Structured Multidomain Cognitive Rehabilitation for Stroke: Findings From an Observational Cohort Study

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Abstract

Background

Persons with mild stroke experience minimal functional difficulties; nonetheless, they are at elevated risk for post-stroke cognitive impairment (PSCI) and cognitive decline.

Aims

We report outcomes from an observational cohort study of a structured, multidomain intervention for persons with mild strokes.

Methods

The Stroke Memory RehabiliTation (SMaRT) program comprises weekly two-hour group sessions for six weeks on cognitive strategies, lifestyle and relaxation. Participants were recruited from a tertiary hospital between June 2018 to September 2019. They had MRI-confirmed ischemic strokes with mild functional difficulties (modified Rankin Scale score ≤3). Participants underwent assessments and questionnaires at baseline, 1-week post-program, 3 months post-program, and 6 months post-program.

Results

Participants (N=108, mean age=63.54±9.22, 31.5% female) demonstrated significant improvement in cognition, mood, activities of daily living (ADL) and quality of life (QOL) (*p*s<0.05) across timepoints. Participants performed significantly better at 6 months post-program compared to baseline on cognitive tests (MoCA 24.47±3.22 vs. 25.80±2.83, Beta=1.26, 95% CI(0.78,1.74)), *p*<.001; Visual Cognitive Assessment Test (22.74±3.98 vs. 24.76±3.68, Beta=2.04, 95% CI(1.44,2.65), *p*<.001); 87% of participants maintained or improved in performance. At 6 months post-program, participants reported greater functional independence (Nottingham Extended ADLs Questionnaire Beta=4.20, 95% CI(2.63,5.77), *p*<.001); fewer depressive symptoms (Geriatric Depression Scale Beta=-1.44, 95% CI(-1.94, -0.94), *p*<.001); and improved QOL (Dementia-QOL Questionnaire Beta=5.28, 95% CI(1.09, 2.57), *p*<.001).

Conclusions

The SMaRT program is a cost-effective, scalable, structured program for PSCI. Findings suggest its potential effectiveness in reducing cognitive decline and improving other domains of well-being, with carry-over benefits after 6 months.

1. Introduction

Approximately one in four adults is likely to experience a stroke in their lifetime[1]. Of these, 70-80% will not experience immediate cognitive or functional deficits[2,3]. Current typical post-stroke rehabilitation focuses on patients with immediate deficits, neglecting the majority who do not show immediate significant

physical or functional decline[4]. However, studies have shown that in this group of stroke survivors, the prevalence and risk of post-stroke cognitive impairment (PSCI) is elevated[5,6]. PSCI refers to the onset of cognitive impairment after a stroke in the absence of pre-existing cognitive deficits[7]. It can undermine quality of life and physical recovery through its insidious effects on work, social interaction, self-esteem, and other aspects of daily functioning. Worse, cognition can continue to decline between 3 months to 1 year or even longer after the stroke[8]. Hence, effective and scalable interventions that raise patient awareness of PSCI, relevant modifiable lifestyle factors, and strategies to manage mild cognitive difficulties will benefit the large number of patients with mild ischaemic strokes.

The multidomain, scalable Stroke Memory RehabiliTation (SMaRT^{TM}) intervention program for persons with mild strokes was designed to meet the needs of this group. The objectives of the SMaRT intervention program can be summarized as follows: (1) to teach skills for self-management of mild cognitive symptoms; (2) to increase awareness of preventive strategies against PSCI; (3) to support participants' re-engagement in community activities and employment; (4) to lower participants' risk for cognitive decline. In this paper, we outline the SMaRT intervention approach and outcomes from a single center in Singapore.

2. Methods

2.1 Research Ethics and Patient Consent

This study has been approved by the SingHealth Centralized Institutional Review Board (study reference number 201806-00133). Anonymized data will be shared upon reasonable request to the Corresponding Author from any qualified investigator. Informed consent was obtained from all participants.

2.2 Study Design

In this prospective observational cohort study, participants underwent a battery of assessments and questionnaires at baseline. Subsequently, participants attended the SMaRT program as a group. Participants were then assessed with the same test battery one week, three months and six months after completing program content (participant timeline summarized in Fig. 1) To cater to the multilingual Singaporean geriatric population, the program and assessments were conducted in English or Mandarin depending on participants' preferred language.

2.3 Inclusion and Exclusion Criteria

Patients screened for eligibility included those admitted to a stroke ward in a hospital in Singapore from April 2018 to September 2019, or referred from other doctors in affiliated organizations. Inclusion criteria comprise (1) ischaemic stroke confirmed on MRI, (2) self-reported cognitive difficulties, (3) ages 18-80, (4) functional independence, defined as a score of 3 or lower on the Modified Rankin Scale (mRS), (5) basic literacy in English or Mandarin, (6) able to attend the program within 3 to 12 months of their stroke. This time frame accounts for the fact that many persons with stroke spontaneously recover some level of

cognition or resolve acute symptoms such as psychosis and delirium within 3 months of their stroke, after which improvement plateaus[9]. However, beyond 12 months, PSCI is likely to have set in and stabilized[10], making rehabilitation less beneficial. In sum, these criteria ensure that participants do not have cognitive and functional difficulties that might interfere with their comprehension of and participation in the program.

Exclusion criteria included pre-existing dementia prior to stroke, psychiatric conditions, behavioral symptoms, or physical difficulties that may impede participation in program activities.

2.4 Program Structure

The eight-week program was designed based on previous research highlighting common deficits in PSCI, potentially effective cognitive strategies, and lifestyle factors influencing PSCI and cognitive decline. The first and last sessions include pre- and post-rehabilitation assessments respectively. As persons with mild strokes have minimal difficulties with independent function and comprehension, they are likely to benefit from exposure to a large variety of PSCI-relevant topics and strategies, from which they can subsequently choose preferred strategies and lifestyle modifications. Further, as PSCI is multifactorial, a holistic program which discusses cognitive, lifestyle and emotional factors relevant to PSCI will be helpful [11,12]. Finally, given the large proportion of persons who experience mild strokes, ensuring accessibility to such services within communities is paramount; hence, a manualized program which can be scaled to multiple centers will be best suited to this group. For these reasons, the program was designed to be multi-domain, to provide participants with a variety of PSCI-relevant strategies, and to have a structured curriculum scalable to multiple centers.

An overview of the program's components is provided in Fig. 1. For each 8-week run, up to 12 participants could enroll, with a facilitator-participant ratio of at least 1:4. Program components are summarized in Table 1.

2.5 Ethics and Patient Consent

Approval for this study has been obtained from the SingHealth Centralised Institutional Review Board. Participant consent is obtained prior to the use of their data. All research was performed in accordance with relevant guidelines and regulations.

2.6 Statistical Analysis

Linear mixed models were performed separately for MoCA, VCAT, TMT-A, GDS, NEADL and Dem-QOL respectively. Outcome variables were changes in scores across timepoints, with intercepts for participants' scores as a random effect and unstructured covariance matrix. Two models for each outcome variable were run with time as fixed effect: (1) to examine differences between each timepoint from baseline; (2) to estimate average change across timepoints from baseline.

To further understand possible individual differences in score changes across time, we computed the proportion of participants whose cognitive performance were maintained or improved at 6 months post-program, defined as a change in MoCA or VCAT scores greater than or equals to -1 between baseline to 6 months post-program.

To test whether trends of the scores may differ across demographic and stroke type variables, the respective interactions of time with age (dichotomized using median split), gender, ethnicity, stroke lacunarity, stroke lateralization and presence of stenosis were tested in separate linear mixed models.

All *p*-values are reported with Bonferroni adjustments for multiple comparisons of 6 outcome variables, with statistical significance set at p=.05. Statistical analysis was performed in STATA software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.).

3. Results

From June 2018 to September 2019, 117 participants were recruited. Of these, 9 participants dropped out from the program due to conflicting commitments (N=8) or death (N=1), and were excluded from analysis. 27 participants were lost to follow-up at 3 months, and 16 participants at 6 months due to conflicting commitments or inability to participate during the peak of the COVID outbreak in Singapore. Nonetheless, these participants provided valid scores on other time points andwere not removed from analysis. As such, adherence rates were high, with only 8 of 117 participants (6.8%) voluntarily dropping out from the program. Baseline characteristics and outcome measures of the 108 included participants are summarized in Tables 2 and 3. The mean MoCA scores of participants at baseline was 24.47 (*SD* 3.22), suggesting potential for rehabilitation.

Linear mixed model analysis demonstrated improvements at all timepoints from baseline (Table 4); these improvements were also statistically significant. The exception was the difference between baseline and post-program for TMT-A (units in seconds); between these timepoints, absolute TMT scores improved (Beta coefficient=-3.49, 95% CI (-7.53, -0.55)) but did not remain statistically significant after Bonferroni adjustment. At month 6 compared to baseline, improvements in MoCA (Beta coefficient=1.26, 95% CI (0.78, 1.74)) and VCAT (Beta coefficient=2.04, 95% CI (1.44, 2.65)) were small but statistically significant, suggesting that on average, participants' cognitive performance improved slightly or was maintained. Further, performance on the TMT-A (units in seconds) improved at month 6 compared to baseline (Beta coefficient=-6.43, 95% CI (-10.65. -2.22)), suggesting improvements in processing speed. At month 6, participants' NEADL scores also improved (Beta coefficient=4.20, 95% CI(2.63,5.77)), suggesting increased independence in activities of daily living. The coefficient for the GDS (Beta coefficient=-1.44, 95% CI (-1.94, -0.94)), suggested that participants endorsed fewer symptoms of depression at month 6. Finally, the DemQOL also improved significantly (Beta coefficient=5.28, 95% CI(2.96,7.60)), suggesting improvements in quality of life after the program. Beta coefficients for participants' scores over time indicated small but statistically significant linear trends of improvement across timepoints for all outcome measures (adjusted *p*s <.001) (Table 4). In all, these results suggest that on average,

participants maintained or improved in global cognition, processing speed, ADL, mood, and quality of life at each timepoint up to 6 months after the program.

Further, from baseline to 6 months post-program, the proportion of participants who had maintained their cognitive performance or improved was substantial across MoCA (N=84, 91.3%) and VCAT (N=80, 87.0%), suggesting that a large majority of participants managed to maintain cognitive performance even at 6 months post-program. Both measures yielded highly consistent findings, supporting the reliability of this observation.

Additionally, the respective interactions between age, gender, ethnicity, stroke lacunarity, lateralization and presence of stenosis were also non-significant (adjusted *p*s>0.5), suggesting that these demographic variables and stroke characteristics are unlikely to affect participant outcomes.

4. Discussion

The SMaRT program is a structured, multi-domain group intervention program, conducted over six, two-hour, weekly, group sessions targeting patients with mild strokes. The program differs from other stroke rehabilitation programs as it: 1) takes a multidomain approach to cognitive rehabilitation 2) targets mild strokes, 3) has a scalable design. The findings thus far demonstrate that the program has a low dropout rate, providing support for its potential to engage participants.

This study's findings indicate small but significant improvements in cognition, mood, ADL and quality of life at 1 week, 3 months, and 6 months post-program, suggesting that on average, participants managed to improve or maintain their cognitive performance at 6 months post-program. 88% of participants maintained or improved in performance on cognitive tests from baseline to 6 months post-program. These trends were not moderated by age, gender, ethnicity, stroke lacunarity, stroke laterality, and presence of stenosis, further suggesting that the program is likely to be similarly effective for persons across these groups. Overall, these results suggest that participants may have been able to make lifestyle changes and apply cognitive strategies taught in the program that not only helped them improve in terms of cognitive performance, but also in mood, quality of life, and activities of daily living. Nonetheless, this interpretation is qualified by the design of this study and remains to be confirmed in further controlled trials of this program.

The SMaRT Program specifically targets persons with mild strokes and minimal cognitive impairment. It remains to be established if such cognitive and behavioural interventions will reduce cognitive decline, or even improve cognition in stroke survivors with non-specific, relatively mild cognitive impairment. To date, lifestyle interventions targeting only vascular risk factors for the reduction of post-stroke cognitive decline have shown promising results for participants with minimal cognitive and functional difficulties[13]. In this study, participants who completed the SMaRT program showed small but significant improvements on two cognitive screening tests from baseline to 6 months post-program; further, at 6 months post-program, nearly 88% of participants were found to have improved or maintained their cognitive performance from

baseline. These promising findings point to the feasibility of a holistic, multi-domain program as a measure against post-stroke cognitive decline in this often-neglected demographic. Further, the SMaRT program's participants were recruited after screening all patients who were admitted to stroke wards during the recruitment period, and hence participants should be fairly representative of patients with mild strokes typically seen in the hospital setting. Nonetheless, our findings are qualified by the lack of a control group for comparison, and will benefit from replication in future controlled studies for a stronger conclusion.

The SMaRT intervention's holistic approach to PSCI rehabilitation is a unique one, with cognition, lifestyle and emotion regulation as essential topics of emphasis. Although previous studies have demonstrated the potential for such multidomain programs to improve cognitive function in persons with cognitive impairment[14,15], it remains to be established if holistic programs tailored for PSCI will also be effective. Two lifestyle interventions targeting multiple vascular risk factors for post-stroke cognition[16,17] showed promising findings on a pooled analysis of their results[13]; however, these interventions did not include components on cognition or emotion regulation. Another study on a combined exercise and cognitive training found greater improvements in cognition in stroke survivors compared to controls, only physical exercise, or only cognitive training[18]. Our study adds to these previous findings, supporting the feasibility of multidomain programs in the treatment of PSCI. Additionally, participants showed gains in other PSCI-relevant domains such as functioning in ADLs, mood, and quality of life, suggesting that the benefits of such programs extend beyond maintaining cognitive capabilities. Nonetheless, these conclusions are qualified by the lack of a control group in our present study, and our findings will benefit from replication in a future controlled study.

Strengths of this study include the use of two measures of global cognition, which increases the reliability of findings relating to cognition. Further, the availability of follow-up data at 4 timepoints, up to 6 months post-program allows investigation of long-term gains and provides a large number of observations with which participants' trajectories of change could be tracked. Finally, outcome measures include domains beyond cognition, such as ADL functioning, mood, and quality of life, which allowed us to quantify the effects of the program beyond cognitive gains. However, a limitation of this study is the lack of a control group. Nonetheless, we were able to show intra-individual change over a period of 6 months for the subjects in the study, which is of clinical importance. Further, while absolute improvements in points seen on cognitive measures were small, this program aims to help participants retain existing cognitive abilities and prevent future decline, beyond improving cognitive performance per se. Hence, we believe that findings from this open-label trial will set invaluable groundwork for designing future randomized controlled trials of the SMaRT intervention.

Given the promising findings in this study, moving forward, we hope to hold controlled trials of the SMaRT program across multiple centers to ascertain its scalability. Further, to supplement participants' learning of cognitive strategies, the development of a complementary mobile application for this program is underway. Ultimately, based on the findings of the present study, the SMaRT Program for PSCI rehabilitation shows promise in meeting its objectives and potential for continued development.

5. Conclusions

The SMaRT intervention is a structured group program which is scalable to multiple centers, and targets key lifestyle, cognitive and emotional factors relevant to PSCI. Its intervention and study design account for a range of methodological and program delivery considerations for persons with mild strokes. Improvements in participants' global cognition, daily functioning and quality of life from baseline up to 6 months post-program, suggesting the potential for the program in reducing PSCI. These findings provide promising support for a follow-up controlled trial for this program, where the feasibility of a complementary mobile application and involvement of multiple centres can be further tested.

Declarations

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Authors' Contributions

SCN contributed to study design; collection and analysis of data; drafting and revision of manuscript for intellectual content. APXO contributed to data collection, drafting and revision of manuscript. FCCW contributed to data collection, drafting and revision of manuscript. EVC contributed to data collection, drafting and revision of manuscript. SES contributed to data analysis, drafting and revision of manuscript. LLHL contributed to data collection, drafting and revision of manuscript. ES contributed to study design, drafting and revision of manuscript for intellectual content. KPN contributed to study design, drafting and revision of manuscript for intellectual content. NK contributed to study design, drafting and revision of manuscript for intellectual content.

Competing Interests

The authors declare no competing interests.

Data Availability

Anonymized data will be shared upon request to the Corresponding Author from any qualified investigator.

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Tables

Table 1. Cognitive and lifestyle topics and strategies taught in SMaRT

Components		Strategies
Cognition	Sensory Input	· Attending to sensory input as key to memory · Mindful sensing
	Attention	· Self-monitoring · Squeezing actions to sustain attention
	Encoding	· Chunking · Categorization · Acronyms · 5W1H: Who, What, When, Where, Why, How · Visual Imagery
	Executive Functions	· Self-monitoring: Stop, Think, Plan, Do
Brain Essentials (Lifestyle)	Exercise	· Sign up for exercise groups and programs · Standing chair exercises · Seated arm strengthening exercises
	Diet	· Healthy portioning · Important nutrients for the brain
	Stress Management	· Five A's: Alter, Avoid, Adapt, Accept, Adopt · Healthy lifestyle tips: 'me' time, exercise, eat and sleep right
	Sleep	· Good sleeping habits
	Social Support	· Stroke-relevant organizations that participants can join activities
Emotion Regulation	Deep Breathing	· Technique and practice in Sessions 2-4
	Progressive Muscle Relaxation	· Technique and practice in Sessions 5-7
Self-Guided Components	Goal-setting	· Setting SMART (Specific, Measurable, Achievable, Relevant and Time-bound) Goals
	Weekly Assignments	· Logs, practices and thinking questions relevant to session content
Return to Community and Work	Return to Work	· Process of returning to work, lifestyle and activity adjustments, relevant agencies in re-employment

	Return to Community	· Examining challenges in engaging in community activities, applying taught strategies to challenges

Note. SMaRT=Stroke Memory Rehabilitation

Table 2. Demographic and Stroke Characteristics of SMaRT Participants

Variables	Mean±SD/Frequency (%)
Age (Years)	63.54±9.22
Education (Years)	9.67±3.77
Gender (Female)	34(31.5)
Ethnicity	
Chinese	94(87.0)
Malay	10(9.3)
Other	4(3.7)
Stroke Type (Lacunar)	59(54.6)
Stroke Lateralization (Left)	58(53.7)
Stenosis (Presence)	21(19.4)

Note. SMaRT=Stroke Memory Rehabilitation; SD=standard deviation

Table 3. Outcome Scores of SMaRT Participants

Score	Baseline	Post-Program	Month 3 Post-Program	Month 6 Post-Program
N	108	105	81	92
MoCA	24.47±3.22*	25.52±3.13	25.68±2.80	25.80±2.83
VCAT	22.74±3.98	24.47±3.64	24.59±3.61	24.76±3.68
TMT-A(Seconds)†	51.31±26.90	47.50±24.34	44.66±18.74	45.30±24.03
NEADL	51.37±11.40	55.31±9.85	55.31±9.37	55.45±10.86
GDS†	4.28±3.46	3.41±3.19	2.78±2.71	2.66±3.33
Dem-QOL	88.66±15.14	91.59±12.30	94.54±12.36	94.95±13.14

Note. SMaRT=Stroke Memory Rehabilitation; MoCA=Montreal Cognitive Assessment; VCAT=Visual Cognitive Assessment Test; TMT-A=Trail-Making Test-A; NEADL=Nottingham Extended Activities of Daily Living Scale; GDS=Geriatric Depression Scale; Dem-QOL=Dementia Quality of Life Scale

†Higher scores indicate poorer performance

*Mean Scores ± standard deviation

Table 4. Linear mixed regression model coefficients of outcome variables against visits

Score	Post-Program‡	Month 3 Post-Program‡	Month 6 Post-Program‡	Overall§
MoCA	1.05 (0.60,1.51)***	1.27 (0.77,1.77)***	1.26 (0.78,1.74)***	0.41 (0.25,0.56)***
VCAT	1.66 (1.08,2.24)***	2.06 (1.43,2.69)***	2.04 (1.44,2.65)***	0.66 (0.47,0.86)***
TMT-A †	-3.49 (-7.53,0.55)	-7.09 (-11.51,-2.68)**	-6.43 (-10.65,-2.22)**	-2.29 (-3.64,-0.94)***
NEADL	3.85 (2.33,5.39)***	3.94 (2.27,5.61)***	4.20 (2.63,5.77)***	1.29 (0.77,1.80)***
GDS†	-0.82 (-1.31,-0.37)***	-1.22 (-1.75,-0.69)***	-1.44 (-1.94,-0.94)***	-0.47 (-0.63,-0.31)***
Dem-QOL	2.81 (0.57,5.04)*	5.32 (2.87,7.76)***	5.28 (2.96,7.60)***	1.83 (1.09,2.57)***

Note. MoCA=Montreal Cognitive Assessment; VCAT=Visual Cognitive Assessment Test; TMT-A=Trail-Making Test-A; NEADL=Nottingham Extended Activities of Daily Living Scale; GDS=Geriatric Depression Scale; Dem-QOL=Dementia Quality of Life Scale. Beta coefficients can be interpreted as the average change in score across each timepoint.

†Higher scores indicate poorer performance

‡Beta coefficients interpreted as the difference in scores at the stated timepoint minus baseline

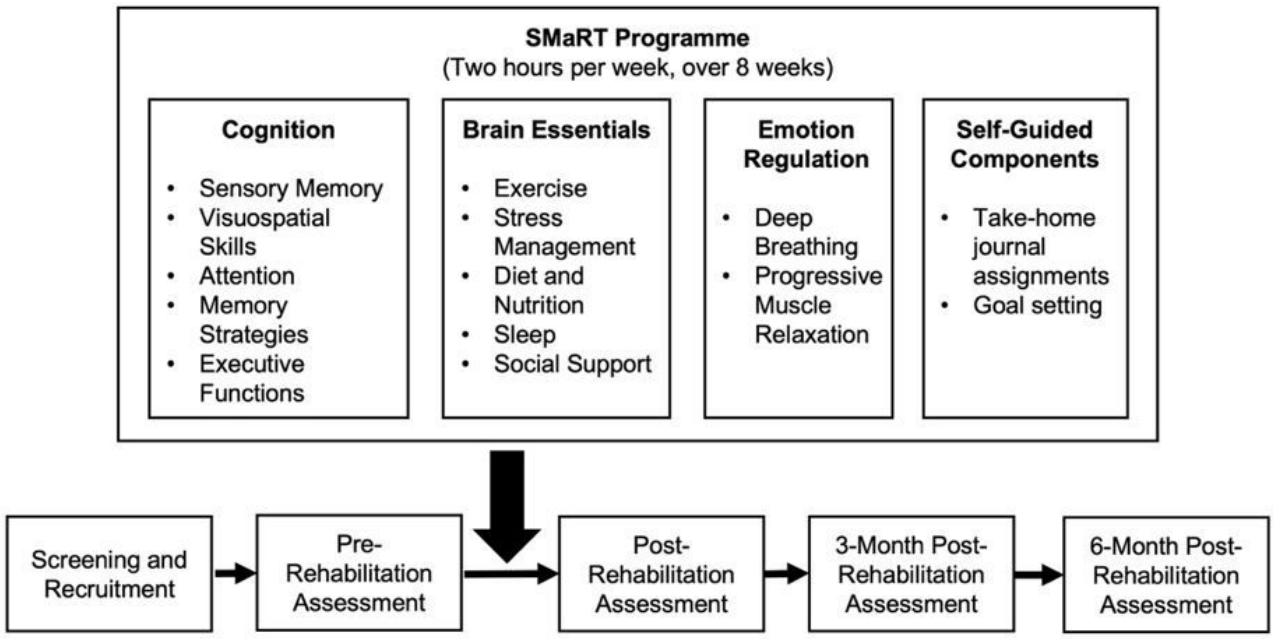
§Beta coefficients interpreted as the average change in score between consecutive time points

*statistically significant, $p<.05$

**statistically significant, $p<.01$

***statistically significant, $p<.001$

Figures



Note. SMaRT=Stroke Memory Rehabilitation

Figure 1

Structure of the SMaRT program