

**The Relationship between Tumour Characteristics, Depressive Symptoms, and
Neuropsychological Profiles in Brain Tumour Patients**

by
Carike Jordaan

*Thesis presented in fulfilment of the requirements for the degree of
Master of Science (Psychology) in the Department of Psychology at
the University of Stellenbosch*



Supervisor: Dr Renata Schoeman

Co-supervisor: Prof Abraham Petrus Greeff

March 2015

Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

Copyright © 2015 Stellenbosch University

All rights reserved

Summary

Worldwide there are various reports on the prevalence of depression in patients diagnosed with brain tumours. In South Africa, psychological research in relation to psychiatric symptoms among patients with brain tumours is lacking.

The aims of this study were to determine the incidence of depression in patients diagnosed with brain tumours and to clarify our understanding of the relationship between depression and tumour localisation, histopathological type of tumour, and participant characteristics. The study sample consisted of 35 patients (11 males and 24 females) aged between 21 and 64 years with a solitary primary brain tumour. The patients were treated at the neurosurgery clinics located at Tygerberg Hospital in the Western Cape and Universitas Hospital in the Free State between mid-2010 and 2013. The major histological subgroup consisted of meningiomas (47%), glioblastomas (22%), astrocytomas (19%), gliomas (9%) and ependymomas (3%). The tumour distribution was as follows: 52% in the left hemisphere, 37% in the right hemisphere, and 11 % in the midline. The psychiatric symptoms of the patients were assessed before treatment by the Beck Depression Inventory and Mini International Neuropsychiatric Interview. In addition, the patients' neuropsychological functions were evaluated by a short neuropsychological test battery (Mini Mental State Examination, Trail Making Test (Part A), Letter Number Sequencing subtest, Hopkins Verbal Learning Test – Revised, and Brief Visuospatial Memory Test – Revised).

Results from the quantitative data, showed the prevalence of mild depression was 26% for men and 43% for women. Overall 37% of the total sample had depressive symptoms. No significant relationship was found between depression and tumour location or between the various neuropsychological characteristics and neurological symptoms and tumour location.

The study showed that depression is a common symptom in patients diagnosed with brain tumours and therefore depression symptoms have to be recognised and treated by psycho-educating the patients and their families, pharmacotherapy, or psychotherapy as soon as possible. However, due to the relatively small sample size, the results are of limited generalisability.

Opsomming

Wêreldwyd is daar verskeie verslae oor die voorkoms van depressie in pasiënte gediagnoseer met breingewasse. In Suid-Afrika is daar 'n tekort aan sielkundige navorsing met betrekking tot psigiatriese simptome by pasiënte.

Die doel van hierdie studie was om die voorkoms van depressie te bepaal in pasiënte gediagnoseer met breingewasse en om duidelikheid te kry oor die verband tussen depressie en die ligging van breingewasse, histopatologiese tipe gewas en karakter eienskappe van die deelnemers. Die steekproef van die studie het bestaan uit 35 pasiënte (11 mans en 24 vroue) tussen die ouderdomme 21 en 64 jaar met 'n soliede breingewas. Die pasiënte is behandel by die neurochirurgiese klinieke by Tygerberg Hospitaal in die Wes-Kaap en by Universitas Hospitaal in die Vrystaat vanaf middel 2010 tot 2013. Die mees algemene histologiese subgroep het bestaan uit meningiome (47%), glioblastomas (22%), astrocytomas (19%), gliomas (9%) en epidiomas (3%). Die verspreiding van die gewasse was soos volg: 52% in die linkerhemisfeer, 37% in die regterhemisfeer en 11% in die middel. Die psigiatriese simptome van die pasiënte is voor behandeling geëvalueer met behulp van die Beck Depression Inventory en die Mini International Neuropsychiatric Interview. Bykomend is die pasiënte se neurosielkundige funksies geëvalueer met behulp van 'n neurosielkundige toetsbattery (Mini Mental State Examination, Trail Making Test (Part A), Letter Number Sequencing subtest, Hopkins Verbal Learning Test – Revised en Brief Visuospatial Memory Test – Revised).

Die resultate van die kwantitatiewe data het getoon die voorkoms van matige depressie was 26% vir mans en 43% vir vroue. In geheel het 37% van die totale steekproef depressiewe simptome getoon. Daar was geen beduidende verhouding tussen depressie en die ligging van

die gewas of tussen die verskeie neurosielkundige eienskappe en die ligging van die gewas nie.

Die studie het getoon dat depressie 'n algemene simptome is in pasiënte gediagnoseer met bringewasse en daarom moet depressiewe simptome herken en so gou as moontlik behandel word deur psigo-opvoeding van die pasiënte en hul familie, farmakoterapie of psigoterapie. As gevolg van die relatiewe klein steekproef grootte het die resultate 'n beperkte veralgemeenbaarheid.

Acknowledgements

My sincere appreciation goes to:

Professor Awie Greeff and Dr Renata Schoeman, my supervisors, particularly Dr Renata Schoeman who guided me through my study.

Professor Martin Kidd for the assistance with the data analysis.

The doctors and staff of the neurosurgery clinics at Tygerberg and Universitas Hospitals for all their help throughout the data collection period.

The patients who were willing and allowed me to be part of their journeys.

My family and husband who supported me and provided many words of comfort.

Hettie Human for your editorial assistance.

God Almighty, for the dream and the strength.

Table of Contents

Declaration.....	ii
Summary.....	iii
Opsomming.....	v
Acknowledgements	vii
List of Figures.....	xii
List of Tables.....	xiii
Chapter One: Introduction	14
1.1. Chapter Overview	14
1.2. Introduction	14
1.3. Outline of Thesis	16
Chapter Two: Theoretical and Methodological Issues	18
2.1. Chapter Overview	18
2.2. Introduction	18
2.3. Theoretical Framework	19
2.3.1.The biopsychosocial model.....	19
2.3.2.Psychoneuroimmunology.....	24
2.4. Depression.....	24
2.4.1.Epidemiological Features of Depression.....	25
2.4.2.Diagnosis of depression	25
2.5. Conclusion.....	28
Chapter Three: Review of the literature.....	29
3.1. Chapter Overview	29
3.2. Brain Tumours.....	29
3.2.1.Introduction	29

3.2.2.Epidemiology of brain tumours.....	29
3.2.3.Mortality rates	30
3.2.4.Categorisation of brain tumours.....	31
3.2.5.Brain tumour symptoms	33
3.3. Depression amongst Patients with Brain Tumours	37
3.3.1.Incidence of depression in patients diagnosed with a brain tumour	37
3.3.1.Depressive symptoms due to the diagnosis of a brain tumour	41
3.3.2.Depression incidence and tumour treatment.....	43
3.4. Clinical Outcomes of Brain Tumour Patients	44
3.5. Conclusion.....	46
Chapter Four: Research Methodology	47
4.1. Chapter Overview	47
4.2. Aims of this study	47
4.3. Research Method.....	47
4.3.1.Research design	47
4.3.2.Setting	48
4.3.3.Participants.....	48
4.4. Measuring Instruments	49
4.4.1.Patient data form.....	49
4.4.2.Mini International Neuropsychiatric Interview (MINI) and DSM-IV-TR criteria	49
4.4.3.Beck Depression Inventory–II (BDI-II)	50
4.4.4.A short neuropsychological test battery.....	50
4.5. Procedure.....	53
4.6. Ethical Concerns	55

4.7. Data Analysis.....	56
4.8. Conclusion.....	56
Chapter Five: Results	57
5.1. Chapter Overview	57
5.2. Descriptive Statistics	57
5.2.1. Demographics	57
5.2.2. Sample characteristics.....	58
5.2.3. Clinical symptomatology	64
5.2.4. Tumour characteristics.....	66
5.2.5. Neuropsychological findings	67
5.3. Comparisons of Mean Scores.....	69
5.3.1. Relationships between depression mean scores and demographic variables	69
5.3.2. Differences between tumour location and neurological symptoms.....	71
5.3.3. Differences between tumour location and depressive symptoms.....	71
5.3.4. Differences between tumour location and neuropsychological functioning	72
5.4. Conclusion.....	74
Chapter Six: Discussion.....	75
6.1. Chapter Overview	75
6.2. Sample.....	75
6.3. Psychiatric Symptoms	75
6.3.1. Depression	75
6.3.2. Demographical variables	77
6.3.3. Tumour location.....	80

6.3.4. Other psychiatric disorders	81
6.4. Neurological Symptoms	82
6.4.1. Sample	82
6.4.2. Tumour location	83
6.5. Neuropsychological Characteristics	84
6.6. Limitations of this Study	86
6.7. Conclusion.....	88
References	90
Appendix A	108
Appendix B	133

List of Figures

<i>Figure 2.1.</i> A diagram of the interchange of systems in the BPS model and the various measures administered.	21
<i>Figure 2.2.</i> The biopsychosocial interactions in depression.	22
<i>Figure 3.1.</i> Cognitive dysfunction according to tumour location.	35
<i>Figure 5.1.</i> Tygerberg Hospital participants: Number of patients excluded from study, and reason for exclusion (n = 16).	58
<i>Figure 5.2.</i> All the most frequently reported symptoms on the BDI-II (N = 35).	63
<i>Figure 5.3.</i> Symptom severity according to the BDI-II scores (N = 35).	64
<i>Figure 5.4.</i> Presenting complaints and symptoms of the participants (n = 28).	65
<i>Figure 5.5.</i> Tumour characteristics of the sample (n = 32).	66
<i>Figure 5.6.</i> Results of the three trails of the HVLT-R and BVMT-R (n = 31).	68
<i>Figure 5.7.</i> Comparison of mean tumour location depression scores for total group (N = 35).	72

List of Tables

Table 3.1 <i>Distribution of Primary Brain Tumours by Histology</i>	32
Table 3.2 <i>Prevalence of Depression among Patients with Brain Tumours according to Sample Sizes and Measures of Depression</i>	39
Table 5.1 <i>Demographic Characteristics of the Participants (N = 35)</i>	59
Table 5.2 <i>Psychiatric Comorbidity according to the MINI (N = 35)</i>	61
Table 5.3 <i>Types of Depression/Depression Disorders and Symptoms in the Sample (N = 35)</i>	62
Table 5.4 <i>Tumour Location and Isolated Symptom Frequency (n = 28)</i>	65
Table 5.5 <i>Neurocognitive T-scores of the Individual Measures</i>	69
Table 5.6 <i>Results from Independent t-tests between BDI-II Total Scores and various Demographic Variables (N = 35)</i>	70

Chapter One: Introduction

1.1. Chapter Overview

The chapter provides the reader with a brief overview of depression in cancer and brain-tumour patients. Furthermore, the specific motivation for undertaking this study is explained by placing the study within the neuropsychological context.

1.2. Introduction

Patients diagnosed with primary brain tumours can experience feelings of depression, together with cognitive and physical symptoms (Pasquini, Kelly, & Pangillnan, 2007). These feelings of depression are not surprising, given the magnitude of their diagnosis and probable shortened lifespan. Depression, pain, and fatigue are of the most frequently occurring symptoms with all types of cancers (Pasquini & Biondi, 2007; Tu, Hsu, Chi, Lin, & Yen, 2014). Depressive disorders, such as major depressive disorder (MDD), adjustment disorder with a depressed mood, and depression secondary to a medical condition, commonly co-occur in patients suffering from cancer. Pasquini and Biondi (2007) argue that the prevalence rates of depression in cancer patients may be underestimated. Several symptoms of depression, such as weight loss, fatigue, and loss of appetite or sleep, closely reflect the physiological effects of cancer; therefore the rates can only be seen as an estimate (Katon, 2003).

Only in recent times has the research community started to investigate the relationship between depression and medical illnesses. Growing evidence suggests that the presence of depressive symptoms/MDD is linked to increased morbidity and mortality of heart disease patients (Baune et al., 2012). Patients suffering from human immunodeficiency virus (HIV)-related illness, diabetes mellitus, Parkinson's disease, and cancer all have higher rates of

MDD than patients without these disorders do. Depression coexisting with a chronic medical illness is associated with a greater symptom burden (Katon, 2003), decreased quality of life (Wikman, Wardle, & Steptoe, 2011), more functional impairment, and decreased devotion to self-care regimens (Evans et al., 2005). Primary brain tumours are one of the cancer types that result in the highest psychosocial burden for cancer patients (Chochinov, 2001). Depression can influence a person's way of life and it is evident that depression can be a frequent complication in patients diagnosed with brain tumours. It can be difficult to identify depressive symptoms in a patient diagnosed with cancer because, as mentioned, the depressive symptoms closely reflect the physiological effects of cancer (Katon, 2003).

Depression can develop in patients with cancer as a consequence to the medical illness itself, or due to treatment-associated variables (Gross, Smith, & Stern, 2007). Personal attributes such as marital status, financial position, and the presence of a support system consisting of friends or family, are all moderator variables affecting the way the patient copes with depression. Lack of psychosocial support and reduced capability to cope with the medical diagnosis may add to the development of depression in patients diagnosed with cancer (Gross et al., 2007).

The occurrence of depression is related to cancer type; the highest prevalence of depression is associated with pancreatic cancer, followed by lung cancer and third, head and neck cancer (Brintzenhofe-Szoc, Levin, Li, Kissane, & Zabora, 2009; Zabora, Brintzenhofeszoc, Curbow, Hooker, & Piantadosi, 2001). For instance, primary and metastatic brain tumours, including tumour cells in the cerebrospinal fluid, frequently lead to changes in mood (Gross et al., 2007). Some chemotherapeutic agents are also associated with depression because of the hormonal effect of the treatment.

In review of 1 000 articles Pirl (2004) found 350 articles reporting on the rates of depressive symptoms and MDD co-morbid with cancer, ranging from 10% to 25%. A South African study concluded that newly diagnosed cancer patients had significantly higher levels of depressive symptoms than a control group without cancer (Pillay, 2001). This strong body of evidence illustrates the coexistence of cancer and depressive symptoms or MDD.

The literature remains limited regarding the relationship between depression and brain tumours (Fox, Lyon, & Farace, 2007; Litofsky & Resnick, 2009; Mainio, Hakko, Niemelä, Koivukangas, & Räsänen, 2005a). This study found no studies with relevance to the South African context at the date of thesis submission (2014). Brain tumours are different from other cancer types in that they can affect a patient's personality, cognition, speech, motor and other capabilities (Beadles, 2006; Bunevicius et al., 2014).

Grounded in the biopsychosocial research model and psychoneuroimmunology, the present study focuses on the South African context to expand the current knowledge. This study explores the incidence of depression in brain tumour patients at Tygerberg and Universitas Hospitals in the Western Cape and Free State, respectively. Furthermore, the relationships between tumour characteristics (location and histological type), depression, and neurocognitive deficits are investigated.

1.3. Outline of Thesis

Chapter 1 sets out the theoretical framework, the motivation and purpose of the study. The following chapters provide an overview of the theoretical framework and literature on brain tumours, depression, and the relationships between them.

Chapter 2 provides an outline of the biopsychosocial model, psychoneuroimmunology, and depression. Chapter 3 entails the epidemiology of brain tumours and provides a description of

a tumour and presenting symptoms upon being diagnosed with a brain tumour. The chapter also provides literature about the relationship between patients diagnosed with brain tumours and depression. Cognitive functioning is also discussed briefly. This chapter ends with the research aims. Chapter 4 describes the research design, procedure of data collection, and measuring instruments used in the study, as well the ethical considerations. Chapter 5 reports the quantitative results followed by a discussion of the findings, the conclusion of the study, recommendations for future research, and the limitations of the study are all discussed in Chapter 6.

Chapter Two: Theoretical and Methodological Issues

2.1. Chapter Overview

This chapter describes the theoretical model with the aim to contextualise brain tumour patients within the biopsychosocial model. The chapter consists of two main sections. First, the theoretical framework consisting of the biopsychosocial model and psychoneuroimmunology are explained and discussed. Second, this chapter focuses on depression, namely on the epidemiological features and the various types of depression.

2.2. Introduction

The biomedical model was the dominant disease model in the 1970s, embedded in molecular biology as its basic cornerstone (Engel, 1977). Somatic processes, such as neurophysiological abnormalities or biochemical imbalances, were used to describe illness in the past (Taylor, 2006). However, in 1977 George Engel challenged this view, stating that interactions of psychological and social factors must be taken into account, rather than only biological factors, when it comes to health and illness (Engel, 1977). Thereafter, the biopsychosocial (BPS) model was developed - a theoretical scheme that emphasises the coexistence of psychological events, neurocognitive factors, and the social environment. These factors are interactively involved in the physical health and illness of a patient (Suls & Rothman, 2004). Starkweather et al. (2011) searched for the most common theoretical model with regard to the relationship between depressive symptoms and patients diagnosed with brain tumours, which resulted in the biopsychosocial framework. Hence, the BPS model is used in this study to explore the factors related to depression.

2.3. Theoretical Framework

2.3.1. The biopsychosocial model

Engel recognised that each individual person consists of and partakes in numerous systems (Engel, 1977, 1981). A human being, is not a unitary system. Engel (1981) further realised that the fundamental matters of health and illness reside in the convoluted interconnections amongst these diverse systems. Hence, the BPS model makes use of the systems approach, which provides a framework within the BPS model to study biological parts (internal system), and psychological and social parts (external system) (Engel, 1981; Taylor, 2006). For the most authoritative explanation of systems theory in biology, one must refer to the writings of Weiss (as cited in Engel, 1981) and von Bertalanffy (1950a, 1950b).

Systems theory is formulated on the observation that “nature is a hierarchically arranged continuum, with the complex larger units being superordinate to the less complex smaller units” (Engel, 1981, p. 2-3). The systems theory framework complements the BPS perspective, in that different factors (biological, psychological, and social) explain disease and are always interrelated (Myatt, 2007; Taylor, 2006). All “three factors affect and are affected” by the patient’s health (Taylor, 2006, p. 13); disease is described as multifaceted. For example, a patient’s body is viewed as a system, and the internal components are made up of atoms, molecules, cells, tissues, organs, and the nervous system (Engel, 1981). The external components relating to a patient incorporate the levels of hierarchy within the patient, and in his/her family, community, society, and the biosphere.

Integrating the systems theory approach within the BPS model, patient care can be established within a hierarchical level of organisation, from the lowest level to past the scope of family, to take account of the community and the biosphere (Engel, 1981). Each system is

at the similar time a part of higher systems. In other words, the systems hierarchy is applied to a patient's experience with disease, in this case a brain tumour.

In the BPS model, each system consists of component systems, for example, psychological components are depression and cognition, which are measured by the listed measures (see Figure 2.1). The experiences of the patient after the diagnosis of a brain tumour depend on both the structured function of the system components (i.e., psychosocial support of family or friends) and the biological components that include internal system changes (i.e., the nervous system), both of which could contribute to the development and nature of depression in the patient with a brain tumour. More specifically, depression is related to a multitude of interacting processes in the areas of biological processes (e.g., stress hormones and genes), psychological processes (e.g., social withdraw and negative beliefs), and social processes (e.g., life events like cancer and social support) that interrelate across time, as mentioned in Akiskal and McKinney's research about depression (as cited in Gilbert, 2004). Note the continuing reciprocal nature of these interactions. See Figure 2.1 for a visual illustration of the interchange of systems in the BPS model and the measures administered.

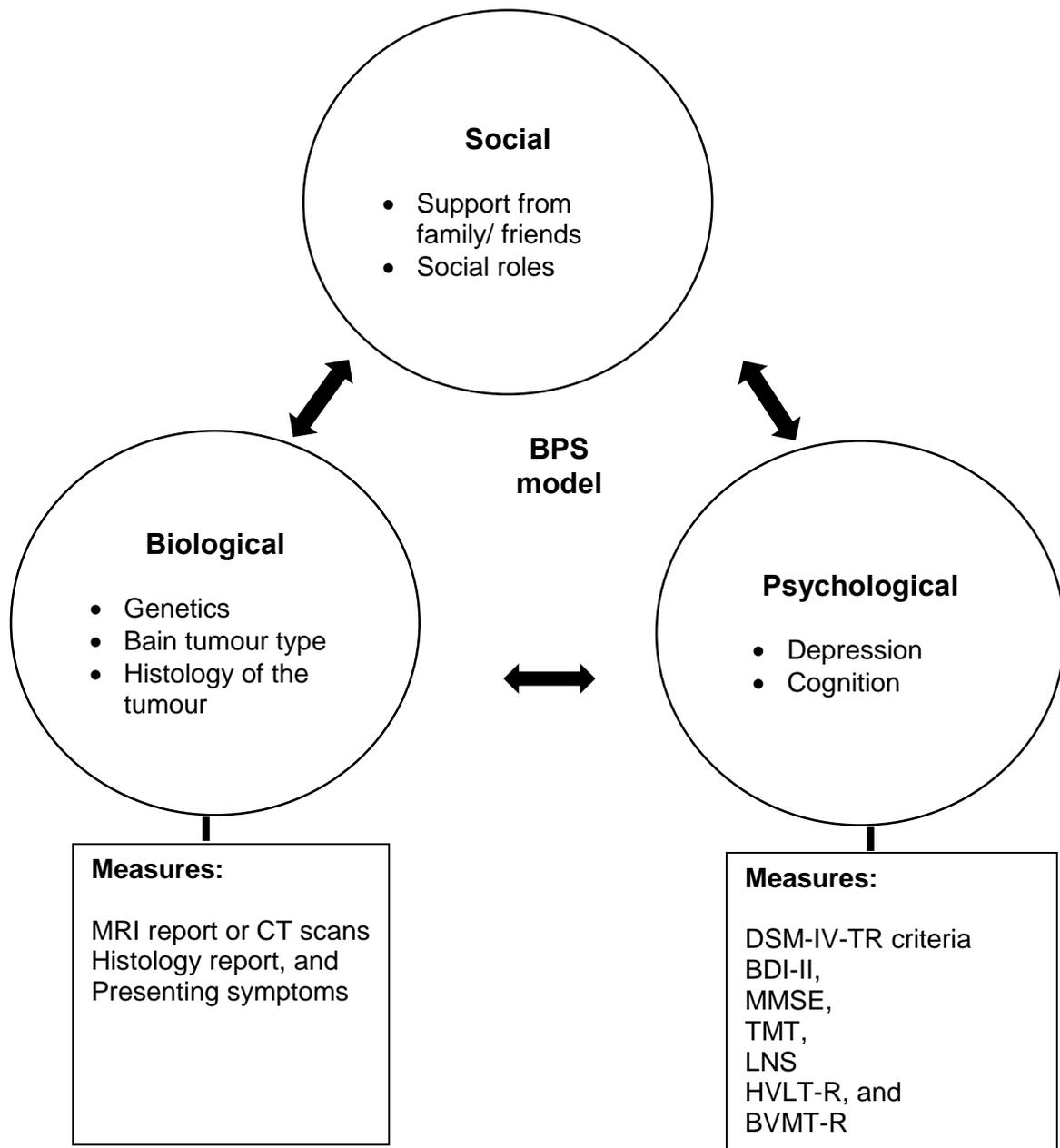


Figure 2.1. A diagram of the interchange of systems in the BPS model and the various measures administered. MRI = magnetic resonance imaging; CT = computed tomographic; DSM-IV-TR = Diagnostic and Statistical Manual of mental disorders fourth-text-revision edition; BDI-II = Beck Depression Inventory-II; MMSE = Mini Mental State Examination; TMT = Trail Making Test; LNS = Letter Number Sequencing; HVLT-R; Hopkins Verbal Learning Test – Revised; BVMT-R = Brief Visual Memory test – Revised.

The biopsychosocial approach focuses on interactions, consequently it is important to conceptualise what type of interactions are salient and to identify the significance of feedback when it comes to treatment of a patient. Gilbert (2004) summarised the possible domains of interactions relevant to depression, which are illustrated in Figure 2.2.

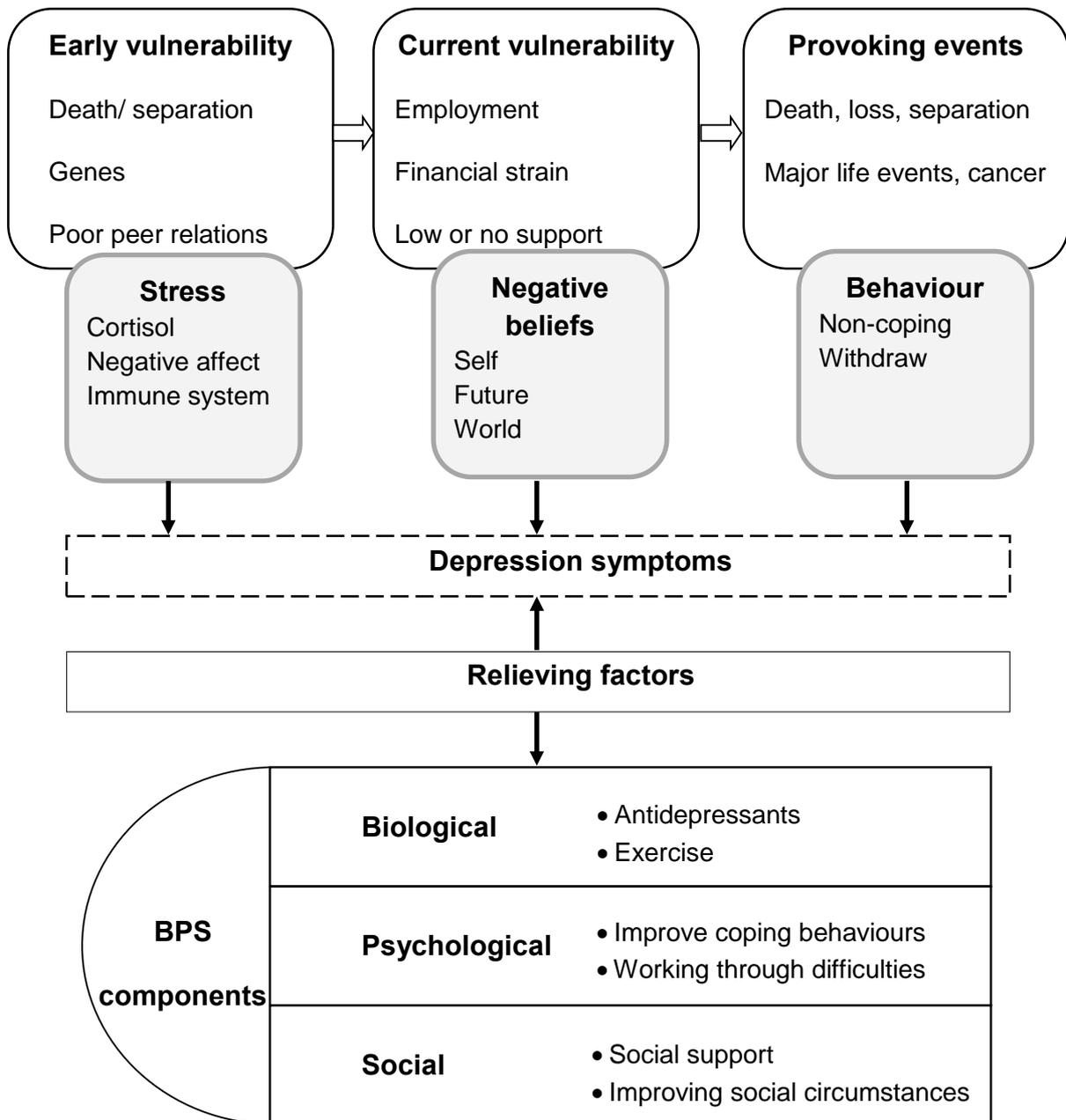


Figure 2.2. The biopsychosocial interactions in depression. BPS = Biopsychosocial. Adapted from “Depression: A biopsychosocial, integrative, and evolutionary approach,” by P. Gilbert, 2004, *Mood disorders: A handbook of science and practice*, p. 105.

Figure 2.2 depicts the possible vulnerability factors and provoking triggers associated with depression. Each of these or combined affects biological states, appraisal processes (negative beliefs), and coping behaviours that results in symptoms of depression (Gilbert, 2004). There are arrows across and between processes. For example, early vulnerability factors (e.g., poor peer relations) can affect how the participant engages in his/her social life (e.g., has difficulty in developing supportive and stable relationships), making the participant more currently vulnerable (e.g., poor social support) and susceptible to stressors. Biological changes, which may stem from major life stress (loss of employment due to hospitalisation), can interrelate, as, for example, the learned interactions between the endocrine and immune systems, each of which effect neurotransmitter systems and mood (Bufalino, Hepgul, Aguglia, & Pariante, 2013).

Therefore, this study applies both the systems theory approach and the BPS model to brain tumour patients. The BPS approach is holistic (Gilbert, 2004). The BPS model provides a framework for studying the relationships between patients diagnosed with brain tumours and their experiences with depression and neurocognitive changes. For instance, patients with brain tumours experience compounding neurological effects, psychological adjustment problems (as depression), and social-role changes, which emphasise the value of the biopsychosocial perspective.

To integrate the multitude of possible interactions between depressive symptoms and biological factors, the integrative concept of psychoneuroimmunology (PNI) could be incorporated to help research in this area (Fox, Shephard, & McCain, 1999). It is especially useful for examining the factors related to depression (Starkweather et al., 2011).

2.3.2. Psychoneuroimmunology

PNI is a behavioural framework (Starkweather et al., 2011) focused on the study of interactions among behaviour, the brain, and the immune system (Maier, Watkins, & Fleshner, 1994). Significant cofactors are seen as moderators of neuroendocrine-immune (biological) connections that could predispose a patient to depressive symptoms (Starkweather et al., 2011). The cofactors can include personal attributes (demographics, current symptoms, or social support), disease attributes (tumour location and type), and treatment options (radiation, chemotherapy, and extent of surgery). Implementing the PNI framework enables the study of the psychosocial and biological factors that influence symptoms of depression. Depressive symptoms and psychological stress are known to increase morbidity and mortality rates, especially among cardiovascular patients, where the effects of depression on other diseases are still somewhat unclear (Irwin, 2002).

2.4. Depression

Depression is the most frequently diagnosed mental disorder among adults, with a lifetime prevalence of 16.2% (Richards, 2011). Recently it was projected that depression affects approximately 350 million people worldwide (World Health Organization [WHO], 2012). Depression, first viewed as an acute and self-limiting illness, is now described as a chronic, lifelong illness (Richards, 2011). The WHO postulates that depression is the primary cause of disability (WHO, 2012) and that depressive disorders are one of the leading contributors to the global burden of disease (Ustün, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004). In 2008, depression was the third most common cause of the disease burden in the world, ranked eighth in low-income countries, and first in middle to high-income countries (Mathers, Fat, Boerma, & WHO, 2008). Globally, 65.5 million people suffer from unipolar depressive disorders, accounting for 4.3% of total disability-adjusted life-years (Mathers et al., 2008) and 12.1% years lost to disability (Ustün et al., 2004).

2.4.1. Epidemiological Features of Depression

Depression is a worldwide public health problem, contributing to significant morbidity and even mortality (Richards, 2011; WHO, 2012). MDD is common in all populations, with a global lifetime prevalence of 17%; the yearly incidence of depression is 1.59% (Saddock & Saddock, 2007) and prevalence of MDD is 7% in the United States of America (American Psychiatric Association [APA], 2013). Globally, 16/100 000 men/year, and 25/100 000 women/year experience depressive episodes (Ustün et al., 2004). The South African Stress and Health Study (SASH), a nationally representative survey of 4 351 South Africans conducted between 2002 and 2004, reported a 9.7% lifetime prevalence estimate for major depression in South Africa (Tomlinson, Grimsrud, Stein, Williams, & Myer, 2009), 13.7% in the Western Cape province and 14.6% in the Free State (Stein et al., 2007). The sample areas of this study are in the Free State and Western Cape Province, which surprisingly, were the two provinces with the highest prevalence rates for mood disorders.

2.4.2. Diagnosis of depression

Patients diagnosed with brain tumours can experience varying degrees of depressive symptoms. Researchers have found that it can be difficult to measure depression in patients diagnosed with brain tumours because of the physical manifestations of the brain tumour (Pringle, Taylor, & Whittle, 1999; Wellisch, Kaleita, Freeman, Cloughesy, & Goldman, 2002). Depressive symptoms, especially symptoms such as decreased appetite, sleep problems and fatigue, are often associated with medical conditions (Mainio, 2005). It is therefore of the utmost importance to exclude underlying medical conditions in the development of a mood disorder such as depression.

Reaction to the diagnosis

A patient's reaction to the diagnosis of a brain tumour could contribute to depressive symptoms. Patients can feel angry and experience shock as well as disbelief, despair, and anxiety (Litofsky & Resnick, 2009). Cognitive functioning and mood changes can occur due to the pathological effects of the tumour (Anderson, Taylor, & Whittle, 1999). Daily living activities of the patient can be impaired, concentration may also be impaired and the patient can experience grief reactions after diagnosis. The reaction of family and friends and the effect of the diagnosis on the patient's social support network can also influence the psychological wellbeing of the patient (Anderson et al., 1999).

Adjustment disorder

An emotional response to a stressful situation or event, such as the diagnosis of having a brain tumour, characterises an adjustment disorder. The varying reactions of patients diagnosed with brain tumours may cause an adjustment disorder because of the situation the patients find themselves in. In a population the prevalence of an adjustment disorder ranges from 2% to 8% (APA, 2000). Patients diagnosed with advanced cancer have a higher prevalence, of 14% to 34% (Miovic & Block, 2007). The Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.; *DSM-IV-TR*; APA, 2000) criterion for an adjustment disorder is the development of emotional or behavioural symptoms in reaction to a stressful event or experience. The symptoms must occur within three months of the onset of the stressor and are clinically significant by either marked distress that is in excess of that would be expected from contact to the stressor, or marked impairment in occupational or social functioning (APA, 2000).

Major depressive disorder

The diagnostic criteria for a major depressive episode require that five out of nine symptoms must be present for a period of two weeks (APA, 2000). These symptoms include a depressed mood, a decreased interest or pleasure in almost all or all daily activities, a significant weight loss or increase, insomnia or hypersomnia, psychomotor retardation or agitation, loss of energy or fatigue experienced almost every day, feelings of worthlessness or excessive feelings of guilt, indecisiveness or diminished ability to think or concentrate and, last, recurrent thoughts of death or suicidal ideation (APA, 2000).

Depression can lead to substantial morbidity with regard to substance abuse, unemployment, financial difficulties, or relationship strains. Depression is also associated with increased mortality, with two thirds of depressed patients contemplating suicide and 10% to 15% committing suicide (Saddock & Saddock, 2007). Satin, Linden, and Phillips (2009) conducted a meta-analysis of how depression can predict the progression and mortality of cancer patients. They found that depression is a significant though minor predictor of mortality, but not of disease recurrence in cancer patients.

Mood disorder secondary to a general medical condition (GMC)

Depressive disorders can accompany many medical problems (Saddock & Saddock, 2007). The DSM-IV-TR criteria for a mood disorder secondary to a GMC is change in mood, such as depressed mood, loss of pleasure, or diminished interest in almost all activities, irritability, expansiveness, or elevated mood (Saddock & Saddock, 2007). All these symptoms should be the direct physiological effect of a medical condition and cannot be accounted for any another mental disorder. With reference to this study, the DSM-IV-TR listed cerebral neoplasms (i.e., brain tumours) as one of the possible causes of depressive disorders due to a GMC (Saddock & Saddock, 2007).

2.5. Conclusion

This study explores depression in patients diagnosed with brain tumours from a biopsychosocial perspective. The BPS model makes use of the systems approach, which provides a framework within the BPS model for exploring the impact of a brain tumour on a patient and the link between predictive factors of depression. The patient's biological, psychological, and social parts are all key elements that must be noted when a patient is examined.

Chapter Three: Review of the literature

3.1. Chapter Overview

A review of previous literature regarding brain tumours, depression, and their relationship with each other are discussed in this chapter as well as the clinical outcome of patients' diagnosed with brain tumours.

3.2. Brain Tumours

3.2.1. Introduction

The diagnosis of a brain tumour can be devastating for a patient. Patients diagnosed with brain tumours have assorted somatic and psychological symptoms, with changes in emotional and cognitive processes (Mainio, 2005).

Brain tumours, whether benign or malignant, can be life threatening. Regardless of the various treatment options available, i.e., surgery, chemotherapy, and radiotherapy, the prognosis of malignant tumours has remained unchanged (Klein et al., 2001). Only during recent years has there been a focus on the psychological impact of brain tumours on patients (Klein et al., 2001; Litofsky et al., 2004; Mainio et al., 2005a).

3.2.2. Epidemiology of brain tumours

The central brain tumour registry of the United States calculated the incidence of primary brain and central nervous system (CNS) tumours at 21.03/100 000 people in the United States of America (USA) between 2006 and 2010 (Ostrom et al., 2013). The National Cancer Institute expected 23.13/100 000 people to be diagnosed with CNS tumours in 2013 in the USA (American Cancer Society, 2013). This implies that 12.77/100 000 men and 10.36/100 000 women are affected by brain tumours in the USA. Research estimated that

brain and CNS tumours would be the 10th leading cause of deaths among women in the USA in 2013 (American Cancer Society, 2013).

The global age-standardised incidence of primary malignant brain tumours is approximately 3.7/100 000 for men and 2.6/100 000 for women per year (Bondy et al., 2008). Incidence rates of primary brain tumours appear to be higher in more developed regions such as western Europe, North America, and Australia, with approximately 6 to 11 new cases of primary intracranial tumours (including meningiomas) per 100 000 population for men and 4 to 11 new cases for 100 000 women per year, a higher incidence than in less developed regions, such as Africa (Ferlay et al., 2010).

The age-standardised incidence of brain and other nervous system tumours is 1.5/100 000 in Southern Africa, for all ages. In central Africa the age-standardised incidence is 0.8/100 000 and in South Africa it is 1.7/100 000 (Ferlay et al., 2013).

Tygerberg Hospital, in Cape Town, Western Cape, offers healthcare to over 3.6 million people, either directly or through its secondary hospitals (Western Cape government, 2010). Approximately 100 brain tumour patients are treated at Tygerberg hospital per year (H. B. Hartzberg, personal communication, March 2, 2010). Roughly 363 870 patients were seen at Universitas Hospital in Bloemfontein, Free State, between April 2011 and March 2012; these patients originated from several provinces: Free State, Northern Cape, Eastern Cape, and North West, and from Lesotho (N. R. J van Zyl, personal communication, May 2, 2012).

3.2.3. Mortality rates

Significant morbidity and mortality rates are present in primary brain tumour patients (Armstrong, Cohen, Erikson, & Hickey, 2004; Rijmen, Edward, Rapp, & Shaw, 2008). Worldwide, age-standardised mortality rates for malignant primary brain tumours are

3.0/100 000 population for men and 2.1/100 000 for women (Ferlay et al., 2013). As is the case with the incidence rates, the estimated mortality rates are higher in more developed countries than in less developed countries. In the USA mortality rates for brain tumours are 5.19/100 000 for men and 3.46/100 000 for women (Ostrom et al., 2013). In Africa the estimated age-specific mortality rate for brain and other nervous system tumours is 1.4/100 000 for both sexes – lower than in South Africa, where it is 1.5/100 000 in the population (Ferlay et al., 2013). In South Africa the estimated brain or other nervous system tumours in 2012 were 1.7 for both sexes, 2.1/100 000 for men and 1.3/100 000 for women (Ferlay et al., 2013).

According to Ferlay et al. (2013) 370 men and 278 women who had been diagnosed with brain and other nervous system cancers in South Africa in 2012, died.

3.2.4. Categorisation of brain tumours

A brain tumour is defined as neoplastic lesions of the brain, which can be primary or metastatic (secondary) and either benign or malignant (Price, Goetz, & Lowell, 2008). Brain tumours can further be classified according to their histological cell type and location. Tumours are classified as malignant or benign based on location, characteristics of the tumour cells, rapidity of growth, and invasiveness (Beadles, 2006). A benign brain tumour consists of slow-growing cells and it rarely spreads (American Brain Tumor Association, 2012). In contrast, a malignant tumour grows rapidly, is aggressive and can be life-threatening. Primary brain tumours originate in the brain, from intracranial cells, while metastatic tumours originate in another part of the body, most commonly the lung, kidney, breast, and malignant melanomas, from where they spread either via adjacent tissue to the brain or are carried by blood to the brain (Price et al., 2008). Primary tumours are further divided into intra- and extra-parenchymal divisions. Extra-parenchymal tumours are, for example, meningiomas and

solitary fibrous tumours (Price et al., 2008). Intra-parenchymal tumours consist out of glial and non-glial tumours. Non-glial tumours (meningiomas) originate on or within structures in the brain, for example, blood vessels, glands, and nerves (McLean, 2010). Common glial tumours are astrocytomas, glioblastomas, oligodendrogliomas, and ependymomas (McLean, 2010). Table 3.1 contains the most prevalent brain tumours as listed by the central brain tumour registry of the United States.

Table 3.1

Distribution of Primary Brain Tumours by Histology

Tumour type	Percentage of brain tumours (%) ^a
Astrocytoma	6.1
Ependymomas	1.9
Glioblastoma	15.6
Gliomas	28.0
Meningiomas	35.8
Oligodendrogliomas	15.6

Note. ^a Prevalence of frequently reported primary brain tumours (Ostrom et al., 2013).

Approximately a third of all primary brain and other nervous system tumours form from glial cells (McLean, 2010). Glial cells, non-neuronal cells, offer support and nutrition to the brain (van den Toorn, 2011).

The most regularly occurring non-glial tumours are neuronal and mixed-neuronal tumours, embryonal, germ cell, and choroid plexus tumours (S. D. Zaharie, personal communication, March 8, 2010). The majority of tumours (35.6%) are meningeal of origin, while 21% of

tumours are located within the frontal (8.7%), parietal (4.2%), temporal (6.5%), and occipital (1.2%) lobes of the brain (Ostrom et al., 2013).

Gliomas account for 28% of all tumours and 80% of malignant tumours as presented in Table 3.1 (Mainio, 2005, Ostrom et al., 2013) (see section 3.2.4). Centred on histological appearance, the WHO categorises the various types of gliomas into prognostic grades ranging from I to IV (Louis et al., 2007). The cerebral hemispheres are the most common site of origin for gliomas (61%).

3.2.5. Brain tumour symptoms

Brain tumours can cause direct brain-tissue damage by shifting of normal brain tissue or by pressure on the brain (American Brain Tumor Association, 2012). Patients are often seen in acute settings, usually in emergency rooms, where they present with seizures or focal neurological deficits because of brain oedema (Berger & Prados, 2005). Seizures can involve either partial or generalised convulsions (Behin, Hoang-Xuan, Carpentier, & Delattre, 2003). In other words, the flow of cerebrospinal fluid (CSF) between the ventricles can be blocked because of the tumour, which leads to build-up of CSF (McLean, 2010). Elevated intracranial pressure leads to breakdown of the blood-tumour barrier causing vasogenic oedema. Patients may develop a range of symptoms, such as headaches, vomiting, nausea, drowsiness, visual abnormalities, and focal neurological symptoms (Behin et al., 2003). Focal neurological symptoms include difficulty in language comprehension, speech problems, and contralateral hemiparesis (McLean, 2010).

Cognitive function

The diagnosis of a brain tumour can have a physiological and functional impact on the patient and may cause cognitive, behavioural, and neuropsychiatric manifestations (Arnold et al.,

2008). Neurocognitive changes can include deficits in memory, problem solving and reasoning ability and attention, and delirium or dementia (Arnold et al., 2008; Weitzner & Meyers, 1997).

Cognitive functions include “higher” and “basic” cerebral functions of the central nervous system (CNS). “Higher” functions include language, attention, memory, and executive functioning, and the “basic” functions include motor and autonomic, perceptual, and primary sensory functions (Taphoorn & Klein, 2004). As mentioned in previous research (Fox, Mitchell, & Booth-Jones, 2006), cognitive functioning can be categorised into nine domains: attention; concentration; executive function; language; memory; intellectual function, mood, thought content, personality, and behaviour; sensory and perceptive function; and visuospatial and constructional skills.

Cognitive dysfunction can be influenced by various factors, for example, it can be the consequence of compression or shift of intracranial structures accompanying cerebral oedema (Fox et al., 2006). Figure 3.1 lists each of the symptoms in the respective domains with reference to the anatomical location of the tumours.

Frontal

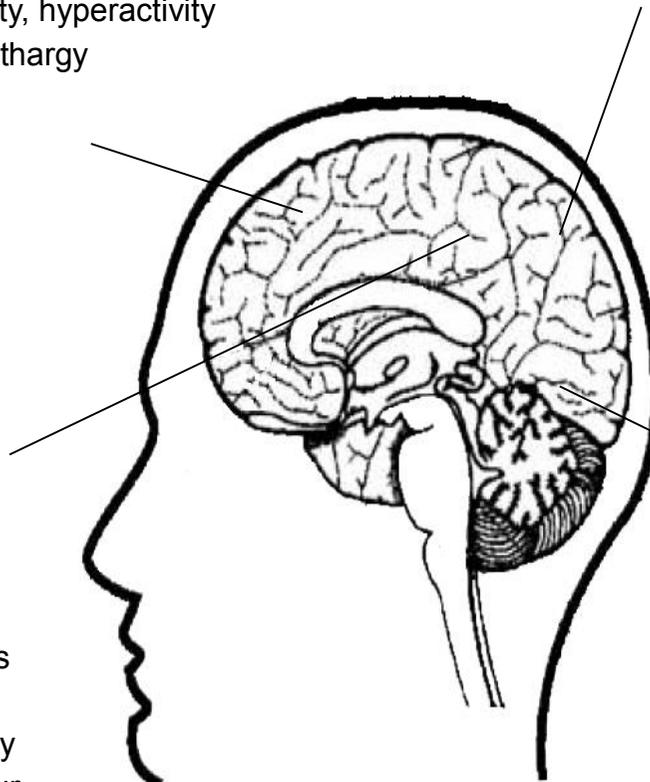
- Expressive aphasia
- Personality changes
- Disinhibition, impulsivity, hyperactivity
- Apathy, depression, lethargy
- Executive dysfunction
- Memory disorders

Parietal

- Impaired sensory modalities
- Apraxia (disorders of skilled movement)
- Somatosensory changes
- Spatial cognition
- Contralateral homonymous hemianopsia (decreased vision in half of the visual field)
- Agnosia (nonperceptual disorders of recognition)
- Alexia (disorders of reading)

Temporal

- Impaired long-term memory
- Language problems
- Visual and auditory perception
- Emotional alterations
- Auditory hallucinations and tinnitus
- Changes in personality and affective behaviour



Occipital

- Visual agnosias
- Alexia (disorders of reading)
- Colour anomia (can't identify colours by name)
- Achromatopsia (color perception impairment)

Figure 3.1. Cognitive dysfunction according to tumour location. Based on information from Joseph (1990), Kolb and Wishaw (2003), Lezak, Howieson, Loring, Hannay, and Fischer (2004), and Zillmer, Spiers, and Culbertson (2007).

It is clinically important to assess the cognitive functioning of patients with brain tumours before neurosurgical intervention. Data obtained from a neuropsychological assessment add valuable information about the clinical state of the patient, such as cognitive, affective, and behavioural impairments (Weitzner & Meyers, 1997). Cognitive functioning, together with age of the patient or histology of the tumour are of prognostic nature for patients with gliomas (Meyers, Hess, Yung, & Levin, 2000). Cognitive deterioration may also be a first indication of tumour growth before the tumour is noted on magnetic resonance imaging (MRI) or computed topographic (CT) scans (Armstrong, Goldstein, Shera, Ledakis, & Tallent, 2003; Meyers & Hess, 2003).

Risk factors for the onset, progression, and severity of cognitive impairment include the histology and location of the tumour (Giovagnoli, 2012). Zillmer, Spiers and Culbertson (2001) found that the location, size, and grade of the tumour, rather than the histology, influence the neuropsychological manifestations of brain tumours.

Certain brain areas are associated with certain cognitive fallouts/patterns, but only if psychological-behavioural changes and confusion are not present (Schoeman & Louw, 2003). Smaller tumours adjacent to primary motor areas may lead to seizures and loss of motor function, in contrast to deeper intracranial tumours, which can grow to a large size before presenting with clinical symptoms.

Irrespective of the tumour's degree of malignancy, patients with left-hemisphere tumours are more prone to cognitive deficits (writing, arithmetic), language and verbal learning impairments or depression-like symptoms (Joseph, 1990; Kolb & Whishaw, 2003). Tumours in the right hemisphere lead to impaired depth perception and impaired visuoperceptual skills (Armstrong et al., 2003; Joseph, 1990).

Tucha et al. (2003) found in their study of cognitive deficits in patients diagnosed with a brain tumour that, before surgery, more than 90% of the patients showed impairment in at least one area of cognition. Impairments of memory and attention were noted in more than 60% of the patients and 78% of the patients displayed executive functioning impairments.

Glioma patients are inclined to have a wider range of cognitive deficits, in contrast with stroke patients where the tendency is site-specific deficits (Taphoorn & Klein, 2004). Weitzner and Meyers (1997) stated that the reason for this can be the continuing displacement and plasticity of neuronal structures in brain tumour patients in contrast to the destruction of neurons in stroke patients.

Compared to lung cancer patients, brain tumour patients have more cognitive deficits and self-reported complaints, for example, memory, attention, visual motor, and communication problems (Catt, Chalmers, & Fallowfield, 2008). These cognitive impairments, such as executive functioning, and language regularly occur in most patients with brain tumours (Hottinger, Yoon, DeAngelis, & Abrey, 2009).

Apart from depression, the most common psychiatric symptoms in patients diagnosed with brain tumours are fatigue and pain (Fox et al., 2007). Depression may even contribute to the course of disease before and after operation (i.e., a prognostic factor) (Mainio, 2005).

3.3. Depression amongst Patients with Brain Tumours

3.3.1. Incidence of depression in patients diagnosed with a brain tumour

In examining the relationship between brain tumours and depression, research has found that a number of factors influence the rates of depression in patients diagnosed with brain

tumours. It is important to take into account the methods and sample sizes used in previous studies, as these factors result in different findings being reported (Beadles, 2006).

Previous studies with large sample sizes, of $N = 109$ to $N = 598$, reported the incidence of depression in patients diagnosed with brain tumours ranging from 15 to 41 percent (Arnold et al., 2008; Bunevicius, Deltuva, Tamasauskas, Tamasauskas, & Bunevicius, 2013; Litofsky et al., 2004; Pringle et al., 1999), while smaller studies report higher rates, of 20 to 38 percent (Mainio, Hakko, Niemelä, Koivukangas, & Räsänen, 2005b; Pelletier, Verhoef, Khatri, & Hagen, 2002; Wellisch et al., 2002). These different findings could be due to variations in sample sizes and the use of different measuring instruments for depression by each study, as illustrated in Table 3.2.

Table 3.2

Prevalence of Depression among Patients with Brain Tumours according to Sample Sizes and Measures of Depression

Research articles	N	Histology of tumour	Prevalence	Measuring Instrument	Time of assessment	Year of study
Armstrong, Goldstein, Cohen, Jo, and Tallent (2002)	57	Glioma, meningiomas, and neuroendocrine	33%	MMPI-2 ^a and BDI ^b	6 weeks after surgery	2002
Arnold et al. (2008)	363	Anaplastic astrocytoma, Glioblastoma multiforme, Anaplastic oligodendroglioma, and other	41%	Brief PHQ ^c	Not informed	2007
Bunevicius, Deltuva, et al. (2013)	226	Meningioma, glioma and other	18% moderate to severe depression preoperatively	BDI-II, PHQ-2, and HADS	Before and after surgery	2010 - 2011
D'Angelo et al. (2008)	72	Glioma, meningioma's, pituitary adenomas, and vestibular schwannomas	9.7% preoperatively 27.7% at 1 month, 36.1% at 3 months, 38.8 at 6 months, and 44.4% at 1 year postoperative	Zung SDS ^d	Before operation, at 1 month, 3 months, 6 months and at 1 year postoperative	2005 - 2006

Table 3.2 continued

Research articles		Histology of tumour	Prevalence	Measuring instrument	Time of assessment	Year of study
Litofsky et al. (2004)	98	High-grade glioma	15.2% of 537 patients 22% at 3 months and 6 months	DSM-IV diagnostic criteria	At perioperative period, at 3 months and at 6 months postoperative	1997 - 2000
Mainio et al. (2005b)	77	Glioma, meningioma, vestibular schwannomas, pituitary adenomas, and other	35% preoperatively	BDI	Before operation	2005
Pelletier et al. (2002)	60	Glioma, meningioma, and other	38%	BDI	6 months or later	2002
Pringle et al. (1999)	109	Glioma, meningioma, metastatic tumours	16% preoperatively, 6% postoperative	HAD ^c	Before operation and 7 days postoperative	1992 - 1995
Wellisch et al. (2002)	89	Glioma, meningioma, and lymphoma	28%	DSM-IV diagnostic criteria	Not informed	2002

Note. ^aMinnesota Multiphasic Personality Inventory-2. ^bBeck Depression Inventory. ^cBrief Patient Health questionnaire. ^dZung Self-rating Depression Scale. ^eHospital Anxiety and Depression Scale.

There is little concordance between physician-reported depression and patient self-reports of depression (Litofsky et al., 2004). In the Glioma Outcomes Project, comprising 598 glioma patients, 93% of patients reported depressive symptoms, while only 15.2% of the physicians reported the patients as depressed in the immediate postoperative timeframe. The study suggests that physicians may fail to identify depression in the beginning phase of the postoperative period (Litofsky et al., 2004).

3.3.1. Depressive symptoms due to the diagnosis of a brain tumour

Depressive symptoms may originate from either the neuropsychological effects of the brain tumour, or from the patient's psychological reaction to the diagnosis. It is important to differentiate the origin of the depressive symptoms, to establish if depression is a mood disorder secondary to a general medical condition, an adjustment disorder, or a major depressive disorder (Mainio et al., 2005b).

Various predictors of depressive symptoms have been described in patients with brain tumours. Demographic variables can be linked with depressive symptoms, namely, gender, educational level, a prior history of psychiatric illness, or marital status (Parker, Baile, de Moor, & Cohen, 2003).

A previous study found that patients with a degree of social support or who are married report depression less often (Parker et al., 2003). Gender was found to be a leading predictor of depressive symptoms, with female patients experiencing more depressive symptoms than their male counterparts (Arnold et al., 2008; D'Angelo et al., 2008; Mainio et al., 2005b; Weitzner, Meyers, & Byrne, 1996). A recent study by Seddighi, Seddighi, Ashrafi, and Nohehsara (2010) reports a higher prevalence of depression in female patients diagnosed with brain tumours than for male patients. Before operation, 10.4% of men and 19.7% of women

reported depressive symptoms. One hypothesis that could explain why female patients are more inclined to depressive symptoms than male patients, is that women generally communicate their emotions more openly than men do and therefore admit to experiencing symptoms of depression more readily (Arnold et al., 2008).

Educational level may contribute to the degree of depressive symptoms in a patient (Arnold et al., 2008). Patients with higher college-level education were found to be less prone to depression. A possible explanation may be that better-educated patients are more likely to have access to healthcare resources due to a higher socioeconomic status than patients with a lower educational level.

Depression is known to be a recurrent disorder (Beshai, Dobson, Bockting, & Quigley, 2011). Mainio et al. (2005b) found, in their study of patients with brain tumours and depression, that 74% of their patients with depression had previous depressive episodes, while only 35% of patients with depression were experiencing the disorder for the first time.

Risk factors for behavioural and psychiatric symptoms in patients diagnosed with brain tumours include a history of previous psychiatric diagnosis, tumour-related mental symptoms, and reactions to stress (Weitzner, 1999).

Tumour factors, such as localisation and histopathological nature, were described as direct predictors of depression in patients with brain tumours. Patients with anterior-frontal-located tumours were more inclined to depression and temporal lesions (Litofsky & Resnick, 2009). Mainio et al. (2005b) found that patients with anterior-located tumours had higher mean depression scores before surgery than patients with posterior-located tumours had, but they found no difference in depression scores after surgery, regardless of tumour location. However, they also found that depression levels decreased in patients with anterior-located

tumours from after surgery, up to the three-month postoperative assessment. In contrast, Armstrong et al. (2002) found higher depression scores in patients with left-posterior tumours.

Tumours located in the left hemisphere were noted to contribute more to the development of depressive symptoms than right-hemisphere-located tumours (Hahn et al., 2003).

The effect of these factors (location of tumours) on depression is not completely understood at this point. One hypothesis is that the cortical interconnections to limbic structures could be more important than the location of the tumour (Weitzner, 1999). Litofsky and Resnick (2009) suggest that larger tumours are more likely to disrupt the limbic connections.

3.3.2. Depression incidence and tumour treatment

A longitudinal study of 72 patients diagnosed with brain tumours examined depressive symptoms after surgical treatment, and found a significant increase in depression scores at both one and three months follow-up (D'Angelo et al., 2008). This finding was confirmed by the Glioma Outcomes Project, where 22.2% and 21.8% patients reported depressive symptoms at one and three months post-surgery, compared to 17.2% reporting depressive symptoms in the year prior to surgery (Litofsky et al., 2004). In contrast, Mainio et al. (2005b) report no difference in depression levels before surgery and three months post-operatively for 77 high-grade glioma patients. Radiotherapy had no effect on the presence of depression in primary-brain-tumour patients (Litofsky et al., 2004).

Glucocorticosteroids, which are used to reduce cerebral oedema, was found to be the treatment with the strongest link to depressive symptoms (Litofsky & Resnick, 2009). Patients treated with glucocorticosteroids often experience dysphoria; they are also prone to developing anxiety with psychomotor agitation and racing thoughts (Wellisch et al., 2002).

The use of glucocorticosteroids can also contribute to depressive features (Litofsky & Resnick, 2009). Various pathophysiological factors contribute to depression in cancer patients. According to Seddighi et al. (2010) numerous researchers believe that deregulation of the hypothalamic-pituitary-adrenal axis and fluctuations in cytokine levels in the brain may explain the relationship between depression and cancer.

Litofsky and Resnick (2009) believe that the deregulations of the hypothalamic-pituitary-adrenal axis cause the fatty acids and phospholipid metabolism to change together with serotonergic systems near the tumour location. It is also suggested that this dysregulation adds to the reasons for the association between depression and cancer (Spiegel & Giese-Davids, 2003).

3.4. Clinical Outcomes of Brain Tumour Patients

Quality of life can be described as a multidimensional construct that includes social, emotional, psychological, and physical components that are connected to medical conditions and treatment (Huang, Wartella, Kreutzer, Broaddus, & Lyckholm, 2001). Increased depression levels in brain tumour patients were significantly associated with a poor quality of life (Fox et al., 2007; Tsay, Chang, Yates, Lin, & Liang, 2012) at three months and one year after tumour surgery (Mainio et al., 2006). The increased rates of depression can be explained partly by the uncertainty experienced by the patient following the brain tumour diagnosis, and his or her adjustment to budding social and functional constraints, or the different treatment modalities (Huang et al., 2001).

A prior study of 75 primary brain-tumour patients who underwent surgery, found that patients who had experienced preoperative depression had a shorter post-operative survival time (Mainio et al., 2005a). Mainio et al. (2005a) concluded that the survival time for high-grade

glioma patients was about 22.5 months, while the corresponding time for low-grade glioma patients was 50.2 months, and 58.2 months for histological benign tumour patients. A 13-year longitudinal study examined the survival rate of 101 patients who had been diagnosed with a low-grade glioma (Mainio et al., 2006) and it was found that patients who were depressed had a shorter survival rate (3.3 to 5.8 years) than non-depressed patients (10.0 to 11.7 years).

In general, the prognosis of brain tumour patients is not good, with a survival period after diagnosis varying from 6 to 8 years for patients with low-grade astrocytoma, 2 to 5 years for patients with anaplastic gliomas, and 12 to 15 months for patients with glioblastomas (Berger & Prados, 2005; Wen & Kesari, 2008). A previous study, spanning the period 1980 to 2000, examined 415 patients with glioblastomas and found the overall survival rate to be 8.2 months (Lutterbach, Sauerbrei, & Guttenberg, 2003). Consequently, glioblastoma patients have the poorest five-year survival rate, namely, 4.7% (Ostrom et al., 2013). The one-year survival rate for patients diagnosed with brain tumours is 57.2%, compared to the five-year survival rate of 33.7% (Ostrom et al., 2013). Poorer prognosis can be ascribed to the histological features of the tumour, such as advanced age of patient, or if the tumour is unresectable (Lutterbach et al., 2003; Wen & Kesari, 2008). Good prognostic factors are a younger age and histology of tumour, where low-grade gliomas have a better prognosis than anaplastic glioma patients (Behin et al., 2003).

The perioperative morbidity and mortality rates for brain tumour patients have been reduced over the years (Oertel, von Buttlar, Schroeder, & Gaab, 2005). This can be due to the availability of diagnostic methods, such as MRI or CT scans, and advances made in the treatment of these patients. Even so, the general prognosis for patients with gliomas has not changed within the last 30 years (Oertel et al., 2005) and further research is clearly needed.

3.5. Conclusion

This chapter provides an overview of brain tumours, i.e., the epidemiology of tumours, different tumour types, mortality rates, as well as the type of symptoms experienced and how an individual is affected cognitively. The relationship between being diagnosed with a brain tumour and depression is discussed in the last section of the chapter. The focus is specifically on the incidence of depression under various circumstances, i.e., depression in patients before treatment, depression as a reaction due to the diagnoses of a brain tumour, and depression during or after treatment. At the end of the chapter, the clinical outcomes of the patients diagnosed with brain tumours are mentioned. The next chapter will describe the research methods used in this study. It is expected that identification of the personal, psychosocial, or medical factors that may lead to depression in patients diagnosed with brain tumours will inform clinicians regarding patient's depressive symptomatology and thereby help to improve patients' quality of life.

Chapter Four: Research Methodology

4.1. Chapter Overview

The chapter begins with highlighting the aims of the study. This chapter describes the research design and methods used in this study. Measuring instruments used in this study and ethical considerations are discussed. The chapter ends with an explanation of the data-analysis procedures used in this study.

4.2. Aims of this study

Research into depressive symptoms in patients diagnosed with brain tumours is limited. There is an absence of research about the relationship between brain tumours and depression in South Africa. Therefore, this study aims to contribute to the literature on the relationship between brain tumours and depression within a South African context. The secondary aim of the study is to examine whether the presence of depressive symptoms is linked to (a) tumour localisation, (b) histopathological type of tumour, or (c) participant characteristics (demographic variables like age and gender). Neuropsychological assessments were done to determine the relationships between tumour characteristics, participant characteristics, and the presence of depressive symptoms.

4.3. Research Method

4.3.1. Research design

An exploratory study was undertaken of all patients who were referred by their general practitioners to the neuro-oncology units at Tygerberg and Universitas Hospitals and newly diagnosed brain-tumour patients already at these hospitals.

4.3.2. Setting

The study took place at the neurosurgery clinics located at Tygerberg and Universitas Hospitals. Both hospitals are academic hospitals and each one has an alliance with a university, i.e., Tygerberg Hospital with Stellenbosch University and Universitas Hospital with the University of the Free State. Tygerberg and Universitas are fairly large provincial hospitals that receive a good representation of the different racial groups in the Western Cape and Free State respectively. Tygerberg Hospital in Cape Town admits over 90 747 patients as well as more than 500 000 outpatients visit the hospital annually, offering healthcare to over 3.6 million people (Western Cape government, 2010). Patients come from the North Eastern parts of Cape Town, the Boland region of the Western Cape Province and the Cape West Coast region. Universitas Hospital admitted 363 870 patients in the year April 2011 to March 2012 (N. R. J. van Zyl, personal communication, May 2, 2012). The Free State province alone is home to roughly 2.74 million people (“South Africa info: Free State province,” 2012). Patients are referred to Universitas Hospital in Bloemfontein from Lesotho, and the North West, Northern and Eastern Cape, and the Free State provinces.

4.3.3. Participants

Patients suitable for inclusion in the study were identified by Prof. Hartzenberg (head of the Neurosurgery Department at Tygerberg Hospital) and Dr. Basson (Neurosurgery Department at Universitas Hospital). To be included in this study, patients had to be at least 18 years old and not older than 65, diagnosed with a solitary, primary brain tumour as confirmed by MRI or CT scan, and competent to read and understand the informed consent forms (see Appendix A for the informed consent forms in the various languages) in order to give their permission to participate in the study. In addition, patients had to be Afrikaans or English speaking, and an education level of at least Grade 6 **was** necessary in order to complete all the

questionnaires. Participants had to be without sedatives such as benzodiazepines, for eight or more hours prior to neuropsychological assessment.

Patients were excluded from the study if they had depressed levels of consciousness, if emergency care was necessary (for example surgical intervention for coning), or if they had been diagnosed with pituitary or metastatic tumours.

4.4. Measuring Instruments

4.4.1. Patient data form

The patient data form contains a brief demographic background, Beck Depression Inventory–II (BDI-II) score, relevant clinical information, MRI or CT scan results, and a histological report for each of the patients participating in this study (see Appendix B).

4.4.2. Mini International Neuropsychiatric Interview (MINI) and DSM-IV-TR criteria

The MINI is a specific psychiatric interview used to screen for patients who have psychiatric disorders and to screen out patients without psychiatric disorders (Sheehan et al., 1998). It is easily administrated because of its short, clear and simple design. The MINI was used in conjunction with the DSM-IV-TR criteria to screen for the major Axis psychiatric disorders, especially depression, and to rule out psychiatric co-morbidities (Sheehan et al., 1998). The MINI is organised into modules identified by letters, each related to a diagnostic category. At the start of each diagnostic module (excluding psychotic disorders), screening question(s) equivalent to the key criteria of the disorder are shown in a grey box. At the end of each module, the clinician refers to diagnostic box(es) that helps to determine whether the diagnostic criteria are met or not.

4.4.3. Beck Depression Inventory–II (BDI-II)

The BDI-II (Beck et al., 1996) was used to measure the presence and severity of depression in the brain tumour patients. The intensity of depression can be assessed in individuals from the age of 13 to 80 years. The BDI-II consists of 21 four-point Likert-type items, where a three indicates the most severe symptom and a zero the less severe symptom (Beck et al., 1996). Therefore a higher total score would indicate more severe symptoms. The BDI score will not be used to diagnose, nor categorise, the patients. It will merely be an indication of the presence and severity of depressive symptoms. An internal consistency reliability coefficient of .92 was found for a clinical sample and .93 for a college sample (Beck et al., 1996). This study also found that the BDI-II obtained a good internal consistency (Cronbach's $\alpha = .847$). A test-retest reliability coefficient of .93 was found (Beck et al., 1996). The BDI has been used in previous studies to assess depressive symptoms in patients with primary brain tumours (Kaplan & Miner, 2000; Mainio et al., 2005a; Pelletier et al., 2002).

4.4.4. A short neuropsychological test battery

Previous research found that emotional distress or mood changes can lead to impairments in vigilance, motivation, and attention, ultimately leading to several cognitive deficits, especially in brain tumour patients (Anderson et al., 1999; Pringle et al., 1999; Wellisch et al., 2002). Other researchers highlighted that mood changes are found to be more common in brain tumour patients than in other neurological disease patients (Andrewes et al., 2003). Neuropsychological testing is referred to as an information-gathering tool within the medical environment to gain data related to illness, psychosocial factors, and behaviour (Engel, 1977). Therefore, a battery of neuropsychological tests were used to evaluate (1) cognitive ability, (2) speed of processing, (3) working memory, (4) verbal learning, and (5) visual learning and memory.

Mini mental state examination (MMSE)

The MMSE (Folstein, Folstein, & McHugh, 1975) was incorporated in the test battery in order to screen for cognitive impairment in the brain tumour patients. The MMSE consists of 11 items, created to establish the individual's orientation to time and place, awareness and calculation, language, and last, immediate and delayed recall (Spreen & Strauss, 2006). The test-retest reliability correlations are between .80 and .95 and the internal consistency range from .31 to .96. The MMSE was confirmed to be valid and reliable for examining depressed individuals with cognitive impairment (Folstein et al., 1975). A prior study made use of the MMSE to examine the overall cognitive performance in high-grade glioma patients (Klein et al., 2001).

Trail Making Test (TMT)

The TMT is a measuring instrument that is used to assess processing speed, attention and mental flexibility (Davies, 1968). It can be divided into two parts, namely Part A, which assesses visual-conceptual skills, visuo-motor tracking and scanning, and Part B, for executive functioning and cognitive flexibility. Part A of the TMT requires the individual to join 25 encircled numbers as quickly as possible in numerical order (Lezak et al., 2004). Part B entails the opposite, connecting the 25 numbers and letters in alternating order as quickly as possible. Only Part A was administered to the participants.

The test-retest reliability correlations range from .41 to .65 (Anderson, 2001; Spreen & Strauss, 2006). The TMT is described as one of the five measuring instruments predominantly used by neuropsychologists to assess attention and executive functioning (Rabin, Barr, & Burton, 2005). The TMT is also used to establish cognitive outcome in brain tumour patients in conjunction with other neuropsychological tests (Kaleita et al., 2004; Meyers & Hess, 2003).

Wechsler Memory Scale, Third Edition (WMS-III) (using only 1 of 11 subtests)

The WMS-III assesses declarative memory (auditory and visual) and working memory (Wechsler, 1997). The one subtest of the WMS-III that was used as part of the neuropsychological test battery in this study is Letter Number Sequencing (LNS). Working and auditory memory are assessed through administering the LNS. The LNS entails a list of numbers and letters that are read to the subject, who must recite it in a specific order, first numbers in ascending order and then letters in alphabetical order. The WMS-III has good reliability coefficients, ranging from .82 to .93 (Lezak et al., 2004). The stability coefficients for the primary subtests vary between .62 and .82 and the internal consistency for the LNS is .80 to .89 (Spreeen & Strauss, 2006).

Hopkins Verbal Learning Test – Revised (HVLT-R)

The HVLT-R is a measuring instrument that gives a quick assessment of verbal learning and memory (Benedict, Schretlen, Groninger, & Brandt, 1998). It consists of a list of 12 words, four for each of the three semantic groups that assess immediate recall across three trials, recognition of the words, and delayed recall (Brandt & Benedict, 2001). The delayed recall was not done with the participants of the present study, in order to increase the measuring time significantly. The HVLT-R is divided into three primary variables: total recall, delayed recall, and percentage words retained. The reliability coefficients for the three subtests are .74, .66, and .39 respectively (Spreeen & Strauss, 2006). The test-retest correlations are for total recall (.70 to .79), delayed recall (.60 to .69), and retention percentage (less than .59). The HVLT-R is quite brief and suitable for severely impaired individuals. It has been used to investigate cognitive deterioration in brain tumour patients in the past (Meyers & Hess, 2003).

Brief Visuospatial Memory Test – Revised (BVMT-R)

The BVMT-R is based on a multiple-trial list-learning model to assess visual learning and memory (Benedict, Schretlen, Groninger, Dobraski, & Shpritz, 1996). The BVMT-R consists of six different forms of measures, namely, immediate recall, rate of acquisition, delayed recall, and recognition (Benedict, 1997). In this study only the immediate recall was performed, in order to keep the measuring time as short as possible. The participant is shown an 8 x 11 inch plate containing six basic geometric visual designs in a 2 x 3 matrix. The matrix is shown for 10 seconds, after which the individual must reproduce as many of the designs as possible, in the identical locations as they appear on the plate (Spreeen & Strauss, 2006). This is then repeated in three trails. The reliability coefficient for the total recall scale is .80 and .60 for Trail 1 and .84 for Trail 3. The BVMT-R is a helpful instrument for clinical and research-based neuropsychological assessment; among its numerous advantages are inclusion of visual learning ability, delayed recall and recognition recall. The BVMT-R's other advantages are its construct and predictive validity, and its preciseness and ease of administration (Benedict et al., 1996). The test manual was used to score each reproduction according to standardised criteria. Two points are awarded if the production was accurately reproduced and placed correctly. If either the responses were accurately placed or correctly drawn, then one point was awarded. In the case of missing designs on the answer sheet, or if an unrecognisable attempt was found, a score of 0 was given. The range of the scores is from 0 to 12 for each of the three trails.

4.5. Procedure

A suitable qualified research assistant (she worked for the Medical Research Council unit at Tygerberg hospital) was recruited in 2011 to help with recruitment and to continue with data collection at Tygerberg Hospital, while the principle investigator started with the study at Universitas Hospital in April 2012. Patients who fulfilled inclusion criteria were interviewed

at the hospitals during their admission to hospital. All the participants were seen pre-operatively.

Written consent was obtained from all the participants before assessment started. The test battery was administered with pen and paper. The investigator asked the questions in the questionnaires and wrote down the responses during the interview, except where some of the neuropsychological tests required the participant to complete it by him or herself.

The presence of depression was determined according to DSM-IV-TR criteria and information obtained with the MINI (Sheehan et al., 1998). Second, the severity of depression was measured with the BDI-II (Beck, Steer & Brown, 1996). The cut-off score that was used was 20. According to Lykouras et al. (1998) the high cut-off point of 20 optimised sensitivity and specificity in neurological settings. A short neuropsychological test battery (refer to the measurements in section 4.3.4) was then administered to determine cognitive functioning of the participants. The radiological diagnosis of each brain tumour was obtained from the MRI or CT scan reports.

The participants' clinical characteristics were collected from the participants' files after the data collection period had ended. The investigator was blind to the results of both the radiological diagnosis and chart review until the data collection period was finished and the data had been analysed. The reason for this was to prevent bias regarding the BDI scores, neuropsychological assessment, and location and histopathological type of the brain tumour.

Scoring and interpretation of both neuropsychological data and chart reviews was done under supervision of a trained psychiatrist with experience in neuropsychology.

The scan results of the MRI or CT were recorded from the participant's medical records by a medical doctor and the location of the brain tumour was specified as being positioned in the left or right hemisphere; the position in the lobe was also specified.

4.6. Ethical Concerns

The research was carried out in accordance with the principles of the Declaration of Helsinki. The Health Research Ethics Committee (HREC) at the Faculty of Health Sciences and the department of Psychology at Stellenbosch University awarded ethical clearance. The HREC of the University of the Free State also awarded ethical clearance. Consent was also obtained from the superintendent at Tygerberg Hospital and the Chief Executive Officer (CEO) of Universitas Hospital.

Each participant's questionnaires received a research number to protect the anonymity of the participants. No personal identifier (name) was recorded. The information obtained from the participants' folders and MRI scans was recorded in a data capturing form. The researcher did not see the data capturing form until all the data had been analysed. A separate folder, to whom only the investigators had access, was used to link the patient research number with his/her patient file, scan, and histopathological report.

Each participant gave written consent by means of an informed consent form (ICF) (see Appendix A). The ICF was read with the participant and the procedures of the study were explained. Participation was voluntary and the participants were free to withdraw at any time without affecting their treatment.

Participants identified with depressive symptoms in need of treatment were referred to the relevant mental-health service provider in their area.

4.7. Data Analysis

Data analyses were performed with STATISTICA version 9 (StatSoft, 2009) and the assistance of a biostatistician. Descriptive statistics were performed to determine frequency counts and distributions (mean and standard deviation) of the demographic variables in the sample. The prevalence of depression was calculated for the sample if the BDI-II raw score was larger than 20. Differences between depression mean scores and demographic variables were analysed by means of independent t-tests. One-way ANOVAs were performed to determine differences among the BDI-II total score and tumour location along with neuropsychological variables and tumour location. Pearson's chi-square tests for independence were used to investigate differences between categorical groups of the BDI-II (minimal, mild, moderate, and severe) and demographic variables as well as neurological symptom variables and between the MINI and BDI-II scores.

4.8. Conclusion

This chapter outlined the research methodology of this study. The research design, setting of data collection, participants, measuring instruments, as well as the ethical considerations were discussed. The data analysis methods were described at the end of the chapter. A descriptive correlation study was undertaken to determine primarily, the relationship between patients diagnosed with brain tumours and depression. Quantitative data was obtained by administering eight measuring instruments. One-way ANOVAs and Pearson's chi-square tests for independence were used to analyse the quantitative data.

In the next chapter the results of this study are reported.

Chapter Five: Results

5.1. Chapter Overview

This chapter represents the quantitative results of this study. First, the descriptive statistics are reported, namely, the demographics, sample as well as tumour characteristics, and clinical symptomology. Results are presented as means (with standard deviations in parentheses). Second, mean score comparisons are reported.

Differences between depression mean scores and demographic variables were analysed by means of independent t-tests. One Way ANOVAs were used to evaluate the differences among the BDI-II scores and tumour location as well as between various individual cognitive measures and tumour location. Chi-square tests for independence were used to examine differences between groups on categorical variables.

5.2. Descriptive Statistics

5.2.1. Demographics

A total of 49 potential participants were identified, of whom 46 fulfilled the inclusion criteria at that time. Three patients were excluded because they lacked the required inclusion criteria of an education level of at least Grade 6 and being competent to read and understand. These patients all agreed to participate. However, after participation the patients' medical records were obtained and as a result of their diagnoses 11 patients were excluded, ending with a total of 35 participants who complied with the inclusion criteria.

The participants were almost equally spread over two provinces, with 54% of patients from the Free State and 46% from the Western Cape. With regard to Free State participants at Universitas Hospital, 19 fulfilled the inclusion criteria and only three patients were excluded

due to their diagnosis. The information regarding the participants included and excluded at Tygerberg Hospital is illustrated in Figure 5.1.

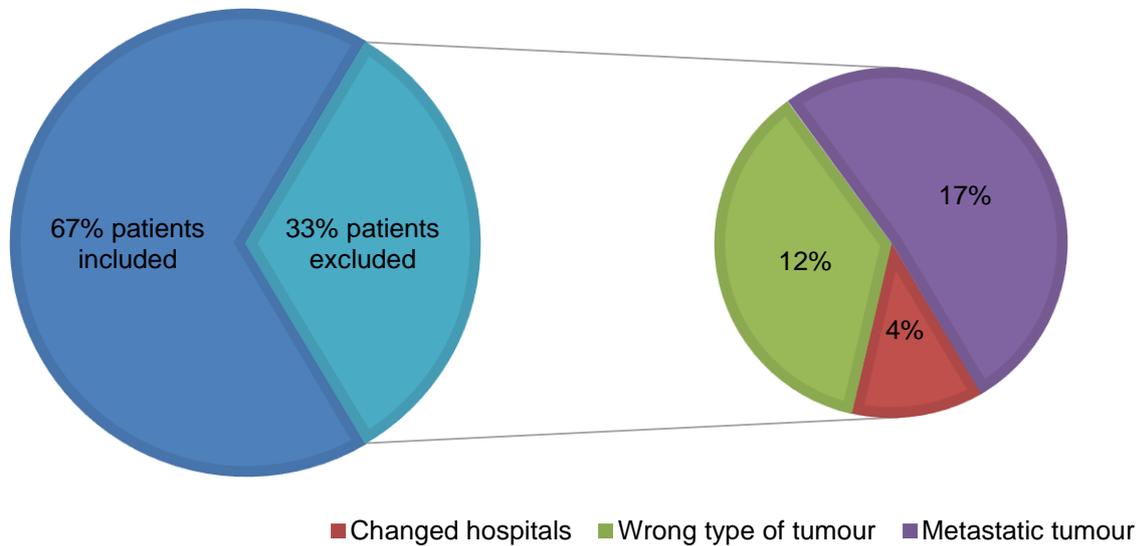


Figure 5.1. Tygerberg Hospital participants: Number of patients excluded from study, and reason for exclusion ($n = 16$).

For participants at Tygerberg Hospital in the Western Cape, 67% of patients fulfilled the inclusion criteria and 33% were excluded mostly because of their diagnosis (metastatic tumour).

5.2.2. Sample characteristics

The final sample consisted of 24 women and 11 men. Table 5.1 lists the sample's demographic features. Afrikaans was the home language of most of the participants.

Table 5.1

Demographic Characteristics of the Participants (N = 35)

Variable	Frequency	%
Relationship status		
Married	25	71
Single	7	20
Divorced	3	9
Gender		
Male	11	31
Female	24	69
Occupation status		
Employed	21	60
Unemployed	14	40
Education qualification		
Grade 6 to Grade 7	5	14
High school	22	63
Diploma	6	17
Degree	2	6
Postgraduate	0	0
First language		
Afrikaans	23	66
English	4	11
Sesotho	6	17
Xhosa	2	6
Referred from		
Casualties	3	13
Emergency rooms	3	13
General practitioners	7	29
Internal medicine	3	13
Neurology	2	8
Ophthalmology	3	13
Ward consult	3	13

The average age of the participants was 45.71 (SD = 12.27) years at the time of assessment, with the majority (71%) of the participants being middle to late adults, with ages between 40 and 65 years.

Psychiatric symptoms and complaints

Major depressive episodes (MDE) were the most commonly reported psychiatric symptom, with 46% of participants experiencing current MDE and 19% of the participants reporting that they experienced past and current MDE. With reference to the participants from the two different hospitals, 63% of participants reported MDE at Tygerberg Hospital in the Western Cape compared to 32% of participants reporting MDE at Universitas Hospital in the Free State. The presence of depression was screened by DSM-IV-TR criteria and information obtained with the MINI. Based on findings from the MINI only 46% of the total sample fulfilled the criteria of a major depressive disorder, of which 37% were women and 9% men.

The overall results obtained from the MINI are summarised and shown in Table 5.2. The majority of participants had no psychiatric disorders.

Table 5.2

Psychiatric Comorbidity according to the MINI (N = 35)

Variable		Frequency	%
Suicide risk	Low	3	9
	Moderate	3	9
	High	4	11
Hypomanic	Yes	1	3
Manic	Yes	2	6
Panic disorder	Yes	0	0
Agoraphobia	Yes	0	0
Social phobia	Yes	2	6
Obsessive compulsive disorder (OCD)	Yes	2	6
Post-traumatic stress disorder (PTSD)	Yes	1	3
Alcohol dependence/abuse	Yes-abuse	2	6
	Yes-dependence	1	3
Psychotic disorder	Yes	0	0
Generalised anxiety disorder	Yes	1	3

As can be observed in Table 5.2, there were 25 participants from the total sample of 35 with no risk of attempting suicide, while four participants had a high suicide risk.

With reference to self-reported depression, the mean depression score on the BDI-II for the total group ($N = 35$) was 18.66 ($SD = 10.13$). The majority (63%) of participants had total BDI-II scores below the cut-off score of 20. This implies that 37% of the sample reported depressive symptoms. Table 5.3 specifically displays the presence of depression found in the sample based on the findings of the MINI and BDI-II.

Table 5.3

Types of Depression/Depression Disorders and Symptoms in the Sample (N = 35)

Variable		Frequency	%
Dysthymia	Yes	0	0
	No	35	100
Major depressive episode (current)	Yes	16	46
	No	19	54
Major depressive episode (past)	Yes	3	9
	No	32	91
Self-report history of depressive symptoms	Yes	13	37
	No	22	63

Table 5.3 demonstrates that depression and/or depressive symptoms were prevalent in the participants of this study.

The frequent symptoms reported by participants on the BDI-II are represented in Figure 5.2. The most common symptom was loss of sexual pleasure (31%), followed by pessimism (20%), sadness, irritability, difficulty sleeping and lack of energy.

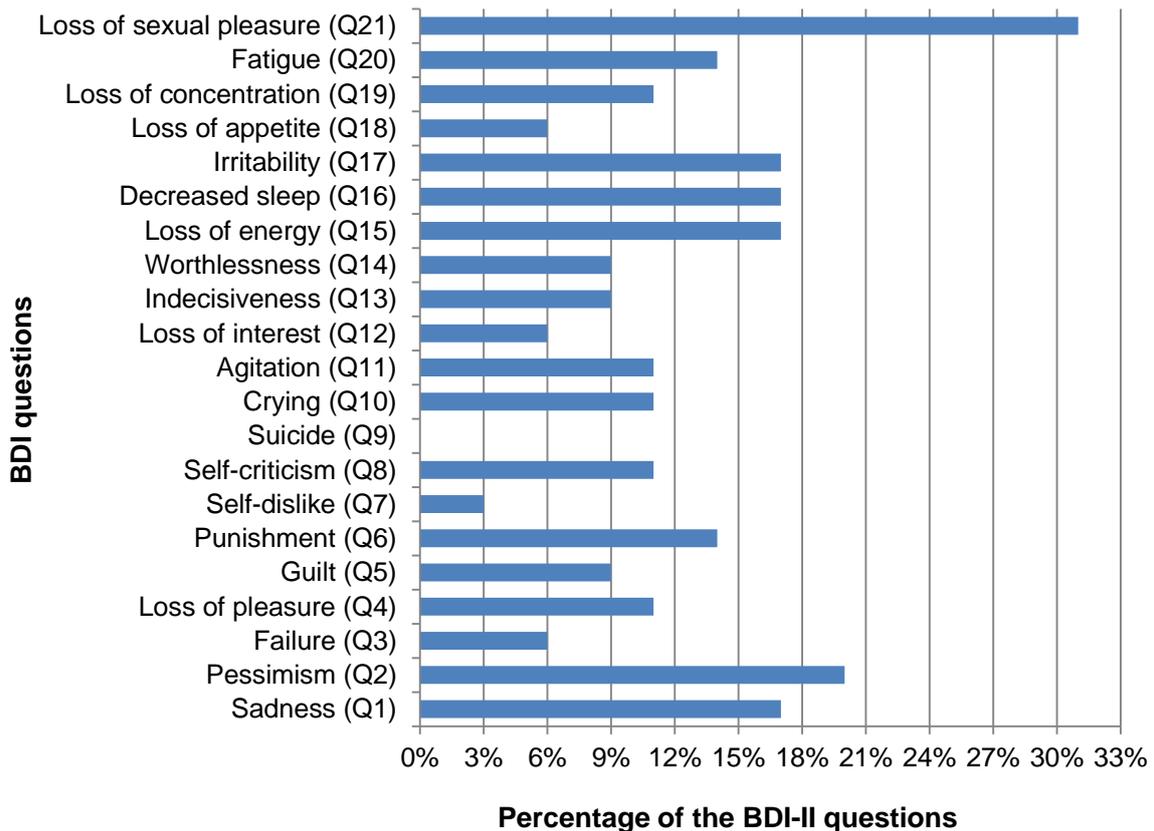


Figure 5.2. All the most frequently reported symptoms on the BDI-II ($N = 35$).

The total scores obtained with the BDI-II were categorised into four groups according to severity of symptoms: minimal (BDI-II score ≤ 13), mild (BDI-II score 14-19), moderate (BDI-II score 20-28), and severe (BDI-II score ≥ 29). There were 11 participants with minimal depression, 11 with mild depression, eight with moderate depression, and five with severe depression. Refer to Figure 5.3 for the percentages in each category and for the BDI-II mean scores. It can be concluded that 37% of the total sample suffered moderate to severe depression.

The prevalence of at least mild depressive symptoms involved 26% of men and 43% of women.

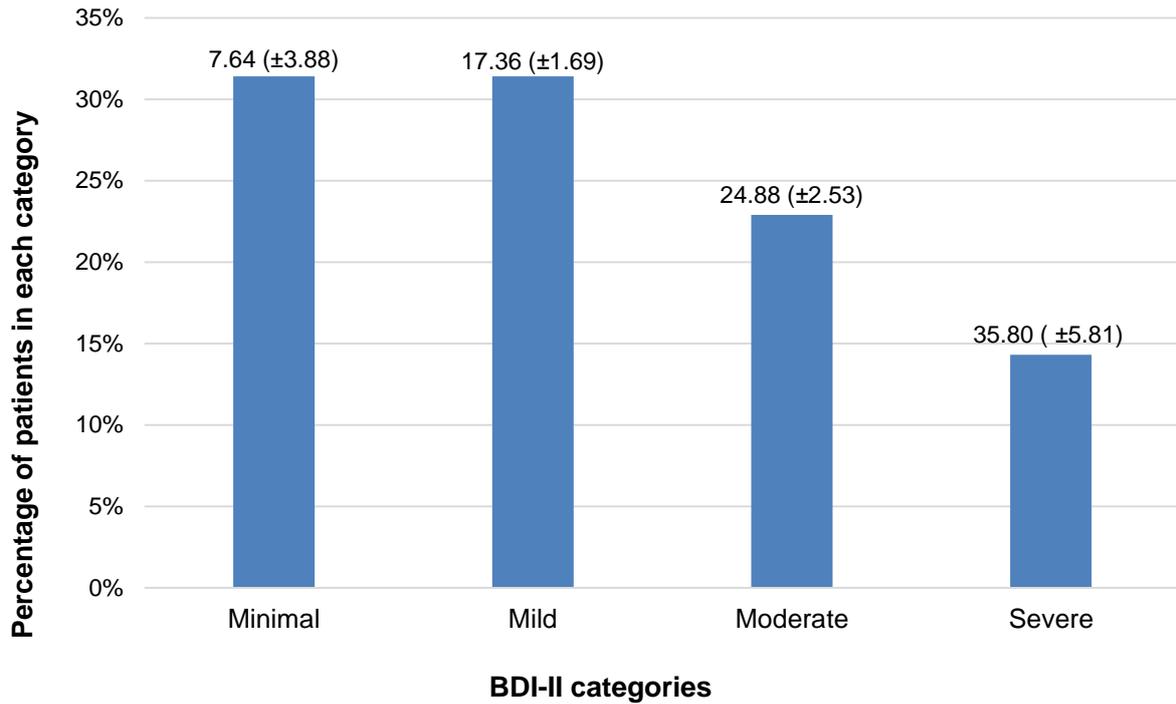


Figure 5.3. Symptom severity according to the BDI-II scores ($N = 35$).

As can be observed in Figure 5.3, the majority of the sample were in the minimal to mild depressive categories based on the groupings on their BDI-II responses.

5.2.3. Clinical symptomatology

Neurological symptoms and complaints

Most of the participants presented with a combination of symptoms, including headaches, seizures, weakness in either the left or right side of the body and impaired vision (see Figure 5.4).

With regard to tumour location and occurrence of individual neurological symptoms, refer to Table 5.4. Only 6% of the sample had headaches without any other symptoms.

Table 5.4

Tumour Location and Isolated Symptom Frequency (n = 28)

Laterality	Frequencies for isolated symptoms		
	Headaches	Seizures	Hemiparesis
Left	11	4	7
Midline	7	0	3
Right	1	2	3

From Table 5. 4 and Figure 5. 4 it is evident that the most common symptom was headaches, especially if the tumour was located in the left hemisphere.

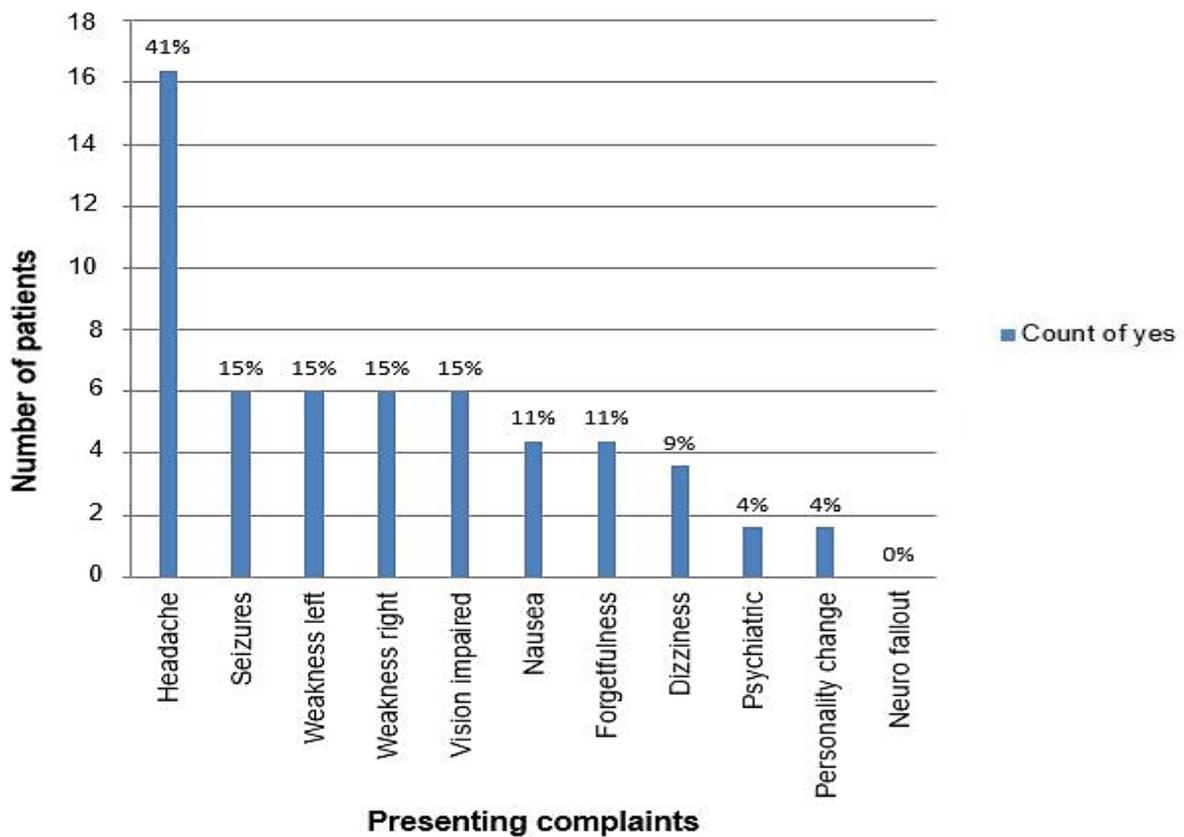


Figure 5.4. Presenting complaints and symptoms of the participants (n = 28).

5.2.4. Tumour characteristics

Figure 5.5 visually represents the tumour-histology frequencies, categorised according to the tumour locations based on the MRI or CT scan results.

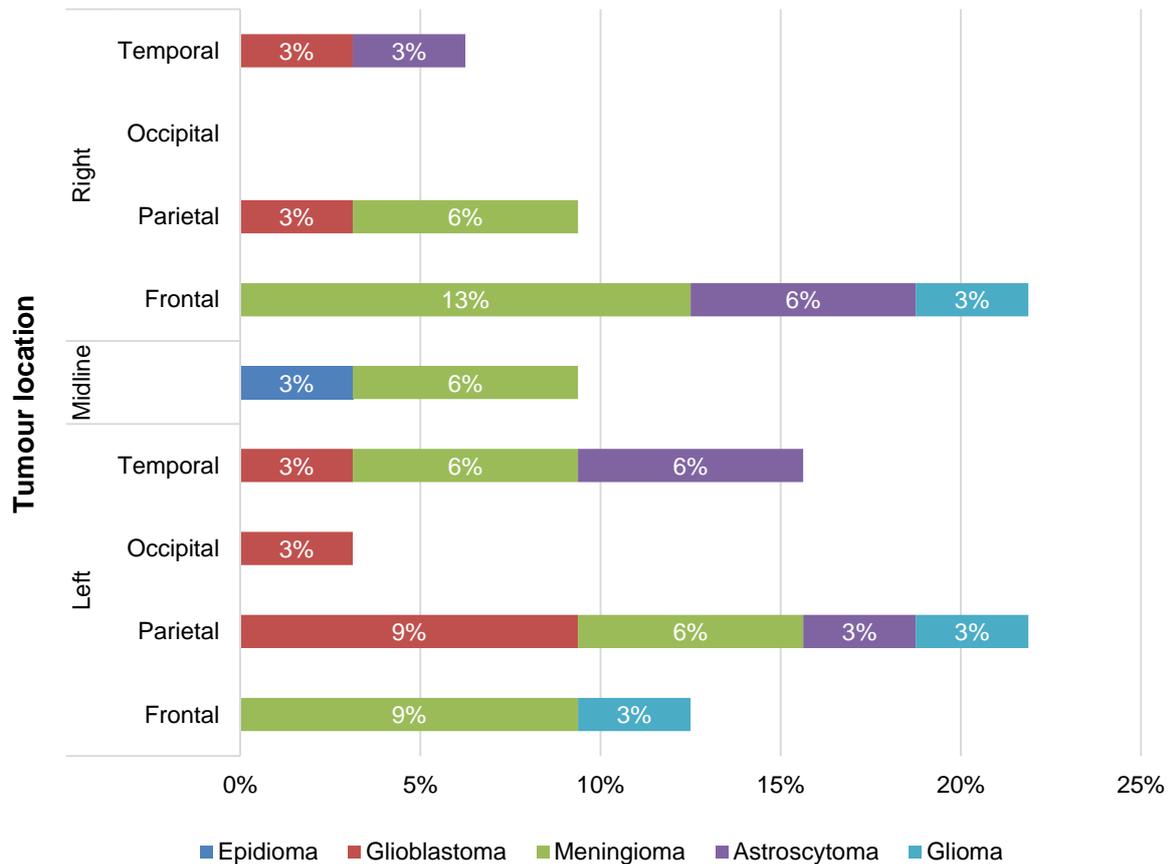


Figure 5.5. Tumour characteristics of the sample ($n = 32$).

The majority of the participants' tumours were located in the left hemispheres (52%) with meningiomas (47%) as the predominant tumour histology.

5.2.5. Neuropsychological findings

A short neuropsychological test battery was used to determine cognitive functioning of the participants. The test battery of neuropsychological tests was used to evaluate (1) cognitive ability, (2) speed of processing, (3) working memory, (4) verbal learning, and (5) visual learning. Although 35 participants were included, total scores could not be calculated for all participants due to some assessments missing data. The primary cause of incomplete data was the physical symptoms of the participants, for example, poor eyesight and hemiplegia.

The cognitive orientation of the whole sample was mildly impaired, with a mean score of 24 (SD = 5.10). The Mini Mental State Examination (MMSE), was the only measure of cognitive ability.

The individual measure, contributing to speed of processing, is the Trail Making Test (TMT). Speed of processing was poor – this conclusion is reached on the basis of the mean score equalling 78. For this test, 29% of the participants obtained a score above 90 seconds, indicating cognitive impairment, mostly impairments in terms of visual scanning, numeric sequencing, and visuomotor speed.

Working memory was measured by the Letter-Number Span (subtest of the Wechsler Memory Scale – 3rd ed.) which measures verbal memory specifically. Working memory was severely impaired. The maximum score for the test is 24, with only 9% of the sample obtaining a score of at least 12.

Verbal learning improved over the three trails (illustrated in Figure 5.6). The Hopkins Verbal Learning Test – Revised (HVLT-R) measures the cognitive domain of verbal learning.

Visual learning also displayed improvement over the three trails (as measured by the Brief Visuospatial Memory Test – Revised; BVMT-R); results are presented in Figure 5.6.

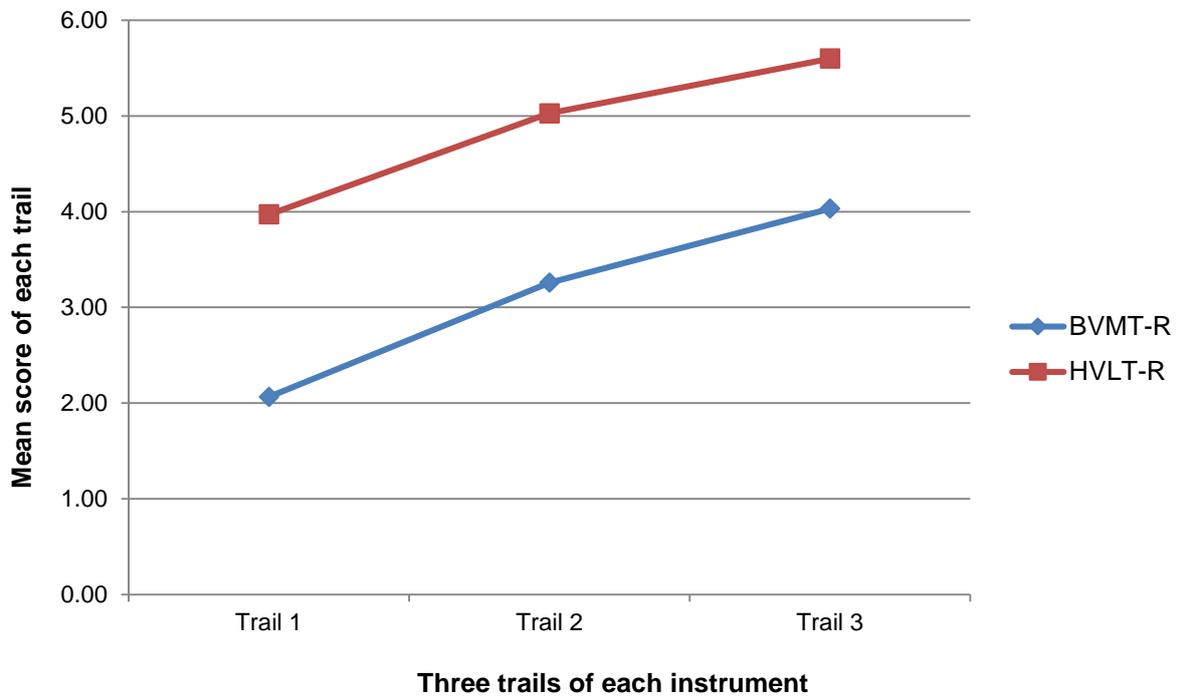


Figure 5.6. Results of the three trails of the HVLTR and BVMT-R ($n = 31$).

The sample appeared to perform better in the verbal learning trails of the HVLTR compared to the visual learning trails of the BVMT-R.

Changes in the individual measures are listed in Table 5.5, which also provides the mean scores for the different trails.

Table 5.5

Neurocognitive T-scores of the Individual Measures

		First trail	Second trail	Third trail
Variable	N	Mean (SD)	Mean (SD)	Mean (SD)
BVMT-R	31	9 (6.96)	2 (2.07)	3 (2.58)
HVLT-R	35	15 (5.82)	4 (1.82)	5 (2.19)
LNS	34	5 (3.81)		
TMT (Part A)	31	78 (48.31)		

Note. BVMT-R, Brief Visuospatial Memory Test – Revised; HVLT-R, Hopkins Verbal Learning Test – Revised; LNS, Letter-Number Span; TMT, Trail Making Test: Part A.

With reference to the TMT mean score, the participants completed part A of the TMT in 78 seconds. Refer to section 6.5 for a brief discussion regarding this mean score.

5.3. Comparisons of Mean Scores

5.3.1. Relationships between depression mean scores and demographic variables

In examining the prevalence of depression in the sample, the relationship between various demographic variables (gender, marital status, and occupational status) and depression is also of interest; in other words, this study wish to determine whether there is a difference in depression scores between men and women; participants who are married and single; and those who have jobs versus those who are unemployed.

Table 5.6 lists the results from the independent t-tests. Single participants as well as unemployed participants obtained slightly higher mean BDI-II scores than married participants and employed participants.

Table 5.6

Results from Independent t-tests between BDI-II Total Scores and various Demographic Variables (N = 35)

Variable	<i>M</i>	<i>SD</i>	<i>df</i>	<i>t</i>	ρ
Gender			33	.49	.63
Male	19.91	11.68			
Female	18.08	9.56			
Marital status			33	.98	.34
Single	21.30	9.90			
Married	17.60	10.23			
Employment			33	-.91	.37
Employed	17.38	10.23			
Unemployed	20.57	10.06			

From Table 5.6 it can be observed that there is no statistical difference in depression scores between the various demographic variables – gender, marital status and occupational status.

BDI-II and MDE findings

An independent-sample t-test revealed higher depression mean scores in participants with current major depressive episode (MDE), with a mean of 23.88 (SD = 10.35), compared to participants with no current MDE, who had a lower mean score of 14.26 (SD = 7.52). As a result, the differences were significant: the presence of current MDE was found to be a predictor of depression $t(33) = 3.14, p = .004$. On the contrary, the presence of past MDE did

not predict depression. Although participants with past MDE have a higher mean depression score, namely 24.67 (SD = 5.86), than participants with no past MDE, who had a mean score of 18.09 (SD = 10.33). However, there are no significant statistical differences between the mean depression score and participants with past MDE $t(33) = 1.08, p = .29$.

5.3.2. Differences between tumour location and neurological symptoms

Chi-square analyses indicated no significant association between tumour location (left, right hemisphere or midline) and any of the following predominant neurological symptoms: headaches, $\chi^2(2, 35) = 1.72, p = .42$, location of hemiparesis, $\chi^2(2, 35) = 3.58, p = .17$ or impaired vision, $\chi^2(2, 34) = .35, p = .84$; neither was there a significant difference between the occurrence of seizures and location of tumours in either one of the lobes or midline, $\chi^2(4, 34) = 2.18, p = .70$. Tumour location is thus not a significant predictor of various neurological symptoms.

5.3.3. Differences between tumour location and depressive symptoms

The mean depression score on the BDI-II for tumours located in the right hemisphere was 21.62 (SD = 8.26), for tumours located in the left hemisphere it was 18.29 (SD = 11.31) and for midline-located tumours it was 10.25 (SD = 5.80). Based on the BDI-II means, it can be deduced that moderate depressive symptoms are experienced if the tumours are located in the right hemisphere. Mild depressive symptoms are experienced by this sample when the tumours are located in the left hemisphere.

Although the mean depression score for tumours in the right hemisphere was higher than the tumours located in the left hemisphere and midline, this difference was not statistically significant, $F(2, 32) = 2.06$, $\rho = .14$ as shown in Figure 5.7.

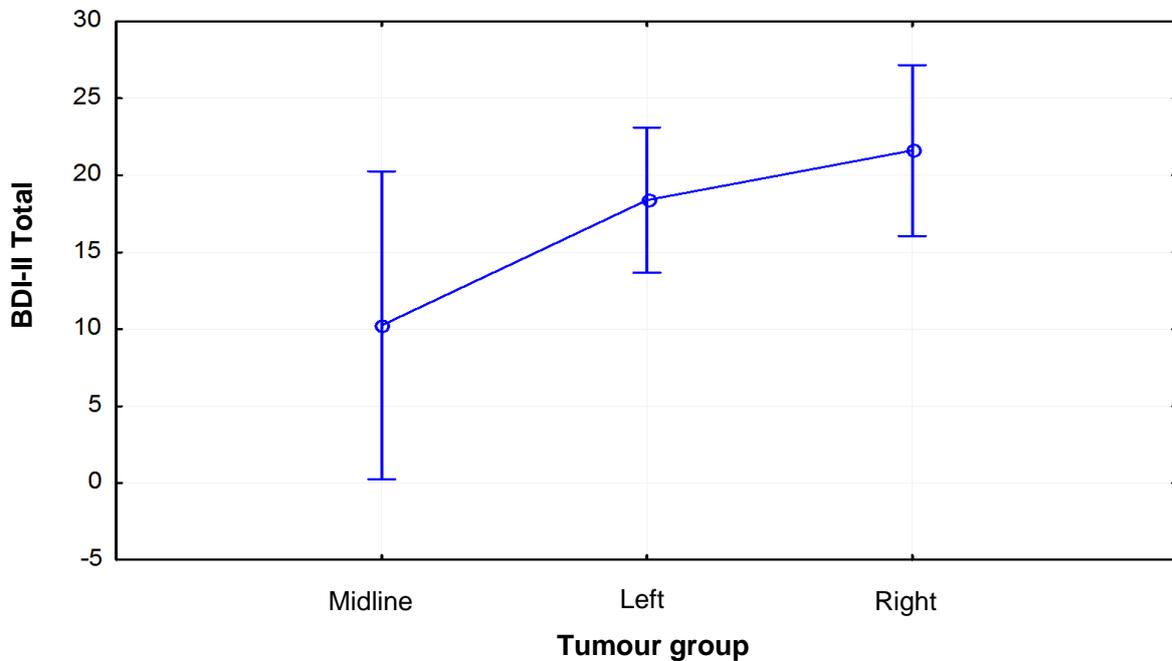


Figure 5.7. Comparison of mean tumour location depression scores for total group ($N = 35$). Vertical bars denote 0.95 confidence intervals.

A chi-square analysis indicated no significant association between tumour location and having depressive symptoms (a BDI-II higher than the cut-off score of 20), $\chi^2(2, 35) = 2.84$, $\rho = .24$. This confirms that tumour location is not a significant predictor of depression in this study.

5.3.4. Differences between tumour location and neuropsychological functioning

Analysis of variances were performed to determine whether group means differ, i.e., between tumour location and the various individual cognitive measures.

The mean cognitive ability score on the MMSE for right-sided tumours was 23.31 (SD = 6.09), for left-sided tumours 23.28 (SD = 4.74) and midline tumours 27.00 (SD = 1.83). The mean MMSE score for tumours located in the midline was higher than for the tumours located in either the right or left hemispheres. This difference was not statistically significant, $F(2, 32) = 0.93, \rho = .40$.

The mean processing speed score on the TMT for tumours located in the right hemisphere was 78.11 (SD = 31.93), for tumours located in the left hemisphere 83.6 (SD = 58.45) and midline-located tumours 50.50 (SD = 7.85). Though the mean TMT score for tumours in the left hemisphere was higher than the tumours located in the right hemisphere and midline, this difference was not statistically significant, $F(2, 28) = 0.76, \rho = .48$.

The mean working memory score on the LNS for tumours located in the right hemisphere was 4.50 (SD = 3.18), for tumours located in the left hemisphere 4.78 (SD = 4.49) and midline-located tumours 6.75 (SD = 1.71). Although the mean LNS score for tumours in the midline was higher than for tumours located in the right or left hemispheres, this difference was not statistically significant, $F(2, 31) = 0.53, \rho = .59$.

The mean verbal learning score, according to HVLT-R, was 5.46 (SD = 1.71) for right-sided tumours, for left-sided tumours 4.50 (SD = 2.02) and midline-located tumours 4.58 (SD = 2.31). The mean HVLT-R score for right-sided tumours was higher than for left-sided and midline tumours, but this difference was not statistically significant, $F(2, 32) = 0.97, \rho = .39$.

The mean visual learning score on the BVMT-R for right-sided tumours was 2.57 (SD = 1.62), for left-sided tumours 3.13 (SD = 2.57) and midline located tumours 4.41 (SD = 2.74). The mean BVMT-R score for tumours located on the midline was higher than for tumours

located in either the left or right hemispheres. This difference was not statistically significant, $F(2, 28) = 0.90, \rho = .42$.

5.4. Conclusion

In this chapter the results of this study were reported. The quantitative data were analysed by means of One-way ANOVAs and Pearson's chi-square tests for independence.

The results showed that major depressive episodes were the most commonly reported psychiatric symptom. Some participants in the sample also reported depressive symptoms. No demographical characteristics of the participants were found to predict depression in this sample.

Last, the results indicated no statistical significant relationship between tumour location and occurrence of depressive symptoms.

In the next chapter the results of this study are discussed.

Chapter Six: Discussion

6.1. Chapter Overview

The primary aim of this study was to determine the prevalence of depression in patients diagnosed with brain tumours. The secondary aim of the study was to examine whether the presence of depressive symptoms were linked to (a) tumour localisation, (b) histopathological type of tumour, or (c) participant characteristics (demographic variables like age and gender). This is one of the first studies of its kind undertaken in South Africa (as to date of thesis submission). Another study only investigated the prevalence of meningiomas in Johannesburg (Ibebuike, Ouma, & Gopal, 2013). This chapter starts with a discussion of the sample, followed by the psychiatric and neurological symptoms that were found in the sample and it ends with the neuropsychological characteristics of the sample.

6.2. Sample

The sample consisted of an almost equal number of participants from two provinces; 16 (46%) from the Western Cape and 19 (54%) of the participants from the Free State. The Western Cape is home to 11.4% and the Free State only of 5.2% of the total South African population (Statistics South Africa, 2013).

6.3. Psychiatric Symptoms

6.3.1. Depression

Depression, a major psychiatric symptom among primary brain tumour patients, can complicate the course of diseases (Mainio, 2005). With regard to this study, the prevalence of at least mild depressive symptoms in brain-tumour patients was remarkably high, at 26% for men and 43% for women. The average depression score for the sample was 18.66, indicating that the sample can be categorised as having mild depressive symptoms; only 37% of the

sample scores were above the cut-off score of 20. The prevalence of major depressive episodes (MDE) was 45.7% for the total sample and 9% for men and 37% for women at the time of assessment. In the adult South African population the data for prevalence of a depressive disorder is limited. The South African Stress and Health Study estimated the lifetime prevalence of MDE at 9.7% (Stein et al., 2007). The prevalence for women was 1.75 times greater than for men. Furthermore, 12-month prevalence of any mood disorder is 4.9% for the general South African population (Stein et al., 2007).

However, the two provinces with the highest lifetime prevalence estimates for mood disorders are the Free State with the highest lifetime prevalence, at 14.6%, while the prevalence estimate is 13.7% in the Western Cape (Stein et al., 2007). This study found that the prevalence of MDE in participants diagnosed with brain tumours was 63% for the Western Cape sample and 32% for the Free State sample.

This study's findings correspond with those of Mainio (2005), who found that the prevalence of depression was 30% for men and 38% for women. In another study, Mainio et al. (2005b) found that 35% of the sample had depressive symptoms. In both of Mainio's studies the BDI-II cut-off score was above 10, while the BDI-II score was above 20 for this study. If this study also used 10 as the BDI-II cut-off score it would imply a depression prevalence of 77%, which is a much higher prevalence than that reported by the two studies mentioned.

In clinical samples among patients diagnosed with a meningioma, a glioma, or other primary tumours, the prevalence of depression varied between studies: starting with 9.7% (D'Angelo et al., 2008), to 16% (Pringle et al., 1999), up to 38% (Pelletier et al., 2002) and even 41% (Arnold et al., 2008). Bunevicius, Deltuva, et al. (2013) found that 33% of their sample had a BDI-II score above 14 and 18% had a score above 20. Therefore, the findings of this study

regarding the high prevalence of depression are consistent with previous studies. The depression prevalence discrepancies may be linked to different depression measures together with different cut-off scores used for the same measure, and also the variance in sample sizes.

6.3.2. Demographical variables

Gender

The gender representation in this sample and the 2013 population estimate for both the Western Cape and Free State provinces together are as follows: 31% male (study) vs. a 49% male (provincial) representation, and 69% female (study) vs. a 51% female (provincial) representation (Statistics South Africa, 2013). This indicates that this study had a nearly equal male and female representation according to the population statistics. The central brain tumour registry of the United States found that approximately 42% of all brain and CNS tumours are diagnosed in men and 58% in women (Ostrom et al., 2013).

There were no significant differences between men and women with regard to depression. Fourteen percent of male participants had no depressive symptoms compared to 17% males with a BDI-II score above 20. Interestingly, 45.7% of female participants reported no depressive symptoms. Goebel and Mehdorn (2012) and Pelletier et al. (2002) also found no significant difference between genders in their studies of patients with benign intracranial meningiomas. In contrast, other studies found that female patients obtained higher depression scores than their male counterparts (Arnold et al., 2008; Beadles, 2006; Pringle et al., 1999).

A possible explanation for the discrepancies in these findings may be that women communicate their emotions more freely and are likely to admit to symptoms of depression. Importantly, physiological factors (e.g., sex hormones and immune system) may add to the

differences in susceptibility related to sex in major depression (Pitychoutis & Papadopoulou-Daifoti, 2010).

Employment status

The unemployment rate in South Africa is 24.9% representing 13 million people without jobs (National Planning Commission, 2011). Sixty percent of the sample was employed at time of assessment and 30% of participants were unemployed.

No statistical significant difference was found between employment status and depression. Nevertheless, 46% of participants who were employed, compared to 17% of participants with no employment, had a BDI-II score below 20, indicating minimal to mild depressive symptoms. Educational status has not yet been found to predict depression in patients with brain tumours. The presumption tends to be that if someone is unemployed, he or she will also have limited or scarce resources available to deal with depression. The burden of the diagnosis, stress about his/her financial situation and leaving his or her family well looked after, are all believed to add to the burden of someone who is unemployed. A recent study about access to mental health in primary care did find that patients with limited resources (e.g., the homeless, long-term unemployed, and advanced cancer sufferers) are more prone to depression (Lamb, Bower, Rogers, Dowrick, & Gask, 2011).

Marital status

The majority (70%) of participants were married. The single participants reported more depressive symptoms (50% vs. 32% of married participants), though, this is not a statistically significant difference between the two groups.

Disparity is found in the literature in relation to marital status, from studies claiming that being married is a predictor of depression (Kaplan & Miner, 2000; Litofsky & Resnick, 2009) to marriage being a protective variable against developing depression (de Graeff et al., 2001).

Depression can influence interpersonal relationships of patients with brain tumours (Litofsky & Resnick, 2009). Married versus single patients with brain tumours have different factors influencing depression. A study about relationship importance for patients with cerebral tumours found that married patients complained about problems with their sexual relationship, marital difficulties, inactivity, and finances (Kaplan & Miner, 2000). To the contrary, single patients were more concerned with bodily deterioration, problems with social activities, cognition, and also finances. Previous research suggests that married patients may have better overall health habits, seek immediate medical care when symptomatic, and have better social support than single patients (de Graeff et al., 2001).

Similarly, in this study the married participants were more inclined to be free from depressive symptoms than the single participants. One previously mentioned factor, problems with their sexual relationship, was associated with a greater likelihood of depression in married patients (de Graeff et al., 2001). The current study did not investigate this specific factor. Loss of sexual pleasure (item 21 in the BDI-II) was the item with the highest frequency, with 31% of participants reporting absence of sexual desire. Interestingly, only 20% of married samples, compared to a high of 40% single participants, had lost their interest in sex.

To conclude, this study agrees with de Graeff et al. (2001), namely, that married patients are less prone to depression than single patients. This may be due to various reasons; one being better social support being available for married patients, either emotionally or physically (for example, help with household tasks).

6.3.3. Tumour location

In this sample, no statistical significant relationship was found between tumour location and occurrence of depressive symptoms. Nearly equal percentages of depressive symptoms were found in participants with tumours in the left and right hemispheres, 20% and 17%, respectively. This finding is in concordance with previous studies (Brown et al., 2005; D'Angelo et al., 2008; Litofsky et al., 2004; Pelletier et al., 2002).

The relationship between tumour location and depression is still being debated. Various researchers did indeed find that the location of a tumour plays a role in influencing depressive symptoms. Left-hemispheric tumours were more inclined to accompany depression than right hemispheric tumours (Hahn et al., 2003), while Pringle et al. (1999) only found this to be true for female patients in their study. Wellisch et al. (2002) found that tumours located in the frontal lobes can predict major depressive disorder. Anteriorly located tumours were also found to be more associated with tumours rather than those with posterior location (Mainio et al., 2005b).

The one thing the above mentioned studies had in common was a sample size larger than 60. There are however several differences between the studies cited, one being that they used different measuring instruments for depression, namely, the Zung self-rating depression scale, SF-36 mental health score, Profile of mood states short form and BDI-II. It can be concluded that the different depression instruments used contributes to the difficulty of obtaining a clear understanding of the relationship between depressive symptoms and patients diagnosed with brain tumours. This also adds to the difficulty of comparing studies with different criteria for depression.

Depression, as measured by the BDI-II, is not necessarily a one dimensional variable, but merely a complex response to biological, psychological, or social factors that can all be influenced by medical conditions (e.g., energy levels, changes in appetite and sleep patterns, and sociability), thus increasing the depressive symptoms in patients diagnosed with brain tumours. For example, a study about psychological distress in brain tumour patients, found that 35% of the BDI-II scores' total variance was accounted for by somatic symptoms (Bunevicius, Tamasauskas, Deltuva, Tamasauskas, & Bunevicius, 2013). This emphasises the importance of identifying somatic depressive symptoms in brain tumour patients. These symptoms can be due to brain-tumour-related impairment, side effects of the treatment (fatigue), or psychological distress induced by the diagnosis (crying).

Consequently, the results of this study confirm that depressive symptoms are prevalent and vital clinical matter among brain tumour patients. The high prevalence of depressive symptoms may be due to various experiences a brain tumour patient undergoes that, in return, demonstrate the validity of the biopsychosocial model (Engel, 1977). The biological (tumour location), psychological (depression), and social factors (family) must all be taken into consideration to comprehend depression amongst brain tumour patients.

This study agrees with Litofsky and Resnick (2009), namely that more research needs to be carried out to determine if tumour location actually has an effect on depressive symptoms and if depressive symptoms are related in any way to the medical condition of having a brain tumour.

6.3.4. Other psychiatric disorders

No statistical differences were found when comparing BDI-II total scores with psychiatric disorders screened with the MINI. The only exception was for MDE. This result confirms

that participants with current MDE had a higher severity of depression than participants without current MDE (refer to Table 5.3). Although not significant, the results showed that 22.9% of participants with a BDI-II score greater than 20 had current major depressive episodes. Because the current study examined self-reported rates of depression, it is likely that the participants underestimated or even overestimated their depressive symptoms, based on their emotional state of having been diagnosed with a brain tumour.

6.4. Neurological Symptoms

6.4.1. Sample

Seizures (15%) was one of the other most commonly reported symptoms in this sample. This finding is consistent with previous studies (Armstrong et al., 2004; Fox et al., 2007), which also found seizures as one of the most frequent symptoms experienced by brain tumour patients. In contrast with this study, a previous integrative literature search by Cahill, LoBiondo-Wood, Bergstrom, and Armstrong (2012) found seizure was the least reported symptom.

Seizures are commonly associated with tumours that are cortical and slow growing (Behin et al., 2003). Meningioma (47%) was the predominant histology type in this sample, followed by glioblastomas and astrocytomas. These tumours are all described as possible, slow-growing tumours, depending on the tumour grade (American Brain Tumor Association, 2012; Lynam et al., 2007). As the majority of tumours in this study were of a slow-growing nature, it can explain why seizures were a common symptom in this sample.

The onset of seizures and progressive headaches are the key symptoms that would warrant an imaging study, leading to diagnosis of a brain tumour (Armstrong et al., 2004). Screening for primary brain tumours is not done routinely and the incidence of a neurological symptom

often helps to form a diagnosis. For example, two participants were diagnosed after they had been admitted for head injuries after they fell off ladders due to suffering seizures.

Headache is another common symptom of brain tumours – it occurs occasionally as a single symptom, as evident in only 6% of this sample. However, the majority of the sample experienced headaches (with a prevalence of 41%) as the predominant neurological symptom. Similarly, a study of 206 patients with intracranial tumours found the prevalence of tumour-related headache was 47.6% (Valentinis et al., 2010). According to Valentinis et al. (2010), 64% of patients with a history of longstanding headaches, had headache accompanying their brain tumours while only 38% without prior history of headache developed headache as a symptom. Therefore, the patient's previous headache history, among other variables, can influence the prevalence of headache after diagnosis with a brain tumour. This study's findings of neurological symptoms are only of a descriptive nature, comprising symptoms reported by the doctor when reports were submitted to the hospitals. No additional information was obtained regarding the history of the symptoms.

6.4.2. Tumour location

The left hemisphere was found to have the highest frequency of isolated neurological symptoms (headaches, seizures, and hemiparesis), but no significant relationship was found between tumour location and occurrence of neurological symptoms. This is congruent with findings of Schankin et al. (2007) with regard to tumour location and headaches, and the finding that headache location does not predict tumour location (Kirby, 2014).

Further, no relationship was found between the location of the tumour, in either one of the lobes or midline, and occurrence of seizures. A study of tumour laterality and presenting

symptoms had similar findings (Inskip et al., 2003). The researchers concluded that seizures and weakness were not significantly associated with tumour laterality.

Previous reports about seizure risk found that the location of the tumours in fact, plays a role in seizure occurrence (Lynam et al., 2007). According to these authors, tumours in the parietal lobe, temporal, and frontal lobes have the highest risk for seizures. Tumours located in the occipital lobes have the least likelihood of being related to seizure occurrence. The majority of this study's sample tumours were indeed located in either the parietal or frontal lobes. However, this finding in this study was not congruent with that of Lynam et al. (2007), possibly due to the smaller sample size of 35 compared to theirs of 112 participants.

6.5. Neuropsychological Characteristics

In this study no significant relationship was found between MSSE scores (screening for cognitive impairment) and tumour location. An average score of 24 was obtained with the MMSE. Scores between 20 and 25 indicate mild cognitive impairment (Folstein et al., 1975). Thus the sample's average score of 24 can be due to mild cognitive impairment indicative of brain tumour. The MMSE has been found to be less sensitive to patients of an advanced age and those with lower educational status. This critique may be relevant to this study. Fourteen percent of participants obtained at least grade 6 or 7 and only four participants finished high school. The effectiveness of the MMSE in identifying cognitive impairment can be largely dependent on the sample. Researchers have started to suggest that the cut-off score can be raised to 27 or 29 to increase the sensitivity in symptomatic samples (Lezak et al., 2004).

The LNS test (working and auditory memory) average score was 5 for this sample, with scores ranging from 0 to 18 and a maximum score of 20. This low average score indicates that this sample possibly have a poor working memory. For example, tumours located in the

temporal lobes are more associated with causing a poor working memory (McLean, 2010; Zillmer et al., 2007). However, no statistically significant relationship was found between poor LNS performance and tumour location.

The TMT (Part A) test (measuring processing speed, attention, and mental flexibility) revealed no statistically significant relationship between processing speed performance and tumour location. The total sample completed the test in 78 seconds, indicating a deficient performance. This result is congruent with the purpose of the Trail Making Test (Part A), as it is used to test psychomotor speed and visual search ability (Crowe, 1998).

Interestingly, a previous study (Hahn et al., 2003) found that patients diagnosed with glioblastoma multiforme have poorer psychomotor speed and visual tracking than patients with non-glioblastoma multiforme types of tumours. Hahn et al. (2003) hypothesised that it may be due to the rapid progression of the more aggressive tumour.

The BVMT- R (measuring visual learning and memory) results indicate that visual learning took place from the first to the third trail (see Figure 5.6). No significant relationship was found between tumour location and BVMT-R scores. A study of epilepsy patients with left and right temporal lobe seizures also found no difference in patients' performance on each of the BVMT-R trails (Barr, Morrison, Zaroff, & Devinsky, 2004). Their conclusion was that the BVMT-R lacks sensitivity for identifying memory impairments. In contrast, another study measuring cognitive functioning in glioma patients found that, among other cognitive deficits, visuospatial memory is one of the most frequently affected functions in patients with brain tumours (Talacchi, Santini, Savazzi, & Gerosa, 2011). The discrepancies in these studies may be due to different measures of visual spatial memory tests, sample sizes, or the type of sample. The first-mentioned study's sample included only epilepsy participants. The

second study's sample included participants diagnosed with gliomas, while this study's sample included all the primary brain tumour types.

Verbal learning also took place from the first to third trail, as indicated by the HVLT-R results. No statistically significant relationship between test performance and brain tumour location was found. In a sample of 68 patients with primary brain tumours a prospective study found that tumour lateralisation did play a role in cognitive performance (Hahn et al., 2003). Patients with left-sided tumours were significantly more prone to memory loss, poorer verbal learning, and verbal fluency. Hahn et al. (2003) also suggested that verbal impairment may be a reason why tumours located in the left hemisphere were more likely to lead to depressive symptoms.

Memory and attention are found to be the most common impairments associated with brain tumours (Giovagnoli, 2012). The cognitive patterns also vary due to brain tumour location. Giovagnoli (2012) found in his review of the literature on cognitive impairments in patients with brain tumours that the prevalence of cognitive deficits varies from 29% in low-grade glioma patients to 90% in patients with different types of tumours. This variability may be due to different tumour types, differences in neuropsychological measuring instruments and, importantly, different population types.

6.6. Limitations of this Study

First, this study used the BDI-II to measure depression, which was originally intended for psychiatric and chronic health conditions and not specifically for individuals with cancer or, in this case, brain tumours. In order to facilitate comparison and evaluation of findings amongst studies, it would be valuable for future researchers in this field to use valid and reliable measures, especially for patients with brain tumours. It is recommended that

researchers make use of the same measuring instrument, for example when screening for depression.

Second, the sample size was small compared to some other studies (Bunevicius, Deltuva et al., 2013; Mainio et al., 2005b). To adequately test for the possible effects of predictors of depression, it is important for future studies to involve a larger sample size to comply with the conventions and requirements of multivariate statistical techniques. It was not feasible in this study to recruit a larger sample due to various obstacles (e.g., delayed diagnosis and access to healthcare).

Third, there are various histological types of tumours and some may be more inclined to cause depressive symptoms than others. For example, gliomas (e.g., astrocytomas and oligodendrogliomas) may cause more depressive symptoms than other brain tumours (e.g., meningiomas), due to involvement of immunocompetent cells (Litofsky & Resnick, 2009). Meningiomas were the most prominent tumour histology in this study. Because tumour grade and histology may have an influence on biological factors that are connected with depressive symptoms, it is recommended to conduct a study only with a specific type of tumour histology, like gliomas.

Last, the education level of the participants could also be a limitation. As previously mentioned, only a few participants had obtained a matric qualification, which could mean they had difficulty in understanding some of the questions. Also, a few participants completed the evaluation in their second language, which is not ideal. However, this was unavoidable due to the limited cultural friendly and standardised instruments available in South Africa.

6.7. Conclusion

This is the first South African study (at the date of thesis submission) to investigate the incidence of depression in patients diagnosed with brain tumours and to clarify our understanding of the relationship between depression and tumour localisation, histopathological type of tumour, and participant demographical characteristics.

The results of this study indicate that depression is a common symptom in patients diagnosed with brain tumours, therefore, it is recommended to screen for signs of depression soon after diagnosis. This will prevent unnecessary complications that may lead to a poor prognostic outcome, which may add a complicating dimension to the diagnosis and implying a poorer prognostic outcome for the patient.

Very few, if any, psychological interventions or rehabilitation programmes have been specifically established to meet the needs of patients diagnosed with brain tumours (Kanter, D'Agostino, Daniels, Stone, & Edelstein, 2014). For that reason it is recommended that the care of brain tumour patients be improved by means of psycho-education, pharmacotherapy, and psychological therapies. Areas that are of great concern for these patients are cognitive impairment, depression, anxiety, and communication. Emotional support, advice, and practical support by a health-care professional or brain tumour support groups can assist the patients with their concerns about their diagnoses. According to the biopsychosocial perspective, the various systems (i.e., biological, psychological, and social) interact with each other and may be different for each individual. Therefore, each individual's needs and responses to treatment will be different. Future clinicians can incorporate these individual differences to help guide therapy to determine the most suitable treatment or combination of treatments for the specific individual.

No significant results were found regarding the relationship between depression and tumour localisation, histology of the tumours, and demographic characteristics of the patients. The neuropsychological assessments revealed no statistically significant relationships between tumour characteristics, participant characteristics, and the presence of depressive symptoms.

In conclusion, with regard to the South African context, further research is required to explore the relationship between depression and these variables. A larger representative sample of South Africa's population is required.

To summarise, determining the characteristics associated with depression throughout the diagnosis can help detect patients at risk of developing depression, and assist in developing interventions centred on these factors.

References

- American Brain Tumor Association. (2012). *A primer of brain tumors: A patient's reference manual*. Chicago, IL: Author.
- American Cancer Society. (2013). *Cancer facts and figures: 2013*. Atlanta, GA: Author.
- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.
- Anderson, S. I., Taylor, R., & Whittle, I. R. (1999). Mood disorders in patients after treatment for primary intracranial tumours. *British Journal of Neurosurgery*, *13*(5), 480–485. doi:10.1080/02688699908540622
- Anderson, S. J. (2001). On the importance of collecting local neuropsychological normative data. *South African Journal of Psychology*, *31*(3), 29–34. doi:10.1177/008124630103100304
- Andrewes, D. G., Kaye, A., Murphy, M., Harris, B., Aitken, S., Parr, C., & Bates, L. (2003). Emotional and social dysfunction in patients following surgical treatment for brain tumour. *Journal of Clinical Neuroscience*, *10*(4), 428–433. doi:10.1016/S0967-5868(03)00086-9
- Armstrong, C. L., Goldstein, B., Cohen, B., Jo, M.-Y., & Tallent, E., M. (2002). Clinical predictors of depression in patients with low-grade brain tumors: Consideration of a neurologic versus a psychogenic model. *Journal of Clinical Psychology in Medical Settings*, *9*(2), 97–107. doi:10.1023/A:1014987925718
- Armstrong, C. L., Goldstein, B., Shera, D., Ledakis, G. E., & Tallent, E. M. (2003). The predictive value of longitudinal neuropsychologic assessment in the early detection of brain tumor recurrence. *Cancer*, *97*(3), 649–656. doi:10.1002/cncr.11099

- Armstrong, T. S., Cohen, M. Z., Erikson, L. R., & Hickey, J. V. (2004). Symptom clusters in oncology patients and implications for symptom research in people with primary brain tumors. *Journal of Nursing Scholarship*, *36*(3), 197–206. doi:10.1111/j.1547-5069.2004.04038
- Arnold, S. D., Forman, L. M., Brigidi, B. D., Carter, K. E., Schweitzer, H. A., Quinn, H. E., ... Raynor, R. H. (2008). Evaluation and characterization of generalized anxiety and depression in patients with primary brain tumors. *Neuro-Oncology*, *10*(2), 171–181. doi:0.1215/15228517-2007-057
- Barr, W., Morrison, C., Zaroff, C., & Devinsky, O. (2004). Use of the Brief Visuospatial Memory Test-Revised (BVM-T-R) in neuropsychological evaluation of epilepsy surgery candidates. *Epilepsy & Behavior*, *5*(2), 175–179. doi:10.1016/j.yebeh.2003.12.010
- Beadles, N. M. (2006). *Resilience and depression in patients with brain tumors* (Doctoral dissertation). Retrieved from ProQuest Dissertations and Theses. (Accession No. 3198412)
- Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Beck Depression Inventory manual* (2nd ed.). San Antonio, TX: Psychological Corporation.
- Behin, A., Hoang-Xuan, K., Carpentier, A. F., & Delattre, J. (2003). Primary brain tumours in adults. *The Lancet*, *361*(9354), 323–331. doi:10.1016/S0140-6736(03)12328-8
- Benedict, R. H. B. (1997). *Brief Visuospatial Memory Test–Revised: Manual*. Odessa, TX: Psychological Assessment Resources.
- Benedict, R. H. B., Schretlen, D., Groninger, L., & Brandt, J. (1998). Hopkins Verbal Learning Test–Revised: Normative data and analysis of inter-form and test-retest reliability. *Clinical Neuropsychology*, *12*(1), 43–55. doi:10.1076/clin.12.1.43.1726

- Benedict, R. H. B., Schretlen, D., Groninger, L., Dobraski, M., & Shpritz, B. (1996). Revision of the Brief Visuospatial Memory Test: Studies of normal performance, reliability, and validity. *Psychological Assessment*, 8(2), 145–153. doi:10.1037/1040-3590.8.2.145
- Berger, M. S., & Prados, M. D. (2005). Textbook of neuro-oncology. In M. S. Berger & M. D. Prados (Eds.), *Basic science* (pp. 3–7). Philadelphia, PA: Elsevier Saunders.
- Beshai, S., Dobson, K. S., Bockting, C. L. H., & Quigley, L. (2011). Relapse and recurrence prevention in depression: Current research and future prospects. *Clinical Psychology Review*, 31(8), 1349–1360. doi:10.1016/j.cpr.2011.09.003
- Baune, B. T., Stuart, M., Gilmour, A., Wersching, H., Arolt, V., & Berger, K. (2012). Moderators of the relationship between depression and cardiovascular disorders: A systematic review. *General Hospital Psychiatry*, 34(5), 478–492. doi:10.1016/j.genhosppsych.2012.05.013
- Bondy, M. L., Scheurer, M. E., Malmer, B., Barnholtz-Sloan, J. S., Davis, F. G., Il'yasova, D., ... Brain Tumor Epidemiology Consortium. (2008). Brain tumor epidemiology: Consensus from the Brain Tumor Epidemiology Consortium. *Cancer*, 113(Suppl.7), 1953–1968. doi:10.1002/cncr.23741
- Brandt, J., & Benedict, R. H. B. (2001). *The Hopkins Verbal Learning Test-Revised: Professional manual*. Odessa, TX: Psychological Assessment Resources.
- Brintzenhofe-Szoc, K. M., Levin, T. T., Li, Y., Kissane, D. W., & Zabora, J. R. (2009). Mixed anxiety/depression symptoms in a large cancer cohort: Prevalence by cancer type. *Psychosomatics*, 50(4), 383–391. doi:10.1176/appi.psy.50.4.383

- Brown, P. D., Maurer, M. J., Rummans, T. A., Pollock, B. E., Ballman, K. V., Sloan, J. A., ... Buckner, J. C. (2005). A prospective study of quality of life in adults with newly diagnosed high-grade gliomas: The impact of the extent of resection on quality of life and survival. *Neurosurgery*, 57(3), 495–504. doi:10.1227/01.NEU.0000170562.25335.C7
- Bufalino, C., Hepgul, N., Aguglia, E., & Pariante, C. M. (2013). The role of immune genes in the association between depression and inflammation: A review of recent clinical studies. *Brain, Behavior, and Immunity*, 31, 31–47. doi:10.1016/j.bbi.2012.04.009
- Bunevicius, A., Deltuva, V., Tamasauskas, S., Tamasauskas, A., & Bunevicius, R. (2013). Screening for psychological distress in neurosurgical brain tumor patients using the Patient Health Questionnaire-2. *Psycho-Oncology*, 22(8), 1895–1900. doi:10.1002/pon.3237
- Bunevicius, A., Tamasauskas, S., Deltuva, V., Tamasauskas, A., & Bunevicius, R. (2013). Psychological distress symptoms' clusters in brain tumor patients: Factor analysis of depression and anxiety scales. *Psycho-Oncology*, 12(2), 2860–2863. doi:10.1002/pon.3354
- Bunevicius, A., Tamasauskas, S., Deltuva, V., Tamasauskas, A., Radziunas, A., & Bunevicius, R. (2014). Predictors of health-related quality of life in neurosurgical brain tumor patients: Focus on patient-centered perspective. *Acta Neurochirurgica*, 156(2), 367–374. doi:10.1007/s00701-013-1930-7
- Cahill, J., LoBiondo-Wood, G., Bergstrom, N., & Armstrong, T. (2012). Brain tumor symptoms as antecedents to uncertainty: An integrative review. *Journal of Nursing Scholarship*, 44(2), 145–155. doi:10.1111/j.1547-5069.2012.01445.x

- Catt, S., Chalmers, A., & Fallowfield, L. (2008). Psychosocial and supportive-care needs in high-grade glioma. *The Lancet Oncology*, 9(9), 884–891. doi:10.1016/S1470-2045(08)70230-4.
- Chochinov, H. M. (2001). Depression in cancer patients. *The Lancet Oncology*, 2(8), 499–505. Retrieved from http://scholar.google.co.za/scholar_url?hl=en&q=http://www.researchgate.net/publication/11458006_Depression_in_cancer_patients/file/d912f50bced8fbb781.pdf&sa=X&scisig=AAGBfm3_ooORzjuxsH7mu5NC4HsTiZD2UA&oi=scholarr&ei=4hzhU8KzI43B7AbbnoHoCQ&ved=0CBoQgAMoADAA
- Crowe, S. F. (1998). The differential contribution of mental tracking, cognitive flexibility, visual search, and motor speed to performance on parts A and B of the Trail Making Test. *Journal of Clinical Psychology*, 54(5), 585–591. doi:10.1002/(SICI)1097-4679(199808)54:5<585::AID-JCLP4>3.0.CO;2-K
- D'Angelo, C., Mirijello, A., Leggio, L., Ferrulli, A., Carotenuto, V., Icolaro, N., ... Addolorato, G. (2008). State and trait anxiety and depression in patients with primary brain tumors before and after surgery: 1-year longitudinal study, *108*(2), 281–286. doi:10.3171/JNS/2008/108/2/0281
- Davies, A. (1968). The influence of age on Trail Making Test performance. *Journal of Clinical Psychology*, 24(1), 96–98. doi:10.1002/1097-4679(196801)24:1<96::AID-JCLP2270240131>3.0.CO;2-U
- De Graeff, A., de Leeuw, J. R. ., Ros, W. J. ., Hordijk, G. ., Blijham, G. ., & Winnubst, J. A. (2001). Sociodemographic factors and quality of life as prognostic indicators in head and neck cancer. *European Journal of Cancer*, 37(3), 332–339. doi:10.1016/S0959-8049(00)00385-3

- Engel, G. L. (1977). The need for a new medical model: A challenge for biomedicine. *Science*, 196(4286), 129–136. doi:10.1126/science.847460
- Engel, G. L. (1981). The clinical application of the biopsychosocial model. *Journal of Medicine and Philosophy*, 6(2), 101–124. doi:10.1093/jmp/6.2.101
- Evans, D. L., Charney, D. S., Lewis, L., Golden, R. N., Gorman, J. M., Krishnan, R., ... Valvo, W. J. (2005). Mood disorders in the medically ill. *Biological Psychiatry*, 58(3), 175–189. doi:10.1016/j.biopsych.2005.05.001
- Ferlay, J., Shin, H., R., Bray, F., Forman, D., Mathers, C., & Parkin, D. M. (2010). *GLOBOCAN 2008: Cancer incidence and mortality worldwide* (IARC CancerBase No. 10). Lyon, France: International Agency for Research on Cancer
- Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., ... Bray, F. (2013). *GLOBOCAN 2012: Cancer incidence and mortality worldwide* (IARC CancerBase No. 11). Lyon, France: International Agency for Research on Cancer
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12(3), 189–198. doi:10.1016/0022-3956(75)90026-6
- Fox, S., Shephard, T. J., & McCain, N. (1999). Neurologic mechanisms in psychoneuroimmunology. *Journal of Neuroscience Nursing*, 31(2), 87–96. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/14964608>
- Fox, S. W., Lyon, D., & Farace, E. (2007). Symptom clusters in patients with high-grade glioma. *Journal of Nursing Scholarship*, 39(1), 61–67. doi:10.1111/j.1547-5069.2007.00144.x
- Fox, S. W., Mitchell, S. A., & Booth-Jones, M. (2006). Cognitive impairment in patients with brain tumors: Assessment and intervention in the clinic setting. *Clinical Journal of Oncology Nursing*, 10(2), 169–176. doi:10.1188/06.CJON.169-176

- Gilbert, P. (2004). Depression: A biopsychosocial, integrative and evolutionary approach. In M. Power (Ed.), *Mood disorders: A handbook of science and practice* (pp. 99–142). Chichester, England: John Wiley & Sons Ltd.
- Giovagnoli, A. R. (2012). Investigation of cognitive impairments in people with brain tumors. *Journal of Neuro-Oncology*, *108*(2), 277–283. doi:10.1007/s11060-012-0815-6
- Goebel, S., & Mehdorn, H. M. (2012). Development of anxiety and depression in patients with benign intracranial meningiomas: A prospective long-term study. *Supportive Care in Cancer*, *21*(5), 1365–1372. doi:10.1007/s00520-012-1675-5
- Gross, A. F., Smith, F. A., & Stern, T. A. (2007). Is depression an appropriate response to having cancer: A discussion of diagnostic criteria and treatment decisions. *Journal of Clinical Psychiatry*, *9*(5), 382–387. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2040285/>
- Hahn, C. A., Dunn, R. H., Logue, P. E., King, J. H., Edwards, C. L., & Halperin, M. D. (2003). Prospective study of neuropsychologic testing and quality-of-life assessment of adults with primary malignant brain tumors. *International Journal of Radiation Oncology, Biology & Physics*, *55*(4), 992–999. doi:10.1016/S0360-3016(02)04205-0
- Hottinger, A. F., Yoon, H., DeAngelis, L. M., & Abrey, L. E. (2009). Neurological outcome of long-term glioblastoma survivors. *Journal of Neuro-Oncology*, *95*(3), 301–305. doi:10.1007/s11060-009-9946-9
- Huang, M. E., Wartella, J., Kreutzer, J., Broaddus, W., & Lyckholm, L. (2001). Functional outcomes and quality of life in patients with brain tumours: A review of the literature. *Brain Injury*, *15*(10), 843–856. doi:10.1080/02699050010013653

- Ibebuike, K., Ouma, J., & Gopal, R. (2013). Meningiomas among intracranial neoplasms in Johannesburg, South Africa: Prevalence, clinical observations and review of the literature. *African Health Sciences, 13*(1), 118–121. doi:10.4314/ahs.v13i1.16
- Inskip, P. D., Tarone, R. E., Hatch, E. E., Wilcosky, T. C., Selker, R. G., Fine, H. A., ... Linet, M. S. (2003). Laterality of brain tumors. *Neuroepidemiology, 22*(2), 130–138. doi:10.1159/000068747
- Irwin, M. (2002). Psychoneuroimmunology of depression: Clinical implications. *Brain, Behavior, and Immunity, 16*(1), 1–16. doi:10.1006/brbi.2001.0654
- Joseph, R. (1990). *Neuropsychology, neuropsychiatry, and behavioral neurology*. New York, NY: Springer.
- Kaleita, T. A., Wellisch, D. K., Cloughesy, T. F., Ford, J. M., Freeman, D., Belin, T. R., & Goldman, J. (2004). Prediction of neurocognitive outcome in adult brain tumor patients. *Journal of Neuro-Oncology, 67*(1), 245–253. doi:10.1023/B:NEON.0000021900.29176.58
- Kanter, C., D'Agostino, N. M., Daniels, M., Stone, A., & Edelstein, K. (2014). Together and apart: Providing psychosocial support for patients and families living with brain tumors. *Supportive Care in Cancer, 22*(1), 43–52. doi:10.1007/s00520-013-1933-1
- Kaplan, C. P., & Miner, M. E. (2000). Relationships: Importance for patients with cerebral tumours. *Brain Injury, 14*(3), 251–259. doi:10.1080/026990500120727
- Katon, W. J. (2003). Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. *Biological Psychiatry, 54*(3), 216–226. doi:10.1016/S0006-3223(03)00273-7
- Kirby, S. (2014). Headaches and brain tumors. *Neurologic Clinics, 14*(2), 423–432. doi:10.1016/j.ncl.2013.11.006

- Klein, M., Taphoorn, M. J. B., Heimans, J. J., van der Ploeg, H. M., Vandertop, W. P., Smit, E. F., ... Aaronson, N. K. (2001). Neurobehavioral status and health-related quality of life in newly diagnosed high-grade glioma patients. *Journal of Clinical Oncology*, *19*(20), 4037–4047. Retrieved from <http://jco.ascopubs.org/content/19/20/4037>
- Kolb, B., & Whishaw, I. Q. (2003). *Fundamentals of human neuropsychology* (5th ed.). New York, NY: Worth.
- Lamb, J. D., Bower, P., Rogers, A., Dowrick, C., & Gask, L. (2011). Access to mental health in primary care: A qualitative meta-synthesis of evidence from the experience of people from “hard to reach” groups. *Health (London)*, *16*(1), 76–104. doi:10.1177/1363459311403945
- Lezak, M. D., Howieson, D. B., Loring, D. W., Hannay, H. J., & Fischer, J. S. (2004). *Neuropsychological assessment*. New York, NY: Oxford University Press.
- Litofsky, N. S., Farace, E., Anderson, F., Meyers, C. A., Huang, W., & Laws, E. R. (2004). Depression in patients with high-grade glioma: Results of the glioma outcomes project. *Neurosurgery*, *54*(2), 358–367. doi:10.1227/01.NEU.0000103450.94724.A2
- Litofsky, N. S., & Resnick, A. G. (2009). The relationships between depression and brain tumors. *Journal of Neuro-Oncology*, *94*(2), 153–161. doi:10.1007/s11060-009-9825-4
- Louis, D. N., Ohgaki, H., Wiestler, O. D., Cavenee, W. K., Burger, P. C., Jouvett, A., ... Kleihues, P. (2007). The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathologica*, *114*(2), 97–109. doi:10.1007/s00401-007-0243-4
- Lutterbach, J., Sauerbrei, W., & Guttenberg, R. (2003). Multivariate analysis of prognostic factors in patients with glioblastoma. *Strahlentherapie Und Onkologie*, *179*(1), 8–15. doi:10.1007/s00066-003-1004-5

- Lykouras, L., Oulis, P., Adrachta, D., Daskalopoulou, E., Kalfakis, N., Triantaphyllou, N., ... Christodoulou, G. N. (1998). Beck Depression Inventory in the detection of depression among neurological inpatients. *Psychopathology*, *31*(4), 213–219. doi:10.1159/000029042
- Lynam, L. M., Lyons, M. K., Drazkowski, J. F., Sirven, J. I., Noe, K. H., Zimmerman, R. S., & Wilkens, J. A. (2007). Frequency of seizures in patients with newly diagnosed brain tumors: A retrospective review. *Clinical Neurology and Neurosurgery*, *109*(7), 634–638. doi:10.1016/j.clineuro.2007.05.017
- Maier, S. F., Watkins, L. R., & Fleshner, M. (1994). Psychoneuroimmunology: The interface between behavior, brain, and immunity. *American Psychologist*, *49*(12), 1004–1017. doi:10.1037/0003-066X.49.12.1004
- Mainio, A. (2005). *Depressive and anxious symptomatology in relation to a primary brain tumor: Prospective study of neurosurgical patients in Northern Finland*. Retrieved from <http://herkules.oulu.fi/isbn9514277163/isbn9514277163.pdf>
- Mainio, A., Hakko, H., Niemelä, A., Koivukangas, J., & Räsänen, P. (2005a). Depression in relation to survival among neurosurgical patients with a primary brain tumour: A 5-year follow-up study. *Neurosurgery*, *56*(6), 1234–1242. doi:10.1227/01.NEU.0000159648.44507.7F
- Mainio, A., Hakko, H., Niemelä, A., Koivukangas, J., & Räsänen, P. (2005b). Depression and functional outcome in patients with brain tumors: A population-based 1-year follow-up study. *Journal of Neurosurgery*, *103*(5), 841–847. doi:10.3171/jns.2005.103.5.0841

- Mainio, A., Tuunanen, S., Hakko, H., Niemelä, A., Koivukangas, J., & Räsänen, P. (2006). Decreased quality of life and depression as predictors for shorter survival among patients with low-grade gliomas: a follow-up from 1990 to 2003. *European Archives of Psychiatry and Clinical Neuroscience*, 256(8), 516–521. doi:10.1007/s00406-006-0674-2
- Mathers, C., Fat, D., M., Boerma, J., & WHO (2008). *The global burden of disease: 2004 update*. Geneva, Switzerland: World Health Organization.
- McLean, R. (2010). *The essential guide to brain tumors*. Newton, MA: National Brain Tumor Society.
- Meyers, C. A., & Hess, K. R. (2003). Multifaceted end points in brain tumor clinical trials: Cognitive deterioration precedes MRI progression. *Neuro-Oncology*, 5(2), 89–95. doi:10.1093/neuonc/5.2.89
- Meyers, C. A., Hess, K. R., Yung, W. K. A., & Levin, V. A. (2000). Cognitive function as a predictor of survival in patients with recurrent malignant glioma. *Journal of Clinical Oncology*, 18(3), 646–646. Retrieved from <http://jco.ascopubs.org/content/18/3/646>
- Miovic, M., & Block, S. (2007). Psychiatric disorders in advanced cancer. *Cancer*, 110(8), 1665–1676. doi:10.1002/cncr.22980
- Myatt, C. A. (2007). *Cognitive affect in adult brain tumor patients*. (Doctoral dissertation). Retrieved from ProQuest Dissertations and Theses. (Accession No. 3262592)
- National Planning Commission. (2011). *National development plan 2030: Our future-make it work*. Retrieved from <http://www.npconline.co.za/medialib/downloads/home/NPC%20National%20Development%20Plan%20Vision%202030%20-lo-res.pdf>

- Oertel, J., von Buttlar, E., Schroeder, H. W. S., & Gaab, M. R. (2005). Prognosis of gliomas in the 1970s and today. *Neurosurgery Focus*, *18*(4), 1–6. doi:10.3171/foc.2005.18.4.13
- Ostrom, Q. T., Gittleman, H., Farah, P., Ondracek, A., Chen, Y., Wolinsky, Y., ... Barnholtz-Sloan, J. S. (2013). CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2006-2010. *Neuro-Oncology*, *15*(Suppl. 2), ii1–ii56. doi:10.1093/neuonc/not151
- Parker, P. A., Baile, W. F., de Moor, C. de, & Cohen, L. (2003). Psychosocial and demographic predictors of quality of life in a large sample of cancer patients. *Psycho-Oncology*, *12*(2), 183–193. doi:10.1002/pon.635
- Pasquini, M., & Biondi, M. (2007). Clinical practice and epidemiology depression in cancer patients : A critical review. *Clinical Practice and Epidemiology in Mental Health*, *3*(2), 1–9. doi:10.1186/1745-0179-3- 2
- Pasquini, P., H., Kelly, B. M., & PangilInan, J. M. (2007). Depression in the patient with brain cancer. *Community Oncology*, *4*(9), 533–536. Retrieved from <http://www.oncologypractice.com/co/journal/articles/0409533.pdf>
- Pelletier, G., Verhoef, M. J., Khatri, N., & Hagen, N. (2002). Quality of life in brain tumor patients: The relative contributions of depression, fatigue, emotional distress, and existential issues. *Journal of Neuro-Oncology*, *57*(1), 41–49. doi:10.1023/A:1015728825642
- Pillay, A. (2001). Psychological symptoms in recently diagnosed cancer patients. *South African Journal of Psychology*, *31*(1), 14–18. doi:10.1177/008124630103100104
- Pirl, W. F. (2004). Evidence report on the occurrence, assessment, and treatment of depression in cancer patients. *Journal of the National Cancer Institute. Monographs*, *2004*(32), 32–39. doi:10.1093/jncimonographs/lgh026

- Pitychoutis, P. M., & Papadopoulou-Daifoti, Z. (2010). Of depression and immunity: Does sex matter? *The International Journal of Neuropsychopharmacology*, *13*(5), 675–89. doi:10.1017/S1461145710000465
- Price, T., R., Goetz, K., L., & Lowell, M., R. (2008). The American psychiatric press textbook of neuropsychiatry. In S. C. Yudofsky & R. E. Hales (Eds.), *Neuropsychiatric aspects of brain tumors* (5th ed., pp. 735–764). Washington, DC: American Psychiatric Publishing.
- Pringle, A. M., Taylor, R., & Whittle, I. R. (1999). Anxiety and depression in patients with an intracranial neoplasm before and after tumour surgery. *British Journal of Neurosurgery*, *13*(1), 46–51. doi:10.1080/02688699944177
- Rabin, L. A., Barr, W. B., & Burton, L. A. (2005). Assessment practises of clinical neuropsychologists in the United States and Canada: A survey of INS, NAN, and APA division members. *Archives of Clinical Neurology*, *20*(1), 33–65. doi:10.1016/j.acn.2004.02.005
- Richards, D. (2011). Prevalence and clinical course of depression: A review. *Clinical Psychology Review*, *31*(7), 1117–1125. doi:10.1016/j.cpr.2011.07.004
- Rijmen, F., Edward, H., Rapp, S., & Shaw, E. G. (2008). Qualitative longitudinal analysis of symptoms in patients with primary and metastatic brain tumours. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, *171*(3), 739–753. doi:10.1111/j.1467-985X.2008.00529.x
- Saddock, B., J., & Saddock, V. A. (2007). *Kaplan & Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry* (10th ed.). Philadelphia, PA: Wolter Kluwer.
- Satin, J. R., Linden, W., & Phillips, M. J. (2009). Depression as a predictor of disease progression and mortality in cancer patients. A meta-analysis. *Cancer*, *115*(22), 5349–5361. doi:10.1002/cncr.24561

- Schankin, C., Ferrari, U., Reinisch, V., Birnbaum, T., Goldbrunner, R., & Straube, A. (2007). Characteristics of brain tumour-associated headache. *Cephalalgia*, 27(8), 904–911. doi:10.1111/j.1468-2982.2007.01368.x
- Schoeman, R., & Louw, D. A. (2003). Neuropsychological assessment versus neuro-imaging in the diagnosis of cerebral lesions: An explorative study. *Medical Technology SA*, 17(1), 386–392.
- Seddighi, A., Seddighi, A. S., Ashrafi, F., & Nohehsara, S. (2010). Neuropsychological disorders in patients with brain tumor. *Iranian Journal of Cancer Prevention*, 3(1), 42–47. Retrieved from <http://journals.sbmu.ac.ir/index.php/cp/article/viewFile/2998/2681>
- Sheehan, D. V., Lecrubier, Y., Sheehan, H., Amorim, P., Janava, J., Weiller, E., ... Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development of validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry*, 59(Suppl. 20), 34–57. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9881538>
- South Africa info: Free State province. (2012). Free State province, South Africa. Retrieved from <http://www.southafrica.info/about/geography/free-state.htm#UhIXkm0UauI>
- Spiegel, D., & Giese-Davids, J. (2003). Depression and cancer: Mechanisms and disease progression. *Society of Biological Psychiatry*, 54(3), 269–282. doi:10.1016/S0006-3223(03)00566-3
- Spreen, O., & Strauss, E. (2006). *A compendium of neuropsychological tests: Administration, norms and commentary* (3rd ed.). New York, NY: Oxford University Press.

- Starkweather, A. R., Sherwood, P., Lyon, D. E., McCain, N. L., Bovbjerg, D. H., & Broaddus, W. C. (2011). A biobehavioral perspective on depressive symptoms in patients with cerebral astrocytoma. *Journal of Neuroscience Nursing*, *43*(1), 17–28. doi:10.1097/JNN.0b013e3182029859
- Statistics South Africa. (2013). *Statistical release: Mid-year population estimates 2013* (No. P0302). Retrieved from <http://beta2.statssa.gov.za/>
- StatSoft. (2009). STATISTICA (Version 9) [data analysis software]. Tulsa, OK: StatSoft
- Stein, D. J., Seedat, S., Herman, A. A., Heeringa, S. G., Moomal, H., Myer, L., ... Williams, D. (2007). *Findings from the first South African stress and health study*. Johannesburg, South Africa: South African Medical Research Council.
- Suls, J., & Rothman, A. (2004). Evolution of the biopsychosocial model: Prospects and challenges for health psychology. *Health Psychology*, *23*(2), 119–125. doi:10.1037/0278-6133.23.2.119
- Talacchi, A., Santini, B., Savazzi, S., & Gerosa, M. (2011). Cognitive effects of tumour and surgical treatment in glioma patients. *Journal of Neuro-Oncology*, *103*(3), 541–549. doi:10.1007/s11060-010-0417-0
- Taphoorn, M. J. B., & Klein, M. (2004). Cognitive deficits in adult patients with brain tumours. *Lancet Neurology*, *3*(3), 159–168. doi:10.1016/S1474-4422(04)00680-5
- Taylor, S., E. (2006). *Health Psychology* (6th ed.). New York, NY: McGraw-Hill.
- Tomlinson, M., Grimsrud, A. T., Stein, D. J., Williams, D. R., & Myer, L. (2009). The epidemiology of major depression in South Africa: Results from the South African stress and health study. *South African Medical Journal*, *99*(5), 367–373. Retrieved from <http://ajol.info/index.php/samj/article/view/50768>

- Tsay, S. L., Chang, J. Y., Yates, P., Lin, K. C., & Liang, S. Y. (2012). Factors influencing quality of life in patients with benign primary brain tumors: Prior to and following surgery. *Supportive Care in Cancer*, *20*(1), 57–64. doi:10.1007/s00520-010-1053-0
- Tu, C. H., Hsu, M. C., Chi, S. C., Lin, H. Y., & Yen, Y. C. (2014). Routine depression screening and diagnosing strategy for cancer inpatients. *Psycho-Oncology*. Advanced online publication. doi:10.1002/pon.3547
- Tucha, O., Smely, C., Preier, M., Becker, G., Paul, G. M., & Lange, K. W. (2003). Preoperative and postoperative cognitive functioning in patients with frontal meningiomas. *Journal of Neurosurgery*, *98*(1), 21–31. Retrieved from <http://thejns.org.ez.sun.ac.za/doi/pdf/10.3171/jns.2003.98.1.0021>
- Ustün, T. B., Ayuso-Mateos, J. L., Chatterji, S., Mathers, C., & Murray, C. J. L. (2004). Global burden of depressive disorders in the year 2000. *The British Journal of Psychiatry*, *184*(5), 386–392. doi:10.1192/bjp.184.5.386
- Valentinis, L., Tuniz, F., Valent, F., Mucchiut, M., Little, D., Skrap, M., ... Zanchin, G. (2010). Headache attributed to intracranial tumours: A prospective cohort study. *Cephalalgia*, *30*(4), 389-398. doi:10.1111/j.1468-2982.2009.01970.x
- Van den Toorn, R. (2011). *Spatial attentional functioning in adult brain tumor patients* (Unpublished master's thesis). Utrecht University, Netherlands.
- Von Bertalanffy, L. (1950a). An outline of general system theory. *The British Journal for the Philosophy of Science*, *1*(2), 134–165. Retrieved from <http://www.jstor.org/stable/685808>
- Von Bertalanffy, L. (1950b). The theory of open systems in physics and biology. *Science*, *111*(2872), 23–29. Retrieved from <http://www.jstor.org.ez.sun.ac.za/stable/1676073>
- Wechsler, D. (1997). *Wechsler Memory Scale. Third edition manual*. San Antonio, TX: The Psychological Corporation.

- Weitzner, M. A. (1999). Psychosocial and neuropsychiatric aspects of patients with primary brain tumors. *Cancer Investigation*, 17(4), 285–291. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10225009>
- Weitzner, M. A., & Meyers, C. A. (1997). Cognitive functioning and quality of life in malignant glioma patients: A review of the literature. *Psycho-Oncology*, 6(3), 3–169. doi:10.1002/(SICI)1099-1611(199709)6:3<169::AID-PON269>3.0.CO;2-#
- Weitzner, M. A., Meyers, C. A., & Byrne, K. (1996). Psychosocial functioning and quality of life in patients with primary brain tumors. *Journal of Neurosurgery*, 84(1), 29–34. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8613832>
- Wellisch, D. K., Kaleita, T. A., Freeman, D., Cloughesy, T., & Goldman, J. (2002). Predicting major depression in brain tumor patients. *Psycho-Oncology*, 11(3), 230–238. doi:10.1002/pon.562
- Wen, P. Y., & Kesari, S. (2008). Malignant gliomas in adults. *New England Journal of Medicine*, 359(5), 492–507. doi: 10.1056/NEJMra0708126
- Western Cape government. (2010). Tygerberg academic hospital information pamphlet. [Brochure]. Retrieved from http://www.westerncape.gov.za/other/2009/10/brochure_facts_figures_tygerberg_2009_2010.pdf
- Wikman, A., Wardle, J., & Steptoe, A. (2011). Quality of life and affective well-being in middle-aged and older people with chronic medical illnesses: A cross-sectional population based study. *PLoS ONE*, 6(4), 1-9. doi:10.1371/journal.pone.0018952
- World Health Organization. (2012). Depression. Retrieved from <http://www.who.int/mediacentre/factsheets/fs369/en/index.html>

Zabora, J., Brintzenhofesoc, K., Curbow, B., Hooker, C., & Piantadosi, S. (2001). The prevalence of psychological distress by cancer site. *Psycho-Oncology*, *10*(1), 1–19. doi:10.1002/1099-1611(200101/02)10:1<19::AID-PON501>3.0.CO;2-6

Zillmer, E. A., Spiers, M. V., & Culbertson, W. C. (2001). *Principles of Neuropsychology*. Belmont, CA: Thomson Wadsworth.

Zillmer, E., Spiers, M., & Culbertson, W. (2007). *Principles of Neuropsychology* (2nd ed.). Belmont, CA: Thomson Wadsworth.

Appendix A

Deelnemerinligtingsblad en -toestemmingsvorm

Titel van die navorsingsprojek: Die verhouding tussen tumor-eienskappe, depressie-simptome en neuropsigologiese profiele in breintumor-pasiënte

Verwysingsnommer: N10/05/149

Hoofnavorsers: Carike Vermaak

Adres: Sielkunde Departement, R.W. Wilcocks Gebou, Ryneveld Straat, 7600 Stellenbosch.

Kontaknommer: [REDACTED]

U word genooi om deel te neem aan hierdie navorsingsprojek wat kyk na die verhouding tussen breintumors en depressie. Die hoofdoel van hierdie studie is om te ondersoek hoeveel breintumor-pasiënte het depressie-simptome by Universitas Hospitaal in Bloemfontein. Tweedens, wil die studie poog om na te vors of depressie verwant is aan óf die spesifieke posisie van die gewas (waar die tumor geleë is), tipe gewas (hoe dit lyk onder die 'n mikroskoop), óf aan sekere deelnemer eienskappe soos ouderdom en geslag. Laastens, sal die effek van die gewas op kognitiewe funksies (m.a.w. u denke, taal en visualiteit) geëvalueer word.

Neem asseblief die tyd om meegaande inligting wat die detail van die projek verduidelik, deur te lees en neem vrymoedigheid om die studiepersoneel of -dokter enige vrae te vra oor enige deel van hierdie projek wat u nie ten volle verstaan nie. Dit is belangrik dat u ten volle tevrede is dat u duidelik verstaan wat die projek behels en hoe u betrokke gaan wees. U betrokkenheid is heeltemal vrywillig en u is vry om te weier om deel te neem. As u sou weier,

sal dit nie u behandeling enigsens negatief beïnvloed nie. U is ook vry om enige tyd te onttrek van die studie, selfs as u sou instem om deel te neem.

Hierdie studie is goedgekeur deur die Komitee vir Mensnavorsing aan die Universiteit van Stellenbosch asook Universiteit van die Vrystaat en sal uitgevoer word volgens die etiese riglyne en beginsels van die Internasionale Verklaring van Helsinki, Suid-Afrikaanse Riglyne vir Goeie Kliniese Praktyk en die Mediese Navorsingsraad (MNR) se Etiese Riglyne vir Navorsing.

Waarom is u genooi om deel te neem?

Pasiënte gediagnoseer met 'n breintumor, gaan deur 'n moeilike tyd en mag selfs depressie ontwikkel. Depressie kan gesondheid en herstel negatief beïnvloed. Daar is baie min navorsing gedoen oor breintumors en depressie in Suid Afrika. Omdat jy onlangs gediagnoseer is met 'n breintumor word jy genooi om deel te neem aan hierdie studie.

Wat gebeur tydens die studie?

Die doelstellings van die studie sal aan u verduidelik word en as u instem om deel te neem sal die navorser dat u die toestemmingsvorm teken. Die navorser sal dan 'n onderhoud met u voer. Sy sal dan vrae aan u voorlees en sal ook u antwoorde tydens die onderhoud neerskryf. Die eerste vrae sal wees om basiese inligting (geslag, ouderdom ens.) van u te verkry. Die tweede vraelys gaan oor depressie. Sy sal dan vir u vra om 'n paar papier-en-pen toetse te voltooi. Hierdie toetse kyk na jou geheue, aandag en konsentrasie. Dit bestaan uit eenvoudige take wat u moet voltooi. As u moeg raak tydens die onderhoud, is u welkom om te rus voor ons verder aangaan.

Die navorser sal ook 'n opsomming van jou mediese rekord soos jou diagnose, brein skandering, histologiese aspekte van tumor opsom in 'n verslag. Jou naam sal anoniem bly want die navorser sal 'n navorsingsnommer vir jou gee. Daarom sal daar geen persoonlike inligting soos u naam, neergeskryf word op enige van die vorms wat gebruik word nie.

Ons sal u geen addisionele medikasie gee nie of u blootstel aan ander ondersoeke of prosedures nie.

Kan ek kies om nie deel te neem aan die studie nie?

As u kies om nie deel te neem aan die projek nie, sal dit nie u behandeling enigsins beïnvloed nie. Indien u sou besluit om deel te neem, en later van plan verander, vir watter rede ook al, is u vry om te onttrek. Die studie sal nie u huidige of toekomstige mediese behandeling enigsins affekteer nie. U sal onttrek word van hierdie navorsingsprojek indien u dringende chirurgie nodig het of ongeskik raak om die vraelyste te voltooi en te verstaan.

Wat sal u verantwoordelikhede wees?

U enigste verantwoordelikheid is om die vrae tot die beste van u vermoë te beantwoord.

Sal u voordeel trek deur deel te neem aan hierdie navorsingsprojek?

As ons vind dat u ernstige depressie-simptome het, sal u verwys word na geskikte geestes gesondheidsdienste. U deelname aan die studie kan toekomstige pasiënte help deur dokters se kennis te verbreed oor pasiënte met breintumors en depressie.

Is daar enige risiko's verbonde aan u deelname aan hierdie navorsingsprojek?

Ons voorsien nie enige risiko's in u deelname aan hierdie navorsing nie, maar 'n aantal mense kan dalk emosioneel en moeg wees na voltooiing van die vraelyste as gevolg van hul mediese toestand nl. gediagnoseer met 'n breingewas.

Watter alternatiewe is daar indien u nie instem om deel te neem nie?

Soos voorheen genoem, indien u nie instem om deel te neem aan die projek nie, maar 'n behoefte het om met iemand te praat oor u mediese diagnose, kan u steeds verwys word na geskikte geestes gesondheidsdienste.

Wie sal toegang tot u mediese rekords hê?

Die inligting wat versamel word, sal as konfidensieel en beskermd beskou word, en sal nie met enigeen buitekant die spektrum van die navorsing, gedeel word nie. Indien dit gebruik word in 'n publikasie of tesis, sal u naam en dié van ander deelnemers, nie bekendgemaak word nie. Slegs die navorser en haar toesighouers, sowel as die dokters betrokke in u behandeling, sal toegang hê tot die resultate van die vraelyste gedurende die onderhoud. U naam sal nie aangeteken word op enige van die vorms nie. Laastens indien van toepassing, sal daar van die borge van die studie, die studie-toesighouers of REC lede verwag word om die navorsingsrekords te inspekteer.

Wat sal gebeur in die onwaarskynlike geval van 'n besering wat mag voorkom as gevolg van u deelname aan hierdie navorsingsprojek?

Niks hiervan word voorsien nie; die studie sal slegs bestaan uit 'n eenmalige onderhoud en evaluering.

Sal u betaal word vir deelname aan hierdie navorsingsprojek en is daar enige koste verbonde aan deelname?

Nee, u sal nie betaal word vir deelname aan die studie nie. As ons 'n bykomende afspraak moet maak by die hospitaal om die vraelyste te voltooi, sal ons u reis koste betaal.

Wat is die verwagte tydsduur van die onderhoud (dit is, hoe lank sal dit nee mom die vraelyste te voltooi)?

Daar word verwag dat die onderhoud tussen 60 en 90 minute sal wees. Dit is 'n eenmalige evaluasie; die enigste betrokkenheid wat u sal hê by die navorsingsprojek.

Is daar enigiets anders wat u moet weet of doen?

U kan [REDACTED] kontak by [REDACTED] as u enige verdere navrae het of enige probleme ondervind met verwante navorsingskwessies.

U kan die Komitee vir Mensnavorsing kontak by [REDACTED] indien u enige bekommernis of klagtes het wat nie bevredigend deur u studie-dokter hanteer is nie.

U sal 'n afskrif van hierdie inligtings- en toestemmingsvorm ontvang vir u eie rekords.

Verklaring deur deelnemer

Met die ondertekening van hierdie dokument onderneem ek,.....
om deel te neem aan 'n navorsingsprojek getiteld: Die verhouding tussen tumor-eienskappe, depressie-simptome en neuropsigologiese profiele in breintumor-pasiënte.

Ek verklaar dat:

Ek hierdie inligtings- en toestemmingsvorm gelees het of aan my laat voorlees het en dat dit in 'n taal geskryf is waarin ek vaardig en gemaklik mee is.

Ek geleentheid gehad het om vrae te stel en dat al my vrae bevredigend beantwoord is.

Ek verstaan dat deelname aan hierdie navorsingsprojek vrywillig is en dat daar geen druk op my geplaas is om deel te neem nie.

Ek te eniger tyd aan die navorsingsprojek mag onttrek en dat ek nie op enige wyse daardeur benadeel sal word nie.

Ek gevra mag word om van die navorsingsprojek te onttrek voordat dit afgehandel is indien die studiedokter of navorser van oordeel is dat dit in my beste belang is, of indien ek nie die ooreengekome navorsingsplan volg nie.

Geteken te (*plek*) op (*datum*) 2013.

.....

Handtekening van deelnemer

.....

Handtekening van getuie

Verklaring deur navorser

Ek (*naam*) verklaar dat:

Ek die inligting in hierdie dokument verduidelik het aan
.....

Ek hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.

Ek tevrede is dat hy/sy al die aspekte van die navorsingsprojek soos hierbo bespreek, voldoende verstaan.

Ek 'n tolk gebruik het/nie 'n tolk gebruik het nie. (*Indien 'n tolk gebruik is, moet die tolk die onderstaande verklaring teken.*)

Geteken te (*plek*) op (*datum*)2013.

.....

Handtekening van navorser

.....

Handtekening van getuie

Patient Information and Consent Form

Title of the research project: The relationship between tumour characteristics, depressive symptoms and neuropsychological profiles in brain tumour patients

Reference number: N10/05/149

Principal investigator: Carike Vermaak

Address: Department of Psychology, R.W. Wilcocks Building, Ryneveld Street, 7600 Stellenbosch.

Contact number: [REDACTED] or [REDACTED]

You are being invited to take part in this research project which looks at the relationship between brain tumours and depression. The main aim of this study is to examine how many brain tumour patients at Tygerberg hospital in Cape Town has depressive symptoms. Secondly, the study wants to see if depression is linked to either specific tumour location (i.e., where the tumour is), type of tumour (i.e., what it looks like when seen through a microscope) or to certain participant characteristics (e.g., age or gender). Lastly, the effect of the tumour on your cognition (i.e., your attention, memory, language and visual functions) will be assessed.

Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you or your treatment negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the **Health Research Ethics Committee (HREC) at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

Why have you been invited to participate?

Patients diagnosed with a brain tumour go through a difficult time and may even develop depression. Depression can affect your health and recovery negatively. There are very little research done in South Africa on brain tumours and depression. Since you have recently been diagnosed with a brain tumour you are invited to partake in this study.

What happens during the study?

The goals of the study will be explained to you and if you agree to participate in the study the researcher will require you to sign the consent form. You will then be interviewed by the researcher. She will read you some questions, and will write down your answers. The first questions are to get more information about you, like your age and home language. The second set of questions will be about depression. She will then ask you to do some paper-and-pencil tests, to assess your memory, attention, and concentration. It will consist of simple tasks which you need to complete. If you get tired during the interview, you are welcome to rest before we continue with the process.

The researcher will also compile a summary from your medical record with regard to your illness, the brain scan, and the histopathology (microscopic appearance of the tumour) report. Your name will be kept anonymous/ secret because the researcher will be giving you a

research number. Therefore no personal identifier (name) will be recorded on any of the forms on which we collect your data.

We are not going to give you any additional medication, or subject you to any other investigations or procedures.

Can I choose not to partake in this study?

If you do not wish to participate in this project, it will not affect your treatment in any way. Should you decide to participate, and you then change your mind, for whatever reason, you are free to withdraw your consent. You will be withdrawn from this research study if you need to have emergency surgery or become unable to complete and understand the questionnaires.

What will your responsibilities be?

Your only responsibility is to answer the questions to the best of your capabilities.

Will you benefit from taking part in this research?

If we find that you have depressive symptoms in need of treatment, you will be referred to appropriate mental health services. Your participation in the study can help future patients by increasing doctors' knowledge about patients with brain tumours, and depression.

Are there in risks involved in your taking part in this research?

We do not foresee any risks in you taking part in this research, but a number of people do feel emotional and tired after completing the questionnaires, because of their medical condition of being diagnosed with a brain tumour.

If you do not agree to take part, what alternatives do you have?

As previously mentioned, if you do not agree to take part in this research, but feel the need to talk to someone regarding your medical diagnosis, you can still be referred to the appropriate mental health services.

Who will have access to your medical records?

The information collected will be treated as confidential and protected, and will not be shared with anyone outside the scope of this research. If it is used in a publication or thesis, your name and those of other people who took part in the study will not be made known to others. Only the researcher and her supervisors, as well as the doctors involved in your treatment, will have access to the results of the questionnaires completed during the interview and the other information collected from your folder. Your name will not be recorded anywhere on any of the forms.

Lastly if applicable, the sponsors of the study, study monitors or auditors or REC members may need to inspect research records.

What will happen in the unlikely event of some form injury occurring as a direct result of your taking part in this research study?

None of these is foreseen, the study will only have a once off interview and assessment.

Will you be paid to take part in this study and are there any costs involved?

No, you will not be paid to take part in the study. If we need to schedule an additional visit to the hospital to complete the assessment, we will reimburse your travelling costs.

What is the expected duration for the interview (that is, how long will it take to complete the questionnaire)?

The interview is expected to take between 60 and 90 minutes. It is a once off evaluation, the only involvement you will have with the research study.

Is there any thing else that you should know or do?

You can contact [REDACTED] at [REDACTED] if you have any further queries or encounter any problems in the event of research related issues.

You can contact the **Health Research Ethics Committee** at [REDACTED] if you have any concerns or complaints that have not been adequately addressed by your study doctor. You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I agree to take part in a research study entitled: The relationship between tumour characteristics, depressive symptoms and neuropsychological profiles in brain tumour patients.

I declare that:

I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.

I have had a chance to ask questions and all my questions have been adequately answered.

I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.

I may choose to leave the study at any time and will not be penalised or prejudiced in any way.

I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests.

Signed at (*place*) on (*date*)2013.

.....

Signature of participant

.....

Signature of witness

Declaration by investigator

I (*name*) declare

that:

I explained the information in this document to

.....

I encouraged him/her to ask questions and took adequate time to answer them.

I am satisfied that he/she adequately understands all aspects of the research, as discussed above

I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.*)

Signed at (*place*) on (*date*)

2013.

.....

Signature of participant

.....

Signature of witness

Ifomu yesivumelwano

Isihloko sophando: Unxibelelwano kwempawu zoxinezeleko kunye nokujongwa kobunjani bokuthatha kwizigulana ezinokuphazamiseka engqondweni

Inombolo yonxulumano: N10/05/149

Umphandi oyintloko: Carike Vermaak

Idilesi: Isebe le Psychology, R. W. Wilcocks Building, Ryneveld Street, 7600, Stellenbosch.

Umnxeba: [REDACTED] okanye [REDACTED]

Uyamenywa ukuba uthathe inxaxheba koluphando lweprojekti olujonga unxibelelwano phakathi kwento esengqondweni kunye noxinezekelo. Injongo yesisifundo kukuvavanya into eyenzeka ngethuba loxinezeleko olukwizigulana eziphazamiseke engqondweni e Tygerberg isibhedlele e Kapa.

Ukuba zingaphi izigulana ezinophazamiseko engqondweni kwisibhedlele i Tygerberg e Kapa ezinempawu zoxinezeleko. Okwesibini isifundo sifuna ukubona ukuba uxinezeleko lunxulumene kwindawo enophazamiseko (oko kukuthi apho kukho uphazamiseko, uhlobo lophazamiseko, injani indawo uxinezeleko olukuyo phantsi kwe- mayikroskopu) okanye ezinye impawu zomthathi -nxaxheba (umzekelo isini okanye ubudala). Okokugqibela okwenziwa luphazamiseko kuqiqo lwakho okokukuthi ukuqaphela, ukukhumbula, intetho kunye nendlela esebenza ngayo ukubonwa ziyakuhlolwa.

Nceda thatha ixesha lokufunda le ngcaciso unikezwe yona, eyakukucacisela ngale nkukacha ngale projekti. Nceda buza kubasebenzi besifundo okanye ugqirha nayiphi imibuzo ngayo le projekti oyakube ungayiqondi .Kubalulekile ukuba waneliseke kwaye ucacelwe uqonde

ukuba lungantoni uphando kwaye luku bandanyakanya njani? Kwaye ukuthatha inxaxheba akusosinyanzelo kwaye ukhululekile ukuyeka ukuthatha inxaxheba. Ukuba uthi Hayi, oko akusayi kuchaphazela wena okanye unyango lwakho nangayo nayiphi indlela .Uvumelekile ukurhoxa kwesi sifundo nangaliphi ithuba nangona ubuvumile ukuthatha inxaxheba. Esi sifundo siye savunyelwa yi Komiti yezoPhando emele uLuntu kweze Mpilo kwi Dyunivesti yase Stellenbosch kwaye siya kuqhutywa ngokwemiyalelo nemiqathango ka Zwelonke u Helsinki (Declaration of Helsinki) , imiqathango yo mZantsi - Afrika yoxilongo olusulungekileyo kunye ne Qumrhu lemiqathango yamalungelo oluntu ezonyango kwezophando.

Kutheni umenywa uthathe inxaxheba?

Izigulana ezinophazamiseko engqondweni zitsala nzima kwaye zingavelelwa luxinezeleko .Kukho uphando oluncinci olukhe lwenziwa emZantsi -Afrika olungophzamiseko kunye noxinezeleko. Njengoko usanda kufunyaniswa nophazamiseko, uyamenywa uthathe inxaxheba kwesi sisifundo.

Kwenzeka ntoni ngexesha lesifundo?

Iinjongo zesifundo uyakuzicaciselwa kwaye ukuba uyavuma ukuthatha inxaxheba esifundweni, umphandi uyakukucela ukuba usayine isivumelwano .Uyakwenza udliwano-ndlebe kunye nomphandi. Uyakukufundela imibuzo, wena ubhale impendulo phantsi. Imibuzo yokuqala ingokufumana inkcukacha ngawe, kanje ngobudala bakho kunye nolwimi lwakho. Imibuzo yesibini iyakuba ngoxinezeleko. Uyakukucela wenze imvavanyo zephepha nosiba, ukujonga inkumbulo, ukuqaphela kunye nokuqononondisa. .Iya kuba yimisetyenzana elula oyakufuneka uyigqibe. Ukuba udiniwe ngexesha lo dliwano ndlebe, wamkelekile ukuba uphumle phambi kokuba uqhubeke.

Umphandi uyakuqokelela ubume bempilo yakho kwi fayile yonyango lwakho, iscan sengqondo, kunye nengxelo yokubonakala kokuphazamiseka. Igama lakho liyakugcinwa liyimfihlo. Kuba umphandi uyakukunika inombolo yophando. Ngoko ke akukho magama ayakushicilelwa nakulo naluphi uhlobo lwefomu esiqokelele kulo. Akukho mayeza ayakusetyenziswa kwesisi fundo.

Ndinga khetha ukungathathi nxaxheba kwesi sifundo?

Ukuba akunqweneli ukuthatha inxaxheba kule projekti oko akusayi kuchaphazela unyango lwakho. Xa uthi wagqiba ekubeni uthtathe inxaxheba waze watshintsha ingqondo, nangasiphi isizathu, ukhululekile ukusiyeka isivumelwano sakho. Uyakuyekiswa kwesi sifundo sophando ukuba ufuna unyango olungxamisekileyo okanye ongakwaziyo ukuzalisa kwaye aqonde imibuzo.

Luyintoni uxanduva lwakho?

Oloni xanduva lwakho kukuba uphendule imibuzo kangangoko unako.

Uyakuzuzisa ntoni ngokuthatha inxaxheba kwesisifundo?

Ukuba sifumanisa ukuba unempawu zoxineleko olunzima olufuna unyango, uyakuthunyelwa kwindawo enonyango olwaneleyo lwentloko .kumelulek olululo.

Ukuthatha kwakho inxaxheba, kunganceda izigulana kwixa elizayo ngokwenza ogqirha bazi amathuba oxinelezeko kwizigulana ezinento engqondweni.

Zintoni ingozi ekuthatheni kwakho inxaxheba koluphando?

Asiboni ngozi kuwe ngokuthatha inxaxheba kwesi sifundo kodwa inani labantu okanye luve luchaphazekile emva kokuzalisa imibuzo ngenxa yempilo eya yavela engqondweni.

Ukuba akuvumanga ukuthatha inxaxheba yeyiphi enye into onokuyenza?

Njengoko bekutshiwo ngaphambili, ukuba akuvumi ukuthatha inxaxheba koluphando, kodwa yiva imfuno yokuthetha nomnye ngokunxulumene nempilo yakho.

Usenakho ukuthunyelwa kugqirha wengqondo okanye umeluleki wendawo ekufutshane nendawoyokuhlala ukulungiselela wena ukukunceda oko kuya kwenza ube ngcono kwimpilo yakho.

Ngubani onemvume kwinkcukacha zonyango lwakho?

Ulwazi oluqokelelweyo luyakugcinwa luyimfihlo kwaye lukhuselekile kwaye alusayi kwabelana nabani ongaphandle kwesifundo. Ukuba luye lwasetyenziswa ekupapashweni, igama lakho kunye nabo bathatha inxaxheba kwesi sifundo abasayi kwaziswa. Ngumphandi kunye nabaphathi bakhe, kunye nogqirha abakhoyo kunyango lwakho abaya kuba nemvume kwiziphumo zemibuzo zodliwano ndlebe. Igama lakho alisayi kushicilelwa kuyo nayo nyiphi ifomu.

Okokugqibela ukuba kufanele, abaxhasi besifundo, abahloli besifundo okanye amalungu equmrhu lozophando ayokuphengulula oluphando.

Kwenzeka ntoni apho kwenzeke into eyehla ngethuba leziphumo lesifundo oyakube uthathe inxaxheba kuso?

Akukho nanye ekhe yabonwa, isifundo siyakuba nodliwano ndlebe olunye nohlolo.

Ingaba uyakuhlawulwa ngokuthatha inxaxheba okanye kukho indleko?

Hayi, akusayi kuhlawulwa ngokuthatha inxaxheba kwesi sifundo kodwa ukuba sifuna utyelelo olongezelekieyo ukuza esibhedlela ukugqibezela uvavanyo, siyakukubuyisela indleko zokukhwela.

Kulindeleke ntoni ngexesha lodliwano-ndlebe? (Oko kukuthi luthatha ixesha elingakanani ukugcwalisa imibuzo)?

Udliwano-ndlebe lulindeleke ukuthatha imizuzu engamashumi amathandathu ukuya kwimizuzu engamashumi alithoba. Luvavanyo olunye, kuphela kwento onxulumene ngayo koluphando

Ingaba ikhona enye into ekufuneka uyenze okanye uyazi?

Ungaqhagamshelana nonkosazana Carike Vermaak ku 021 886 9447 ukuba uneminye imibuzo okanye uhlangana nengxaki ezinxulumene nesisifundo.

Ungaqhagamshelana neQumrhu lezempilo kwezophando kule nombolo [REDACTED] ukuba unazo unezikhalazo okanye inxalabo eziyakube zichaziwe ngugqirha wesifundo.

Uya kufumana ikopi yenkcukacha kunye neyesivumelwano ezize zakho.

Isifungo somthathi nxaxheba

Ngokutyikatya ngezantsi, Mna.....

Ndivuma ukuthatha inxaxheba kuphando oluthi.

Unxibelelwano lwempawu zoxinezelelo kunye nokujongwa kobunjani bokuthatha ebuchotsheni kwizigulane ezinto engqondweni.

NDIYAFUNGA UKUBA

Ndifundile okanye ndifundelwe ngale nkcukacha kunye nesivumelwano kwaye ibhalwe ngolwimi endilwaziyo nendililungeleyo.

Ndibe nethuba lokubuza imibuzo kunye nayo imibuzo iphendulwe kakuhle.

Ndiyaqonda ukuba ukuthatha inxaxheba kwesisifundo akusosinyanzelo kwaye andinyanzelwanga ukuthatha inxaxheba.

Ndinga khetha ukuyeka kwesisifundo nangaliphi ixesha kwaye andisayi kutshutshiswa nangayiphi indlela.

Ndingacelwa ukuyeka kwesisifundo phambi kokuba sigqitywe, ukuba ugqirha wesifundo okanye umphandi uva ndikulungele.

.....

Umsayino womthathi nxaxheba

.....

Umsayino wengqina

Isifungo somphandi

Mna.....ndifunga ukuba:

Ndicacise ngale ngcaciso ikule nkcukacha ku.....

Ndimkhuthazile ukuba abuze imibuzo kwaye athathe ixesha ukuphendule imibuzo.

Ndanelisekile ukuba uqonde ukuba zonke izinto zophando njengaphambili.

Ndisebenzise/Andisebenzisanga toliki (ukuba itoliki isetyenziswe ngoko itoliki mayisayine isifungo ngezantsi).

Isayinwe e (indawo).....ngomhla.....

.....

Umsayino womphandi

.....

Umsayino wengqina

Lebitso la morero yena: Ha o na le seso sa boko, na o tla fumana kगतello (leuba) (depression).

Nomoro ya thomelo: N10/05/149 le ECUFS NR 47/2012

Hloho ya morero: [REDACTED]

Adrese: Depatemente ya tsebo ya maikutlo, R.W.Wilcocks Mohaho, Ryneveld Straat, Stellenbosch 7600

Nomoro: [REDACTED]

O a memelwa ho re thusa ho bona na batho ba ba kae ba na leng seso sa boko, ba fumana leuba mona sepetlele sa Universitas.

Hape re batla ho bona kapa moo seso seo se leng teng bokong, le mofuta wa sona na ho a tswana ho basadi le banna ha ba fumana pheko.

Bala hantle pele o dumela ho re thusa. Ha o sa batle, o ka hana. Diuniversity tsa Stellenbosch le Freistata ke bona ba etsang morero ona.

Hobaneng ke wena a kopwang ho re thusa?

Hobane batho ba na leng seso sa boko, ke bona ba ka fumana pheko, jwale re batla ho sheba se etsa eng bophelong.

Ho tlo etswa eng?

Ba tla o bolela kaufela pele ba o kopa ho saena. Motho yena o tla o botsa dithaba, hape o tla di ngola. Tse ding wena o tla di ngola. Ha o kgathetse, o bolele, o ka phomola.

Ska tshaba ba tla ngola lebitso la hao, hobane ba o fa nomoro feela. Ha ba o fe moriana o mong.

Ke ka hana ho le thusa?

Ha o hana ha ho na taba. O tla fumana phekolo ska o no e fumana.

Ke tlo etsa eng?

O tlo araba dipotso feela, tseo ba tlo o botsa tsona.

Ke tlo fumana thuso?

Ha re bona o kula ho feeta, re tla fumana ngaka e tla o thusang. Dingaka tseo di tseba hantle, hobane wena o ile wa araba hantle.

Ha ke tlo utlwa bohloko kapa ha ke tlo kula ho feeta?

Tjhee, o ka kgatala feela mohlomong hobane o kula.

Ha ke hana, ke tlo etswa eng?

Ha o hana, empa o batla ho bua le motho o mong, re tla mo fumana o tsebe ho bua le yena.

Ke bomang ba tlo sheba dipampiri tsa ka?

Ha ho motho kante ho batho ba morero ona. Le lebitso la hao ha le hlahe mono.

Ha ke ka tswa kotsi?

Thjee, o tlo bua feela ha ba o botsa dipotso.

Ke tlo fumana tjhelete ha ke le thusa?

Tjhee, ha o tlo fumana tjhelete. Ha ba o lokolla sepetlele, re o batla hape, re tla o fa tjhelete ya transport ho kgutla mono sepetlele.

E tlo nka nako e kae?

Re tlo bua metsotso o 60-90.

Tse ding o batlang ho di botsa?

Bua le [REDACTED] [REDACTED] kapa Komiti [REDACTED] ha o batla ho tseba tse ding. O tla fumana foromo ya hao.

Totobatsa

Nna ke kenya lebitso mona.

Ke dumela ho le thusa .

Ke totobatsa hore ke ile ka bala foromo yena ka puo eo ke e utlang.

Ke ile ka botsa dipotso,ka fumana karabo.

Ke a utlwisisa ke le thusa ka boithaopo.

Ke ka tswa ha ke batla.

Ba ka ntsa ha ba bona ha ke kgone ho e qeta le ha ke sa ba thuse hantle.

Saena..... ka letsatsi

la.....2013.

.....

.....

Tshaeno (nna a dumelang)

Tshaeno (mopaki)

Totobatsa

Nna (lebitso) ke totobatse:

Ke boletsekaufela tse ngotswing mona.

O ile a botsa a di batlang.Ke mo arabile kaufela.

Ke a tseba o ile a utlwa hantle.

Ke a thuswa /ha ke thuswe ke toloko.

Saenaka letsatsi

la.....2013.

.....

Tsaeno (nna a etsang fuputsa)

.....

Tsaeno (mopaki)

--	--	--

Appendix B

Patient data form

Demographic background

- Gender: _____
- Age: _____
- Years of education: _____
- First language: _____
- Marital status: _____
- Occupational status: _____

BDI Score

--	--	--

Neuropsychological test scores

TMT Score

--	--	--

LNS total score

--	--

HVLT-R total correct responses

Trail 1 Trail 2 Trail 3

--	--	--

BVMT-R score

Trail 1 Trail 2 Trail 3

--	--	--

Patient

--	--	--

Relevant clinical information

• Referred from: _____

○ 1st Consultation (with whom, where):

○ Presenting complaints/features:

• Neurological examination:

• Working diagnosis:

MRI results (*from scan summary*)

Histological report

