Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Vascular Cognitive Impairment Evidence Tables

7th Edition, Update 2024

Cognitive Rehabilitation

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Vascular Cognitive Impairment Writing Group and in collaboration with the
Canadian Stroke Consortium CanStroke Recovery Clinical Trials Platform.

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Published Guidelines

Guideline	Recommendations
General Vascular Cognitive Impairment Guidelines	
Guideline Adaptation Committee. Clinical Practice Guidelines and Principles of Care for People with Dementia. Sydney. Guideline Adaptation Committee; 2016. **https://cdpc.sydney.edu.au/wp-content/uploads/2019/06/CDPC-Dementia-Guidelines_WEB.pdf**	109 recommendations addressing diagnosis, assessment, neuroimaging, organization of services, treatment and support for carers. Most recommendation are practice points or consensus based recommendations. Of the evidence-based recommendations, the quality was assessed as being low or very low (n=22) and moderate (n=7).
Stroke-specific guidelines	
Quinn TJ, Richard E, Teuschl Y et al. **European Stroke Organisation and European Academy Neurology joint guidelines on post-stroke cognitive impairment.** ***Eur J Neurol*. 2021, Vol. 6(3) I–XXXVIII**	PICO question 15: In people with post-stroke cognitive impairments, does cognitive rehabilitation (cognitive skill training or compensation strategies), compared to no rehabilitation, delay cognitive decline or progression to dementia, improve behavioural and psychological symptoms, improve performance in ADL or decrease caregiver burden? Recommendation Due to a lack of methodologically robust trials, for most cognitive rehabilitation interventions, there is continued uncertainty on the benefits and limitations associated with these interventions for stroke survivors. Quality of evidence: Very low ⨁ Strength of recommendation: no recommendation Expert consensus statement Although many of the available studies did not meet our inclusion criteria for this PICO, there is emerging evidence that cognitive rehabilitation, particularly compensatory strategies in the context of individually relevant functional tasks, may be beneficial for people with PSCIs. Methodologically robust trials to support definitive recommendations for clinical practice are needed.
VA/DoD clinical practice guideline for the management of stroke rehabilitation 2019.	There is insufficient evidence to recommend for or against the use of any specific cognitive rehabilitation methodology or pharmacotherapy to improve cognitive outcomes.
Stroke Foundation. Clinical Guidelines for Stroke Management 2017. Melbourne Australia. (Part 6)	Weak Recommendation For stroke survivors with cognitive impairment, meta-cognitive strategy and/or cognitive training may be provided. Consensus-based recommendation For stroke survivors with attentional impairments or those who appear easily distracted or unable to concentrate, a formal neuropsychological or cognitive assessment should be performed. Weak Recommendation For stroke survivors with attention and concentration deficits, cognitive rehabilitation may be used.

Guideline	Recommendations
	Weak recommendation New For stroke survivors with attention and concentration deficits, exercise training and leisure activities may be provided. Practice statement Consensus-based recommendations New Stroke survivors with identified perceptual difficulties should have a formal perceptual (i.e. neurological and neuropsychological) assessment. Stroke survivors with an identified perceptual impairment and their carer should receive: • verbal and written information about the impairment; • an assessment and adaptation of their environment to reduce potential risk and promote independence; • practical advice/strategies to reduce risk (e.g. trips, falls, limb injury) and promote independence; • intervention to address the perceptual difficulties, ideally within the context of a clinical trial.
Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, Lang CE, MacKay-Lyons M, Ottenbacher KJ, Pugh S, Reeves MJ, Richards LG, Stiers W, Zorowitz RD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. **Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke* 2016;47:e98–e169.**	Enriched environments to increase engagement with cognitive activities are recommended. Class I; LOE A Use of cognitive rehabilitation to improve attention, memory, visual neglect, and executive functioning is reasonable. Class IIa; LOE B Use of cognitive training strategies that consider practice, compensation, and adaptive techniques for increasing independence is reasonable. Class IIa: LOE B Compensatory strategies may be considered to improve memory functions, including the use of internalized strategies (eg, visual imagery, semantic organization, spaced practice) and external memory assistive technology (eg, notebooks, paging systems, computers, other prompting devices). Class IIb; LOE A Some type of specific memory training is reasonable such as promoting global processing in visual-spatial memory and constructing a semantic framework for language-based memory. Class IIb; LOE B Errorless learning techniques may be effective for individuals with severe memory impairments for learning specific skills or knowledge, although there is limited transfer to novel tasks or reduction in overall functional memory problems. Class IIb; LOE B
Intercollegiate Stroke Working Party. National clinical guideline for stroke, *5th* Edition. London: Royal College of Physicians, 2016.	**Cognitive Impairment (general)** People with cognitive problems after stroke should receive appropriate adjustments to their multidisciplinary treatments to enable them to participate, and this should be regularly reviewed. People with continuing cognitive difficulties after stroke should be considered for comprehensive interventions aimed at developing compensatory behaviours and learning adaptive skills.
Gorelick PB, Scuteri A, Black SE, et al. **Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American heart association/America stroke association.**	Only limited evidence exists to support non-pharmacological modalities for management of VCI. • No formal recommendations for therapy are offered. More research with rigorous designs to study the effects of nonpharmacological interventions, including cognitive rehabilitation and acupuncture, is needed.

Guideline	Recommendations
***Stroke* 2011;42:2672-2713.**	

Evidence Tables

Cognitive Rehabilitation for Persons with Dementia or VCI

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Tang et al. 2019 **China** **RCT** ***Cog-VACCINE: Cognitive Training in Patients with Vascular Cognitive Impairment, no Dementia (Cog-VACCINE)***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☒	60 participants were recruited from neurology and geriatric clinics from 3 hospitals, aged >50 years, with complaints of cognitive impairment involving memory or other cognitive domains lasting ≥3 months, who were neither normal nor demented (Clinical Dementia Rating [CDR] ≥0.5 on at least one domain and a global score ≤0.5; with an MMSE score ≥20 or ≥24, depending on education level). In addition, there were MRI criteria. Mean age was 64 years, 66.7% were men.	Participants were randomized to a multi-domain adaptive internet-based training program, including processing speed, attention, long-term memory, working memory, flexibility, calculation, and problem solving (intervention group) or a placebo program with a fixed, primary difficulty level task, 5 x 30 minutes per week, for 7 weeks. Specific training paradigms in the intervention group included a time perception task, visual search task, attention blink, delayed mapping task, attention span task, Go-No go task, Stroop task, task switching, and name-face match task, among others.	**Primary outcomes:** Changes in MoCA scores and time to complete Trail Making Test (TMT) **Secondary outcomes:** Changes in left and right hippocampal volume, change in brain white matter integrity (scale of 0-1) Assessments were conducted at baseline and after intervention Change in MoCA scores were also evaluated at 6 months	Mean baseline MoCA score was 21.9 in the intervention group and 21.2 in the control group. Mean change from baseline to 7 weeks was 3.36 (95% CI 1.47 to 5.24) in the intervention group and -0.085 (95% CI -2.06 to 1.89) in the control group. Mean time to completion on the TMT at baseline was 74.0 seconds in the intervention group and 77.0 seconds in the control group. Mean change from baseline to 7 weeks was -5.96 seconds (95% CI -38.6 to 26.6) in the intervention group and -10.7 seconds (95% CI -45.3 to 23.9) in the control group. Mean changes in left hippocampal volume were -105.7 mm (95% CI -287.6 to 76.2) in the intervention group and -70.3 mm (95% CI (-269.4 to 128.9) in the control group. Mean changes in right hippocampal volume were -0.28 mm (95% CI -185.7 to 185.1) in the intervention group and -103.7 mm (95% CI (-316.4 to 109.0) in the control group. Mean change in brain white matter integrity were -0.008 (95% CI -0.031 to 0.014) in the intervention group and 0.004 (95% CI -0.015 to 0.023) in the control group. Mean change from baseline to 6 months in MoCA score was 2.2 (95% CI 0.26 to 4.192) in the intervention group and 1.4 (95% CI 0.9 to 3.6) in the control group.
Bahar-Fuchs et al. 2019	Using the Cochrane RoB	33 RCTs including persons with mild to moderate	Trials compared a cognitive rehabilitation intervention	**Primary outcome:** Composite score of global	Compared with a control intervention, cognitive training was associated with a

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Australia **Cochrane review**	tool, most rials had a high or unclear risk of bias in ≥1 domain	dementia.	compared with a control intervention or alternative intervention. Of the cognitive training interventions, 26 were classified as multi-domain interventions and 13 as single-domain interventions. 13 trials were classified as augmented interventions as they included additional elements. The control conditions included passive (n=18) and active interventions (n=13). The 15 alternative treatment conditions, included occupational therapy, mindfulness, reminiscence therapy etc. The duration of interventions ranged from 2 to 104 weeks. In 9 trials, the intervention was delivered ≥3 sessions per week.	cognition	significantly greater improvement in the composite measure of global cognition, when assessed immediately after the intervention (SMD=0.42, 95% CI 0.23 to 0.62). Results from 27 trials included. When assessed 3-12 months post intervention, the result remained significant (SMD=0.65, 95% CI 0.11 to 1.2). Results from 8 trials included. Compared with an alternative intervention, cognitive training was not associated with a significantly greater improvement in the composite measure of global cognition, when assessed immediately after the intervention (SMD=0.21, 95% CI -0.23 to 0.64). Results from 7 trials included. When assessed 3-12 months post intervention, the result remained nonsignificant (SMD=1.31, 95% CI -1.03 to 3.65). Results from 2 trials included.

Cognitive Rehabilitation Following Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
General					
O'Donoghue et al. 2022 **Ireland** **Systematic review & meta-**	Using the Cochrane Risk of Bias Tool, 34 trials had a high risk of bias in ≥1	64 RCTs including 4,005 persons with/without cognitive impairment following ischemic or hemorrhagic stroke, in the acute (n=20), subacute (n=12), and chronic (n=18)	Trials compared cognitive rehabilitation strategies to improve cognitive function with a control group (usual care, active control, waitlist, or no treatment).	**Primary outcome:** Change in cognitive outcome measures after treatment (general cognition, memory) **Secondary outcomes:**	Data from 42 trials were available for pooling. *Multiple component intervention vs. standard care* Pooling data from 3 trials, in persons with stroke ≤3 months previously, the mean MoCA score, (indicator of general cognition) was significantly

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
analysis	domain	stages. 14 trials did not provide data on stroke chronicity. Participants were recruited from acute inpatient units (n=24), inpatient rehabilitation units (n=15), outpatient clinics (n=18) and both inpatient and outpatient settings (n=7). Mean age was 62.5 years.	Among the included trials, 21 were multiple component interventions, 16 were cognitive rehabilitation interventions, 11 were physical activity interventions, 6 were non-invasive brain stimulation (NIBS), 5 were occupational-based interventions, and 5 were other interventions (acupuncture, prism adaptation, TENS, music therapy).	Functional status, depression, QoL, balance	higher in the intervention group (MD=1.56, 95% CI, 0.69 to 2.43). Pooling data from 4 trials, measures of memory (including the letter-number sequencing test, and the Digital Span), were improved significantly in the intervention group (SMD=0.49, 95% CI, 0.27 to 0.72). Pooling data from 4 trials, measures of functional status (BI and FIM) memory were improved significantly in the intervention group (SMD= 0.33, 95% CI, 0.05–0.62). *Cognitive Rehabilitation Interventions vs. standard care* Pooling data from an unknown number of trials, there were no significant differences between groups in measures of general cognition, memory, executive function, or QoL. There were no significant differences between groups comparing cognitive rehabilitation interventions vs an active control in any of the outcomes assessed (general cognitive functioning, memory, executive function, or attention, nor was there a difference between groups comparing cognitive rehabilitation interventions vs. wait list control (memory) *Physical activity interventions vs. active control* Physical activity interventions were not associated with significantly greater improvement in executive function, compared with an active control (MD= –1.92, 95% CI –28.68 to 24.84). Berg Balance Scale scores were significantly higher in the intervention group (MD=2.97, 95% CI 0.71–5.23). *NIBS vs. active control* Pooling the results from 3 trials, measures of neglect (line bisection test) were significantly better in the rTMS group (MD=20.79, 95% CI

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					14.53– 27.04). Measures of functional status (mBI and Korean mBI) were also significantly higher in the rTMS group (MD=14.02, 95% CI, 8.41–19.62). *Occupational-based interventions vs. standard care* Pooling data from an unknown number of trials, there were no significant differences between groups in measures of general cognition (MD= 0.45, 95% CI −1.33 to 2.23) or functional status (SMD=0.31, 95% CI −0.03 to 0.65). Pooling the results from 2 trials, prism therapy did not improve neglect compared with an active control (SMD=0.40, 95% CI −0.06 to 0.85).
Saa et al. 2021 **Australia** **Meta-analysis & meta-regression**	Using the *Study Quality Assessment Using the Tools of the National Institutes of Health and National Heart, Lung and Blood Institute*, 47 studies were rated as good quality, 50 were of fair quality and 25 were of poor quality.	43 intervention trials (RCT and non RCT) and 79 observation studies (prospective/retrospective cohort) including 28,222 persons recovering from ischemic or hemorrhagic stroke, in which cognitive outcomes were reported.	Effect sizes for short-term and long-term cognitive recovery were estimated, based on factors that moderate changes over time (eg., age intervention type).	**Primary outcome:** Effect size (Hedge's *g*) for cognitive recovery	Across all moderators including intervention (y/n), intervention type, study quality, recovery stage, cognitive domain, stroke etiology and age, the overall effect size for recovery across all studies was small (*g* = 0.35, CI 0.29-0.42). Effect sizes were greatest for recovery within 61-180 days (*g*=0.43), compared with 1-61 days (g=0.36) and 181-729 days (g=0.38). Effect sizes were larger in the intervention studies. The effect size for recovery was greatest among intervention studies compared with observational studies (*g*=0.47 vs. 0.28). Among intervention studies, the effect sizes were 0.57 for nonroutine/alternative intervention studies, 0.52 for pharmacological studies, 0.46 for therapist-led studies, and 0.28 for usual care studies. When assessing the interaction between chronicity of stroke and therapy type, the largest effect sizes were for nonroutine therapy provided at 1-60 days (*g*=0.89) and at 61-180 days (*g*=0.82), pharmacological interventions provided at 61-180 and 181-729 days (*g*=0.7) and therapist-led interventions provided at 61-180

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					days (*g*=0.7). The effect sizes for different cognitive domains used to assess overall cognitive recovery were small (ranging from 0.53 [praxis] to 0.40 [consciousness] and were higher in intervention studies. Effect sizes for cognitive recovery were highest for persons aged 65 to 70 years (*g* = 0.43). Effect sizes were higher for all age groups (<65; 65-70; >70-81 years) in intervention studies
Rogers et al. 2018 **Australia** **Systematic review & meta-analysis**	Mean PEDro score was 7.8.	22 RCTs including 1,098 persons with cognitive deficits following stroke. Mean age was 62 years (range 48–78 years). The average time post stroke ranged from 3 days to 6.7 years. 10 studies were conducted during the sub-acute stage (≤ 3 months) and 12 studies were conducted during the chronic stage (> 3 months).	Trials compared cognitive remediation (CR) strategies vs. treatment as usual, placebo, or a waitlist control. Non-inferiority trials were excluded. Types of interventions included computer training (n=8), therapist led interventions (n=7), pen/paper or workbook (n=3), and group therapy (n=4). Cognitive domains targeted in the intervention were memory (n=3), language (n=6), attention (n=4), visuo-spatial (n=4), general function (n=2), executive function (n=2), and processing speed (n=1) Mean frequency of therapy provided was 3.5 sessions per week	**Primary outcome:** Cognitive outcomes assessed at the impairment level	CR was associated with a small overall effect (Hedge's *g*=0.48, 95% CI 0.35–0.60). Where outcomes were assessed at the end of the intervention, effect sizes were higher in trials that provided interventions earlier following stroke, and trials that provided an intervention for a longer duration. Lower-quality trials were associated with higher effect sizes. Factors that were not effect size moderators included generalizability to trained or untrained processes, control group type, remediation approach, and intervention frequency. In 9 trials, outcomes were assessed at follow-up (ranging from 2 weeks to 12 months), the effect size on cognitive outcomes was lower and remained small (*g*=0.27, 95% CI 0.04–0.51). Variations in study quality, frequency, duration, recovery stage, remediation type, control group, or generalizability to trained or untrained processes were not found to be effect size moderators. *Domain specific outcomes at the end of the intervention (Hedge's g, 95% CI)* Attention: 0.40, 0.55-0.59 (10 trials) Language: 0.66, 0.35-0.96 (8 trials) Memory: 0.47, 0.03-0.92 (5 trials) Visio-spatial: 0.75, 0.18-1.31 (4 trials)

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			(range: 1-6), mean duration of a session was 63 minutes (range: 15 minutes-2.5 hours) and mean duration was 8 weeks (range: 2-26 weeks).		Processing speed: 0.37, 0.06-0.68 (3 trials) Executive function: 0.47, 0.21-0.73 (6 trials)
Feng et al. 2017 **China** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☒ ITT: ☒	80 patients with first-ever stroke with vascular cognitive impairment with no dementia, who were admitted to hospital. Mean age was 66 years, 57% were men.	Participants were randomized 1:1 to receive a 12-week systematic cognitive training program (30 minutes, 2x per day), with training gradually becoming more difficult or to a control group that received standard rehabilitation. When the patients were discharged from the hospital, the cognitive training was performed by a trained and eligible family caregiver. The cognitive training program also included 3 months of telephone follow-up, provided every 2 weeks. Specific content included training of attention, memory, orientation, visual spatial perception and retelling and naming training.	**Primary outcomes:** Rey-Osterrieth Complex Graphics Test (CFT), Clock Drawing Test (CDT), Logic Memory Test (LMT), Auditory Verbal Learning Test (AVLT), Stroop Color-Word Test (SCWT), Trail Making Test (TMT), Verbal Fluency Test (VFT), Digit Span Test, Picture-Naming Test Assessments were completed 3 months prior to the intervention and at the end of the intervention.	There were 4 dropouts in the intervention group and 3 in the control group. Mean change scores from baseline were significantly greater among persons in the intervention group for all outcomes assessed, except for the SCWT.

Abbreviations

CA: concealed allocation	CI: confidence interval	ITT: intention-to-treat
MMSE: Mini Mental State Examination	MoCA: Montreal Cognitive Assessment	
OR: odds ratio	RCT: randomized controlled trial	RR: relative risk

Reference List

Bahar-Fuchs A, Martyr A, Goh AM, Sabates J, Clare L. Cognitive training for people with mild to moderate dementia. *Cochrane Database Syst Rev*. 2019 Mar 25;3(3):CD013069.

Feng H, Li G, Xu C, Ju C, Qiu X. Training rehabilitation as an effective treatment for patients with vascular cognitive impairment with no dementia. *Rehabil Nurs*. 2017 Sep/Oct;42(5):290-297.

O'Donoghue M, Leahy S, Boland P, Galvin R, McManus J, Hayes S. Rehabilitation of cognitive deficits poststroke: Systematic review and meta-analysis of randomized controlled trials. *Stroke.* 2022 May;53(5):1700-1710

Rogers JM, Foord R, Stolwyk RJ, Wong D, Wilson PH. General and domain-specific effectiveness of cognitive remediation after stroke: systematic literature review and meta-analysis. *Neuropsychol Rev*. 2018 Sep;28(3):285-309.

Saa JP, Tse T, Baum CM, Cumming T, Josman N, Rose M et al. Cognitive recovery after stroke: A meta-analysis and metaregression of intervention and cohort studies. *Neurorehabil Neural Repair*. 2021 Jul;35(7):585-600.

Tang Y, Xing Y, Zhu Z, He Y, Li F, Yang J, Liu Q, Li F, Teipel SJ, Zhao G, Jia J. The effects of 7-week cognitive training in patients with vascular cognitive impairment, no dementia (the Cog-VACCINE study): A randomized controlled trial. *Alzheimers Dement*. 2019 May;15(5):605-614.