COMPARATIVE EFFECTS OF OVERGROUND WALKING EXERCISE AND COGNITIVE REHABILITATION ON COGNITION, BRAIN-DERIVED NEUROTROPHIC FACTOR, QUALITY OF LIFE AND PARTICIPATION RESTRICTION AMONG STROKE SURVIVORS

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CERTIFICATION

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DEDICATION

This piece of work is dedicated to Almighty Allah, my parents - Alhaji Aliyu Abba and Hajiya Aisha Sule Minjibir, and stroke survivors.

ABSTRACT

Post-Stroke Cognitive Impairment (PSCI) is a major cause of disability, dependence on Activities of Daily Living (ADL), Participation Restriction (PR) and poor Quality of Life (QoL). Evidence has shown that the gold standard for PSCI rehabilitation is Cognitive Rehabilitation (CR). Studies have also shown that aerobic exercises with treadmills and bicycle ergometers are effective in the management of PSCI. However, only few studies have examined the effects of Overground Walking Exercise (OWE), which is an inexpensive, accessible and natural form of aerobic exercise. This study was conducted to investigate the comparative effects of an eight-week OWE and Cognitive Rehabilitation (CR) on cognition, Brain-Derived Neurotrophic Factor (BDNF), QoL and PR among stroke survivors.

The study design was randomised-controlled trial, which involved 53 stroke survivors with mild-to-moderate cognitive impairments, purposively recruited from three tertiary hospitals in Kano, and randomly assigned into three groups using computer-generated random numbers. The participants received moderate-intensity self-paced OWE, Zoltan protocol CR and combined interventions in the respective groups (OWEG=17, CRG=18 and OWECRG=18). Each group received thrice weekly interventions for eight weeks. About 5 ml venous blood sample was collected aseptically, allowed to clot and centrifuged to harvest the serum sample. Cognition, serum BDNF (ng/ml), QoL and PR were assessed using Montreal Cognitive Assessment, Enzyme-Linked Immunosorbent Assay (ELISA) technique, Stroke-Specific Quality of Life questionnaire and London Handicap Scale, respectively at baseline, 4th week and 8th week. Data were summarised using descriptive statistics and ANOVA at $\alpha_{0.05}$.

Age of participants was 48.42±27.39 years. At baseline, duration since stroke onset was 26.70±27.25 months. The OWEG, CRG and OWECRG were comparable in cognition (18.06±3.60; 19.00±3.90; 19.50±3.85); BDNF levels (13.05±8.27; 13.81±11.04; 9.54±6.46); QoL (191.00±28.85; 202.72±28.83; 197.44±39.83) and PR (12.06±4.02; 10.39±4.24; 10.56±3.31) at baseline. Within-group comparisons at week 4 showed significant improvements in cognition (20.53±2.83; 22.78±3.95; 22.44±3.37); BDNF levels (13.88±8.26; 15.62±12.98; 11.54± 9.17) and QoL (202.24±22.49; 211±21.99; 204.17±41.24) for the OWEG, CRG and OWECRG, respectively. The PR significantly decreased to 9.00±2.45; 9.56±2.73 and 9.44±3.47 at week 4 for the OWEG, CRG and OWECRG, respectively. Similarly, within-group comparisons at week 8 showed significant improvements in cognition (26.24±2.51; 25.22±3.26; 25.17±3.47); BDNF levels (14.69±8.85; 18.13±14.96; 13.35±10.56) and QoL (243.53±17.84; 222.89±18.35; 221.28±25.72) for the OWEG, CRG and OWECRG, respectively. There were significant reductions in PR to 7.24±2.05; 8.39±2.70; 8.39±2.43 at week 8 for the OWEG, CRG and OWECRG, respectively. There was no significant across-group difference in cognition, BDNF levels and PR. The percentage mean changes at week 8 in cognition (45.3%, 32.7%, 30.5%) and PR (40.0%, 19.3%, 20.6%) were highest for the OWEG, while the percentage mean change in BDNF level was highest in the OWECRG (12.6%, 31.3%, 38.3%). There was a significant across-group difference in QoL at week 8, with the best improvement observed in the OWEG.

Overground walking exercise, cognitive rehabilitation and a combination of both had comparable positive effects on cognition, level of brain-derived neurotrophic factor, and participation. However, overground walking exercise resulted in better improvement in participants' quality of life.

Keywords: Cerebrovascular accident, Post-stroke impairment, Aerobic exercise
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CHAPTER ONE
INTRODUCTION

1.1 Background to the Study

Stroke is one of the leading causes of disability worldwide, with about 24 to 49% of stroke survivors presenting with some forms of disability or the other (do Carmo, 2015). Ekeh et al. (2015) described stroke as a major reason for death in Nigeria, with about one-third of deaths occurring within 24 hours of admissions and another third within 30 days. It has been reported that stroke contribute significantly to the cost of medical rehabilitation in Africa (Badaru et al., 2015). Stroke causes significant neurological deficits including motor, sensory/perceptual and cognitive impairments (Lawrence et al., 2001). Cognitive dysfunction, affecting one or more domains, has been associated with history of stroke (Sun et al., 2014). Qu et al. (2015) noted that stroke ranks second only to Alzheimer's disease in the aetiologies of cognitive impairment in outpatient clinics.

Cognitive impairment following a stroke or Post-Stroke Cognitive Impairment (PSCI), is a dysfunction in overall cognitive function or sub-domains of cognition such as memory, problem solving, and language (Sun et al., 2014). Its prevalence varies from 30-70% among stroke survivors depending on factors such as the characteristics of the individuals and the geographic locations (Sun et al., 2014; Mellon et al., 2015). PSCI is a leading cause of impairments and dependence among stroke survivors (Sun et al., 2014). It has significant negative impact of patients' functional abilities (Mercier et al., 2001) and quality of life. It is worth noting that while Singam et al. (2015) had suggested an association between PSCI and reduced community participation, Cawood et al. (2016) reported that physical and perceptual impairments also contribute to participation restriction among stroke survivors.

Quality of Life (QoL) is often moderately reduced among stroke survivors compared to non-stroke individuals (Teng et al., 2012). Factors such as stroke severity, disability and depression were reported as important predictors of QoL among stroke survivors in Nigeria

(Badaru et al., 2015). Mellon et al. (2015) had also identified cognitive impairment as a factor affecting QoL among stroke survivors. Studies conducted in Nigeria have consistently reported poor QoL among stroke survivors, which was influenced by factors such as level of education, marital status and functional abilities (Hamzat and Peters, 2009; Badaru et al., 2015). However, there is a dearth of research on how cognitive dysfunction affects QoL of stroke patients in Nigeria (Fatoye et al., 2007).

Community participation among stroke survivors is closely linked on their functional abilities (Hamzat et al., 2014). Cognitive function, particularly executive function, has been associated with adherence to rehabilitation among adults with cognitive impairment after stroke (Skidmore et al., 2009). Additionally, a reduction in community participation after stroke has been associated with cognitive deficits (Spitzer et al., 2011). This has led to the recommendations for incorporating the International Classification of Function and Disability (ICF) concept in the rehabilitation of individuals with PSCI (Wolf, 2011). The ability to perform Activities of Daily Living (ADL) has been reportedly associated with cognitive skills required for planning and executing tasks among stroke patients (Claesson et al., 2005). According to Oros et al. (2016) cognitive impairment had significant negative impact on ADL among stroke survivors. Prosper et al. (2017), on the other hand, suggested that low to moderate PSCI may not necessarily affect ADL, indicating that recovery can still occur.

Research has also shown a correlation between cognitive function and motor recovery post-stroke. Better global cognition at early to later stages of stroke had been associated with improved motor function in the later stages (Verstraen et al., 2016). Cognitive function, including executive function, has been associated with physical functions such as balance in stroke patients (Cho & Lee, 2013) and balance, in turn, has been associated with participation (Hamzat & Kobiri, 2008). Deficits in specific cognitive functions, such as memory and abstraction have been found to be accompanied by disturbances in gait, balance and limb functions post-stroke (Verstraen et al., 2016). Attention has also been directly associated with mobility, explaining the improvements in gait and balance that occur following combined cognitive and motor intervention (Choi et al., 2015).

Brain-Derived Neurotrophic Factor (BDNF), a type of neurotrophins (Lasek-Bal et al., 2015), is an important regulator of neural survival, development, function, and plasticity (Nassenstein et al., 2003). BDNF mediates nerve existence, learning and plasticity in adults (Staats et al., 2005). It elicits changes in synaptic structure and chemical messenger secretion in nerve morphology (Rezaei et al., 2016). Reduced BDNF levels in the brain have been linked with cognitive dysfunction, memory problems and depression (Staats et al., 2005). BDNF levels have also been associated with motor function after stroke (Chang et al, 2017), with higher levels at the acute phase predicting better functional independence (Lasek-Bal et al., 2015).)

Physiotherapy is recognised as an important intervention at all levels of stroke (Olaleye et al., 2014). Adherence to treatment is considered an important determinant of neurorehabilitation outcomes (Hamzat et al., 2014). However, adherence to post-stroke rehabilitation has been linked to cognitive function (Skidmore et al., 2010). Therefore, strategies to prevent or slow down cognitive decline are important in stroke rehabilitation (Rohde et al., 2017), highlighting the importance of diagnosing and treating cognitive impairment alongside motor and sensory impairments (Cawood et al., 2016). Rehabilitation strategies employed in the management of PSCI include restoration, compensation and behavioural strategies (Hochstenbach et al., 2003). Occupational therapists are the professionals typically involved in the rehabilitation of cognitive dysfunction (Cawood et al., 2016). A systematic review by Abba et al. (2020b) highlighted the role of physiotherapy in the management of cognitive impairment post-stroke, and one approach that had been reported to improve cognition among stroke patients is aerobic exercise (Abba et al., 2020b).

1.2 Statement of the Problem

Neurological deficits following a stroke include motor, sensory/perceptual and cognitive impairments (Lawrence et al., 2001). Stroke is the second leading cause of cognitive impairment (Qu et al., 2015). Existing literature has highlighted the effectiveness of aerobic exercise, administered through treadmill or cycle ergometer, in managing PSCI (Abba et al., 2020b). However, a notable limitation of the reviewed studies was that the outcome assessed was solely cognitive impairment, which is just a single component of the

International Classification of Functioning, Disability and Health (ICF), without consideration for the QoL issues and participation restriction experienced by patients with PSCI. Furthermore, reports showed a lack of adequate stroke management and human resources in many African countries (Olawale et al., 2011). Hence, the need for an economical and pragmatic form of aerobic exercise that can be as effective as or more effective than treadmill training and can be easily implemented as a treatment option for stroke survivors, particularly in regions lacking advanced equipment like treadmills or bicycle ergometers. Overground walking has been suggested as a potential solution, but empirical studies on its efficacy are lacking. Therefore, this randomised control trial was designed to assess the comparative effects of overground walking exercise and cognitive rehabilitation on cognition, BDNF, QoL, and participation restriction among stroke with PSCI. The following questions were also addressed:

a) What would be the effects of Over-ground Walking Exercise (OWE) on cognition, BDNF, QoL and participation restriction among stroke survivors with PSCI?
b) What would be the effects of Cognitive Rehabilitation (CR) on cognition, BDNF, QoL and participation restriction among stroke survivors with PSCI?
c) What would be the effect of combined OWE and CR (OWECR) on cognition, BDNF, QoL and participation restriction among stroke survivors with PSCI?
d) What would be the comparative effects of OWE, CR and OWECR on cognition, BDNF, QoL and participation restriction among stroke survivors with PSCI?

1.3 Aim of the Study

The aim of this study was to investigate the comparative effects of an 8-week over-ground walking exercise (OWE), cognitive rehabilitation (CR) and combined OWE and CR (OWECR) on cognition, BDNF, QoL and participation restriction (PR) among stroke survivors with PSCI.

1.4 Objectives of the Study

The specific objectives of this study were to:

a. investigate the effects of an 8-week over-ground walking exercise (OWE) on cognition, BDNF, QoL and PR among among stroke survivors with PSCI.
b. evaluate the effects of an 8-week cognitive rehabilitation (CR) cognition, BDNF, QoL and PR among among stroke survivors with PSCI.
c. assess the effects of an 8-week combined OWE and CR on cognition, BDNF, QoL and PR among among stroke survivors with PSCI.
d. compare the effects of 8-week OWE, CR and combined OWE and CR (OWECR) on cognition, BDNF, QoL and PR among among stroke survivors with PSCI.

1.5 Hypotheses

1.5.1 Main Hypotheses

1. There would be no significant difference in the effect of OWE on cognition, BDNF, QoL and PR among stroke survivors with PSCI in Kano, Nigeria, across baseline, 4th week and 8th week.
2. There would be no significant difference in the effect of CR on cognition, BDNF, QoL and PR among stroke survivors with PSCI in Kano, Nigeria, across baseline, 4th week and 8th week.
3. There would be no significant difference in the effect of OWECR on cognition, BDNF, QoL and PR among stroke survivors with PSCI in Kano, Nigeria, across baseline, 4th week and 8th week.
4. There would be no significant difference in the effects of overground walking exercise (OWE), cognitive rehabilitation (CR), combined overground walking exercise and cognitive rehabilitation (OWECR) on each of cognition, BDNF, QoL and participation restriction among stroke survivors with PSCI in Kano, Nigeria across baseline, 4th week and 8th week.

1.5.2 Sub-Hypotheses

1. There would be no significant difference in cognition across baseline, 4th week and 8th weeks of Over-ground Walking Exercise (OWE) among stroke survivors with PSCI in Kano, Nigeria.
2. There would be no significant difference in BDNF across baseline, 4th week and 8th weeks of OWE among stroke survivors with PSCI in Kano, Nigeria.
3. There would be no significant difference in QoL across baseline, 4th week and 8th weeks of OWE among stroke survivors with PSCI in Kano, Nigeria.
4. There would be no significant difference in participation restriction across baseline, 4th week and 8th weeks of OWE among stroke survivors with PSCI in Kano, Nigeria.
5. There would be no significant difference in cognition across baseline, 4th week and 8th weeks of cognitive rehabilitation (CR) among stroke survivors with PSCI in Kano, Nigeria.
6. There would be no significant difference in BDNF across baseline, 4th week and 8th weeks of CR among stroke survivors with PSCI in Kano, Nigeria.
7. There would be no significant difference in QoL across baseline, 4th week and 8th weeks of CR among stroke survivors with PSCI in Kano, Nigeria.
8. There would be no significant difference in participation restriction across baseline, 4th week and 8th weeks of CR among stroke survivors with PSCI in Kano, Nigeria.
9. There would be no significant in cognition across baseline, 4th week and 8th week of combined overground walking exercise and cognitive rehabilitation (OWECR) among stroke survivors with PSCI in Kano, Nigeria.
10. There would be no significant in BDNF across baseline, 4th week and 8th week of OWECR among stroke survivors with PSCI in Kano, Nigeria
11. There would be no significant in QoL across baseline, 4th week and 8th week of OWECR among stroke survivors with PSCI in Kano, Nigeria
12. There would be no significant in participation restriction across baseline, 4th week and 8th week of OWECR among stroke survivors with PSCI in Kano, Nigeria
13. There would be no significant difference in cognition among stroke survivors with PSCI across 4 weeks of OWE, CR, and OWECR.

14. There would be no significant difference in BDNF among stroke survivors with PSCI across 4 weeks of OWE, CR, and OWECR.
15. There would be no significant difference in QoL among stroke survivors with PSCI across 4 weeks of OWE, CR, and OWECR.
16. There would be no significant difference in participation restriction among stroke survivors with PSCI across 4 weeks of OWE, CR, and OWECR.
17. There would be no significant difference in cognition among stroke survivors with PSCI across 8 weeks of OWE, CR, and OWECR.
18. There would be no significant difference in BDNF among stroke survivors with PSCI across 8 weeks of OWE, CR, and OWECR.
19. There would be no significant difference in QoL among stroke survivors with PSCI across 8 weeks of OWE, CR, and OWECR.
20. There would be no significant difference in participation restriction among stroke survivors with PSCI across 8 weeks of OWE, CR, and OWECR.

1.6 Delimitation

The study was delimited as follows:

a. Settings: Aminu Kano Teaching Hospital (AKTH), Murtala Mohammed Specialist Hospital (MMSH) and Muhammad Abdullahi Teaching Hospital (MAWTH) which are tertiary health institutions in Kano state, Nigeria.

b. Participants: First documented incident stroke patients with mild to moderate cognitive impairments.

c. Interventions: Over-ground walking exercise, cognitive rehabilitation using Zoltan protocols, combined over-ground walking exercise and cognitive rehabilitation protocol.

d. Instruments: Montreal Cognitive Assessment, Melsin ELISA reagent, Stroke Specific Quality of Life Questionnaire and London Handicap Scale to assess cognition, BDNF, QoL and participation restriction respectively.

1.7 Significance of the Study

The outcomes of this study have shown that overground walking exercise, cognitive rehabilitation and a combination of both all improved cognition and quality of life, increased the level of serum BDNF, and reduced participation restriction among cognitive-impaired chronic stroke survivors. The best performance in QoL was however, among participants in the overground walking exercise group. Also, the highest percentage mean changes in cognition and participation restriction were among participants in overground walking exercise group. Therefore, overground walking exercise, an inexpensive, accessible and natural medium of aerobic exercise, could be used to improve cognition, increase social and community participation and enhance QoL among chronic stroke survivors in low-resource settings like Nigeria.

1.8 Limitations of the study

A major limitation of this study was that the combined intervention group received half the duration of each individual intervention, rather than the full duration of each separate intervention. This could have accounted for why the combined intervention group did not show significant improvement beyond those observed in the individual intervention groups.

1.9 Definition of Terms

a) **Quality of Life:** is the individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns (Colver, 2009).

b) **Participation:** is involvement in life situations for example responsibilities, maintaining relationships, education, and recreation (Colver, 2009).

CHAPTER TWO
LITERATURE REVIEW

2.1 Stroke

Stroke is defined as a clinical syndrome of presumed vascular origin, characterised by rapidly developing signs of focal or global disturbance of cerebral functions lasting more than 24hours or leading to death (WHO, 1988). However, American Heart Association (AHA) and American Stroke Association (ASA) critiqued the old definition of stroke for being mainly clinical and not accounting for clinical research, developments in science and technology (Sacco et al., 2013). Ischaemic stroke specifically refers to central nervous system infarction accompanied by overt symptoms, while silent infarction causes no known symptoms (Sacco et al., 2013). Central nervous system infarction is defined as brain, spinal cord, or retinal cell death attributable to ischaemia, based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury (Sacco et al., 2013).

2.1.1 Epidemiology of Stroke

The incidence of stroke is relatively lower in females than in males. However, the prevalence of stroke is more in women than in men because women generally live longer than men (Niewada et al., 2006). The annual incidence of stroke is estimated to be between 21 and 42 per 100 000 population in Europe (Liu et al., 2006). In England, the incidence of stroke is 178/100,000 population among men and 139/100,000 population among women, while in Scotland, there are 202 stroke events per 100,000 population among men and 160 per 100,000 population among women (Tomasik et al., 2003). In the UK approximately 152,000 strokes occur annually, accounting for more than one case for every five minutes (Liu et al., 2006). About 50% of stroke victims are dependent on others for their activities of daily living (Liu et al., 2006). Stroke is the third leading cause of mortality in the United States, coming closely behind cardiac diseases and cancers. It is estimated that stroke occurs more commonly among the black race than the Caucasians.

Approximately 50–70% of stroke survivors regain functional independence, while about a third remain permanently dependent (Cooper, 2006).

The World Health Organization (WHO, 2002) estimates showed that the second most common cause of death among individuals 60 years and above, was stroke. The Republic of China recorded the highest number of stroke deaths globally, which represent about 30% (Liu et al., 2006). Stroke accounts for 7% of mortality among males and 10% among females (Tomasik et al., 2003). It was reported that after cancers, cardiovascular and pulmonary diseases, stroke is the leading cause of death in the United Kingdom (Tomasik et al., 2003).

In Africa, the annual incidence ranges from 87,000–625,300 new cases, and a prevalence of 2,060,000–4,930,000 stroke survivors (Adeloye, 2014). There is inadequate data on the current epidemiology of stroke in African and other low- and middle-incomes countries (Owolabi et al., 2018). This is due to the nature of studies conducted in Africa which were mostly hospital-based case series (Owolabi et al., 2018). In Nigeria, the 24-hour case fatality of stroke is about 31%- and 30-days case fatality is 38.4% (Abubakar & Sabir, 2013). The annual stroke prevalence rate is 131/100,000 population in the Middle-belt (Sanya et al., 2015), 13.31/1000 in the Niger delta (Ezejimofor et al., 2017) and accounts for 2.4 % of all emergency admissions in South-west of Nigeria (Ogun et al., 2005).

2.1.2 Risk Factors for Stroke

Elevated blood pressure is the major risk factor for stroke (Tomasik et al., 2003). Hypertension was reported to be responsible for about half of the death due to stroke among adults (WHO, 2013). Hypertension is the leading risk factor for stroke in sub-Saharan Africa, with a Nigerian study reporting more than 80% prevalence of hypertension in stroke patients (Richard, 2013). Atrial fibrillation, coronary artery disease, myocardial infarction (MI), previous stroke, hyperlipidaemia, alcohol consumption, smoking, diabetes mellitus and sickle cell disease are other major risk factors (Tomasik et al., 2003; Abubakar & Sabir, 2013). Diabetes mellitus and hypertension have been identified as the more prevalent risk factors in individuals of African descent, whereas hypertension and atrial fibrillation appear to be greater risk factors among Caucasians (Richard, 2013). However, study has

found no gender differences in risk factors other than hypertension (Watila et al., 2011). In addition to other risk factors, Human Immunodeficiency Virus (HIV) increases the risk of ischaemic stroke in young adults (Richard, 2013). Stroke from ischaemia occur from reduced circulation due to embolism, or other conditions affecting blood coagulation (Cooper, 2006).

2.1.3 Classification of Stroke

Stroke is classified based on several criteria, such as duration of onset, severity, mechanism and regions of the brain affected among others. According to the Stroke Recovery and Rehabilitation Roundtable (SRRR), stroke can be classified as: hyperacute, occurring within 0-24 hours of onset; acute, ranging from one to seven days after onset; sub-acute stroke, ranging from seven days to three months after onset; and chronic stroke, starting from six months after onset and above (Bernhardt et al., 2017).

In terms of the mechanism of stroke injury, strokes are classified as either ischaemic or haemorrhagic strokes. Ischaemic strokes occur when there is a blockage or occlusion of the arterial blood supply to the brain, leading to infarction (WHO, 2005). Ischaemic strokes account for approximately 80% of cases in high-income countries, and about 60% of cases in low- and middle-income countries (Alkali et al., 2013). The second type of stroke occurs when there is rupture of the arterial blood supply to the brain leading to haemorrhage (WHO, 2005). Haemorrhagic strokes can manifest as either intracerebral haemorrhage or subarachnoid haemorrhage, depending on whether there is there is bleeding within the brain tissues or between the two meninges known as the pia and arachnoid. Haemorrhage strokes make up about 20% of cases in advanced countries and approximately 40% of cases in developing countries (Ogun et al., 2005).

2.1.4 Motor and sensory impairment post-stroke

Motor and sensory impairments resulting from stroke are consequences of damage to the arterial blood supply to the specific areas of the brain responsible for such motor and sensory functions (Frías et al., 2018). Stroke-related motor impairments can be unilateral or bilateral, taking the form of hemiplegia or hemiparesis (WHO, 2006). Stroke survivors

often experience paralysis of the facial muscles, upper limbs, trunk and lower limbs. The severity of this paralysis can range from mild to moderate or severe, depending on the extent of the brain injury. Typically, stroke survivors initially present with flaccidity, which gradually transitions to spasticity in the later stages (Kuo & Hu, 2018). Spasticity manifests as impairment of muscle tone, primarily in the antigravity muscles of the upper and lower limbs (Kuo & Hu, 2018). This spasticity, which is a sign of an upper motor neuron injury, presents as resistance to passive movements of the joints affected, with the resistance increasing as the velocity of passive movement increases. The onset of spasticity restricts coordinated voluntary movements, and these movements tend to improve as spasticity decreases in the later stages (Zeng et al., 2020).

Stroke can also lead to impairments in sensory function, which may be unilateral or bilateral. Stroke can affect both superficial and deep sensations. Common superficial sensory impairments include altered temperature perception, tactile sensitivity and nociception (Bolognini et al., 2015). Stroke survivors may also experience impairments of speech, vision, perception and hearing. Additionally, movement disorders, balance and gait impairments can occur when there is impaired proprioception or ataxia (WHO, 2006). These impairments manifest when affect individuals attempt to stand or ambulate. Balance impairment is categorised into static balance impairment, occurring during stationary or standing positions, and dynamic balance impairment, which affects activities involving gait or mobility (Khan & Chevidikunnan, 2021).

2.1.5 Post-Stroke Cognitive Impairment

Stroke is the second leading cause of cognitive dysfunction, following Alzheimer's disease (Cengic et al., 2011). Post Stroke Cognitive Impairment (PSCI) is a significant long-term consequence of stroke (Danovska et al., 2012). Cognitive abilities encompass memory, spatial manipulation, executive skills, language proficiency, perception, reasoning, perceptual speed, which collectively contribute to the broader concept of intelligence (Giles, et al., 2013). Dysfunction of cognition refers to impairments in these cognitive domains. It is important to note that PSCI is a distinct disability, which is a consequence of stroke, and not related to any other underlying disorders (Danovska et al., 2012).

2.1.5.1 Epidemiology of Post-Stroke Cognitive Impairment

Post-Stroke Cognitive Impairment (PSCI) is particularly common in cases of ischaemic stroke, accounting for up to 80.97% of cases (Sun et al., 2014; Qu et al., 2015). It typically reaches its peak around three months after a stroke (Danovska et al., 2012). The prevalence of PSCI varies significantly across different countries, regions and cultures (Sun et al., 2014). Global data on PSCI reveals that European countries, such as Britain and Sweden had reported prevalence rates ranging from 24% to 39% at three months post-stroke when assessed using the Mini-Mental Status Examination (MMSE), and prevalence of up to 96% have been reported in the same population when comprehensive neuropsychological test batteries were used (Sun et al., 2014). This variance can be attributed to the limited sensitivity of the MMSE to mild cognitive impairment and executive function (Douiri et al., 2013). In the United States, the prevalence of PSCI is around 19.3%, while in the Caribbean, it can reach as high as 58.9%. Asian countries also exhibit varying rates, with prevalence reported at 69.8% and 21.8% in South Korea and Hong Kong respectively (Sun et al., 2014).

In Nigeria, different studies have reported varying prevalence rates of PSCI. Akinyemi et al. (2014) documented a prevalence of 39%, whereas Fatoye et al. (2007) reported a rate of 17% in hospital-based studies. A study among patients attending physiotherapy out-patient clinics found a prevalence of up to 67.14% (Abba et al., 2020a). These discrepancies may be attributable to the differences in the assessment tools used in these studies. Akinyemi et al. (2014) and Fatoye et al. (2007) employed the Vascular Neuropsychological Battery and modified Mini-Mental State Examination (mMMSE) respectively, while Abba et al. (2020a) used MMSE to assess cognitive function.

Despite the high prevalence of PSCI, it has received limited attention from clinicians, because it is often masked by other physical disability (Sun et al., 2014). Higher education has been associated with better cognitive performances among stroke patients (Cengic et al., 2011; Sun et al., 2014). Additionally, American-Mexicans with PSCI tend to have more

cognitive decline than non-Hispanic whites, and bilingual stroke patients have been shown to have better cognitive function (Alladi et al., 2010).

2.1.5.2.1 Risk Factors for Post-Stroke Cognitive Impairment

The risk factors for PSCI include age (Sun et al., 2014), previous history of stroke (Zhuo, 2015), vascular factors such as large hemispheric or lacunar infarct (Mellon et al., 2015), polypharmacy, hypertension, diabetes mellitus, hyperlipidaemia, smoking and atrial fibrillation (Mellon et al., 2015). Higher education was associated with better cognitive performances among stroke patients (Cengic et al., 2011; Sun et al., 2014). American-Mexicans with PSCI tend to have more cognitive impairment than in non-Hispanic whites. However, bilingual stroke patients have been proved to have better cognitive function especially executive function (Carlson & Meltzoff, 2008).

2.1.5.2.2 Assessment and Diagnosis of Post-Stroke Cognitive Impairment

The diagnosis of PSCI involves two diagnostic criteria which include presence of a cognitive impairment detected using neuropsychological tests and clinical history of stroke (Federico, 2013). The procedure for the diagnosis involves the following steps:

Neuropsychological tests for post-stroke cognitive impairment

The National Institute for Healthcare Excellence (NICE) guidelines recommended cognitive assessment of stroke patients within 6 weeks of their stroke as it relates to their normal ADLs (Mellon et al., 2015). Neuropsychological deficit should always be linked to the patient's functional abilities (Tatemichi et al., 1994). The neuropsychological tests include cognitive assessment for either global cognitive functions, specific cognitive domains functions or both. The global cognitive function is obtained by summing up of all individual cognitive domains scores. There are several paper and pencil outcome measures used to assess global cognitive function such as Mini-Mental Status Exam (MMSE), Montreal Cognitive Assessment (MoCA), Addenbrooke's Cognitive Examination Revised (ACER), Cambridge Cognitive examination (CAMCOG) and Wechsler Adult Intelligence Scale (WAIS). On the other hand, specific outcome measures are used based on the domain of interest. For example, Digit Span Test is used to assess memory, while Stroop test and Trails A and B used for assessing attention Blanchet et al. (2016).

The screening, assessment and diagnosis of PSCI involve the global assessment using instruments such as Mini mental status examination (MMSE) (Quaney et al., 2009; Blanchet et al., 2016), Montreal Cognitive Assessment (MoCA) (Marzolini et al., 2013; Tang et al., 2016) and Addenbrooke's Cognitive Examination-Revised ACER (El-Tamawy et al., 2014) among others.

Cognitive assessment encompasses the individual domain usually integrated to produce the global scores. The specific domain assessment includes that of memory, attention, orientation, language etc. Memory domains of the various instruments Stroke Impact Scale (SIS) version 2.0 (Kluding et al., 2011), memory component of MMSE (Marzolini et al., 2012) were used to assess memory. Other instruments used for assessing memory are Revised-Hopkins Verbal Learning Test (Blanchet et al., 2016), digit Span Backwards (Kluding et al., 2011) and Brown–Peterson paradigm (Tang et al., 2016). Attention among patients with PSCI can be assessed using Trail-Making Task, Paced Auditory Serial Addition Test (Ploughman et al., 2008), Stroop test (Quaney et al., 2009) Flanker test (Kluding et al., 2011) and continuous performance test (Blanchet et al., 2016). On the other hand, Concentration was assessed by Symbol digit substitution test (Ploughman et al) and concentration domains can be assessed using of MMSE and MoCA test (Marzolini et al., 2012).

a. Mini-Mental Status Examination: It is uni-dimensional scale that comprises of eleven tasks. It assesses several domains such ability to recall, language, attention etc. It is easy to administer in duration of not more than 10 minutes. Total point between 23 and below reveals dysfunction of cognition, while between 24 and 30 shows good cognition. It has an excellent psychometric property (Blake et al., 2002).

b. Montreal Cognitive Assessment (**MoCA):** Evaluates cognition. The MoCA has a reliability of $\alpha = 0.71$. when compared to mini-mental state examination, it has a concurrent validity with $r=0.62$, $p<0.001$(Ramírez et al., 2014). Administration of MoCA assessment of patients based on sub-sections visuospatial skills, memory recall, clock drawing test, language, abstraction memory index scale etc. it is easy to administer but requires training

to make diagnosis using the test. The overall points are summed up to determine presence, absence and level of cognition/ cognitive impairments.

Radiological investigations

Radiological investigations are used to determine the extent and severity of stroke as it to PSCI (Huang et al., 2020). The Computed Tomography (CT) Scan and Magnetic Resonance Imaging (MRI) are used to determine the areas and size of brain lesion. Brain MRI is used in addition to assess brain atrophy. Positron-Emission Tomography (PET) scans are used to determine amyloid plaque positivity

Laboratory investigations

Laboratory investigations for PSCI consist of assessment of biomarkers. Emphasis on the disease specific biomarkers is placed which helps in the advancement of diagnosis and treatment of diseases. Therefore, the detection of biomarkers in circulating blood serum, plasma and cerebrospinal fluid (CSF) may improve the accuracy of diagnosis and prognosis in PSCI. Changes in the levels of these molecular biomarkers in the blood and urine are related to a decline in cognitive function post-stroke. There are two major biomarkers used for laboratory investigations in PSCI namely; growth factors and metabolic biomarkers.

Growth factors

There are basically two major growth factors (Brain-Derived Neurotrophic Factor and Insulin-like Growth Factor-1) assessed during laboratory investigations of biomarkers related to PSCI. The measurement of circulating BDNF appears to be of great interest for the diagnosis, the prognosis and treatment monitoring of various diseases of the central nervous system (Staats et al., 2005). BDNF is present in the blood and is widely used as an indicator of brain BDNF levels by neurologists and psychiatrists (Lasek-Bal et al., 2015). BDNF was also reported to be a determinant of motor function post-stroke (Chang et al., 2017). BDNF concentration correlates with the degree of vasogenic damage to white matter of the brain. The normal reference range for BDNF is 15.83-79.77ng/ml. The Insulin-like Growth Factor-1 (IGF-1) levels in acute stroke were related to the recovery of neurological

function and prognosis (Zhang & Bi, 2020). Level of serum IGF-1 at baseline during intervention could significantly predict the improvement of cognition in stroke patients undergoing cognitive rehabilitation (Ploughman et al 2019). A higher level of IGF-1 was associated with recovery of neurological function and better outcome (Sonntag et al., 2013). A range outside 90-370ng/ml is associated with pathology.

Metabolic Biomarkers: Metabolic biomarkers involved in PSCI include Homocysteine (Hcy), Trimethylamine-N-Oxide (TMAO) and Retinoic Acid (RA). Studies have shown that there is a relationship between high plasma level of Hcy and PSCI. Higher level of Hcy (>15micromoles/L) from onset of predicts high risk of developing PSCI at 3-6 months post-stroke. Other biomarkers involved in PSCI include inflammatory biomarkers, oxidative damage biomarkers, genetic biomarkers and elevated plasma C- reactive protein (CRP) levels.

2.1.5.4 Differential diagnosis of post-stroke cognitive impairment

The differentials diagnosis for post-stroke cognitive impairment are:

a. Dementias
b. Alzheimer's disease
c. Parkinson’s Disease
d. Post-stroke Depression

2.1.5.5 Prognosis for Post-Stroke Cognitive Impairment

Low scores on MMSE in the early stage of ischaemic stroke is an important predictor of disability after three months (Tatemichi et al., 1995) Patients with PSCI significantly suffer dependent life, which interfered with community ambulation (Tatemichi et al., 1995) About 25% of stroke survivors will develop Dementia Later in life and Dementia after stroke is related to high risk of recurring stroke (Danovska et al., 2012) PSCI patients and caregivers are vulnerable and have poor functions, quality of life (Fatoye et al., 2007).

2.1.6 Treatment Approaches for Stroke

Stroke rehabilitation is a complex process that poses challenge to health care providers, patients and families due to the difficulty in the administration of appropriate procedure on patients with varying level of severity and availability of rehabilitation therapies (Chen et al., 2014). Improvement in stroke depends on level of disabilities at early stages (Mercier et al., 2001). Rehabilitation training is important in improving the abilities and participation of stroke (Lum et al., 2009). Stroke rehabilitation is focused on performing meaningful, repetitive and intensive tasks based on principle of motor learning and neuroplasticity (Takeuchi & Izumi, 2013). There are a range of treatment strategies for the rehabilitation of stroke at a certain level of recovery such as aerobic exercises (Hamzat & Nelson, 2015), Bobath concept, Proprioceptive Neuromuscular Facilitation (Kawahira et al., 2004) and Constraint Induced Movement Therapy (Abdullahi, 2014), among others.

A range of methods of exercise approaches are available for the treatment of stroke survivors. Strategies for stroke management include the Bobath's approach, Brunnstrom's approach, Proprioceptive Neuromuscular Facilitation (PNF) techniques, therapeutic electric stimulation, electromyographic biofeedback, intensive rehabilitation therapy and constraint-induced therapy, were deployed for management of stroke survivors (Kawahira et al., 2004).

Constraint Induced Movement Therapy (CIMT) is a treatment strategy for stroke (Wolf et al., 2006). The CIMT can be administered across all levels of severity of motor impairments (Bonifer and Anderson 2003) and as well be administered in hospitals and home setting (Tariah et al., 2010). Studies on upper limb recovery post-stroke revealed substantial enhancement of recovery in favour of CIMT than the counterparts (Corbetta et al., 2015).

Proprioceptive Neuromuscular Facilitation (PNF) is applied as a strategy to manage impairments of nervous system (Lee et al., 2013). PNF concept is an approach that can be applied on post-stroke patients. PNF improves limb functions by reducing impairments of motor and sensory functions (Akosile et al., 2011; Yeole et al., 2017) and trunk

(Hariharasudhan & Balamurugan, 2016). It improves recovery of motor impairment through correction in the order of muscle contraction (Shimura & Kasai, 2002).

2.1.6.1.1 Management of Post-Stroke Cognitive Impairment

Cognitive impairment post-stroke constitutes as burden during care giving (Rohde et al., 2017). Rehabilitation adherence of post-stroke patients was related to level of cognition (Skidmore et al., 2010). Therefore, approaches that will avert or slowdown cognitive decline are important in stroke rehabilitation (Rohde et al., 2017), this underscores the recommendation that assessment and management of dysfunction of cognition should be considered as important as motor and sensory impairments (Cawood et al., 2016). Assessment and management of dysfunction of cognition should be considered as important as motor and sensory impairments (Cawood et al., 2016). New guidelines for stroke rehabilitation programme suggested integration of cognition rehabilitation into motor and other components of stroke rehabilitation procedures (Cengic et al., 2011; Mellon et al., 2015). The procedure for cognitive intervention includes screening for cognitive functions, planning, selecting suitable technique (Giles et al., 2013). Cognitive rehabilitation is broadly classified into approaches 3 namely: Compensatory approach, Remedial approach and Dynamic interactional (Hoffmann et al., 2010). Other managements include acupuncture (Liu et al., 2014) and aerobic exercise (Oberlin, et al., 2017).

Cognitive Rehabilitation

This is a scientifically treatment method applied to enhance cognitive function (Olukolade & Osinowo, 2017). The development and administration of this rehabilitation method is mainly carried out by an occupational therapist (Cawood et al., 2016). However, neuropsychologists are also involved in the evaluation and management of cognitive function (Olukolade & Osinowo, 2017). The two major categories of cognitive rehabilitation are restorative and compensatory (Hochstenbach et al., 2003).

The restorative approach involves patients with mild to moderate impairment while the compensatory approach involves the severe form of cognitive impairment (Hochstenbach

et al., 2003). Cognitive rehabilitation is applied through different modes such as computer based, paper and pencil among others (Shin & Kim, 2015; Wentink et al., 2015). Numerous studies described the relevance of cognitive rehabilitation on different conditions such as depression (Olukolade & Osinowo, 2017), cognitive impairment following brain injury (Langenbahn et al., 2013), and cognitive dysfunction after stroke (das Nair, 2016).

A very significant component of stroke rehabilitation is the cognitive rehabilitation (Zucchella et al., 2014). It is applicable to overall global cognition or specific domains such as memory (das Nair, 2016), and attention among others (Loetscher & Linclon, 2013). Cognitive rehabilitation improves overall quality of life (QoL) of various neurological deficits (Guàrdia-Olmos et al., 2015). However, a study by Wentink et al. (2015) reported that cognitive rehabilitation did not have effect on QoL patients post stroke.

Physiotherapy approach to management of post-stroke cognitive impairment

Some physiotherapy approaches have been shown to be effective in the management of PSCI. Example of the approaches are aerobic exercise, resistance training, constraint induced movement therapy etc. The reported types of interventions to be effective are aerobic exercise alone or combined with other activities. The exercises could be in the form of treadmill, Lower body cycle (Blanchet et al., 2016) Bicycle ergometery (El-Tamawy et al., 2014) and BWSTT (Ploughman et al., 2008). These aerobic exercises are sometimes administered combined with resistance exercise on treadmill or cycle ergometer (Marzolini et al., 2012). The combined aerobic and resistance exercise may be in the form of fixed or progressive resistance (Quaney et al., 2009; Kluding et al., 2011)

Aerobic Exercises

A therapeutic exercise includes aerobic, resistance or both (Tiozzo et al., 2015). Aerobic exercise was reported to be under-utilised in stroke rehabilitation (Billinger et al., 2015). Therefore, studies on stroke rehabilitation recommend the incorporation of aerobic exercise in the routine management (Hamzat & Nelson, 2015). Structured aerobic exercise programmes for stroke survivors are recommended by level 1 evidence (Lomaglio & Perry, 2016). Aerobic exercise can be administered to stroke survivors in the form of cycle

ergometer, overground waking, treadmill training among others (Stoller et al., 2012). Post stroke survivors are trained within 40-70% HRR (Lomaglio & Perry, 2016). The duration of the treatment sessions lasts between 20 to 60 minutes, with the frequency of 3-5 times per week depending on the intensity (Lomaglio & Perry, 2016).

A study by Potempa et al. (1996) reported that aerobic exercises are useful in enhancing physical function of individuals with stroke. Exercises can be used to improve impairments of motor, balance and cognition post-stroke (Tiozzo et al., 2015). Aerobic exercise also improves cardio-respiratory fitness with QoL of stroke survivors (Hamzat, 2002). However, a study by Murdoch et al. (2016) reported lack of evidence to support aerobic exercise training to improve motor and sensory functions, rather it can be used to enhance stamina, fitness and performance. Treadmill training has been shown to be useful in enhancing spatiotemporal gait parameters in stroke survivors (Patterson et al., 2008). However, researches have described a contradictory finding for effect of aerobic exercises on cognitive function post stroke (Ploughman et al., 2008; Quaney et al., 2009; Kluding et al., 2011; Marzolini et al., 2012; El-Tamawy et al., 2014; Blanchet et al., 2016; Tang et al., 2016).

Mechanism of action of exercises on post-stroke cognitive impairment

Aerobic exercise improves BDNF level by stimulating its productions in the peripheral blood cells (mononuclear cell, T & B lymphocytes). This process augments for the relative lack of BDNF in the nervous system especially the hippocampus & cortex (Miranda et al., 2019). It also increases hippocampal volume with better cardio-respiratory fitness (Cui et al., 2018).

In another report, the combined resistance training with aerobic exercise affects the outcomes of cognition following stroke by influencing the production of IGF-1. In human brain, IGF-1 receptors are predominantly found in the hippocampus, parahippocampal areas, amygdala, cerebellum and cortex. Moderate to high intensity resistance training increases the levels of IGF-1 which promotes neuronal growth (Cui et al., 2018). The exercise increases the peripheral IGF-1 productions to from liver (Gubbi et al., 2018). A

higher level of IGF-1 was associated with recovery of neurological function & better outcome (Sonntag et al., 2013).

On the other hand, combined resistance training improves post-stroke cognitive function by acting on the level of serum homocysteine. Combined resistance training and aerobic exercise leads to lower levels of Hcy. Due to its overall negative effect on neural function, reduction in homocysteine results in better cognitive function post-stroke (Cui et al., 2018). PSCI is a threat to the recovery of stroke survivors. Moderate to high intensity aerobic exercise is reported to be effective in the management of PSCI. Early routine aerobic exercise be used in the management of stroke-related PSCI by Physiotherapists. Cognitive tests and biological investigations be included as stroke outcomes of for effective management.

2.1.7 Association between PSCI and characteristics of stroke survivors

Studies have revealed that with advancing age, the risk for developing PSCI increases (Kang et al., 2021; Kaddumukasa et al., 2023; Utomo & Pinzon, 2023). Studies conducted on the effect of aerobic exercise on PSCI have mean age of participants of 60 years and above. (Ploughman et al., 2008; Quaney et al., 2009; Kluding et al., 2011; Marzolini et al., 2012; Blanchet et al., 2016). The lower the academic qualification the higher the chance of PSCI and vice versa (Kaddumukasa et al., 2023; Utomo & Pinzon, 2023). On the other hand, a study by Aam et al. (2020) revealed that PSCI affects any type of stroke. Studies on the effect aerobic exercise on PSCI involved all type of stroke (Ploughman et al., 2008; Marzolini et al., 2012; Tang et al., 2016). In terms of duration of stroke, it was stated that stroke is affected by PSCI at any time of the occurrence or duration of stroke (Kaddumukasa et al., 2023). However, cognitive impairment after stroke is most common within the few weeks of occurrence.

2.1.8 Association between cognitive impairment and activities of daily living post-stroke

The ADLs are self-care activities carried out by individuals independently in their everyday life (Proper et al., 2017). ADL consist of basic activities such as feeding, grooming,

toileting bathing and transfer collectively referred to as Basic ADLs (BADLs) (Makoshi, 2005). Activities for example shopping, laundering, food preparation, housekeeping among others are termed Instrumental Activities of Daily Living (IADL) (Lee, 2014).

Singam et al., (2015) showed that 84% of patients post stroke were able to partake in difficult and social everyday task. Performance on ADL was found to be associated with cognitive skills in order to plan and execute tasks (Claesson et al., 2005). Moreover, cognitive impairment was reported to have substantial effect on the ADL of patients post stroke (Oros et al., 2016). Therefore, impairment of participation among stroke is remarkably linked with cognition (Spitzer et al., 2010). However, a study by Prosper (2017) reported that mild to moderate cognitive impairment post stroke does not affect ADL hence recovery not affected. The ADL of patients with dysfunction of cognition after stroke indicates the overall severity and hence the recovery after intervention (Claesson et al., 2005). Interventions focusing on improvement of cognitive function greatly depends on the utilisation of ADL as an outcome (Mokashi, 2005).

2.1.9 Association between cognitive impairment and participation post-stroke

Participation can be defined as the involvement of life situations and things that give meaning to the lives of people (Skidmore et al., 2009). The life situations include employment, homemaking, sports, leisure activities, community and spiritual activities (Wolf et al., 2011). Social participation has been shown to affect patients post stroke across mobility, employment, leisure activities and physical dependence (Vincent-Onabajo, 2013). Cognitive function post stroke plays a significant role on the activities and participation of patients. (Cawood et al., 2016).

Cognitive function greatly affects the social participation of patients with neurological disorders (Glei et al., 2005). Cognitive function especially executive function was found to be associated with adhesion to rehabilitation participation among adults with cognitive impairment after stroke (Skidmore et al., 2009). Therefore, incorporation of International Classification of Function and Disability (ICF) was recommended in the management of patients with post stroke cognitive impairment (Wolf, et al., 2011).

2.1.10 Association between cognitive impairment and quality of life post-stroke

QoL is used is a determinant of a condition and evaluate effectiveness of interventions (Gill & Feinstein, 1994). Disability following neurological condition was reported to as independent determinant of health-related QoL (Abubakar & Isezuo, 2012). The overall QoL in patients with nervous system disorders for example stroke deteriorate progressively over a period of time (Badaru et al., 2015), including stroke survivors with cognitive impairment (Teng et al., 2012).

The importance of QoL assessment in stroke rehabilitation is underscored by its relevance in the quantification of the impact of, and as an outcome for, cognitive impairment among stroke patients (Abubakar & Isezuo, 2012; Baumstarck et al., 2014). It is endorsed that quality of life of stroke survivors be considered as an outcome when offering rehabilitation intervention aimed at improving their cognitive functions (Lee et al., 2013; Takemasa et al., 2016).

2.1.11 Association between cognitive impairment and Brain-Derived Neurotrophic Factor (BDNF) post-stroke

The BDNF is a type of neurotrophins (Lasek-Bal et al., 2015). Neurotrophins play crucial roles in neural existence, growth, function, and plasticity (Nassenstein et al., 2003). Four neurotrophins have be characterized in humans, namely: Nerve Growth Factor (NGF), BDNF, neurotrophin-3 (NT-3), and neurotrophin-4 (NT-4) (Huang & Reichardt, 2001). These neurotrophins share a common inherited gene, and display similar sequences and structures (Huang & Reichardt, 2001).

The synthesis of BDNF involves precursor production called proBDNF, which is proteolytically cleaved to produce mature BDNF (Chang et al., 2017). BDNF is an important mediator of neuronal survival, synaptic plasticity, and adult learning (Staats et al., 2005). It produces extended transformation in nerve junction structures and chemical messenger secretion within neuronal morphology of the nervous system (Rezaei et al., 2016).

Measuring circulating levels of BDNF has become a valuable indicator for assessing brain BDNF levels in the field of neurology and psychiatry (Lasek-Bal et al., 2015). The measurement of circulating BDNF holds significant interest for diagnosing, prognosing and monitoring the treatment of various disorders of the nervous system. Decreased levels of BDNF in the brain have been associated with cognitive impairment, memory deficits and depression (Staats et al., 2005). Furthermore, BDNF has been identified as a determinant of motor function recovery following stroke (Chang et al., 2017). Patients with higher level of BDNF during the acute phase of a stroke tend to have better prognosis in terms of achieving functional independence (Lasek-Bal et al., 2015).

2.2 Systematic Review Studies on the Effect of Aerobic Exercise on Cognitive Function among Stroke Survivors

Several reviews have examined the impact of aerobic exercises on post-stroke cognitive impairment (PSCI), but they have yielded conflicting and inconclusive results due to the varying methodologies used (Cummings et al., 2012; Garcia-Soto et al., 2013; Mahmudul-Hasan et al., 2016; Zheng et al., 2016; Vanderbeken & Kerckhofs, 2017). For instance, the reviews by Cummings et al. (2012), Vanderbeken & Kerckhofs (2017) and Mahmudul-Hasan et al. (2016) involved studies with diverse populations, including those with traumatic brain injuries or animal subjects. Zheng et al. (2016) employed a single search item for interventions, while Garcia-Soto (2013) focused on the effects of combined aerobic and resistance exercises on cognition. Consequently, reaching a definitive conclusion has proven challenging. Therefore, a systematic review was conducted to examine the available scientific evidence and provide a comprehensive analysis of the effectiveness of aerobic exercise in improving cognitive function after a stroke.

2.2.1 Materials and Methods for the Systematic Review

The systematic review followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) by Moher et al. (2009). The guideline provides checklist on effective writing of systematic review which include setting objectives, writing method and result.

2.2.1.1 Search Terms and Search Strategy for the Systematic Review

Comprehensive searches were conducted in PubMed, Embase and Web of Science databases, spanning their respective inception dates to July 13, 2017, in order to identify relevant published articles. The search strategy employed specific terms for the various databases as shown in Table 2.1. Additionally, search filters were applied across all databases to restrict the search output for type of article to clinical trials involving human subjects and that are published in English language (Figure 2.1).

Table 2.1: Search strategy adopted in the review process for each database

Database	**Search strategy using PICO terms**
PubMed	*#1: "cerebral hemorrhage [MeSH]" OR "stroke" [MeSH] OR "cerebrovascular disorders" [MeSH] OR "brain infarction" [MeSH] OR "cerebral infarction" [MeSH]* *#2: "cerebral hemorrhage" OR "stroke" OR "cerebrovascular disorders" OR "brain infarction" OR cerebral infarction* *#3: #1 OR #2* *#4: "exercise" [MeSH] OR "exercise therapy" [MeSH] OR "aerobic exercise" [MeSH] OR "activity, physical" [MeSH]* *#5: "exercise" OR "physical activity" OR "aerobic exercise" OR "treadmill" OR "running" OR physical conditioning* *#6: #4 OR #5* *#7: "executive function" [MeSH] OR "cognition disorders" [MeSH] OR "recovery of function" [MeSH] OR "cognition" [MeSH] OR "memory" [MeSH]* *#8: "cognition" OR "cognitive" OR "neuroplasticity" OR "cognitive function" OR "functional recovery" OR executive function* *#9: #7 OR #8* *#10: #3 AND #6 AND #9* *#11: Search (#10) Filters; English, Clinical Trials, Humans*
Embase	*#5: #4 AND ('clinical article'/de OR 'clinical trial'/de OR 'human'/de OR 'randomized controlled trial'/de) AND 'article'/it* *1,585* *#4: #1 AND #2 AND #3* *3,184* *#3: cerebral AND hemorrhage OR stroke OR (cerebrovascular AND disorders) OR (brain AND infarction) OR (cerebral AND infarction)* *445,780* *#2: exercise OR (physical AND activity) OR (aerobic AND exercise) OR treadmill OR running OR (physical AND conditioning)* *718,239* *#1: cognition OR cognitive OR neuroplasticity OR (cognitive AND function) OR (functional AND recovery) OR (executive AND function)*
Web of Science	*#4: (#3 AND #2 AND #1) AND **LANGUAGE:** (English) AND **DOCUMENT TYPES:** (Article) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Time span* *#3: TS= (cognition OR cognitive OR neuroplasticity OR cognitive function OR functional recovery OR executive function) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Time span= All years)* *#2: TS=(exercise OR physical activity OR aerobic exercise OR treadmill OR running OR physical conditioning) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Time span=All years* *#1: TS=(cerebral hemorrhage OR stroke OR cerebrovascular disorders OR brain infarction OR cerebral infarction)*

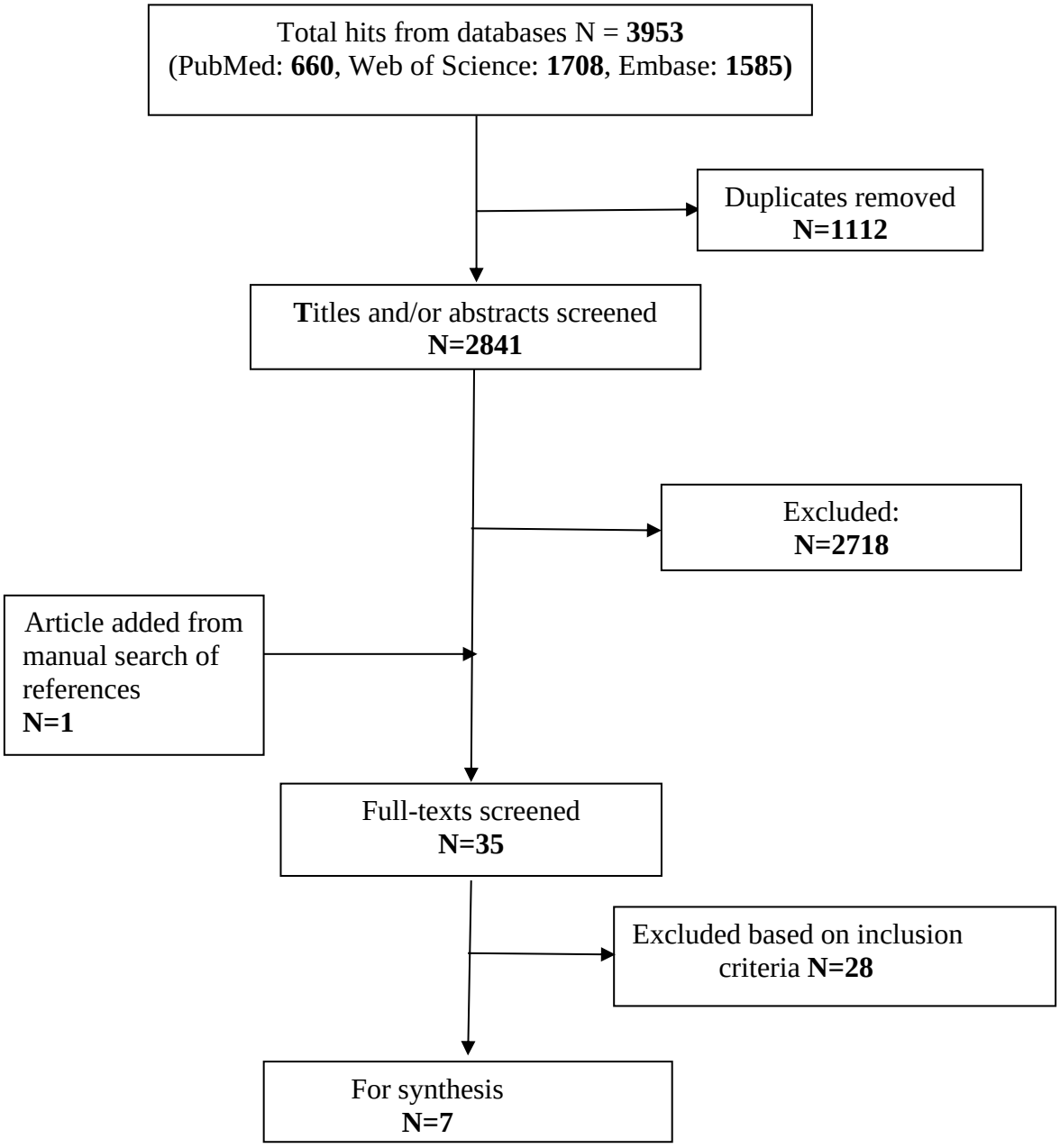

Figure 2.1: Flowchart of the of the Review

Eligibility Criteria for Studies including the Systematic Review

The eligibility criteria for the review encompassed studies that investigated the short and long-term effect of aerobic exercises interventions (I) on different domains of cognitive function, including memory, attention, and executive function outcomes (O) among stroke survivors (P).

Eligibility criteria for the review

The PICOS abbreviation method proposed by Liberati et al. (2009) was employed to guide the study selection process:

a. The population (P) consisted of adult humans who had been diagnosed with a stroke or cerebrovascular accident.
b. The intervention (I) encompassed all forms of physical exercise, physical activities or aerobic exercises such as overground walking, bicycle ergometry or treadmill walking.
c. The comparator (C) referred to a second type of physiotherapy intervention or an intervention that did not involve physical activity, which is used to isolate the effects of the intervention.
d. The outcome (O) specifically focused on cognitive impairments
e. The study design (S) was limited to randomized controlled trials (RCT), clinical controlled trials (CCT) and clinical trials (CT).

Data items and collection for the systematic review

Data was collected by extracting information about: author and year of publication, study design, sample size and characteristics of participants, inclusion criteria, intervention details, outcomes assessed, main results, and conclusion from each of the included studies (Table 2.2).

Assessment of risk of bias for the reviewed studies

The methodological quality of the studies was independently evaluated by two reviewers to assess the risk of bias. In cases that were uncertain, a third reviewer was consulted for consensus. The PEDro scale, a commonly used tool for assessing the quality of studies in physiotherapy interventions was employed to evaluate the methodological quality of the

studies. Scores on the PEDro scale ranged from 1 to 10 points, and were transformed to percentages indicating low (10-50%) or high (60-100%) methodological quality (Appendix 3). This scale has been recognized as a comprehensive measure for evaluating the quality of stroke rehabilitation studies (Bhogal et al., 2005). Due to the heterogeneity of the included studies in terms of population, intervention, and outcomes, a qualitative data synthesis was conducted. The synthesis considered the number of studies and exposure in each study to arrive at meaningful conclusions.

Evidence synthesis for the systematic review

For evidence synthesis, the approach used in a previously published systematic review was followed (Bakker et al. 2009). The evidence levels were categorized as strong, moderate, limited, inconsistent, and no evidence. Strong evidence required consistent findings in at least two high-quality studies. Moderate evidence indicated consistent findings in one high-quality and one low-quality study. Limited evidence referred to situations where only one study was available. Inconsistent evidence arose when conflicting findings were reported across the available studies, while no evidence was assigned when no studies were found. For findings in multiple studies (>3) to be considered consistent, at least 75% of the available studies needed to report similar results and conclusions.

2.2.2 Results of the systematic review

Study selection

As illustrated in figure 2.1, a total of 3953 articles were returned from the database hits. After screening the titles and abstracts, 2718 articles were excluded due to inappropriate population, study design, intervention, or outcome parameters. Full-text copies of 35 articles were obtained for further evaluation. Out of these, 28 articles were excluded for not meeting the inclusion criteria. Ultimately, only seven articles were included for evidence synthesis.

Study Characteristics

Among the reviewed studies, Kluding et al. (2011) and Marzolini et al. (2013) utilised a single group method, and therefore lacks comparator. The design for these two studies was

reported as pre-test post-test design. Four studies were randomized controlled trials (Ploughman et al., 2008; Quaney et al., 2009; Tang et al., 2016; Blanchet et al., 2016), and one study was a clinical control trial (El-Tamawy et al., 2014).

In most of the studies, the average age of the participants was around 60 years (Ploughman et al., 2008; Quaney et al., 2009; Kluding et al., 2011; Marzolini et al., 2012; Blanchet et al., 2016; Tang et al., 2016). Only the participants in the study of El-Tamawy et al. (2014) had a mean age of 48 years. Three of the studies involved participants with ischaemic stroke, ranging from 38.0% (Tang et al., 2016), to 65.9% (Marzolini et al., 2012) and 90.5% (Ploughman et al., 2008). Quaney et al. (2009) involved only ischaemic stroke patients in their study. The type of stroke was not indicated in three of the studies (Kluding et al., 2011; El-Tamawy et al., 2014; Blanchet et al., 2016). All the studies included only chronic stroke patients with a minimum duration of 5 months post stroke event (Ploughman et al., 2008; Quaney et al., 2009; Kluding et al., 2011; Marzolini et al., 2012; El-Tamawy et al., 2014; Blanchet et al., 2016; Tang et al., 2016).

General cognitive function outcomes measures of the reviewed studies

Four studies used the Mini-Mental Status Examination (MMSE) to screen participants for eligibility, and as one of the study outcomes (Blanchet et al., 2016; Kluding et al., 2011; Quaney et al., 2009; Ploughman et al., 2008). Two studies used the Montreal Cognitive Assessment (MoCA) to screen participants and those included scored less than 24 (Marzolini et al., 2012 and Tang et al., 2016). El-Tamawy et al. (2014) used the Addenbrooke's Cognitive Examination Revised (ACER) to assess cognition, with a cutoff score of 82. Only one study reported the effect of aerobic exercise on brain-derived neurotrophic factor, as a measure of cognition post-stroke (El-Tamawy et al., 2014).

Specific domains outcomes measures of cognitive function of the reviewed studies

Memory was assessed in three studies. In the study by Kluding et al. (2011) the memory component of Stroke Impact Scale (SIS) version 2.0 was used to assess memory. Marzolini et al. (2012) used the memory component of MMSE, while Blanchet et al. (2016) used the Revised-Hopkins Verbal Learning Test (episodic memory). Three studies assessed

working memory as study outcomes. Kluding et al. (2011) and Tang et al. (2016) assessed working memory using the Digit Span Backwards, while Blanchet et al. (2016) used Brown–Peterson paradigm.

The third domain of cognition assessed in the reviewed studies was attention. Three studies assessed attention using Trail-Making Task A and B or part B (Ploughman et al., 2008; Quaney et al., 2009; Tang et al., 2016). In two of these studies, resistance to interference was assessed using the Stroop test (Quaney et al., 2009; Tang et al., 2016). Kluding et al. (2011) assessed attention with Flanker test, while, the Continuous Performance Test and Paced Auditory Serial Addition Test was used to assess attention in the studies by Blanchet et al. (2016) and Ploughman et al. (2008).

Concentration, as a domain of cognition, was measured in two studies. Ploughman et al. (2008) used the symbol digit substitution test, while Marzolini et al. (2012) used the concentration domains of the MMSE. Other domains of cognition assessed in the reviewed studies included learning and resistance to perseveration using the Wisconsin Card Sorting Task (WCST) (Quaney et al., 2009), as well as naming, language, abstraction and orientation components of the MMSE (Marzolini et al., 2012).

Exercise training parameters of the reviewed studies

Aerobic exercises either alone or in combination with other activities, were the main interventions in the reviewed studies. Different forms of aerobic exercises were administered, including high or low intensity (Tang et al., 2016), treadmill and lower body cycle (Blanchet et al., 2016), bicycle ergometry (El-Tamawy et al., 2014) and Body Weight Support Treadmill Training (BWSTT) (Ploughman et al., 2008). One study administered aerobic exercise in the form of treadmill, over ground or cycle ergometer exercise combined with resistance training (Marzolini et al., 2012). Quaney et al. (2009) administered aerobic exercise on a stationary bicycle with progressive resistance, while Kluding et al. (2011) administered aerobic exercise combined with resistance training on a total body recumbent stepper.

The intensity of the aerobic exercises varied from low to high across the studies. Some studies used 70% maximal heart rate or 60 to 70% of heart rate reserve (Quaney et al., 2009; Blanchet et al., 2016), or the Borg's scale category ratio 10 rating to quantify exercise intensity. Two studies administered low to high intensity individualized exercise based on between 40% to 80% of heart rate reserve or peak oxygen uptake (VO_2 max (Marzolini et al., 2012; Tang et al., 2016). One study administered low to moderate intensity exercise at 50% VO_2 max and/or the rate of perceive exertion (RPE) scale of 11–14, which indicates a light-to-moderate level of intensity (Kluding et al., 2011). Ploughman et al. (2008) used 70% of estimated target heart rate or level 13 on the Borg RPE as intensity of the exercise, However, El-Tamawy et al. (2014) did not specify the intensity of exercise used in their study.

Exercise duration in the studies ranged from short to long, with some studies including warm up and warm down periods of 2-10 minutes (Ploughman et al., 2008; Quaney et al., 2009; Kluding et al., 2011; El-Tamawy et al., 2014; Blanchet et al., 2016). Exercise was administered for 60 minutes in one study (Tang et al., 2016), while the participants in another study were allowed to exercise in the range of 20 to 60 minutes to accommodate the needs of individual participants (Marzolini et al, 2012).

Exercise training frequency ranged from three and five times per week (Quaney et al, 2009; Kluding et al, 2011; Marzolini et al., 2012; El-Tamawy et al., 2014; Tang et al., 2016). Only one study utilised a frequency of twice weekly (Blanchet et al 2016).

A summary of the reviewed study and the assessment of the methodological quality of the studies are presented in tables 2.2 and 2.3 respectively.

Table 2.2: Summary of Reviewed Studies

Author	Study design	Sample	Inclusion criteria	Intervention	Outcome	Results	Conclusion
Blanchet, et al., 2016	RCT	61.93±9.90 years M 9 F5 Chronic stroke	ischemic or hemorrhagic stroke Cognitive deficit on a standard neuropsychological test battery Fluency in French Not on rehabilitation services/ Living at home Able to walk with an aid or independently leg impairment score of ≥3 on CMSA	Aerobic exercises Treadmill, Lower Body Cycle 2 times/ week for 20-30 minutes 2–3mins training and 2–3min of rest intensity of 60–70 % of the HRR/Borg category ratio 10 rating=6–7) with 5–10 % increase in intensity for the last 4 weeks.	Episodic memory Working memory Attention	↑ attention ↑ Working memory ↓ attention errors	Attention may improve in chronic stroke survivors with clearly identified cognitive impairment following short-term training that has anaerobic component
El-Tamawy, et al., 2014	**CCT**	30 chronic stroke survivors, M21, F30, 48.4±6.39yrs 3–18Mos	ACER score < 82 CI following stroke in the territory of AC	**Physiotherapy program** "25–30" min Rest period "10–15" min, **Aerobic exercise** Bicycle ergometer for "40–45" min slow progression followed by the active phase of exercise for 30min 5-10 mins warming up 5-10 mins cooling down speed decreased until reaching the RHR performed 3 times for 8 weeks	BDNF ACER scores	↑ ACER scores ↑ BDNF	Aerobic exercises are considered as an effective method for improving cognitive impairment in stroke. This improvement is strongly correlated to the elevation in BDNF

Kluding, et al., 2011	pre-	9 chronic stroke 50.4± (37.9) Mo post stroke 63.7± (9.1) years	Able to transfer from a sitting to a standing position able to walk 30 feet without assistance of another person MMSE, score ≥ 23	Aerobic exercise 12-week TBRS And LE muscle strengthening exercise, 3 times each week. The 30-minute session (5-minute warm up period, maintenance of THR for 20 minutes, and a 5-minute cool down period) Strengthening exercises for the lower extremities were performed in a sitting position using resistive bands A light-to-moderate level of intensity for older adults.	Working memory Attention and executive function Memory	↑ working memory ↑ SIS total score ↑ FM total score.	12-week aerobic and strengthening exercise improved selected measures of executive function in people with stroke.
Marzolini, et al., 2012	**Pre-**	63.6 ± 13.5 (27-88) years 30 M 11 F 74 ± 13.5 W post stroke (10-650W)	Ischemic/hemorrhagic/unknown type stroke ≥ 10 weeks post stroke Stroke-related motor impairment score of <7 on the CMA of hand, leg, or foot Ambulate ≥ 10 m independently with/without an assistive device, with no significant limitations caused by pain	Treadmill Over ground Cycle ergometer exercise 20 to 60 minutes of exercise 5 times per week 40% to 70% of heart rate reserve or VO2 max RT- hand-held dumbbells, exercise bands or patients' body weight. load equivalent 50% to 60% of 1 RM NAL& AL =50% of 1 RM and/or a resistance rated as 13 to 14 on the RPE Scale	Depression VO2max Muscle strength Motor recovery Gait speed Fat-free mass	↑ MoCA score ↑ visuospatial/ executive function ↑ attention/concentration	AT+RT resulted in improvements in overall cognition and in the subdomains of attention/concentration and visuospatial/executive function.
Ploughman, et al., 2008	RCT	21 stroke survivors, 0.5-5years post- stroke,	≥2 of 7 levels of motor control on the CMII for Arm and Hand > 24 MMSE > 16 years of age only1documented stroke event,	BWSTT 70% estimated THR or level 13 Borg RPE 20 minutes: 5-minute incremental increase, 10-	Speed of visuomotor processing cognitive flexibility	cognitive tests=	Treadmill exercise does not improve cognitive performance

		61.4±10.2 years	not receiving active rehabilitation intervention able to walk with or without a cane	minute steady-state, and 5-minute slow down	Psychomotor performance &concentration. General attentional ability		
Quaney, et al., 2009	RCT	38 Chronic stroke ≥ 6 Mo post stroke	single ischemic stroke ≥ 6 M hemiparetic deficit (LE or UE) MMSE score > 23 perfect score on the 3-step command adequate cardiac function	Aerobic exercise stationary bicycle progressive, resistive for 45 minutes 3 times per week for 8 weeks 5-minute warm-up and cool down periods 70% max HR (based on Karvonen's formula)	selective attention visual search ability working memory, attention switching	Executive function=	Aerobic exercise did not improve cognitive function
Tang, et al., 2016	RCT	47 stroke 1.8-6.7 years post-stroke 62–75 years	50–80 years old were eligible if they were > 1 year Able to walk ≥5Mo	high or low intensity exercise 3 times/week in 60-min 40 to 80% of heart rate reserve	Verbal Digit Span Trail Making Part B Stroop tests	Memory= Executive function=	No changes in cognitive function were observed following high- and low-intensity exercise after stroke
Blanchet, et al., 2016	RCT	61.93±9.90 years M 9 F5 Chronic stroke	ischemic or hemorrhagic stroke Cognitive deficit on a standard neuropsychological test battery Fluency in French Not on rehabilitation services/ Living at home Able to walk with an aid or independently leg impairment score of ≥3 on CMSA	Aerobic exercises Treadmill, Lower Body Cycle 2 times/ week for 20-30 minutes 2–3mins training and 2–3min of rest intensity of 60–70 % of the HRR/ Borg category ratio 10 rating=6–7) with 5–10 % increase in intensity for the last 4 weeks.	Episodic memory Working memory Attention	↑ attention ↑ Working memory ↓ attention errors	Attention may improve in chronic stroke survivors with clearly identified cognitive impairment following short-term training that has anaerobic component

El-Tamawy, et al., 2014	**CCT**	30 chronic stroke M21 F30 48.4±6.39 years 3–18Mo	ACER score < 82 CI following stroke in the territory of AC	**Physiotherapy program** "25–30" min Rest period "10–15" min, **Aerobic exercise** Bicycle ergometer for"40–45"min slow progression followed by the active phase of exercise for 30min 5-10 mins warming up 5-10 mins cooling down speed decreased until reaching the RHR performed 3 times for 8 weeks	BDNF ACER scores	↑ ACER scores ↑ BDNF	Aerobic exercises are considered as an effective method for improving cognitive impairment in stroke. This improvement is strongly correlated to the elevation in BDNF
Kluding et al., 2011	pre-test post-test design	9 chronic stroke 50.4± (37.9) Mo post stroke 63.7± (9.1) years	Able to transfer from a sitting to a standing position able to walk 30 feet without assistance of another person MMSE score ≥ 23	Aerobic exercise 12-week TBRS and LE muscle strengthening exercise, 3 times each week. The 30-minute session (5-minute warm up period, maintenance of THR for 20 minutes, and a 5-minute cool down period) Strengthening exercises for the lower extremities were performed in a sitting position using resistive bands A light-to-moderate level of intensity for older adults.	Working memory Attention and executive function Memory	↑ working memory ↑ SIS total score ↑ FM total score.	12-week aerobic and strengthening exercise improved selected measures of executive function in people with stroke.

Marzolini et al., 2012	**Pre-test post test**	63.6 ± 13.5 (27-88) years 30 M 11 F 74 ± 13.5 W post stroke (10-650W)	Ischemic/hemorrhagic/unknown type stroke ≥ 10 weeks post stroke Stroke-related motor impairment score of <7 on the CMA of hand, leg, or foot Ambulate ≥ 10 m independently with/without an assistive device, with no significant limitations caused by pain	Treadmill Over ground Cycle ergometer exercise 20 to 60 minutes of exercise 5 times per week 40% to 70% of heart rate reserve or VO2 max RT- hand-held dumbbells, exercise bands or patients' body weight. load equivalent 50% to 60% of 1 RM NAL& AL =50% of 1 RM and/or a resistance rated as 13 to 14 on the RPE Scale	Depression VO2max Muscle strength Motor recovery Gait speed Fat-free mass	↑ MoCA score ↑ visuospatial/ executive function ↑ attention/concentration	AT+RT resulted in improvements in overall cognition and in the subdomains of attention/concentration and visuospatial/executive function.
Ploughman et al., 2008	RCT	21 stroke 0.5-5 years post- stroke 61.4±10.2 years	≥2 of 7 levels of motor control on the CMII for Arm and Hand > 24 MMSE > 16 years of age only1documented stroke event, not receiving active rehabilitation intervention able to walk with or without a cane	BWSTT 70% estimated THR or level 13 Borg RPE 20 minutes: 5-minute incremental increase, 10-minute steady-state, and 5-minute slow down	Speed of visuomotor processing cognitive flexibility Psychomotor performance and concentration. General attentional ability	cognitive tests=	Treadmill exercise does not improve cognitive performance
Quaney et al., 2009	RCT	38 Chronic stroke ≥ 6 Mo post stroke	single ischemic stroke ≥ 6 M hemiparetic deficit (LE or UE) MMSE score > 23 perfect score on the 3-step command adequate cardiac function	Aerobic exercise stationary bicycle progressive, resistive for 45 minutes 3 times per week for 8 weeks 5-minute warm-up and cool down periods 70% max HR (based on Karvonen's formula)	selective attention visual search ability working memory, attention switching	Executive function=	Aerobic exercise did not improve cognitive function

Tang et al., 2016	RCT	47 stroke 1.8-6.7 years post-stroke 62–75 years	50–80 years old were eligible if they were > 1 year Able to walk ≥5Mo		high or low intensity exercise 3 times/week in 60-min 40 to 80% of heart rate reserve	Verbal Digit Span Trail Making Part B Stroop tests	Memory= Executive function=	No changes in cognitive function were observed following high- and low-intensity exercise after stroke

Key: W=week M=male F=female RT= resistance training RM=repetition maximum NAL=Non affected Limb AL= affected lower limb RPE=rate of perceived exertion AT=aerobic training MoCA=Montreal cognitive assessment ↑=increase Mo=month W=week ♀=female BDNF=brain derived neurotrophic factor LE=lower extremity UE=upper extremity MMSE=mini-mental status examination BWSTT= body weight support treadmill HRR= heart rate reserve ACER=Addenbrooke's Cognitive Examination Revised AC=anterior cerebral artery SIS= stroke impact scale =same/no change ↓=decrease CMII= chedoke McMaster impairment inventory RHR=resting heart rate FM= fugl-meyer CMA= Chedoke McMaster stroke assessment scale TBRS= Total body recumbent stepper THR= target heart rate

Table 2.3: Assessment of Methodological Quality of the Studies

Authors	1*	2	3	4	5	6	7	8	9	10	11	Total score	MQ100%
Blanchet et al., 2016	√	√	√	×	×	×	√	√	√	×	√	6/10	60
El-Tamawy et al., 2014	√	×	×	√	×	×	×	√	√	√	√	5/10	50
Kluding et al., 2011	√	×	×	×	×	×	×	√	√	×	√	3/10	30
Marzolini et al., 2013	√	×	×	×	×	×	√	√	√	×	√	4/10	40
Ploughman et al., 2008	√	√	√	×	√	×	×	√	√	×	√	6/10	60
Quaney et al., 2009	√	√	×	√	√	×	√	√	√	√	√	8/10	80
Tang et al., 2013	√	√	×	√	×	×	√	√	√	√	√	7/10	70

Key: √=yes, ×=No, MQ=methodological quality, 1= eligibility criteria were specified, 2= subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received), 3= allocation was concealed, 4= the groups were similar at baseline regarding the most important prognostic indicators, 5= there was blinding of all subjects, 6= there was blinding of all therapists who administered the therapy, 7= there was blinding of all assessors who measured at least one key outcome, 8= measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups, 9= all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat", 10 the results of between-group statistical comparisons are reported for at least one key outcome, 10=the study provides both point measures and measures of variability for at least one key outcome.

2.2.3 Evidence Synthesis for the Effect of Aerobic Exercise on Cognitive Function Post-Stroke

Effects of Aerobic Exercise on Global Cognitive Function among Stroke Survivors

Two studies (Marzolini et al., 2012; El-Tamawy et al., 2014) on the effect of aerobic exercise on the global cognition of stroke patients were of low methodological quality. The results from these studies indicated that aerobic exercise improved the global cognitive function of post stroke patients. Based on the quality, level of evidence and results from those studies, we conclude that only moderate level evidence supports the efficacy of aerobic exercise in improving global cognitive impairment in post-stroke.

Effects of Aerobic Exercise on Attention among Stroke Survivors

Studies of high (Ploughman et al., 2008; Blanchet et al., 2016) and low quality reported on the effect of aerobic exercise (Marzolini et al.,2012; El-Tamawy et al., 2014) on attention in post-stroke individuals. One high quality study (Blanchet et al., 2016) and two low quality studies (Marzolini et al., 2012; El-Tamawy et al., 2014) were consistent in their findings that aerobic exercise is effective in the improvement of attention post-stroke. However, one high quality study (Ploughman et al., 2008) reported that aerobic exercise has no effect on attention. Therefore, it was concluded that the evidence to support the effect of aerobic exercise in improving attention in post-stroke cognitive impairment is moderate.

Effects of Aerobic Exercise on Memory among Stroke Survivors

One high quality study (Blanchet et al., 2016) and three low quality studies (Kluding et al., 2011; Marzolini et al., 2012; El-Tamawy et al., 2014) reported on the effect of aerobic exercise on memory among post-stroke patients. While two of the three low quality studies reported better memory in post-stroke following aerobic exercise intervention (El-Tamawayi et al., 2014; Kluding et al., 2011), the other low-quality study and the only high-quality study both reported otherwise. Therefore, it is inferred there is conflicting evidence on the effect of aerobic exercise on memory post-stroke.

Effects of Aerobic Exercise on Executive Function among Stroke Survivors

Two studies of high (Tang et al., 2008; Quaney et al., 2009) and one of low quality (Marzolini et al., 2012) reported the effect of aerobic exercise on the executive function in post stroke patients. The results from two high quality studies (Tang et al., 2008; Quaney et al., 2009) reported consistent finding that aerobic exercise did not improve executive function post-stroke. Therefore, we concluded that strong evidence supports the efficacy of aerobic exercise in not improving the executive function in post-stroke patients.

Effects of Aerobic Exercise on Working Memory among Stroke Survivors

For assessing the effect of aerobic exercise on working memory of post stroke individuals, one studies of high quality (Blanchet et al., 2016) and low quality (Kluding et al., 2011) were reviewed. The results from both studies indicated a consistent finding that aerobic exercise improved working memory post-stroke. Based on these results, the evidence supporting the effect of aerobic exercise on working memory in post stroke patient is moderate.

Effects of Aerobic Exercise on Brain-Derived Neurotrophic Factor among Stroke Survivors

Only one study of low quality reported the effect of aerobic exercise on brain-derived neurotrophic factor post-stroke (El-Tamawi et al., 2014). Although the result from this study indicates that aerobic exercises improve brain-derived neurotrophic factor in post-stroke patients, the evidence to support this result is currently limited.

2.2.4 Discussion of the Evidence on the Effect of Aerobic Exercise on Cognitive Function Post-stroke

The objective of this review was to determine the evidence to support the effects of aerobic exercise on the cognitive function of post-stroke patients. A total of seven studies were included in the review comprising 200 stroke survivors. The review showed that most of the study participants have ischaemic-type stroke, this is in concordance with literature on stroke epidemiology that ischaemic-stroke is the most commonly occurring type worldwide (Centers for Disease Control and Prevention, CDC, 2018)

The review also showed that evidence on effect of aerobic exercise on global cognitive function post-stroke is moderate. The studies that reported the effect of aerobic exercise on global cognitive function post-stroke have several limitations such as recruitment of relatively younger stroke participants (El-Tamawi et al., 2014) and administration of combined aerobic-strengthening exercises (Marzolini et al., 2013) thus affecting the conclusion on effect of aerobic exercise on global cognitive function.

The results of this review also showed that evidence aerobic exercise improves attention post-stroke is moderate. Among the studies that reported on the effect on attention, Ploughman et al., (2008) indicated that aerobic exercise does not improve attention post-stroke. This finding contradicts those of other studies by Marzolini et al. (2012), El-Tamawy et al. (2014) and Blanchet et al. (2016) that were reviewed. However, the disparity may be due to the differences in the duration of intervention administered. In particular, the participants in the study of Ploughman et al. (2008) engaged in aerobic exercise for only 20 minutes, which may inadequate to elicit cognitive effects as earlier opined (Winter et al., 2007; McMorris et al., 2008). Moreover, post stroke patients are known to present with a varied range of cognitive impairments, or even normal cognitive function.

Findings from the review further revealed that there is conflicting evidence regarding the effect of aerobic exercise on memory post-stroke. The studies that reported significant improvement in memory were limited in the area of characteristic of participants included such as younger stroke participants (El-Tamawy et al., 2014), mild cognitive impairment and normal cognition (Kluding et al., 2011). On the other hand, studies that reported no improvement in memory after administration of aerobic exercise had study design limitations i.e single group (Marzolini et al., 2013) and small sample size (Blanchet et al., 2016). These findings are indicative of a possible role of the baseline individual stroke patient characteristics in post aerobic exercise stroke cognitive function outcomes.

One of the important findings of this review is that strong evidence supports the role of aerobic exercise does not improve executive function in post-stroke patients. Nevertheless, the studies had several imitations. For example, Quaney et al. (2009) administered a

combination of aerobic and strengthening exercise. In addition to aerobic exercises, other varied interventions were reported in other studies. One study administered cognitive training, performed once weekly for 1.5 hours using a computer programme (Blanchet et al., 2016). Another study administered general physiotherapy for 25–30 minutes with a rest period of 10–15 minutes (El-Tamawy et al., 2014). The study by Ploughman et al. (2008) also incorporated home exercises at the clinic for the control group. One study administered stretching exercises for 45 minutes of upper and lower extremities three times per week (Quaney et al., 2009). The last also by Tang et al. (2016) also reported administering Balance and Flexibility (BF) programs, three times a week for 60 minutes per session, at an intensity of less than 40% heart rate reserve. We suspect that these differences or confounding variables turn will affect the validity of the study as regards to the effect of aerobic exercise on executive function post-stroke.

Another aspect of our systematic review also revealed that majority of the evidence level reached to support the effect of aerobic exercise on working memory, is moderate. However, these were likely as a result of study design limitations like in the study of Kluding et al. (2011). Moreover, only a few high-quality studies such as the study of Blanchet et al. (2016) compared aerobic exercise with the gold standard for managing cognitive impairment i.e. cognitive behavioural therapy (Cawood et al., 2016).

This review had a few limitations. The major limitation being that there is only a small number of studies existing on the topic area. Secondly, the available studies are highly heterogeneous thereby making a meta-analyses or quantitative evidence synthesis difficult. Nevertheless, our systematic review is a necessary attempt toward exploring evidence-based intervention for the cognitive impairment in post stroke-patients.

Evidence suggests that aerobic exercise is effective in improving several aspects of cognitive function in post-stroke individuals. Therefore, aerobic exercise should remain a major component in post-stroke rehabilitation. Nevertheless, more high-quality clinical trials are needed to conclusively answer the review question, mainly because existing studies were either of limited quality or scanty.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Participants

The participants in this study were stroke survivors with mild to moderate cognitive-impairment receiving physiotherapy at Aminu Kano Teaching Hospital, Murtala Mohammed Specialist Hospital and Muhammad Abdullahi Wase Teaching Hospital in Kano State.

3.1.1 Inclusion Criteria

Stroke survivors with the following characteristics were included in the study:

1. First incident stroke, clinically diagnosed by a neurologist and with blood pressure under control
2. Scores of between 10 and 25 on the Montreal Cognitive Assessment (MoCA)
3. Adequate balance control of ≤ 30sec on Timed up-and-go (TUG) test.
4. Mild to moderate upper limb impairment with wrist, metacarpophalangeal and interphalangeal joints extension of more than 20^0 and preserved ability to grasp.
5. Scores of ≤15 on the Physical Health Questionnaire (PHQ) for assessing level of depression.
6. Ability to complete self-paced 6-Minute Walk Test (6MWT) at an intensity of perceived exertion of 12 to 14 on the Borg 6-20 Scale.
7. Able to write/read in either English or Hausa language

3.1.2 Exclusion criteria

The following categories of stroke survivors were excluded from the study:

a) Stroke survivors with severe cardiac problems, determined using exercise testing. This group of participants may not be able to cope with the exercise intensity.

b) Stroke survivors with comorbidity that could negatively impact cognitive function and quality of life such as Parkinson's disease, Alzheimer's disease or history of traumatic head injury.

c) Stroke survivors with severe joint disorders such as osteoarthritis, rheumatoid arthritis that could become worse during exercise or could make performance of exercise difficult.

3.2 Materials

3.2.1 Instruments

The materials deployed for the research were:

a. Physical Health Questionnaire (PHQ): The PHQ is a 9-item self-administered questionnaire that is used to screen for depression in clinical settings. It is relatively short and easy to administer (de Man-van Ginkel, Gooskens, & Schepers, 2012). It is a reliable and valid instrument for the assessment of depression in neurological conditions such as stroke. The interrater reliability (intraclass correlation [ICC]=0.98, 95% CI [0.96, 0.99]), test-retest reliability (ρ= 0.75, $p < 0.001$), and internal consistency (Cronbach's $\alpha = 0.79$) of the PHQ-9 were good (de Man-van Ginkel, Gooskens, & Schepers, 2012). (Appendix 1). It was used to screen participants for depression.

b. Borg Rating of Perceived Exertion (RPE): was used to screen for aerobic capacity of the participants (Appendix 2). It was also used to monitor the intensity of the intervention on Borg original version of 6-20 coupled with the HR monitor. RPE is an indicator of exercise intensity after stroke at moderate (60%-70% Vo2peak) (Sage et al., 2013).

c. Montreal Cognitive Assessment (MoCA): The MoCA test was used to screen and assess level of cognitive functions (Appendix 3). It is easy and takes approximately 10 minutes to administer. It assesses different domains of cognition such as attention, concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculations and orientation (Aggarwal & Kean, 2010). The total obtainable score is 30 points, a score of 26 and above is considered normal (Chiti & Pantoni, 2014). A score of 18-25 signifies mild cognitive impairment, 10-17 indicates moderate cognitive impairment and less than 10 shows severe cognitive impairment

(Chiti & Pantoni, 2014). It is a valid and reliable instrument used in acute, sub-acute and chronic stroke survivors. The MoCA has internal consistency of α= 0.71 (Ramírez et al., 2014). The MMSE and MoCA scores were highly correlated (r^2=0.80, P<0.001) (Pendlebury et al., 2010).

d. Stroke-Specific Quality of Life (SSQoL): The questionnaire was used to assess quality of life among the participants. It was developed by Williams et al. (1999) to address the need for a disease-specific tool to assess quality of life of stroke patients. The questionnaire consists of 49 items grouped into 12 domains (Appendix 4). Each individual domain consists of 3 to10 items that are averaged to generate an overall score, with a minimum value of 1(meaning the worst outcome). The reliability coefficients analysed by the Rasch model were 0.91 for the items and 0.87 for the patients while the intra-class correlation coefficient was (ICC ≥ 0.60) (Silva et al., 2015). The scale has previously been validated in Hausa language (Odetunde et al., 2017).

e. London Handicap Scale (LHS): The scale is a self-administered questionnaire and was used to assess participation restriction. It was developed by Harwood et al. (1994) based on the descriptive framework of handicap developed by the World Health Organisation (WHO) in the International Classification of Impairments, Disabilities, and Handicaps (ICIDH). It was developed for different conditions and as such can also be applied to conditions such as stroke (Vincent-Onabajo, 2013). The scale consists of six domains namely; mobility, orientation, occupation, physical independence, social integration and economic self-sufficiency (Appendix 5). Each domain is scored on a six-point likert scale from 1 (extreme disability) to 6 (no disability). For each of the six dimensions of LHS, scores are added together. It takes about five minutes and no training required to administer. The scale's reliability coefficient is 0.85 and its Pearson separation is 2.42 in stroke patients, (Jenkinson et al., 2000). It has been used in previous studies (Hamzat & Peters, 2009; Hamzat et al., 2014).

f. Melsin brand Enzyme Linked Immunosorbent Assay (ELISA) kit: Enzyme linked immunosorbent assay applies a technique called a quantitative sandwich immunoassay. It was used to assess the level of serum brain-derived neurotrophic factor.

g. Stopwatch, digital type (Leisure life brand): This was used to time participants during the timed up and go test. Values were recorded in seconds.

h. **Digital blood pressure monitor (Omron):** it evaluated the blood pressure of participants to screen individuals with high blood pressure or uncontrolled hypertension. It consists of the arm cuff, digital display and parameter buttons. Values obtained were recorded in mmHg

i. **Heart rate monitor (Bowflex):** was used to determine the target heart rate of the participants, values were recorded in beats per minute (BPM). It consists of wrist strap, digital display and parameter buttons.

j. **Goniometer:** was used to screen for the active range of motion (AROM) of the wrist, metacarpophalangeal and interphalangeal joints among participants. The goniometer is a valid instrument for assessment of ROM among stroke survivors (Beebe & Lang, 2009)

k. **Blood sample collection instruments:** 10-millimeter blood spectrum tube, 5-millimeter serum bottle, 5-millimeter syringe, cotton wool and methylated spirit and hand gloves were used in the collection and storage of blood samples by a medical laboratory scientist.

l. **Hettich Universal 32 Centrifuge (Germany):** was used for separating serum from whole blood, which was subsequently stored at the Center for Infectious diseases of Bayero University Kano located at Aminu Kano Teaching Hospital Kano for storage.

m. **ELISA machine (Rayto, China):** was used to the read the absorbance of colour spectrophotometrically to detect presence of serum BDNF.

3.2.2 Venues of the study

The venues for the research were Physiotherapy Departments of Aminu Kano Teaching Hospital, Murtala Mohammed Specialist Hospital and Muhammad Abdullahi Wase Teaching Hospital in Kano state.

3.3 METHODS

3.3.1 Research Design

The research design for this study was a Randomized Control Trial (RCT). This RCT was conducted according to the Consolidated Standards of Reporting Trials (CONSORT)

guideline which involves controlled study with random assignment of eligible participants into groups, blinding of assessment of outcomes or intervention (Moher et al., 2010).

3.3.2 Sampling Technique

The technique used to recruit participants was purposive sampling of which the eligible participants were recruited from Aminu Kano Teaching Hospital, Murtala Mohammed Specialist Hospital and Muhammad Abdullahi Wase Teaching Hospital in Kano state.

3.3.3 Sample Size

The sample size (n) for this study was determined using the Cohen's table. The effect size was first determined using the following formula:

$$\text{Effect size} = \frac{M2 - M1}{d}$$

Where M2, M1and d represents average scores of the experimental group, control group, and standard deviation of the of the intervention group. Therefore, M1, M2 and d were obtained from El-Tamawy et al. (2014) for the effect size calculation:

M2= 23.83

M1=20.66

d= 2.77

$$\text{Effect size} = \frac{23.88 - 20.66}{2.77}$$

Effect size = 1.14

Power of 0.8 (80%) was adopted as the commonly used power for RCTs. For each group, a sample size of 17 subjects were obtained from the Cohen's table, giving a total of 51 patients for the study. An attrition rate of 10% (5.1) was added to 51 which brought the number of participants to 56.1, which was approximated to 57. Thus, a total of 60 stroke were recruited and randomised into three groups of 20 patients per each.

3.3.4 Procedure for Data Collections

Ethical approvals were obtained from the ethical committees of Aminu Kano Teaching Hospital and Ministry of Health Kano state before commencement of the study (Appendix 6 and 7 respectively). The study was also registered with Pan African Clinical Trial Registry

(PACTR) (PACTR201903762696119) (Appendix 8). The ethical approvals were used to obtain permission from the Departments of Physiotherapy of the respective hospitals to recruit participants and conduct the study at the clinics. The procedure for the study is as described below:

a) **Screening for Eligibility**

The participants were screened for eligibility as follows:

1. **Blood pressure:** The blood pressure was measured in the physiotherapy clinics with background noise, such as ringing telephones, eliminated. It was measured in seated position. A rest period of 5 minutes was given before readings. The cuff was wrapped around the arm of the participant. Start button on the apparatus was pressed and the readings from the screen were recorded and documented on the data collection sheet (Plate 3.1). The measurement procedure took about 2 minutes. Two measurements were taken each from both the right and left arms. The arm with the highest average was used for all subsequent measurements.

2. **Aerobic capacity**: The 6-Minute Walk Test (6MWT) was used to assess the aerobic capacity of participants. It measures the distance that a patient can quickly walk on a flat, hard surface in a period of six minutes. The patients' aerobic capacity was determined using the Borg rating of perceived exertion (RPE). Test was terminated when there was chest pain, intolerable dyspnoea, leg cramps, staggering, diaphoresis, and pale appearance. Patients who were unable to complete the 6MWT were excluded (Appendix 9).

3. **Depression:** A brief version of the PHQ was used to screen for depression before commencement of the study. The participants responded by providing self-report on the level of depression. Participants who scored 15 or more were excluded.

4. **Upper limb range of motion:** The upper limb range of motion (ROM) was assessed using the goniometer. The range of wrist, metacarpophalangeal and interphalangeal joint extension was assessed with the patient in sitting and affected arm positioned on a table in front of the patient.

5. **Balance:** The Timed up and go (TUG) test was used to assess balance control. It involved the patient standing up from a chair, walking at self-paced speed along a 3meters (10 feet) line on the floor, and turning around to go and sit back on the chair (Appendix 10). The test has an excellent intra-rater and inter-rater reliability, with ICC values greater than 0.95

(Hafsteinsdottir et al., 2014). Participants with balance scores of 30 seconds or less were recruited into the study.

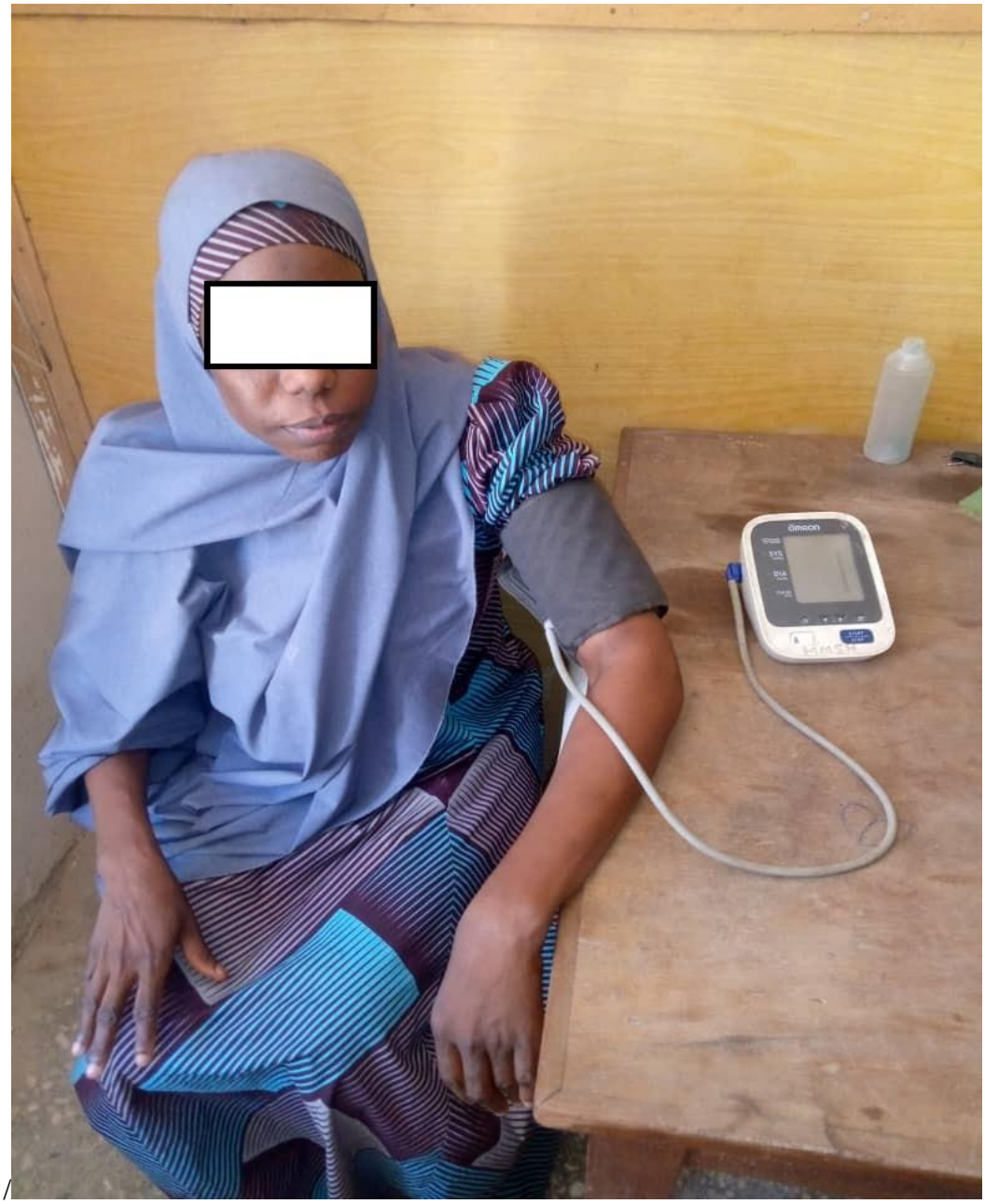

Plate 3. 1: Blood Pressure Measurement

6. **Cognition:** Cognition was assessed using the MoCA test. The participants were asked questions to which they responded, and were given specific tasks to complete by the researcher. Participants with overall score of 9 or below (severe cognitive impairment) and 26 or above (normal cognitive function) were excluded.

b) Randomization and Blinding

Participants who met the eligibility criteria were then asked to sign the consent form in either English or Hausa language (Appendix 11). Written or thumb printed informed agreements were requested from the patients. The subjects that signed the informed consent were assigned randomly into in each of the three hospitals that served as venue for the study using stratified random assignment. Strata were developed based on the level cognitive dysfunction as mild and moderate with scores of 10-17 and 18-25 respectively. A computer application (Random Number generator) was used to generate random numbers for allocation of participants into groups: Overground Walking Exercise Group, Cognitive Rehabilitation Group and combined Overground Walking Exercise and Cognitive Rehabilitation Group, which was supervised by a research assistant. Assessors were blinded to the intervention for each group. Furthermore, participants for each group were treated on alternate days to avoid contamination.

c) Assessment of baseline characteristics

The socio-demographic characteristics were obtained using a data collection form. Information such as age, sex, occupation, level of education, duration of stroke, and side of affectation were obtained.

Training of researcher and research assistants on assessment of outcomes

Prior to baseline assessments of all participants, the researcher received a training and certification on the use of the MoCA (Appendix 12). Two research assistants were also trained on how to carry out the assessment and re-assessment of the outcomes. The outcomes assessed were: cognition using MoCA, level of brain-derived neurotrophic factor using the ELISA kit, quality of life using the SSQoL and participation restriction using LHS.

The research assistants who conducted the assessments of the outcomes were blinded to the intervention for each group. Re-assessments of all outcomes were administered at 4th and 8th week of intervention.

1. Assessment of cognition using Montreal Cognitive Assessment

Prior to the commencement of the study, permission to use the instrument was sought and obtained from the developers of the MoCA test. The approval to use the questionnaire was granted on the condition that the researcher would attend an online certification training for the administration of the MoCA test (Appendix 12).

The participants in the study responded to each of the items in the domains of the scale. Visuospatial abilities were assessed using a clock-drawing task (3 points) and a three-dimensional cube copy (1 point). Multiple aspects of executive functions were assessed using an alternation task adapted from the trail-making B task (1 point), a phonemic fluency task (1 point), and a two-item verbal abstraction task (2 points). The short-term memory recall task (5 points) involved two learning trials of five nouns and delayed recall after approximately 5 minutes. Attention, concentration and working memory were evaluated using a sustained attention task (target detection using tapping; 1 point), a serial subtraction task (3 points), and digits forward and backward (1 point each). Language was assessed using a three-item confrontation naming task with low-familiarity animals (lion, camel, rhinoceros; 3 points), repetition of two syntactically complex sentences (2 points), and the aforementioned fluency task. Finally, orientation to time and place were evaluated (6 points). The instrument was administered at baseline, 4th and 8th week of intervention.

2. Assessment of Quality of Life using the SSQoL: The participants responded to the items in each domain of the scale. The SSQoL takes about 10 minutes to complete. The Hausa version of the instrument was used for participants who could not communicate in English language. The scale was administered in each of the following domains: energy, family roles, language, mobility, mood, personality, self-care, social roles, thinking, upper extremity (UE) function, vision, and work/productivity, at baseline and subsequently at 4th

and 8th weeks of intervention. The domains were scored separately, and a total score was calculated. Scoring of the SS-QoL involves activities in the past week and is rated on a 5-point Likert scale. The SS-QoL provides domain scores and a summary score, with higher scores indicating better function. The domain scores are composed of unweighted averages while summary scores are composed of an unweighted average of the 12 domain average scores. Scores range from 49-245.

3. Assessment of Participation using the London Handicap Scale: The participants indicated the statements they identified with the most in each of the six subscales of the following domains: mobility (getting around), physical independence (looking after yourself), occupation (work and leisure activities), social integration (getting on with people), orientation (awareness of your surroundings) and economic self-sufficiency (affording the things you need). It took about five minutes to administer and was conducted at baseline, and subsequently 4th and 8th weeks of intervention. Each subscale represented a different level of disability in relation to the subscale scoring. Each statement is associated with a number, which are summed together to give a total handicap score. The statements were scored on a six-point scale. For each of the six dimensions of LHS, scores are added together, and minimum possible score is six and maximum obtainable score is 36.

4. Assessment of BDNF using the ELISA tool kit (MELSIN brand)

The serum BDNF was assessed by a licensed medical laboratory scientist with expertise in chemical pathology following the procedure below:

Serum sample: 5 ml venous blood was aseptically drawn from each participant (Plate 3.2), dispensed into a blood spectrum tube and allowed to clot for 30 minutes. Samples were retracted and centrifuged for five minutes at approximately 15,000 revolutions per minute using Hettich Universal 32 Centrifuge (Germany). The serum was harvested and dispensed into a serum bottle, and was immediately stored at -20°C or -80°C, at the Center for Infectious Diseases Research of Bayero University Kano located at Aminu Kano Teaching Hospital, until needed.

Principle: The BDNF enzyme-linked immunosorbent assay applies a technique called a quantitative sandwich immunoassay. The microtiter plate provided in this kit had been pre-

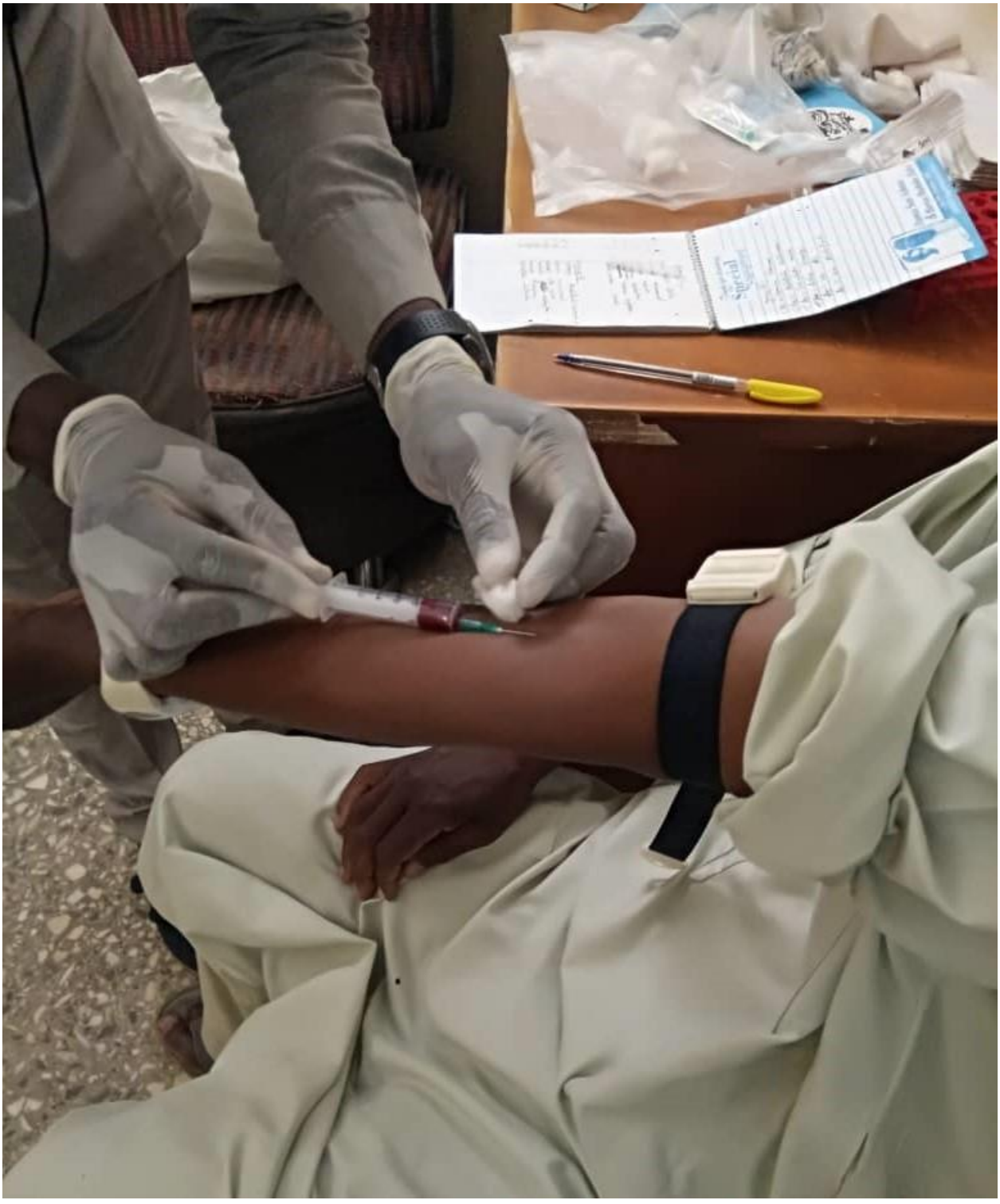

Plate 3.2: Collection of Blood Sample for Assessment of BDNF

coated with a polyclonal antibody specific for BDNF. Calibrators or samples were then added to the microtiter plate wells, and BDNF if present, bound to the antibody pre-coated wells. In order to quantitatively determine the amount of BDNF present in the sample, a standardized preparation of horseradish peroxidase (HRP)-conjugated polyclonal antibody, specific for BDNF were added to each well to "sandwich" the BDNF immobilized on the plate. The microtiter plate was incubated, and then the wells were thoroughly washed to remove all unbound components. Thereafter, A and B substrate solution was added to each well. The enzyme (HRP) and substrate were allowed to react over a short incubation period. Only those wells that contain BDNF and enzyme-conjugated antibody exhibited a change in colour. The enzyme-substrate reaction was terminated by the addition of a sulphuric acid solution and the colour change was measured spectrophotometrically at a wavelength of 450 nm.

Assay procedure

1. Calibrators and samples were added in duplicates to the Microtiter Plate as recommended.
2. Conjugate (100µL) was added to each well and mixed properly. The mixture was covered and plate incubated for 1 hour at 37°C.
3. Microtiter Plate was washed manually by aspirating contents of the plate into a sink or proper waste container. Each well was completely filled with diluted wash solution, and contents of the plate were aspirated into a sink or proper waste container. The procedure was repeated five times for a total of five washes. After washing, the plate was inverted, and blotted dry by hitting it on an absorbent paper or paper towels until no moisture appeared. The sides of the plate frame were held firmly when washing the plate to ensure that all strips remained securely in the frame. Complete removal of liquid at each step was essential to good performance.
4. A 50µL of Substrate A and 50µL of Substrate B were subsequently aadded to each well. The plate was covered and incubated for 15 minutes at 20-25°C.
5. A 50µL of stop solution was added to each well and was mixed well.
6. The optical density (O.D.) was immediately read at 450nm using a microtiter plate reader.

Calculation of results

1. Calibration curves are used to determine the amount of an unknown sample. A calibration curve is usually constructed by plotting the average O.D. (450 nm) for each calibrator on the vertical (Y) axis against the concentration on the horizontal (X) axis, and a best fit curve is then drawn through the points on the graph.
2. For the BDNF, the mean O.D. value was calculated for each calibrator and sample.
3. All O.D. values were subtracted from the mean value of the blank control before result interpretation.
4. Calibration curve was constructed using a graph paper.
5. To determine the amount in each sample, a horizontal line was drawn from the O.D. value on the Y-axis to the calibration curve. At the point of intersection, a vertical line was drawn to the X-axis, and the corresponding concentration was read off. The sensitivity was 1.0 ng/ml

3.3.5 The Intervention

Training of the researcher and research assistants for intervention administration

The researcher and four research assistants (R.A) were trained in administration of cognitive rehabilitation (Zoltan protocol) by three occupational therapists. Two other RA received training for the administration of the walking exercise interventions. In addition, familiarisation with various instruments and parameters was carried out.

a) Overground Walking Exercise Group (OWEG)

A moderate-intensity over-ground walking exercise, adapted from Olawale et al., (2011), was the intervention. The participants walked in the clinics (Plate 3.3) at an intensity of 40 to 59% (moderate) of Heart Rate Reserve (HRR) and/or a rating of RPE of 12 to 14 on the Borg 6-20 Scale (Franklin and Swain, 2003). A wrist heart rate monitor was further used to ensure the participants performed the exercise within the intensity boundary set. Exercise was stopped the moment participants experienced negative signs of exercise or they walk outside of the set the intensity. The exercise-intensity remained the same and the exercise time was increased from 20 minutes in the first week and second week to 50 minutes by the 8^{th} week. There was a warm-up and cool-down period of five minutes each at the intensity of 30% of HRR prior to commencement and as well towards the end of the training session

Plate 3.3: Participant Performing the Overground Walking Exercise

(Macko et al., 1997). Participants were encouraged to refrain from alcohol consumption and to avoid smoking and caffeine consumption on the day of intervention to avoid the possible influence of these substances on cognition.

The intensity of the exercise was determined using the HRR method of Karvonen et al. (1957). The formula stated as: THR= (HR_{max}- HR_{rest}) x (desired intensity) + $HR_{rest.}$ Where;

1. **Maximum Heart Rate (**HR_{max}**)** = was computed using the formula:

   HR_{max} =220-age
2. **Heart Rate Rest (**HR_{rest}**)** =The Resting Heart Rate was measured using the heart rate monitor
3. **Heart rate reserve (HRR)** = Maximum heart rate – resting heart rate
4. **Desired intensity**= 40 to 59% of HR

b) Cognitive Rehabilitation Group (CRG)

The cognitive rehabilitation protocol for this study was adapted from Zoltan (2007) which was developed for training cognitive task among stroke survivors with cognitive impairments.

Procedure for the Cognitive Intervention

The intervention was administered thrice weekly for a total of eight weeks. Each session lasted 30 minutes. The first part of the session was a paper and pencil task, star cancellation activity, which was targeted at the individuals' attention (Plate 3.4). The second part of the session included intervention to improve memory. Task that utilized Preview, Question, Read, State, Test (P. Q. R. S. T) method was administered.

The cognitive rehabilitation was performed in a room free from distractions in the first four weeks. Subsequently, cognitive rehabilitation was conducted at venues with environmental distractions (e.g., noise from television, noise and movements from people in clinic reception) in the last four weeks.

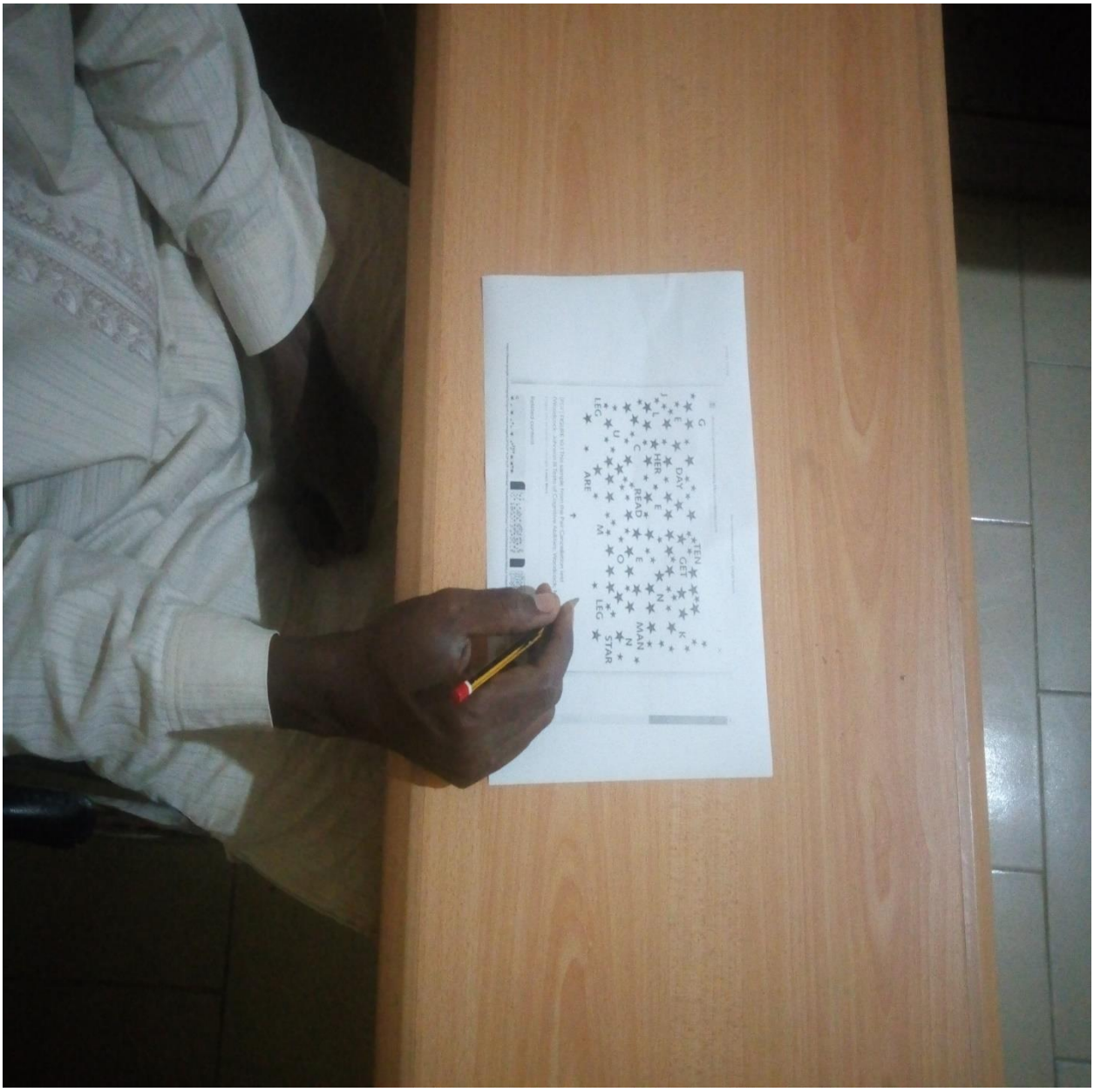

Plate 3.4: Star Cancellation Task for Attention during Cognitive Rehabilitation

c) Combined Overground Walking Exercise and Cognitive Rehabilitation Group (OWECRG)

The combined interventions were administered in sessions. First part included the over-ground-walking exercise while the second part was the cognitive rehabilitation.

i. Overground Walking Exercise

A moderate-intensity over-ground walking exercise adapted from Olawale et al. (2011) was conducted. The participants walked in the clinics (Plate 3.3) at an intensity of 40 to 59% (moderate) of HRR and/or a rating of RPE of 12 to 14 on the Borg 6-20 Scale (Franklin & Swain, 2003). A wrist heart rate monitor was further used to ensure the participants performed the exercise within the intensity boundary set. Exercise was stopped the moment participants experienced negative signs of exercise or they walk not within the intensity. The exercise-intensity remained the same and the exercise time was increased from 10 minutes in the first week and second week to 25 minutes by the 8^{th} week. There was a warm-up and cool-down period of five minutes each at the intensity of 30% of HRR prior to commencement and as well towards the end of the training session (Macko et al., 1997). Participants were advised to refrain from alcohol consumption and to avoid smoking and caffeine consumption on the day of intervention.

The intensity of the exercise was determined using the HRR method of Karvonen et al. (1957). The formula stated as: THR= (HR_{max}- HR_{rest}) x (desired intensity) + $HR_{rest.}$ Where;

1. **Maximum Heart Rate (**HR_{max}**)** = was computed using the formula:

   HR_{max} =220-age
2. **Heart Rate Rest (**HR_{rest}**)** =The Resting Heart Rate was measured using the heart rate monitor
3. **Heart rate reserve (HRR)** = Maximum heart rate – resting heart rate
4. **Desired intensity**= 40 to 59% of HR

ii. Cognitive Rehabilitation

The cognitive intervention adapted from Zoltan (2007) protocol was used in this study.

Procedure for the cognitive intervention:

The intervention was administered thrice weekly for a period of 8 weeks. Each session lasted 30 minutes. The first part of the session was a paper and pencil task, star cancellation activity, which was targeted at the individuals' attention (Plate 3.4). The second part of the session included intervention to improve memory. Task that utilized Preview, Question, Read, State, Test (P. Q. R. S. T) method was administered.

The cognitive rehabilitation was conducted in a place free from interferences in the first four weeks. Subsequently, cognitive rehabilitation was carried out at venues with environmental distractions (e.g., noise from television, noise and movements from people in clinic reception) in the last four weeks.

3.3.6 Data Analyses Procedure

The data obtained were analysed using Statistical Package for Social Sciences (SPSS) version 20.0

a. Descriptive statistics was used to summarise the sociodemographic and clinical characteristics of participants such as age, gender, cognition, BNDF, participation restriction and quality of life.
b. Normality test was conducted using Kolmogorov-Smirnov.
c. Repeated measures ANOVA was used to compare the variables at baseline, 4^{th} and 8^{th} weeks within the study groups.
d. One-way ANOVA was used to compare BDNF levels, cognition, QoL and participation restriction at baseline, 4^{th} and 8^{th} weeks across the groups.
e. Post-hoc analysis was further performed to determine where the differences lay across the weeks.

   The level of significance for the data analysis was set at $p \leq 0.05$.

CHAPTER FOUR

RESULTS

4.1 Participants

A total of 197 stroke survivors were contacted for the study. After an initial screening, 132 recruits were excluded based on the stipulated eligibility criteria and presence of co-morbidities (Figure 4.1). Among the eligible participants, five declined to participate. Sixty consenting stroke survivors who were eligible, were randomly assigned into each of the three groups namely: Overground Walking Exercise Group (OWEG), Cognitive Rehabilitation Group (CRG), and Combined Overground Walking Exercise and Cognitive Rehabilitation. (OWECRG). However, 53 participants comprising 35 males completed the eight-week intervention (Figure 4.1).

4.2 Socio-demographic and Clinical Characteristics of Study Participants

The average ages of the subjects in the OWEG, CRG and OWECRG were 49.56±14.56, 48.39±12.85 and 47.56±10.14 years respectively. The mean time since onset of stroke were 31.94±32.55 months, 26.17±29.31 months and 20.28±18.46 months for the OWEG, CRG and OWECRG respectively. There were more males than females across the groups (Table 4.1). The three groups were similar in terms of age, mean time since onset of stroke, cognition, BDNF level, quality of life and participation restriction ($p>0.05$) (Table 4.2). More than half of the participants in the OWEG (52.90%) and about two-thirds of the participants in the OWECRG (66.70%) had left hemiplegia, while participants in the CRG mostly had right hemiplegia (61.10%). Just above half of the participants (n=27; 50.9%) had ischaemic stroke (Table 4.1).

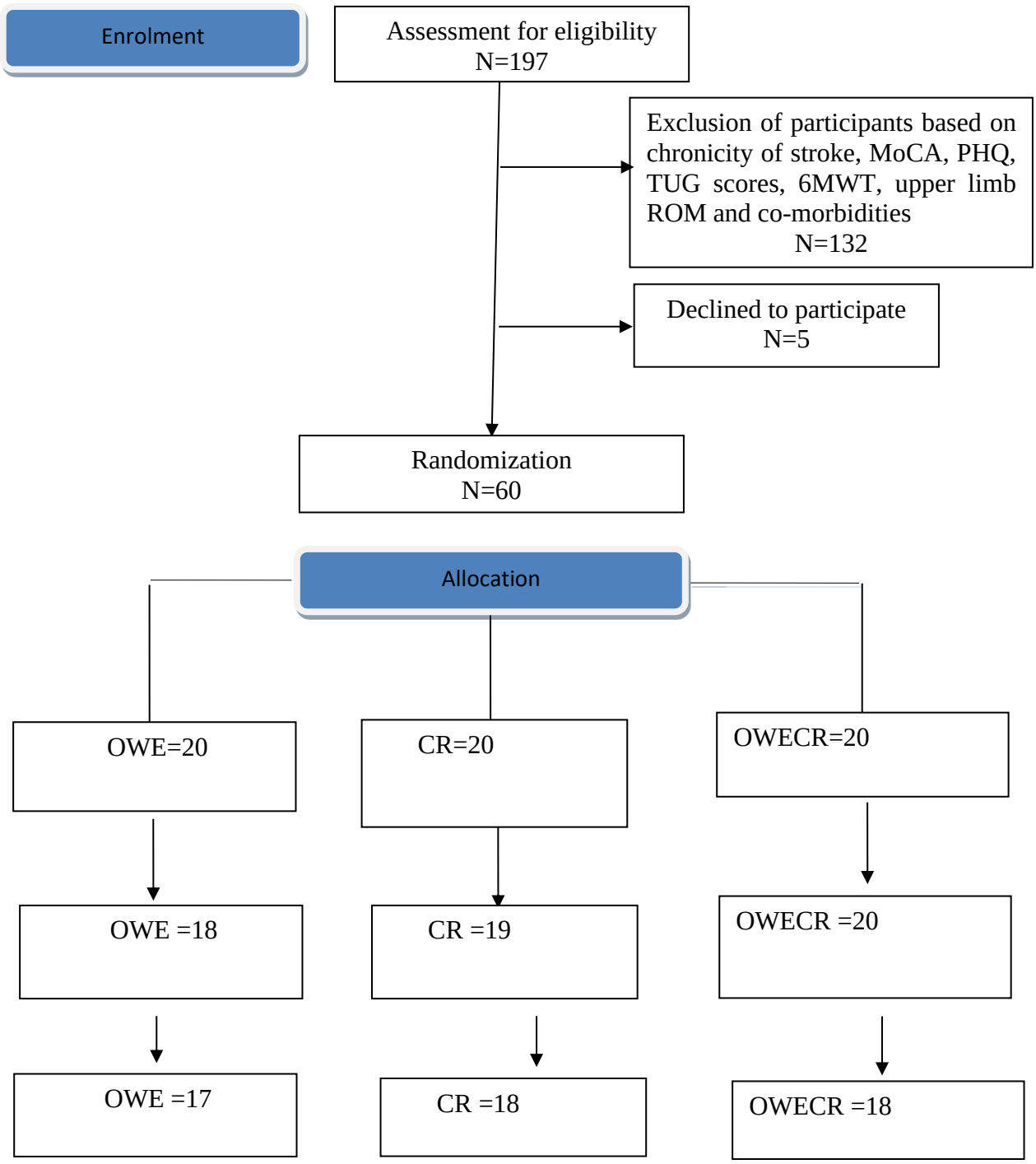

Figure 4.1: Flowchart of Participant

Table 4.1: Socio-demographic and Clinical Characteristics of Participants (N=53)

Variables	OWEG (n=17) n (%)	CRG (n=18) n (%)	OWECRG (n=18) n (%)	Total (N=53) n (%)
Sex				
Male	11(64.7)	11(61.1)	13 (72.2)	35 (72.2)
Female	6 (64.7)	7(38.9)	5 (27.8)	18 (34.0)
Marital Status				
Married	16 (94.1)	18 (100.0)	17 (94.4)	51 (96.2)
Divorced	1 (5.9)	0 (0.0)	0 (0.0)	1 (1.9)
Single	0 (0.0)	0 (0.0)	1 (5.6)	1 (1.9)
Level of Education				
Primary	5 (29.4)	2 (11.1)	2 (11.1)	9 (16.9)
Secondary	8 (47.1)	13 (72.2)	11 (61.1)	32 (60.4)
Post Secondary	3 (17.6)	2 (11.1)	5 (27.8)	10 (18.9)
Tertiary	1 (5.9)	1 (5.6)	0 (0.0)	2 (3.8
Type of Stroke				
Ischaemic	9 (52.9)	8 (44.4)	10 (55.6)	27 (50.9)
Haemorrhagic	8 (47.10	10 (55.6)	8 (44.4)	26 (49.1)
Side of Affectation				
Left	8 (47.1)	11(61.1)	6 (33.3)	25 (47.2)
Right	9 (52.9)	7(38.9)	12 (33.7)	28 (52.8)
Mean Age (years)	49.56±14.56	48.39±12.85	47.56±10.14	48.42±27.39
Mean time since stroke onset (months)	31.94±32.55	26.17±29.31	20.28±18.46	26.70±27.25

Key: OWEG= Overground Walking Exercise Group, CRG= Cognitive Rehabilitation Group, OWECRG= combined OWE and CR group, n= frequency, %= percentage

Table 4.2: Baseline Characteristics of Participants Across Groups

Variables	OWEG (n=17) $\bar{X}$±S.D	CRG (n=18) $\bar{X}$±S.D	OWECRG (n=18) $\bar{X}$±S.D	Total (N=53) $\bar{X}$±S.D	f-value	p-value
Cognition	18.06±3.60	19.00±3.90	19.50±3.85	19.50±3.85	**0.65**	**0.53**
BDNF level (ng/ml)	13.05±8.27	13.81±11.04	9.54±6.46	12.05±8.82	**1.12**	**0.34**
Quality of Life	191.00±28.85	202.72±28.83	197.44±39.83	197.17±32.71	**0.55**	**0.58**
Participation Restriction	12.06±4.02	10.39±4.24	10.56±3.31	10.99±3.88	**0.98**	**0.39**
Mean Age (yrs)	49.56±14.56	48.39±12.85	47.56±10.14	48.42±27.39	**0.84**	**0.92**
Mean time since stroke onset (mos)	31.94±32.55	26.17±29.31	20.28±18.46	26.70±27.25	**0.09**	**0.44**

Key: BDNF= Brain-Derived Neurotrophic Factor, OWEG= overground walking exercise group, CRG= Cognitive Rehabilitation group, OWECRG= combined OWE and CR group, n= frequency, SD=standard deviation, ng/ml= Nanogramme per milliliter, yrs = years; mos = months

4.3. Changes in Cognition, BDNF Level, QoL and Participation Restriction across Eight weeks in the OWEG

Repeated measures ANOVA was used for comparison of all outcomes among participants in the OWEG. The results showed significant improvements in cognition across the time intervals ($f = 75.48$; $p<0.01$). The post-hoc analysis showed a significant improvement in cognition from 18.06±3.60 at baseline to 20.53±2.83 at week 4, and to 26.24±2.51 at week 8 (Table 4.3). There was also a significant difference in BDNF levels across the time intervals ($f = 31.88$; $p<0.01$). Post-hoc analysis showed significant increases in BDNF levels from 13.05±8.27ng/ml at baseline to 13.88±8.26ng/ml at week 4, and to 14.69±8.85ng/ml at week 8 (Table 4.3).

The OWEG demonstrated a significant improvement in QoL across time intervals ($f = 24.77$; $p<0.01$)**.** Post-hoc analysis revealed that the significant improvement in QoL was from 202.24±22.49 at week 4 to 243.53±17.80 at week 8 (Table 4.3). Similarly, there was a significant reduction in participation restriction across the time interval ($f =11.54$, $p<0.05$). The results of post-hoc analysis showed that there was a significant reduction in participation restriction from 12.062±4.02 at baseline to 9.00±2.45 at week 4, and 7.249.00±2.05 at week 8 (Table 4.3).

4.4. Changes in Cognition, BDNF Level, QoL and Participation Restriction across Eight weeks in the CRG

There were significant differences in cognition (MoCA scores) across the different time intervals in CRG ($f=35.62$; $p<0.01$). Post-hoc analysis showed significant improvements in cognition from baseline (19.00±3.90) to week 4 (22.78±3.95), and to week 8 (25.22±3.26) as presented in table 4.4. There was also a significant difference in BDNF levels across the time intervals among participants in CRG ($f=4.58$; $p=0.03$). Post-hoc analysis showed the significant improvement in BDNF level was from 13.81±11.04ng/ml at baseline to 18.13±14.96ng/ml at week 8 (Table 4.4).

There were significant differences in QoL across different time intervals in the CRG ($f=10.03$; $p<0.01$). Post-hoc analysis showed significant improvement in the QoL was from

Table 4.3: Within- Group Comparison of Cognition, BDNF, QoL and PR from Baseline to Week 8 for the OWEG

Variables	Baseline $\bar{X}$±S.D	Week 4 $\bar{X}$±S.D	Week 8 $\bar{X}$±S.D	f-value	p-value	η_p^2
Cognition	18.06±3.60[a]	20.53±2.83[b]	26.24±2.51[c]	**75.48**	**<0.01***	**0.83**
BDNF level (ng/ml)	13.05±8.27[a]	13.88±8.26[b]	14.69±8.85[c]	**31.88**	**<0.01***	**0.67**
Quality of Life	191.00±28.85[a]	202.24±22.49[a]	243.53±17.8[b]	**24.77**	**<0.01***	**0.61**
Participation Restriction	12.06±4.02[a]	9.00±2.45[b]	7.24±2.05[bx]	**11.54**	**<0.01***	**0.42**

Key: BDNF= Brain-Derived Neurotrophic Factor, *=significant @ p< 0.05, ng/ml= Nanogramme per milliliter, **Items with the same or have at least one same superscript were not significantly different (X^a and Y^a or X^a and Y^{ax}), Items with entirely different superscript were significantly different (X^a and Y^b or X^x and Y^y), OWEG= Overground Walking Exercise Group, CRG= Cognitive Rehabilitation Group, OWECRG= combined OWE and CR group**

Table 4.4: Within- Group Comparison of Cognition, BDNF, QoL and PR from Baseline to Week 8 for the CRG

Variables	Baseline $\bar{X}$±S.D	Week 4 $\bar{X}$±S.D	Week 8 $\bar{X}$±S.D	f-value	p-value	η_p^2
Cognition	19.00±3.90^{a}	22.78±3.95^{b}	25.22±3.26^{c}	**35.61**	**<0.01***	**0.67**
BDNF level (ng/ml)	13.81±11.04^{a}	15.62±12.98^{ax}	18.13±14.96^{b}	**4.58**	**0.03***	**0.21**
Quality of Life	202.72±28.83^{a}	211.22±21.99^{a}	222.89±18.35^{b}	**10.**03	**<0.01***	**0.37**
Participation Restriction	10.39±4.24^{ab}	9.56±2.73^{a}	8.39±2.70^{b}	**8.02**	**<0.01***	**0.50**

Key: BDNF= Brain-Derived Neurotrophic Factor, *=significant @ p<0.05, ng/ml= Nanogramme per milliliter, η_p^2= Partial eta squared items with the same or have at least one same superscript were not significantly different (X^a and Y^a or X^a and Y^{ax}), Items with entirely different superscript were significantly different (X^a and Y^b or X^x and Y^y), CRG= Cognitive Rehabilitation Group

week 4 (211.22± 21.99) to week 8 (222.89±18.35), and from baseline to week 8 (Table 4.4). Similarly, there was a significant difference reduction in participation restriction across the time intervals ($f=8.02$; $p<0.01$). Post-hoc analysis showed that the significant decrease in participation restriction was from the 4th week (9.56±2.73) to the 8th week (8.39±2.70) (Table 4.4).

4.5. Changes in Cognition, BDNF Level, QoL and Participation Restriction across Eight weeks in the OWECRG

Repeated measures ANOVA was used to compare the study outcomes among the participants in OWECRG across the time intervals. The result from the study showed that there were significant differences in cognition among the participants across the time interval ($f=35.40$, $p<0.05$). Post-hoc analysis revealed that there was a significant improvement in cognition from baseline (19.50±3.85) to 4th week (22.44±3.37), and from 4th week to 8th week (25.17±3.47) (Table 4.5). The result of the study also showed that there was a significant difference in BDNF levels among the participants across the time interval. Post-hoc analysis showed that the significant improvement in BDNF level was from baseline (9.54±6.46 ng/ml) to 8th week (13.35±10.56ng/ml).

There was a significant difference in QoL scores in the OWECRG across time intervals ($f=7.19$, $p<0.01$). Post-hoc analysis revealed significant improvement in quality-of-life scores from 197.44±39.83 at baseline to 221.28±25.72 at week 8 (Table 4.5). There was also a significant decrease in PR across time interval ($f=5.31$, $p<0.05$). Post-hoc analysis showed the significant difference in participation restriction was between baseline (10.56±3.31) and 4th week (9.44±3.47) (Table 4.5).

Table 4.5: Within- Group Comparison of Cognition, BDNF, QoL and PR from Baseline to Week 8 for the OWECRG

Variables	Baseline $\bar{X}$±S.D	Week 4 $\bar{X}$±S.D	Week 8 $\bar{X}$±S.D	f-value	p-value	η_p^2
Cognition	19.50±3.85^{a}	22.44±3.37^{b}	25.17±3.47^{c}	**35.40**	**<0.01***	**0.67**
BDNF level (ng/ml)	9.54±6.46^{a}	11.54±9.17^{ax}	13.35±10.56^{bx}	**6.46**	**<0.01***	**0.28**
Quality of Life	197.44±39.83^{a}	204.17±41.24^{ax}	221.28±25.72^{bx}	**7.19**	**<0.01***	**0.30**
Participation Restriction	10.56±3.31^{a}	9.44±3.47^{b}	8.39±2.43^{ab}	**5.31**	**0.03***	**0.24**

Key: BDNF= Brain-Derived Neurotrophic Factor, *=significant difference, ng/ml= Nanogramme per milliliter, η_p^2= Partial eta squared items with the same or have at least one same superscript were not significantly different (X^a and Y^a or X^a and Y^{ax}), Items with entirely different superscript were significantly different (X^a and Y^b or X^x and Y^y), OWECRG= combined Overground Walking Exercise and Cognitive Rehabilitation Group

4.6. Across-Groups Comparison of Cognition, BDNF Level, QoL and Participation Restriction

One-way ANOVA was used to compare the study outcomes among participants across the groups from baseline to week 8. The results showed no significant difference in cognition, BDNF level and participation restriction across the three groups at the 4^{th} and 8^{th} week of intervention ($p>0.05$) (Table 4.6). The time-trend effects and differences across groups are as illustrated in Figures 4.2 to 4.5. The percentage mean changes in cognition across the three groups at week 8 was highest in the OWEG (45.3%) and least in the OWECRG (Table 4.7), while the percentage mean changes in PR were highest for the OWEG and least in the CRG (Table 4.7). The percentage mean change in BDNF level was highest in the OWECRG (12.6%, 31.3%, 38.3%). There was however, a significant difference in quality of life across the three groups at the 8^{th} week of intervention ($f=6.05$, $p=0.05$). Post-hoc analysis showed a significant difference in QoL between the OWEG (243.53±17.84) and CRG (222.89±18.35), and also between the OWEG (243.53±17.84) and the OWECRG (221.28±25.72) (Table 4.6).

Table 4.6: Comparison of Cognition, BDNF, QoL and PR across Groups Over 8 Weeks of Intervention

Variables	OWEG $\bar{X}$±S.D	CRG $\bar{X}$±S.D	OWECRG $\bar{X}$±S.D	f-value	p-value
Cognition					
Baseline	18.08±3.60	19.00±3.90	19.50±3.85	**0.65**	**0.53**
Week 4	20.53±2.83	22.78±3.95	22.44±3.37	**2.18**	**0.12**
Week 8	26.24±2.51	25.22±3.26	25.17±3.47	**0.64**	**0.53**
BDNF level (ng/ml)					
Baseline	13.05±8.27	13.81±11.04	9.54±6.46	**1.12**	**0.34**
Week 4	13.88±8.26	15.62±12.98	11.54±9.17	**0.70**	**0.50**
Week 8	14.69±8.85	18.13±14.96	13.35±10.56	**0.78**	**0.46**
Quality of Life					
Baseline	191.00±28.85	202.72±28.83	197.44±39.83	**0.55**	**0.58**
Week 4	202.24±22.49	211.22±21.99	204.17±41.24	**0.44**	**0.65**
Week 8	243.53 ± 17.84^{a}	222.89 ± 18.35^{bx}	221.28 ± 25.72^{cx}	**6.05**	**<0.01***
Participation Restriction					
Baseline	12.06±4.02	10.39±4.24	10.56±3.31	**0.98**	**0.38**
Week 4	9.00±2.45	9.56±2.73	9.44±3.47	**0.95**	**0.39**
Week 8	7.24±2.05	8.39±2.70	8.39±2.43	**2.70**	**0.08**

Key: SD= standard deviation, QoL=Quality of Life, PR=Participation Restriction, BDNF= Brain-Derived Neurotrophic Factor, *=significant difference, df=degree of freedom, ng/ml= Nanogramme per milliliter, **Items with the same or have at least one same superscript are not significantly different (X^{a} and Y^{a} or X^{a} and Y^{ax}), Items with entirely different superscript are significantly different (X^{a} and Y^{b} or X^{x} and Y^{y}), OWEG= overground walking exercise group, CRG= Cognitive Rehabilitation group, OWECRG= combined OWE and CR group**

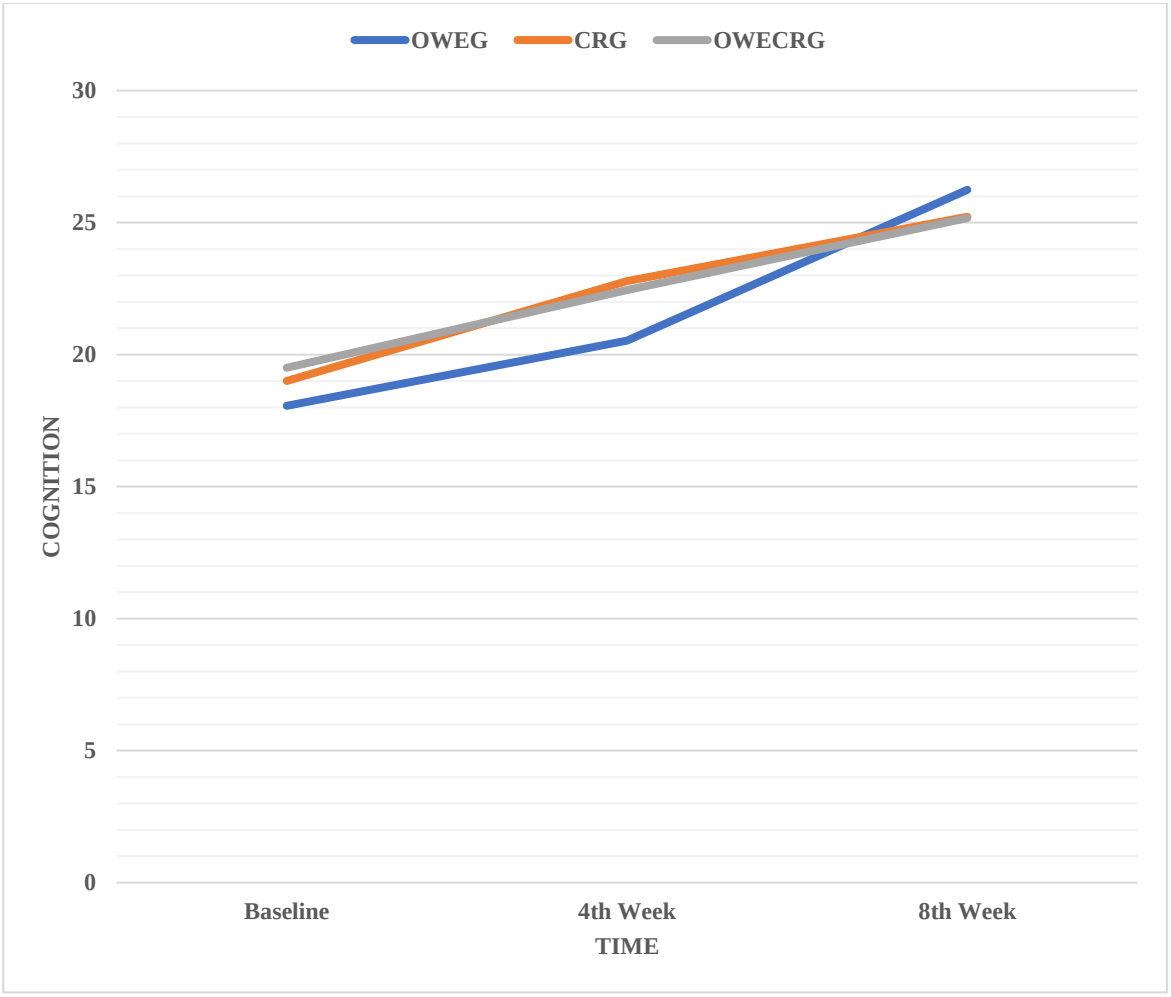

Figure 4.2: Time-Trend of Scores for Cognition across Groups at Baseline, 4th Week and 8th Week of Intervention

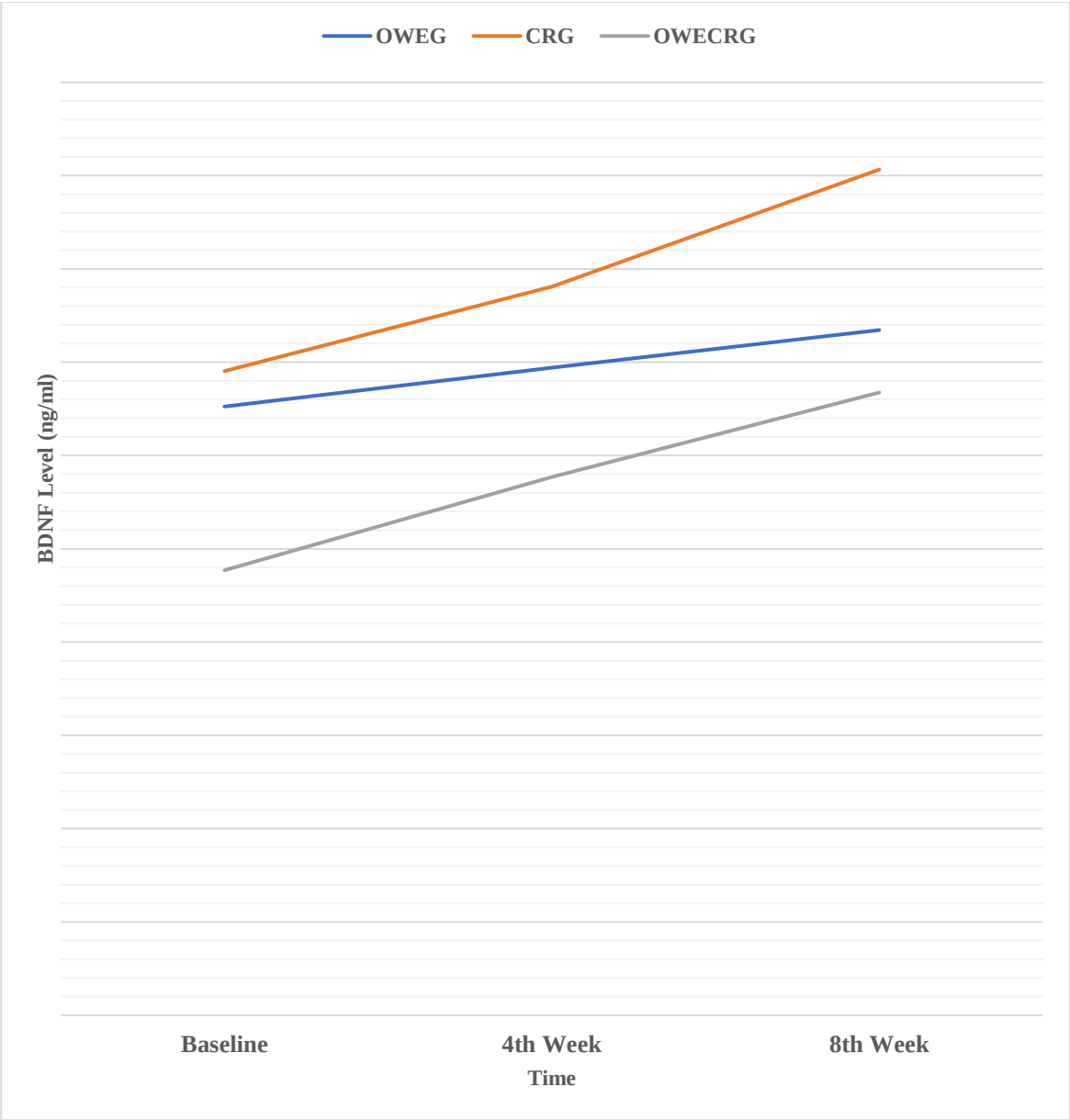

Figure 4.3: Time-Trend of Scores for BDNF Levels across Groups at Baseline, 4th Week and 8th Week of Intervention

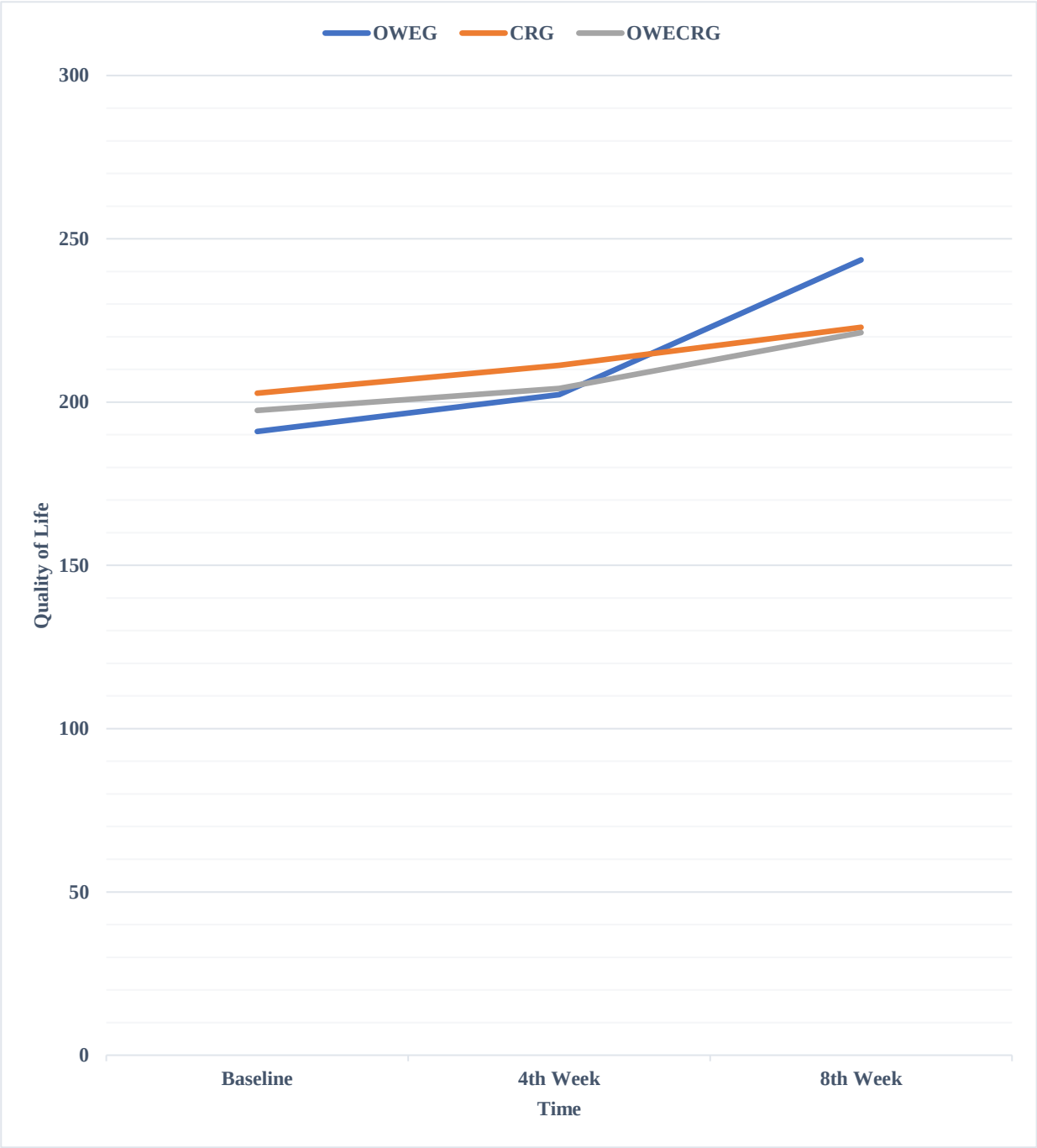

Figure 4.4: Time-Trend of Scores for Quality of Life across Groups at Baseline, 4th Week and 8th Week of Intervention

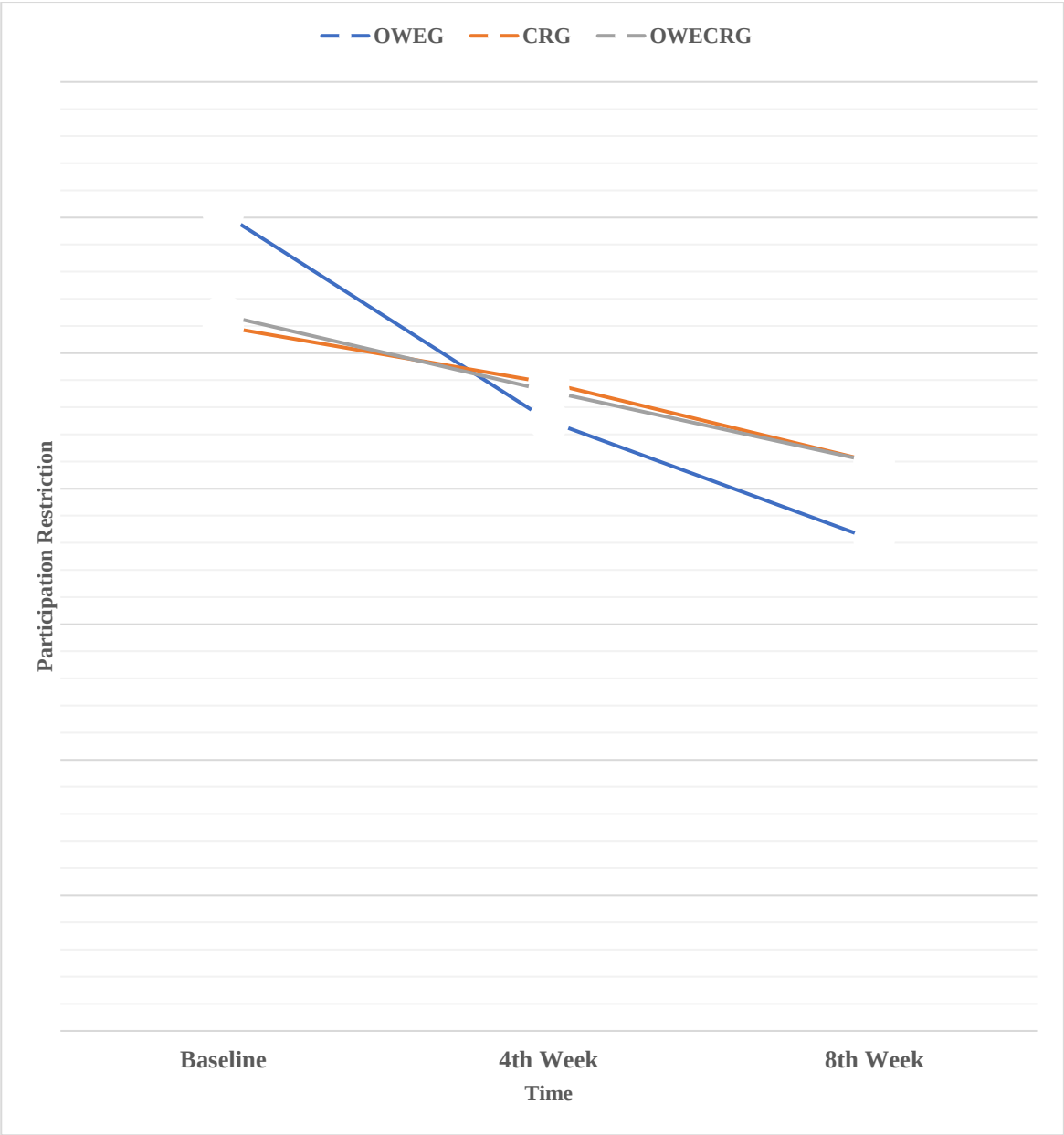

Figure 4.5: Time-Trend of Scores for Participation Restriction across Groups at Baseline, 4th Week and 8th Week of Intervention

Table 4.7: Percentage Changes in Cognition, BDNF levels, QoL and PR after 8 Weeks of Intervention

Variable	Percentage Change (%)		
	OWEG	**CRG**	**OWECRG**
Cognition	45.29	32.74	30.46
BDNF Level	12.57	31.28	38.29
QoL	27.50	9.95	12.07
Participation Restriction	39.97	19.25	20.55

Key: OWEG= overground walking exercise group, CRG= Cognitive Rehabilitation group, OWECRG= combined OWE and CR group QoL= quality of life, BDNF= Brain derived neurotrophic factor, %= percentage

4.7 Hypotheses Testing

1. There would be no significant difference in cognition across baseline, 4th week and 8th weeks of Over-ground Walking Exercise (OWE) among stroke survivors with PSCI in Kano, Nigeria.

Alpha level: 0.05

Observed p = 0.000

Test statistics: Repeated measures ANOVA

Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

2. There would be no significant difference in BDNF across baseline, 4th week and 8th weeks of OWE among stroke survivors with PSCI in Kano, Nigeria.

Alpha level: 0.05

Observed p = 0.000

Test statistics: Repeated measures ANOVA

Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

3. There would be no significant difference in QoL across baseline, 4th week and 8th weeks of OWE among stroke survivors with PSCI in Kano, Nigeria.

Alpha level: 0.05

Observed p = 0.000

Test statistics: Repeated measures ANOVA

Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

4. There would be no significant difference in participation restriction across baseline, 4th week and 8th weeks of OWE among stroke survivors with PSCI in Kano, Nigeria.

Alpha level: 0.05

Observed p = 0.000

Test statistics: Repeated measures ANOVA

Judgment: Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

5. There would be no significant difference in cognition across baseline, 4th week and 8th weeks of cognitive rehabilitation (CR) among stroke survivors with PSCI in Kano, Nigeria.
Alpha level: 0.05
Observed p = 0.000
Test statistics: Repeated measures ANOVA
Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

6. There would be no significant difference in BDNF across baseline, 4th week and 8th weeks of CR among stroke survivors with PSCI in Kano, Nigeria.
Alpha level: 0.05
Observed p = 0.031
Test statistics: Repeated measures ANOVA
Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

7. There would be no significant difference in QoL across baseline, 4th week and 8th weeks of CR among stroke survivors with PSCI in Kano, Nigeria.
Alpha level: 0.05
Observed p = 0.004
Test statistics: Repeated measures ANOVA
Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

8 There would be no significant difference in participation restriction across baseline, 4th week and 8th weeks of CR among stroke survivors with PSCI in Kano, Nigeria.
Alpha level: 0.05
Observed p = 0.004

Test statistics: Repeated measures ANOVA

Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

9. There would be no significant in cognition across baseline, 4th week and 8th week of combined overground walking exercise and cognitive rehabilitation (OWECR) among stroke survivors with PSCI in Kano, Nigeria.

Alpha level: 0.05

Observed p = 0.000

Test statistics: Repeated measures ANOVA

Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected**.

10. There would be no significant in BDNF across baseline, 4th week and 8th week of OWECR among stroke survivors with PSCI in Kano, Nigeria.

Alpha level: 0.05

Observed p = 0.004

Test statistics: Repeated measures ANOVA

Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected.**

11. There would be no significant in QoL across baseline, 4th week and 8th week of OWECR among stroke survivors with PSCI in Kano, Nigeria.

Alpha level: 0.05

Observed p = 0.002

Test statistics: Repeated measures ANOVA

Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected.**

12. There would be no significant in participation restriction across baseline, 4th week and 8th week of OWECR among stroke survivors with PSCI in Kano, Nigeria.
Alpha level: 0.05
Observed p = 0.034
Test statistics: Repeated measures ANOVA
Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected.**

13. There would be no significant difference in cognition among stroke survivors with PSCI across 4 weeks of OWE, CR, and OWECR.
Alpha level: 0.05
Observed p = 0.124
Test statistics: One-way ANOVA
Judgment: Since the observed p-value was greater than the 0.05 Alpha level, the null hypothesis **failed to be rejected**

14. There would be no significant difference in BDNF among stroke survivors with PSCI across 4 weeks of OWE, CR, and OWECR.
Alpha level: 0.05
Observed p = 0.502
Test statistics: One-way ANOVA
Judgment: Since the observed p-value was greater than the 0.05 Alpha level, the null hypothesis **failed to be rejected.**

15. There would be no significant difference in QoL among stroke survivors with PSCI across 4 weeks of OWE, CR, and OWECR.
Alpha level: 0.05
Observed p = 0.648
Test statistics: One-way ANOVA
Judgment: Since the observed p-value was greater than the 0.05 Alpha level, the null hypothesis **failed to be rejected.**

16. There would be no significant difference in participation restriction among stroke survivors with PSCI across 4 weeks of OWE, CR, and OWECR.
Alpha level: 0.05
Observed p = 0.394
Test statistics: One-way ANOVA
Judgment: Since the observed p-value was greater than the 0.05 Alpha level, the null hypothesis **failed to be rejected.**

17. There would be no significant difference in cognition among stroke survivors with PSCI across 8 weeks of OWE, CR, and OWECR.
Alpha level: 0.05
Observed p = 0.529
Test statistics: One-way ANOVA
Judgment: Since the observed p-value was greater than the 0.05 Alpha level, the null hypothesis **failed to be rejected.**

18. There would be no significant difference in BDNF among stroke survivors with PSCI across 8 weeks of OWE, CR, and OWECR.
Alpha level: 0.05
Observed p = 0.462
Test statistics: One-way ANOVA
Judgment: Since the observed p-value was greater than the 0.05 Alpha level, the null hypothesis **failed to be rejected.**

19. There would be no significant difference in QoL among stroke survivors with PSCI across 8 weeks of OWE, CR, and OWECR.
Alpha level: 0.05
Observed p = 0.004
Test statistics: One-way ANOVA
Judgment: Since the observed p-value was less than the 0.05 Alpha level, the null hypothesis was **rejected.**

20. There would be no significant difference in participation restriction among stroke survivors with PSCI across 8 weeks of OWE, CR, and OWECR.

Alpha level: 0.05

Observed p = 0.077

Test statistics: One-way ANOVA

Judgment: Since the observed p-value was greater than the 0.05 Alpha level, the null hypothesis **failed to be rejected.**

CHAPTER FIVE
DISCUSSION

5.1 Discussion

This study investigated the comparative effects of an eight-week over-ground walking exercise, cognitive rehabilitation and the combined interventions on cognition, BDNF level, Quality of life (QoL), and participation restriction among stroke survivors with post-stroke cognitive impairment (PSCI). PSCI had been shown to improve following treatment with aerobic exercise (Abba et al., 2020). Interventions in most of the previous studies involved the use of cycle ergometers or treadmills which are not readily affordable and not easily applicable in Nigerian clinics. Overground walking exercise is an inexpensive and natural form of aerobic exercise which could be used in place of cycle ergometer or treadmill. However, its effects on important indicators of recovery of cognition among stroke survivors needed to be investigated.

5.2 Socio-demographic and Clinical Characteristics of Study Participants

The mean age of the participants in this study was 48.42±27.39 years. This indicates that majority of the participants in the study were middle-aged stroke survivors. This is similar to the findings of El-Tamawy et al. (2014), where the majority of the participants were middle aged stroke survivors. About two-thirds of the participants were males. This is in line with findings from an earlier study by Ploughman et al. (2008) in which there were more male participants than females. Most of the participants in this study had low educational attainment of less than or equal to 12 years. This is similar to the reports from a study by Blanchet et al. (2016) where participants had mean years of educational attainment of 13.71±3.38years.

The mean time since stroke onset of 26.70±27.25 months recorded in this study is similar to what was reported by Ploughman et al. (2008). This suggests that participants in this study were chronic stroke survivors just like participants in previous studies on post-stroke cognitive impairment. The most commonly affected side of the body among the participants

in this study was the left side. According to Marzolini et al. (2012), the left side is the most commonly affected side of the body among stroke survivors. More than half of the participants in this study had ischaemic stroke, which is comparable to findings of Ploughman et al. (2008). The three groups were comparable in terms of age, mean time since onset of stroke, cognition, BDNF level, quality of life and participation restriction. Therefore, differences and changes observed in the groups post-intervention could be attributable to the effects of the interventions.

5.3 Changes in Cognition, BDNF Level, QoL and Participation Restriction across Eight weeks in the OWEG

The result of this study revealed significant improvement in cognition among the stroke survivors following 8-week of over-ground walking exercise. This implies that 8-week over-ground walking exercise was associated with improvement in cognitive function among stroke survivors with PSCI. This finding is in agreement with the finding of El-Tamawy et al. (2014), who reported that eight weeks of aerobic exercise resulted in improvement in cognitive function among stroke survivors with PSCI. This is corroborated by the study of Aghjayan et al. (2021) which stated that aerobic exercise improves cognitive function through enhancement of the size of hippocampal area of the brain.

The result of this study also showed a significant increase in BDNF levels across the time intervals in response to 8 weeks of OWE. This is similar to the findings of El-Tamawy et al. (2014) which revealed significant increase in BDNF levels among stroke survivors following aerobic exercise. Aerobic exercise, such as overground walking, increases BDNF level by stimulating its productions in the peripheral blood cells (mononuclear cells, T and B lymphocytes) (Miranda et al., 2019). This process augments the relatively low level of BDNF in the nervous system especially the hippocampus and cerebral cortex (Miranda et al., 2019).

There was also a significant improvement in quality of life across the time interval following overground walking exercise in this study. This is similar to the finding from the study by Kluding et al. (2011), where an improvement in quality of life was observed following

aerobic exercise intervention. Quality of life is a multidimensional concept that involves all aspect of life including mobility, social roles, self-care and work (Post, 2014). According to Ahmed et al. (2020), quality of life among stroke survivors, is dependent on cognitive function. The improvement in quality of life observed in this study may be related to the observed improvement in cognitive function.

There was a significant reduction in participation restriction across the time interval following overground walking. Cognitive function is associated with increased participation (Annemarie et al., 2021). This is because participation in activity requires certain level of functioning in cognitive domains of memory, attention and concentration. Thus, the better the cognition, the more likely the participation in activities. This suggests the need to improve cognitive function for improved performance of activity among stroke survivors, and overground walking exercise appears to be effective in improving both cognition and participation among stroke survivors with PSCI.

5.4 Changes in Cognition, BDNF Level, QoL and Participation Restriction across Eight weeks in the CRG

There was a significant improvement in cognition following eight weeks of cognitive rehabilitation among stroke survivors. This is comparable to the findings of Oh and Jung (2017) which showed significant improvement in cognitive function among stroke survivors with cognitive impairment following cognitive rehabilitation. Cognitive rehabilitation has been proven to be the gold standard for managing cognitive impairments in patients with neurological conditions.

There was also a significant increase in BDNF levels following cognitive rehabilitation among the participants. Lower levels of BDNF have been associated with poor functional outcome post-stroke (Stanne et al., 2016), whereas higher BDNF levels positively correlate with neural plasticity and recovery of cognition (Mojtabavi et al., 2022). The outcome of this study suggests that the cognitive rehabilitation protocol used in this study was effective in increasing BDNF level among stroke survivors with PSCI. There was also a significant improvement in quality of life of the stroke survivors following cognitive rehabilitation. A

strong association has been reported between cognitive impairment poor quality of life following stroke (Akpalu et al., 2018). Therefore, improving cognitive function may result in better quality of life among stroke survivors, as observed in this study.

There was a significant reduction in participation restriction among the stroke survivors after undergoing the eight-week cognitive rehabilitation protocol. This suggests that the cognitive rehabilitation protocol used in this study was associated with a reduction in participation restriction. This is comparable to the findings of Oh and Jung (2017), that cognitive rehabilitation improved activity participation among stroke survivors with cognitive impairment. Multiple components of activity-participation require some form of cognition or the other. Therefore, improving cognition may subsequently improve participation.

5.5 Changes in Cognition, BDNF, QoL and Participation Restriction across Eight weeks in the OWECRG

The result of this study showed a significant improvement in cognition among participants in the combined overground walking exercise and cognitive rehabilitation group. This suggests that the combined intervention was also effective in improving cognitive function among stroke survivors. This is similar to the finding of Blanchet et al. (2016) who reported an improvement in cognitive function of stroke survivors following combined aerobic exercise and cognitive rehabilitation. The result also revealed a significant increase in BDNF level across the time intervals following combined interventions. This is expected, as both individual interventions had been shown to be effective in improving BDNF level.

The result of this study showed that there was significant improvement in quality of life among the participants after eight weeks of combined over-ground walking and cognitive rehabilitation. This suggests that the combined intervention proved effective in improving QoL among stroke survivors. This is similar to the findings of Jiang et al. (2022) where it was reported that the administration of combined aerobic exercise and cognitive rehabilitation significantly improved quality of life among stroke survivors. Similarly, there was a significant decrease in participation restriction among the participants in this group.

This is comparable to the findings from a study by Jiang et al. (2022) that showed a significant improvement in participation in activities following combined aerobic exercise and cognitive rehabilitation among stroke survivors.

5.6 Across-Groups Comparison of Cognition, BDNF, QoL and Participation Restriction

The result of this study showed that there was no significant difference in cognition, BDNF level, QoL and participation restriction across the groups from baseline to week 4 of interventions. This suggests that all three interventions were equally effective in improving cognition, BDNF levels, QoL and reducing participation restriction among stroke survivors midway through the intervention period. Previous studies investigating the effect of aerobic exercise on PSCI typically assessed outcomes at a minimum period of eight weeks. Therefore, this study represents the initial effort to determine the differences or potential superiority of interventions at four weeks of the interventions. Moreover, this provides a broader range of treatment options for stroke survivors with mild to moderate cognitive impairment, as none of the interventions was shown to be clearly superior.

The results of this study also revealed that there was no significant difference in cognition among the participants across the three groups from baseline to week 8. This suggests that all three interventions are effective in improving cognition among stroke survivors. Contrarily, studies conducted by Jiang et al. (2022) and Ye et al. (2021) reported significant differences in cognition across interventions, in favour of combined aerobic exercise and cognitive rehabilitation. One potential reason for this disparity could be that the other studies assessed outcomes at 6 months and 12 weeks for Jiang et al. (2022) and Ye et al. (2021) respectively. This suggests that over a longer term, the combined intervention was superior to other individual interventions. It could also be because the participants in the combined intervention group received half the duration of each individual interventions.

In addition, the result of the study revealed no significant difference in BDNF levels among the participants across the three groups from baseline to week 8. It has been reported that BDNF levels are associated with level of cognition among stroke survivors (Hassan &

Yarube, 2018). However, the results from this study indicated no significant difference in cognition among the three groups, and also in the BDNF. Additionally, a previous study that reported the effect of aerobic exercise on BDNF level among stroke survivors (El-Tamawy et al., 2014) observed only within-group effects. Therefore, in terms of improving BDNF levels among stroke survivors, no intervention was found to be superior.

Furthermore, the result of this study revealed that there was no significant difference in participation restrictions among the stroke survivors across the three groups. This aligns with the findings from the study by Ye et al. (2021), which reported that no intervention was superior to the others in reducing participation restriction pot-stroke. In contrast, there was a significant improvement in quality of life across the groups at week 8 of the interventions. The observed difference improvement was in favour of the overground walking exercise group. This is contrary to the findings of Ye et al. (2021), which showed that there was no significant difference in quality of life among participants across the groups in their study. The variation in the findings between this study and the study by Ye et al. (2021) may be attributed to differences in the instruments used to assess quality of life. Quality of life was assessed in this study using the Stroke Specific Quality of Life (SSQoL) scale, whereas Ye et al. (2021) assessed quality of life with the Stroke Impact Scale (SIS).

CHAPTER SIX

SUMMARY, CONCLUSION AND RECOMMENDATIONS

6.1 Summary

Neurological deficits following a stroke include motor, sensory/perceptual and cognitive impairments. Post-stroke Cognitive Impairment (PSCI) is a major cause of disability, Participation Restriction (PR) and poor Quality of Life (QoL). Evidence has shown that the gold standard for PSCI rehabilitation is Cognitive Rehabilitation (CR). A systematic review of studies investigating the effects of aerobic exercise on cognitive function has shown its effectiveness in improving various aspects of cognitive function among stroke survivors, and that it should remain an essential component of post-stroke rehabilitation. Nevertheless, further high-quality randomized controlled trials are needed to provide additional evidence to support its use. Additionally, the effects of Overground Walking Exercise (OWE), a relatively inexpensive form of aerobic exercise, on cognitive function among African stroke survivors had not been fully investigated. Therefore, this research was conducted to examine the comparative effects of overground walking exercise and cognitive rehabilitation on cognition, BDNF levels, quality of life and participation restriction among stroke survivors with post-stroke cognitive impairments.

The study was a randomised controlled trial. 60 stroke survivors with mild to moderate cognitive impairment were recruited from three tertiary hospitals in Kano and randomly assigned into three groups: Over-ground Walking Exercise Group (OWEG), Cognitive Rehabilitation Group (CRG) and combined OWE and CR Group (OWECRG). The participants in each group received moderate-intensity self-paced OWE, Zoltan protocol CR and combined interventions. All interventions were administered thrice weekly for 8 weeks. Cognition, BDNF level, QoL and participation restriction were assessed using Montreal Cognitive Assessment (MoCA), ELISA reagent, SSQoL and LHS respectively at baseline, 4th and 8th week of interventions. Descriptive statistics of frequency, percentages, mean and standard deviations was used to summarise data. Repeated measures ANOVA was used

for within-group comparison of variables at baseline, 4th and 8th weeks. One-way ANOVA was used for across-groups comparison of variables at baseline, 4th and 8th weeks. The level of significance was set at 0.05.

Fifty-three stroke survivors comprising 35 males, and aged 48.42±27.39 years completed the study. The mean duration since stroke onset was 26.70±27.25 months. Participants in the groups were comparable in age, time since onset of stroke and other baseline characteristics. The results of the study showed a significant difference in cognition, BDNF levels, quality of life and participation restriction within the OWEG, CRG and OWECRG ($p<0.05$). No difference in cognition, BDNF levels and participation restriction was observed across the OWEG, CRG and OWECRG ($p>0.05$). There was however a significant difference in quality of life across the OWEG, CRG and OWECRG ($p<0.05$).

6.2 Conclusions

Based on the findings from this study the following conclusions were drawn:

1. Overground walking exercise, cognitive rehabilitation, and a combination of both were similarly effective in improving cognitive function, BDNF levels, QoL and in reducing participation restriction among stroke survivors with post-stroke cognitive impairment.
2. Overground walking exercise seemed to be more effective in improving quality of life among stroke survivors with post-stroke cognitive impairment than cognitive rehabilitation or combined overground walking exercise and cognitive rehabilitation.

6.3 Recommendations

Based on the results of this study, it is recommended that:

1. Overground walking exercise could be administered alone or in combination with cognitive rehabilitation in the management of stroke survivors with PSCI.
2. Overground walking exercise was associated with the greatest improvement in quality of life and should be the most preferred choice of intervention for improving quality of life among stroke survivors with PSCI.

3. Future studies should investigate the effect of upper extremity aerobic exercise on cognitive function, participation, QoL and BDNF levels among non-ambulant stroke survivors.
4. Future studies should also investigate the effects of aerobic exercise on cognitive function, participation, QoL and BDNF levels among stroke survivors with severe cognitive impairment, and who have no formal education.

6.4 Contributions to knowledge

This study provided information on the effectiveness of overground walking in improving cognition and quality of life among stroke survivors with post-stroke cognitive impairment. The findings from the study have also shown that overground walking exercise appeared to reduce participation restriction among stroke survivors. Overground walking exercise is a user-friendly activity that requires minimal supervision. It could be recommended for the cognitive rehabilitation of stroke survivors with post-stroke cognitive impairments, and for enhancing their quality of life and promoting community participation among them. Additionally, overground walking exercise could be used as a viable alternative to bicycle ergometers and treadmills, in setting where this equipment is not available.

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APPENDIX 1

Patient Health Questionnaire

PHQ9P

PATIENT HEALTH QUESTIONNAIRE - 9

Comments:

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
	0 + ____ + ____ + ____			
	= Total Score: ____			

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

Developed by Drs. Robert L. Spitzer, Janet B. W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc.

Patient's name:	Date:

APPENDIX 2

Borg RPE scale

While doing physical activity, we want you to rate your perception of exertion. This feeling should reflect how heavy and strenuous the exercise feels to you, combining all sensations and feelings of physical stress, effort, and fatigue. Do not concern yourself with any one factor such as leg pain or shortness of breath, but try to focus on your total feeling of exertion. Look at the rating scale below, choose the number that best describes your level of exertion while you are engaging in an activity. It ranges from 6 to 20, where 6 means "no exertion at all" and 20 means "maximal exertion." This will give you a good idea of the intensity level of your activity, and you can use this information to speed up or slow down your movements to reach your desired range.
Try to appraise your feeling of exertion as honestly as possible, without thinking about what the actual physical load is. Your own feeling of effort and exertion is important, not how it compares to other people's.

After a few minutes, assess your RPE from the scale. If you are still at an RPE under 12, pick up your pace to increase your intensity by going faster. If you are feeling an intensity of 19 you might want to slow your pace or decrease the resistance until you are back in the moderate-intensity zone.

9 correspond to "very light" exercise. It is like walking slowly at his or her own pace for some minutes

13 on the scale is "somewhat hard" exercise, but it still feels OK to continue.

17 "very hard" is very strenuous. A healthy person can still go on, but he or she really has to push him- or herself. It feels very heavy, and the person is very tired.

19 on the scale is an extremely strenuous exercise level. For most people this is the most strenuous exercise they have ever experienced.

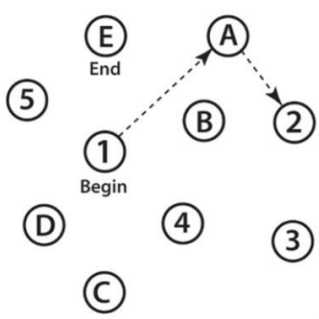
#	
6	No exertion at all
7	
7.5	Extremely light (7.5)
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

APPENDIX 3

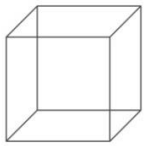
Montreal Cognitive assessment test

MONTREAL COGNITIVE ASSESSMENT (MOCA®) Name:
Version 8.1 English Education: Date of birth:
Sex: DATE:

VISUOSPATIAL / EXECUTIVE — POINTS



Copy cube



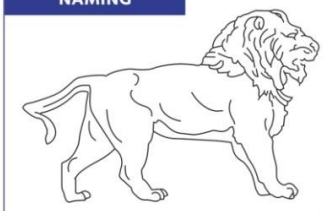
[ ] [ ]

Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

__/5

NAMING



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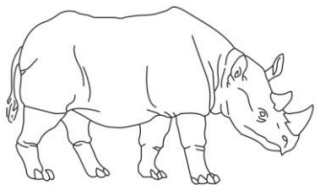
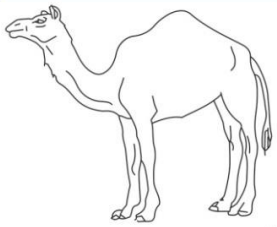


[ ]



[ ]

__/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1ST TRIAL					
2ND TRIAL					

NO POINTS

ATTENTION Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order. [ ] 2 1 8 5 4
Subject has to repeat them in the backward order. [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100. [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0**

__/3

LANGUAGE Repeat: I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency: Name maximum number of words in one minute that begin with the letter F. [ ] _____ (N ≥ 11 words)

__/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train - bicycle [ ] watch - ruler

__/2

DELAYED RECALL

(MIS)	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
X3		[ ]	[ ]	[ ]	[ ]	[ ]	
X2	Category cue						MIS = ____ /15
X1	Multiple choice cue						

Memory Index Score (MIS)

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

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Administered by: _____

Training and Certification are required to ensure accuracy

MIS: /15
(Normal ≥ 26/30)
Add 1 point if ≤ 12 yr edu

TOTAL __/30

APPENDIX 4

Stroke-Specific Quality of Life Scale Version 2.0-Original English Version

Instructions: We will like to know how you are doing with activities or feelings that can sometimes be affected by stroke. Each question will ask about a specific activity or feeling. For each question think about how that activity or that feeling has been for you in the last one week. The first group of questions asks about how much trouble you have with specific activities. Each question deals with problems that some people have after their stroke. Circle a number in the box that best describes how much trouble you have with the activity in the past week.

DURING THE LAST WEEK:

Energy

My energy level is	Total help - Couldn't do it at all – Strongly Agree 1	A lot of trouble – Moderately Agree 2	Some help - Some trouble – Neither agree or disagree 3	A little help - A little trouble – Moderately disagree 4	No help needed - No trouble at all – Strongly disagree 5
1.10 I felt tired most of the time					
1.11 I had to stop and rest often during the day					
1.12 I was too tired to do what I wanted to do					

Family Roles

My role in the family is	Couldn't do it at all 1	A lot of trouble 2	Some trouble 3	A little trouble 4	No trouble at all 5
1. I didn't join in activities just-for- fun with my family					
2. I felt I was a burden to my family					
3. My physical condition interfered with my family life					

Language

My language is	Couldn't do it at all 1	A lot of trouble 2	Some trouble 3	A little trouble 4	No trouble at all 5
1. Did you have trouble speaking? For example, get stuck, stutter, stammer or slur your words?					
2. Did you have trouble speaking clearly enough to use the telephone?					
3. Did other people have trouble in understanding what you said?					
4. Did you have trouble finding the word you wanted to say?					
5. Did you have to repeat yourself so others could understand you?					

Mobility

My mobility is	Total help 1	A lot of trouble 2	Some help 3	A little help 4	No help needed 5
1. Did you have trouble walking? (if you can't walk, circle 1 and go to question M7)					
2. Did you lose your balance when bending over to or reaching for something?					
3. Did you have trouble climbing stairs?					
4. Did you have trouble with needing to stop and rest when walking or using a wheelchair?					
5. Did you have trouble with standing?					
6. Did you have trouble getting out of a chair?					

Mood

My Mood is	Strongly Agree 1	Moderately Agree 2	Neither agree or disagree 3	Moderately disagree 4	Strongly disagree 5
1. I was discouraged about my future					
2. I wasn't interested in other people or activities					
3. I felt withdrawn from other people					
4. I had little confidence in myself					
5. I was not interested in food.					

Personality

My personality is	Strongly Agree 1	Moderately Agree 2	Neither agree or disagree 3	Moderately disagree 4	Strongly disagree 5
1. I was irritable					
2. I was impatient with others					
3. My personality has changed					

Self-Care

I can take care of myself	Total help 1	A lot of trouble 2	Some help 3	A little help 4	No help needed 5
1. Did you have trouble preparing food?					
2. Did you have trouble eating? For example, cutting food or swallowing?					
3. Did you have trouble getting dressed? For example, putting on socks or shoes, buttoning buttons or zipping.					
4. Did you have trouble taking a bath or a shower?					

5. Did you have trouble using the toilet?					

Social Roles

My role in the society is	Strongly Agree 1	Moderately Agree 2	Neither agree or disagree 3	Moderately disagree 4	Strongly disagree 5
1. I didn't go out as often as I would like.					
2. I did my hobbies and recreation for shorter period of time than I would like.					
3. I didn't see as many of my friends as I would like					
4. I had sex less often than I would like					
5. My physical condition interfered with my social life					

Thinking

My thinking is	Strongly Agree 1	Moderately Agree 2	Neither agree or disagree 3	Moderately disagree 4	Strongly disagree 5
1. It was hard for me to concentrate.					
2. I had trouble remembering things.					
3. I had to write things down to remember them.					

Upper Extremity Function

The use of my arm and hand is	Total help 1	A lot of trouble 2	Some help 3	A little help 4	No help needed 5
1. Did you have trouble writing or typing?					
2. Did you have trouble putting on socks?					
3. Did you have trouble buttoning buttons?					
4. Did you have trouble zipping a zipper?					

5. Did you have trouble opening a jar?					

Vision

My vision	Strongly Agree 1	Moderately Agree 2	Neither agree or disagree 3	Moderately disagree 4	Strongly disagree 5
1. Did you have trouble seeing the television well enough to enjoy a show?					
2. Did you have trouble reaching things because of poor eye sight?					
3. Did you have trouble seeing things off to side?					

Work/Productivity

I do my jobs at home or at work	Strongly Agree 1	Moderately Agree 2	Neither agree or disagree 3	Moderately disagree 4	Strongly disagree 5
1. Did you have trouble doing daily work around the house?					
2. Did you have trouble finishing jobs that you started?					
3. Did you have trouble doing the work you used to do?					

HAUSA VERSION OF SS-QOL 2.0

SHANYEWAR BARIN JIKI: Tambayoyi a kan Inganta Hanyoyin Gudanar da rayuwa. Kashi na 2.0

UMARNI

Wadannan jerin tambayoyi ne da akayi don bincike da sanin halin da kuke ciki dangane da ayyukanku na yau da kullum da kuma yadda kuke ji a jikinku, wanda a wasu lokuta matsalar shanyewar jiki kan iya shafa. Ga kowace tambaya ana bukatar ka bayyana yadda kaji ko yaddaka gudanar da ayyukanka suka kasance a makon da yawuce. Kashin farko na tambayoyin, ana bukatar sanin irin yanayin matsalar da kukan ci karo da su yayin gudanar da wasu ayyuka kebantattu. Kowace tambaya ta tabo wasu matsaloli da mutane kan fuskanta bayan samun matsalar shanyewar barin jikinsu. Ka zagaye amsa ko zabin da kake ganin ya fi dacewa da irin matsalar da ka fuskanta yayin gudanar da wasu ayyuka, a satin da yagabata.

A SATIN DA YA GABATA:

Kuzari

Kuzarina	Ban iyayi sam-sam - Na yarda kwarai - (yayi) muni sosai kamin na samu rashin lafiyar 1	Da matukar wahala - Na yarda sama-sama - (yayi) muni kamin na samu rashin lafiyar 2	Da kyar - Ba ni da zabi - (yayi) muni kadan kamin na samu rashin lafiyar 3	Da iyar matsala kadan - Ban yarda ba - Daida iyake da kamin na samu rashin lafiyar 4	Ban sami wata matsala ba sam-sam - Ban yarda ba sam-sam 5
1. Ka samu cikas na yin magana? Kamar sarkewar harshe ko in'ina yayin magana?					
2. Na ji gajiya a mafi yawan lokaci.					
3. Da rana, ina tsayawa na huta yayin tafiya.					
4. Saboda gajiya sosai ba na iya yin abin da nake son yi.					

Matsayina a Iyali

Matsayina a cikin iyali	(yayi) muni sosai kamin na samu rashin lafiyar 1	(yayi) muni kamin na samu rashin lafiyar 2	(yayi) muni kadan kamin na samu rashin lafiyar 3	Daida iyake da kamin na samu rashin lafiyar 4	Ban sami wata matsala ba sam-sam 5
1. Ban shawar shiga sha'anonin mutane					
2. Na ji kamar na zame wa iyalina wata matsala					

3. Yanayin da na shiga ya kawo cikas a rayuwata da iyalina					

Harshena

Harshena/Maganata	Ban iyayi sam-sam 1	Da matukar wahala 2	Da kyar 3	Da iyar matsala kadan 4	Ban sami wata matsala ba sam-sam 5
1. Ka sami matsalar yin Magana yadda ya kamata? Musamman wajen yin amfani da wayar hannu?					
2. Shin mutane sun sami matsalar fahimtar maganarka?					
3. Ka samu matsalar laluben Kalmar da za ka furta?					
4. Shin sai ka maimaita Magana sannan ake iya fahim tarka?					

Zirga / Zirga

Zirga-zirgata	Ban iyayi sam-sam 1	Da matukar wahala 2	Da kyar 3	Da iyar matsala kadan 4	Ban sami wata matsala ba sam-sam 5
1. Ka samu cikas wajen yin tafiya? (idan ba ka iya tafiya to ka kewaye tambaya M1 sannan ka tafi tambaya ta M7)					
2. Ka yi tangadi (taga-taga) yayin sunkuyawa ko wajen kokarin kaiwa ga wani abu?					
3. Ka samu matsalar hawa matattakalar bene?					
4. Ka samu matsalar bukatar neman tsayawa ko hutawa yayin tafiya ko wajen amfani da kujerar guragu?					
5. Ka samu matsala wajen tsayawa?					
7. Ka samu matsalar iya mikewa daga kan kujera?					

Yanayi

Halin zuciyata/yanayina	Na yarda kwarai 1	Na yarda sama- sama 2	Ba ni da zabi 3	Ban yarda ba 4	Ban yarda ba sam-sam 5
1. Banajin dadin rayuwata					
2. Ban samu sha'awar shiga harkokin mutane ko wasu ayyuka ba					
3. Na ji kamar na yi nesa da mutane.					
4. Na karaya da kaina.					
5. Ban jisha'awar cin abinci ba.					

Kamala

Kamalata	Na yarda kwarai 1	Na yarda sama- sama 2	Ba ni da zabi 3	Ban yarda ba 4	Ban yarda ba sam-sam 5
1. Na kasance mai saurin fushi					
2. Ba na iya hakuri (jure wa) da mutane					
3. Yanayina ya sauya					

Kula da kai

Zan iya kula da kaina	Ban iyayi sam-sam 1	Da matukar wahala 2	Da kyar 3	Da iyar matsala kadan 4	Ban sami wata matsala ba sam-sam 5
1. Kun samu matsala wajen girka abinci, ko zuwa sayen kayan abinci?					
2. Ka samu matsala wajen tauna ko hadiyar abinci?					
3. Ka samu matsala wajen sa kaya? Kamar sa safa ko takalmi ko sa maballi da jan zif na riga/da mazagi na wando, ko daura zani, ko kalabi, ko hijabi?					
4. Ka samu matsala wajen yin wanka?					
5. Ka samu matsala wajen yin amfani da bandaki?					

Mu'amula

Matsayina a cikin al'umma	Na yarda kwarai 1	Na yarda sama- sama 2	Ba ni da zabi 3	Ban yarda ba 4	Ban yarda ba sam-sam 5
1. Ban samu fita kamar yadda niske so ba					
2. Inayin wasannina da nikeyi ba kamar yadda na sababa.					
3. Ban samu ganin mafiyawan abokaina kamar yadda nake so.					
4. Ban samu kusantar iyalina ba (jima'i) kamar yadda nake so.					
5. Yanayin jikina ya kawo tarnaki wajen gudanar da rayuwata a cikin jama'a.					

Tunanina

Tunanina	Na yarda kwarai 1	Na yarda sama 2	Ba ni da zabi 3	Ban yarda ba 4	Ban yarda ba sam-sam 5
1. Samun nutsuwa ya yi min wuya sosai					
2. Na samu matsalar tuna abubuwa					
3. Sai na rubuta abubuwa domin kadana manta su					

Yanayin amfani da hannuna

Yin amfani da hannayena	Ban iyayi sam-sam 1	Da matukar wahala 2	Da kyar 3	Da iyar matsala kadan 4	Ban sami wata matsala ba sam-sam 5
1. Ka samu matsalar yin rubutu da hannu ko da naura mai kokoiwa?					
2. Ka samu matsala wajen saka safa?					
3. Ka samu matsalar saka maballin riga?					
4. Ka samu matsalar jan zif?					
5. Ka samu matsala wajen bude murfin kwalba?					

Ganina

Ganina	Na yarda kwarai 1	Na yarda sama- sama 2	Ba ni da zabi 3	Ban yarda ba 4	Ban yarda ba sam-sam 5
1. Ka samu cikas wajen jin dadin kallon talabijin kamar yadda ya kamata?					
2. Ka samu matsalar rashin iya kai wa ga wasu abubuwa saboda rashin karfin gani?					
3. Ka samu matsalar na gani da gefe guda na idanun ka?					

Ayyukan Gida / Sana'a

Ina yin ayyukana a gida ko wajen aiki/Sana'a	Ban iyayi sam-sam 1	Da matukar wahala 2	Da kyar 3	Da iyar matsala kadan 4	Ban sami wata matsala ba sam-sam 5
1. Ka samu matsala wajen yin ayyukan yau da kullum na gida?					
2. Ka samu matsalar kasa karasa ayyukan da ka fara?					
3. Ka samu matsalar gudanar da ayyukan da ka saba yi?					

APPENDIX 5

London Handicap Scale

This questionnaire is about the way your health affects your everyday life. Please read the instructions for each question and then answer by ticking the box next to the sentence which describes you best.

When answering the questions, it may help to think about the things you have done over the last week and compare yourself with someone like you who is in good health.

1. Getting around: Think about how you get from one place to another, using any help, aids or means of transport that you normally have available.

Does your health stop you from getting around?

Tick one box

Not at all:	You go everywhere you want to, no matter how far away.	☐ 1
Very slightly:	You go most places you want, but not all.	☐ 2
Quite a lot:	You get out of the house, but not far away from it.	☐ 3
Very much:	You don't go outside, but you can move around from room to room indoors	☐ 4
Almost completely:	You are confined to a single room, but can move around in it.	☐ 5
Completely:	You are confined to a bed or a chair. You cannot move around at all. There is no one to move you.	☐ 6

2. Looking after yourself: Think about things like housework, shopping, looking after money, cooking, laundry, getting dressed, washing, shaving and using the toilet.

Does your health stop you looking after yourself?

Tick one box

Not at all:	You do everything to look after yourself.	☐ 1
Very slightly:	You need a little help now and again.	☐ 2
Quite a lot:	You need help with some tasks (such as heavy housework or shopping), but no more than once a day.	☐ 3
Very much:	You do some things for yourself, but you need help more than once a day. You can be left alone safely for a few hours.	☐ 4

Almost completely:	You need help to be available all the time. You cannot be left alone safely.	☐ 5
Completely:	You need help with everything. You need constant attention, day and night.	☐ 6

3. Work and leisure: Think about things like work (paid or not), housework, gardening, sports, hobbies, going out with friends, travelling, reading looking after children, watching television and going on holiday.

Does your health limit your work or leisure activities?

Tick one box

Not at all:	You do everything you want to do.	☐ 1
Very slightly:	You do almost all the things you want to do	☐ 2
Quite a lot:	You find something to do almost all the time but cannot do some things for as long as you would like.	☐ 3
Very much:	You are unable to do a lot of things, but can find something to do most of the time.	☐ 4
Almost completely:	You are unable to do most things, but can find something to do some of the time	☐ 5
Completely:	You sit all day doing nothing. You cannot keep yourself busy or take part in any activities	☐ 6

4. Getting on with people: Think about family, friends and the people you might meet during a normal day.

Does your health stop you getting on with people?

Tick one box

Not at all:	You get on well with people, see everyone you want to see, and meet new people	☐ 1
Very slightly:	You get on well with people, but your social life is slightly limited.	☐ 2
Quite a lot:	You are fine with people you know well but you feel uncomfortable with strangers.	☐ 3
Very much:	You are fine with people you know well but you have few friends and little contact with neighbours. Dealing with strangers is very hard.	☐ 4
Almost completely:	Apart from the people who look after you, you see no-one. You have no friends and no visitors.	☐ 5

Completely:	You don't get on with anyone, not even people who look after you.	☐ 6

5. Awareness of your surroundings: Think about taking in and understanding the world about you and finding your way around in it.

Does your health stop you understanding the world around you?

Tick one box

Not at all:	You fully understand the world around you. You see, hear speak and think clearly, and your memory is good	☐ 1
Very slightly:	You have problems with hearing, speaking, seeing or your memory, but these do not stop you doing most things.	☐ 2
Quite a lot:	You have problems with hearing, speaking, seeing or your memory, which makes life difficult a lot of the time, but you understand what is going on.	☐ 3
Very much:	You have (he/she has) great difficulty understanding what is going on.	☐ 4
Almost completely:	He/she is unable to tell where he/she is or what day it is. He/she cannot look after him/herself at all.	☐ 5
Completely:	He/she is unconscious, completely unaware of anything going on around him/her	☐ 6

6. Affording the things you need: Think about whether health problems have led to any extra expenses, or have caused you to earn less than you would if you were healthy.

Are you able to afford the things you need?

Tick one box

Yes, easily:	You can afford everything you need. You have easily enough money to buy modern labour saving devices, and anything you may need because of ill-health.	☐ 1
Fairly easily:	You have just about enough money. It is fairly easy to cope with expenses caused by ill-health.	☐ 2
Just about:	You are less well off than other people like you; however, with sacrifices you can get by without help.	☐ 3
Not really:	You only have enough money to meet your basic needs. You are dependent on state benefits for any extra expenses you have because of ill-health.	☐ 4

No	You are dependent on state benefits, or money from other people or charities. You cannot afford things you need.	☐ 5
Absolutely not:	You have no money at all and no state benefits. You are totally dependent on charity for your most basic needs.	☐ 6

APPENDIX 6

Ethical Approval

AMINU KANO TEACHING HOSPITAL
P.M.B. 3452, ZARIA ROAD, KANO.
(☎07068297399)www.akth.info/www.akth gov.ng, email: equiries@akth.info/akthkano@yahoo.com

CHAIRMAN BOARD OF MANAGEMENT	CHIEF MEDICAL DIRECTOR	CHAIRMAN M.A.C	DIRECTOR OF ADMINISTRATION
HON. EMMA ENEUKWU	PROF. AMINU ZAKARI MOHAMMED MBBS, FMC PATH	DR. ABDULRAHMAN ABBA SHESHE MBBS, FMCS, FICS	ZAINAB AHMED GWADABE (MRS) B.A. Ed M.Ed (Admin/ Planning)

NHREC/21/08/2008/AKTH/EC/2471

AKTH/MAC/SUB/12A/P-3/VI/2571 **2nd April, 2019**

Muhammad Aliyu Abba
Department of Physiotherapy
College of Medicine
University of Ibadan
Ibadan, Nigeria.

ETHICS APPROVAL

Further to your application in respect of your research proposal titled "Walking Exercise Versus Cognitive Rehabilitation Protocols on Brain-derived Neurotrophic Factor, Cognition, Participation and Quality of Life among Stroke Survivors", The Committee reviewed the proposal and noted same as a prospective study.

In view of the above, Ethics approval is hereby granted to conduct the research.

However, the approval is subject to periodic reporting of the progress of the study and its completion to the Research Ethics Committee.

Regards,

Abubakar S. Mahmud
Secretary, Research Ethics Committee
For: Chairman

APPENDIX 7

Ethical Approval

KANO STATE OF NIGERIA
MINISTRY OF HEALTH
2nd & 3rd Floor, Post Office Road,
P.M.B. 3066, Kano.

Commissioner: 08023337417
Permanent Secretary: 09096619985
website: www.kanostateministryofhealth.gov.ng

Ref: MOH/Off/797/T.I/1171 *Date:* 15th March, 2019

Abba Muhammad Aliyu,
Department of Physiotherapy,
Faculty of Clinical Sciences,
College of Medicine,
University of Ibadan,
Oyo.

RE: APPLICATION FOR ETHICAL APPROVAL

Reference to your letter dated 19th February, 2019 on the above request addressed to the Chairman Health Research Ethics Committee of the Ministry requesting for ethical approval to conduct a Research work at Aminu Kano Teaching Hospital, Murtala Muhammad Specialist and Muhammad Abdullahi Wase Specialist Hospitals, Respectively Kano State.

2. The research entitled ***"Walking Exercise versus Cognitive Rehabilitation Protocols on Brain-derived Neurotrophic Factor, Cognition, Participation and Quality of Life among Stroke Survivors"*** is for the award of Doctor of Philosophy Degree in Physiotherapy.

3. In view of the foregoing, I wish to convey the Ministry's approval for you to conduct the research at the above mentioned hospitals.

4. You are also requested to share your findings with the Ministry of Health, Kano state.

5. Best Regards

Liti Gwarzo, Abdullahi
Ag. DPRS
Secretary (HREC)
For: Honourable Commissioner

APPENDIX 8

18 March 2019

To Whom It May Concern:

RE: Walking Exercise Versus Cognitive Rehabilitation Protocols on Brain-Derived Neurotrophic Factor, Cognition, Participation and Quality of Life among Stroke Survivors

As project manager for the Pan African Clinical Trial Registry (www.pactr.org) database, it is my pleasure to inform you that your application to our registry has been accepted. Your unique identification number for the registry is **PACTR201903762696119**.

Please be advised that you are responsible for updating your trial, or for informing us of changes to your trial.

Additionally, please provide us with copies of your ethical clearance letters as we must have these on file (via email or post or by uploading online) at your earliest convenience if you have not already done so.

Please do not hesitate to contact us at +27 21 938 0835 or email epienaar@mrc.ac.za should you have any questions.

Yours faithfully,

Elizabeth D Pienaar
www.pactr.orgProject Manager
+27 021 938 0835

The South African Medical Research Council
Cochrane South Africa | PO Box 19070, Tygerberg, 7505
Tel: +27 (0)21 938 0438 | Email: cochrane@mrc.co.za | Web: www.southafrica.cochrane.org

APPENDIX 9

6-Minute Walk Test (6MWT)

The test measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 minutes. It will be performed in a gymnasium which is well-ventilated. Marks were placed on the ground at 0 meter and 10 meters long respectively. There were markings at every 1 meter on the ground up to the 10^{th} meter. The researcher/ research assistant practically demonstrate to the patients how the test will be performed. Two individuals, that is the researcher and a research assistant conducts the test (one will time the patient and the other will count the number of laps). The patient will rest for about 15-20 minutes and had fasted for at least two hours after his/ her last meal before commencement of the test. Each patient will stand and then walk to the 10 meters and return to the 0 meter repeatedly for 6 minutes. A stop watch will be used to record the total time for the test (6 minutes)

Administering test

1. Prior to walking say to patient:

The objective of this test is to walk as **FAR AS POSSIBLE** for 6 minutes. You will walk back and forth along this course (demonstrate one lap for the patient) for six minutes

You may slow down if necessary. If you stop, I want you to continue to walk again as soon as possible. You will be informed of the time and encouraged each minute.

Please do not talk during the test unless you have a problem or I ask you a question. You must let know if you have any chest pain or dizziness.

When six minutes is up, I will ask you to STOP where you are.

Do you have any questions?

2. To begin say to patient:

Start now, or whenever you are ready (start stopwatch when walking starts).

3. During the test:

Provide the following standard encouragements in even tones. Do not use other words of encouragement or body language to speed up.

1 minute: You are doing well. You have 5 minutes to go.

2nd minute: Keep up the good work. You have 4 minutes to go.

3rd minute: You are doing well. You are halfway done.

4th minute: Keep up the good work. You have only 2 minutes left.

5th minute: You are doing well. You have only 1 minute to go.

When the timer is at 15 seconds, tell the patient, "in a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you."

When the timer buzzes, tell the patient to stop walking. Walk over to the patient, bringing a chair if necessary. Place a marker on the floor where the patient stopped.

Record the post-test vital signs and the number of laps on the worksheet, plus the additional distance covered. Calculate the total distance walked, rounding to the nearest foot, and record on the worksheet. Congratulate the patient on good effort and offer a drink of water.

Stopped or paused before 6 minutes completed?

No/Yes, reason _____

Other symptoms at the end of test: angina dizziness hip, knee, calf pain

other _____

Number of laps_____ + final partial lap _____meters =

Total distance walked in 6 minutes: _____ meters

APPENDIX 10

Timed Up & Go (TUG)

Begin by having the patient sit back in a standard arm chair

Identify a line 3 meters (10 feet) away, on the floor from chair to the cone.

Instruct the patient:

When I say **"Go,"** I want you to:

1. Stand up from the chair.
2. Walk to the line on the floor at your normal pace.
3. Turn around the cone
4. Walk back to the chair at your normal pace.
5. Sit down again.

On the word **"Go,"** begin timing.

1. Stop timing after patient sits back down.

2. Record time.

Time _____ (seconds)

APPENDIX 11

Informed Consent Form

IRB research approval number:
This approval will elapse on:

Title of the research: Walking exercise versus cognitive rehabilitation protocols on brain-derived neurotrophic factor, cognition, participation and quality of life among stroke survivors.

Names and affiliations of researchers:
This study is being conducted by Abba Muhammad Aliyu a PhD student under the supervision of Professor T. K Hamzat and Dr Olubukola A. Olaleye, Department of Physiotherapy, faculty of clinical sciences college of Medicine, University of Ibadan.

Sponsor of the research:
This study is sponsored by Bayero University Kano

Purpose of the study:
The purpose of this study is to find out whether 8-week over-ground walking exercise will be effective in improvement of brain-derived neutrophic factor, cognition, participation and quality of life of stroke survivors cognitive impairment

Procedure:
A total of 57 participants will be recruited and will be assigned randomly into 3 groups using the computer random number generator. You will be required to visit the clinic to receive over-ground-walking exercise, cognitive rehabilitation or combined over-ground-walking exercise / cognitive rehabilitation 3 times per week for a period of 8 weeks. Assessments will be conducted at the initial then 4^{th} and 8 weeks of intervention.

Expected duration of research and participants' involvement:
In total, we expect you to be involved in this research for 8 weeks. You should not spend more than 1 hour at each clinic visit.

Risks:
The over-ground walking, like other exercises, will not cause you any harm

Costs to the participants of joining the research:
You will not be requested to pay for the treatment received

Benefits:

The goal of this study is to find ways of improving cognitive function in stroke survivors as well as the level of their quality of life and participation. It is hoped that over-ground walking exercise will improve cognition, quality of life and participation,

Confidentiality:

All information collected in this study will be given code numbers and no name will be recorded. This cannot be linked to you in anyway and your name or any identifier will not be used in any publication or reports from this study.

Voluntariness:

Your participation in this research is entirely voluntary. You are to opt out of this study anytime you wish to do so

Alternatives to participation:

If you choose not to participate, this will not affect your treatment in this hospital in anyway.

Due inducement:

You will be compensated for lost wages, cost of transport to and fro the research site but you will not be paid any fees for participating in this research.

Use of research data when participant withdraws from research

When you choose to withdraw from research at anytime. Please note that some of the information that has been obtained from you may have been modified or used in reports or publications. These cannot be removed anymore. However, the researchers promise to make effort in good faith to comply with your wishes as much as practicable.

Consent Statement of participant for study participation:

Now that I have read and fully understand the research procedure, I wish to voluntarily participate in the study

Date: _____ Signature: _____

Name: _____

Signature of researcher

Date: _____ Signature: _____

Name: _____

Consent Statement of participant for taking photos/media

I have agreed and fully understand that photos/media of me taken while participating in the study may be used for the purpose of publication, but my face will be pixilated/ covered to avoid recognition

Date: _____ Signature: _____

Name: _____

Signature of researcher

Date: _____ Signature: _____

Name: _____

TAKARDAR BAYANAI

Lambar amincewa da bincike ta Kwamitin Xa'ar Bincike (IRB):

Wannan amincewa za ta daina aiki zuwa:

Taken Bincike: Gwajin tafiya da tsarin magance matsalar tunani dangane da sinadaran da suke fitowa daga qwaqwalwa da tunani da shiga cikin jama'a da kuma ingancin rayuwar waxanda suka kamu da cutar mutuwar varin jiki

Sunaye da adireshin masu bincike:

Wannan bincike ne wanda Abba Muhammad Aliyu yake gudanarwa don samun digiri na uku bisa jagorancin Farfesa T. K Hamzat da kuma Dr Olubukola A. Olaleye na sashen Physio, Tsangayar Kimiyyar ayyukan kulawa da marasa lafiya ta Kwalejin Likitanci, Jami'ar Ibadan.

Waxanda suka xauki nauyin binciken:

Jami'ar Bayero, Kano ce ta xauki nauyin Binciken

Manufar Binciken:

Manufar wannan bincike ita ce domin a gano ko aikin da za a yi a dandaryar qasa na mako 8 zai kasance mai inganci wajen inganta sinadaran da ke fitowa daga qwaqwalwa da tunani da shiga cikin jama'a da ingancin matsalar tunani ta masu ciwon varin jiki

Matakan Bincike:

Za a zavi mutum 57 waxanda za a yi binciken da su, sannan za a kasa su gida uku ba tare da wani la'akari da wani abu ba ta amfani da tsarin samar da lambobi ta kwamfuta. Za a nemi ka je asibiti don yin gwajin tafiya a dandaryar qasa da magance matsalar tunani ko a haxa duka biyun sau 3 a kowane mako na tsawon makwanni 8. Da farko za a yi awo sannan a mako na 4 a sake aunawa, sai kuma a sake awon a mako na qarshe wanda za a tunkari lamarin.

Tsayin lokacin da ake tunanin bincike zai kai da kuma daxewar da waxanda za a yi a binciken a kansu za ta kasance:

A gabakixaya, muna sa ran shafe makwanni 8 muna wannan bincike. Kada ku zauna sama da awa xaya a duk asibitin da kuka ziyarta.

Haxura:

Idan dai har an yi gwajin tafiyar da za a yi a dandaryar qasar yadda ya dace, to babu wani haxari da za a iya gamuwa da shi.

Abin da waxanda za su shiga bincike za su kasha sakamakon shiga bincike:

Ba za a nemi ku biya komai ba sakamakon duba lafiyarku da za a yi

Alfanu:

Manufar wannan bincike it ace gano hanyoyin da za a inganta tunanin waxanda suka kamu da cutar shanyewar varin jiki da kuma matakin ingancin rayuwarsu da shigar su cikin al'umma. Ana sa ran aikin tafiyar da za su yi a dandaryar qasa zai inganta tunaninsu da rayuwarsu da kuma shigarsu cikin al'umma.

Sirrintawa:

Dukkan wani bayani da za a tattara a wannan bincike za a ba shi wata lamba ta musamman kuma babu wani suna da za a rubuta. Don haka ba za a alaqanta bayanan da ku ba ta kowace hanya kuma ba za a sa sunayenku ko wata alama da za ta sa a gane ku ba a dukkan rahotannin da za a fitar daga binciken.

Sa kai/ganin dama:

Shigarka cikin wannan bincike ganin damarka ce. Kana iya fita daga binciken a duk lokacin da ka so.

Wani zavin idan ba a son shiga binciken:

Idan ka zavi qin shiga binciken, wannan ba zai shafi dubaka da ake a asibiti ba ta kowace siga.

Hasafin da za a samu:

Za a biya ka abin da ka rasa sakamakon zuwanka da kuxin mota na zuwa da komawa amma ba za a biya wani kuxi na musamman sakamakon shiga binciken ba.

Amfani da bayanan da aka tattara don binciken idan wani daga cikin waxanda ake binciken a kansu ya janye

Idan ka yi niyyar fita daga binciken a kowane lokaci. Ka sani cewa wasu bayanan da aka samu daga wajenka tana iya yiyuwa an sauya musu kama ko kuma an yi amfani da su an fitar da wani rahoton. Don haka ba za a iya cire wannan ba. Duk da haka, masu binciken sun yi alqawarin yin qoqarinsu da gaskiya don ganin sun daxaxa maka a kodayaushe.

Bayanin amincewar waxanda ake binciken da su kan shigarsu binciken:

Yanzu na karanta kuma na fahimci matakan binciken, don haka na sa kaina zan shiga wannan bincike bisa raxin kaina.

Kwanan wata: _____ Sa hannu: _____

Suna: _____

Sa hannun mai bincike

Kwanan wata: _____ Sa hannu: _____

Suna: _____

Bayanin amincewar mai shiga bincike don xaukar hotonsa ko sanya shi a jarida

Na amince kuma na fahimci cewa hotona da za a iya xauka yayin bincike za a iya amfani da shi don buga wani abu, amma za a yi dishi-dishi da fuskata don kada a gane ni.

Kwanan wata: _____ Sa hannu: _____

Suna: _____

Sa hannun mai bincike

Kwanan wata: _____ Sa hannu: _____

Suna: _____

APPENDIX 12

MoCA Online Course Certificate

MoCA
MONTREAL
COGNITIVE ASSESSMENT

CERTIFICATE OF COMPLETION

This certificate acknowledges that

Muhammad Abba

has successfully completed a one hour training and certification to administer and score the Montreal Cognitive Assessment, MoCA. Only health professionals with expertise in cognition can interpret test results.

Completion date: 2020/05/24

Expiration date: 2022/05/24

NGABBMU206829-01

Dr Nasreddine, Ziad