on the latency scores of the Stroop Word-Colour Test.

Figure 8.14 Executive functioning - Stroop Word-Colour Test: latency scores (age 10 to 13)



The plot of means for birth weight and gender of the 10 to 13 age group for executive functioning on latency scores on the Stroop Word-Colour Test, is illustrated in Figure 8.14.

Table 8.19 reflects the results of the ANOVA for the Stroop Word-Colour Test (latency scores) for the birth weight, gender and age groups.

Table 8.19 Executive functioning - Stroop Word-Colour Test: latency scores – ANOVA results for birth weight, gender and age groups

Variable	ANOVA								
		Neutral		Blocks		Interference		Interference difference	
	Df	*F*	*P*	*F*	*P*	*F*	*P*	*F*	*p*
Group	1, 150	4.932	0.028*	6.385	0.013*	10.787	0.001***	4.220	0.042*
Gender	1, 150	3.322	0.070	2.617	0.108	0.016	0.900	1.073	0.302
Age	1, 150	14.569	0.000***	24.624	0.000***	9.982	0.002**	1.097	0.297
Group x gender	1, 150	0.058	0.810	0.000	0.994	0.024	0.877	0.193	0.661
Group x age	1, 150	0.428	0.514	0.370	0.544	0.778	0.379	0.143	0.706
Gender x age	1, 150	1.038	0.310	2.552	0.112	2.757	0.099	0.434	0.511
Group x gender x age	1, 150	0.146	0.703	0.634	0.427	0.005	0.944	0.273	0.602

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$

The ANOVA showed significant group differences on all latency scores: neutral (p=0.028), blocks (p=0.013), interference (p=0.001) and interference difference (p=0.042). Poorer performance was indicated in the LBW group than in the NBW cohort. Age effects were also determined for latencies pertaining to neutral, blocks and interferences, where the age groups were analysed separately. There were no effects of gender, neither main nor interacting, therefore the gender groups were not analysed separately.

The results of the *post hoc* (Newman-Keuls) test for the latency scores on the Stroop Word-Colour Test for the birth weight and age groups are depicted in Table 8.20.

Table 8.20 Executive functioning - Stroop Word-Colour Test: latency scores – Post hoc (Newman-Keuls) results for birth weight and age groups

Group	Neutral		Blocks		Interference	
	6-9	**10-13**	**6-9**	**10-13**	**6-9**	**10-13**
LBW v NBW	0.041*	n/s	n/s	0.027*	n/s	0.009**

* $p \leq 0.05$; ** $p \leq 0.01$

The *post hoc* (Newman-Keuls) test indicated significantly more symptoms of executive dysfunction by the LBW 6 to 9 group on the neutral latency score (p=0.041) only, in comparison to the NBW cohort. For the blocks (p=0.027) and interference (p=0.009) scores there were significant differences in performance for the 10 to 13 age group, with the LBW group having the poorer performance.

Table 8.21 gives an overview of the results on the Stroop Word-Colour Test (error scores), for the LBW and controls, as a function of gender and age.

Table 8.21 Executive functioning - Stroop Word-Colour Test: error scores – Descriptive statistics for birth weight, gender and age groups

Group	Gender	Age group	N	Neutral	Blocks	Interference
LBW	**Male**	**6-9**	23	3.609 ± 5.366	3.826 ± 2.229	7.913 ± 5.334
		10-13	15	1.267 ± 1.100	3.267 ± 2.815	9.267 ± 5.612
	Female	**6-9**	26	1.654 ± 2.432	3.115 ± 3.983	8.231 ± 8.856
		10-13	15	1.467 ± 1.302	3.667 ± 2.160	8.667 ± 4.731
NBW	**Male**	**6-9**	23	1.696 ± 2.704	3.043 ± 1.692	6.435 ± 4.470
		10-13	15	0.600 ± 0.910	2.000 ± 1.648	4.467 ± 2.900
	Female	**6-9**	26	0.346 ± 0.629	1.769 ± 1.142	4.808 ± 5.068
		10-13	15	0.533 ± 0.640	2.933 ± 1.534	6.667 ± 5.010

Figure 8.15 Executive functioning - Stroop Word-Colour Test: error scores (age 6 to 9)

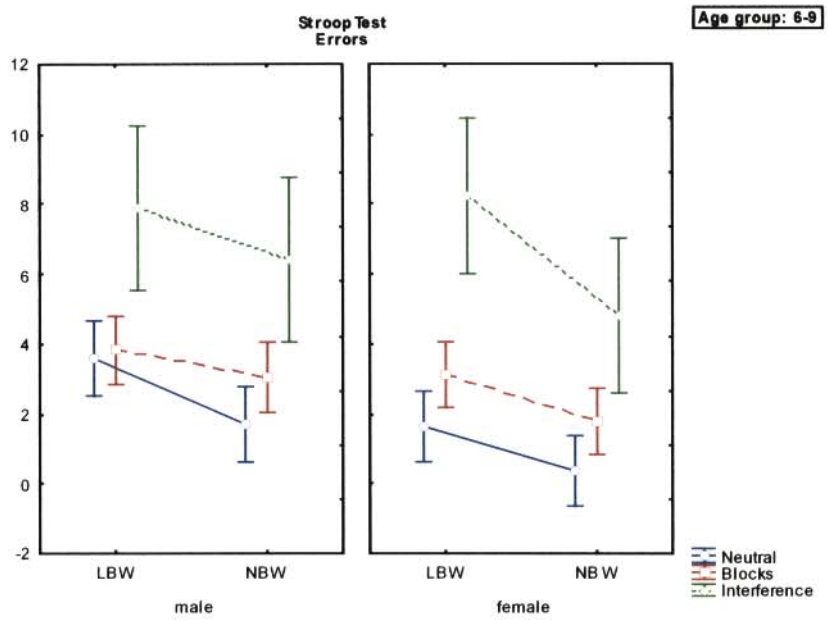
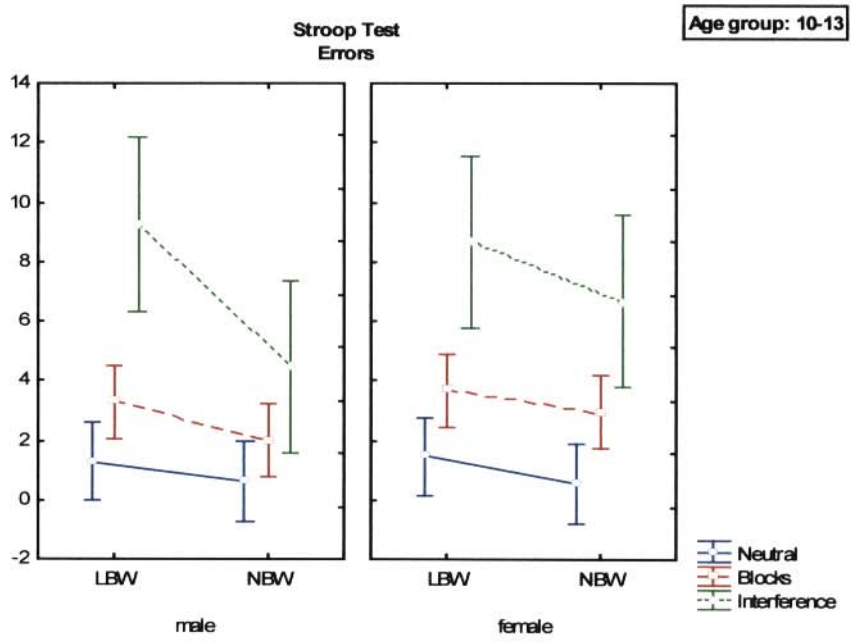


Figure 8.15 illustrates the plot of means for birth weight and gender of the 6 to 9 age group, for error scores on the Stroop Word-Colour Test.

Figure 8.16 Executive functioning - Stroop Word-Colour Test: error scores (age 10 to 13)



The plot of means for birth weight and gender of the 10 to 13 age group for error scores on the Stroop Word-Colour Test, is indicated in Figure 8.16.

Table 8.22 reflects the results of the ANOVA for the Stroop Word-Colour Test (error scores) for the birth weight, gender and age groups

Table 8.22 Executive functioning - Stroop Word-Colour Test: error scores - ANOVA results for birth weight, gender and age groups

Variable	ANOVA						
		Neutral		Blocks		Interference	
	Df	*F*	*p*	*F*	*p*	*F*	*p*
Group	1, 150	8.015	0.005**	6.998	0.009**	9.752	0.002**
Gender	1, 150	3.468	0.065	0.174	0.677	0.006	0.938
Age	1, 150	4.076	0.045*	0.005	0.943	0.201	0.654
Group x gender	1, 150	0.040	0.843	0.000	0.985	0.052	0.820
Group x age	1, 150	0.906	0.343	0.007	0.934	0.257	0.613
Gender x age	1, 150	4.076	0.045*	4.520	0.035*	0.603	0.439
Group x gender x age	1, 150	0.262	0.609	0.494	0.483	1.604	0.209

* $p \leq 0.05$; ** $p \leq 0.01$

The ANOVA showed significant group differences for the error scores of the Stroop Word-Colour Test pertaining to neutral (p=0.005), blocks (p=0.009) and interferences (p=0.002). Error scores were significantly more in the LBW cohort than in NBW participants. Only in the case of neutral errors was an effect of age determined, where the age groups were analysed separately. There were no effects of gender, neither main nor interacting, therefore the gender groups were not analysed separately.

The result of the *post hoc* (Newman-Keuls) test performed on the Stroop Word-Colour Test (error scores) for the birth weight groups, is demonstrated in Table 8.23.

Table 8.23 Executive functioning - Stroop Word-Colour Test: error scores – Post hoc (Newman-Keuls) results for the number of errors for birth weight and age groups

Group	Neutral	
	6-9	**10-13**
LBW v NBW	0.022*	n/s

* $p \leq 0.05$

The *post hoc* (Newman-Keuls) test indicated that the 6 to 9 LBW cohort scored significantly poorer (p=0.022) than their NBW counterparts on the neutral errors. No difference in performance was indicated on this measure in the 10 to 13 birth weight group.

8.3 Hypotheses testing

Based on the presented research results, the following can be concluded regarding the research hypotheses:

The primary research hypothesis, which stated that there is a higher incidence of psychological disorders and neuropsychological deficits in primary school children born with low birth weight than in children with normal birth weight, can be partially accepted, as reflected in secondary hypotheses 1 and 2.

Secondary hypothesis 1, which stated that there is a higher incidence of internalising (Separation Anxiety Disorder, Overanxious Disorder and Major Depressive Disorder) and externalising (Attention-Deficit/Hyperactivity Disorder, Oppositional Defiant Disorder and Conduct Disorder) psychological disorders in children born with low birth weight than in children with normal birth weight, can be partially accepted, in view of the following:

- Children with LBW did not show significantly more internalising symptoms of separation anxiety and overanxiousness than the NBW cohort. Significantly more

symptoms of Major Depressive Disorder were however indicated in the LBW group. A tendency towards increasing symptoms of separation anxiety and overanxiousness, although statistically not significant, was observed in the LBW group.

- Generally more externalising symptoms were observed in the LBW group than in their NBW counterparts. LBW children showed significantly more hyperactive/impulsive and inattentive symptoms, as indicated on the parent DBD rating scale, but not more ODD and CD symptoms. The LBW 6 to 9 age group was rated by parents as displaying significantly more hyperactive/impulsive symptoms. Parent reports did not indicate gender differences. There were significantly more hyperactive/impulsive, inattentive, ODD and CD symptoms in the LBW group, when rated by teachers. Moreover, teachers indicated significantly more hyperactive/impulsive, inattentive and ODD symptoms in LBW males than in their NBW counterparts. LBW females were also rated by teachers as displaying significantly more inattentive symptoms than the NBW cohort.

Secondary hypothesis 2, which stated that there is a higher incidence of neuropsychological deficiencies (motor, visual-spatial, memory and executive functions) in children born with low birth weight than in children with normal birth weight, can be accepted, in view of the following:

Significant differences between children with LBW and NBW controls were shown in all neuropsychological tests:

- The LBW group showed significantly more fine motor problems with the dominant and non-dominant hand than the NBW cohort. The LBW 6 to 9 age group had significantly more motor problems with both the dominant and non-dominant hand

than the NBW participants, whereas the LBW 10 to 13 age group only differed significantly in respect of the non-dominant hand on the Grooved Pegboard tasks. Significantly more visual-motor deficits were shown in both 6 to 9 and 10 to 13 LBW groups than in their NBW counterparts on the ROCF Test. Insufficient improvement in visual-motor tasks was indicated with increasing age on the ROCF Test. According to the findings the motor deficiencies continued with increasing age. No gender differences were identified.

- There were significant differences between children with LBW and the control group concerning visual-spatial functions, for both the 6 to 9 and 10 to 13 age groups. Therefore it seems that visual-motor deficits do not resolve with increasing age. Gender differences were not shown.

- Significant deficiencies in short-term verbal memory, working memory and visual-spatial memory were determined for the LBW group in comparison to the NBW controls. After analysis, only the 10 to 13 LBW females showed poorer performance on the digits backward test, measuring working memory, in comparison to their NBW counterparts. Both the LBW age groups showed significantly more visual-spatial and working memory impairments on the ROCF Test in comparison to the NBW cohort. Therefore, there was a tendency for the older group to continue experiencing these deficits.

- There were significantly more EF deficits in children with LBW than in the NBW group. Both the LBW age groups performed significantly poorer than their NBW counterparts on the ROCF Test, measuring EFs such as spatial organisation, planning, problem-solving and attention. Also, both the LBW age groups

experienced significantly more difficulty than the NBW cohort with interference control, inhibition, cognitive flexibility and control (Stroop Word-Colour Test). The LBW 10 to 13 group took significantly longer than the NBW participants to complete EF tasks of interference control, whereas the LBW 6 to 9 group did not differ from the NBW participants in this regard. No significant gender differences were identified.

A discussion of the results obtained will follow in the next chapter.

Chapter 9

DISCUSSION OF RESULTS

9.1 Introduction

The South African context enhances the risk of a high incidence of LBW or premature births in view of factors such as poverty (Campbell, 2001a) and high HIV/AIDS infection rates (The MRC Unit for Maternal and Infant Health Care Strategies et al., 2001). These risk factors will probably have an adverse impact on child development and prognosis, with significant cost implications and burdening of public health services.

There is no doubt from international studies that LBW/prematurity enhances the risk of physiological, emotional, behavioural, cognitive, psychiatric and other problems. Some of these difficulties persist throughout childhood and adolescence and into adulthood (Berk, 2006).

International prevention and intervention programmes to reduce LBW/premature births and the sequelae thereof seem to be better established. Ideally this study will contribute to the development of similar programmes locally. The present study proposed to determine the number of internalising and externalising psychological symptoms among LBW children in comparison with NBW children, as well as to determine whether LBW children performed more poorly on neuropsychological tests than NBW children. Similarities and differences between birth weight, gender and age groups were determined pertaining to the focus areas mentioned. Results of the comparison groups (the specific LBW gender and age group with their NBW counterparts) on all measuring instruments are summarised in Table 9.1.

Table 9.1 Summary of results

Measurement/function tested	LBW v NBW	Age		Gender		Age/ Gender
		6 to 9	10 to 13	Male	Female	
Psychological symptoms: internalising						
Separation anxiety	n/s					
Overanxiousness	n/s					
Depression	*					
Psychological symptoms: externalising						
Hyperactivity/impulsiveness (parent ratings)	*	*				
Inattention (parent ratings)	***					
ODD (parent ratings)	n/s					
CD (parent ratings)	n/s					
Hyperactivity/impulsiveness (teacher ratings)	*			*	n/s	
Inattention (teacher ratings)	***			**	*	
ODD (teacher ratings)	**			**	n/s	
CD (teacher ratings)	*					
Neurospychological functions						
Grooved pegboard (fine motor skills): Dominant hand Non-dominant hand	***	 * ***	 *			
ROCF (visual-spatial, visual-motor, visual-spatial memory, working memory, EF, attention): Administration Immediate recall Delayed recall	 *** *** ***	 *** *** ***	 *** * *			
Digits forward (attention, short-term verbal memory, few EF connotations)	**					* age 10-13 female
Digits backward (working memory, EF)	***		**			
Stroop (EF, inhibition, cognitive flexibility) Latencies: neutral blocks interference interference difference Errors: neutral blocks Interference	 * * *** * ** ** **	 * *	 * **			

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$

9.2 Discussion of results

This study demonstrated a trend among LBW children towards poorer performance than their NBW counterparts in most domains or functions investigated, referring to internalising and externalising psychological symptoms, as well as neuropsychological functions. This tendency towards poorer performance was observed in both LBW genders and age groups in comparison with the NBW cohort. The only exception to this finding was qualitatively more symptoms, although not statistically significant, of ODD among NBW males (6 to 9 group), NBW females (10 to 13 group) (as rated by parents) and NBW females (6 to 9 group) according to teacher ratings, as well as more CD symptoms among NBW males (age 6 to 9) as indicated by parents. Only a few gender differences were shown in the focus areas investigated.

9.2.1 Internalising psychological symptoms

This study investigated the magnitude of internalising psychological symptoms, namely separation anxiety, overanxiousness and major depression, as reported by LBW children in comparison to the NBW cohort.

9.2.1.1 Anxiety

The LBW children of both age and gender groups reported more symptoms, however not significantly more, of separation anxiety and overanxiousness. Inconsistent findings regarding the prevalence of internalising symptoms among LBW children were noted (Aylward, 2002). There is a discrepancy between findings related to the prevalence of anxiety disorders in LBW children. Similar to the present study, certain studies found no association between LBW and childhood anxiety disorders (Breslau et al., 1996a; Klebanov & Brooks-Gunn, 1994). In contrast, more recent investigations showed a significant prevalence of anxiety disorders in VLBW children (Hoff et al., 2004; Indredavik et al., 2004). In addition,

overanxiousness was observed in children born with VLBW (Botting et al., 1997) and ELBW (Saigal et al., 2003b). During this investigation no distinction was made between LBW, VLBW and ELBW. This might have given a clearer indication of the impact of LBW on internalising psychological functioning. The prevalence of separation anxiety in LBW children was not indicated in the literature consulted.

Though the LBW group's tendency to experience more internalising symptoms than the NBW cohort did not always reach statistical significance or the diagnostic level of a psychiatric disorder, psychiatric problems may still affect their overall functioning, development and management (Indredavik et al., 2004). This is in keeping with the suggestion to refer to a continuum instead of an absolute diagnosis (Harrison, 1996).

The tendency to increasing separation anxiety and overanxious symptoms among LBW participants in comparison to the NBW group may be ascribed to significantly more pregnancy complications (see Table 7.8), which is consistent with the explanation of Hirshfeld-Becker et al. (2004). Parents may consequently have experienced elevated levels of anxiety due to pregnancy complications and their infant's medical condition(s), as shown by the study of Chapieski and Evankovich (1997). The possibly elevated levels of parental anxiety may contribute to "anxiety-enhancing" parenting (Bögels & Siqueland, 2006; Hack et al., 2005). Other sequelae of LBW indicated in this study, such as poor motor skills (Section 9.2.3.1), may be a significant risk factor in anxiety symptoms, which was also indicated by Botting et al. (1997).

Age differences in anxiety: Symptoms of separation anxiety appear to decrease in prevalence from childhood through adolescence in the general population (American Psychiatric Association, 2000; Simonoff et al., 1997). This tendency was qualitatively

demonstrated, although not statistically significant, in this study, since the separation anxiety scores for both LBW genders in the 6 to 9 age groups were qualitatively higher, although they did not reach significance, when compared to the corresponding LBW genders in the 10 to 13 age groups.

The observation that overanxiousness seems to increase with age (Simonoff et al., 1997) was qualitatively observed in the LBW male groups only.

Gender differences in anxiety: Separation anxiety symptoms were qualitatively, although not statistically significant, more prevalent in both LBW female age groups in comparison with the LBW males. This tendency is in keeping with findings of higher rates of separation anxiety in females of the general population (Last et al., 1987a; Mash & Wolfe, 2002).

More symptoms of overanxiousness in the younger LBW female group than in the younger LBW male group were demonstrated in this study, though the prevalence did not reach statistical significance. This finding supports other observations that generalised anxiety was more common in females than in males of the VLBW group (Botting et al., 1997; Simonoff et al., 1997). The tendency towards more overanxious symptoms in females than in males was not confirmed in the older LBW gender groups.

9.2.1.2 Depression

The LBW group displayed significantly more symptoms of depression in comparison with the NBW counterparts. This observation coincides with similar research, in which depressive symptoms were found to be perceptibly more common among ELBW adolescents (Saigal et al., 2003a), LBW adolescents (Patton et al., 2004) and VLBW children of 12 years

(Botting et al., 1997). Indredavik et al. (2004), on the contrary, did not identify any group differences between the 10-to-14-year-old VLBW adolescents and the NBW cohort.

The high rate of depressive symptoms found in the LBW group could be ascribed to the fact that significantly more perinatal insults (see Table 7.8), as well as motor deficits (Section 9.2.3.1) and behavioural problems (Section 9.2.2), were indicated in the LBW group in comparison to the NBW participants. The study by Jaffee et al. (2002) found that perinatal insults and motor skills deficits and psychopathology in the family of origin, as well as behavioural and socio-emotional problems, were important indicators during early childhood (irrespective of birth weight) of juvenile-onset depression. Moreover, other neuropsychological impairments shown in this study (see Section 9.2.3) may be considered predictors of childhood depression, similar to the findings of Botting et al. (1997).

Age differences in depression: Mood disorders tend to increase with increasing age in the general population (Berk, 2006; Johnson et al., 2000; Mash & Wolfe, 2002; Sadock & Sadock, 2003). The peak risk period for the onset of depression is middle to late adolescence (Barlow & Durand, 2002; Gale & Martyn, 2004). In this study the LBW 10 to 13 groups for both genders exhibited qualitatively more, although statistically insignificant, depressive symptoms than the LBW 6 to 9 groups for both genders. A possible explanation may be that puberty is accompanied by cortical maturation and synaptic pruning (Whitaker et al., 1997). This process seems to enhance vulnerability to mood disorders.

Gender differences in depression: Qualitatively, the LBW female participants of both age groups showed more depressive symptoms than the LBW males, although not statistically significant. This finding is inconsistent with other studies, which indicate extensive gender differences in depression among all LBW children (Botting et al., 1997;

Masi et al., 2001). Findings on gender differences however are inconclusive. Gale and Martyn (2004) found that women whose birth weight was low or at the lower end of the normal range had an increased risk of depression at age 26 years.

A strong correlation between the internalising disorders investigated in this study was shown between separation anxiety and overanxiousness (r=0.76), separation anxiety and depression (r=0.62) and overanxiousness and depression (r=0.63). This is presented in Appendix K. These moderate to strong correlations may be explained by comorbidity tendencies in the general population. Anxiety disorders, especially separation anxiety in children and GAD in adolescents, were found to be more commonly comorbid with Dystymic Disorder (Masi et al., 2001).

The research results from this study thus point to a relationship, either direct or indirect, between LBW and vulnerability to symptoms associated with internalising psychological disorders, particularly depression.

9.2.2 Externalising psychological symptoms

Hyperactivity/impulsiveness, inattention, ODD and CD were investigated and will be discussed subsequently.

9.2.2.1 Hyperactivity/impulsiveness and inattention

Parents and teachers indicated significantly more hyperactive/impulsive and inattentive symptoms in the LBW group than in the NBW comparisons. The LBW group also performed more poorly than the NBW controls on all neuropsychological tests measuring attention and impulsiveness (see Section 9.2.3). An association between LBW and ADHD-related symptoms, similar to the findings of this study, is well documented (Aylward, 2002; Barlow & Lewandowski, 2000; Bhutta et al., 2002; Botting et al., 1997; Breslau et al., 2000; Harrison,

1996; Haycock, 2004; Hoff et al., 2004; Huddy et al., 2001; Marlow, 2004; Mick et al., 2002; Olness, 2003; Peterson et al., 2002; Saigal et al., 2001; Saigal et al., 2003a; Szatmari et al., 1990; Ulvund et al., 2001; Winders & Burns, 2001). On the other hand, the finding of significant group differences regarding hyperactivity/impulsiveness and inattention is in contrast with some studies (Cooke & Abernethy, 1999; Indredavik et al., 2004; O'Keeffe et al., 2003; Rickards et al., 2001; Sauver et al., 2004; Sommerfelt et al., 1996; Stathis et al., 1999; Zappitelli et al., 2001).

A higher rate of ADHD-related symptoms in the LBW group than in the NBW comparisons is a tendency that could be ascribed to the presence of considerably more pre-, peri- and postnatal complications, as indicated in Table 7.8. Shortage of oxygen, lengthy hospitalisation and epilepsy or seizures/convulsions were some of the key complications among the LBW cohort in this study. The occurrence of pre- and perinatal complications (Asherson et al., 2005; Zappitelli et al., 2001), particularly hypoxic-ischaemic events (Krageloh-Mann et al., 1999; Lou, 1996), were found to increase the risk of ADHD symptoms.

The findings of this study indicated that parents and teachers of the LBW group reported a stronger significance for inattention than for hyperactivity/impulsiveness, thus supporting observations of more significant attention deficits among LBW children, but less hyperactivity (Haycock, 2004; York & DeVoe, 2002). The teacher DBD rating scale demonstrated more inattentive than hyperactive symptoms in both age groups of the LBW cohort in this study. A similar tendency was observed in the LBW 10 to 13 males and females on the parent DBD rating scale. These findings are contradictory to observations of Elgen et al. (2004) and Potgieter et al. (2003), who indicated no specific identifiable attention dysfunctions in the LBW group, as well as continued uncertainty about the nature of the reported impaired attention among LBW children.

Teacher-rated hyperactivity/impulsiveness correlated with their ratings of inattention, ODD and CD, whereas inattention correlated only with hyperactivity/impulsiveness and ODD (all within a correlation range of between 0.5 and 0.8). On the other hand, parent-rated hyperactivity/impulsiveness only correlated with their observations of inattention and ODD. Unlike teachers' ratings, parent-rated inattention only correlated with hyperactivity/impulsiveness. The correlations of parents' ratings varied between 0.5 and 0.7 (see Appendix K). The LBW participants seem to experience symptoms of both hyperactivity/impulsiveness and inattention, which often co-exist. Hyperactive-impulsive behaviour is more closely associated with externalising problems, such as oppositional and delinquent behaviour (Johansen et al., 2002), which may explain the correlation with ODD and CD. The correlation between inattention and ODD is unique to the present study. Hyperactive/impulsive and inattentive symptoms often result in cognitive and scholastic problems. Behavioural problems are mediated by the influence of the environment via cognitive impairments in children (Hoff et al., 2004). Other sequelae of VLBW, such as motor deficits and other neuropsychological deficiencies observed in the present study, may increase the risk of more oppositional behaviour (Botting et al., 1997; Mash & Wolfe, 2002).

Age differences in hyperactivity/impulsiveness and inattention: There is a discrepancy in available research on the age at which LBW children are at higher risk of ADHD-related symptoms. Significantly more symptoms of hyperactivity/impulsiveness than in the NBW cohort were only indicated by parents of children in the younger LBW group. This is in keeping with a finding of an excess in externalising problems only at age 6 (Breslau et al., 2000). This increased risk of higher hyperactivity/impulsiveness in the younger LBW group in the present study contradicts the findings that LBW infants appear to be at risk of hyperactivity (Klebanov & Brooks-Gunn, 1994; Peterson et al., 2002) and poorer attention

control at later ages (Lawson & Ruff, 2004). No differences in inattentive symptoms between the younger and older LBW groups compared to the NBW cohort were found in this study. According to Hernandez et al. (2003) attention control develops progressively between the ages of 8 and 12 years in relation with the maturation of the frontal lobes. Possible deficient frontal lobe maturation may explain this observation.

More symptoms of impulsiveness, including insufficient forethought, planning or control (Solanto et al., 2001), were indicated in both LBW age groups on the Stroop Word-Colour Test and ROCF Test than in the control group, as indicated in Section 9.2.3. As previously noted, impulsiveness has both a motor and a cognitive component (Johansen et al., 2002). Both LBW age groups also performed more poorly on the motor task in comparison with the NBW counterparts. Impulsiveness was also seen as one of the frequently reported behavioural problems among preterms (Sajaniemi et al., 2001), though the effects of age were not reflected in the literature consulted.

Gender differences in hyperactivity/impulsiveness and inattention: Parents and teachers do not seem to share similar opinions on the incidence of hyperactivity/impulsiveness and inattention in LBW males and females when compared to the NBW participants. Teachers only indicated significantly more symptoms of hyperactivity/impulsiveness and inattention in LBW males than in the NBW comparisons, as well as noticeably more symptoms of inattention in LBW females than their NBW counterparts. Parents' observations of no significant differences between LBW genders with their NBW complement are in keeping with findings of Hoff et al. (2004), indicating no meaningful gender differences after controlling for differences in IQ. Teachers' observations are consistent with other findings indicating that LBW males appear to be at

increased risk of hyperactive/impulsive and inattentive symptoms (Breslau & Chilcoat, 2000; Chapieski & Evankovich, 1997; Haycock, 2004; Sajaniemi et al., 2001; Whitaker et al., 1997).

According to the teachers' ratings, there were definitive symptoms of inattention among LBW females when compared with the NBW cohort, but the symptoms of hyperactivity/impulsiveness did not reach statistical significance. This is consistent with the finding that females are more vulnerable to inattentive (Swanson, 2003) and internalising (Abikoff et al., 2002; Heptinstall & Taylor, 2002) symptoms than males. The significantly higher prevalence of hyperactivity/impulsiveness among males confirms the findings that males tend to be prone to more hyperactive symptoms (Hunt et al., 2001) and externalising behaviour (Abikoff et al., 2002; Crijnen et al., 1997; Heptinstall & Taylor, 2002). On the other hand, teachers also rated the LBW males as more inclined to inattention than the NBW males.

A possible explanation for these higher rates of inattention in both LBW genders than in their NBW counterparts may be the occurrence of more pre-, peri- and postnatal complications (see Table 7.8). However, Abernethy et al. (2002) mention that attention deficit in children born with VLBW does not correlate with conventional markers of perinatal brain injury, but may be related to global brain growth and the development of key structures (such as the caudate nuclei and hippocampal formations). Potgieter et al. (2003) conclude that reported poor attention in preterm children with ADHD cannot be explained by a simple maturational delay in the development of attention and inhibition mechanisms. Moreover, in a study of event-related potentials during attention tasks, no specific brain dysfunction in children born prematurely could explain the higher incidence of ADHD in prematurely born children (Potgieter et al., 2003).

Findings of considerably more symptoms of both hyperactivity/impulsiveness and inattention in LBW males in comparison to only significant inattentive symptoms among LBW females when compared to controls, underscore the theory that LBW males are more likely than females to present with neuropsychological deficits and ADHD. This may be due to foetal testosterone that slows the lateralisation of the left hemisphere of the brain and increases vulnerability to prenatal injury, LBW and neuropsychological problems (Martel et al., 2007). Females may have more protecting factors (e.g. hormones such as oestrogen), which keep them from developing ADHD and buffer them from some of the impact of risks associated with LBW (Martel et al., 2007). The extent to which females are buffered is questioned however since the LBW females still showed a substantial prevalence of inattention symptoms and a tendency to more hyperactive/impulsive symptoms when compared with the NBW cohort.

9.2.2.2 Oppositional Defiant Disorder and Conduct Disorder

Teachers' reports indicated a statistically significant prevalence of ODD and CD symptoms in the LBW participants when compared to the control group. These reports are in contrast with the reports by parents, which indicated no significance. Findings on the prevalence of ODD and CD in LBW children, which are reported in literature, are also contradictory. There are studies that indicate more externalising problems (Breslau & Chilcoat, 2000; Mash & Wolfe, 2002; Nadeau et al., 2001), delinquent behaviour (Lui et al., 2001) and CD (Aylward, 2002) among children born with LBW, confirming the teachers' ratings of the present study. More CD symptoms may be related to the higher rate of pregnancy and birth complications observed in the LBW group (Table 7.8). Such complications were identified as significant contributing factors to CD in the general population (Burke et al., 2002; Mash & Wolfe, 2002). In addition, biologically based traits,

such as a difficult temperament or impulsiveness, may further predispose children to develop aggressive and antisocial behaviour (Mash & Wolfe, 2002). In this study more temperamental difficulties were indicated by parents of LBW children during the first year of life (see Table 7.8). Increased impulsiveness was also pointed out by both parents and teachers (Section 9.2.2.1), as well as confirmed by results on neuropsychological tests.

There are, however, also studies that deny a higher prevalence of ODD and CD symptoms in LBW children (Burke et al., 2002; York & DeVoe, 2002; Zappitelli et al., 2001). CD in particular was not found to be more prevalent in studies with children born prematurely (Chapieski & Evankovich, 1997), as well as among VLBW adolescents (Indredavik et al., 2004) and during mid-childhood (Saigal et al., 2003b).

Teacher-rated ODD correlated with their observations of hyperactivity/impulsiveness, inattention and CD. Parent-rated ODD showed a similar pattern of correlation to that of teachers, with both sets of correlations ranging from 0.5 to 0.72. Also, teacher-rated CD correlated with their observations of hyperactivity/impulsiveness and ODD, whereas parents' ratings of CD only correlated with ODD, all ranging from 0.50 to 0.54 (see Appendix K). The comorbidity between ADHD and ODD/CD in the general population (American Psychiatric Association, 2000; Mash & Wolfe, 2002) is reflected in these correlations. However, these correlations oppose the study by Botting et al. (1997), which reported that LBW children with hyperactivity do not develop antisocial behaviour or CD as frequently as matched peers with NBW. The correlations mentioned also contradict the statement that VLBW children are more likely to suffer a "pure" form of ADD, often without hyperactivity, which is not associated with the development of CD or ODD (Marlow, 2004).

Family and parenting problems are among the strongest and most consistent correlates of antisocial behaviour, including general family disturbances (e.g. parental psychopathology and family instability) (American Psychiatric Association, 2000; Mash & Wolfe, 2002; Newcorn et al., 2005). In addition, internalising, externalising and neuropsychological problems have an adverse impact on the family system. Negative home environmental factors, though not the focus of this investigation, may increase problem behaviour in the LBW group in this study in collaboration with increased internalising, ADHD and neuropsychological deficit symptoms. Furthermore, Oosterlaan et al. (2005) noted that EF deficits in ADHD may be a risk factor for the maintenance of ADHD in later development, and possibly for the development of other DBDs, including ODD and CD.

Thus, significant symptoms of ADHD observed in this study, together with EF deficiencies and neuropsychological impairment (see Section 9.2.3), may have contributed to increased vulnerability of the LBW group to ODD and CD.

Gender differences in ODD and CD: Teachers indicated more ODD symptoms in the LBW male group than in the NBW comparisons, which is in line with the observation that ODD appears to occur more frequently in males than females before puberty in the general population (American Psychiatric Association, 2000; Cantwell, 1996; Levy et al., 2005; Mash & Wolfe, 2002; Swanson, 2003; Whitaker et al., 1997). More ODD among the LBW males however is in contrast with the finding of increased risk of behavioural problems in both genders, but that these sequelae become evident at an earlier age in boys than in girls (Papageorgiou & Bardin, 1999). Neither LBW gender experienced significantly more symptoms of CD than the NBW counterparts. The reported increased incidence of CD among LBW males as documented by Chapieski and Evankovich (1997) was not evident in this study.

Although the findings of this study were not always identical to those of earlier researchers, there can be no doubt about the role of LBW in the development of externalising symptoms. Moreover, the complex interaction between more internalising symptoms and neuropsychological deficiencies may increase the vulnerability of LBW children to the development of externalising symptoms even further.

Conflicting reports: Both parents and teachers indicated a significant prevalence of hyperactive/impulsive and inattentive symptoms in the LBW group. Reports of parents and teachers were however inconsistent in some regards, with teachers also indicating significantly more symptoms of ODD and CD in the LBW cohort than in controls. Unlike parents, teachers rated more symptoms of inattention in both LBW genders in comparison with the NBW counterparts, as well as significantly more symptoms of hyperactivity/impulsiveness and ODD in LBW males than in the NBW group. Research offers different perspectives on the value of parent and teacher reports by authors. According to Meyer and Sagvolden (2006b) and Wolraich, Lambert, Baumgaertel, Garcia-Tornel, Feurer, Bickman et al. (2003), teacher ratings are regarded as an accurate measure of assessment. Teachers, as opposed to children and parents, are considered to be the optimal informants for ADHD symptoms (Oosterlaan et al., 2005). Teacher reports are perceived to be more objective, as they are not influenced by the effect of birth weight on behaviour or by previous knowledge of illness or development. According to Oosterlaan et al. (2005) teachers' ratings of ADHD, but not that of parents, credibly predicted EF task performance. In this study both teacher and parent ratings of inattention correlated with executive dysfunction in the LBW group (see Appendix K). Moreover, teachers have greater experience in observing children over time, during a variety of tasks and relative to the peer group (Klebanov & Brooks-Gunn, 1994).

Conflicting reports from multiple reporters give rise to uncertainty in deciding which reporter to use (Dick et al., 2005). Differences in reports may be ascribed to differences in children's behaviour in different contexts, leading to different observations regarding psychiatric problems by parents and teachers (Johnson et al., 2000; Klebanov & Brooks-Gunn, 1994). Certain behaviours are more perceptible to teachers than to parents or similar behaviour may be interpreted differently by different observers (Klebanov & Brooks-Gunn, 1994). Potential bias from parent reports of behaviour problems associated with LBW status should be considered (Breslau & Chilcoat, 2000; Johnson et al., 2000; Klebanov & Brooks-Gunn, 1994; Lui et al., 2001). Bias was checked in the present study by collecting data from both parents and teachers (Breslau & Chilcoat, 2000). Teachers were assumed to be generally unaware of children's birth weight status.

Different parent and teacher reports on symptoms of hyperactivity/impulsiveness, inattention, ODD and CD are confirmed by rather weak correlations between the two sets of data. Only the hyperactive/impulsive, inattentive and CD scales of parents and teachers correlated, with a correlation of $r=0.36$ for hyperactivity/impulsiveness, $r=0.45$ for inattention and $r=0.23$ for CD.

9.2.3 Neuropsychological functions

Neuropsychological functions pertaining to motor, visual-spatial, memory and EF were investigated in the present study. It is important to note that cognitive tasks were used to understand the nature of brain functions in children and brain dysfunction in CNS disorders specific to children (Espy, 2004). Anderson et al. (2004) also emphasise that identifying the nature of cognitive deficits associated with premature birth will provide some indication of the neural systems compromised.

9.2.3.1 Fine motor functions

The time taken to complete the Grooved Pegboard task and the scores on the ROCF Test were significantly poorer in the LBW group than in the NBW counterparts. This finding of motor dysfunction in LBW children is of particular concern, as confirmed by other studies (Aylward, 2002; Blondis, 1999; Burns et al., 2004; Cuddihy et al., 1999; Dewey et al., 1999; Hemgren & Persson, 2004; Huddy et al., 2001; Nadeau et al., 2001; O'Brien et al., 2004; Rickards et al., 2001; Taylor et al., 2000a; Whitaker et al., 1997). Very few studies did not find significant neuro-motor impairments in the SGA group (Sommerfelt et al., 2002).

Neuropsychological impairments occur partially as a result of the sequelae of medical complications, such as hypoxia or respiratory distress syndrome (Curtis et al., 2002) and stressful environmental conditions in hospital (Perlman, 2001). In fact, respiratory problems or prolonged oxygen therapy (Brandt et al., 2000; Stoelhorst et al., 2003) were indicated to have a significant impact on psychomotor outcome. Troubled breathing with subsequent delivery of oxygen, injury during delivery, infections, as well as lengthy hospitalisation, were found to be more prevalent in the LBW cohort in comparison to the NBW group (see Table 7.8). Perinatal insults (Lui et al., 2001; Torrioli et al., 2000), postnatal treatment of respiratory problems (Stoelhorst et al., 2003) and biological risk factors (Dewey et al., 1999; Kilbride et al., 2004) are some of the adversities to consider in motor development. All these complications mentioned were less prevalent in the control group than in the LBW participants, as reflected in Table 7.8.

In addition, fine motor functioning in the LBW group may also be influenced by a significant prevalence of other psychiatric symptoms, such as symptoms of depression and ADHD. Motor milestones have been found to be delayed in children with affective

disturbances (van Os et al., 1997) and ADHD (Gillberg & Kadesjö, 2000; Meyer & Sagvolden, 2006b). Martel et al. (2007) also mention a relation between inattention/hyperactivity at age 6 and low arousal, slower motor speed and poorer fine motor control.

Age differences in motor functions: The younger LBW group showed undeniably poorer performance with both hands on the Grooved Pegboard than the NBW participants, as well as on visual-motor skills measured by the ROCF Test. The older LBW group also experienced significantly more motor deficits than the NBW counterparts on the Grooved Pegboard but with the non-dominant hand only. However, there was a tendency towards poorer scores with the dominant hand as well. The visual-motor skills of the older boys were also significantly poorer than those of their NBW cohort. The finding of significantly more motor problems in the older group is consistent with studies of continuation of motor difficulties (Holsti et al., 2002), whereas others identified improvement of motor deficits with increasing age (O'Brien et al., 2004). Insufficient or delayed maturation may be responsible for continuous motor problems in the older group (Meyer & Sagvolden, 2006b).

Gender differences in motor functions: No significant differences between LBW males and females and their NBW counterparts in motor abilities were observed, which is in line with findings of Liebhardt et al. (2000). On the other hand, Sajaniemi et al. (2001) mentioned an increased tendency among preterm boys to exhibit visual-motor problems.

Various reasons are advanced for the impairment of motor functions among LBW children. Both physical and psychological issues seem to be involved in this concerning phenomenon, which affects the overwhelming majority of children in this group.

9.2.3.2 Visual-spatial functions

The LBW group scored significantly lower than the NBW comparisons on visual-spatial functions, as measured by the ROCF Test. This finding is in keeping with other studies (Aylward, 2002; Dieterich et al., 2004; Liebhardt, 2000; Maalouf et al., 2001; Taylor et al., 2000a; Torrioli et al., 2000) that also indicate significant visual-spatial and visual-motor problems among LBW children.

Children born with LBW may be at risk of visual-perceptual or visual-motor deficits due to abnormal pre- and perinatal brain development (Hille et al., 2001; Lui et al., 2001), including brain injury (Hille et al., 2001). Table 7.8 reflects various pre-, peri- and postnatal complications in the LBW group that may have affected brain development and visual-perceptual functioning.

The strongly significant prevalence of both visual-perceptual and motor difficulties observed in the LBW group in this study seems to support the finding that visual- and perceptual-motor deficits may be interrelated disorders (Torrioli et al., 2000). The possible interrelatedness between visual- and perceptual-motor functions is confirmed in the present study by a moderate correlation ($r=-0.62$, $r=-0.59$) between scores on the visual-spatial test (ROCF) and time to complete the motor task (Grooved Pegboard) (see Appendix K).

Age differences in visual-spatial functions: Visual-spatial deficiencies were observed in both LBW age groups of this study in comparison to their NBW counterparts. Problems with visual memory, visual processing and visual-perceptual organisation were also indicated at age 8 and 14 years in the LBW group in other studies (Rickards et al., 2001). It may be possible that developmental delays in LBW children do not completely resolve, although Campbell (2001b) indicates that they catch up by 12 to 18 months.

Gender differences in visual-spatial functions: The present study showed no differences in performance between the LBW males and females and the NBW participants, which contradicts the finding that males appear to have an advantage in visual-spatial tasks (Hindmarsh et al., 2000; Taylor et al., 2000a). However, Sajaniemi et al. (2001) observe that preterm boys tend to have more visual-perceptual problems than preterm girls. Inconsistent findings in this regard necessitate further research.

Deficient visual-spatial functions are bound to have a crucial effect on the functioning of an individual. It is therefore of the utmost importance to examine the exact nature and impact of this problem in future research.

9.2.3.3 Memory functions

The LBW group scored significantly poorer on measures of visual-spatial memory (immediate and delayed recall) (ROCF Test), working memory (ROCF Test and digits backward) and short-term verbal memory (digits forward) than the NBW group. Problems with visual memory (Aylward, 2002; Dewey et al., 1999; Rickards et al., 2001), spatial working memory (Anderson et al., 2004; Curtis et al., 2002; Lindeke et al., 2002; Vicare et al., 2004), working memory (Lindeke et al., 2002), verbal memory (Taylor et al., 2000b), immediate (Curtis et al., 2002) and delayed memory (Curtis et al., 2002; Taylor et al., 2000b) were also found by other researchers to be more significant in LBW participants than the NBW cohort.

Perinatal complications (such as hypoxic-ischaemic damage) have an adverse impact on the hippocampus (Curtis et al., 2002; Nosarti et al., 2002). Neurobiological risk factors during the neonatal stage, particularly factors that influence oxygenation, play a vital role in predicting spatial working memory (Curtis et al., 2002). These perinatal and neurobiological

risk factors mentioned were indicated significantly more often in the LBW group than in the NBW comparisons (see Table 7.8), which may partially explain memory deficiencies. Childhood depression (Section 9.2.1.2) was found to be associated with memory impairment, particularly verbal memory (Günther et al., 2004). This association between depression and verbal memory was weak in the present study (memory for digits forward: r=-0.15; digits backward: r=-0.25).

Age differences in memory functions: The occurrence of visual-spatial memory problems was unmistakably higher in both LBW age groups than in the NBW counterparts. Visual memory, visual processing and visual perceptual organisation impairments were also indicated at age 8 and 14 years in the LBW group in another study (Rickards et al., 2001). The older LBW group also experienced significantly more short-term verbal memory and working memory deficits (as shown on the digits forward and backward subtest) than the NBW participants. Several age-related processes coincide with the increase in working memory capacity (Klingberg et al., 2002). It seems that older children who had been born with LBW do not recover from visual-spatial, short-term verbal and working memory difficulties. These memory problems, which are also experienced by the older age group, contradict evidence of neural plasticity (Curtis et al., 2002).

Gender differences in memory functions: Only the older LBW females performed significantly more poorly than the NBW cohort on the short-term verbal memory task, which is difficult to explain. This specific memory task also tapped attention functions, which was noticeably deficient in both LBW genders compared to their NBW counterparts. The relation between memory, LBW and gender is an under-researched domain, as literature consulted did not show differences in memory performance between the LBW males and females and their NBW comparisons that may explain this finding in the present study. Impaired memory

functioning among LBW children will probably have an adverse impact on daily functioning and scholastic progress.

9.2.3.4 Executive functioning

The LBW group clearly experienced more difficulty with EF in comparison with their NBW counterparts, as shown on the ROCF Test, digits forward, digits backward and Stroop Word-Colour Test. This supports the findings of Anderson et al. (2004) (reasoning ability, working memory, planning, organisational abilities, impulse control, starting activities, generating new ideas, mental flexibility and strategic decision-making), Aylward (2002) (organisation, planning, problem-solving and abstracting), Dieterich et al. (2004) (self-regulation), as well as Nadeau et al. (2001) and Sajaniemi et al. (2001) (problem-solving, global deficits).

The significant prevalence of some pre-, peri- and postnatal complications in the LBW group, particularly those relating to oxygen shortage, may have contributed to suboptimal development of essential brain structures involved in EF, such as the striatum (Böhm et al., 2004) and frontal lobe (Frisk et al., 2002).

Age differences in EF: More significant EF deficits were observed in both age groups of the LBW cohort than in the control group, indicating that children born with LBW do not develop the ability to engage effectively in EF as they grow older, like the general population (Barkley, 2006). The finding of EF deficits in both age groups in this study contradicts the observation that improvement in executive impairment in preterm children occurs (Curtis et al., 2002). The younger LBW group performed significantly more poorly than the NBW cohort on the neutral latency and errors of the Stroop Word-Colour Test, probably because of

more impulsiveness during younger developmental stages, as well as insufficient reading skills (especially the grade 1 participants).

Gender differences in EF: Only the older LBW 10 to 13 female group performed significantly more poorly in the short-term verbal memory task, which measures attention and a few other EF connotations (also see Section 9.2.3.3). Literature consulted did not indicate differences in EF between LBW males and females and their NBW counterparts to assist in explaining the observation in this study. This needs further investigation.

The high incidence of EF deficiencies among LBW children, which is evident from both the present research and literature, coupled with the fact that age does not solve the associated problems, necessitates further research into this aspect.

The previously mentioned findings of this study show that birth weight indeed predicts neuropsychological functioning directly or indirectly. Moreover, these neuropsychological functions are in reciprocal interaction with each other, as well as with internalising and externalising psychological functioning.

Prognosis: Poorer performance in the LBW 10 to 13 group than in the NBW participants were identified on fine motor skills, visual-spatial abilities, executive functioning (such as organisation, strategic decision making, problem-solving strategies, planning, attention, impulsiveness, interference control/response inhibition, working memory and cognitive flexibility) and memory (short-term verbal, working and visual-spatial). This finding may indicate that problem areas do not resolve with increasing age, which is inconsistent with other studies (Brandt et al., 2000; Tideman, 2000). This observation also questions evidence of neural plasticity, which refers to the process by which compensatory neural events, brought about either by endogenous, genetically driven mechanisms or through

environmental experience, facilitate change or reorganisation in the neural substrate (Curtis et al., 2002). Distinct levels of maturation and integration occur at age 6 years, age 10 years and in adolescence, possibly reflecting an extended period of maturation of the prefrontal cortex during the first two decades of life. Increased pre-, peri- and postnatal complications among the LBW cohort, as indicated in Table 7.8, may include some of the possible variables contributing to early neurological insults experienced by children born preterm, slowing down the normative developmental process in the prefrontal cortex during the first 8 to 10 years. Opposed to the present findings, Grodzinsky and Diamond (1992) observed improvement with age on most tasks (e.g. inhibition, cognitive flexibility, planning and organisation), which was consistent with a hypothesis of maturation of frontal regions. Curtis et al. (2002) confirm this hypothesis, noting that by adolescence LBW children may to some extent overcome the developmental lag by normal brain maturation mechanisms (Curtis et al., 2002).

However, results on the prognosis of LBW or premature children are inconsistent. Different researchers postulate that neurodevelopmental functioning improves with increasing age (Kesler et al., 2004; Tideman, 2000), continues to lag behind in cognitive development (Brandt et al., 2000; Rickards et al., 2001; Tully et al., 2004) or deteriorates with increasing age (Aylward, 2002; O'Brien et al., 2004; Pietz et al., 2004), owing to possible underlying cognitive deficiencies to meet increasing, higher-level demand at school level (Aylward, 2002).

Comorbid symptoms: It is possible that impairment in a specific domain(s) places a child at risk of a cascade of other delays or impairment. The problems identified in this study raise new questions regarding their primary and secondary development. For example, motor dysfunctioning in this study may be enhanced by depressive symptoms or vice versa. A mediational model posits that behaviour problems emerge as a result of the mediating effects

of both neuro-motor and cognitive delays associated with birth status (prematurity). Thus, birth status was not considered as the best predictor for school-age behaviour problems, but rather a factor influencing the developmental processes (Nadeau et al., 2001). Aylward (2002) also hypothesises that prematurity and its effects act through the association with health, cognitive and neuro-motor function to explain behavioural and emotional problems at school age.

Possible comorbidity may be confirmed by moderate correlations between neuropsychological functions, all in a range of between 0.5 and 0.7, as reflected in Appendix K. Fine motor functioning correlated with EF (some Stroop Word-Colour Test scales), working memory (digits backwards) and visual-spatial/visual-motor skills (ROCF Test). A correlation was indicated between visual-spatial tasks (ROCF Test) with motor functions (Grooved Pegboard) and executive dysfunction (some scales of the Stroop Test). Working memory (digits backward) correlated with motor skills and executive dysfunctioning (Stroop Test). EF (Stroop Test) showed correlations with some variables, such as motor skills (Grooved Pegboard), working memory (digits backward) and visual-spatial tasks (ROCF). Some of the correlations may be explained by measurement instruments tapping similar functions. For example, both the Grooved Pegboard and ROCF Test measure fine motor functions. The ROCF and Stroop Word-Colour Tests are sensitive to aspects of EF. Moreover, working memory, motor skills and EF seem to be interrelated, since EF is defined as a complex system of functions including or dependent on executive processes that include higher-level skills, such as focused and divided attention, planning abilities, impulse control (inhibition), mental flexibility and working memory (Anderson et al., 2004; Böhm et al., 2004; Boonstra et al, 2005; Geurts et al., 2005). A deficit in inhibition causes difficulties with various EFs such as working memory, self-regulation and motor control

(Boonstra et al., 2005). The correlation between the functions mentioned may also be explained by hierarchical developmental processes occurring according to a sequence from basic concept formation, visual-perceptual skills, visual-motor integration to cognitive development. Motor skills develop from gross, diffuse activities to fine movements (Berk, 2006). Thus, well-developed fine motor skills seem to be the gateway to higher cognitive development. Visual-spatial problems are some of the problems that often co-occur with minor motor impairment, which suggests a cortical developmental problem (Abernethy et al., 2003). Moreover, the interrelatedness between the motor, executive, working memory and visual-spatial functions may be ascribed to overlapping neural networks (Torrioli et al., 2000). The frontal lobes seem to mediate the most complex behavioural and cognitive functions, also known as frontal lobe functions or EFs (Demakis, 2004).

It can be concluded that the neuropsychological impairments (motor, visual-spatial, memory and EF) observed in this study among the LBW children, exacerbated by significantly more ADHD symptoms, may increase the risk of subsequent externalising (conduct and oppositional behavioural problems) and internalising (depressive) psychological symptoms. More pre-, peri- and postnatal complications in the LBW cohort than in the NBW comparisons are some of the risk factors contributing to the increased symptoms in the LBW group. Continued neuropsychological deficiencies in the older LBW group indicate ineffective resolution of delays or impairments. This assumption is in keeping with the hypothesis of Botting et al. (1997) who postulate that other sequelae of VLBW, such as motor deficits and neuropsychological impairments found in this study, may increase the risk of more anxiety, depression or oppositional behaviour.

9.3 Clinical implications of the study

Previous studies indicated that early problem behaviour was clearly linked to later psychopathology (Weiss & St. Jonn Seed, 2002). Powerful evidence exists that most psychiatric disorders originate early in life. The risk of adult-onset disorders is often increased by childhood adversities. Disorders experienced in early years often recur in adulthood. The World Health Organisation emphasises that psychiatric disorders with their origins in childhood are a major contributor to the 'global burden of disease' (Costello et al., 2005).

9.3.1 Psychological symptoms

Internalising and externalising psychological symptoms have implications for all levels of functioning.

Internalising symptoms: Symptoms of depression during childhood probably have adverse implications for social, emotional, cognitive and behaviour development/functioning. On a cognitive level, school performance of depressed children is affected by a combination of difficulty in concentration, slowed thinking, lack of interest and motivation, fatigue, sleepiness, depressive ruminations and preoccupations. These symptoms of depression during childhood may be misdiagnosed as a learning disorder. Secondary learning problems are corrected after a child's recovery from the depressive disorder (Sadock & Sadock, 2003). Childhood depression was also found to be associated with memory impairment, particularly verbal memory, but not with attention deficit (Günther et al., 2004). Motor milestones were delayed in children with affective disturbances, who also ran a greater risk of speech defects between the ages of 6 and 15 years, decreased psychomotor alertness and an excess of twitching and grimacing motor behaviours in adolescence (van Os et al., 1997). In addition, symptoms of depression and

often poor scholastic performance increase the risk of LBW children to the development of more severe emotional problems, as well as behavioural and social dysfunctioning.

Childhood onset MDD accounts for a disproportionately high percentage of depression in adults with two or more comorbid Axis 1 disorders (Alpert et al., 1999). Children with prepubertal-onset major depression have a high risk of suicide attempts, bipolar disorders, substance abuse and CD in adulthood (Weissman et al., 1999). CD and/or ADHD often co-occur with depression (Barlow & Durand, 2002).

Externalising symptoms: Childhood ADHD has implications for academic progress, since it appears to be characterised by impairments in motor coordination and perceptual-motor skills (Tucha & Lange, 2001), EF (especially inhibitory control) (Böhm et al., 2004; Boonstra et al., 2005; Heptinstall & Taylor, 2002; Max et al., 2005), visual-motor ability, deficient motivation and difficulties with serial information processing (Kalff et al., 2002), including working memory (Böhm et al., 2004; Kalff et al., 2002; Wilens et al., 2002). Impaired inhibition causes difficulties with various EFs such as working memory, self-regulation and motor control (Boonstra et al., 2005). Dysregulation of EF is assumed to be intrinsic to ADD (Böhm et al., 2004) or ADHD (Heptinstall & Taylor, 2002; Max et al., 2005).

According to Tannock (2005) ADHD is a major public health concern because of its chronicity and increased risk of additional and serious psychopathology in adulthood, including its detrimental effects on the individual's educational, social and occupational attainments. Meyer and Sagvolden (2006b) state that repeated accidents, depressive and anxiety disorder, later substance abuse, learning disabilities and school failure are associated with ADHD. ADHD teenagers with more pronounced comorbid ODD and CD symptoms

seem to be at highest risk of defiant driving habits and negative driving-related outcomes (Abikoff et al., 2002).

Significant ODD symptoms in the LBW group increase the risk of developing CD, since comorbid ODD is often a precursor of CD (Burke et al., 2002; Dick et al., 2005). Children with both hyperactivity and CD tend to continue having ADHD symptoms and to display aggressiveness, non-compliance, antisocial behaviour and alcohol use at follow-up. Adolescents with ADHD who were comorbid for CD were found to indulge in more cigarette and cannabis use (but not alcohol) and experienced more school expulsions and suspensions (Hechtman, 1999).

Hyperactive individuals had significantly higher juvenile (46% versus 11%) and adult (21% versus 7%) arrest rates. Conduct problems in childhood and serious antisocial behaviour in adolescence are considered to be significant risk factors for becoming an adult offender. The authors concluded that children with both hyperactivity and CD problems are at increased risk of later criminality (Dick et al., 2005; Fischer et al., 2002; Hechtman, 1999; Olson, 2002; Spencer et al., 1999). Early identification of deficits or dysfunctional symptoms in the LBW group and intervention are essential to prevent symptoms from reaching a full diagnosis. Parents and teachers should be included in prevention and intervention strategies.

9.3.2 Neuropsychological functions

Neuropsychological impairments have an important impact on academic and behavioural functioning, as reflected in the discussion below.

Motor: Visual-motor problems have an impact on mathematics (Abernethy et al., 2003; Aylward, 2002; Holsti et al., 2002), written language (Aylward, 2002; Dewey et al., 1999), reading problems (Aylward, 2002; Holtsti et al., 2002), later learning disabilities (Cooke &

Abernethy, 1999; Elgen et al., 2003; Huddy et al., 2001; Pietz et al., 2004) and school failure (Burns et al., 2004). Holsti et al. (2002) further note that children who were labelled as clumsy in elementary school continued to experience motor difficulties at ages 15 to 17 years. They were also more prone to behavioural problems and high-risk behaviour, including suicide, drug use, bullying and poor concentration, as well as a higher risk of psychiatric disorders (Holsti et al., 2002). Poor motor control appears to predict worse outcomes for children with ADHD (Martel et al., 2007).

Visual-spatial: Later reading problems (Dewey et al., 1999; Liebhardt et al., 2000) and comorbid deficits in mathematics (Bellinger et al., 2003) are associated with visual-spatial impairments. Dewey et al. (1999) note that VLBW children with perceptual problems are more likely to have problems with cognition and behaviour.

Memory: Memory impairment is considered one of the most important cognitive deficits, because in the immature brain it may be responsible for learning disabilities at school (Giménez et al., 2004). According to Klingberg et al. (2002) the amount of information kept in working memory increases throughout childhood and early adulthood, which is essential for the development of a wide range of cognitive skills (e.g. reading and logical reasoning). Working memory is essential in more sophisticated capabilities such as reasoning, planning and language comprehension (Boonstra et al., 2005; Donohoe et al, 2005; Golob & Starr, 2004). Isaacs et al. (2000) note that lack of attention or even disobedience may be linked to or coexist with a specific memory deficit.

Executive functioning: Oosterlaan et al. (2005) note that early developmental EF deficits may cause a cascade of other future executive dysfunctions leading to gross EF deficits and severe impairments in planning, execution and goal-directed behaviour. Executive

functioning includes an array of functions essential for effective scholastic performance, social adjustment and responsible, self-serving adult conduct (Lezak et al., 2004). Impaired executive functioning has a detrimental effect on daily functioning concerning inhibition of undesirable responses or considering consequences before acting (Oosterlaan, 1996), planning (Anderson et al., 2004), decision-making and judgement (Anderson et al., 2004; Boonstra et al., 2005; Cheung et al., 2004; Geurts et al., 2005), carrying out goal-directed behaviour (Cheung et al., 2004), as well as problem-solving (Barkley, 2006).

EF deficits in ADHD may be a risk factor for the maintenance of ADHD in later development, and possibly for the development of other DBDs, including ODD and CD (Oosterlaan et al., 2005). Results on the parent and teacher rating scales and measures of EF demonstrated and confirmed this association in this study. Executive dysfunction among premature children of ELBW with normal intelligence increased the likelihood of learning difficulties at school (Nadeau et al., 2001). Even slight deficits in EF affected educational progress and adaptive functioning, requiring neuropsychological assessment and specialist assistance (Sajaniemi et al., 2001).

Learning problems (Abernethy et al., 2003, Huddy et al., 2001; Potgieter et al., 2003; York & DeVoe, 2002), educational difficulties and lower IQ (Gross et al., 2001; O'Keeffe et al., 2003; Peterson et al., 2002), school failure (Kilbride et al., 2004; Marlow, 2004; Pietz et al., 2004; Pinto-Martin et al., 2004; Tully et al., 2004) and special/remedial education (Aylward, 2002; Bhutta et al., 2002; Frisk et al., 2002) are most probably associated with the neuropsychological impairments identified in this study. Children with these problems place increasing demands on school systems and often require multidisciplinary coordination of intervention (Aylward, 2002).

The neuropsychological deficiencies observed in the LBW group in the present study not only increase vulnerability to scholastic, emotional and behavioural problems, but may also encourage early school drop-out. Intervention programmes based on research findings should therefore aim at continuous monitoring of development, including identification, diagnosis and treatment of problem areas. These programmes should focus on preventing possible pathological symptoms from reaching a full diagnostic level. Early identification of LBW children at risk of behaviour, emotional and neuropsychological problems and tailoring early intervention to address behavioural competence are of paramount importance (Saylor et al., 2003) in developing prevention programmes (Olness, 2003; Saigal et al., 2001). The prognostic significance of the problem areas identified in this study requires follow-up assessment as children mature, including assessment of comorbid disorders (Lui et al., 2001). Significant internalising and externalising psychological symptoms, as well as neuropsychological deficits in this study, clarify why premature birth is one of the most challenging and costly public health problems (Wolke, 1998).

The development of prevention and intervention programmes in South Africa should include aspects such as establishment of a birth weight register, psycho-education with parents regarding the risk factors associated with LBW, as well as periodic monitoring of development. These programmes should be available to individuals from all socio-economic groups.

9.4 Integration of results

The LBW group generally tended towards increased internalising and externalising psychological symptoms, as well as poorer neuropsychological functioning, in comparison to the NBW counterparts. This was particularly relevant in the domains of internalising

symptoms (depression), externalising symptoms (hyperactivity/impulsiveness, inattention, ODD and CD) and neuropsychological impairments (motor, visual-spatial/visual-motor, memory and EF).

The problem areas that were mentioned may be in reciprocal interaction, placing the LBW children at risk of further delay in different domains at specific developmental stages. The neuropsychological impairments (motor, visual-spatial, memory and EF) observed in this study among the LBW children, probably exacerbated by symptoms of ADHD, may increase the risk of subsequent externalising (conduct and oppositional behavioural problems) and internalising (depressive) psychological symptoms. Significantly more pre-, peri- and postnatal complications in the LBW cohort than the NBW participants may predispose them to neuropsychological deficiencies and subsequent internalising/ externalising symptoms. These impairments most probably affect academic, emotional, social and other important areas of functioning. The neuropsychological effect of LBW is possibly more adverse, since only normal functioning children were included in the sample.

This study generally did not reveal critical differences between the LBW males and females and their NBW comparisons. Statistically, considerably more symptoms of hyperactivity/impulsiveness, inattention and ODD were indicated in LBW males than in the NBW cohort. The LBW females experienced markedly more symptoms of inattention than their NBW counterparts. Differences in performance between the LBW and NBW age groups were mostly observed in both LBW age groups, indicating deficient resolution of impairments with increasing age.

The LBW cohort seems to be biologically vulnerable to increasing internalising and externalising symptoms, as well as neuropsychological impairments, owing to significantly

more pre-, peri- and postnatal complications than the NBW participants, as shown in Table 7.8. Current difficulties may be explained by previous unresolved developmental delays or developing impairments in an increasingly demanding environment.

The South African context may exacerbate impairments in LBW children, as shown by significant group differences in almost all areas investigated, which are probably more secured in a developed country. Follow-up programmes and intervention strategies appear to be better established in developed countries to optimise the long-term outcomes of LBW/premature children. Monitoring of the development of these children may be restricted to the higher SES group in developing countries, such as South Africa.

This study is one of only a few conducted in a developing country. Continuous research on the nature of the relation between LBW and developmental difficulties, such as psychological disorders and neuropsychological impairments, will ensure awareness, early detection of impairments and the optimisation of the treatment and outcomes of these children, given the context that the number of LBW children is increasing, with a corresponding increase in public health cost.

Discriminating properties of measurement instruments: The measurement instruments utilised in the present study generally discriminated effectively between the birth weight groups in the domains investigated. The Grooved Pegboard task was sensitive to motor impairments in both LBW age groups. The ROCF Test discriminated effectively between both LBW age groups and their NBW counterparts in visual-spatial, visual-motor and visual-spatial memory, working memory and EF tasks. The digits forward (measuring mostly short-term verbal memory) and digits backward (tapping working memory and EF) subtest also showed poorer performances in the LBW group, with the poorest performance

in the LBW 10 to 13 group. The Stroop Word-Colour Test indicated greater sensitivity to inhibition, cognitive flexibility and other EF in both LBW age groups than in their NBW comparison groups. The Stroop Word-Colour Test however does not seem to be a reliable measurement for the 6 to 9 group, since some of the younger participants had insufficient reading skills.

9.5 Limitations of the study

No formal method was used to determine SES. SES factors, such as demographic characteristics (particularly the suburb where the participant attends school) and caregiver income, were used as far as possible to match the experimental and control group. Other requirements for matching pertaining to gender, age and home language were regarded as priorities. Participants from 11 language groups were included, which complicated the matching process. Seven LBW participants had to be discarded from the sample because of a lack of suitable control group participants or uncertainty about their birth weight.

Administration of the neuropsychological test battery occurred at the particular school the child attended. Environmental conditions differed between schools, particularly regarding the level of noise in general and at different times of day. These differences may have influenced test performance.

The study was conducted in a developing country with no nationally coordinated register or regional data base of birth weight. Only 25% of parents/guardians submitted proof of birth weight (copy of immunisation/clinic cards). Birth weight was crosschecked on the return slips and biographical data questionnaire. Participants were excluded in cases where birth weight was uncertain or did not meet the requirements.

Generalisations from results obtained in this sample, particularly in the age groups, would be more reliable if a bigger sample had been used. The sample consisted of children attending urban schools only.

Assessment in this study did not include any medical examination or neuro-imaging techniques (such as MRI) to rule out unknown medical conditions (for example brain injury) that can mimic psychiatric symptoms. Findings on the implications of medical conditions are however inconsistent. Some researchers note that cognitive and behavioural problems occur as commonly in the presence or absence of neuro-imaging abnormalities (Cooke & Abernethy, 1999; Perlman, 2001). The biographical data questionnaire did explore aspects of medical history. In future the neuropsychological tasks may be combined with functional imaging techniques to delineate the brain structures involved in LBW children.

Only the "Terry" picture questionnaire was administered to participants for measurement of internalising symptoms. Though children are sometimes considered as better reporters of internal distress (Chavira et al., 2004), making use of multiple reporters may reflect a more holistic clinical impression of emotional functioning.

There appears to be a gradient effect of LBW and gestational age on development, with the smallest and youngest having the highest incidence of impairment (Avery et al., 1999; Aylward, 2002; Berk, 2006; Harrison, 2002; Lou, 1996; Piecuch & Leonard, 1997; Pietz et al., 2004; Potgieter et al., 2003; Vohr et al., 2000), particularly concerning motor dysfunctioning (Kilbride et al., 2004) and EF (spatial organisation and mental flexibility [Anderson et al., 2004]). However, Elgen et al. (2002) found that behavioural problems and psychiatric disorders were as common in children born with a birth weight of less than 1 500 g as in children born with a birth weight of between 1 500 and 2 000 g. Others observed increased

risk in all levels of LBW (Breslau & Chilcoat, 2000; Elgen et al., 2003; Lindeke et al., 2002; Pietz et al., 2004). Levels or degrees of LBW were not considered in this study. Significant problems in most areas investigated were identified in spite of 49% of the LBW cohort belonging to the LBW level, and only 35% to the VLBW and 15% to the ELBW level.

The relationship between LBW and some problem areas, such as ADHD (Breslau et al., 2000; Kalff et al., 2002) and EF (Böhm et al., 2004), seems to vary by level of IQ. The intellectual functioning of those with possible borderline (IQ between 71 and 84) or mild mental retardation (IQ between 55 and 70) was only screened with the CPM Test. No comprehensive intellectual assessment was conducted.

This study was limited to a number of internalising symptoms (SAD, OAD and MDD), externalising symptoms (ADHD, ODD and CD) and neuropsychological functions. Other comorbid disorders were not taken into account.

Parental mental illness was not included in this investigation. Children born at LBW or preterm are genetically predisposed to psychiatric illness, as a previous study indicated that women with a history of psychiatric illness, substance use or both diagnoses had an appreciably higher risk of delivering VLBW, LBW and preterm infants (Kelly et al., 2002). Differences in alcohol intake were not shown in this study. The possibility of a history of parental mental illness may explain the higher prevalence of depressive symptoms, and symptoms of ADHD, ODD and CD in the LBW group than the NBW cohort, though it was not investigated in this study.

Research results on the role of environmental factors in the expression of psychological disorders and neuropsychological impairments among LBW children seem to be inconsistent. A study of premature children found that family factors were stronger predictors of school

performance than were perinatal complications (Gross et al., 2001). The impact of environmental influences was not investigated in this study, though various aspects were included in the biographical data questionnaire. It would be enlightening to explore the extent to which environmental influences (such as low parental education, single mother status, SES, family composition, foetal exposure to toxins, postnatal nutrition) predict emotional, behavioural and school problems (Abernethy et al., 2004; Breslau et al., 2001; Gross et al., 2001; Hack et al., 2005; Jobe, 2001).

Birth status is not considered the best predictor of school-age behaviour problems, but rather a factor influencing the developmental processes (Nadeau et al., 2001). Significant differences observed in this study between the birth weight groups may not be caused by LBW or gestational age independently, but by other variables. Substantially more pre-, peri- and postnatal complications (included in the biographical data questionnaire) were shown in the LBW group than in the LBW cohort, as indicated in Table 7.8. Generally more psychological/neuropsychological impairments, as well as pre-, peri- and postnatal complications (see Table 7.8), raise the question whether the impairments mentioned are related to LBW as such or rather caused by pre-, peri- and/or postnatal problems, environmental factors or by an interplay of them all.

9.6 Possibilities for further research

The areas of limitation discussed in Section 9.5 should be considered in follow-up investigations.

Limited research on LBW and its outcomes is available in the South African context. Large differences in SES and high HIV infection rates might imply more pronounced and

long-lasting effects on child development and neuropsychological functioning in LBW children in South Africa. HIV status should be taken into account in follow-up studies.

The sample included children from 11 ethnic groups. Cultural differences in neuropsychological measures (Meyer, 2005) and the expression of anxiety (American Psychiatric Association, 2000; Hack et al., 2005) have been noted. Investigating the sequelae of LBW in South Africans is of paramount importance in developing culture appropriate prevention and intervention strategies.

Longitudinal studies in the South African context should focus on all developmental stages, in order to determine developmental trends, predictors, prognosis and preventative strategies. Research findings of Breslau et al. (2001) imply that most of the differences between LBW and NBW academic achievements at age 11 could be eliminated by reducing differences in cognitive abilities at age 6. Berk (2006) and Breslau et al. (2001) postulate that frequently encountered behavioural and cognitive difficulties persist throughout childhood and adolescence and into adulthood.

This investigation will contribute to a data base in order to identify problem areas, their frequency, nature and severity and will determine tendencies, predictors, the course of psychopathology from childhood to adolescence and beyond, cultural determinations and appropriate interventions from a South African perspective. Patterns of disability seem to change over time, implying continuous updating of research findings (Saigal et al., 2003b). All LBW children, including low-risk populations, should be included in follow-up programmes for early detection of deficits and treatment before school entry (Pietz et al., 2004).

9.7 Concluding remarks

As expected, this study demonstrated that LBW children, in comparison to the NBW cohort, are associated with a tendency towards increased internalising symptoms (depression), externalising symptoms (hyperactivity/impulsiveness, inattention, ODD and CD) and neuropsychological impairments (motor, visual-spatial/visual-motor, memory and EF). These symptoms and functions seem to be in reciprocal interaction. The impaired domains mentioned may be explained by significantly more pre-, peri- and postnatal complications in the LBW group than the NBW counterparts.

Only a few differences were observed between the LBW males and females and their NBW counterparts. Differences in performance were mostly indicated in both the LBW 6 to 9 and 10 to 13 age groups, indicating deficient resolution of impairments with increasing age. The findings of the present study indicate that birth weight is an important aspect to consider in assessment in view of its potentially adverse impact on short- and long-term outcomes.

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Human Sciences Research Council
Lekgotla la Dinyakisišo tša Semahlale tša Setho
Raad vir Geesteswetenskaplike Navorsing
Umkhandlu Wezokucwaninga Ngesayensi Yesintu
Ibhunga Lophando Ngenzulu-Lwazi Kantu

Social Aspects of HIV/AIDS and Health

HSRC
Social science that makes a difference

27 January 2005

Population

The target population for this survey consists of learners at the schools situated in Tshwane North and South Districts. However, schools with boarding facilities; schools that combine primary and secondary or schools with low number of pupils were excluded from the sampling population.

Sampling process

The sample is stratified to enable the reporting of results at the stratification level. The explicit stratification variable was Race. That is, the dominant racial group of learners at the school. The intention of the study is to report the results of the survey at district and racial levels.

(a) Districts

Two districts were used for selection of the schools. These are the Tshwane North and South Districts.

(b) School sampling

The schools were first identified and classified according to the dominant racial group at school. Schools that are dominated by Coloureds or Indians were grouped together. In the case were the learners were racially mixed and there was no clear indication of the dominant race, the school was classified as Multiracial. The other two racial groups consisted of Whites and Africans. A total of five schools were selected in each racial group. A stratified random sampling was used. The schools were sampled within each stratum using the Probability Proportional to Size (PPS). The estimated total number of learners at the school was used as a measure of size (MOS).

Sincerely yours

Dr Khangelani Zuma, BssEd, MSc,PhD
E-mail: kzuma@hsrc.ac.za

UMnyango WezeMfundo
Department of Education

Lefapha la Thuto
Departement van Onderwys

Date:	**28 February 2005**
Name of Researcher:	**Haycock Anna Cornelia**
Address of Researcher:	**3 Kuisis Street**
	Amarilla no 5
	Brummeria, 0027
Telephone Number:	**0824899498**
Fax Number:	**N/A**
Research Topic:	**Psychological functioning in children with low birth weight**
Number and type of schools:	**9 Primary Schools**
District/s/HO	**Tshwane South & North**

Re: Approval in Respect of Request to Conduct Research

This letter serves to indicate that approval is hereby granted to the above-mentioned researcher to proceed with research in respect of the study indicated above. The onus rests with the researcher to negotiate appropriate and relevant time schedules with the school/s and/or offices involved to conduct the research. A separate copy of this letter must be presented to both the School (both Principal and SGB) and the District/Head Office Senior Manager confirming that permission has been granted for the research to be conducted.

Permission has been granted to proceed with the above study subject to the conditions listed below being met, and may be withdrawn should any of these conditions be flouted:

1. ***The District/Head Office Senior Manager/s concerned must be presented with a copy of this letter that would indicate that the said researcher/s has/have been granted permission from the Gauteng Department of Education to conduct the research study.***
2. ***The District/Head Office Senior Manager/s must be approached separately, and in writing, for permission to involve District/Head Office Officials in the project.***
3. ***A copy of this letter must be forwarded to the school principal and the chairperson of the School Governing Body (SGB) that would indicate that the researcher/s have been granted permission from the Gauteng Department of Education to conduct the research study.***

4. *A letter / document that outlines the purpose of the research and the anticipated outcomes of such research must be made available to the principals, SGBs and District/Head Office Senior Managers of the schools and districts/offices concerned, respectively.*
5. *The Researcher will make every effort obtain the goodwill and co-operation of all the GDE officials, principals, chairpersons of the SGBs, teachers and learners involved. Persons who offer their co-operation will not receive additional remuneration from the Department while those that opt not to participate will not be penalised in any way.*
6. *Research may only be conducted after school hours so that the normal school programme is not interrupted. The Principal (if at a school) and/or Senior Manager (if at a district/head office) must be consulted about an appropriate time when the researcher/s may carry out their research at the sites that they manage.*
7. *Research may only commence from the second week of February and must be concluded before the beginning of the last quarter of the academic year.*
8. *Items 6 and 7 will not apply to any research effort being undertaken on behalf of the GDE. Such research will have been commissioned and be paid for by the Gauteng Department of Education.*
9. *It is the researcher's responsibility to obtain written parental consent of all learners that are expected to participate in the study.*
10. *The researcher is responsible for supplying and utilising his/her own research resources, such as stationery, photocopies, transport, faxes and telephones and should not depend on the goodwill of the institutions and/or the offices visited for supplying such resources.*
11. *The names of the GDE officials, schools, principals, parents, teachers and learners that participate in the study may not appear in the research report without the written consent of each of these individuals and/or organisations.*
12. *On completion of the study the researcher must supply the Senior Manager: Strategic Policy Development, Management & Research Coordination with one Hard Cover bound and one Ring bound copy of the final, approved research report. The researcher would also provide the said manager with an electronic copy of the research abstract/summary and/or annotation.*
13. *The researcher may be expected to provide short presentations on the purpose, findings and recommendations of his/her research to both GDE officials and the schools concerned.*
14. *Should the researcher have been involved with research at a school and/or a district/head office level, the Senior Manager concerned must also be supplied with a brief summary of the purpose, findings and recommendations of the research study.*

The Gauteng Department of Education wishes you well in this important undertaking and looks forward to examining the findings of your research study.

Kind regards

ALBERT CHANEE
ACTING DIVISIONAL MANAGER: OFSTED

The contents of this letter has been read and understood by the researcher.	
Signature of Researcher:	
Date:	

UNIVERSITY OF THE NORTH
SCHOOL OF SOCIAL SCIENCES
PSYCHOLOGY

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01 October 2006

Dear Sir or Madam

DOCTORATE STUDY: A.C. HAYCOCK : PSYCHOLOGICAL FUNCTIONING IN CHILDREN WITH LOW BIRTH WEIGHT

This is an approved departmental research project of the University of Limpopo in collaboration with the Department of Physiology, University of Oslo, Norway.

The Human Science Research Council selected your school as part of a sample to participate in the above mentioned project.

Background information, purpose of the study, the proposed method of this study and expectations of schools will be the focus of this letter.

Background information

The future welfare of low-birth-weight (LBW) or premature infants (birth before 37th week of gestation) has stimulated research for several decades. The improved survival of low-birth-weight (birth weight below 2 500 g) infants owing to improved techniques of newborn intensive care, even those with birth weights lower than 1 000 g, compelled researchers to investigate the later development of these children, in order to optimise their chances of leading a healthy, productive life.

LBW children seem to be vulnerable to neurodevelopmental disturbances due to prenatal complications and neonatal risk factors. Preterm children are at increased risk of developmental difficulties due to a central nervous system that is not fully organized at the time of birth for sustaining itself in the extra-uterine environment. Preterm neonates are at higher risk of postnatal complications, such as intraventricular haemorrhage or chronic lung disease. They are consequently subjected to painful procedures and maternal separation for prolonged periods. These factors can promote or precipitate neuronal cell death in the immature brains.

Specific types of developmental morbidities are described in LBW cohorts, for example social problems, lower attention, cognitive delays (for example lower IQ), remedial assistance, mathematic problems, speech and language disorders, persistent neuro-motor abnormalities, perceptual problems and disobedience. Greater rates of behavioural problems are associated with decreasing birth weight.

Preterm children seem to be particularly vulnerable to psychiatric disturbances. Ten percent of a sample of premature children exhibited an emotional disturbance severe enough to interfere with their development and to make them

difficult to manage. 27 percent of LBW children compared to 9 percent of normal-birht-weight (NBW) children were diagnosed with a psychiatric disorder.

The purpose of the study

The main focus of this study is to investigate the associated externalising psychological disorders (attention-deficit/hyperactivity disorder, opposi- tional defiant disorder and conduct disorder) and internalising psychological disorders (anxiety and depression) with LBW, as well as neuropsychological functioning among current primary school children born with LBW. Similarities and differences between birth weight and gender groups will be determined pertaining to the focus areas mentioned.

Method

If you should agree in participating in this project, the researcher will visit your school and screen the children for low birth weight by sending out a letter to the parents. A control group (consisting of normal birth weight children) will be selected according to age, language, socio-economic status and gender in order to compare results.

The following questionnaires/tests will be administered:

- Biographical data questionnaire (to be completed by parents)
- Disruptive Behaviour Disorder (DBD) Rating Scale (to be completed by parents and one teacher)
- Self-report questionnaire measuring symptoms of anxiety and depression
- Tests for fine motor co-ordination
- Tests for planning abilities
- Test for perceptual organisation abilities
- Tests for over-activity, impulsiveness and impaired sustained attention
- Tests for visual and working memory

Selected pupils will be tested individually for approximately 40-50 minutes, depending on the child's pace.

The data will be used for statistical analysis only and in no circumstances will the identity of the child and the school be revealed. The children selected will not necessarily be suffering from any disorder.

The involved schools will receive feedback regarding general results of the study. Individual feedback will be given to parents of participants.

Expectations from selected schools

We need your assistence regarding the following:

- Sending out letters (appendix A) to and receiving it from parents via all pupils in order to identify low birth weight and normal birth weight children. Each school will be provided with the necessary letters. Return slips will be collected by the researcher.
- Children with an IQ below 75 have to be excluded from the study. Therefore we need class teachers to indicate the level of intellectual functioning of each participant, based on class observation (appendix B). Should this not be possible, every participant has to be screened by the researcher, which is much more time consuming.
- Completion of **one** Disruptive Behaviour Disorder (DBD) rating scale (appendix C) by the class teacher or all involved teachers of every participant.
- Sending of documentation (such as a DBD rating scale and Biographical data questionnaire) to the parents via participants in your school, as well as receiving these documentation. The researcher will again collect these data.
- Practical arrangements (e.g. room for testing, time of testing, etc.) will be made with every school regarding the testing of children.

All documentation will be provided at the researcher's cost. There will be no financial implication for your school.

We will limit the involvement and responsibilities of school personnel as far as possible.

The number of participants in your school depends on the response of parents with low birth weight children. From previous experience a maximum of 46 pupils were selected in a school (23 in the low birth weight group and 23 in the normal birth weight group).

Statistically the number of low birth weight children are increasing, with consequent increased morbidities (e.g. intellectual and neuro-developmental problems). Research will enable professionals to enhance the longterm outcomes of these low birth weight children by developing appropriate treatment strategies for their special needs.

Your co-operation will be appreciated. A valid and reliable study will not be possible without your support.

.....

Anelia Haycock
Researcher
Cellphone number: 082 489 9498
e-mail: haycocke@tut.ac.za

Dear parent/guardian

RESEARCH PROJECT: PSYCHOLOGICAL FUNCTIONING IN CHILDREN WITH LOW BIRTH WEIGHT

The Discipline of Psychology of the University of Limpopo is investigating the relationship between low birth weight and possible psychological problems.

Current primary school children, born with a birth weight below 2.5 kg, are needed for this research project. We also need children with normal birth weight, above 2.5 kg, in order to compare the results of the two groups. The children selected will not necessarily experience any problem.

The following areas will be evaluated at the school through games: executive functions, working memory, perceptual and motor skills, as well as emotional aspects. Parents of selected children will be required to complete a questionnaire. The school will also complete a questionnaire. Parents will receive individual feedback afterwards. Confidentiality is guaranteed.

Involvement in the project is free of charge. Free psychological services will be offered in relevant cases.

We would appreciate it if **all parents** who are willing to allow their child or children to participate in the study could complete the slip and return it to the class teacher on/before Thursday, ……..

Thank you for your co-operation. Your involvement will contribute to more effective psychological treatment of children with special needs.

Anelia Haycock
Researcher
Cell no: 082 489 9498

Place return slip in envelope, if preferred

I hereby grant permission for …….. (name/s of child/children) to participate in the study.

Grade and class: …… Name of school: ……

Birth weight: …… Gender: ……

Date of birth: …….. Age in months: ……

Home language: ……

Name of parent/guardian:……

Telephone number: ……

Monthly income of mother (please indicate relevant category):

unemployed	R0 – R3000	R3001 – R7000	R7001 – R11000	R11001 – R15000	above R15000

Monthly income of father (please indicate relevant category):

unemployed	R0 – R3000	R3001 – R7000	R7001 – R11000	R11001 – R15000	above R15000

PO Box 1473
Groenkloof
0027

Dear parent/guardian

RESEARCH PROJECT: PSYCHOLOGICAL FUNCTIONING IN CHILDREN WITH LOW BIRTH WEIGHT

Thank you for responding to the previous letter. As previously noted, the Discipline of Psychology of the University of Limpopo is investigating the relationship between low birth weight and possible psychological problems.

Your child has been included in the sample. Current primary school children, born with a birth weight below 2 kg, are needed for this research project. We also need children with normal birth weight, above 2.5 kg, in order to compare the results of the two groups. The children selected will not necessarily experience any problem.

The following areas will be evaluated at the school during school time through games: executive functions, working memory, perceptual and motor skills, as well as emotional aspects. Parents of selected children will be required to complete a questionnaire. The school will also complete a questionnaire. Parents will receive individual feedback afterwards. Confidentiality is guaranteed.

Involvement in the project is free of charge. Free psychological services will be offered in relevant cases.

We would appreciate it if you could complete the following documents and return to the class teacher on or before .....:

- Biographic Information
- DBD questionnaire
- Please send a copy of your child's clinic chart to confirm his/her birth weight, if possible.

Thank you for your co-operation. Your involvement in this research project will contribute to more effective psychological treatment of children.

.....
Anelia Haycock
Researcher
Cell nr: 082 489 9498

BIOGRAPHICAL DATA

CHILD NO: .....

CHILD AND FAMILY INFORMATION

Child's name and surname: .....

Date of birth: ..... **Age:**.....

Sex: **M / F** **Language:** .....

Height: ..... **Weight:** .....

School: ..... **Grade:** .....

Is child in special education? Y / N **If so, what type?** .....

Computer experience: Y / N

Dominant hand: Left / Right **Dominant foot: Left / Right**

Medication (if any): .....

Father's name: ..... **Age:** .....

Years of education: ..... **Occupation:** .....

Contact number: .....

Mother's name: ..... **Age:** .....

Years of education: ..... **Occupation:** .....

Contact number: .....

Address: .....

Home phone: .....

Please list all the other children in the family:

Name:	**Age:**	**Grade:**
_____	_____	_____
_____	_____	_____
_____	_____	_____

	YES	**NO**
Does the family have a TV?		
A car?		
Electricity in the house?		
Water in the house?		
Is the child adopted?		
Are parents married?		
Separated?		
Divorced?		

DEVELOPMENTAL AND MEDICAL HISTORY

PREGNANCY AND DELIVERY

A. Length of pregnancy (e.g. full term, 40 weeks, 32 weeks, etc.) _____

B. Length of delivery (number of hours from initial labor pains to birth) _____

C. Were you a low birth weight baby yourself? _____

D. Mother's age when child was born _____

E. Do you (mother) have a small body build? _____

F. Child's birth weight _____

G. Where was this child born (e.g. home, hospital etc.) _____

H. Did you give birth to other premature babies? Yes / No

I. Did any of the following occur during pregnancy / delivery?

1.	Received proper medical care	No Yes
2.	Followed a well balanced diet	No Yes
3.	Bleeding	No Yes
4.	Excessive weight gain (more than 66 kg)	No Yes
5.	Low weight gain by mother	No Yes
6.	Toxemia / preeclampsia	No Yes
7.	Rh factor incompatibility	No Yes
8.	Frequent nausea or vomiting	No Yes
9.	Maternal anemia	No Yes
10.	Serious illness (e.g. genital, urinary tract or other infections, hypertension or diabetes mellitus) or injury	No Yes
11.	Took prescription medications	No Yes
	a. If yes, name of medication _____	
12.	Took illegal drugs	No Yes
13.	Used alcoholic beverage	No Yes
	a. If yes, approximate number of drinks per week _____	
14.	Smoked cigarettes	No Yes
	a. If yes, approximate number of cigarettes per day (e.g. ½ pack) _____	
15.	Was given medication to ease labor pains	No Yes
	a. If yes, name of medication _____	
16.	Delivery was induced	No Yes
17.	Forceps were used during delivery	No Yes
18.	Had a breech delivery	No Yes

19. **Had a cesarean section delivery** **No** **Yes**

20. **Other problems – please describe** _____.

J. **Did any of the following conditions affect your child during delivery or within the first few days after birth?**

1.	**Injured during delivery**	**No**	**Yes**
2.	**Cardiopulmonary (heart) distress during delivery**	**No**	**Yes**
3.	**Delivered with cord around neck**	**No**	**Yes**
4.	**Had trouble breathing following delivery**	**No**	**Yes**
5.	**Needed oxygen**	**No**	**Yes**
6.	**Turned blue**	**No**	**Yes**
7.	**Was jaundiced, turned yellow**	**No**	**Yes**
8.	**Had an infection**	**No**	**Yes**
9.	**Had seizures**	**No**	**Yes**
10.	**Was given medications**	**No**	**Yes**
11.	**Born with a congenital defect**	**No**	**Yes**
12.	**Was in hospital more than 7 days**	**No**	**Yes**

INFANT HEALTH AND TEMPERAMENT

A. **During the first 12 months, was your child:**

1.	**Difficult to feed**	**No**	**Yes**
2.	**Difficult to get to sleep**	**No**	**Yes**
3.	**Colicky**	**No**	**Yes**
4.	**Difficult to put on a schedule**	**No**	**Yes**
5.	**Alert**	**No**	**Yes**
6.	**Cheerful**	**No**	**Yes**
7.	**Affectionate**	**No**	**Yes**
8.	**Sociable**	**No**	**Yes**
9.	**Easy to comfort**	**No**	**Yes**
10.	**Difficult to keep busy**	**No**	**Yes**
11.	**Overactive, in constant motion**	**No**	**Yes**
12.	**Very stubborn, challenging**	**No**	**Yes**

EARLY DEVELOPMENTAL MILESTONES

A. **At what age did your child first accomplish the following:**

1. **Sitting without help** _____

2. **Crawling** _____

3. **Walking alone, without assistance** _____

4. **Using single words (e.g. "mama", "dada", "ball", etc.)** _____

5. **Putting two or more words together (e.g. "mama up")** _____

6. **Bowel training, day and night** _____

7. **Bladder training, day and night** _____

HEALTH HISTORY

A. **Date of child's last physical exam:** _____

B. **At any time has your child had the following:**

1.	**Asthma**	**Never**	**Past**	**Present**
2.	**Allergies**	**Never**	**Past**	**Present**
3.	**Diabetes, arthritis, or other chronic illness**	**Never**	**Past**	**Present**
4.	**Epilepsy or seizures**	**Never**	**Past**	**Present**
5.	**Febrile seizures**	**Never**	**Past**	**Present**
6.	**Heart or blood pressure problems**	**Never**	**Past**	**Present**
7.	**High fever (over 103°)**	**Never**	**Past**	**Present**
8.	**Head injury with loss of consciousness**	**Never**	**Past**	**Present**
9.	**Lead poisoning**	**Never**	**Past**	**Present**
10.	**Lengthy hospitalization**	**Never**	**Past**	**Present**
11.	**Speech or language problems**	**Never**	**Past**	**Present**
12.	**Chronic ear infections**	**Never**	**Past**	**Present**
13.	**Hearing difficulties**	**Never**	**Past**	**Present**
14.	**Eye or vision problems**	**Never**	**Past**	**Present**
15.	**Fine motor / handwriting problems**	**Never**	**Past**	**Present**
16.	**Gross motor difficulties, clumsiness**	**Never**	**Past**	**Present**
17.	**Appetite problems (overeating / under-eating)**	**Never**	**Past**	**Present**
18.	**Sleep problems (falling asleep, staying asleep)**	**Never**	**Past**	**Present**
19.	**Soiling problems**	**Never**	**Past**	**Present**
20.	**Wetting problems**	**Never**	**Past**	**Present**

21. **Other health difficulties – please describe** _____.

TEACHER / PARENT DBD RATING SCALE

ID: _____

Child's name: _____ **Form completed by:** _____

Sex: M / F **Age:** _____ **School:** _____

Grade: _____ **Date Completed:** _____

Home language: English/Afrikaans/N-Sotho/Xitsonga/Tshivenda/Other: _____

CHECK THE COLUMN THAT BEST DESCRIBES THIS CHILD. PLEASE PUT A QUESTION MARK NEXT TO ANY ITEM FOR WHICH YOU DON'T KNOW THE ANSWER.

	Not at All	Just a Little	Pretty Much	Very Much
1. often interrupts or intrudes on others (e.g. butts into conversations or games)				
2. has run away from home overnight at least twice while living in parental or parental surrogate home (or once without returning for a lengthy period)				
3. often argues with adults				
4. often lies to obtain goods or favours to avoid obligations (i.e. "cons" others)				
5. often initiates physical fights with other members of his or her household				
6. has been physically cruel to people				
7. often talks excessively				
8. has stolen items of nontrivial value without confronting a victim (e.g. shoplifting, but without breaking and entering; forgery)				
9. is often easily distracted by extraneous stimuli				
10. often engages in physically dangerous activities without considering possible consequences (not for the purpose of thrill-seeking), e.g. runs into the street without looking				
11. often truant from school, beginning before age 13 years				
12. often fidgets with hands or feet or squirms in seat				
13. is often spiteful or vindictive				
14. often swears or uses obscene language				
15. often blames others for his or her mistakes or misbehaviour				
16. has deliberately destroyed others' property (other than by fire setting)				
17. often actively defies or refuses to comply with adults' request or rules				
18. often does not seem to listen when spoken to directly				
19. often blurs out answers before questions have been completed				

PLEASE ALSO COMPLETE REVERSE SIDE

	Not at all	Just a little	Pretty much	Very much
20. often initiates physical fights with others who do not live in his or her household (e.g. peers at school or in the neighbourhood)				
21. often shifts from one uncompleted activity to another				
22. often have difficulty playing or engaging in leisure activities quietly				
23. often fails to give close attention to details or makes careless mistakes in schoolwork, work or other activities				
24. is often angry and resentful				
25. often leaves seat in classroom or in other situations in which remaining is expected				
26. is often touchy or easily annoyed by others				
27. often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behaviour or failure to understand instructions)				
28. often looses temper				
29. often has difficulty sustaining attention in tasks or play activities				
30. often has difficulty awaiting turn				
31. has forced someone into sexual activities				
32. often bullies, threatens, or intimidates others				
33. is often "on the go" or often acts as "driven by a motor"				
34. often loses things necessary for tasks or activities (e.g. toys, school assignments, pencils, books, or tools)				
35. often runs about or climbs excessively in situations in which it is inappropriate				
36. has been physically cruel to animals				
37. often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)				
38. often stays out at night despite parental prohibitions, beginning before age 13 years				
39. often deliberately annoys people				
40. has stolen while confronting a victim (e.g. mugging, purse snatching, extortion, armed robbery)				
41. has deliberately engage in fire setting with the intention of causing serious damage				
42. often has difficulty organising tasks and activities				
43. has broken into someone else's house, building, or car				
44. is often forgetful in daily activities				
45. has used a weapon that can cause serious physical harm to others (e.g. a bat, brick, broken bottle, knife, gun)				

UNIVERSITY OF LIMPOPO
ETHICS COMMITTEE

PROJECT TITLE: Psychological functioning in children with low birth weight

PROJECT LEADER: Prof. Anneke Meyer

CONSENT FORM

I, _____ hereby voluntarily consent for my child to participate in the following project: **Psychological functioning in children with low birth weight**

I realise that:

1. The study deals with the relationship between psychological problems and low birth weight;

2. The procedure or treatment envisaged may hold some risk for me that cannot be foreseen at this stage;

3. The Ethics Committee has approved that individuals may be approached to participate in the study;

4. The experimental protocol, i.e., the extent, aim and methods of the research, has been explained to me;

5. The protocol sets out the risks that can be reasonably expected as well as possible discomfort for persons participating in the research, an explanation of the anticipated advantages for myself or others that are reasonably expected from the research and alternative procedures that may be to my advantage:

6. I will be informed of any new information that may become available during the research that may influence my willingness to continue my participation;

7. Access to the records that pertain to my participation in the study will be restricted to persons directly involved in the research;

8. Any questions that I may have regarding the research, or related matters, will be answered by the researchers;

9. If I have any questions about, or problems regarding the study, or experience any undesirable effects, I may contact a member of the research team;

10. Participation in this research is voluntary and I can withdraw my participation at any stage;

11. If any medical or psychological problem is identified at any stage during the research, or when my child is vetted for participation, such condition will be discussed with me in confidence by a qualified person and/or my child be referred to a doctor or psychologist;

12. I indemnify the University of Limpopo and all persons involved with the above project from any liability that may arise from my participation in the above project or that may be related to it, for whatever reasons, including negligence on the part of the mentioned persons.

.....	.....
SIGNATURE OF RESEARCHED PERSON	SIGNATURE OF WITNESS
.....	.....
SIGNATURE OF PERSON THAT INFORMED THE RESEARCHED PERSON	SIGNATURE OF PARENT/GUARDIAN

SIGNED AT _____ this _____ day of _____ 2003

P.O Box 1473
GROENKLOOF
0027

30 September 2007

Dear school principal

Research 2006/7: The psychological functioning in children with low birth weight

I would like to thank you for your collaboration. A reliable and valid study would not be possible without your support.

Specific aspects were investigated in this study, namely:

1. Psychological symptoms
    - Internalising psychological symptoms: separation anxiety, overanxiousness and major depression; and
    - Externalising psychological symptoms: attention difficulties, hyperactivity/impulsivity (attention-deficit/hyperactivity disorder), including oppositional defiant and conduct disorders). Oppositional defiant behaviour includes negativistic, hostile and defiant behaviour (e.g. often loses temper, often argues with adults, blaming others for his/her misbehaviour, touchy or easily annoyed by others, spiteful or vindictive). Conduct behaviour refers to the violation of the basic rights of others or important societal norms/rules (e.g. serious violations of rules, aggression to people or animals, destruction of property, deceitfulness or theft).

2. Neuropsychological functions
    - Fine motor skills;
    - Visual-spatial abilities
    - Memory (short-term verbal -, working – and visual-spatial memory); and

- Executive functioning, such as cognitive flexibility, attention shifting, sustained attention, problem-solving, planning, forming of abstract concepts, and inhibition of inappropriate responses

This study has demonstrated that low birth weight is associated with a tendency towards increased internalising and externalising psychological symptoms, as well as poorer neuropsychological functioning. This was particularly significant in the domains of internalising symptoms (depression), externalising symptoms (hyperactivity/impulsivity, inattention, oppositional defiant- and conduct disorders) and neuropsychological impairments (motor, visual-spatial/visual-motor, memory and executive functions).

The mentioned problem areas may be in reciprocal interaction, placing the low-birth-weight children at risk of further delay in different domains at specific developmental stages. The neuropsychological impairments (motor, visual-spatial, memory and executive functions) observed in this study among the low-birth-weight children probably increase the risk of subsequent externalising (conduct and oppositional behavioural problems) and internalising (depressive) psychological symptoms. Increased complications before, during and after birth in the low-birth weight group may increase their risk of neuropsychological deficiencies and subsequent internalising/externalising symptoms. These impairments most probably affect academic, emotional, social and other significant areas of functioning. The neuropsychological effect of low birth weight is possibly more adverse, since only normal functioning children from mainstream schools were included in the sample.

Generalisations should however be done with caution. Some low-birth-weight children did perform in the average and above average ranges in some domains. The low-birth-weight children as a group do however seems to be at increased risk of psychological and neuropsychological impairments than the normal-birth-weight comparisons.

Parents are to be individually informed regarding the performance of their child. They are referred to the following professional people closest to them, should their child need help:

- Clinical psychologists (addressing emotional and behavioural problems)
- Occupational therapists (specialising in neuropsychological problems)

It is an honor to work with you in the process of enhancing the well-being of the future, our children.

Should you require more information please feel free to contact me.

Regards

.....

Anelia Haycock
Researcher
Cellphone number: 082 489 9498

P.O. Box 1473
GROENKLOOF
0027

25 March 2007

Dear parent / guardian

Research 2006/7: Psychological functioning in children with low birth weight

The psychological functioning of low-birth-weight children was investigated by the University of Limpopo in collaboration with the University of Oslo, Norway. Children with a birth weight below 2000g and above 3000g were needed, in order to compare the results of normal-birth-weight and low-birth-weight children.

I would like to thank you for your co-operation. Reliable and valid results would not be possible without your support.

Specific aspects were measured in this study, namely:

- Fine motor skills;
- Visuospatial construction/perceptual organization;
- Executive functions such as cognitive flexibility, sustained attention, problem-solving, planning;
- Working and visual memory;
- Cognitive impulse control: Inhibition of inappropriate responses;
- Attention;
- Hyperactivity and impulsivity;
- Conduct behaviour: Violation of the basic rights of others or important societal norms/rules (e.g. serious violations of rules, aggression towards people or animals, destruction of property, deceitfulness or theft);
- Oppositional defiant behaviour: Negativistic, hostile and defiant behaviour (e.g. often loses temper, often argues with adults, blames others for his/her misbehaviour, touchy or easily annoyed by others, spiteful or vindictive); and

- Symptoms of separation anxiety, overanxiousness and depression.

An extensive test battery could not be used due to time restriction. Feedback is based on available data obtained from the parents/guardian, teachers and individual assessment of children. If a problem area(s) is indicated below, it is in your child's best interest to obtain a second opinion whether therapy is needed. The 2004/5 teachers can be consulted. Your child can be assessed by a psychologist or occupational therapist to determine the necessity of therapy.

According to available tests results and the rating scales, your child's performance is indicated in the table below in the following categories: above average, average (within the group norm) and below average.

Skills or behaviour measured	**Above average**	**Average/ normal**	**Below average**	**Needs therapy or assessment: Yes**	**No**
Fine motor skills					
Visiouspatial construction/perceptual organization					
Executive functions (e.g. problemsolving, planning, sustained attention)					
Visual memory					
Working memory					
Cognitive impulse control					
Hyperactivity/impulsivity					
Attention					
Oppositional behaviour					
Conduct behaviour					
Separation anxiety					
Overanxiousness					
Depression					

Psychological input is more applicable in the case of emotional or behavioural problems (such as depression, anxiety, inattention, hyperactivity, conduct or oppositional behaviour), while occupational therapy should be considered when cognitive

impairments (such as memory problems, executive dysfunctions, perceptual problems, motor impairments etc.) are identified.

The following institutions can be contacted for more information, should you consider involving your child in assessment and/or therapy:

- Child Therapy Clinic at the Pretoria Academic Hospital: A multi-professional team approach is followed at the Child Therapy Centre, including a psychologist, occupational therapist, speech therapist and social worker.
  Contact person: Mampho Sekonyela
  Contact number: 012-3546177
- Laudium Community Health Centre
  Psychologist: Tfibe, contact number: 012-3749952
  Occupational therapist: Babani Kolopen, contact number: 012-3749957
- Any other governmental hospital nearest to your home can be contacted to determine if any services are rendered by a psychologist or occupational therapist.
- Various professional people visit specific schools on a weekly basis, where they render services to children in need during school time. Contact numbers of the psychologist and/or occupational therapist involved at your child's school is included, if such a service is available. These professionals usually render there services on a private practice basis, claiming from the parent's medical fund or by other means of payment. Contact reception at the school if you experience any difficulty contacting these professionals, should you prefer to make use of their service.
  Psychologist: Ursula Pretorius – contact number: 012-6568779
  Occupational therapist: Louisa Nortier – contact number: 012-6531456

Remember to take this letter with to your child's appointment.

Please do not hesitate to contact me if you require more information.

Regards

Anelia Haycock (Researcher)
Cell phone number: 082 489 9498

Variable	Spearman Rank Order Correlations (phd anelia) MD pairwise deleted Marked correlations are significant at p <.05000						
	BWEIGHT	TERRYSAD	TERRYOAD	TERRYMDD	PEGS_DH	PEGS_NDH	DIGITS_F
BWEIGHT	1.000000	-0.038732	-0.078640	-0.152426	*-0.249088*	*-0.256854*	*0.225503*
TERRYSAD	-0.038732	1.000000	*0.759370*	*0.618142*	*0.284101*	*0.288495*	-0.148411
TERRYOAD	-0.078640	*0.759370*	1.000000	*0.624946*	*0.202451*	*0.205044*	-0.064208
TERRYMDD	-0.152426	*0.618142*	*0.624946*	1.000000	*0.234224*	*0.176148*	-0.149757
PEGS_DH	*-0.249088*	*0.284101*	*0.202451*	*0.234224*	1.000000	*0.803006*	*-0.393129*
PEGS_NDH	*-0.256854*	*0.288495*	*0.205044*	*0.176148*	*0.803006*	1.000000	*-0.372759*
DIGITS_F	*0.225503*	-0.148411	-0.064208	-0.149757	*-0.393129*	*-0.372759*	1.000000
DIGITS_B	*0.249926*	*-0.337243*	*-0.217703*	*-0.246487*	*-0.522579*	*-0.479431*	*0.498646*
ROCF_1	*0.434960*	*-0.185773*	-0.149410	-0.109565	*-0.616969*	*-0.587642*	*0.315704*
ROCF_2	*0.263001*	-0.141148	-0.116222	-0.122898	*-0.464505*	*-0.443007*	*0.302040*
ROCF_3	*0.293489*	*-0.159119*	-0.111177	-0.086755	*-0.485827*	*-0.462727*	*0.328205*
TDBD_HI	*-0.159976*	*0.158555*	0.112460	*0.171618*	0.032772	0.015863	-0.122199
TDBD_INA	*-0.346783*	*0.176337*	*0.167085*	*0.211202*	0.145619	0.148440	*-0.245929*
TDBD_ODD	*-0.239408*	0.036370	0.075511	0.134175	-0.023282	-0.055888	-0.153031
TDBD_CD	*-0.284862*	0.016417	-0.015475	0.063290	0.012446	-0.042367	-0.121478
PDBD_HI	*-0.209187*	0.114820	0.122767	0.020190	0.141519	0.164372	-0.133868
PDBD_INA	*-0.335168*	*0.185541*	*0.192670*	*0.181714*	*0.183801*	*0.197923*	-0.163770
PDBD_ODD	-0.041641	0.072241	0.044583	0.071659	-0.033548	-0.042108	-0.159986
PDBD_CD	*-0.219638*	0.031458	0.043513	0.071484	0.064008	0.045753	-0.140604
STROOPLN	*-0.164091*	*0.186322*	0.127580	0.043099	*0.590997*	*0.585756*	*-0.422380*
STROOPEN	*-0.346298*	0.011023	-0.033892	-0.013433	*0.245375*	*0.223185*	*-0.169543*
STROOPLB	*-0.219636*	*0.282257*	*0.188035*	*0.175594*	*0.628215*	*0.631324*	*-0.452187*
STROOPEB	*-0.286826*	0.029255	-0.004909	0.073515	0.083810	0.071851	*-0.157534*
STROOPLS	*-0.251136*	*0.267820*	*0.236447*	*0.268457*	*0.511467*	*0.566122*	*-0.360894*
STROOPES	*-0.234096*	0.011894	0.037754	0.090618	0.015597	0.079970	-0.107490
STROOPLV	*-0.163217*	*0.216739*	*0.226044*	*0.309689*	0.153630	*0.217443*	-0.094505

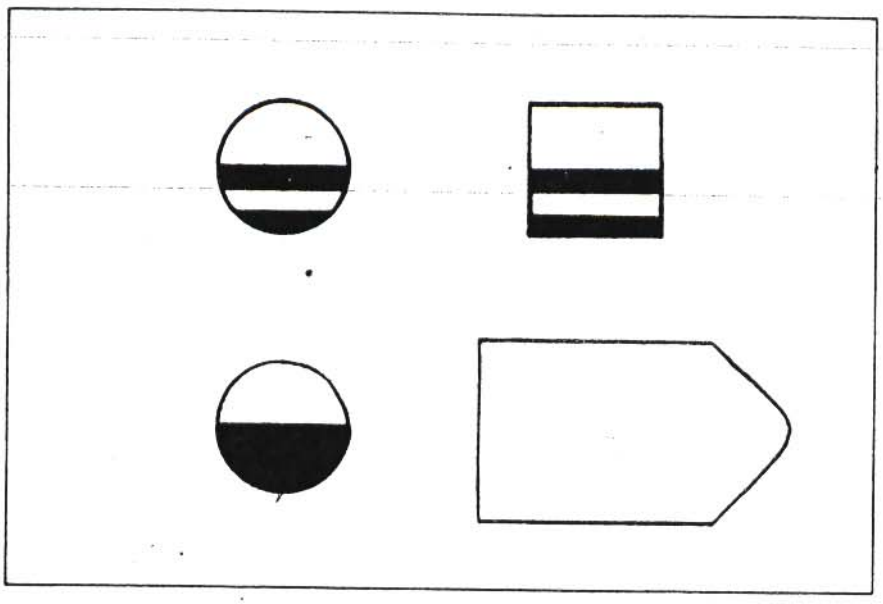
Spearman Rank Order Correlations (phd anelia)
MD pairwise deleted
Marked correlations are significant at p <.05000

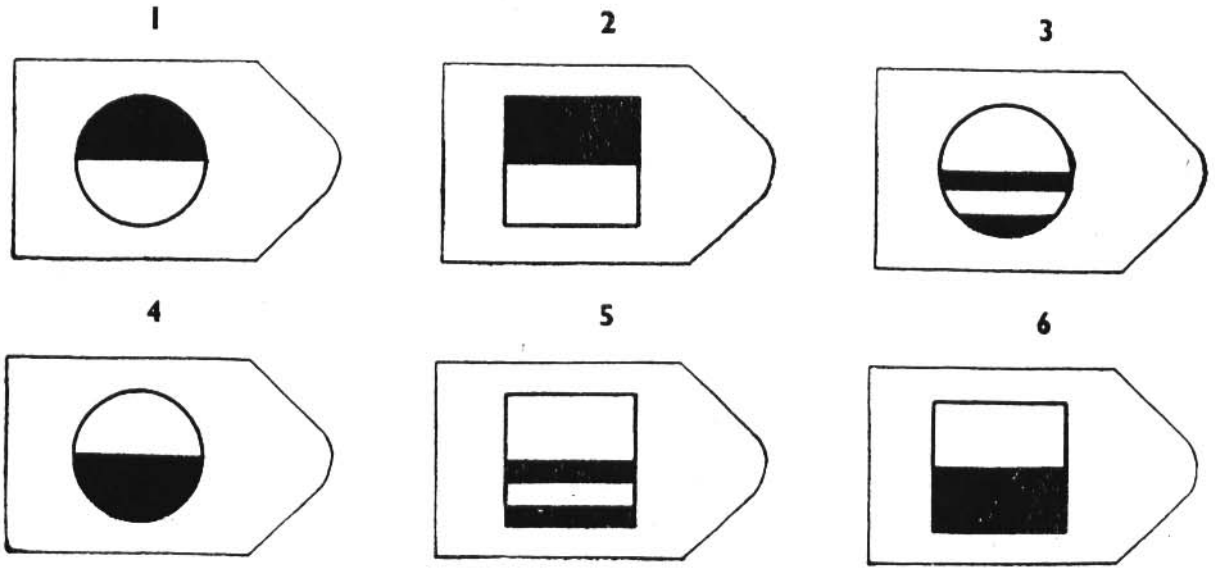
Variable	TDBD_CD	PDBD_HI	PDBD_INA	PDBD_ODD	PDBD_CD	STROOPLN	STROOPEN
BWEIGHT	-0.284862	-0.209187	-0.335168	-0.041641	-0.219638	-0.164091	-0.346298
TERRYSAD	0.016417	0.114820	0.185541	0.072241	0.031458	0.186322	0.011023
TERRYOAD	-0.015475	0.122767	0.192670	0.044583	0.043513	0.127580	-0.033892
TERRYMDD	0.063290	0.020190	0.181714	0.071659	0.071484	0.043099	-0.013433
PEGS_DH	0.012446	0.141519	0.183801	-0.033548	0.064008	0.590997	0.245375
PEGS_NDH	-0.042367	0.164372	0.197923	-0.042108	0.045753	0.585756	0.223185
DIGITS_F	-0.121478	-0.133868	-0.163770	-0.159986	-0.140604	-0.422380	-0.169543
DIGITS_B	-0.090047	-0.166953	-0.215316	-0.144029	-0.167944	-0.480542	-0.229189
ROCF_1	-0.113427	-0.117879	-0.275320	-0.025415	-0.148254	-0.507381	-0.380531
ROCF_2	0.007649	-0.071096	-0.169705	0.001077	-0.086402	-0.336667	-0.236666
ROCF_3	-0.026395	-0.033188	-0.170015	0.018110	-0.109723	-0.331898	-0.216686
TDBD_HI	0.502068	0.355021	0.400470	0.236883	0.156907	0.092298	0.099028
TDBD_INA	0.418482	0.299205	0.450907	0.133746	0.213098	0.196642	0.215057
TDBD_ODD	0.653017	0.342848	0.361336	0.148565	0.032299	0.058931	0.133761
TDBD_CD	1.000000	0.311490	0.280257	0.176253	0.225560	0.083629	0.173297
PDBD_HI	0.311490	1.000000	0.634331	0.590416	0.429637	0.140829	0.189999
PDBD_INA	0.280257	0.634331	1.000000	0.499310	0.465066	0.196948	0.226677
PDBD_ODD	0.176253	0.590416	0.499310	1.000000	0.539335	0.063753	0.099354
PDBD_CD	0.225560	0.429637	0.465066	0.539335	1.000000	0.078538	0.170631
STROOPLN	0.083629	0.140829	0.196948	0.063753	0.078538	1.000000	0.447301
STROOPEN	0.173297	0.189999	0.226677	0.099354	0.170631	0.447301	1.000000
STROOPLB	0.098437	0.150391	0.266944	0.059819	0.106568	0.849290	0.411420
STROOPEB	0.149976	0.158004	0.216920	0.119343	0.178322	0.237080	0.391991
STROOPLS	0.060648	0.179512	0.341227	0.107363	0.198667	0.509017	0.264145
STROOPES	0.007242	0.126810	0.242732	0.181330	0.246243	-0.043950	0.191195
STROOPLV	0.006683	0.133379	0.309671	0.145152	0.192817	-0.029040	-0.027182

Spearman Rank Order Correlations (phd anelia)
MD pairwise deleted
Marked correlations are significant at p <.05000

Variable	STROOPLB	STROOPEB	STROOPLS	STROOPES	STROOPLV
BWEIGHT	-0.219636	-0.286826	-0.251136	-0.234096	-0.163217
TERRYSAD	0.282257	0.029255	0.267820	0.011894	0.216739
TERRYOAD	0.188035	-0.004909	0.236447	0.037754	0.226044
TERRYMDD	0.175594	0.073515	0.268457	0.090618	0.309689
PEGS_DH	0.628215	0.083810	0.511467	0.015597	0.153630
PEGS_NDH	0.631324	0.071851	0.566122	0.079970	0.217443
DIGITS_F	-0.452187	-0.157534	-0.360894	-0.107490	-0.094505
DIGITS_B	-0.564813	-0.272034	-0.455492	-0.151546	-0.143857
ROCF_1	-0.491317	-0.146091	-0.364832	-0.081877	-0.053757
ROCF_2	-0.312155	-0.046046	-0.280114	-0.042742	-0.033808
ROCF_3	-0.361432	-0.034933	-0.314447	-0.027017	-0.042523
TDBD_HI	0.146075	0.105001	0.054094	0.007375	-0.007162
TDBD_INA	0.258670	0.161376	0.237952	0.157680	0.139746
TDBD_ODD	0.085883	0.109778	0.028593	-0.038250	0.004506
TDBD_CD	0.098437	0.149976	0.060648	0.007242	0.006683
PDBD_HI	0.150391	0.158004	0.179512	0.126810	0.133379
PDBD_INA	0.266944	0.216920	0.341227	0.242732	0.309671
PDBD_ODD	0.059819	0.119343	0.107363	0.181330	0.145152
PDBD_CD	0.106568	0.178322	0.198667	0.246243	0.192817
STROOPLN	0.849290	0.237080	0.509017	-0.043950	-0.029040
STROOPEN	0.411420	0.391991	0.264145	0.191195	-0.027182
STROOPLB	1.000000	0.396261	0.746171	0.042038	0.179046
STROOPEB	0.396261	1.000000	0.301788	0.353618	0.017594
STROOPLS	0.746171	0.301788	1.000000	0.393036	0.726662
STROOPES	0.042038	0.353618	0.393036	1.000000	0.511968
STROOPLV	0.179046	0.017594	0.726662	0.511968	1.000000

Variable	Spearman Rank Order Correlations (phd anelia) MD pairwise deleted Marked correlations are significant at p <.05000 DIGITS_B	ROCF_1	ROCF_2	ROCF_3	TDBD_HI	TDBD_INA	TDBD_ODD
BWEIGHT	0.249926	0.434960	0.263001	0.293489	-0.159976	-0.346783	-0.239408
TERRYSAD	-0.337243	-0.185773	-0.141148	-0.159119	0.158555	0.176337	0.036370
TERRYOAD	-0.217703	-0.149410	-0.116222	-0.111177	0.112460	0.167085	0.075511
TERRYMDD	-0.246487	-0.109565	-0.122898	-0.086755	0.171618	0.211202	0.134175
PEGS_DH	-0.522579	-0.616969	-0.464505	-0.485827	0.032772	0.145619	-0.023282
PEGS_NDH	-0.479431	-0.587642	-0.443007	-0.462727	0.015863	0.148440	-0.055888
DIGITS_F	0.498646	0.315704	0.302040	0.328205	-0.122199	-0.245929	-0.153031
DIGITS_B	1.000000	0.447371	0.368125	0.379726	-0.061885	-0.234701	-0.086472
ROCF_1	0.447371	1.000000	0.619723	0.668235	-0.106125	-0.280217	-0.078597
ROCF_2	0.368125	0.619723	1.000000	0.899614	-0.030542	-0.134446	0.058144
ROCF_3	0.379726	0.668235	0.899614	1.000000	-0.030902	-0.168134	0.077080
TDBD_HI	-0.061885	-0.106125	-0.030542	-0.030902	1.000000	0.737171	0.716680
TDBD_INA	-0.234701	-0.280217	-0.134446	-0.168134	0.737171	1.000000	0.634516
TDBD_ODD	-0.086472	-0.078597	0.058144	0.077080	0.716680	0.634516	1.000000
TDBD_CD	-0.090047	-0.113427	0.007649	-0.026395	0.502068	0.418482	0.653017
PDBD_HI	-0.166953	-0.117879	-0.071096	-0.033188	0.355021	0.299205	0.342848
PDBD_INA	-0.215316	-0.275320	-0.169705	-0.170015	0.400470	0.450907	0.361336
PDBD_ODD	-0.144029	-0.025415	0.001077	0.018110	0.236883	0.133746	0.148565
PDBD_CD	-0.167944	-0.148254	-0.086402	-0.109723	0.156907	0.213098	0.032299
STROOPLN	-0.480542	-0.507381	-0.336667	-0.331898	0.092298	0.196642	0.058931
STROOPEN	-0.229189	-0.380531	-0.236666	-0.216686	0.099028	0.215057	0.133761
STROOPLB	-0.564813	-0.491317	-0.312155	-0.361432	0.146075	0.258670	0.085883
STROOPEB	-0.272034	-0.146091	-0.046046	-0.034933	0.105001	0.161376	0.109778
STROOPLS	-0.455492	-0.364832	-0.280114	-0.314447	0.054094	0.237952	0.028593
STROOPES	-0.151546	-0.081877	-0.042742	-0.027017	0.007375	0.157680	-0.038250
STROOPLV	-0.143857	-0.053757	-0.033808	-0.042523	-0.007162	0.139746	0.004506

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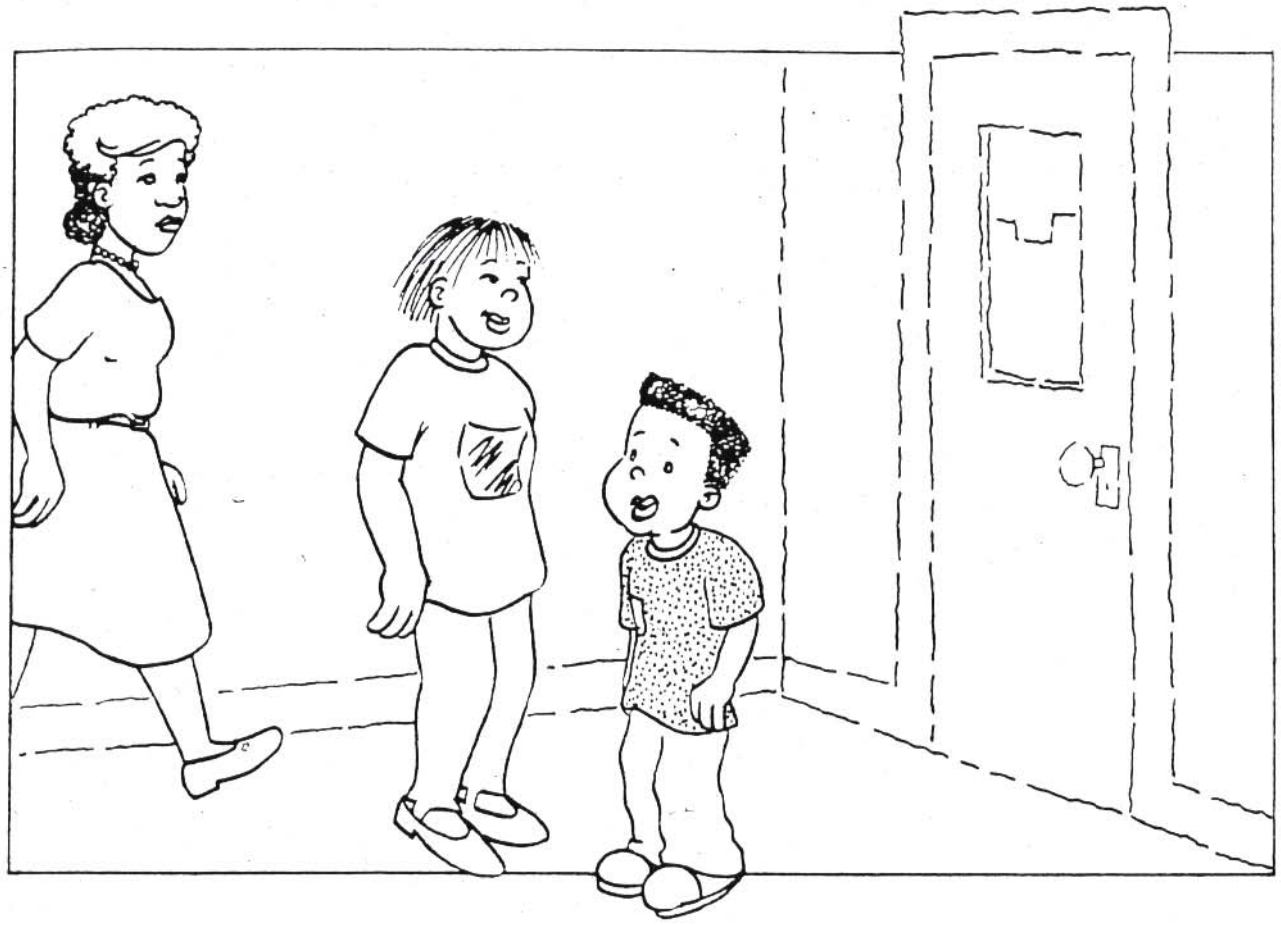
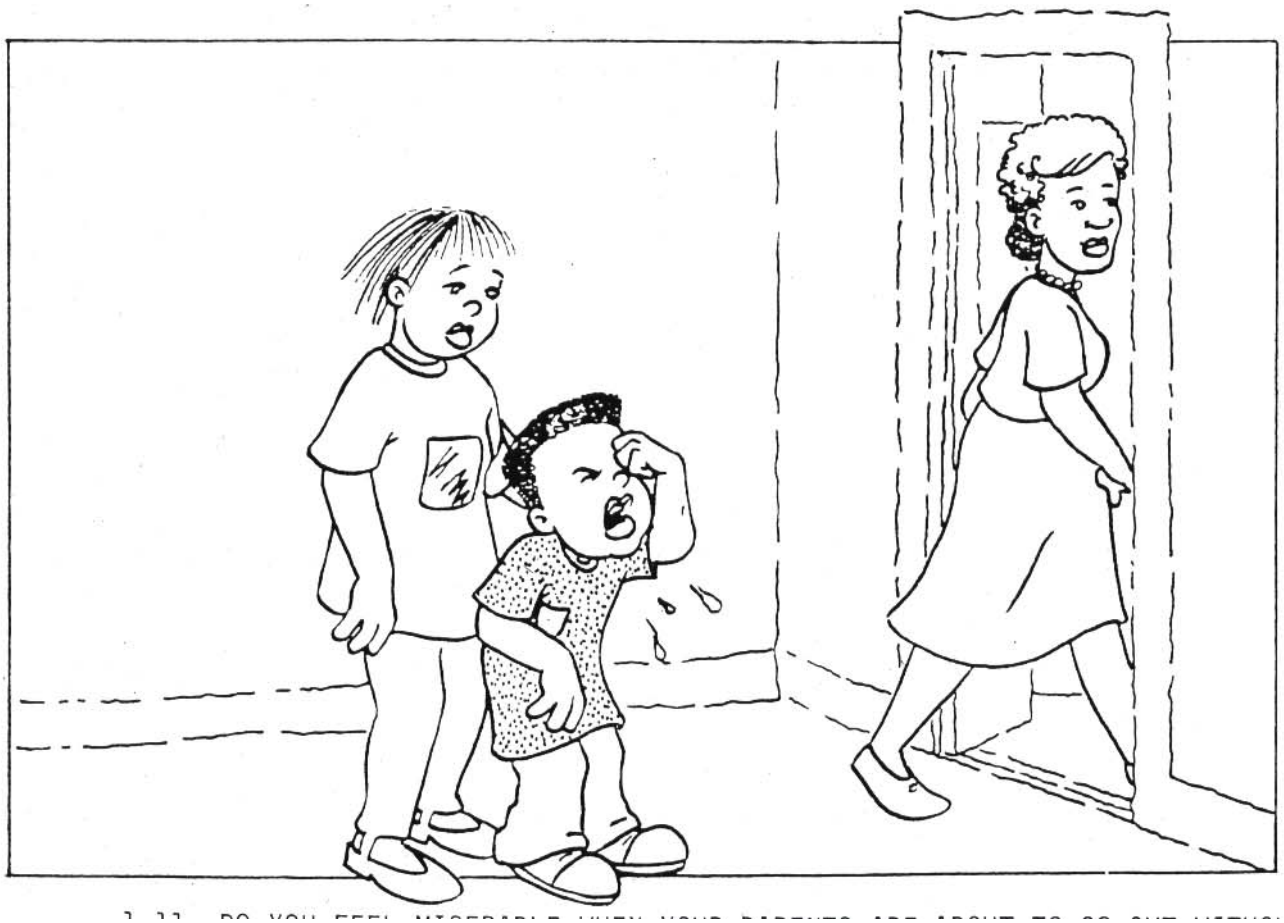
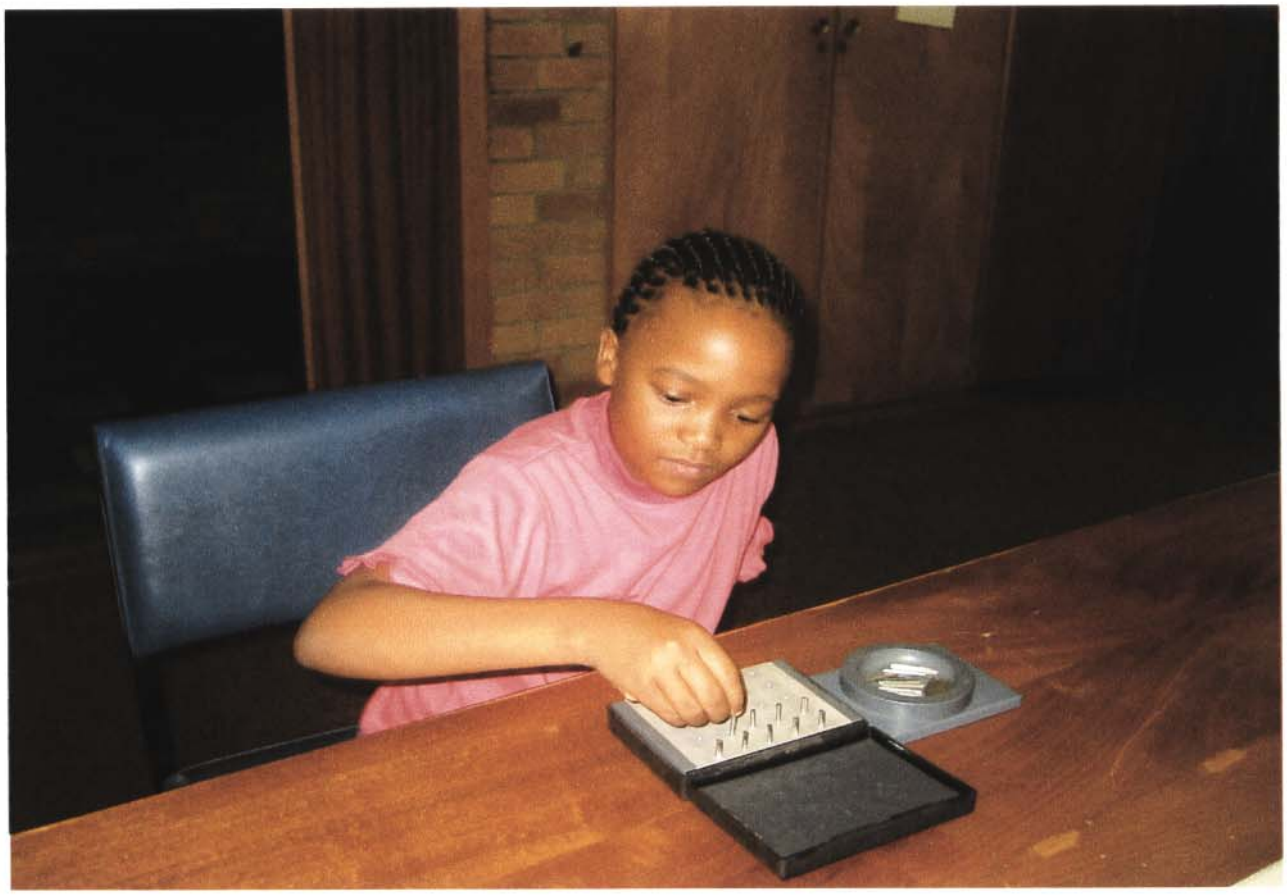


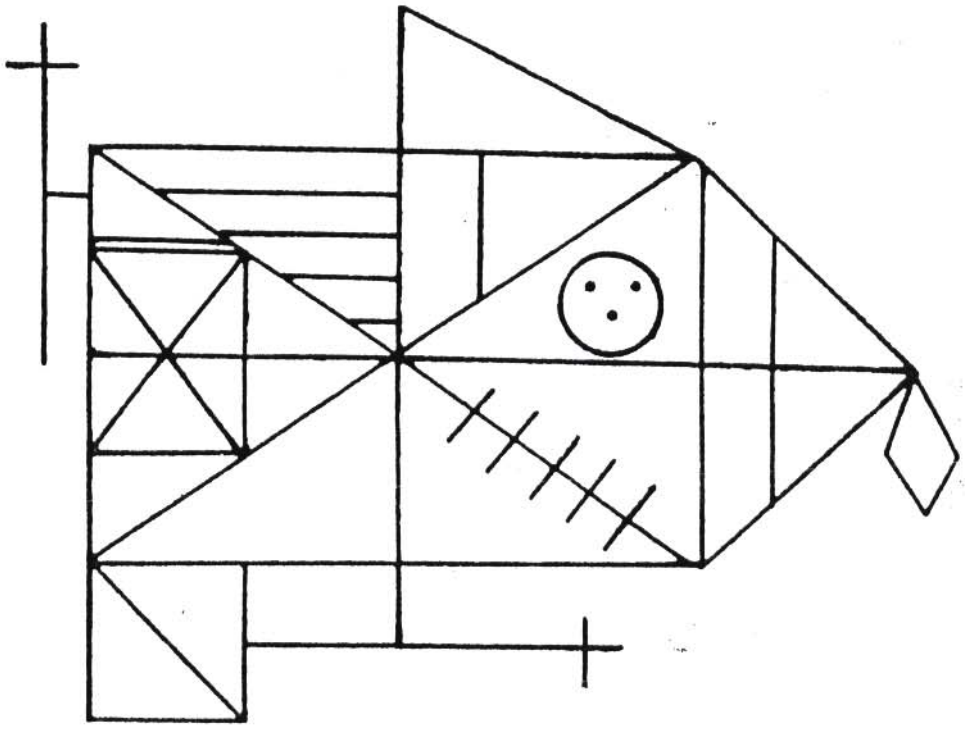


1.11 DO YOU FEEL MISERABLE WHEN YOUR PARENTS ARE ABOUT TO GO OUT WITHOUT YOU

Appendix N

Grooved Pegboard





ITEMS OF TEST 10: MEMORY FOR DIGITS - DIGITS FORWARD

Item	Series 1	Series 2
1.	*1 - 4*	*6 - 3*
2.	*2 - 8 - 5*	*1 - 7 - 4*
3.	*4 - 5 - 1 - 8*	*2 - 6 - 4 - 1*
4.	*6 - 9 - 2 - 8 - 3*	*7 - 2 - 9 - 6 - 5*
5.	*3 - 8 - 4 - 7 - 1 - 9*	*5 - 2 - 7 - 8 - 1 - 6*
6.	*3 - 6 - 7 - 8 - 2 - 4 - 9*	*9 - 3 - 2 - 6 - 4 - 7 - 5*
7.	*8 - 5 - 6 - 2 - 7 - 9 - 5 - 3*	*2 - 5 - 3 - 8 - 6 - 7 - 3 - 9*
8.	*6 - 4 - 8 - 5 - 1 - 3 - 2 - 9 - 7*	*4 - 6 - 5 - 7 - 2 - 3 - 8 - 9 - 1*

ITEMS OF TEST 10: MEMORY FOR DIGITS - DIGITS BACKWARD

Item	Series 1	Series 2
1.	*3 - 1*	*5 - 3*
2.	*2 - 7 - 5*	*4 - 9 - 2*
3.	*9 - 1 - 8 - 2*	*7 - 3 - 4 - 8*
4.	*3 - 5 - 2 - 6 - 7*	*8 - 3 - 4 - 6 - 2*
5.	*8 - 2 - 9 - 4 - 7 - 5*	*3 - 1 - 9 - 6 - 8 - 4*
6.	*6 - 3 - 8 - 9 - 1 - 4 - 7*	*6 - 1 - 3 - 7 - 5 - 2 - 8*
7.	*4 - 6 - 1 - 5 - 9 - 2 - 7 - 8*	*7 - 3 - 6 - 9 - 6 - 5 - 1 - 4*

Introduction

Colour-Word Interference

What colour is this word? **GREEN** The answer is red.

Colour-word interference effects were first used to assess cognitive functions by John Ridley Stroop in 1935. These effects arise when a person is required to name the colour that a word is printed in rather than read the word itself. When the written word is incongruous with the colour it is printed in, interference effects are present.

red **blue** **green**

These effects arise because reading is an automatic cognitive process. In a learner reader these effects are absent because reading is not yet *automatic*, but rather *controlled*. In a fluent reader the ability to name incongruent colours rather than read words depends on the integrity of some brain structures, and measuring performance under Stroop interference conditions provides an index of the functioning of the brain.

Neuroanatomy

Positron emission tomography (PET) studies suggest that when interference effects are present there is a selective activation of the right orbitofrontal cortex (Brodmann's area 47) and the cingulate cortex at the junction of Brodmann's areas 23 and 24. Correlational analysis of PET activity when subjects are engaged in reaction time experiments that utilise Stroop interference conditions indicate bilateral activity which is more prominent on the right in the insular region, orbitofrontal cortex and frontal eye fields. Additionally correlations are shown in the anterior cingulate gyrus and large regions of the superior right frontal lobe, involving both medial and dorsolateral prefrontal cortices. Such studies have also shown that when engaged in a Stroop interference task an inhibitory effect is present in the primary visual cortex, the superior temporal cortices and parietal association cortex.

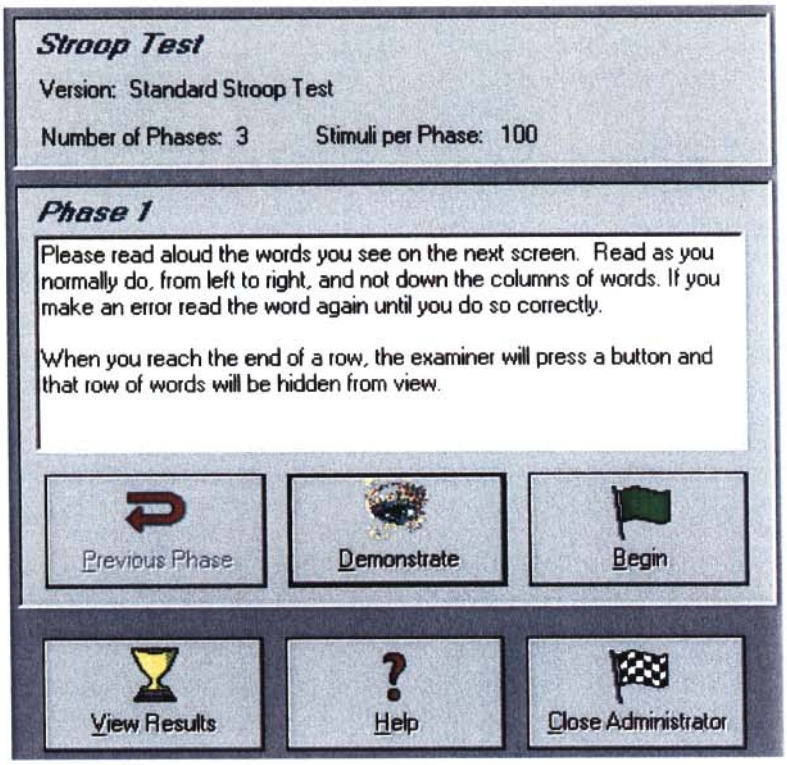
The Software

The software's Test Administrator runs Stroop Tests, the Results Viewer displays performance graphs and statistics. Optionally, you can use the Procedure Editor to create your own custom Stroop procedures.

Test Administrator Main Screen

The Test Administrator main screen looks like this. To find out more about the different items click on the graphic.

See Running a Procedure for more information.



Understanding Conditions and Phase Types

A phase may administered under one of two conditions:

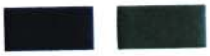
1. Standard Condition. This is the Stroop Test as originally conceived. Stimuli are laid out across the screen as if for a page in a book. The subject's task is to either name colours or read words or both, depending on the phase. Any one of phase types 1 to 4 below may be used with the Standard Condition.

2. Decision Condition. A pair of stimuli are displayed and the subject must decide if the meaning of the word on the left matches the colour of the word to the right. This condition is used only if the phase type is set to Decision Condition

Phase properties interact with stimulus properties to determine how are stimuli are displayed. Since the same stimuli are used for every phase, a subject who makes no errors *says* the same words on each phase, but what they *see* is different on each phase. This controls for the effects of word / syllable length across the phases of the procedure.

There are five phase types:

Coloured Blocks. All stimuli are displayed as coloured blocks. The colour used is the congruent colour/word property of the stimulus. The blocks are also referred to as "patches" in the scientific literature.

e.g. 

2. ***Congruent Text.*** All text is displayed so that the colour of the word matches the meaning of the word. The colour and text of the stimulus is determined by the congruent colour/word property of the stimulus.

e.g. **Blue** **Green**

3. ***Incongruent Text.*** All text is displayed so that there is a mismatch between the colour of the word and the meaning of the word. The colour of the stimulus is determined by the incongruent colour/word property of the stimulus and the text by the congruent colour/word property.

e.g. **Blue** **Green**

4. ***Neutral Text.*** All text is displayed in the colour selected for neutral text, typically black or grey. The text used is determined by the congruent colour/word property of the stimulus.

e.g. Blue Green

Decision Condition. Both stimuli are either congruent, incongruent or neutral, as determined by the flagged text property of the stimulus.

e.g. **Blue** **Green**

The flagged text property determines the appearance of the word on the left: if congruent then the colour and text is set to the congruent colour/word property of the stimulus. If the flagged text property is incongruent then the colour of the word on the left is the incongruent colour/word of the stimulus and the text the congruent colour/word. When flagged text is neutral the colour is always the neutral colour and the text the congruent colour/word.

An additional property, Yes Response, determines the appearance of the stimulus on the right. If the correct answer is "Yes" and the flagged text property is set to congruent then the colour and text of the

word on the right is the congruent colour/word.

e.g. **Blue** **Blue**

If the correct answer is "No" and the flagged text property is set to congruent then the colour and text of the word on the right is the incongruent colour/word.

e.g. **Blue** **Green**

If the correct answer is "Yes" and flagged text is incongruent then the colour of the word on the right is the incongruent colour/word and the text is the congruent colour/word.

e.g. **Blue** **Green**

If the correct answer is "No" and the flagged text property is set to incongruent then the colour of the word on the right is the congruent colour/word the text the incongruent colour/word.

e.g. **Blue** **Green**