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VASCULAR COGNITIVE IMPAIRMENT: RISK FACTORS, PREVENTION AND TREATMENT

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ABSTRACT

Background: Vascular cognitive impairment (VCI) is a major contributor to age-associated cognitive decline, both independently and as a contributor to mixed dementia syndromes. Despite many years of research, an approved therapy has not yet been identified.
Methods: We reviewed preventive and therapeutic strategies tested in VCI and meta-analyzed efficacy data for eligible interventions to assess whether previously tested treatments warranted reconsideration.
Results: VCI clinical trials exhibited substantial heterogeneity. Few interventions were reproducibly tested in adequately sized and designed studies. Nonetheless, some interventions showed modest effects on global cognition and functional outcomes.
Conclusion: Early and effective management of cerebrovascular risk factors, particularly beginning in midlife, plays a crucial role in lowering the likelihood of developing neurodegenerative conditions such a vascular cognitive impairment and other related dementias. Ginkgo biloba extracts and acetylcholinesterase inhibitors have shown the greatest cognitive and functional benefits, though their clinical significance remains uncertain, and certainty of evidence is overall low.

KEYWORDS

Dementia, Cerebrovascular, Cognition, Vascular Cognitive Impairment, Vascular Dementia

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Introduction

Vascular cognitive impairment (VCI) is a neurological disorder that represents clinically significant cognitive impairment directly related to vascular injury to the brain, typically influenced by several vascular risk factors. Vascular dementia (VaD), which represents the most advanced stage of vascular cognitive impairment, is considered the second most common cause of dementia, accounting for about 15–20% of cases. The leading form remains Alzheimer's disease (AD). (Yang 2025)

The range of VCI conditions reflects reductions in mental functioning that arise from various forms of vascular damage, including large strokes or bleeding events, small infarcts, microbleeds, lacunar lesions, white-matter abnormalities, and enlargement of perivascular spaces. (Jiménez-Ruiz i wsp. 2024)

The development of VCI involves multiple interacting mechanisms that ultimately damage neurons and lead to alterations in mental functioning. Vascular abnormalities—such as disruption of the blood–brain barrier—occur frequently in various cognitive impairments and are associated with worsening mental performance. (Bowman i wsp. 2018)

The white matter is especially sensitive to damage from small-vessel pathology, and lesions in this region—often accompanied by myelin loss—are a characteristic feature of VCI. (Ihara i wsp. 2001)

There is an urgent need for effective treatments for VCI because the condition places a heavy strain on affected individuals and their caregivers. In addition, since vascular abnormalities are common across many forms of cognitive impairment, developing successful therapies for VCI could also help reduce the vascular factors that worsen cognitive decline in other disorders. (Masserini i wsp. 2023)

Methodology

A systematic search of the PubMed database was performed to locate publications addressing the prevention and therapeutic management of vascular cognitive dementia. The search strategy initially identified 197 records. Titles and abstracts were subsequently screened for relevance according to predefined eligibility criteria: (1) studies involving human participants, (2) assessment of prevention or treatment outcomes, and (3) a study sample size.

Following full-text evaluation, 51 publications that satisfied all inclusion criteria were retained for the final analysis. No limitations were imposed regarding participants' sex, age, or level of performance. The eligible studies were then integrated in order to assess the impact of various dietary supplements on different aspects of running performance.

Results

2.1 **VCI diagnosis**

The way VCI is defined and diagnosed has changed over time. Earlier criteria for vascular dementia required measurable memory impairment and cognitive deficits severe enough to interfere with daily independence. These standards, however, often failed to identify patients whose symptoms mainly involve executive difficulties or milder levels of mental decline, which are typical features of VCI. (Levine i Langa 2011)

Reaching agreement on a reliable diagnosis of VCI requires combining clinical assessment, neuropsychological testing, and brain imaging, with final confirmation provided by pathological examination. (Kalaria 2016) Moreover, recent studies indicate that advanced neuroimaging techniques and new fluid biomarkers may be also a valuable tools in this area. (Sachdev i wsp. 2025)

Among the various processes that contribute to VCI, cerebral small vessel disease (SVD) is considered the most common and can lead to mental decline even in the absence of stroke. SVD involves structural and functional abnormalities of the brain's small vessels and presents with a range of neurological and imaging findings, including deterioration in mental abilities. It is not a single uniform condition but rather a group of both sporadic and inherited disorders that arise from a combination of genetic influences and vascular risk factors. The likelihood of SVD increases with age. The two most frequent sporadic forms are arteriolosclerosis—also known as hypertensive or deep perforator arteriopathy—and cerebral amyloid angiopathy (CAA). Arteriolosclerosis is typically associated with hypertension and type 2 diabetes, and is marked by thickening of the walls of small arteries, particularly in deep grey nuclei and deep white matter. Autopsy studies report its presence in more than 80% of people over the age of 80. CAA involves the deposition of amyloid-β within the walls of cortical and leptomeningeal small vessels, and it frequently appears alongside AD. (Zanon Zotin i wsp. 2021)

2.2 **VCI Risk factors**

Research indicates that among vascular risk factors, high blood pressure in midlife carries the greatest impact, accounting for as much as 30% of dementia cases that appear later in life.

In a case–control study by Kern et al. 64 participants were matched by age, sex, and educational level. Patients either had normal blood pressure, well-regulated hypertension, or hypertension that remained poorly controlled. Among individuals aged 60 to 86, distinct configuration showing reduced gray-matter volume were found in both temporal and parietal regions, while areas such as the basal forebrain, thalamus, and cingulate cortex were comparatively unaffected. This configuration appeared most strongly in participants with untreated or inadequately managed hypertension and was least apparent in those with normal blood pressure. It was also more visible in older adults. Stronger expression of this pattern corresponded to poorer results on tests of executive skills and memory. (Kern i wsp. 2017)

In another study, midlife systolic blood pressure (SBP) of 120 mmHg or higher was linked to a higher chance of developing dementia and VaD later in life. Treatment to lower SBP reduced the risk of VaD, whereas controlling diastolic blood pressure (DBP) did not show the same effect. (Stewart i wsp. 2009)

Observational studies also show that diabetes substantially increases the likelihood of developing dementia. In the study by Tuligenga et al., middle-aged individuals with type 2 diabetes who had poor blood sugar control experienced a faster decline in memory and reasoning abilities, according to data from the Whitehall II cohort. (Tuligenga i wsp. 2014)

Research indicates that, another risk factor of VCI is obesity. Various pathways have been suggested to explain how obesity affects brain function. These include ongoing low-level inflammation and oxidative stress, greater blood–brain barrier permeability, and higher insulin resistance, which together can impair glucose

metabolism and promote neuronal damage and loss. Additionally, obesity may contribute to vascular cognitive impairment by increasing arterial stiffness and encouraging the development of atherosclerosis and small vessel disease through dysfunction of the endothelium. (Balasubramanian i wsp. 2021)

In a Solomon et al. study, cholesterol levels 200–239 mg/dl were linked to a significantly higher risk of developing vascular dementia about 30 years later. Cholesterol ≥240 mg/dl also showed a tendency to increase VaD risk, although this relationship was not statistically significant, possibly due to the small number of VaD cases in the study. (Solomon i wsp. 2009)

In another study current smokers compared with never smokers, showed an increased risk of dementia including AD and VaD. For all-cause dementia, the risk increased by 34% for every 20 cigarettes per day. (Zhong i wsp. 2015)

Based on these studies, vascular and metabolic risk factors should be seen as key targets for dementia prevention. The timing of prevention efforts seems important: these risk factors show a stronger link to dementia when they are present in midlife rather than in older age, suggesting that midlife represents a particularly vulnerable period.

Protecting healthy cognitive development early in life is also essential, as new evidence shows that childhood and adolescent experiences shape adult health and cognitive outcomes. Adequate nutrition during these formative years supports normal brain development, which continues into late adolescence and forms a foundation for reducing the risk of later cognitive decline. (Gorelick i wsp. 2011)

2.3 **VCI Prevention**

Although severe forms of VCI are widely acknowledged as the second leading cause of dementia globally, milder VCI—often marked by problems with executive functions rather than memory—is likely far more common than current estimates suggest. Therefore, more accurate data on how often VCI occurs and develops over time are needed to guide effective prevention and protective strategies. (Kalaria i wsp. 2024)

High blood pressure is likely the most changeable risk factor contributing to both cardiovascular and cerebrovascular conditions that can result in VCI. Effective treatment—using safe antihypertensive drugs together with lifestyle changes—can lower blood pressure by roughly 10–15%. Although recent clinical trials have not used VCI as their main cognitive endpoint, pooled analyses of randomized studies indicate that blood pressure reduction offers only limited, if any, protection against cognitive decline.

The SPRINT MIND studies drew attention to the fact that stronger treatment targets influenced not only cognitive outcomes but also other indicators of vascular brain injury, such as total brain volume and white-matter hyperintensities. In secondary analyses of SPRINT data, adults around 80 years old who received intensive systolic blood pressure treatment (<120 mm Hg) showed reduced risks of major cardiovascular events, mild cognitive impairment, and mortality, and they did not experience more serious falls than those treated to a standard goal (<140 mm Hg). These advantages, however, were not observed in participants who began the study with poorer cognitive performance. (Pajewski i wsp. 2020)

The World Health Organization recommends aerobic exercise as a way to help preserve cognitive abilities in older adults, including those with normal cognition or mild cognitive impairment. Evidence from the PROMoTE trial showed that a six-month, moderate-intensity walking program improved overall cognitive scores in individuals with CSVD, although no gains were seen in executive functioning. The cognitive improvement appeared to be linked to lower diastolic blood pressure, suggesting this may be one mechanism through which aerobic exercise supports brain health. A follow-up analysis also found that sex influenced the response: women, but not men, showed meaningful enhancement in executive skills, and these benefits lasted for at least six months after the intervention.

In another study, a two-year aerobic dance program for people with CSVD did not produce clear differences between the intervention and control groups. Still, participants in the exercise group improved their memory, executive abilities, and language skills when compared with their own baseline performance.

With respect to resistance training, results from the Study of Mental and Resistance Training indicated that this type of exercise enhanced global cognitive scores on the Alzheimer's Disease Assessment Scale, although memory performance did not improve. (Dao i wsp. 2024)

Research indicates that Oral anticoagulant therapy may help protect cognitive function in patients with atrial fibrillation (AF). A retrospective analysis of registry data from 440,106 Swedish patients with AF showed that those receiving oral anticoagulants at the start of observation had a 29% lower risk of developing dementia. Furthermore, patients who remained on anticoagulation for at least 80% of the follow-up period experienced a 48% reduction in dementia risk compared with those who did not receive these medications. (Friberg i Rosenqvist 2018)

Smoking contributes to cardiovascular disease by causing oxidative damage, raising fibrinogen levels, and creating a hypercoagulable state. Because cerebrovascular infarcts are a main cause of VaD, risk factors for cerebrovascular disease—including smoking—also increase the likelihood of developing vascular dementia. Quitting smoking lowers cardiovascular risk by reducing inflammation and oxidative stress, which may similarly reduce the risk of VaD. A recent meta-analysis of 19 prospective studies with 26,374 participants found that current smokers had a higher risk of AD, VaD, and all-cause dementia compared with those who never smoked. Other research in Western populations has shown that former smokers have a lower dementia risk than current smokers. (Anstey i wsp. 2007) Consistent with these findings, a study in Korean men demonstrated that never smokers had the lowest risk of dementia, and those who quit smoking for a long period experienced a reduced risk of overall dementia. (Choi i wsp. 2018)

Maintaining healthy levels of blood pressure, glucose, and cholesterol, avoiding smoking, staying physically active, keeping a balanced body weight, eating a nutritious diet, and engaging in mentally and socially stimulating activities are all considered important indicators of good brain health and help support cognitive function. Although strong evidence for preventing cognitive decline currently exists for only two of these factors—controlling hypertension and regular physical activity—they remain sensible approaches for reducing overall mortality and lowering the risk of vascular disease. (Jiménez-Ruiz i wsp. 2024)

2.4 **Treatment**

A wide range of therapies has been tested in people with VCI, yet none has been approved as a treatment that can alter the course of the disease or reliably ease its symptoms. One reason for this gap may be the broad and varied nature of VCI itself, which makes it difficult to pinpoint a single intervention that works for all patients. Recent discussions also propose that the benefits of some therapies might have been undervalued because study groups were highly diverse, the assessment tools were not specifically designed for VCI, and many clinical trials were too short to detect meaningful effects.

Experimental studies and clinical findings suggest that VaD may involve a reduction in cholinergic activity, similar to what is observed in AD. This raises the possibility that people with VaD could respond to cholinesterase inhibitor therapy. Supporting this idea, a recent investigation reported benefits of a cholinesterase inhibitor in individuals with both AD and cerebrovascular pathology. In addition, donepezil—an acetylcholinesterase inhibitor known to improve cognition, global status, and daily functioning in mild to moderate AD—also showed positive effects in a 6-month open-label pilot study in participants with probable VaD. (Mendez i wsp. 1999)

In a study by Wilkinson et al. patients with VaD who received donepezil at either 5 mg or 10 mg once daily showed clear advantages over those given placebo on cognitive assessments (ADAS-Cog and mini mental state examination (MMSE)) and on an overall clinical evaluation (CIBIC-Plus). The group taking 10 mg/day also performed significantly better than placebo on the Clinical Dementia Rating–Sum of Boxes, a broader measure of dementia severity. Although treatment with donepezil appeared to slow the decline in daily functioning as measured by the ADFACS, this difference did not reach statistical significance when compared with placebo. (Wilkinson i wsp. 2003)

Several studies have examined rivastigmine—another acetylcholinesterase inhibitor commonly prescribed for Alzheimer's disease—as a possible therapy for VCI.

Study by Narasimhalu et al. included 50 adults (ages 48–84) with post-stroke cognitive impairment but no dementia (CIND). Their baseline MMSE scores were similar (23.7 versus 23.9). Over 24 weeks, they received up to 4.5 mg rivastigmine twice daily or placebo. No significant differences were detected in cognitive performance, daily functioning, behavioural symptoms, or global outcomes, and withdrawal due to adverse effects was rare in both groups. (Narasimhalu i wsp. 2010)

In a second study with 40 adults diagnosed with subcortical VaD (ages 40–90), participants had similar baseline MMSE scores. They received either 3 mg of rivastigmine twice daily or placebo for 26 weeks. The study found no meaningful differences between groups in cognitive outcomes, behavioural symptoms, functional abilities, global clinical assessments, or withdrawal rates. (Mok i wsp. 2007)

Another, much larger study enrolled 710 individuals with vascular dementia of both cortical and subcortical types (ages 50–85). After 24 weeks, participants receiving rivastigmine reached an average dose of 9.4 mg/day. Both groups started with the same MMSE score. At 24 weeks, rivastigmine produced a small but statistically significant improvement in cognitive test scores, although this did not extend to global ratings or non-cognitive measures. Participants assigned to rivastigmine experienced substantially more nausea, vomiting, diarrhoea, anorexia, and treatment discontinuations than those on placebo. (Ballard i wsp. 2008)

Overall, only one of the three trials demonstrated any notable cognitive benefit, and this effect was modest. At the same time, gastrointestinal side effects—especially nausea and vomiting—were common among those taking rivastigmine. Based on current evidence, the effectiveness of rivastigmine for people with VCI remains uncertain.

In another randomized, double-blind, placebo-controlled study, 788 individuals with probable VaD were treated with another acetylcholinesterase inhibitor – galantamine. Treatment effects were assessed using cognitive tests, measures of daily functioning, and behavioral ratings. The main outcomes were the ADAS-Cog/11 and the ADCS-ADL total score, while secondary measures included the CIBIC-Plus. After 26 weeks, patients taking galantamine showed a larger cognitive improvement on the ADAS-Cog/11 than those receiving placebo. However, both groups performed similarly on the ADCS-ADL at week 26. The global clinical rating on the CIBIC-Plus tended to favor galantamine, although the difference did not reach clear significance. A benefit on the EXIT-25, an executive function test, was also observed for the galantamine group. Regarding safety, 13% of participants on galantamine and 6% on placebo stopped treatment because of side effects. Overall, the study indicated that galantamine can enhance cognitive performance, including executive abilities, in people with VaD, and is generally well tolerated—though its effect on everyday functioning did not differ from placebo. (Auchus i wsp. 2007)

A double-blind, placebo-controlled multicenter trial was carried out to assess the effectiveness of pentoxifylline. The study included 289 participants aged 45 or older who had a Hachinski Ischemia Scale score above 7, an MMSE score between 10 and 25 at baseline, and CT scans confirming vascular pathology. The main outcome was the difference between treatment groups on the Gottfries–Bråne–Steen (GBS) scale. In the intention-to-treat analysis of participants who completed the trial, pentoxifylline produced a statistically significant improvement on the overall GBS score compared with placebo. A similar advantage for pentoxifylline was also nearly significant in the intention-to-treat analysis that included all evaluable participants. (European Pentoxifylline Multi-Infarct Dementia Study 1996)

In another study evaluating pentoxifylline, the overall group did not show a statistically significant slowing of decline on the total ADAS score or on its cognitive and non-cognitive subscales, although a significant effect was observed on the cognitive subscales when memory items were excluded. Among the subgroup of 40 participants who showed CT or MRI signs of stroke in addition to meeting all other entry criteria, pentoxifylline was linked to a significantly slower decline on the total ADAS and the cognitive subscale, but not on the non-cognitive subscale. In a second subgroup of 37 patients with at least one clinically documented stroke, pentoxifylline treatment was associated with significantly less deterioration on the total ADAS as well as on both the cognitive and non-cognitive components. (Black i wsp. 1992)

Systematic reviews have indicated that pentoxifylline might have some therapeutic value in VaD. However, most of the available studies were small and had important methodological weaknesses. (Sha i Callahan 2003)

The next medication examined was propentofylline In the randomized controlled trial (RCT) and in two meta-analyses, outcomes were reported for global function, cognition, daily functioning, and adverse events. Global functioning slightly improved over 12 months in the propentofylline group, while the placebo group worsened. The difference in mean change from baseline reached statistical significance in the RCT and in one meta-analysis. Using the CGI scale, the treatment group consistently showed better clinical status across all time points; the RCT also reported a clinically meaningful difference at 12 months, though this was not statistically significant.

For cognitive performance measured by the Syndrome Short Test (SKT), both groups improved at 3 months in the RCT. At 12 months, the improvement persisted only in the propentofylline group, while placebo returned to baseline. The difference in mean change from baseline was statistically significant in the RCT and in the meta-analysis. The RCT also found that MMSE scores increased over 12 months in the propentofylline group but declined in the placebo group; this difference was statistically significant in both the RCT and the meta-analysis.

Regarding daily functioning, both groups in the RCT showed gradual decline on the Nurnburger-Alters-Beobachtungs-Skala (NAB) scale, but the deterioration was greater in the placebo group. The difference in mean change from baseline was statistically significant in the RCT and in the meta-analysis. Reported adverse effects were similar to those typically seen with donepezil. (Chilcott i wsp. 1999)

In the study by Pantoni et al, 230 participants were included in the intention-to-treat evaluation of nimodipine efficiency. After 52 weeks, the nimodipine treatment group and the placebo group showed no meaningful difference in the main outcome, which was the 5-point change on the Sandoz Clinical Assessment

Geriatric scale. Still, people receiving nimodipine did better than those on placebo in tasks involving word generation, and they were less likely to show decline on the MMSE or the Global Deterioration Scale.

Participants taking placebo discontinued the study more often and experienced more adverse events than those taking nimodipine, especially cardiovascular or cerebrovascular problems and behavioral symptoms that required clinical management. When the researchers used a worst-rank approach to account for the high dropout rate in the placebo group, additional significant advantages for nimodipine appeared in the Set Test and the overall MMSE scores. (Pantoni i wsp. 2005)

The efficacy of donepezil hydrochloride combined with nimodipine on treating VaD is systematically reviewed to provide evidence-based references for clinical applications. In the Yang et al. meta-analysis, donepezil hydrochloride combined with nimodipine resulted in a significant improvement in MMSE scores in the treatment group compared with controls, with consistent benefits across 12-, 8-, and 4-week interventions, although high heterogeneity required the use of random-effects models. Although activity daily scale (ADL) scores tended to improve more in the treatment group than in controls, these differences were not statistically significant across the 12-, 8-, or 4-week subgroups. The meta-analysis demonstrated a significant reduction in clinical dementia scale

Clinical Dementia Rating (CDR) scores in the treatment group compared with controls across all time-points, although high heterogeneity was detected within the 12-, 8-, and 4-week subgroups. The findings indicate that using donepezil together with nimodipine leads to greater improvements in MMSE, ADL, and CDR scores in patients with VaD. Sensitivity analyses suggest that the most reliable and favorable effects occur after 12 weeks of treatment. (Yang i wsp. 2022)

Numerous clinical studies have shown that another substance - cerebrolysin can provide therapeutic benefits for vascular dementia (VD). One large randomized multicenter trial reported that using this compound for 24 weeks improved overall clinical outcomes in people with VD. Its beneficial effects were found to continue for many months after treatment ended, suggesting that the drug may promote long-lasting neuroprotection. Follow-up data from an extension study supported this observation by demonstrating that improvements remained for at least 12 weeks after stopping therapy. (Allegri i Guekht 2012)

Several systematic reviews and meta-analyses have also concluded that cerebrolysin is effective in managing different forms of dementia. In VD, its ability to improve cognitive symptoms appears comparable to that of cholinesterase inhibitors. The drug may help compensate for cholinergic deficits by increasing the production of neurotrophic factors. Experimental work indicates that both donepezil and cerebrolysin can enhance cholinergic signaling by raising acetylcholine levels in the prefrontal cortex, and combined treatment has shown added benefit in patients with AD. These findings suggest that cerebrolysin may counter cognitive decline in VaD partly by strengthening cholinergic neurotransmission. (Alvarez i wsp. 2020; Dey i wsp. 2024)

An analysis of six randomized trials including nearly six hundred individuals with VaD reported no serious adverse reactions or deaths associated with the drug, supporting its overall safety. Additional evidence indicates that its neuroprotective properties may also be relevant for AD. Early pilot studies have shown improvements in cognition and EEG patterns in VaD, and electrophysiological investigations suggest dose-dependent enhancement of attention, memory, and general cognitive performance. Observational data further indicate that treatment may delay the progression from mild cognitive impairment to dementia, and that a 20-day course can reduce amnestic symptoms in older adults while increasing circulating brain-derived neurotrophic factor (BDNF) levels. (Cui i wsp. 2019)

In another 28 week randomized, double-blind, parallel-group trial tested memantine at a daily dose of 20 mg in individuals diagnosed with probable VaD. The main outcomes were performance on the ADAS-cog and ratings on the Clinical Global Impression of Change. In total, 579 participants entered the study. By the end of the trial, memantine produced better cognitive results than placebo, the mean difference in ADAS-cog change from baseline was –1.75 points, with a median difference of 2 points. However, the memantine and placebo groups did not differ significantly in global clinical impressions. Adverse events occurred in 77% of people receiving memantine and 75% of those taking placebo, with dizziness reported most often. (Wilcock i wsp. 2002)

In a study by Want et al. eighty individuals diagnosed with VCI with no dementia were randomly assigned to two groups: one receiving standard aspirin therapy alone and the other receiving standard therapy together with Ginkgo biloba. The standard-therapy group was treated with routine anti-platelet medication, specifically aspirin 75 mg taken three times daily for a period of three months. The combined-therapy group followed the same anti-platelet regimen but also took Ginkgo biloba tablets (19.2 mg, three times daily) for the same duration.

Cognitive performance and cerebral blood flow were assessed in both groups before and after treatment using the Montreal Cognitive Assessment (MoCA) and transcranial Doppler ultrasound. After three months, participants in the combined-therapy group showed notable improvements in MoCA sub-scores related to executive function, attention, abstraction, delayed recall, and orientation, both compared with their own baseline and with the standard-therapy group. This group also demonstrated a significant increase in blood-flow velocity in the anterior cerebral artery. (Wang i wsp. 2015)

In another study after six months of treatment, the group receiving Ginkgo biloba showed a meaningful advantage over the placebo group only on the Clinical Global Impression measure. Participants given placebo experienced a noticeable decline in this score compared with their baseline, whereas those treated with Ginkgo biloba did not. Evaluations using transcranial Doppler ultrasound revealed no notable differences between the groups. (Demarin i wsp. 2017)

Compared to medication and surgery, Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Current Stimulation (tCDS) are a non-invasive treatment options with fewer risks and side effects, making it particularly suitable for elderly patients. The results of the gangemi et al. study indicate that transcranial direct current stimulation (tDCS) produces beneficial effects on both brain-related measures and cognitive performance in patients with VaD. The study confirmed changes in P300 event-related potentials and MMSE outcomes. In particular, shorter P300 latency, larger P300 amplitude, and higher MMSE scores together suggest that tDCS may be an effective therapeutic approach for vascular dementia.

Regarding P300 parameters, the decrease in P300 latency suggests faster cognitive processing. Faster processing may support better attention, memory function, and decision-making, which are cognitive processes linked to the P300 response. The increase in P300 amplitude indicates stronger neural responses to cognitive stimuli.

In addition, the increase in MMSE scores further demonstrates the positive effect of tDCS on overall cognitive status. Since the MMSE is commonly used to evaluate cognitive impairment, higher scores after stimulation suggest a general improvement in cognitive abilities. (Gangemi i wsp. 2024)

In a separate study, ten individuals with post-stroke cognitive impairment (PSCI) underwent high-frequency rTMS applied to the ipsilesional dorsolateral prefrontal cortex (DLPFC). The intervention consisted of ten sessions delivered over two weeks. After completing the rTMS treatment, participants showed improvements in several cognitive measures, including the Intelligence Quotient assessed by the Wechsler Adult Intelligence Scale, the Auditory Verbal Learning Test (AVLT), and the Complex Figure Test (CFT).

These cognitive gains persisted at the MMSE three-month follow-up. In addition, scores on global cognitive screening tools, namely the MMSE and the MoCA, were significantly higher than baseline. Overall scores on the Geriatric Depression Scale did not change across the whole group; however, patients with moderate to severe depressive symptoms demonstrated a reduction in depression scores, reaching borderline statistical significance.

Biological analyses showed a reduction in pro-inflammatory cytokine levels immediately after the ten rTMS sessions, with interleukin-1β (IL-1β) remaining reduced at three months. Moreover, decreases in interleukin-6 (IL-6) were strongly associated with improvements in AVLT and CFT scores immediately following treatment. Follow-up functional MRI revealed increased activity in several brain regions, including the medial frontal cortex, hippocampus, and angular gyrus. (Cha i wsp. 2022)

Discussion

Detecting individuals who are vulnerable to cognitive decline, including early or mild conditions, creates an important opportunity to delay or even prevent the onset of dementia and its related complications, while also reducing long-term public health expenditures. This preventive potential can be pursued through careful evaluation of cardiovascular and stroke risk factors, followed by timely and appropriate management of these risks. Despite the fact that cognitive performance is a significant indicator of illness and mortality among older adults, routine cognitive screening is still often omitted from comprehensive cardiovascular risk evaluations and assessments of target-organ damage in everyday clinical practice. (Gorelick i wsp. 2016)

Lifestyle-based strategies play a central role in lowering the risk of cognitive deterioration. Quitting smoking — even at an older age — along with maintaining regular physical activity and ongoing cognitive engagement, contributes meaningfully to brain health. Evidence increasingly favors comprehensive, multidomain prevention programs over isolated, single-component interventions, suggesting that future clinical trials should prioritize combined approaches.

Current findings indicate that moderate levels of aerobic exercise are advantageous for cognitive functions. Interventions designed to improve cardiorespiratory capacity and optimize cerebrovascular performance - including cerebral vasoreactivity and vascular pulsatility - are likely to exert stronger positive effects on cognition.

Growing evidence highlights a bidirectional relationship between cardiovascular disease and mental health conditions, including depression and behavioral disorders. Effective management of cardiovascular risk factors may therefore confer dual benefits, reducing both psychiatric morbidity and the incidence of VCI. Additional influences — such as chronic stress, overall well-being, sleep quality (including sleep apnea), socioeconomic disadvantage, and occupational conditions — may also shape vascular brain outcomes, although they were not examined in detail here. Broad public health initiatives and policies aimed at controlling vascular risk across individual, community, and population levels hold substantial promise for safeguarding brain health and lessening the overall impact of VCI. (Kalaria i wsp. 2024)

A range of pharmacological approaches has been associated with improvements in cognitive performance and, to a lesser degree, everyday functioning. In most cases, however, the magnitude of these effects was small or neutral, with the notable exception of preparations derived from Ginkgo biloba.

Particular attention should be given to therapies whose benefits may not yet be fully appreciated. Among them, Ginkgo biloba extracts were linked to enhanced overall cognitive functioning and better functional outcomes in individuals with VCI. We recognize that the three trials analyzed in this review were heterogeneous, that the pooled estimate for cognitive outcomes showed moderate imprecision, and that the real-world clinical relevance of these effects remains open to debate. Despite these limitations, the results appear encouraging. Considering the oral route of administration, comparatively low cost, and favorable safety profile, Ginkgo biloba extracts warrant more rigorous and extensive future research.

This review is constrained by weaknesses related to both the underlying evidence and the methodological approaches of the included studies. The existing literature varies substantially in study design and overall rigor, and many investigations are affected by residual confounding, limited sample sizes, and reliance on proxy rather than definitive clinical outcomes. Moreover, findings are not consistently replicated across different populations.

Together, these issues may contribute to potential bias and limit the reliability of the conclusions. To provide more robust and generalizable evidence, future research should include adequately powered randomized controlled trials that employ standardized and clinically meaningful cognitive outcome measures. (Zhu i wsp. 2025)

Conclusions

Approximately one in three older adults will experience either stroke or dementia. Nearly 90% of individuals diagnosed with dementia present with either VCI or AD, and about half of these cases involve a combination of both pathologies, commonly referred to as mixed dementia.

Although the diagnostic criteria for VCI continue to evolve and require further confirmation, the concept itself reflects an important change in perspective. It emphasizes the cognitive consequences of vascular brain injury, including its early and potentially reversible stages. Recognizing individuals at these initial phases creates an opportunity to address modifiable risk factors before substantial progression occurs.

Using the VCI framework also supports more precise identification of affected populations and helps guide the development of targeted preventive and therapeutic strategies. Vascular risk factors play a critical role not only in VCI but also in AD, appearing to elevate the likelihood of cognitive decline and dementia beyond their established association with stroke alone.

Future research should clarify whether effective management of hypertension, diabetes, dyslipidemia, smoking, systolic blood presure and obesity can delay or prevent the onset of VCI. Well-designed clinical trials are essential to determine whether reducing vascular brain damage can slow the progression from early cognitive impairment to clinically manifest dementia. (Rincon i Wright 2013)

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