

# Effects of combined intervention of computer-aided self-regulation learning (CA-SRL) and cognitive training on generalization ability and cognitive function in post-stroke patients with cognitive impairment: a randomized controlled trial

**Youze He**

Fujian University of Traditional Chinese Medicine

**Ting Yang**

Fujian University of Traditional Chinese Medicine

**Yaqi Bao**

Fujian University of Traditional Chinese Medicine

**Tianshen Xiao**

Fujian University of Traditional Chinese Medicine

**Tiecheng Wu**

Fujian University of Traditional Chinese Medicine

**Jingsong Wu** (✉ [jingsongwu01@163.com](mailto:jingsongwu01@163.com))

Fujian University of Traditional Chinese Medicine

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## Research Article

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# Abstract

Emerging study suggests the application of self-regulation learning (SRL) for improving generality abilities in post-stroke patients. It is proposed that SRL could generate an added effect on computer-aided cognitive training (CACT). This study aimed to examine the efficacy of the combined intervention of computer-aided SRL (CA-SRL) training and CACT for generalization ability and cognitive function in patients with post-stroke cognitive impairment (PSCI). A total of 75 patients were randomly assigned into CA-SRL group, demonstration learning (DL) group and traditional learning (TL). Over three weeks, patients in these three groups underwent CA-SRL or DL training combining with cognitive training respectively. After intervention, all outcomes have significantly improved after intervention ( $P < 0.05$ ). CA-SRL group showed better improvements in all trained tasks among groups, especially in "wash the dishes" and "change the bed". The analysis of generalization ability found CA-SRL groups obtained the highest scores among groups in untrained tasks. Mean changes of MoCA in both CA-SRL and TL groups were significantly higher than the DL group ( $P < 0.001$ ,  $P = 0.002$ ) after adjusting education year and Lawton Instrumental ADL Scale. In general, the combination of CA-SRL and CACT is effective for PSCI patient and it has a better effect in promoting the skills generalization from cognitive gains than traditional training.

## Introduction

Post-stroke cognitive impairment (PSCI) is a commonly seen dysfunction in patients with stroke<sup>1</sup> It is reported that 76.3% of sub-acute post-stroke patients and 67.3% of chronic post-stroke patients have cognitive impairments in at least one cognitive domain, such as attention, memory, executive function and perceptual disorders.<sup>2,3</sup> Moreover, the impairments in cognitive functions have negatively impacted activities of daily living (ADL) and reduced their abilities to reacquire motor and functional skills, which led to the decrease of quality of life.<sup>4-6</sup>

Cognitive training is one of the most widely used rehabilitation strategies for PSCI patients, and its' effectiveness and safety for recovering cognitive functions has been evidenced.<sup>7,8</sup> However, some previous studies revealed that the improved cognitive functions did not generalize into ADL.<sup>9-11</sup> The possible reason for this phenomenon may be the training scenes and contents unrelated to normal activities of daily life.<sup>12</sup> Moreover, it might be possibly correlated with the injury of brain regions that caused the impairment of learning and relearning abilities to limit the generalization from cognitive functions to ADL.<sup>13</sup>

Self-regulation learning (SRL) training, which includes three steps (decomposition step, self-calibration and mental imagery), is a widely-used method to improve generalization abilities and daily tasks performance in post-stroke patients.<sup>14-16</sup> It was proved that SRL training encourages individuals to adapt task strategies to the tasking environment,<sup>17</sup> but there was little transfer effect of SRL training on cognitive function, such as memory.<sup>18</sup> Moreover, the manual training of SRL have relatively high requirements, such as reliance on the knowledge and experience of therapists, limitations of training sites and training tools, cost of time of therapists to prepare training contents.

With the development of computer-aided technology in recent years, it provides a new solution for the rehabilitation of post-stroke patients. Compared with traditional one-on-one training, computer-aided training can provide various training contents in different forms based on cost-effectiveness.<sup>19</sup> Many systematic review and meta-analysis studies have evidenced the practical efficacy of computer-aided cognitive training (CACT) in improving cognitive functions of post-stroke patients.<sup>20,21</sup> If we combine the cognitive training with SRL training to form a new computer-aided strategy for the rehabilitation of post-stroke patients, it may help to improve patients' cognitive functions and promote the generalization of their skills.

This study designed the first Chinese Computer-aided SRL (CA-SRL) training program and combined the new program with CACT to form a comprehensive intervention scheme for PSCI patients. There we conducted a randomized controlled trial to answer the following questions: 1) Whether this combined intervention of CA-SRL and CACT is effective in improving the generalization ability and cognitive functions for PSCI patients; 2) Does CA-SRL training works better in generalizing the cognitive gains into ADL when compared with traditional manual training.

## Methods

### Study design

This study was a single-blinded randomized controlled trial for post-stroke patients with cognitive impairment. The protocol of this trial had been approved by the Ethics Committee of the Rehabilitation Hospital Affiliated to Fujian University of Traditional Chinese Medicine (Approved number: 2017YJS-004-01) in 2017. This study was performed in accordance with the guidelines of Declaration of Helsinki and the informed consent was obtained from all participants and/or their legal guardians before screening. The details of this trial were also registered in China Clinical Trial Registry (Registration number: ChiCTR-INR-17013042; Registration date: 19/10/2017).

### Participants

Eligible participants were recruited in the Rehabilitation Hospital Affiliated to Fujian University of Traditional Chinese Medicine. All participants included should meet the following inclusion criteria: (1) meet diagnostic criteria for stroke according to the principles of 2010 Chinese guidelines for the management of hypertension<sup>22</sup> and confirmed by computed tomography or magnetic resonance imaging; (2) first-ever stroke and within one year post-stroke; (3) aged between 45 and 80 years old; (4) education level was primary school or above; (5) cognitive impairment was identified by the Fuzhou version of the Montreal cognitive assessment<sup>23</sup> with the scores between 10 and 26 points; (6) cognitive impairment occurred after stroke and excluded other causes; (7) participants included should be conscious and stable in vital signs; (8) participants could understand the operation of computer-aided training; (9) the participants themselves or their legal guardian had informed consent.

Exclusion criteria: (1) had severe visual or hearing impairment, mental disorders for their potential impacts on cognitive examination; (2) history of mental retardation and dementia before the occurrence of stroke; (3) had severe unilateral spatial neglect; (4) had depressive symptom (Hamilton Depression Scale score >7)<sup>24</sup>; (5) had severe heart disease, liver failure, renal failure, malignant tumor, gastrointestinal bleeding or other diseases; (6) participants who were included in other clinical trials that would affect the assessments of outcomes in our study.

### Procedures

After obtaining participants' written informed consent form and screening for inclusion and exclusion, all patients included were randomly assigned to computer-aided self-regulation learning group, demonstration learning group or traditional learning group in a ratio of 1:1:1. Randomization was conducted by an independent researcher who did not participate in intervention and outcomes assessments of our study. The randomized sequence was generated using simple randomization in SPSS 24.0 statistics analysis software. After completing baseline assessments, the independent researcher informed these patients about the results of their group allocation via telephone. Due to the full explanation of interventional contents to eligible participants in the informed consent form, it is impossible to blind these included patients. Outcome assessors, data entry personnel and statistical analysts were blinded to avoid potential bias. Meanwhile, to ensure the quality of training, all interventions were administered by occupational therapists who had over three years of working experience in post-stroke rehabilitation and did not participate in

patients' enrollments and outcome assessments. The schedule and contents of interventions in this study were shown in Figure 1.

## **Intervention**

### **Computer-aided self-regulation learning (CA-SRL) group**

Patients in the CA-SRL group received CA-SRL training, CACT and basic activities of daily living (ADL) training. In the first week, basic ADL training were conducted for an hour per time with five sessions, which was the basis of SRL training. Through the first-week training, patients could be able to understand the contents involved in SRL training. This way was trying to avoid the potential effect of incomprehension of training contents that limit the efficacy of CA-SRL training. The contents of CA-SRL (including ten tasks that related to ADL) were performed for an hour per session five times per week in the next two weeks. In addition, the CACT training was carried out throughout the three weeks for 30 minutes each session.

### **Demonstration learning (DL) group**

Training tasks in the DL group were also divided into three parts. In the first week, patients received the same basic ADL training with the same training dose. Unlike the CA-SRL group, these ten training tasks were conducted in a demonstration learning way with the same training schedule. Moreover, CACT was also conducted throughout these three weeks for 30 minutes each session.

### **Traditional learning (TL) group**

Similar to the training schedule in the DL group, patients in the TL group received traditional cognitive training with the same training dose rather than CACT. Besides, other training parts (basic ADL training and DL training) were the same as the schedule of the DL group.

## **Interventional Contents**

### **Computer-aided self-regulation learning training**

There are three parts to the learning tasks of CA-SRL: step decomposition, self-calibration and mental imagery.<sup>25</sup> As our design, CA-SRL recorded the process of patients' task learning by cameras. Then the videos were displayed to make them self-reflected on their task performance.<sup>14,26</sup> Moreover, there are ten daily tasks in CA-SRL training,<sup>27</sup> including fold the laundry, see the doctor, make the bed, tidy the table after a meal, fry vegetables with meat, prepare fruit, sweep the floor, wash the dishes, change the beds and intake medication. In the CA-SRL training, therapists have guided patients for the pre-programmed instructions to understand the task's actions, self-reflection and think about the solution, and finally complete the tasks. In the second week, patients were trained in five daily tasks: fold the laundry, see the doctor, make the bed, tidy the table after a meal, fry vegetables with meat. Then in the third week, patients were trained with the other five tasks: wash the dishes, change the beds, prepare fruit, take medication and sweep the floor.

### **Computer-aided cognitive training**

In this study, the contents of CACT were developed by the cognitive rehabilitation research team of Hong Kong Polytechnic University, Hong Kong University and Fujian University of Traditional Chinese Medicine. There were two parts of CACT named basic cognitive module and cognitive application module. The primary cognitive module contained simple reaction time, visual perception, visual attention, visual choice, sustained attention, working memory,

maze, one mind for two purposes, psychological rotation and auditory choice, which aimed to improve specific cognitive function. Besides, the cognitive application module was composed by four parts: ability of computer application training, memory application training, logic ability training and attention application training. These training items are purposed to integrate the cognitive training contents into the living scenes for improving comprehensive cognitive abilities. As designed, professional therapists were appointed to arrange the training contents according to the actual situation of patients.

### **Demonstration learning training**

There were three steps in DL training, consisted of step decomposition, error-less calibration and repetitive training.<sup>28</sup> Manipulation of tasks (main steps, needed tools and sequence) would be told in details to patients to make a comparison for error-less calibration. Before completion of all tasks, therapists would give patients enough demonstrations and correct their inaccurate actions timely. Then, patients should practice this item repeatedly until completion of the task independently.<sup>29</sup> All training contents were consistent with CA-SRL contents.

### **Basic ADL training**

The professional therapists would conduct the basic activities of daily living training based on the Code of Practice for Common Rehabilitation Therapy Techniques (2012 edition). The training contents included clothing, decoration, eating, bed and chair transfer, going to the toilet, bathing, and going up and downstairs. According to the conditions and performances of patients, occupational therapists would evaluate patients' activities and then prepare the corresponding tools such as clothes for dressing and spoons for eating. Through observations and evaluations, the missing components of their actions would be told to patients, and then these actions should be trained repeatedly.

### **Traditional cognitive training**

Based on the Code of Practice for Common Rehabilitation Therapy Techniques (2012 edition), the contents of the traditional cognitive training were composed of attention, memory, calculation and discrimination training. Therapists were appointed to conduct traditional cognitive training for the patients according to their results of cognitive assessment.

### **Outcome assessment**

The primary outcomes were Daily Living Task Assessment<sup>27</sup> and Montreal Cognitive Assessment (MoCA), Fuzhou version.<sup>23</sup> Daily Living Task Assessment was applied to assess the abilities to relearn and generalization (Reliability: 0.89-0.98, kappa value: 0.54-0.72).<sup>27</sup> In the relearning test, the previous five trained tasks (wash the dishes, change the beds, prepare fruit, take medication and sweep the floor) were used. Another five untrained daily tasks (including cook and steam fish, put clothes on a hanger, use the telephone, go to the canteen and clean the bathroom) were conducted to assess the generalization ability. These subtests were both scoring from 1 (total assistance, unable to perform 25% or more of task) to 7 (complete independence, perform a task in a timely and safe manner).<sup>27</sup> Higher score means more extraordinary ability in independence. MoCA was used to assess the global cognitive function.

The secondary outcomes were Modified Barthel Index (MBI)<sup>30</sup>, Lawton Instrumental Activity of Daily Living Scale (IADLs)<sup>31,32</sup> and Simplified Fugl-Meyer Assessment (FMA)<sup>33</sup>. MBI and IADLs were applied to evaluate patients' ability of basic ADL and instrumental ADL, respectively. FMA was used to assess the motor functions of post-stroke patients.

### **Statistical analysis**

Except for evaluating the generalization ability after intervention, other outcomes were all assessed at baseline and post-intervention after three weeks. All data included in the analysis were calculated by IBM SPSS Version 24.0 software. The categorical variables were expressed in numbers by several different categories using Chi-square ( $\chi^2$ ) tests. The continuous variables were presented in the form of Mean $\pm$ Standard Deviation (SD) and calculated according to their types of distribution. If these continuous variables were in a normal distribution, a one-way analysis of covariance (ANCOVA) would be applied to compare the differences between these three groups. Otherwise, Kruskal-Wallis rank-sum test would be applied.

Moreover, to clarify the efficacy of the intervention, differences between baseline and after intervention would be compared by paired t-test or Wilcoxon signed-rank test. Due to the significant difference of education and scores of IADLs across three groups at baseline, these factors were added as covariates in ANCOVA for multiple comparisons. *P* values below 0.05 (two-tailed) were considered statistically significant.

## Results

All PSCI patients were recruited from the department of neurological rehabilitation, the Rehabilitation Hospital Affiliated to Fujian University of Traditional Chinese Medicine. A total of 501 patients were screened, but 321 of them did not meet the inclusion criteria, and 105 of them met the exclusion criteria. Therefore, 75 PSCI patients were finally included in this study. (See Fig. 1)

During the intervention, two patients discontinued intervention and discharged from the hospital halfway because of economic reasons. Another patient discontinued because of dissatisfaction with these tests. A total of 72 patients (CA-SRL group: *n* = 23; DL group: *n* = 24; TL group: *n* = 25) completed all interventions, and there was no great harm to participants or severe adverse events happened during this trial.

Table 1  
Demographic and baseline characteristics of three groups [mean (SD)/M (P25, P75)]

Variables	CA-SRL group (n = 23)	DL group (n = 24)	TL group (n = 25)	F/Z/ $\chi^2$	P-value
Age, year <sup>b</sup>	57(51, 65)	57(48.25, 64)	58(51.5, 66)	0.592	0.744
Gender (men/women, n) <sup>c</sup>	19/6	18/7	19/6	0.141	0.932
Education, year <sup>b</sup>	9(9, 12)	9(9, 12)	7(5, 11)	10.923	<b>0.004</b>
Months after stroke <sup>b</sup>	2(1, 7)	2(1, 6.5)	1(1, 3)	3.960	0.138
Location of stroke (Left/Right, n) <sup>c</sup>	19/6	17/8	17/8	0.773	0.537
Types (ischemic/hemorrhagic, n) <sup>c</sup>	15/10	18/7	17/8	0.657	0.551
MoCA <sup>a</sup>	19.22 (4.22)	19.17(4.57)	16.60(6.04)	2.167	0.122
MBI <sup>a</sup>	61.39(19.71)	59.88(17.24)	51.04(27.08)	1.594	0.211
IADLs <sup>b</sup>	6(5, 11)	8(5.25, 9)	4(4, 7)	8.538	<b>0.014</b>
<b>FMA</b>					
Upper limbs <sup>b</sup>	14(10, 28)	19(7, 37.5)	25(6, 49)	0.547	0.761
Lower limbs <sup>b</sup>	22(18, 27)	18.5(16, 24.5)	18(10, 28)	2.365	0.307
<b>Five daily living tasks</b>					
Wash the dishes <sup>b</sup>	4(3, 5)	4(4,5)	3(4,4.5)	2.114	0.348
Change the beds <sup>b</sup>	3(2, 3)	3(3, 3)	3(2, 3)	0.249	0.883
Sweep the floor <sup>b</sup>	4(3, 5)	4(3, 5)	4(3, 4)	0.792	0.673
Take medication <sup>b</sup>	3(3, 4)	3.5(3, 4)	3(3, 4)	0.602	0.740
Prepare fruit <sup>b</sup>	3(3, 4)	4(3, 4)	3(2, 4)	3.499	0.174
Notes: a Calculated by ANOVA; b Calculated by Kruskal-Wallis rank sum test; c Calculated by Chi-square test.					

The demographic and baseline characteristics of these three groups were presented in Table 1. Except for education and IADLs, there was no significant difference in age, sex, duration of stroke, location of stroke, type of stroke and five daily living tasks at baseline evaluation.

Our results showed that all outcomes have significantly improved after intervention ( $P < 0.05$ ). (See Table 2) And there were statistically significant differences in scores of MoCA, IADLs and five tasks of relearning ability ( $P < 0.001$ ) among these groups. Further multiple comparison presented that improvement of MoCA scores in both CA-SRL and TL group were significantly higher than those in DL group ( $P < 0.001$ ,  $P = 0.002$ ). In comparing IADLs, improvements in the CA-SRL group were better than the TL group ( $P = 0.033$ ). The results of relearning ability showed that improvements of all five trained tasks in the CA-SRL group were significantly better than those of the DL group ( $P < 0.05$ ). In addition, the

CA-SRL group also showed better improvements in “wash the dishes” ( $P= 0.046$ ) and “change the bed” ( $P= 0.016$ ) when compared with those in the TL group. In comparison between the DL and TL group of these trained tasks, only one task (take medication) was found that improvement in the TL group was more significant than the DL group ( $P< 0.001$ ). However, there were no significant differences in MBI and FMA found. (See Table 3)

Table 2  
Comparison of outcomes before and after intervention (mean  $\pm$  SD)

Variables	CA-SRL group (n = 23)		DL group (n = 24)		TL group (n = 25)	
	Pre	Post	Pre	Post	Pre	Post
<b>MoCA</b>	19.36 $\pm$ 4.32	23.22 $\pm$ 3.69#	19.08 $\pm$ 4.49	20.42 $\pm$ 4.76#	16.60 $\pm$ 6.04	19.92 $\pm$ 5.78#
<b>MBI</b>	60.24 $\pm$ 20.26	79.52 $\pm$ 13.68#	58.28 $\pm$ 18.66	75.63 $\pm$ 14.61#	51.04 $\pm$ 27.08	67.64 $\pm$ 24.51#
<b>IADLs</b>	7.96 $\pm$ 3.05	11.65 $\pm$ 3.92#	7.68 $\pm$ 2.93	10.13 $\pm$ 2.97#	5.44 $\pm$ 3.71	6.96 $\pm$ 5.73#
<b>FMA</b>						
Upper limbs	21.80 $\pm$ 16.62	27.00 $\pm$ 14.32#	22.12 $\pm$ 14.73	26.38 $\pm$ 18.54#	27.36 $\pm$ 21.08	34.72 $\pm$ 21.81#
Lower limbs	21.60 $\pm$ 6.62	24.04 $\pm$ 5.2#	19.28 $\pm$ 6.07	20.75 $\pm$ 6.71#	18.12 $\pm$ 9.66	20.80 $\pm$ 8.54#
<b>Relearning ability</b>						
Wash the dishes	4.12 $\pm$ 0.88	6.04 $\pm$ 0.98#	4.16 $\pm$ 0.75	5.33 $\pm$ 0.92#	3.80 $\pm$ 0.91	5.00 $\pm$ 1.00#
Change the beds	2.88 $\pm$ 0.73	4.52 $\pm$ 0.79#	2.92 $\pm$ 0.64	3.96 $\pm$ 0.69#	2.84 $\pm$ 0.80	4.00 $\pm$ 0.65#
Sweep the floor	3.96 $\pm$ 0.89	5.65 $\pm$ 1.19#	3.88 $\pm$ 1.05	4.79 $\pm$ 1.06#	3.72 $\pm$ 0.94	5.12 $\pm$ 0.97#
Take medication	3.48 $\pm$ 0.59	4.91 $\pm$ 0.73#	3.68 $\pm$ 0.85	4.46 $\pm$ 0.83#	3.60 $\pm$ 0.76	5.48 $\pm$ 1.33#
Prepare fruit	3.48 $\pm$ 1.05	5.04 $\pm$ 1.02#	3.76 $\pm$ 0.66	4.42 $\pm$ 0.83#	3.28 $\pm$ 1.10	4.48 $\pm$ 0.92#
#: Comparison between Pre- and Post-intervention; $P$ -value $< 0.05$ . These results in this table showed the significant effect of these interventions (CA-SRL, DL and TL) in improving cognitive function, quality of life, activities of daily living, motor functions, and relearning abilities.						

Table 3  
Comparison of mean changes of outcomes after intervention [mean (SD)]

Variables	CA-SRL group (n = 23)	DL group (n = 24)	TL group (n = 25)	F value	Differences P-value	CA-SRL vs DL P value	DL vs TL P value	CA-SRL vs TL P value
MoCA	4.00(2.09)	1.25(1.26)	3.32(1.70)	19.706	<b>0.001</b>	<b>0.001</b>	<b>0.002</b>	0.100
MBI	18.13(12.64)	15.75(10.91)	16.60(15.41)	0.507	0.605			
IADLs	3.84(0.70)	2.67(0.70)	1.15(0.71)	3.414	<b>0.017</b>	0.685	0.452	<b>0.033</b>
<b>FMA</b>								
Upper limbs	7.12(2.06)	3.31(2.06)	7.66(2.11)	1.273	0.287			
Lower limbs	2.26(4.04)	1.42(2.52)	2.68(5.92)	0.221	0.802			
<b>Relearning ability</b>								
Wash the dishes	1.89(0.19)	1.18(0.19)	1.22 (0.20)	4.387	<b>0.016</b>	<b>0.029</b>	1	<b>0.046</b>
Change the bed	1.65(0.14)	1.04(0.14)	1.07(0.14)	6.453	<b>0.003</b>	<b>0.006</b>	1	<b>0.016</b>
Sweep the floor	1.70(1.06)	0.88(0.74)	1.40(1.00)	3.902	<b>0.025</b>	<b>0.021</b>	0.423	0.818
Take medication	1.43(0.84)	0.75(0.53)	1.88(1.20)	11.384	<b>0.001</b>	<b>0.027</b>	<b>0.001</b>	0.077
Prepare fruit	1.61 (0.94)	0.63 (0.58)	1.20(0.96)	8.451	<b>0.001</b>	<b>0.001</b>	0.271	0.117
<b>Note:</b> The table showed the comparison results of mean changes of MoCA, MBI, IADLs, FMA and relearning abilities in Analysis of Covariance after Adjusting education year and scores of IADLs.								

In the assessment of generalization ability, there were significant differences among three groups in these five untrained tasks ( $P < 0.05$ ). The comparison results showed scores of tasks "go to the canteen", "put clothes on hanger" and "use the telephone" in the CA-SRL group were significantly better than those of the DL group ( $P = 0.001$ ,  $P = 0.005$ ,  $P = 0.007$ ). Moreover, the CA-SRL group also showed significantly higher scores than the TL group in tasks "go to the canteen" ( $P = 0.002$ ), "clean the bathroom" ( $P < 0.001$ ) and "cook and steam fish" ( $P = 0.001$ ). (See Table 4)

Table 4  
Comparison of generalization ability assessment between groups [mean (SD)]

Variables	CA-SRL group (n = 23)	DL group (n = 24)	TL group (n = 25)	F value	Differences P-value	CA-SRL vs DL P-value	DL vs TL P-value	CA-SRL vs TL P-value
Go to the canteen	4.87(0.82)	3.96(0.81)	3.76(0.83)	9.779	<b>0.001</b>	<b>0.001</b>	1	<b>0.002</b>
Put clothes on hanger	5.26(0.86)	4.50(0.78)	4.44 (1.04)	5.446	<b>0.006</b>	<b>0.005</b>	0.747	0.190
Clean the bathroom	4.74(0.69)	4.05(0.61)	3.56(0.82)	11.442	<b>0.001</b>	0.078	0.064	<b>0.001</b>
Cook and steam fish	5.00(0.74)	4.54(0.72)	3.88(0.88)	7.531	<b>0.001</b>	0.156	0.152	<b>0.001</b>
Use the telephone	5.65(1.23)	4.75(0.85)	4.72(0.94)	5.513	<b>0.006</b>	<b>0.007</b>	1	0.071

**Note:** The group differences were compared after adjusting education year and scores of IADLs.

## Discussion

To our knowledge, this is the first study that observing the combined efficacy of CA-SRL and CACT for PSCI patients for their generalization abilities and cognitive function. Our results revealed that the combined strategy created significant improvements in generalization abilities and cognitive function compared with the baseline assessment and those in DL or TL training. We also found that patients in the CA-SRL group got higher scores in untrained five tasks after CA-SRL training, which illustrated the effect of CA-SRL in promoting the skill generalization from the cognitive gains.

We found that these three rehabilitation strategies significantly improved the global cognitive function, ADL, motor functions and relearning ability after the 3-week intervention compared with the baseline assessments. Moreover, the between-group analysis indicated that the combined strategy (CA-SRL + CACT) had a better effect in enhancing the performances in most of the trained tasks and half of the untrained tasks compared to demonstration learning training. It might be the benefits of CA-SRL training. Because SRL strategy provided opportunities to make errors and learn to recognize and self-correct these errors,<sup>34</sup> while demonstration learning (also named errorless learning) focused on motion imitations and required a high level of support from the therapist to prevent errors and promote the errorless performance in the daily situation.<sup>35</sup> Thus, patients in the CA-SRL group obtained more opportunities to discover their faults in tasking performance and tried to find the right solutions to solve and correct the faults. At the same time, it is difficult for patients who experienced demonstration learning in the DL or TL group to form self-awareness of self-correction.<sup>36</sup> And this result was consistent with other observations in the previous study. Research demonstrated that significantly fewer errors and greater behavioral competency were found after SRL training than errorless training in patients with traumatic brain injury (TBI), which proved the more effective efficacy in enhancing skills generalization abilities on tasks related to training.<sup>37</sup> Hence, it provided evidence to believe the practical efficacy of the combined strategy (CA-SRL + CACT) in improving generalization abilities in transferring skills to untrained tasks.

In comparing the generalization abilities of PSCI patients between the DL and TL groups, there was no significant difference in scores of these five untrained tasks. This may be the result of demonstration learning which lacked

thinking and reflection of tasking execution during the training process.<sup>12</sup> But higher scores of five untrained tasks were found in the CA-SRL group, which provided further evidence for the efficacy of the combined strategy (CA-SRL + CACT) in promoting skills generalization. In other words, it revealed the better effect of CA-SRL in generalizing the cognitive gains into tasking performances than manual training.

In the analysis of relearning ability, we also found a better improvement of "Take the medication" in the TL group (mean changes = 1.88) rather than the CA-SRL group (mean changes = 1.43) or DL group (mean changes = 0.75). This task is in a simple sequence and requires less comparatively for upper extremity motor function than other tasks. Therefore, the improvement in this task may be associated with the changes in motor functions of the upper limb. Although there was no significant difference, the mean changes of upper limb FMA score in the TL group were higher than those in CA-SRL and DL groups. It might provide a possible explanation for this result. In addition, the therapists used some additional tools in traditional cognitive training, such as pencil, paper and cards, to guide training operations. Some traditional training tasks such as writing, using fingers to recognize cards, and folding paper would improve upper limb motor functions. In another aspect, a previous study declared that the efficacy of CACT in improving motor function was uncertain compared with traditional cognitive training.<sup>38</sup> Therefore, it might be a reasonable explanation for the significant "take medication" task in the TL group.

Additionally, when comparing changes of global cognitive function among these groups, our results presented that both the interventions in CA-SRL and TL group had a more significant effect on global cognitive function than the DL group, but there was no significant difference between them. Although CACT could significantly improve the cognitive function of patients with cognitive impairment after brain injury, its effect was not significantly different from or even lower than that of traditional cognitive training.<sup>11,39-41</sup> It was declared that cognitive intervention mainly concentrated in one cognitive domain might be more effective than multiple domains for stroke patients.<sup>11</sup> In our study, the contents of CACT involved multiple cognitive domains. In contrast, traditional cognitive training was guided by professional therapists to ensure the motivation of PSCI patients to complete complex cognitive tasks. This would make patients obtained more benefits and improvements of cognitive function in some targeted cognitive domains.<sup>42</sup> Moreover, although there was no significant difference between the CA-SRL and TL group, the mean changes of MoCA score in the CA-SRL group was the highest among these groups. The more significant effect may be the benefits from CA-SRL training which motivated patients to use the problem-solving method with active self-reflection and repetitive practice to complete their tasks to activate more changes of cognitive functions.<sup>25</sup> Therefore, it could be believed that the combined strategy (CA-SRL + CACT) was also influential in improving global cognitive function.

There are several limitations to this study. Firstly, the content to whether patients were actively engaged in each training session was impossible to control in this study. Suppose patients were trained with low enthusiasm and effort. In that case, it may increase the between-group variability of results and then might lower the significance of the training effect of CA-SRL. Secondly, we had not considered the patients' personal experience with similar training contents, which may also make a difference to our results to some extent. Future studies could pay more attention to these points to reduce the impacts of these mixed factors.

## Conclusion

The combination strategy of CA-SRL and CACT is an effective tool in improving the generalization abilities, cognitive function and motor functions of PSCI patients. The efficacy of combining CA-SRL with CACT on skills generalization improvements is better than traditional strategies of training. However, its effect on global cognitive function is similar to traditional training. Given the advantages of computer-aided technology, including low cost, high availability, and

not limited by the treatment environment, the combined strategy is worth applying in the rehabilitated interventions of PSCI patients.

## Declarations

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### Author contributions

WJS secured funding and conceived the original idea and designed the study. BYQ and XTS prepared the ethical review application and were responsible for patients' recruitment and coordination. HYZ, YT and WTC contributed to the data collection. HYZ wrote the manuscript, and all authors contributed to further development of this manuscript. All authors read and approved the final manuscript.

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### Competing interests

All authors have declared no conflicts of interest.

Correspondence and requests for materials should be addressed to WJS or HYZ.

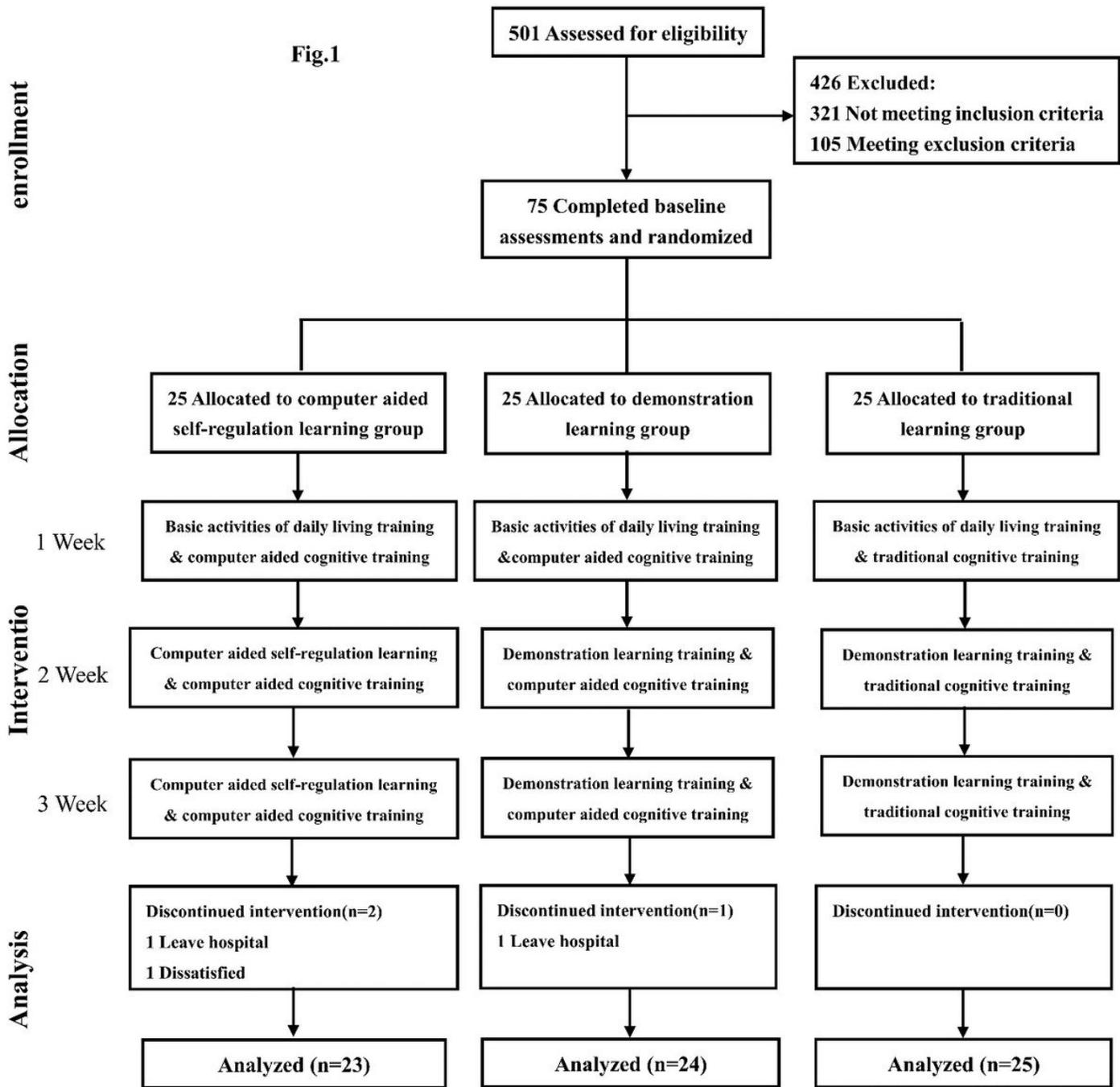
## References

1. Sun, J. H., Tan, L. & Yu, J. T. Post-stroke cognitive impairment: epidemiology, mechanisms and management. *Ann Transl Med* 2 80(2014).
2. Middleton, L. E. *et al.* Frequency of domain-specific cognitive impairment in sub-acute and chronic stroke. *NEUROREHABILITATION* 34 305(2014).
3. Jaillard, A., Naegele, B., Trabucco-Miguel, S., LeBas, J. F. & Hommel, M. Hidden dysfunctioning in subacute stroke. *STROKE* 40 2473(2009).
4. Farokhi-Sisakht, F., Farhoudi, M., Sadigh-Eteghad, S., Mahmoudi, J. & Mohaddes, G. Cognitive Rehabilitation Improves Ischemic Stroke-Induced Cognitive Impairment: Role of Growth Factors. *J Stroke Cerebrovasc Dis* 28 104299(2019).
5. Rohde, D. *et al.* The Impact of Cognitive Impairment on Poststroke Outcomes: A 5-Year Follow-Up. *J Geriatr Psychiatry Neurol* 32 275(2019).
6. Cicerone, K. D. *et al.* Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. *Arch Phys Med Rehabil* 92 519(2011).
7. Valenzuela, M. & Sachdev, P. Can cognitive exercise prevent the onset of dementia? Systematic review of randomized clinical trials with longitudinal follow-up. *Am J Geriatr Psychiatry* 17 179(2009).

8. Aminov, A., Rogers, J. M., Middleton, S., Caeyenberghs, K. & Wilson, P. H. What do randomized controlled trials say about virtual rehabilitation in stroke? A systematic literature review and meta-analysis of upper-limb and cognitive outcomes. *J NEUROENG REHABIL* 15 29(2018).
9. Chung, C. S., Pollock, A., Campbell, T., Durward, B. R. & Hagen, S. Cognitive rehabilitation for executive dysfunction in adults with stroke or other adult non-progressive acquired brain damage. *Cochrane Database Syst Rev* 2013 D8391 (2013).
10. Brueggen, K. *et al.* Cognitive Rehabilitation in Alzheimer's Disease: A Controlled Intervention Trial. *J ALZHEIMERS DIS* 57 1315(2017).
11. Wentink, M. M. *et al.* The effects of an 8-week computer-based brain training programme on cognitive functioning, QoL and self-efficacy after stroke. *NEUROPSYCHOL REHABIL* 26 847(2016).
12. Li, K., Alonso, J., Chadha, N. & Pulido, J. Does Generalization Occur Following Computer-Based Cognitive Retraining?-An Exploratory Study. *Occup Ther Health Care* 29 283(2015).
13. Toglia, J. & Kirk, U. Understanding awareness deficits following brain injury. *NEUROREHABILITATION* 15 57(2000).
14. Liu, K. P., Chan, C. C., Lee, T. M., Li, L. S. & Hui-Chan, C. W. Self-regulatory learning and generalization for people with brain injury. *Brain Inj* 16 817(2002).
15. Liu, K. P. & Chan, C. C. Pilot randomized controlled trial of self-regulation in promoting function in acute poststroke patients. *Arch Phys Med Rehabil* 95 1262(2014).
16. Liu, K. P. *et al.* A randomized controlled trial of self-regulated modified constraint-induced movement therapy in sub-acute stroke patients. *EUR J NEUROL* 23 1351(2016).
17. Hertzog, C. & Dunlosky, J. Metacognition in Later Adulthood: Spared Monitoring Can Benefit Older Adults' Self-regulation. *CURR DIR PSYCHOL SCI* 20 167(2011).
18. Dunlosky, J., Kubat-Silman, A. K. & Hertzog, C. Training monitoring skills improves older adults' self-paced associative learning. *PSYCHOL AGING* 18 340(2003).
19. McCrone, P. *et al.* Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial. *Br J Psychiatry* 185 55(2004).
20. Ye, M., Zhao, B., Liu, Z., Weng, Y. & Zhou, L. Effectiveness of computer-based training on post-stroke cognitive rehabilitation: A systematic review and meta-analysis. *NEUROPSYCHOL REHABIL* 1(2020).
21. Cha, Y. J. & Kim, H. Effect of computer-based cognitive rehabilitation (CBCR) for people with stroke: a systematic review and meta-analysis. *NEUROREHABILITATION* 32 359(2013).
22. Liu, L. 2010 Chinese guidelines for management of hypertension. *Chin J Hypertens* 19 701(2011).
23. Fang, Y. *et al.* Patient and Family Member Factors Influencing Outcomes of Poststroke Inpatient Rehabilitation. *Arch Phys Med Rehabil* 98 249(2017).
24. HAMILTON, M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*, **23**, 56 (1960).
25. Liu, K. P. & Chan, C. C. Pilot randomized controlled trial of self-regulation in promoting function in acute poststroke patients. *Arch Phys Med Rehabil* 95 1262(2014).
26. Leung, D. P. & Liu, K. P. Review of self-awareness and its clinical application in stroke rehabilitation. *INT J REHABIL RES* 34 187(2011).
27. Liu, K. P. *et al.* A randomized controlled trial of mental imagery augment generalization of learning in acute poststroke patients. *STROKE* 40 2222(2009).
28. Ownsworth, T. *et al.* Comparison of error-based and errorless learning for people with severe traumatic brain injury: study protocol for a randomized control trial. *TRIALS* 14 369(2013).

29. Roberts, J. L. *et al.* The benefits of errorless learning for people with amnesic mild cognitive impairment. *NEUROPSYCHOL REHABIL* 28 984(2018).
30. Leung, S. O., Chan, C. C. & Shah, S. Development of a Chinese version of the Modified Barthel Index–validity and reliability. *CLIN REHABIL* 21 912(2007).
31. Lawton, M. P. & Brody, E. M. Assessment of older people: self-maintaining and instrumental activities of daily living. *GERONTOLOGIST* 9 179(1969).
32. Hassani, M. A., Soltanmohamadi, Y., Akbarfahimi, M. & Taghizadeh, G. Validity and reliability of the persian version of lawton instrumental activities of daily living scale in patients with dementia. *Med J Islam Repub Iran* 28 25(2014).
33. Bowden, M. G., Clark, D. J. & Kautz, S. A. Evaluation of abnormal synergy patterns poststroke: relationship of the Fugl-Meyer Assessment to hemiparetic locomotion. *Neurorehabil Neural Repair* 24 328(2010).
34. Toglia, J. P. in *Cognition, Occupation, and Participation Across the Life Span: Neuroscience, Neurorehabilitation, and Models of Intervention in Occupational Therapy*. 3rd edition.(AOTA Press, 2011), pp. 161.
35. Clare, L. & Jones, R. S. Errorless learning in the rehabilitation of memory impairment: a critical review. *NEUROPSYCHOL REV* 18 1(2008).
36. Gandomkar, R. & Sandars, J. Clearing the confusion about self-directed learning and self-regulated learning. *MED TEACH* 40 862(2018).
37. Ownsworth, T. *et al.* Do People With Severe Traumatic Brain Injury Benefit From Making Errors? A Randomized Controlled Trial of Error-Based and Errorless Learning. *Neurorehabil Neural Repair* 31 1072(2017).
38. Faria, A. L., Andrade, A., Soares, L. & I, B. S. Benefits of virtual reality based cognitive rehabilitation through simulated activities of daily living: a randomized controlled trial with stroke patients. *J NEUROENG REHABIL* 13 96(2016).
39. Yoo, C., Yong, M. H., Chung, J. & Yang, Y. Effect of computerized cognitive rehabilitation program on cognitive function and activities of living in stroke patients. *J Phys Ther Sci* 27 2487(2015).
40. Spikman, J. M., Boelen, D. H., Lamberts, K. F., Brouwer, W. H. & Fasotti, L. Effects of a multifaceted treatment program for executive dysfunction after acquired brain injury on indications of executive functioning in daily life. *J Int Neuropsychol Soc*, **16**, 118 (2010).
41. Akerlund, E., Esbjörnsson, E., Sunnerhagen, K. S. & Björkdahl, A. Can computerized working memory training improve impaired working memory, cognition and psychological health? *Brain Inj* 27 1649(2013).
42. Lynch, B. Historical review of computer-assisted cognitive retraining. *J Head Trauma Rehabil* 17 446(2002).

## Figures



**Figure 1**

Flowchart of this study showing the procedure of allocation, intervention, and analysis.