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Clinical and demographic predictors of unilateral spatial neglect recovery after prism therapy among stroke survivors in the sub-acute phase of recovery

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ABSTRACT

BACKGROUND AND AIMS: Unilateral Spatial Neglect (USN) affects the rehabilitation process and leads to poor outcomes after stroke. Factors that influence USN recovery following prism adaptation therapy have not been investigated. This study investigated predictors of USN recovery after prism therapy at the sub-acute phase of recovery.

METHODS: This study was a randomized controlled trial. USN was assessed with the Behavioural Inattention Test and Catherine Bergego scale. Seventy-four patients with USN were divided into control and intervention group (prism). The prism group used 20 dioptre prism lenses for repeated aiming for 12 sessions while the control group used neutral lenses for aiming training. Regression analysis was conducted to establish clinical and sociodemographic factors that influence USN recovery.

RESULTS: Gender, age, years of education, race, employment status, handedness, type of stroke, time since stroke and site of stroke ($p > 0.005$) showed no significant influence on USN recovery following PA treatment. Higher Cognitive function ($OR = 1.52$, $CI = 1.08–2.14$, $p = 0.016$) and group allocationng (being in the prism group) ($OR = 63.10$, $CI = 9.70–410.59$, $P < 0.001$) were found to significantly influence USN recovery following PA treatment session.

CONCLUSIONS: A significant modulating effect on general cognitive ability was found in this study. This suggests that prism adaptation therapy's effect on neural activity and spatial neglect depends on the cognitive function of stroke survivors.

Trial registration: Pan African Clinical Trial Registry identifier: PACTR201903732473573.

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Introduction

Unilateral spatial neglect (USN) is defined as "a failure to report, respond or orient to stimuli presented in the side of space contralateral to the injured cerebral hemisphere, which cannot be explained by primary sensory or motor deficit" (Heilman et al., 2000). USN is observed more with lesions affecting the right side of the brain than with lesions on the left side and is estimated to occur in 13–100% of the patient population with right hemispheric affectation (Bowen et al., 1999). A systematic review by Esposito and colleagues (Esposito et al., 2021) estimated the prevalence of USN after a unilateral stroke to be 30% and this prevalence was reported to decrease from acute to chronic stage of stroke. However, in some post-stroke patients, the severity of neglect symptoms persists chronically (Farnè et al., 2004; Katz et al., 1999) with a negative impact on almost every activity that contributes to daily living and rehabilitation outcomes such as postural balance (Gottlieb & Levine, 1992; Pérennou, 2006; Taylor et al., 1994; van N et al., 2009), functional mobility (Berti et al., 2002; Tromp et al., 1995), quality of life (Franceschini et al., 2010; Sobrinho et al., 2018), activities of daily living (ADLs) (Cherney et al., 2001; Jehkonen et al., 2000; Jehkonen et al., 2001; Vossel et al., 2013), reduced functional mobility and poor gait (Oh-Park et al., 2014), reduced quality of life (QoL) (Sobrinho et al., 2018) and hospital stay duration (Chen et al., 2015; Hammerbeck et al., 2019; Wee & Hopman, 2008) and all these results in increased costs for health care systems need for caregiver assistance and supervision.

Several interventions to ameliorate USN have been proposed by researchers (Luauté et al., 2006; Umeonwuka et al., 2020). Strategies for USN symptom amelioration are broadly classified into bottom-up or top-down methods (Marshall, 2009). With the top-down approach, the patient is actively engaged in the process through external cues and guidance. Therapy based on the top-down approach involves continuous feedback, training and encouragement provided by a therapist. The treatment options that employ such an approach are visual scanning training (VST), sustained attention training and mental imagery training (Marshall, 2009). Treatment based on the bottom-up mechanism involves manipulating endogenous components of the neural axis, mainly sensory input, at the preconscious level of perception. The idea behind this method is that an unbalanced perception and attention system can be corrected without the patient's conscious involvement. Prism glasses, trunk rotation, and eye patches are all examples of bottom-up interventions. Other interventions alter the somatosensory system, such as limb activation, muscle vibration, and optokinetic stimulation.

Prism adaptation (PA)intervention has been of interest to researchers in recent times because of its propensity to ameliorate neglect symptoms in post-stroke patients (Chokron et al., 2007; Luauté et al., 2006; Umeonwuka et al., 2020).

Studies (Gammeri et al., 2020; Jacquin-Courtois et al., 2008; Keane et al., 2006; Shiraishi et al., 2008; Tilikete et al., 2001), have suggested that neglect symptoms improve with PA and these improvements extend to dressing, postural stability (Tilikete et al., 2001), walking (Keane et al., 2006), sit-to-stand transfer (Shiraishi et al., 2008) and wheelchair driving (Jacquin-Courtois et al., 2008). Conversely, studies have also reported no improvement in unilateral spatial neglect following prism adaptation treatment (Bourgeois et al., 2021; Mancuso et al., 2012; Morris et al., 2004; Rode et al., 2015; Rousseaux et al., 2006; Ten Brink et al., 2017; Turton et al., 2010; Vilimovsky et al., 2021).

Several explanations for the heterogeneity of results of the effect of PA on post-stroke USN could be due to differences which include non-harmonisation of treatment apparatus, the severity of the stroke, treatment duration, and phase of stroke recovery of patients included in the study. Several factors such as deficit severity, visual field defects, age and age-related brain atrophy (Campbell & Oxbury, 1976; Farnè et al., 2004 Stone et al., 1992) have been identified to predict successful USN recovery.

Previous studies had identified variables such as the presence of motor intentional aiming deficit, (Goedert et al., 2014), and frontal lobe lesions (Chen et al., 2014; Goedert et al., 2020) to moderate the effect of PA on USN in post-stroke survivors.

Studies on sociodemographic and clinical predictors of recovery following a regimen of PA are necessary to improve the knowledge in this field as this will shed more light on the homogeneity of results following PA treatment of stroke survivors and also guide clinicians in choosing appropriate intervention options for the treatment of post-stroke unilateral spatial neglect.

Consequently, this study was conceptualized to investigate sociodemographic and clinical predictors of USN recovery following PA treatment in post-stroke survivors.

Methods

Study design

This study was a double-blinded randomized controlled trial (RCT). Consenting patients were consecutively recruited from the study sites.

Sample selection and size

Patients who had a stroke and were in the sub-acute phase ($\leq$ 3 months post-stroke) were recruited consecutively from the study sites. Information on the expected effect of prism adaptation on neuropsychological neglect tests or BIT scores was unavailable (Ten Brink et al., 2015). The sample necessary to identify a difference with a power of 80% and alpha 0.05 (2-sided) was estimated using an effect size of 0.5 for medium effect size (Muller & Cohen, 1989) with non-compliance of 5% and 0.7 standard deviations (Ten Brink et al., 2015). A sample size of 35 patients per group (70 patients in total) for sufficient statistical power sans inflation was calculated; 15% inflation for possible dropouts raised the number to 82.

Study setting

Patients were screened and recruited from three clinical facilities (two hospitals and one clinic) in the Gauteng province of South Africa.

Participants

Stroke patients with a clinical diagnosis of symptomatic stroke (initial or recurrent, haemorrhagic, or ischemic stroke) were screened at the respective study site consecutively. The diagnosis was made by the physician after a brain Computed tomography (CT) investigation (Musuka et al., 2015). The inclusion criteria were: first-ever right hemispheric stroke, admission within three months following stroke onset, age 18 years and above, and absence of severe cognitive impairment (Mini-Mental State Examination score > 17). Patients were excluded if they were unable to sit on a wheelchair, had very bad eyesight, had severe hearing loss, unable to reach with upper extremity, had amputation of the post-lesional upper extremity and had poor position sense or deficits of the fingers because of peripheral neuropathy.

Randomization and masking

Participants were assigned to either the control or intervention group by individual randomization. The investigator placed 82 labelled cards (41 intervention and 41 control) in 82 envelopes before the commencement of the study. Following baseline assessment, the research assistant randomly selected an envelope and assigned the patient based on the information written on the card to either the control or the treatment group. The patients were ignorant of the treatment arm to which they were assigned.

Research assistants were recruited for this study and were trained to provide them with a clear understanding of the study and the prism adaptation therapy intervention. The main researcher assessed the patient pre-and post-intervention using the outcome measures and was kept blinded to participant allocation throughout the entire study. The researcher determined the eligibility of patients identified by physiotherapists working at the research sites for the study. Participants that met the inclusion criteria and were willing to participate in the study signed consent and were randomly assigned to the intervention or the control as described previously.

Assessment of patients

Unilateral spatial neglect screening

The standard subtest of the Behavioural Inattention Test (BIT-C) (Halligan et al., 1991; Wilson et al., 1987) was used to measure improvement from USN. This comprises six items: figure and shape copying, line crossing, representational drawing, star cancellation, line bisection, and letter cancellation.

Patients that scored below the BIT-C Cut-off (less than 129 out of 146) were considered to have presence of neglect and the higher the BIT-C score the better the neglect (Halligan et al., 1991; Wilson et al., 1987).

The Catherine Bergego scale was also used to evaluate the functional aspect of USN (Azouvi et al., 2003). The Catherine Bergego Scale is a standardized checklist to check the presence and degree of neglect during observation of everyday life situations. The CBS is comprised of day-to-day tasks which are daily activities the patient performs while the therapist observes. The CBS uses a 4-point grading scale to show the severity of neglect for each item: 0 = no neglect 1 = mild neglect (patient always explores the right hemispace first and slowly or hesitantly explores the left side) 2 = moderate neglect (patient demonstrates constant and clear left-sided omissions or collisions) 3 = severe neglect (patient is only able to explore the right hemispace). The lower the CBS score, the better the neglect. This results in a total score out of 30 (Azouvi et al., 2003).

Socio-demographic and clinical screening

The sociodemographic and clinical variables considered in this study were cognitive ability, gender, age, years of education, race, employment status, handedness, type of stroke, and site of a stroke. A socio-demographic and clinical data form was used to retrieve participating patients' data from the patient's hospital case file.

The mini-mental scale was used to assess the patient for any cognitive impairment before recruitment into the study as per the study inclusion criteria. The patients were recruited for this study if they obtained an MMSE score of >17 (Tombaugh & McIntyre, 1992). The MMSE is a screening tool that identifies cognitive ability quantitatively and is made up of 11 tasks, grouped into seven areas. The usual threshold for cognitive impairment is a score of 23 or less from a total of 30 (Dick et al., 1984).

Prism adaptation protocol

The prism adaptation intervention procedure for reaching the task was adapted from a similar study by Mizuno and colleagues (Mizuno et al., 2011).

Patients recruited for this study were asked to sit at a desk on which a wooden table adapted from Bedford, (Bedford, 1989) (height 30 cm) was placed. The semi-circular shape tabletop with a radius of 60 cm had three targets marked 10 cm apart at the centre, right, and left corners of its edge. During each session, patients were seated upright and assisted if needed. Every patient's target distance was adapted according to their arm length. Therapists then instructed patients to point using the forefinger of their opposite hand at the three targets located at the bottom of the table. The three targets were randomly selected by the therapists. The reaching path was made unseen to the patient by the table. It was only possible for patients to see their fingertips at the table's edge. The patients were instructed to reach and return their hands as quickly as possible without being corrected for pointing errors. Initially, the pointing task was repeated 30 times without prism glasses. Then, wearing 20 dioptre prism glasses that shifted their visual field 11.4° to the right (deluxe Prism google; Bernel 1138KIT28+). The task was repeated 90 times. After pointing at targets, the prism glass was taken off and they pointed 60 more times. This procedure is based on the three steps of prism adaptation which include: pre-exposure baseline measurement of pointing performance, active exposure to prismatic displacement to produce the adaptation, and post-exposure after-effect measurement of adaptation (Pisella et al., 2006; Redding et al., 2005; Rossetti et al., 1998).

Each patient undertook a total of 12 training sessions (one session a day), each lasting about 30 min, every weekday over a period of 16 days. The interventions were provided during regularly scheduled rehabilitation sessions and all other routine interdisciplinary stroke rehabilitation continued as usual. The control and intervention groups underwent the same intervention procedure. However, the control group utilized neutral goggles (sham) whilst the intervention group utilized prism glasses.

Data analysis

STATA version 15 was used for data analysis. Descriptive statistics of percentage, medians and IQR, mean and standard deviation were used to summarize data.

An intention-to-treat analysis approach was utilized to include all participants as originally recruited in the study. The rationale to conduct an intention-to-treat (ITT) analysis in this study is to provide unbiased comparisons among the treatment to forestall the effects of dropout, which may affect the randomization of the treatment groups and to also ensure deviation from the protocol will not have a major effect on the findings of this study. Missing data were handled using simple imputation methods. A comparison of the means of the BIT-C and CBS scores between the control and intervention groups was carried out using a t-test to demonstrate a significant distinction between the two groups. Univariate and stepwise multivariate logistic regression was done to establish sociodemographic and clinical variables that may have significance in the prediction of the outcome of prism adaptation therapy among stroke survivors with USN. The outcome variable was the post-treatment BIT-C score and the Catherine Bergego scale. The BIT-C score was categorized as thus: BIT-C score greater than 129 was categorized as recovery while a BIT-C score less than or equal to 129 was categorized as no recovery. We tested the correlation between the estimated MMS and the total BIT-C and the components of the BIT-C using Pearson's correlation (r).

Ethical considerations

This trial was registered in the Pan African clinical trial registry. The registry identification number is **PACTR201903732473573**. Ethical clearance was obtained from the University of the Witwatersrand Committee for research on the human subject with approval number **M180155.** Patient consent was sought and obtained from prospective study participants before recruitment into the study. The procedure of the research process was explained to the patient and an information sheet was given to the patient for further clarification. Participation was voluntary and participants were free to withdraw from the study at any time with no consequences.

Results

Between October 2018 and December 2020, 221 patients were screened; 74 patients met the eligibility criteria and gave consent to participate in the study and 68 patients completed the study. Six participants dropped out, three in the control and three in the intervention group: Four were discharged prematurely; one was deceased before the intervention was complete and another was infected with COVID-19 and transferred to the isolation ward. Figure 1 shows the flow of participants in the study.

Table 1 shows the sociodemographic and clinical characteristics of the enrolled study participants. The male to female ratio was 1:1 and the mean participant age was 49.15 ± 13.17 years while the median time from stroke onset to study enrolment was 38.5 (28–48) days. The majority of the patients were right-handed (79.73%), of black race (81.08%), and had ischaemic stroke type (78.38%) with a supratentorial lesion (90.54%). The differences in demographics and clinical variables between intervention and control groups were not statistically significant. Clinically relevant improvement was observed more post-treatment, more ($n = 23$; 62.16%) of the patients in the intervention group recovered from USN post-treatment (BIT-C score > 129) than patients in the control group ($n = 3$; 8.11%) and this was statistically significant ($p = <.001$) (Table 2).

Both groups had improved total scores of the BIT-C which generally increased over the study period for both groups at post-treatment (t_1). There were statistically significant differences in BIT-C baseline and post-treatment scores with the intervention group scoring higher than the control group

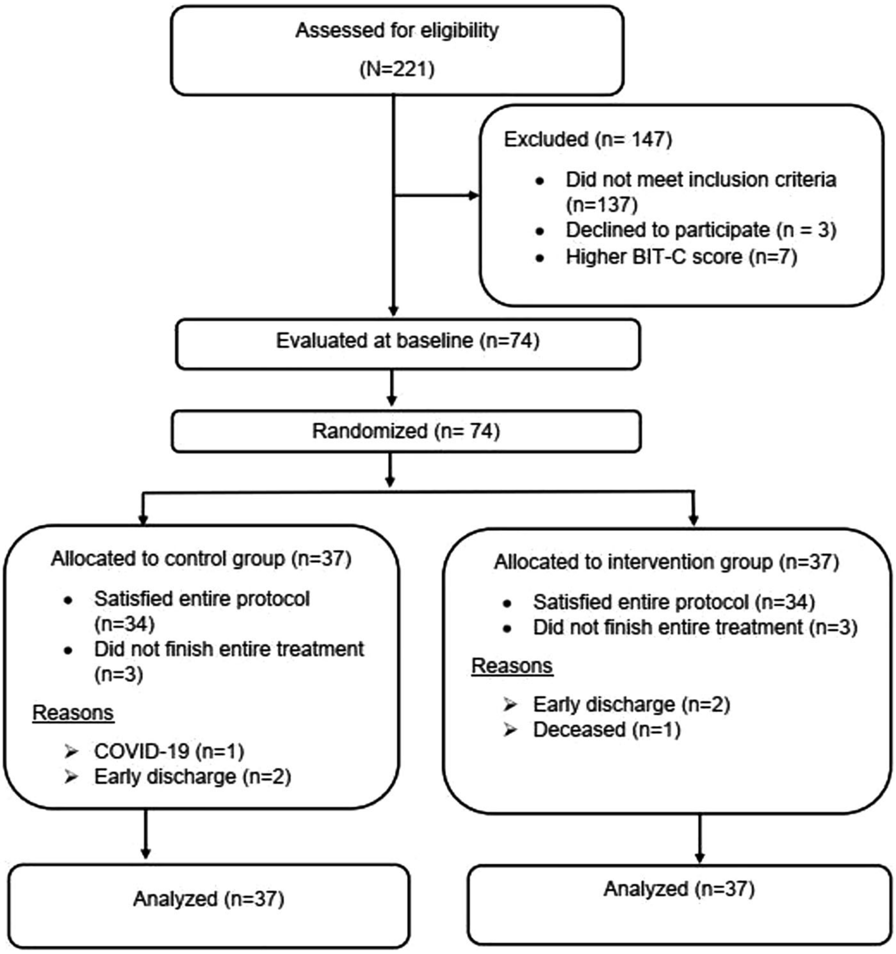

Figure 1. Distribution of the study sample throughout the study.

(Table 3). Items of the BIT-C had statistically significant between-group difference as thus: baseline: Star cancellation test ($p = .024$); post-treatment: line crossing ($p = <.001$), star cancellation test ($p = <.001$), letter cancellation test ($p = <.001$), figure and shape copying ($p = <.001$), line bisection test ($p = .005$).

Tables 4 and 5 show factors that had an influence on USN recovery after prism adaptation therapy: results of the univariate and multivariate analysis (for the BIT-C).

Stroke survivors in the treatment group had 18.62 times more odds of recovery than patients in the control group. This was seen to be overwhelmingly significant ($P < .001$).

The model for the multivariate analysis (using the BIT-C as the outcome variable) was selected following backward stepwise logistic regression. Age was locked into the model as literature has shown that age plays a role in stroke recovery (Bagg et al., 2002).

Table 1. Demographic and clinical characteristics of stroke survivors ($N = 74$).

Variable	Total	Control group ($n = 37$)	Intervention group ($n = 37$)	Comparison	
				Test statistics	p-value
Sex, (n, %)					
Male	37 (50)	20 (45.95)	17 (54.05)	$X^2 = 0.487$	0.485
Female	37 (50)	17 (54.05)	20 (45.95)		
Age, years Mean ± SD	49.15 ± 13.17	46.51 ± 13.56	51.78 ± 13.06	$t = 1.69$	0.095
Time post-stroke onset *(at baseline), days*	38.5 (28–48)	36 (28–47)	42 (26–56)	$z = 0.80$	0.423
Years of education	10 (5–13)	10(6–13)	9(5–12)	$z = -1.028$	0.304
Employment status					
Employed	33 (44.59)	14 (37.84)	19 (51.35)	$X^2 = 1.620$	0.445
Unemployed	29 (39.19)	17(45.95)	12 (32.43)		
Retired	12 (16.22)	6(16.22)	6 (16.22)		
Marital status (%)					
Married	43 (58.11)	20 (54.05)	23 (62.16)	$X^2 = 1.019$	0.601
Single	24 (32.43)	14 (37.84)	10 (27.03)		
widowed	7 (9.46)	3 (8.11)	4 (10.81)		
Race (%)					
Black	60 (81.08)	30 (81.08)	30 (81.08)	$X^2 = 0.311$	0.856
Asian	5 (6.76)	2 (5.41)	3 (8.11)		
Caucasian	9 (12.16)	5 (13.51)	4 (10.81)		
Hand preference (%)					
Right	59 (79.73)	30 (81.08)	29 (78.38)	$X^2 = 0.084$	0.772
Left	15 (20.27)	7 (18.92)	8 (21.62)		
Stroke type (%)					
Ischaemic	58 (78.38)	29 (78.38)	29 (78.38)	$X^2 = 0.000$	1.000
Haemorrhagic	16 (21.62)	8 (21.62)	8 (21.62)		
Lesion site (%)					
Supratentorial	67 (90.54)	33 (89.19)	34 (9.89)	$X^2 = 0.215$	P = 0.898
Infratentorial	2 (2.70)	1 (2.70)	1 (2.70)		
Mixed (diffuse)	5 (6.76)	3 (8.11)	2 (5.41)		
Cognitive ability, *(MMSE score)*	21.61 ± 2.27	21.89 ± 2.51	21.32 ± 1.99	$t = -1.077$	P = 0.285

(t = T-test statistics; z = Man witney U statistics; X^2 = Chi square statistics).

Table 2. Distribution of patients that recovered from unilateral spatial neglect post-treatment.

Recovery from USN	Control (N; %)	Intervention (N; %)	X^2	p-value
No	34(91.89)	14(37.84)	23.717	P < .001**
Yes	3(8.11)	23(62.16)		
Total	37(50.00)	37(50.00)		

(BIT-C score > 129: recovery, BIT-C score < 129:No recovery.
**statistically significant @ p < .005).

Controlling for other confounding factors, patients in the treatment group had 63.10 times the odds of recovery of patients in the non-treatment group. This finding was overwhelmingly significant (p < .001, 95% CI = 9.70–410.59). Also, for every unit increase in cognitive ability (MMSE score), the odds of recovery increased by 1.52 after controlling for confounders. This finding was also statistically significant (p = .016, 95% CI = 1.08–2.14). Females had 0.70 times the odds of recovery compared to the males, although this did not reach statistical significance (P = .139). Likewise, for every unit increase in age, the odds of recovery decreased by 0.96 after adjusting for confounders. This finding was not statistically significant (p = 0.147, CI = 0.90 −1.02). Tables 4 and 5 shows the multivariate analysis of factors that influence post-stroke USN after prism treatment.

There is no significant correlation between the total BIT-C score and the estimated mini-mental scale score (*r* = 0.132, p = 0.262). There is, however, a significant positive correlation between the representational drawing component of the BIT-C and the estimated MMS (*r* = 0.328. p = .006). Table 6 shows these relationships.

For the CBS, univariate analysis showed only treatment allocation had a significant relationship with the CBS being lower by an average of 5.65 in the intervention group compared to the score of participants in the control arm (p < .001) (Table 7). Using backwards stepwise regression, a model was created to assess predictors of USN recovery. We found that adjusting for all other variables, the CB score for participants in the treatment arm was lower by an average of 6.68 compared to that of participants in the control arm (p < .05). Also, for every unit increase in the estimated mini mental health score of participants, the CBS score increased by 0.58 points and this relationship was found to be significant (p = .04) while the relationship with other parameters did not reach statistical significance. Table 8 shows the results of the multivariate analysis of the factors that influence recovery from post-stroke USN (using the CBS as the outcome variable).

Discussion

This study investigated the demographic and clinical factors that influence USN recovery following the PA regimen. Our study is the first to examine

Table 3. Comparison of specific test for BIT-C (primary USN outcome) between control and intervention group.

Variable (maximum obtainable score)	Baseline Assessment (t_0)		Baseline comparison		Post-intervention assessment (t_1)		Post-intervention comparison	
	Control group (ẋ ± SD)	Intervention group (ẋ ± SD)	Mean difference	p-value	Control group (ẋ ± SD)	Intervention group (ẋ ± SD)	Mean difference	p-value
BIT-C Total (146)	82.95 ± 20.46	70.59 ± 23.40	−12.35	.018***	78.08 ± 33.74	117.68 ± 39.49	39.59	<.001***
Line crossing (36)	23.38 ± 7.54	20.97 ± 9.60	−2.41	0.235	23.00 ± 7.09	33.44 ± 5.48	10.44	<.001***
Star cancellation (54)	30.84 ± 11.94	24.70 ± 10.98	−6.14	0.024***	31.71 ± 11.90	47.74 ± 7.52	16.03	<.001***
Letter cancellation (40)	20.43 ± 7.46	17.03 ± 7.82	−3.41	0.059	20.32 ± 8.89	33.91 ± 6.22	13.59	<.001***
Figure and shape copying (4)	2.00 ± 1.20	1.76 ± 1.28	−0.24	0.389	3.11 ± 1.34	4.38 ± 1.13	1.26	<.001***
Line bisection (9)	5.59 ± 1.64	5.03 ± 1.48	−0.57	0.123	6.12 ± 2.10	7.50 ± 1.88	1.38	.005***
Representational drawing (3)	0.70 ± 1.02	1.11 ± 1.15	0.41	0.114	0.71 ± 1.12	1.09 ± 1.42	0.38	.222
Catherine Bergego scale	20.24 ± 4.18	21.22 ± 4.02	0.97	0.311	19.5 ± 4.28	13.85 ± 5.73	−5.65	<.001***

(*** = statistically significant at $p < .005$). The italaicized items in the table are subtests of the BIT-C.

Table 4. Factors that influence recovery from post-stroke USN (BIT-C): Univariate analysis.

	OR	SE	Z	p-value	95% confidence	
Allocation arm						
Control	Ref					
Treatment	18.62	12.87	4.23	<.001***	4.80	72.15
Age	1.01	0.02	0.56	0.574	0.97	1.05
Cognitive ability	1.17	0.13	1.41	0.160	0.94	1.45
Time since stroke onset	1.09	0.02	0.60	0.550	0.98	1.04
Gender						
Male	Ref					
Female	0.72	0.12	−1.92	0.054	0.52	1.01
Marital status						
Married	Ref					
Single	0.84	0.45	−0.32	0.751	0.30	2.41
Widow	0.68	0.60	−0.44	0.660	0.12	3.89
Years of Education	0.98	0.05	−0.41	0.680	0.88	1.08
Employment status						
Employed	Ref					
Unemployed	2.17	1.17	1.43	0.153	0.75	6.25
Retired	1.33	0.97	0.40	0.692	0.32	5.54
Race						
Black	Ref					
Asian	0.40	0.46	−0.79	0.428	0.04	3.82
Caucasian	0.46	0.39	−0.92	0.357	0.09	2.41
Hand Preference						
Right	Ref					
Left	1.3	0.77	0.44	0.659	0.41	4.17
Type of stroke						
Ischemic	Ref					
Hemorrhagic	0.80	0.48	−0.37	0.71	0.24	2.62
Site of stroke						
Supratentorial	Ref					
Infratentorial	1.79	2.57	0.41	0.685	0.11	29.95
Mixed	0.45	0.51	−0.70	0.484	0.05	4.24

(OR: odd ratio, CI: confidence interval, SE: standard error.)
*** = statistical significance.

Table 5. Factors that influence recovery from post-stroke USN (BIT-C): Multivariate analysis.

	OR	SE	z	P-value	CI	
Allocation arm						
Control	Ref					
Treatment	63.10	60.30	4.34	<0.001***	9.70	410.59
Cognitive Ability	1.52	0.26	2.41	0.016***	1.08	2.14
Gender						
Male	Ref					
Female	0.70	0.17	−1.48	0.139	0.44	1.12
Age	0.96	0.03	−1.46	0.145	0.90	1.02
Employment Status	2.21	1.21	1.45	0.147	0.76	6.46

*** = statistical significance at $p < 0.05$.

demographic and clinical predictors of USN predictors following PA treatment regimen in an African population.

Equal gender distribution was observed in this study; this could be linked to chance in the recruitment of patients for this study and not a depiction of the gender distribution of stroke incidence. There is existing evidence that stroke incidence is higher in males than in females in all age classes, and females are, on average, several years older than men when they suffer their first

Table 6. Correlation between the Mini-mental scale and post-treatment BIT-C score.

		Total BITC	Line crossing	Letter cancellation	Star cancellation	Figure and shape Copying	Line bisection	Representational drawing
Estimated mini-mental scale	Pearson correlation (r)	0.1320	0.0518	0.0909	0.1280	0.0623	−0.0510	0.3284
	P-value	0.2623	0.6751	0.4612	0.2982	0.6137	0.6797	0.0063

Table 7. Factors that influence recovery from post-stroke USN (CBS): Univariate analysis.

Variables	Coeff	SE	t	p-value	95% confidence	
Allocation arm						
Control	Ref					
Treatment	−5.65	1.23	−4.60	<0.001***	−8.10	−3.20
Age	0.02	0.05	0.33	0.745	−0.09	−0.13
Cognitive ability	−0.40	0.31	−1.31	0.196	−1.01	0.21
Time to enrolment	−0.08	0.05	−1.58	0.119	−0.17	0.02
Genderc						
Male	Ref					
Female	−0.63	1.41	−0.45	0.657	−3.44	2.18
Marital status						
Married	Ref					
Single	−0.96	1.55	−0.62	0.536	−4.06	2.13
Widow	−1.27	2.55	−0.50	0.622	−6.37	3.84
Years of Education	0.09	0.16	0.54	0.589	−0.24	0.41
Employment status						
Employed	Ref					
Unemployed	−0.82	1.50	−0.55	0.584	−3.81	2.16
Retired	2.80	2.17	1.29	0.202	−1.54	7.14
Race						
Black	Ref					
Asian	1.53	2.66	0.57	0.568	−3.78	6.84
Caucasian	4.18	2.15	1.94	0.057	−0.12	8.48
Hand Preference						
Right	Ref					
Left	−0.10	1.70	−0.06	0.954	−3.49	3.30
Type of stroke						
Ischemic	Ref					
Haemorrhagic	−0.23	1.66	−0.14	0.890	−3.55	3.09
Site of stroke						
Supratentorial	Ref					
Infratentorial	−1.30	4.20	−0.31	0.757	−9.69	7.09
Mixed	−1.20	2.72	−0.44	0.660	−6.63	4.23

*** = statistical significance at $p < 0.05$.

Table 8. Factors that influence recovery from post-stroke USN (CBS): Multivariate analysis.

Variable	Coeff	SE	t	p-value	95% confidence	
Treatment allocation						
Control	Ref					
Case	−6.68	1.25	−5.36	<.001	−9.18	−4.19
Estimated mini mental state	−0.58	0.28	−2.08	0.042	−1.14	−0.02
Age	0.01	0.06	1.77	0.083	−0.01	0.21
Time from stroke	−0.06	0.04	−1.42	0.160	−0.14	0.02
Stroke site						
Supratentorial	Ref					
Mixed	−4.43	2.33	−1.90	0.062	−9.10	2.23
BI total	0.33	0.22	−1.53	0.130	−0.77	0.10
Marital Status						
Married	Ref					
Widowed	−4.71	2.43	−1.94	0.058	−9.58	0.16
Race						
Black	Ref					
Caucasian	2.74	1.98	1.38	0.172	1.22	6.71

stroke. Up until about the age of 80 years, the prevalence of stroke is higher among men, after which it is higher among women (Gibson, 2013; Giralt et al., 2012; Goto et al., 2007; Kes et al., 2016; Wyller, 1999)

Participants in this study averaged 46.51 ± 13.56 years in the control group and 51.78 ± 13.06 years in the intervention group. This age group seems to be younger than previous studies that investigated the effect of prism adaptation in stroke survivors. This is not surprising as the current trend in the incidence of stroke supports that stroke, against the age-long belief, is no longer a disease of the aged. Previous studies (Connor, 2004; Mudzi et al., 2012; Ntsiea M et al., 2013; Rhoda & Hendry, 2003; Röding et al., 2003) had reported the occurrence of stroke in the same age group as this study. This paradigm shift in the age of occurrence of stroke has been attributed to growing poor lifestyle choices such as sedentary habits, smoking and poor dietary intake which leads to stroke risk factors such as dyslipidaemia and hypertension (Maredza et al., 2016; Putaala et al., 2012; Smajlović, 2015). Also, our population for this study is predominantly black African population, studies have shown that blacks are more likely to have stroke than white and Hispanic populations (Gardener et al., 2020; Howard et al., 2011; Sacco et al., 1998).

This study demonstrated that the use of prism adaptation improved recovery from post stroke unilateral spatial neglect in the sub-acute phase of recovery. Patients in the treatment arm for this study had greater odds of recovery than patients in the control arm. This outcome suggests that PA enabled motor and cognitive re-learning following the twelve sessions of prism treatment This result is in tandem with previous study (Fortis et al., 2011; Gossmann et al., 2013; Keane et al., 2006; Maravita et al., 2003; Mizuno et al., 2011; Nys et al., 2008; Turton et al., 2010; Serino et al., 2009; Shiraishi et al., 2008; Yoneda et al., 2011) that had reported improvement following prism adaptation therapy (PAT) and in contrast with studies (Mancuso et al., 2012; Rode et al., 2015) that reported no improvement following PAT. This could be due to a plethora of factor in our study such as the use of higher prism power, and treatment sessions. In our study, higher prism power ((20 diopters, 11.4°), than reported in previous studies that reported use of "10 diopters" (Kerkhoff & Schenk, 2012; Mizuno et al., 2011; Turton et al., 2010) and "5 diopters" (Mancuso et al., 2012).

Also, this study demonstrated that cognitive performance measured by the MMSE influenced improvement in USN symptoms as assessed by both the BIT-C and the Catherine Bergego scale (CBS) after prism adaptation therapy in patients in the sub-acute phase of recovery from stroke. It is not daunting that an impaired initial global cognitive function assessed by the MMSE decreased patient's response following PAT as shown in our study, patients with preserved cognitive function have a better propensity to learn new task, follow instructions and participate in PAT treatment regimen. Previous studies have examined the relationships of cognitive ability and rehabilitation outcome (Adamit et al., 2015; Dignam et al., 2017). This study is in tandem with a previous study by Leem *et al.* (Leem et al., 2019) that reported that less spasticity, better initial cognitive function, and better initial motor function have a significant correlation with the functional outcomes after robot-assisted therapy. Similarly, cognitive impairments have been found to correlate with poor gain in function and are a predictor of adverse outcomes in stroke survivors' rehabilitation outcomes (Zinn et al., 2004; Zwecker et al., 2002). Previous studies have reported that frontal lobe lesions (Chen et al., 2014; Goedert et al., 2020) and aiming deficits (Goedert et al., 2014) could predict better outcomes following PA treatment in stroke survivors. This study expands the knowledge on factors that predict post-stroke USN recovery. Wagle *et al.* (Wagle et al., 2011) had, in a previous study, demonstrated that post-stroke cognitive functioning is an independent predictor of the lasting functional post-stroke outcome. First, cognitive function as assessed by MMSE could be predictive of the primary outcome measured in this study, the BIT-C, because the BIT-C is a cognitive evaluation for neglect (Wilson et al., 1987) and it is more intensely influenced by cognitive function than the intentional task (Kato et al., 2012). Secondly, attentional tasks have been closely associated with cognitive function in patients with right cerebral infarction. Thirdly, cognitive function may have acted as a prognostic factor because patients that participated in prism adaptation needed attention to follow the tasks with visuomotor coordination. Ward et al. (Ward et al., 2003) demonstrated that after visuomotor tasks (such as during PA), there is increased activation of non-primary motor regions in the brain, which culminates in an activity-dependent plastic change in somatotopic representations in the motor system hence increasing the access to alternative pathways.

Several other cognitive functions such as working memory, and executive function (Al-Qazzaz et al., 2014) have been shown to modulate the spatial neglect symptoms. The cognitive domain includes attention, memory, language, and orientation. The most affected domains for stroke survivors are attention and executive functions; at the time of stroke diagnosis, memory problems are often prominent, this correlates with aspects or domain (attention, recall, calculation, language, executive function, orientation and ability to follow simple commands) that the MMSE examines which was used in this study. In our study, the cognitive function should not be seen as a global construct rather as a multifaceted construct characterized by stages which involves different cognitive processes such as learning and memory, visuospatial and motor function, attention/concentration, language, social cognition/emotions and executive functions (Al-Qazzaz et al., 2014).

Although not statistically significant; age, gender, type of stroke, site of stroke, time from stroke to enrollment in the study, handedness and race showed some interesting findings on recovery from USN after prism treatment. Although these variables were not significant it is important to report the relationships.

For instance, age was shown to have no significant effect on recovery after prism adaptation therapy. Previous studies had reported that functional recovery post-stroke increased with decreasing age (Cioncoloni et al., 2013;

Jongbloed, 1986; Khan et al., 2014; Protopsaltis et al., 2009; Veerbeek et al., 2011). Also, the female gender had lesser odds of recovery than the males in this study. Previous studies (Cioncoloni et al., 2013; Tei et al., 2011; Tilling et al., 2001) have reported that females show poorer functional outcomes and lower quality of life than men even though females have a higher incidence of stroke. Stroke differences may be explained by a combination of factors that include coagulation status, sex hormones, genetics, social interactions, and life-style, individually or jointly (Hiraga, 2017)

Stroke patients who had a hemorrhagic stroke had lesser odds of recovery than those with ischemic stroke. Left-handed participants were 1.3 times more likely to recover than those who were right-handed. Currently available data do not provide definitive answers to all of the questions regarding recovery on haemorrhagic strokes versus ischemic strokes; however, patients with haemorrhagic strokes demonstrated functional gains more rapidly than those with ischemic strokes, (Chae et al., 1996; Paolucci et al., 2003) but data from this study appear to be in disagreement with those of a prior study (Franke et al., 1992).

Stroke patients who had infratentorial strokes had 1.79 more odds of recovery while those with mixed type had 0.45 fewer odds of recovery compared to those who had a supratentorial stroke. Supratentorial stroke (STS) and infratentorial stroke (ITS) cause motor deficits that require specific rehabilitative treatment; the main motor deficit for STS is hemiparesis and ataxia for ITS. Very few studies compare the outcome of STS patients with that of ITS patients (De Haan et al., 1995; Gialanella et al., 2008; Marshali & Kaeser, 1961; Turney et al., 1984). Patients with brainstem infarction (ITS) have a worse prognosis than those with hemispheric infarction (STS) (Gialanella et al., 2008). A possibility is that structures in the supratentorial region are responsible for cognitive and perceptual processing. Prism adaptation may have altered spatial cognition in the direction of visual displacement by temporarily adjusting sensorimotor mapping.

In this study, we conducted a further correlational analysis between the primary outcome (Unilateral spatial neglect as assessed by the behavioural inattention test) and Cognitive function as assessed by the mini-mental scale examination (MMSE). Our findings were interesting as they showed a correlation only between the representational drawing subset of the BIT-C. This finding is similar to a previous study by Kato and colleagues (Kato et al., 2012) that found a significant correlation between MMSE score and the number of errors in intentional tasks. This suggests the existence of a strong link between low-level sensorimotor plasticity and high-level cognitive functions and raises important questions about the mechanisms involved in creating unexpected cognitive effects following prism adaptation therapy. The representational drawing subset of the BIT-C involved task is designed to assess the patient's visual imagery independent of sensory input and assesses the representational form of neglect. Execution of representation drawing which forms the basis of the assessment involves preserved cognitive function as the process is a multimodal cognitive stimulation process (Munzert et al., 2009).

The implication of the results of our study to rehabilitation practice is the need to focus on and reinforce early rehabilitation to improve cognitive function. This is further reinforced as a previous study (Mori et al., 2021) had identified that about half of stroke survivors at the sub-acute phase of recovery are affected by cognitive impairment. Also, cognitive impairment is a major impedance to the rehabilitation process affecting ADLs (Joel Yager, 2019), eating and social interaction (Mori et al., 2021).

This study further highlights that Prism adaptation therapy recovery is not devoid of the modulatory effect of cognitive function. This is because patients undergoing PA treatment regimen for post-stroke USN will need a fairly intact cognitive system to, for instance, obey commands, execute and participate in the therapy process. The finding of this study underscores the importance of evaluating cognitive functions using an adequate tool in post-stroke survivors undergoing prism adaptation therapy.

Conclusion

The result of this study suggests that following the PA treatment regimen, stroke survivors with preserved cognitive function show higher chances of attaining significant recovery from neglect following in the sub-acute phase of recovery.

Limitation of study

This study did not consider the stratification of unilateral spatial neglect by severity and subtypes of spatial neglect. Also, follow-up for patients was just for a single time after completion of the treatment regimen. Multiple follow-ups could enable the researcher to establish the lasting effects of prism treatment on USN and if there could be possible relapse in the gains recorded after prism adaptation therapy. It is therefore recommended that future studies should consider multiple follow up times to evaluate factors that predict USN recovery following PAT at long-term.

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Data availability statement

Data emanating from this research is available upon Request.

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