

An investigation into exercise behaviour, preferences and quality of life of primary brain tumour patients

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Abstract

Brain tumors are the second leading cause of cancer deaths in young adults ages 20-39. According to the South African Medical Research Council, there was an estimated 801 deaths from brain cancer in South Africa in 2000. Primary and metastatic tumors are a significant cause of morbidity and mortality in cancer patients worldwide. The purpose of this study was to further the knowledge and expertise on exercise as an adjuvant therapy in brain tumor patients to improve quality of life (QoL). A sample of 14 brain tumor patients in various stages of the illness was recruited. Based on the objectives of this study, an Exercise and Quality of Life questionnaire (Fact-Br) was compiled. It contains 53 questions with high validity and good psychometric properties and efficacy to assess QoL in patients in the population. The main objective of the study was to find a correlation of QoL and physical activity. A positive correlation was evident, which indicated that physical activity would improve the QoL of the brain tumor patient. There was a statistically significant difference between patients who participated in exercise before diagnoses and those who did not in terms of perceptions of QoL ($p=0.034$). In the survey it showed that 59-71% patients engaged in mild to moderate exercise. There is a considerable rationale for promoting multimodal exercise interventions to improve physical capacity, vitality, and physical and mental well-being and to relieve fatigue during chemotherapy, thereby supporting cancer patients' daily activities.

Keywords: Brain tumor, quality of life (QoL), exercise intervention, FACT-Br, well-being.

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Introduction

Cancer is one of the most dreaded diseases of our time because it could strike anybody and may develop or affect the victim in various ways. More research has been done on cancer than on any other disease, yet treatment

changes almost monthly and sometimes daily, due to the physiological differences between patients and the various types and grades of cancers. For many years, researchers did not classify a brain tumor as cancer. A primary brain tumor does not spread to other parts of the body, but is life-threatening. For this very reason it was later classified as cancer (Roberts & Musella, 2005).

Cancerous tumors or malignant tumors are life-threatening due to their invasive and aggressive behaviour. Noncancerous tumors or benign tumors are also life-threatening if they should compromise any vital structures (Yang, 2006). Table 1 shows the classification of the tumor related to the current speed of growth and potential interference with brain functioning (Roberts & Musella, 2005).

Table 1: Four grades of brain tumors

Grade	Name	Status
I	Pilocytic Astrocytoma	Benign
II	Low grade Astrocytoma	Benign
III	Anaplastic Astrocytoma	Malignant
IV	Glioblastoma Multiforme	Malignant

Source: Adamsen *et al.* (2009).

The symptoms from primary brain tumors can be physical (e.g. fatigue, headaches), emotional (e.g. depression and anxiety) and neuro-cognitive (e.g. decrease in attention and concentration, memory loss) (Shaw & Robbins, 2006).

Six symptoms that mostly influence the quality of life of the patients are fatigue, uncertainty of the future, motor difficulties, drowsiness, communication difficulties and headaches. These were reported in more than 50% of patients with a glioma (Molassiotis, Wilson, Brunton, Chaudhary, Gattamaneni & Mcbain, 2010). It was also proved that postsurgical glioma patients have markedly reduced cardiorespiratory fitness, isokinetic strength, and muscle cross-sectional area (CSA) (Jones, Friedman, West, Mabe, Fraser, Kraus, Friedman, Tresch, Major & Readon, 2010).

Pre-treatment of a brain tumor patient sometimes includes the Karnofsky scale (KPS) that is used to assess the patient's performance status (Karnofsky & Burchenal, 1949, cited in Meyers & Hess, 2003). The patient is usually still competent in ADL if his or her KPS score is > 60 (Crooks, Waller, Smith & Hahn, 1991). An explosion of interest was noticeable in the measurement

of quality of life in patients with solid tumors receiving both adjuvant and palliative therapies (Rayson & Reyno, 2003). To sustain quality of life is one of the most important focuses for any brain tumor patient. Quality of life assessments in neuro-oncology are becoming increasingly relevant with the proliferation of intensive research into brain tumors and their therapy (Bampoe, Ritvo & Berstein, 1998).

The word “exercise” derives from a Latin root meaning “*to maintain*”, “*to keep*”, “*and to ward off*” (Kramer, 2003). Exercise is a powerful tool to simulate several brain processes, and it is becoming clear that therapeutic effects of exercise are not only good for cardiovascular and other diseases, but also, and this is important, good for your brain (Meeusen, 2005). Physical activity, such as walking or running on a treadmill, swimming, and weight-bearing exercise, is known to increase neural activity in both the peripheral and central nervous systems (Seo, Kim, Ko, Kim, Shin, Kim, Yoon & Kim, 2010).

Walking is not strenuous, so your leg muscles do not take up extra oxygen and glucose like with other types of exercise. As you walk, you effectively oxygenate your brain. Studies show that cerebral blood vessels can grow in response to exercise. Stroke risk was cut by 57% in people who walked as little as 20 minutes a day (Kramer, 2003). Brain scans confirm the benefits of physical exercise. Exercise is essential for preserving brain function for everyone. To explain how it works: muscles activate brain receptors. When acetylcholine is released at a neuromuscular junction, it crosses the synapse that separates the nerve from the muscle. It binds to the acetylcholine receptor molecules that initiate a chain of events that lead to muscle contraction. This is called the “mind-body connection” or the neuromuscular junction (Kramer, 2003). Exercise also increases the brain’s capillary bed and elevates cerebral blood flow (CBF) which, in turn, serves to help protect against the extensive damage that normally occurs following brain damage such as happens with a stroke. In a study by Davis and Bailey (1997) and Covalt (2006), an approximate 35% improvement in brain blood flow subsequent to stroke over that of the control animals was proved.

Serotonin is of critical importance in many brain functions, including the regulation of mood, heart rate, sleep, appetite, pain and many others. As a result, it is extremely important that the neuron releases the proper amount of serotonin at the right time (Senerth, 2002). Chronic exercise activates not only the synthesis but also the metabolism of serotonin in the cerebral cortex;

this neuronal adaptation is sustained until even one week after the termination of training (Dey, Singh & Dey, 1992).

The Blood Brain Barrier (BBB) consists of capillary endothelial cells that lack fenestrations (openings), have low pinocytotic activity and high electrical resistance, and are connected by continuous tight junctions to keep undesirable agents from entering the brain. Most molecules that cross the BBB are small in molecular weight, non-polar, and hydrophobic, permitting diffusion through lipid bi-layer membranes (Palmieri, Lockman, Thomas, Hua, Herring, Hargrave, Johnson, Flores, Qian, Vega-Valle et al., 2009). A progressively growing tumor usually opens the permeability of the blood brain barrier to create a blood-tumor barrier, but evidence and data are still limited on this topic (Palmieri *et al.*, 2009). According to a recent study from Ivanhoe Newswire, exercise can strengthen the BBB. Ratey summarised the positive influence of exercise on the brain by stating that, “*some exercise is better than nothing*” (Hobson, 2008).

Exercise modulates both plasticity and various supporting systems that participate in maintaining brain function and health (Cotman & Berchtold, 2002). Neglecting the human brain by not taking any exercise could negatively impact in many ways. It could, for example, result in depression and stress, to mention but two undesirable effects.

New studies have shown that exercise improves brain tumor patients’ moods and memories after they have received radiation therapy. Exercise appears to prevent the decline of erasable memory, which is similar to the memory problems patients with brain tumors experience following whole brain radiation (Ivanhoe, 2009).

Exercise intervention and the resultant improvement in the brain tumor patient’s QoL, encouraged further studies at Duke University in North Carolina, America. Studies were undertaken to determine the potential of exercise as an adjuvant therapy for the management of brain cancer patients. Through several systematic reviews and one meta-analysis, the studies showed promising preliminary evidence of physiological and psychological efficacy of exercise during and following the definitive adjuvant therapy (Jones, Guill, Keir, Carter, Friedman, Bigner & Reardon, 2006). Exercise has also been well-established as an effective intervention to prevent, minimize, or decrease fatigue (Ingram & Visovsky, 2007).

Exercise may help a cancer patient to cope in several ways, according to Jefford, MacCallum, Kong, MacCallum and Chapman (2008) and Hoffman (2010):

- It can help patients feel in charge of their lives;
- It can increase patients' energy and reduce fatigue;
- It can reduce nausea and vomiting for some patients receiving chemotherapy;
- It can help digestion and reduce constipation;
- It can increase strength, flexibility and heart and lung function;
- It can improve mood; and
- Improve self-confidence.

It is important in the case of exercise recommendations for the brain tumor patient, to try to maintain some level of physical activity. Exercise, even minimal physical exertion, increases heart rate and muscle activation, while at the same time boosting the body's tolerance to conventional brain cancer treatment (Cancer Treatment Centers of America, 2008).

Exercise rehabilitation during or after treatment is now considered an effective means of restoring physical and psychological health for the brain tumor patient during and after cancer therapy. Therefore, the process of rehabilitation includes dealing with not only the effects of completed treatments, such as surgery and radiotherapy, but also with the side effects of on-going treatments (Ewertz & Jensen, 2011). The approach to the exercise intervention needs careful consideration. Therefore, the goal of this study was to investigate and anticipate the exercise preferences of a brain cancer patient and the effect of the exercise on the quality of a patient's daily activities.

Methodology

This study obtained ethical clearance from the ethics committees of the Faculty of Humanities and the Faculty of Health Sciences at the University of Pretoria.

The design of the study was cross-sectional. Cross-sectional studies enable researchers to simultaneously study a disease and its exposure status in a specific population. The current study gave the researchers an indication of the behaviour of primary brain tumor patients during exercise. The questionnaires and literature supporting this study, helped the researchers to determine that exercise has a positive influence on the quality of life of primary brain tumor patients. The study included 14 subjects; both male and

female, that had been diagnosed with a primary brain tumor (see Table 2). Patients were in different stages after diagnosis. Some had not received treatment, some were undergoing treatment and some patients had recurring brain tumors.

Subjects were recruited through two oncology practices and were approached by postal service to provide the necessary details about the study. They had to state that participation would be voluntary. Informed consent was given, but confidentiality was guaranteed. The participants needed to complete the FACT-Br (QoL) questionnaire. The Exercise and Quality of Life questionnaire (Fact-Br) that was compiled focused on the areas identified in the objectives of this study. The Fact-Br scale contains a variety of measuring areas that are linked to the quality of life and experience of brain tumor patients. It contains 53 questions with high validity and good psychometric properties and efficacy to assess QoL in patients in the population (Preedy & Watson, 2010).

Table 2: Descriptive data of the subjects (n=14)

Participants	Number
Sex:	
Male	6
Female	8
Age (years):	
0-30	1
31-40	3
41-50	2
51-60	8
61-70	0
71 -80	0
Total participants	14

The responses on the questionnaires were captured on a computer and analyzed by means of the SPSS package (Statistical Product and Service Solutions). The following statistical techniques were used to do the analysis.

Spearman rank-order correlations: Spearman’s rho was used to determine the correlations between Physical, Social, Emotional, and Functional Well-being and perceptions of Fatigue and Quality of Life. Spearman’s rho is a non-parametric version of the Pearson correlation coefficient, based on the ranks of the data rather than the actual values. It is appropriate for ordinal data, or for interval data that do not satisfy the normality assumption. Values of the coefficient range from -1 to +1. The sign of the coefficient indicates the direction of the relationship, and its absolute value indicates the strength,

with larger absolute values indicating stronger relationships (SPSS Manual) (Howell, 1992).

The Mann-Whitney Test: The Mann-Whitney test was used for testing differences between means when there are two conditions and different subjects have been used in each condition. This test is a distribution-free alternative to the independent samples t-test. Like the t-test, Mann-Whitney tests the null hypothesis that two independent samples (groups) come from the same population (not just populations with the same mean). The Mann-Whitney statistic is obtained by counting the number of times an observation from the group with the smaller sample size precedes an observation from the larger group. It is especially sensitive to population differences in central tendency (Howell, 1992). This test was used to determine significant differences between those patients who did participate in exercise versus those who did not participate, on each of the indexes calculated.

Frequency analysis was used to describe the sample and also to give an indication of trends in the manner in which patients responded to the various questions in the questionnaire. Descriptive statistics were used to give an indication of patients' scores on the calculated indexes of Physical, Social, Emotional, and Functional Well-being and perceptions of Fatigue and Quality of Life. These descriptive statistics included the number of participants, minimum and maximum values, mean scores and standard deviations.

Since the sample was relatively small and consisted of only 14 patients, non-parametric statistics were used to analyze the data. The recruitment of primary brain tumor patients is fairly difficult due to the patients' time of diagnosis and the time of survivorship, that is very limited. Non-parametric tests, also known as distribution-free tests, are a class of tests that do not rely on a parameter estimation and/or distribution assumptions (Howell, 1992).

Results and Discussion

The study sample consisted of 14 patients with primary brain tumours. Demographic details are as follows: more than half of them were married; a third had high school diplomas or graduate-level qualifications respectively. Half of the patients were employed while 25% were disabled. Two thirds of the patients had smoked more than 100 cigarettes in their lifetimes, but 91.7% were not smoking at the time of the survey.

The results of the correlation analysis indicated that better physical well-being was significantly related to better emotional and functional well-being and better perceptions of QoL. Poorer physical well-being was associated with higher fatigue. Better emotional well-being was strongly correlated to better functional well-being and better perceptions of QoL. Higher emotional well-being scores were also associated with less fatigue. High fatigue was associated with poorer perceptions of quality of life.

The analysis of differences between those patients who did participate in exercise versus those who did not showed one statistically significant difference. There was a statistically significant difference between patients who participated in strenuous exercise before diagnoses and those who did not in terms of their perceptions of QoL ($p=0.034$). The QoL index was negative, thus higher scores were associated with poorer perceptions of quality of life. The mean scores indicated that patients who did participate in strenuous exercise prior to diagnoses had significantly higher scores than those who did not participate in strenuous exercise. The implication is that they have poorer perceptions of their current QoL than those who did not exercise. Patients diagnosed with cancer often experience psychological outfall after diagnosis. Starting with treatment they find the disease is synonymous with an inactive lifestyle, which results in loss of muscle mass and strength (Adamsen, Quist, Andersen, Moller, Herrstadt, Kronborg, Baardsgaard, Vistisen, Midtgaard, Christiansen, Stage, Kronborg & Rorth, 2009). The pooled estimate showed statistically significant increase of greater than 4.0 point on the FACT scale representing a clinically meaningful improvement in QoL from exercise. Literature indicates that patients that are more active will show a higher level of QoL than patients with an inactive daily lifestyle (Dimeo, 2001; Adamsen *et al.*, 2009).

The analysis of the difference between patients who exercised versus those who did not was conducted on all index scores for strenuous, moderate and mild exercise, prior to diagnosis, during treatment and after treatment. The Mann-Whitney U-tests were used due to the small sample size. Only one statistically significant difference was found. There was a statistically significant difference between patients who participated in strenuous exercise before diagnoses and those who did not in terms of perceptions of quality of life ($p=0.034$). The mean scores indicated that those patients who did participate in strenuous exercise prior to diagnoses had significantly higher scores than those who did not participate in strenuous exercise. The implication is that they have poorer perceptions of their current quality of life than those who did not exercise.

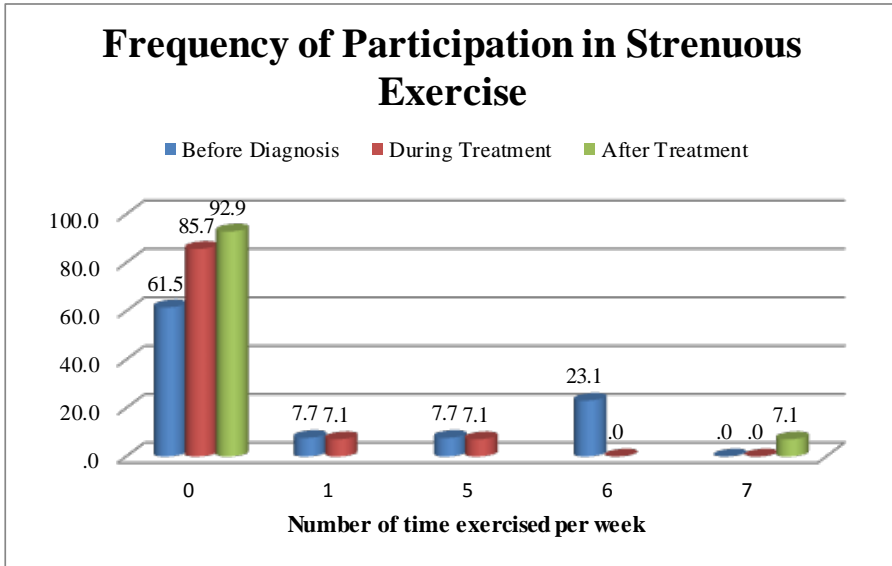


Figure 1: Participation in strenuous exercise by participants

It is clear from Figure 1 that more than half of the patients (61.5%) did not take part in strenuous exercise prior to diagnosis. This number increased to 85.7% during treatment and 92.9% after treatment. Only a small percentage of patients thus participated in strenuous exercise during treatment. Before diagnosis 23.1% exercised 6 times a week with 1 or no patients participating in exercise between 1 and 7 times a week.

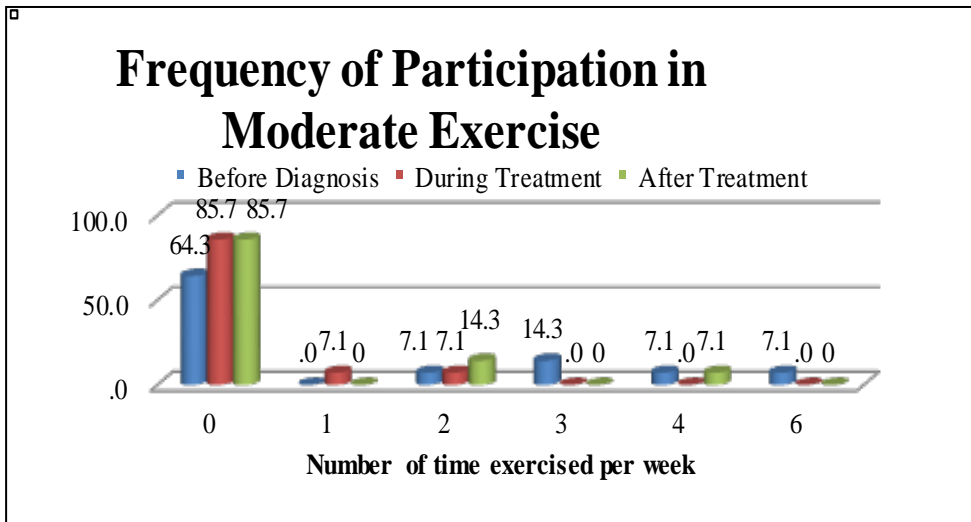


Figure 2: Participation in moderate exercise by participants

From Figure 2, it is once again evident that two thirds (64.3%) of patients did not exercise moderately prior to diagnosis. This figure increased to 85.7% during treatment and after treatment. Slightly more patients participated in moderate exercise twice a week when compared to those doing strenuous exercise.

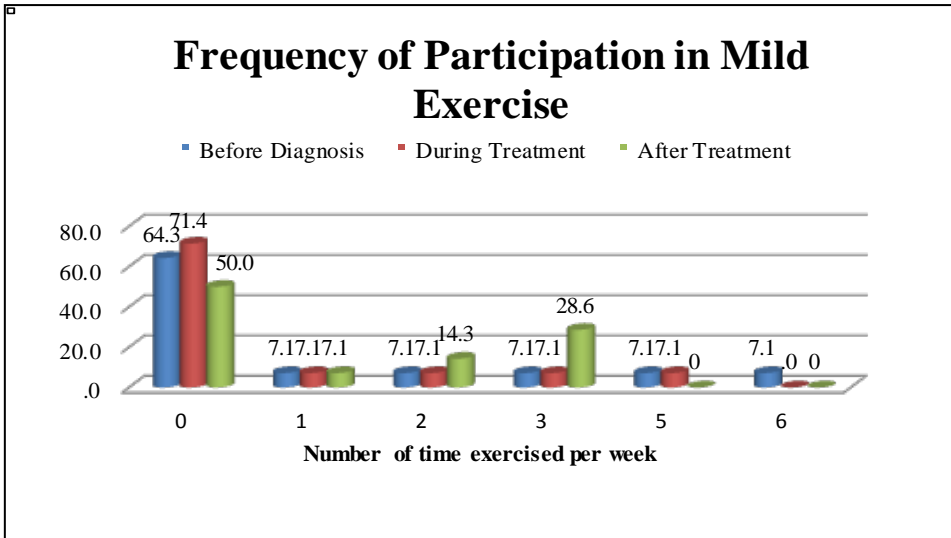


Figure 3: Participation in mild exercise by participants

In Figure 3, about two thirds (64.3%) of patients did not participate in mild exercise prior to diagnosis. This number increased to 71.4% during treatment, but after treatment only half of the patients (50%) indicated that they did not exercise mildly. More patients exercised twice a week, with 28.6% exercising 3 times a week after treatment. Compared to the strenuous and moderate exercises, more patients participated in mild exercise, especially after treatment.

From these figures, it is deduced that patients will rather participate in a mild exercise programme than a strenuous type of exercise programme. To exercise mildly is better than taking no exercise at all. Exercise intervention will improve physical capacity, vitality, and physical and mental well-being and will relieve an individual’s considerable amount of pain during chemotherapy, thereby supporting cancer patients’ daily living activities. Researchers have used high intensity exercise intervention that included aerobic exercises, strength training and relaxation exercises equivalent to 45 MET (Metabolic equivalent of task) on cancer patients a week (Adamsen *et al.*, 2009). It is important to note that brain tumor patients cannot always

follow the same exercise intervention programme that is set for other cancer patients. Primary brain tumor patients are often weaker than patients with breast cancer. Therefore, exercise intervention programmes for brain tumor patients are specifically designed for them.

From this study it was found that it was more likely that the patients would exercise at home, where they can control their movements and are familiar with their surroundings. Home-based exercises are usually moderate to light exercises because the patient controls the intensity of the exercises. Moderate to light exercises may be more effective than continuous rest, therefore walking exercises that are moderate in nature can increase the overall muscle tone, relieve emotional distress and help with ADL (Stasi, Abriani, Beccaglia, Terzoli & Amadori, 2003). According to Wiggins (2004), physical fitness can be increased at lower levels of exercise intensity. The belief therefore is that any exercise, mild or moderate, is better than rest or inactivity. The hypothesis of Durak, Harris and Ceriale (2001) was that not only is exercising safe, but that it will also show substantial improvements in QoL measures, independent of place of exercise or instructional methods used.

The general exercise prescription for people undergoing or having complete cancer therapy is low to moderate intensity, regular frequency (three to five times a week) for at least 20 minutes per session, involving aerobic, resistance or mixed types (Velthuis, Agasi-idenburg, Aufdenkampe & Wittink, 2009). Exercise appears to result in an improvement of the physiologic parameters, including increases in functional capacity and lean tissue, decrease in percentage of body fat, nausea and fatigue. It also shows an improvement in psychological indicators of well-being and quality of life (Freidenreich & Courneya, 1996).

Exercise modulates both plasticity and various supporting systems that participate in maintaining brain function and health (Cotman & Berchtold, 2002). This literature study shows that exercise very positively impacts on the brain. To be able to control both their emotional health and their physical functioning will positively impact on brain tumor patients. The emotional and physiological well-being will definitely impact on how the patient will respond to physical activity. Patients' different preferences and expectations may influence their response to an exercise intervention (Rogers, Vicari & Courneya, 2010).

In this study, a group of patients were recruited that were enthusiastic and positive about exercise. In most cases they were positive towards exercise intervention, even though they were not always capable of performing the exercises. They understood the positive influence of this intervention as an adjuvant therapy to cancer treatment.

To approach a patient holistically is very important. The focus must be on the physical, psychological, social and emotional aspects, which may all influence the patient’s injury or illness. Holistic approach equals quality of life. Quality of life will impact the total of the person’s well-being.

In this study, there was a positive correlation between emotional and physical well-being, which means that being physically active in ADLs helps the patient to be more emotionally stable. The results of this study show that exercise influences behavioural patterns (for example to relieve stress), and can reduce depression and anxiety in humans (Cotman & Berchtold, 2002). Stress and emotions are related. Emotions are a very powerful tool in human life. They usually define a person’s way of thinking. It is important for a brain tumor patient to be as positive as possible throughout the diagnosing and treatment phase.

Table 3: Results of responses on questions pertaining to quality of life

VARIABLES QUALITY OF LIFE	Not at all	A little bit	Some what	Quite a bit	Very much
I am able to concentrate	14.3	14.3	28.6	21.4	21.4
I have had seizures	50.0	21.4		21.4	7.1
I can remember new things	7.1	21.4	14.3	28.6	28.6
I get frustrated that I cannot do things I used to	14.3	28.6		21.4	35.7
I am afraid of having a seizure	35.7	7.1	21.4	7.1	28.6
I have trouble with my vision	14.3	42.9	14.3	14.3	14.3

The correlation of quality of life and physical activity, which is the main objective of the study, is positive. According to the results in Table 3, patients mostly did experience some changes in their QoL to various degrees. Areas of their lives that seemed to be negatively affected were their ability to concentrate, their vision and hearing to some extent, being able to find the right words, putting their thoughts together and expressing their thoughts, as

well as the ability to read, write and drive a vehicle. This, in turn, affected their independence though most (78.6%) indicated that they did not need help in caring for themselves at all. While half (50%) of them have not experienced any seizures, 21.4% did have a small number of seizures (“a little bit”), while 21.4% experienced a moderate number of seizures (“quite a bit”). Only 1 person (7.1%) experienced a great number of seizures. Patients had different opinions as to their ability to remember new things, getting frustrated that they could not do the things they used to and being bothered by the drop in their contribution to their families. A third of the patients (35.7%) indicated that they were not at all afraid of having a seizure, while the rest had some concern. A third (35.7%) was not bothered by the change in their personalities at all, while 28.6% did show a certain amount of (“a little bit of”) concern. Just over a third did show some concern about this issue. Most of the respondents (64.3%) indicated that they were able to make decisions and take responsibility, while 28.6% only felt so “a little bit” or “not at all”. Most patients felt that they were able to put their thoughts into actions to varying degrees. This indicates that physical activity or exercise will improve the QoL of the brain tumor patient. Exercise is a safe and an effective intervention for cancer patients, independent of the location and instructional methods. Therefore, according to Durak *et al.* (2001), any exercise has a positive influence on the cancer patient, no matter where, when and how it is administered. This means that exercise will definitely impact on the patient’s physical well-being and emotional well-being. The growing body of research on exercise for patients with cancer shows dramatic improvements in physiological and psychological functioning in patients participating in aerobic exercise programmes (Young-McCaughan & Arzola, 2007).

Brain tumor patients are a different population of cancer patients. They represent a population with very low survival rates, with only 19% survival of the disease for five years or less. The treatment of brain tumor patients depends on when the patient has been diagnosed, early or in the last stages. Patients with higher grade brain tumors will only survive six months, and in the last two months they will be either hospitalized or in palliative care. Therefore it is important to educate the patients when they are diagnosed and prepare them for exercise as an adjuvant therapy, even though it is only for a very short period. In the last 20 years we have seen advances in the treatment of brain tumor patients, specifically regarding QoL (Janda, Steginga, Langbecker, Dunn, Walker & Eakin, 2007).

Conclusion

Despite the fact that brain tumor patients do not have a high survival rate according to previous studies, exercise has been found to have a positive influence on a brain tumor patient's health. Physical activity, such as walking or running on a treadmill, swimming and weight-bearing exercise, are known to increase neural activity in both the peripheral and central nervous systems (Seo et al., 2010). Brain tumor patients can improve their overall physical strength and aerobic fitness, even if only to cope with ADLs. Again, physical activity or exercise intervention for brain tumor patients only helps these patients to improve their QoL. Ruden *et al.* (2011) maintain that exercise behaviour is a strong predictor of survival that provides incremental prognostic value to the Karnofsky Performance Scale (KPS).

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