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Cognitive Recovery Outcome in a 12 Month Quasi-experimental Study Involving Sub-acute Stroke Survivors in Selected Hospitals in Nnewi, Anambra State, Nigeria

U. P. Okonkwo[1*], G. C. Okoye[2], A. O. Ezeukwu[2], M. J. Nwankwo[3], V. A. Egwuonwu[3], O. P. Ibikunle[3], C. O. Azubike[1] and E. E. Okoye[3]

[1]Department of Physiotherapy, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria.
[2]Department of Medical Rehabilitation, Faculty of Health Sciences and Technology, University of Nigeria, Enugu Campus, Nigeria.
[3]Department of Medical Rehabilitation, Faculty of Health Sciences and Technology, Nnamdi Azikiwe University, Awka, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Authors UPO, GCO and AOE were involved in the design and implementation. Authors MJN, VAE and OPI were involved in analysis of data, interpretation of results and write up of this study, while authors COA and EEO were involved in the design and editing of the main paper. All authors read and approved the final manuscript.

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ABSTRACT

Background: Studies estimate that up to 85 percent of people who suffer a stroke will have cognitive impairments, including deficits in executive function, attention and working memory. New evidence indicates that exercise exerts its effects on cognition by affecting molecular events related to the management of energy metabolism and synaptic plasticity. Therefore, combining Proprioceptive Neuromuscular Facilitation (PNF) and Task-specific Balance Training (TSBT) to

**Corresponding author: E-mail: drchiefprosper@gmail.com;*

facilitate global cognitive recovery and maintenance on cognitive impaired and non-cognitive impaired sub-acute ischemic stroke subtype with first ever cerebral ischemia was the focus of study.

Methods: The study was a 12-month quasi experimental study of cognitive recovery outcome following PNF and TSBT intervention involving 143 stroke survivors in selected hospitals in Nnewi, Nigeria. The ischemic stroke subtypes with first ever cerebral ischemia were recruited using convenience sampling technique after a neuropsychiatric test done under the supervision of a neurologist. About 100 participants that completed the study were allotted into a cognitive impaired group (Cog.) mean age 55.36±10.2 and non-cognitive impaired group (Non-cog.) mean age 50.20± 13. The PNF and TSBT were applied three times a week, 30mins per session, for 12 months. Four research assistants were trained to assist in each treatment session. The outcome measure applied was mini-mental state examination (MMSE) for determining the neuropsychiatric status of participants at baseline and after exercise intervention at 4^{th} month, 8^{th} month and 12^{th} month.

Results: The mean MMSE scores was significantly greater than the baseline values for both Cog.: (F (2.232, 109.366) = 68.671, $p < 0.001$ with large partial eta squared = .584 and Non. Cog.: (F (2.478, 121.409) = 5.787, $p < 0.001$ with large partial eta squared = .541

Conclusion: There was improvement in global cognitive status of the sub-acute stroke survivors after 12 months PNF and TSBT exercise adapted in this study.

Keywords: Stroke; cognitive impairment; proprioceptive neuromuscular facilitation; task specific balance training.

1. INTRODUCTION

Reducing the impact of post stroke cognitive impairment is an important goal. In addition to having a direct influence on the quality of life of patients and their caregivers, cognitive impairment after stroke is associated with higher mortality [1], greater rates of institutionalization [2], and higher health-care costs [3]. Cognition is important for recovery in other neurological domains even when relevant confounders were controlled [4]. Cognitive impairments can reduce a person's ability to understand task instructions, to plan and initiate self-directed activities, and to solve problems. The executive function of stroke patients in inpatient rehabilitation has been independently associated with the level of participation in rehabilitation [5]. Cognitive rehabilitation can be either compensatory or restorative. Compensatory approaches involve adapting the external environment to altered cognitive abilities, whereas restorative approaches aim for the compelling goal of direct restoration of function [6]. One specific external strategy that has been tested is electronic paging systems which were found to be effective in compensating for everyday memory and planning problems after brain injury [7], maintaining these benefits over time may be difficult for stroke survivors [8]. Compensatory strategies can also be internally generated. Rather than attempt to restore reaction time to a normal speed [9] introduced a ‘time pressure management’ strategy: stroke patients were taught to compensate for mental slowness in real-life tasks by reorganizing the execution of sub-tasks that had a time pressure component. Their treatment group significantly outperformed controls on speed of performance on everyday tasks at three-month follow-up. Other cognitive rehabilitation approaches aim for the compelling goal of direct restoration of function. The realization that neural plasticity is present throughout life and can be influenced by training has generated hope in this area, but conclusive studies remain scarce. The strongest evidence of effectiveness is for treatment of focal cortical deficits. A review of evidence- based cognitive rehabilitation identified substantial evidence for cognitive-linguistic therapies to treat aphasia and for visuospatial rehabilitation to treat neglect after stroke, but effective treatments in other domains were lacking [10].

The standard reference method for the assessment of cognition after stroke is the neuropsychological examination. In research, it is usually conducted 3 months after a stroke, but in clinical practice it follows earlier, from 1 week to 1 month after the stroke. However, a neuropsychological assessment is not always available for all stroke patients, and patients may be too disabled or fatigued to complete the test at the acute stage [11]. Treadmill training intensity was suggested to affect memory function recovery which is related to neural activity in the hippocampus [12]. Ploughman considered exercise brain food that ultimately enhances brain functions like memory and learning [13], and additionally suggests that moderate exercise has positive effects on physically disabled young people aided by their high brain plasticity [14]. However, while there was report that mild global cognitive impairment and mild attention loss had negative effect on activity of daily living (ADL) in the older stroke survivors [15,16], another study showed that acute stroke patients with cognitive impairment had significant functional gain after rehabilitation intervention [17].

There is a growing body of evidence that lays credence to the influence of exercise in vitality and function of the central nervous system (CNS) and promoting resistance against neurological disorders. The outcomes of these studies highlighted the extraordinary capacity of exercise to enhance mental health, and currently more efforts are being devoted to use this capacity to reduce cognitive decay in aging and psychiatric disorders. Innovations in neuroimaging have been critical to document the relationship between the cognitive gain and the activity of specific neural networks in the cerebral cortex and hippocampus in individuals who practice exercise. Recent advances in imaging of the human hippocampus stand to more directly bridge the gap between human and animal models [18]. The increasing incidence of stroke survivors with cognitive impairment has made it imperative to evolve a restorative exercise intervention which can impact on the mental health of those stroke survivors with compromised cognition, This is essential as stroke survivors have reduced capacity to participate in exercise volitionally hence threatening their mental health, According to American Heart Association (AHA), because there are no drugs to improve cognitive function, physical activity, such as physical therapy, aerobic and strength training become a low-cost intervention to treat cognitive deficits in stroke survivors [19]. This study sorts to evaluate the cognitive variation in a 12 month quasi-experimental study involving utilization of PNF and TSBT in stroke rehabilitation involving stroke survivors with and without cognitive impairment. The working hypothesis was that there will be no improvement in cognitive status in stroke survivors with impaired cognition after 12 months of PNF and TSBT.

2. METHODS

A multi-center quasi-experimental study of 143 sub-acute ischemic stroke survivors with first ever cerebral ischemia were selected using convenience sampling at four hospitals (one tertiary and 3 specialists hospitals): Nnamdi Azikwe University Teaching Hospital, Myles Specialist Hospital, Hope Specialist Hospital and Mercy Specialist Hospital all located in Nnewi, Anambra State Nigeria. The participants had mostly cerebral ischemia of the middle cerebral artery (MCA). Based on radiological reports, participants in the present study, had the highest frequency of affectation within the middle cerebral artery, at the following regions; the insula, putamen, operculum, and superior temporal cortex, as well as the inferior and superior occipito-frontal fascicles, superior longitudinal fascicle and uncinate fascicle. The patients recruited were treated at facilities with the required equipment: Landmark Physiotherapy Services, Nnewi and Department of Physiotherapy, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria. The sample size was determined using a mathematical relationship recommended by a previous author [20].

$$N= \frac{2\,(Z_1 + Z_2)^2}{(ES)^2}$$

ES= standardized difference of variable with the least possible change = mean difference standard deviation= 1.8/3.0= 0.60; N= sample size for a group; Z_1= percentage point of normal distribution for statistical significance level at 95% confidence interval = 1.96; Z_2= percentage point of normal distribution for statistical power at 80% = 0.8416; N= 2 $(1.96 + 0.84)^2/\ (0.60)^2$ = 15.68/0.36 = 43.56=44; N= 2x44= 88. About 70% of the stroke survivors were expected to be compliant, and therefore an attrition rate of 30% of the calculated sample size, i.e. 30/100 x 88 = 26), was added to the sample size. Therefore, N (total sample size) = 88 + 26 = 114. However, 143 participants was recruited, with only 100 (comprising 85 and 58 participants with and without cognitive impairments, respectively) eventually completing the study.

2.1 Inclusion and Exclusion Criteria

The participants criteria were as follows (i) Adults of between 30-65years of age, (ii) radiological diagnosis of first ever ischemic stroke by a physician, (iii) adjudged cognitively impaired and non-cognitively impaired by a neurologist using the mini mental state examination, (iv) stroke duration ≥3 months but ≤ 6 months, (v) ischemic stroke survivors without history of recurrent stroke or dementia, (vi) no history of other neurological, metabolic (diabetes), neurodegenerative diseases or orthopedics conditions and (vii) domiciled within Nnewi and its environs (Ichi, Amichi, Orifite, Utuh, Ozubulu), and (viii) must be literate. (ix) the present study included only those patients with post stroke cognitive impairment before commencement hence reducing the possibility of cerebral atrophy.

2.2 Ethical Approval

Ethical approval from the Nnamdi Azikiwe University Teaching Hospital Ethical Committee (NAUTHEC), Nnewi, was obtained alongside a supervision approval from a Consultant Neurologist. All the participants gave their informed consent to participate in the study after the purpose was explained to them. They were also assured of the confidentiality of the information they provide. It was made clear to the participants that they have the right to refuse to participate or to withdraw at any stage of the project, and these rights were respected all through the research procedure.

2.3 Intervention Procedures

2.3.1 Proprioceptive neuromuscular facilitation (PNF)

The PNF technique/ strengthening program that was applied comprised rhythmic initiation, repeated contraction, slow reversal and rhythmic stabilization,

a. Rhythmic initiation- the participants were made to progress from passive to active resistance, then followed by active movements. It was applied for those participants to teach movement to the participants.
b. Repeated contraction. Here the participants were allowed to move their limb isotonically through resistance just before fatigue was present.
c. Slow reversal. Participants were made to contract the agonist and immediately after the antagonist. It was intended for developing active range of motion and coordination between agonist and antagonist. It was also used to increase strength of a specific Range of motion.
d. Rhythmic stabilization. This technique was used to elicit isometric contraction of agonist followed by isometric contraction of antagonist. It was also used to achieve the holding power of a targeted range of motion.

Ten repetitions of each pattern were done before proceeding to the next pattern, in line with what obtains in previous PNF studies [21,22]. After a set of patterns were completed, it was repeated twice in each treatment session making 3 sets per session. This usually lasted about 30 minutes per participant per session. However, the PNF training were applied equally in terms of duration irrespective of laterality of stroke and the set used in the study were as described by Knott and Voss [23] for the following:

1. **Lower extremity:**

   a. flexion abduction-external rotation (knee flexed and knee extended)
   b. Extension-adduction –internal rotation (knee flexed and knee extended)
   c. Flexion-adduction-internal rotation (knee flexed and knee extended)
   d. Extension –abduction-external rotation (knee flexed and knee extended)

2. **Upper extremity:**

   a. Flexion-abduction-external rotation (elbow flexed and elbow extended).
   b. Extension-adduction-internal rotation (elbow flexed and elbow extended).
   c. Flexion-adduction-internal rotation (elbow flexed and elbow extended).
   d. Extension-abduction-external rotation (elbow flexed and elbow extended)

A pamphlet containing the described patterns also served as treatment guide during training [24].

2.3.2 Task specific balance training

The Tasks specific activities that were initiated to train balance include;

a. Graded strengthening (repetitive rising from a chair) – 10 repetition
b. Aerobic training (cycle ergometer)- 5 repetitions
c. Walking tasks (stepping over obstacle)- 10 repetitions

d. Standing balance-10 repetitions
e. Forward and backward and forward progression- 5 repetitions
f. Turning task- 10 repetitions [25].

These tasks were participants' specific (made flexible according to the need of the individual patient) and lasted for an average of 30 minutes to reduce the chance of their getting fatigued. However, the duration of treatment administered was same on the participants irrespective of laterality. Patients were dressed in a pair of shorts vest so as to make them comfortable for the exercise. They were also allowed to wear appropriate sized flat-heeled shoes or bare footed as the case may be. An interval of 10 minutes rest was allowed between sets of treatment or as situation may warrant for the individual participant, like early fatigue before completion of a set of exercise. Deep breathing exercises were performed during rest period to enhance recovery. During the rest period also patients could reflect on the activities and receive feedback on their work, with the aim of reorienting or reinforcing their behaviors. In the first case, the feedback served to identify behaviors that did not contribute to the goals, inducing the patients to develop alternative strategies or solutions. In the second case, served to highlight useful and appropriate behaviors for achieving the goal, the feedback stimulated the patients to repeat and improve themselves. Patients were however closely monitored to prevent any adverse cardiovascular or respiratory reactions as a result of the training. The training was timed with a stop watch (diamond model, made in China) and scheduled between 8am -12pm on the appointment days. Data were collected at baseline, 4^{th}, 8^{th} and 12^{th} months, respectively to build a profile and track the trend of change [25].

2.4 Outcome Measures

Mini-mental state examination was used by the researchers to assess global cognition which comprised items concerning orientation, registration and recall, attention, language, following commands and figure copying for those stroke cases that had minimum of 3months duration. The cut off score was 23/24. Those below the cut off were deemed to be cognitively impaired while those above the cut off were deemed to be cognitively normal. Mini-mental state examination is brief, inexpensive, and simple to administer. Its widespread use and accepted cut off scores increases its interpretability. However, it has low sensitivity with people with mild cognitive impairment [26].

2.5 Statistical Analysis

Statistical Analysis was performed using SPSS version 20: Descriptive statistic of Mean± SD was used in the analysis of demographic and baseline characteristics. The raw data was tested for normality using Shapiro-wilks while Log Transformation was utilized to normalize the data. Repeated Analysis of Variance (ANOVA) was adopted to compare variations within each group; independent t-test was applied to compare variations between the two treatment groups. Probability value less than 0.05 was considered statistically significant.

3. RESULTS

Out of 143 participants that commenced the treatment 43 dropped out before the 6^{th} month of the study for different reasons. Thus, in the cognitive group, 10 participants missed their follow-up appointments, 11 deaths were recorded as serious adverse events which was not connected to the exercise intervention but linked to poor compliance to conventional management routine, outright resort to traditional and faith healers as is common in Nigeria, leading to untoward cardiopulmonary complications and eventual death; while 14 others tended towards dementia as there was severe deterioration in their cognitive status making participation in exercise program impossible; this is significant as dementia featured in the exclusion criteria. The non-cognitive group had 6 participants who missed their follow up appointments, 2 deaths were recorded as serious adverse event not connected to the exercise intervention but related with patients poor or non-compliance to conventional management plan leading to cardiopulmonary complications and eventual death. Thus, only 100 participants completed the study. In the cognitive group 58.82% participants completed their exercise program while 41.18% participants did not. This contrasts with 86.21% participants who completed their exercises in the noncognitive group while 13.79% participants did not.

The baseline characteristics in Table 1 showed the number of male and female participants were 23(46%) and 27(54%), respectively, for the cognitive group, while the non-cognitive had

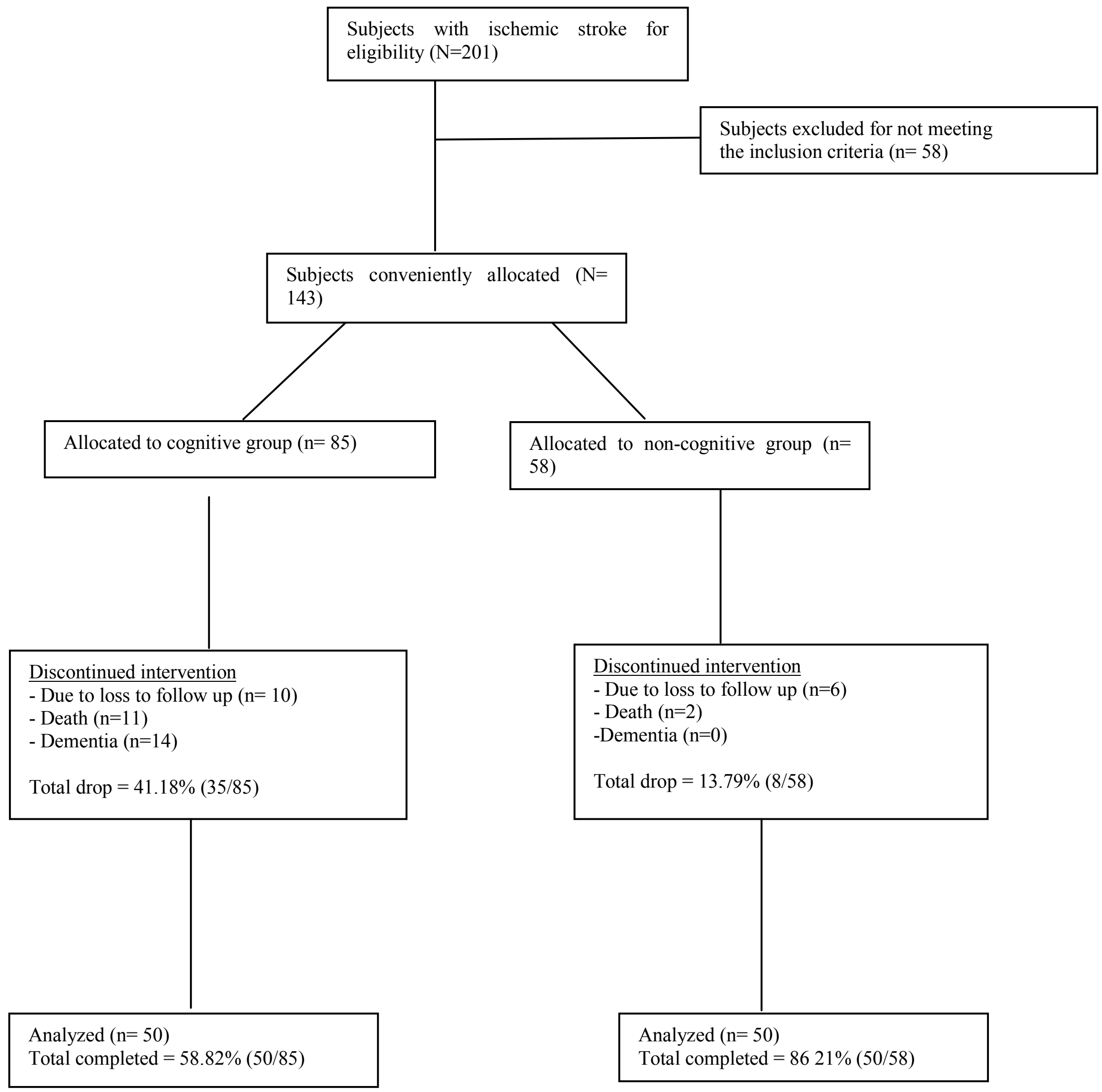

Fig. 1. Subject selection flow chart

22(34%) and 28(56%) for the males and females, respectively. Their mean age differed significantly ($p < 0.05$) and was recorded as 53.94 ± 9.316 years and 49.30 ± 12.214 years for the cognitive and non-cognitive groups, respectively. However, the duration of stroke and body mass index were not significantly different ($p > 0.05$) for both groups. The ischemic stroke subtype was higher among traders (business men) and civil servants with the professional workers having the least incidence of stroke. The other physical characteristics of the participants are presented in Table 1.

Summary of Table 2 shows mauchly's test indicated that assumption of sphericity had been violated by the minimental state examination scores for CIG, therefore degrees of freedom was corrected using Greenhouse Geisser estimates of sphericity. The mean scores for MMSE scores was significantly different: (F (2.232, 109.366) = 68.671, $p < 0.001$. The partial eta squared was large = .584. Also the mauchly's test indicated that assumption of sphericity had been violated by the minimental state examination scores for NCIG, therefore degrees of freedom was corrected using Greenhouse Geisser estimates of sphericity. The mean scores for MMSE scores were significantly different: (F (2.478, 121.409) = 5.787, $p < 0.001$. The partial eta squared was large = .541.

Table 3 reveals mini-mental baseline scores for cognitive group: 19.620 ± 3.469 and non-cognitive stroke survivors 25.040 ± 1.195; t (97) = -10.355, p = 001. After 12th month of intervention with mini-mental mean scores for cognitive: 24.160 ± 3.151 and non-cognitive: 27.700 ± 1.249; t (97) = -7.894, p = .001. The t-value = -7.894 and p-value = .001.

Table 1. Baseline characteristics of participants

Characteristic	Cognitive	Non-cognitive	p- value
Number(n)	50	50	
Age	53.94 ± 9.316	49.30 ± 12.214	.041*
Male	23 (46%)	22 (34%)	
Female	27 (54%)	28 (56%)	
Duration (months)	3.96 ± 1.029	4.04 ± 1.106	.928
Height	1.706 ± .0699	1.711 ± .0453	
Weight	78.760 ± 5.635	79.760 ± 6.1397	
BMI (kg/m^2)	27.20 ± 2.80	27.196 ± 2.80	.863
Ischemic			
Left (%)	30 (60%)	18(36%)	
Right (%)	20 (40%)	32 (64%)	
Occupation			
Business (%)	20 (40%)	23 (46%)	
Civil servant (%)	14 (28%)	13 (26%)	
Professional (%)	1(2%)	2(4%)	
Dependent (%)	9 (18%)	11(22%)	
Others (%)	6 (12%)	1(2%)	

**Indicates significant difference at α = 0.05, BMI=Body Mass Index*

Table 2. Effects of proprioceptive neuromuscular facilitation and balance training on cognitive status

Period	Type	Mean ± SD Raw	Mean ± SD transformed	Mean Diff.	% change	P-value	Conf. inter.
Baseline-4Months	Cog.	19.620 ± 3.469 21.620 ± 2.531	1.284 ± .091 1.332 ± .058	-2.000	10.194	.001*	-1.104- -2.263
Baseline 4 Months	Non.Cog	25.040 ± 1.195 26.020 ± 1.19	1.398 ± .020 1.415 ± .019	-.980	3.013	001*	-1.407- -.553
B/ 12 months	Cog.	19.620 ± 3.469 24.160 ± 3.151	1.284 ± .091 1.384 ± .054	-4.700	23.955	.001*	-5.827- -3.693
B/ 12 months	Non.Cog	25.040 ± 1.195 27.700 ± 1.249	1.398 ± .020 1.442 ± .200	-2.660	10.623	.001*	-3.208- -2.112
4/ months 8months	Cog.	21.620 ± 2.531 23.160 ± 3.152	1.334 ± .055 1.361 ± .059	-1.540	7.123	.001*	-2.372- -.708
4 months/ 8 months	Non.Cog	26.020 ± 1.186 26.360 ± 1.675	1.442 ± .020 1.415 ± .019	-.340	1.307	.001*	-.853- 173
8 months/ 12 months	Cog.	23.160 ± 3.152 24.160 ± 3.151	1.361 ± .059 1.384 ± .054	-1.220	5.268	.001*	-2.004- -376
8 months/ 12 months	Non.Cog	26.360 ± 1.675 27.700 ± 1.249	1.420 ± .028 1.442 ± .020	-1.340	5.083	.001*	-1.981- -.699

*Values are presented as the mean standard Deviation. *Significant difference at α = 0.05; Cog,. = (F (2.232, 109.366) = 68.671, p< 0.001 with large effect size (partial eta squared) of 0.584; Non.cog. (F (2.478, 121.409) = 5.787, p< 0.001 with large effect size (partial eta squared) of 0.54; Sd= standard deviation, Cog. = Cognitive Impaired group, non-cog=Non-cognitive Impaired Group, p-value= Significant difference, Conf. Interv. = Confidence Interval, B= baseline, %= percentage mean change*

Table 3. Independent t-test at baseline, 4th month, 8th month and 12th month

Type	MM0	MM4	MM8	MM12
Cog.	19.620 ± 3.469	21.620 ± 2.531	23.16 ± 3.152	24.160 ± 3.151
Non.Cog.	25.040 ± 1.195	26.020 ± 1.186	26.360 ± 1.675	27.700 ± 1.249
t-value	-10.355	-11.041	-6.312	-.7.894
p.value	.001*	.001*	.001*	.001*
Confidence Interval	-6.468- -4.387	-5.200- -3.615	-4.22- -2.206	-4.171- -2.495

*Values are presented as the mean standard Deviation *Indicates significant difference at α = 0.05, Cog. = cognitive impaired group, Non-cog. = non-cognitive impaired group, Conf. Interv. = Confidence Interval, MM0= minimental at baseline, MM4= Minimental at 4th month, MM8= Minimental at 8th month, MM12= Minimental at 12th month*

4. DISCUSSION

The baseline characteristics revealed that a total of 100 stroke survivors (50 cognitive and 50 non-cognitive) completed this research study. The ratio of the male to female was almost the same in the two groups; therefore, the differences in sex were consistent and indicate the similarity of the samples in this context. It was further revealed that both the duration of stroke and the body mass index were not significantly different between the two groups. It appears that traders and civil servants were vulnerable to stroke than other professionals, which may be induced by work related stress increasing the activities of reactive oxygen species leading to degenerative changes of the vasculature. Therefore, the high incidence of stroke in the two occupations may be attributed to the preponderance of this group of participants in the general population hence increasing the possibility of stroke [25].

5. STRENGTH AND LIMITATIONS OF STUDY

This work was limited by the high level of participants who dropped from the cognitive group and by the limited number of participants. However, there were significant age differences between the two groups which were not unexpected considering that the subjects were not randomly selected. This may be a weakness for the study design, as age is an important confounding variable for cognition, Perhaps, this difference between the groups may add to the explanations that up to the 12th month of the intervention study, there were significant differences in the outcome measures across both groups. This could be an indication that age-related differences and cognitive dysfunction may suppress gains in cognitive recovery in stroke survivors when PNF and TSBT are giving when compared to the non-cognitive recovery [25]. This finding agrees with the results of a previous study which found that old and even very old patients with stroke benefit from specialized inpatient neuro rehabilitation and high amounts of therapy in the same degree as younger patients [27]. The above finding contradicted the earlier views of the American Heart Association (AHA) [28] that the younger stroke patients benefited more by stroke unit rehabilitation compared with older patients. What is however strikingly different from the two studies above was that they were short term studies, unlike this study that was a long-term study.

The global cognitive status as measured by mini-mental scale for the cognitive and non- cognitive impaired post stroke survivors was significantly different throughout the 12 months period of the study. The least mean difference and percentage mean change was recorded between 8 and 12 months for cognitive impaired stroke survivors, while same was recorded between 4 and 8 months for the control group. The highest post intervention change in mean difference and percentage change was recorded between baseline and 4 months for both groups. The improvement in cognition between the baseline and 12 months of intervention was significantly different ($p < 0.001$) with partial eta of .584. Comparatively, the cognitive improvement of the control group was significantly different ($p < 0.001$) between baseline and 12 months with partial eta of (.541) .This means that by the end of 12 months intervention though there was higher percentage change in the cognitive status of stroke survivors with cognitive impairment those of non-cognitive still maintains a better status. A comparison of the two groups using the independent t-test showed a significant difference in mini mental scores between the two groups. The researchers finding that cognitive recovery can be enhanced even when physical activity is introduced in the chronic stroke phase (beyond 3 months after a stroke) is consistent with AHA position [19]. It also agrees with other research studies that repetitive exercises are very good for healthy brain function especially the effect it has on hippocampus which is responsible for long memory function. Treadmill training intensity was suggested to affect memory function recovery which is related to neural activity in the hippocampus [12]. Ploughman considered exercise brain food that ultimately enhances brain functions like memory and learning [13], and additionally suggested that moderate exercise has positive effects on physically disabled young people aided by their high brain plasticity [14]. The improvement recorded in the cognitive status of participants in this study was in line with the work of Ballard et al. (2003), who did a longitudinal study of a small group of stroke patients >75 years of age who underwent a detailed neuropsychological evaluation 3 months after an ischemic stroke and again 1 year later to investigate delayed changes in cognitive functions after stroke. The result showed a cognitive improvement in 50% of the patients, 16 % showed an increase of >2 in the mini mental state examination. The work confirmed that cognitive changes after stroke have a highly dynamic course in the months after the acute event and that cognitive improvement was the usual outcome for those who did not have dementia. Ballard went further to hypothesize that cognitive function improves unless individuals have concurrent cerebrovascular or neurodegenerative disease or develop further cerebral insults [29]. This was consistent with the finding by Desmond that conditions linked to small-vessel were associated with lack of improvement in cognition [30]. The authors may justify the cognitive improvement in this study with the fact that the cerebrovascular or neurodegenerative disease and small vessel diseases such as diabetes were among the exclusion criteria. We are of the opinion that the one year exercise intervention in this study concurs with the research finding that emphasized the need for the rehabilitation team to increase the time spent in meaningful exercises and task practices in order to meet the needs of brain reorganization, skill relearning, and improved physical and mental fitness [31]. It had been also observed according to a research study that most cognitive improvement occurs in the first 3 months after a stroke although recovery may continue for up to a year [32]. We can postulate at this point that since exercise affects brain reorganization and improved mental fitness that Proprioceptive Neuromuscular Facilitation and task specific balance training could have a positive relationship with level of cognitive recovery. Another justifiable explanation for the global cognitive improvement noticed in this study may be linked to the fact that brain has a remarkable capacity for modifying its structure and function according to the influences of the environment and experience. On this basis, abundant progress has been achieved in the last decade unravelling the cellular and molecular mechanisms responsible for the influence of exercise enhancing cognition. Exercise is known to activate the neural circuitry important for learning and memory using molecular systems associated with synaptic plasticity and energy metabolism. It also appears to enhance the process by which information is transmitted across cells at the synapse, in which select neurotrophic factors such as brain-derived neurotrophic factor (BDNF) play a major role. For example, exercise influences the production of (BDNF) in the area vital for learning and memory, the hippocampus [33,34,35]. The authors are of the assumption that the cumulative effects of the length, the intensity and the frequency of exercise training via PNF and TSBT could trigger the production of the BDNF which possesses the extraordinary capacity to enhance neuronal excitability and synaptic plasticity by interacting with energy metabolism, thereby supporting cognitive abilities. According to AHA the meta-analysis of 13 intervention trials that included 735 participants, researchers analysed the effects of various types of physical activity on cognitive function among stroke survivors. They found that structured physical activity training significantly improved cognitive deficits regardless of the length of the rehabilitation program (i.e., training longer than 3 months as well as from 1 to 3 months led to improvements in cognitive performance) [19]. In this study we are not oblivious of the finding that recurrent cerebral infarction causes greater cognitive impairment as reflected in the study by Arboix et al. [36] who amongst other findings reported that lacunar stroke accounted for more than 25% of brain infarcts and that neurological deficit related to a first lacunar infarction is usually mild; whereas recurrent lacunar infarctions may be associated with a more severe clinical picture, including lacunar state and vascular dementia. The same study implicated diabetes as one of the major predictors of recurrent stroke. The implication of this findings on our study is that lacunar stroke is a significant cause of ischemic stroke subtype; hence, inclusion of post stroke survivors with recurrent or multiple cerebral infarction may leave the participants with more adverse clinical pictures like vascular dementia which may significantly impede rehabilitation. Additionally, we took cognisance of the implication of including ischemic stroke survivors with diabetes in our study because of its potential to trigger recurrent lacunar infarctions via accelerating the clinical course of atherosclerosis and contributing to cerebrovascular recurrence [37]. We noted the significant role cerebral atrophy play in the post stroke cognitive impairment especially as a predictor of subsequent cognitive impairment. The study by Duering et al. [38] observed that cortical neurodegeneration following ischemia in the subcortical region probably represents pathophysiological mechanisms for cerebral atrophy in cerebrovascular disease; they showed that subcortical infarcts trigger focal thinning in connected cortical areas. However, it is of importance that Grau-Olivares et al. [39] revealed that patients with mild VCI showed clear progressive gray matter atrophy in cortical (temporal and frontal) and subcortical (pons, caudate and cerebellum) regions after first-ever lacunar stroke. This may be in contrast to patients without initial cognitive impairment. The present study excluded those patients with marked cognitive impairment before the ischemic stroke hence reducing the possibility of cerebral atrophy which could have impacted negatively on exercise training used in this study.

6. CONCLUSION

The findings of this study made the authors to conclude that global cognitive status of sub-acute stokes survivors with compromised cognition can improve significantly as well as those of non-cognitive impaired stroke survivors when subjected to long term PNF/TSBT intervention. We therefore infer that exercise is good both for recovery of lost cognitive function and in maintaining healthy function of non-compromised cognitive status of stroke survivors. It is interesting that researchers observed with interest that the intervention protocol applied in this study was consistent with the finding of American Heart Association, that combined strength and aerobic training programs yielded the largest cognitive gains in stroke survivors. The authors speculated that similarities in outcomes between the two groups were influenced by the interplay of factors thus highlighted: participants not being very old; mild or moderate cognitive impairment; absence of metabolic disease (diabetes), neurodegenerative or small vessel diseases, enriched environment created by the intervention protocol; length and intensity of the exercise; and neuroplasticity.

7. RECOMMENDATIONS

A long term proprioceptive neuromuscular facilitation and task specific balance training that is multi-level in approach and combining strength/aerobic training should be adopted in cognitive rehabilitation program in sub-acute stroke survivors as one of the means of restoring cognitive loss and forestalling its deterioration. A future line of research could be the assessment of physical exercise effects in cognitive function in patients with TIA.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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