

VASCULAR COGNITIVE IMPAIRMENT AND VASCULAR DEMENTIA

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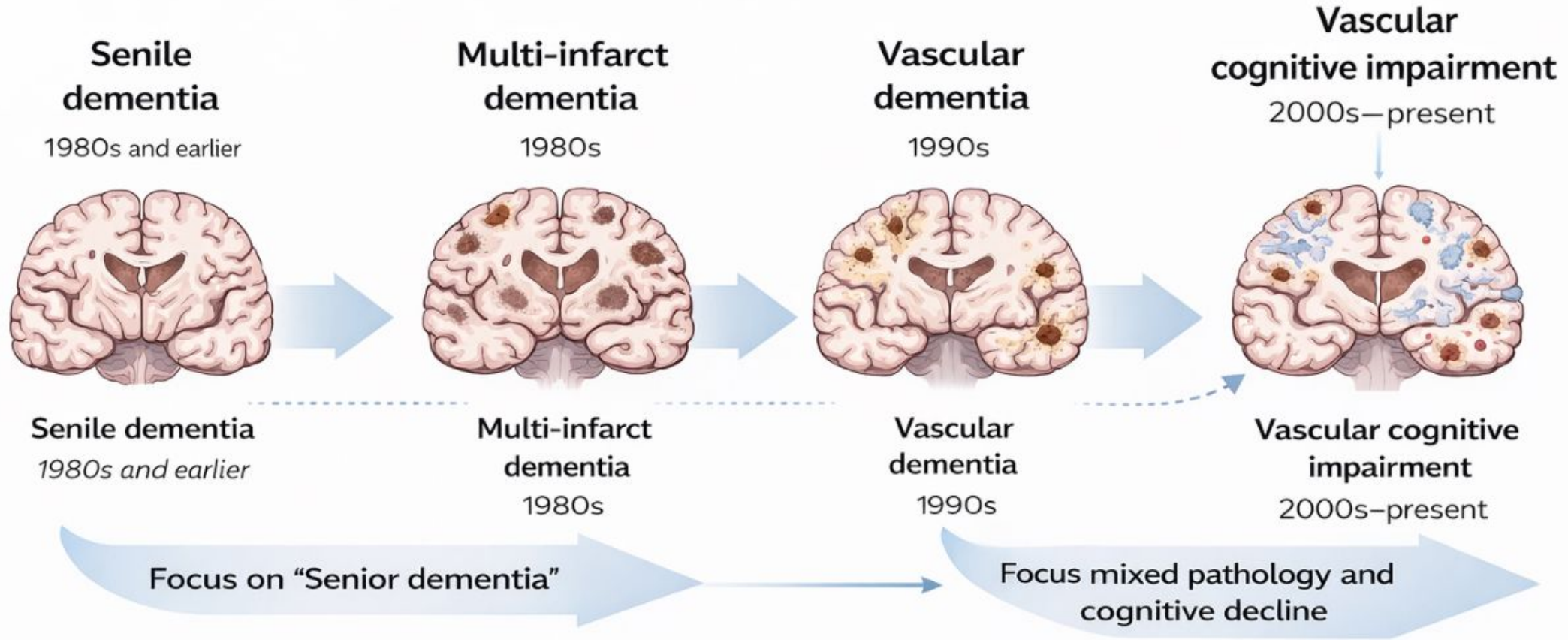
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**Past President, International Society of Interventional Neurology and
Society of Vascular and Interventional Neurology**

Rami Fakh MD

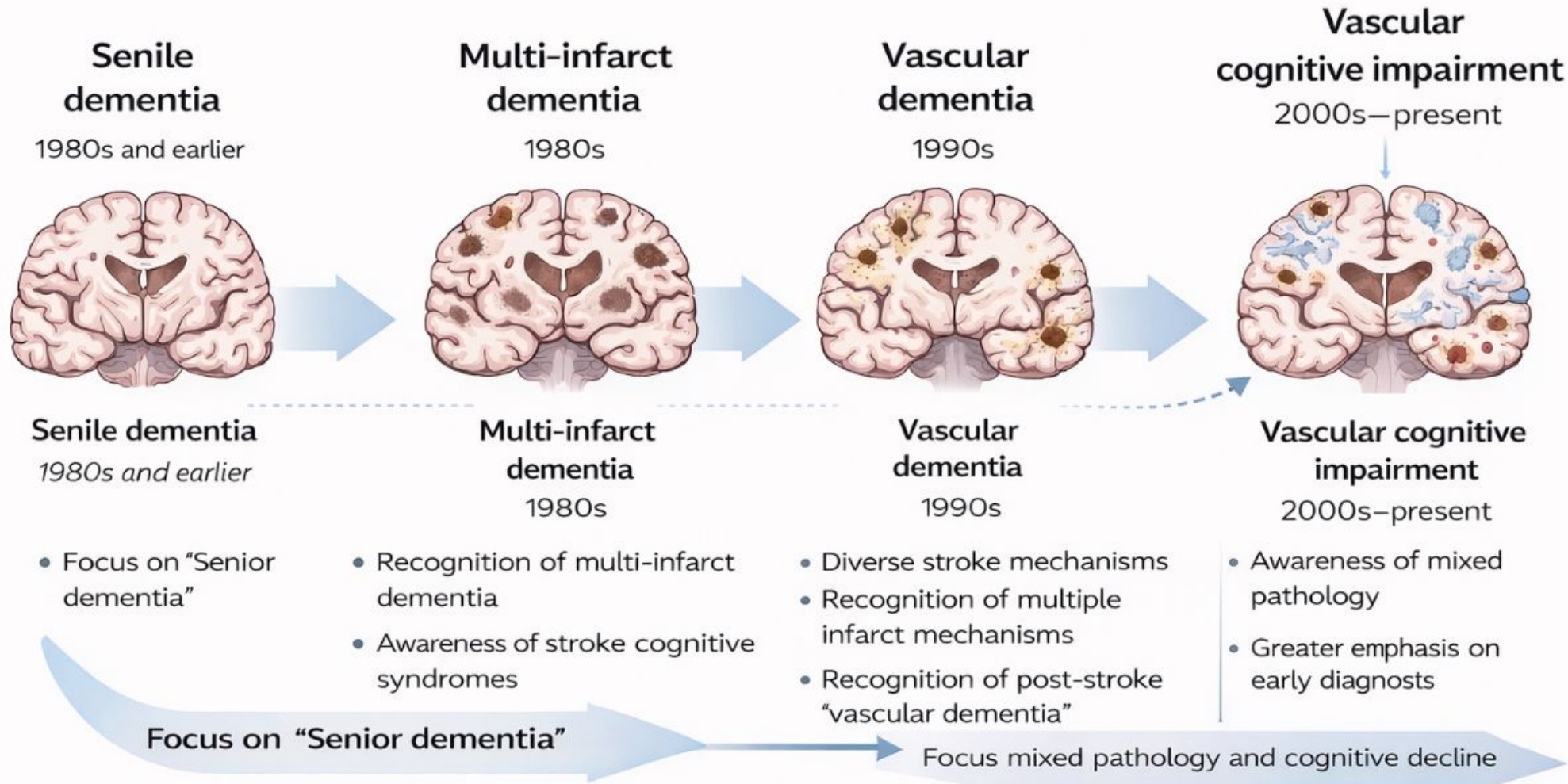
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Manila, Philippines; Zeenat Qureshi Institute of Clinical
Neurosciences, Donka National Hospital, Conakry, Guinea; Qureshi
Medical Education Center, Xuan Wu Hospital, Beijing, China.**

Evolving terminology



**Evolution of the Definition of Vascular Dementia
and Vascular Cognitive Impairment**

Basis of evolution



Evolution of the Definition of Vascular Dementia and Vascular Cognitive Impairment

Evolution and Definitions of Vascular Dementia / VCI

Definition	Era	Core Concept	Cognitive Threshold	Imaging Requirement	Key Limitations
Senile dementia (vascular type)	Pre-1970s	Arteriosclerotic aging	Dementia	None	Non-specific
Multi-infarct dementia	1970s	Cumulative infarcts	Dementia	Limited	Ignored SVD
DSM-IV VaD	1994	Stroke-related dementia	Dementia	Supportive	Low sensitivity
ICD-10 VaD	1992	Vascular causes	Dementia	Supportive	Broad criteria
NINDS-AIREN	1993	Imaging-confirmed stroke dementia	Dementia	Mandatory	Overly restrictive
VASCOG (VCD)	2014	Spectrum disorder	Mild + major	Recommended	Less operationalized
VICCS-2	2018	VCI continuum	VCI ± dementia	Central	New / evolving

Cognitive Criteria and Domains

Domain	NINDS–AIREN	VASCOG	VICCS-2
Cognitive threshold	Dementia required	Mild + major VCD	VCI ± dementia
Domains affected	Memory + ≥2 domains	Any domain; executive focus	Any domain; graded impact
Functional impairment	Required	Only major VCD	Graded by dementia status

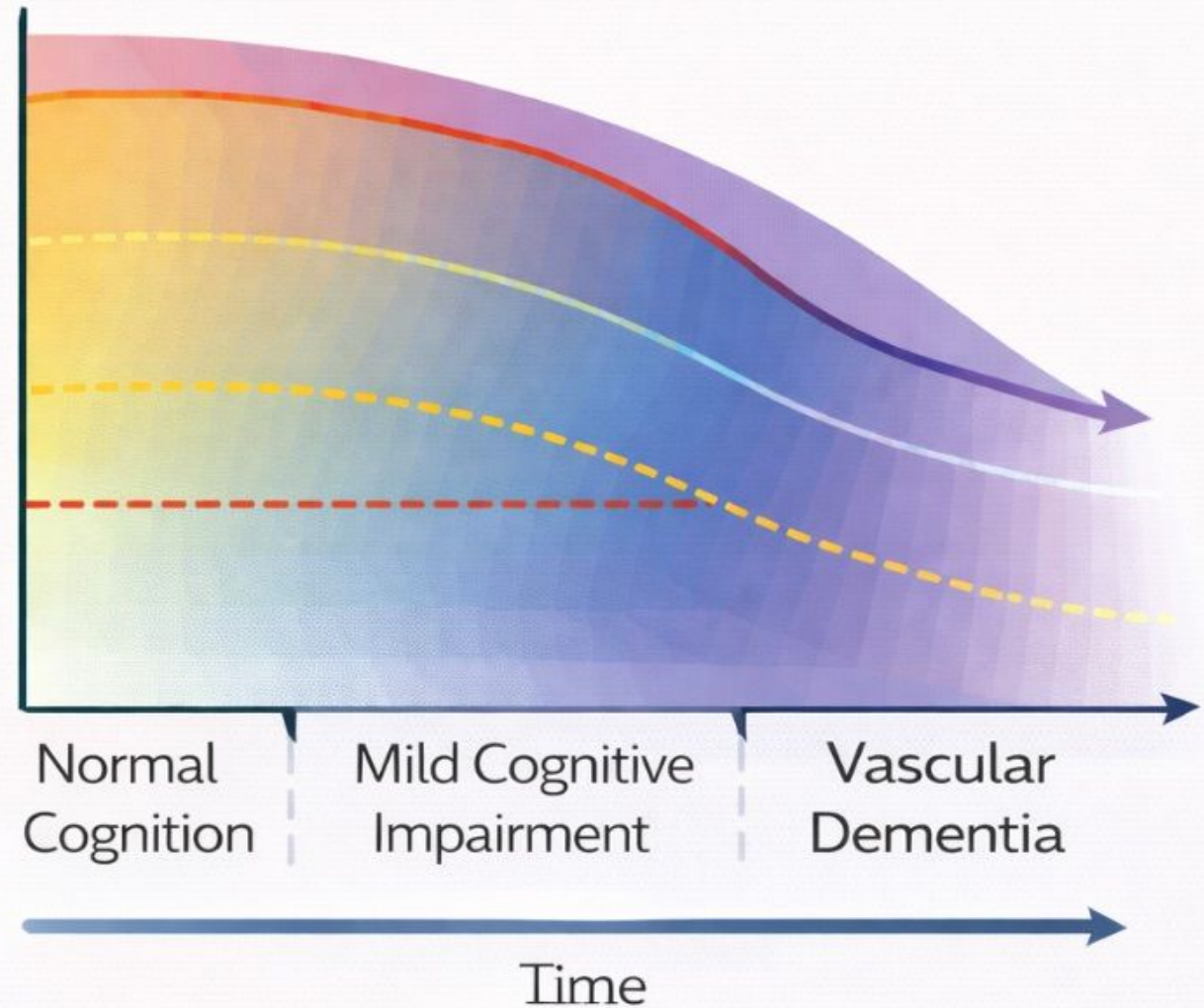
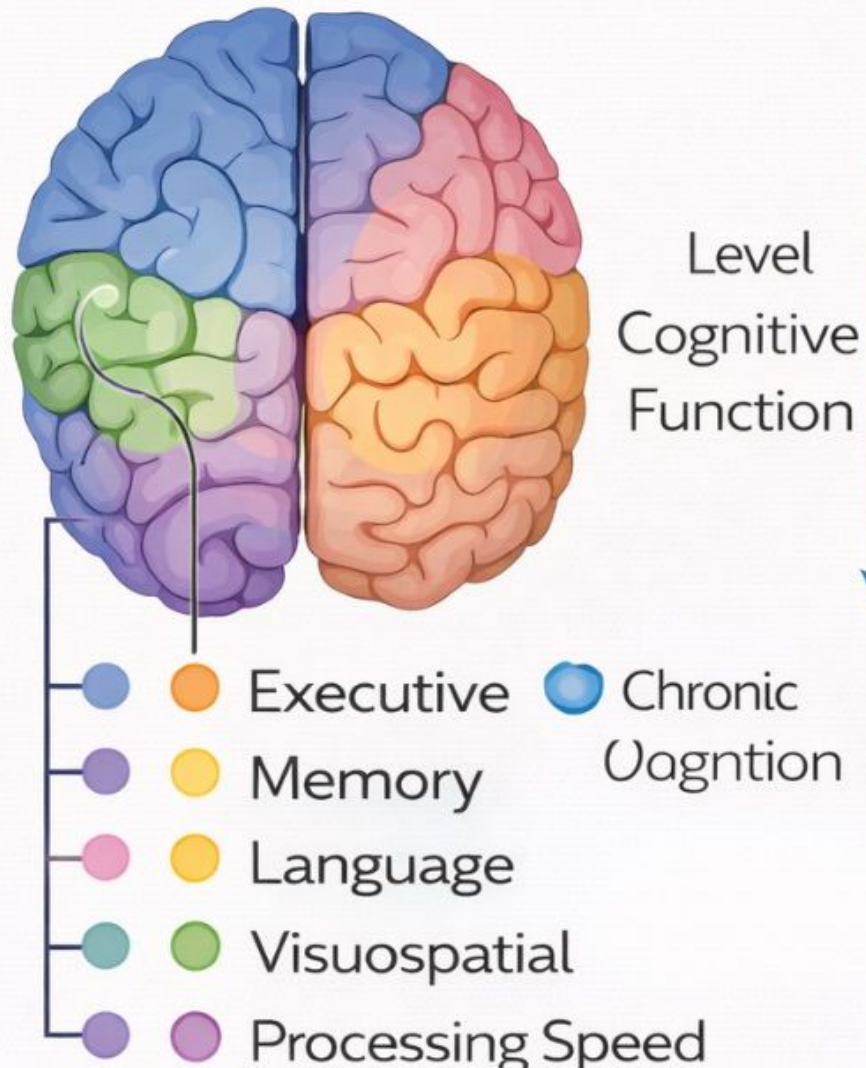
VASCOG = Vascular Cognitive Disorders (VASCOG) Society
VICCS-2 = Vascular Impairment of Cognition Classification System – Version 2

Memory

Multiple domains

Executive functions

Cognitive Criteria and Domains



Pathology and Recognized Subtypes

Domain	NINDS–AIREN	VASCOG	VICCS-2
Vascular lesions	Large/multiple infarcts	Large, small, hemorrhagic	Large, small, mixed
Small-vessel disease	Underemphasized	Emphasized	Central
Mixed pathology	Excluded	Acknowledged	Incorporated
Subtypes	MID, strategic,	Post-stroke, subcortical, mixed	Post-stroke, subcortical, mixed

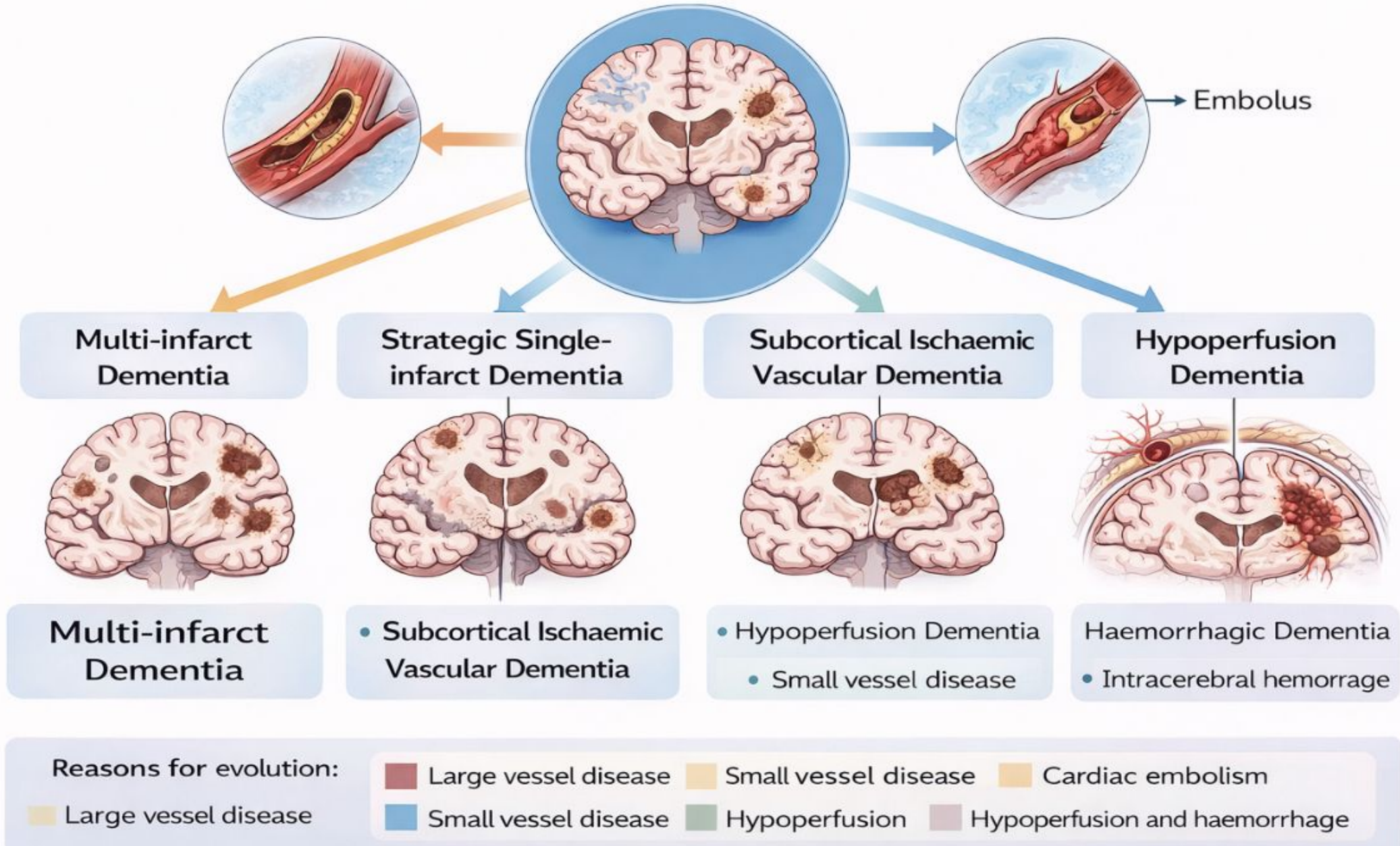
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Cortex involvement

Infarct mechanism

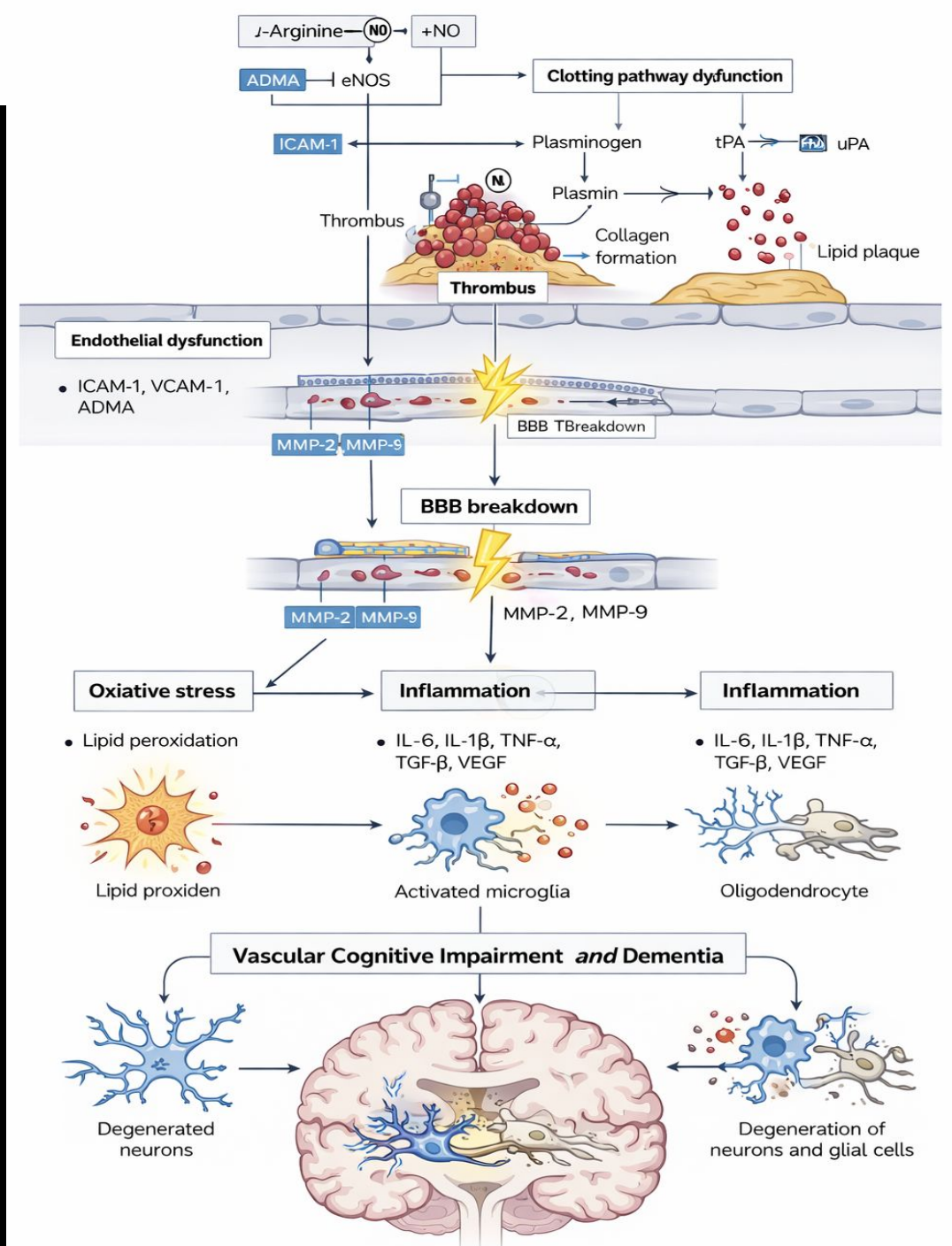
Non infarct mechanism

Subtypes of Vascular Dementia



Pathophysiology

Pathway	Biomarkers (Serum or plasma)	Biomarkers (CSF)
Endothelial dysfunction	ICAM-1, VCAM-1, ADMA, MR-proADM	PIGF
BBB breakdown	MMP-2, MMP-3, MMP-9	sPDGFR β , MMP-2, MMP-3, MMP-9, TIMP-1
Oxidative stress	oxLDL, Lp-PLA2	NA
Inflammation	IL-6, IL-18, VEGF-A	IL-6, VEGF-C, TGF- β , CCL2
Clotting pathway dysfunction	Fibrinogen, D-dimer, vWF	NA
Degeneration of neurons and glial cells	NfL, GFAP	NfL

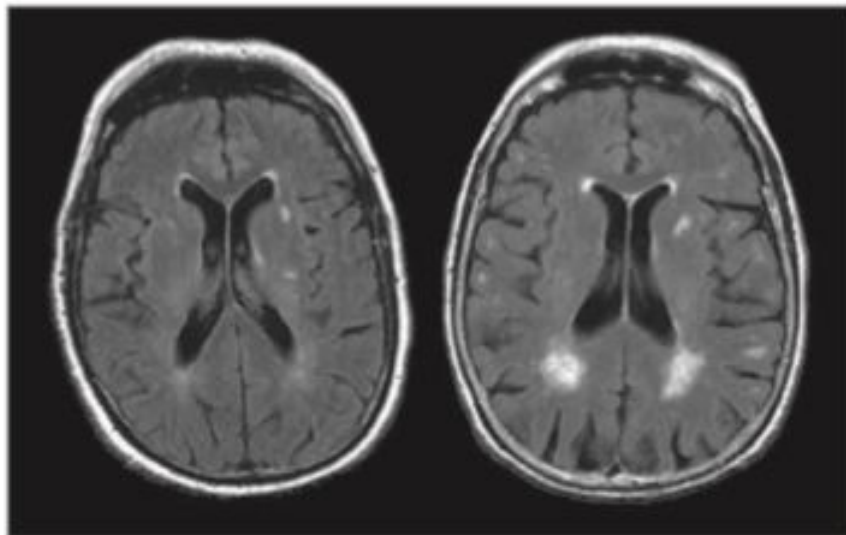


Key MRI Markers

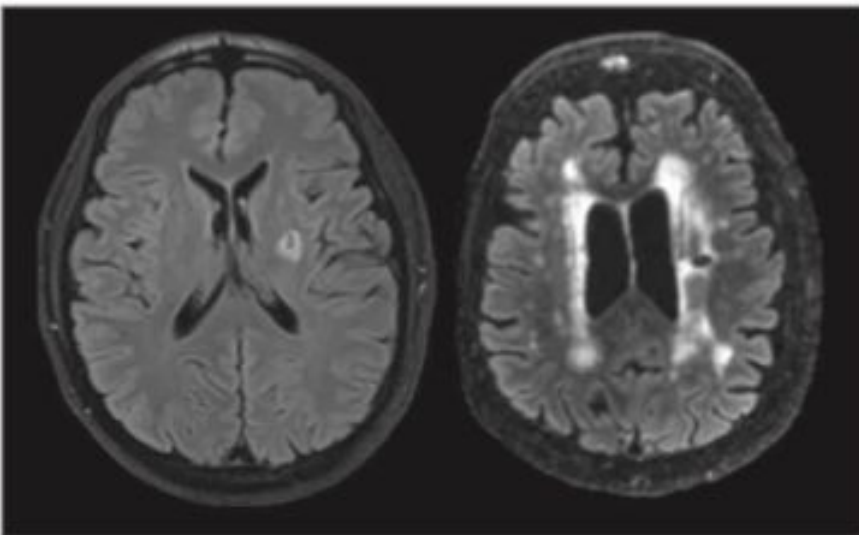
- ❑ White matter hyperintensities (WMH)
 - ❑ Covert brain infarcts (BI)
 - ❑ Cerebral microbleeds (CMB)
 - ❑ Perivascular spaces (PVS)
-
- ❖ MRI markers = powerful risk stratification tools
 - ❖ Support aggressive vascular risk factor control
 - ❖ Need randomized trials for targeted prevention

Figure 1. Magnetic Resonance Imaging (MRI) Markers of Covert Vascular Brain Injury

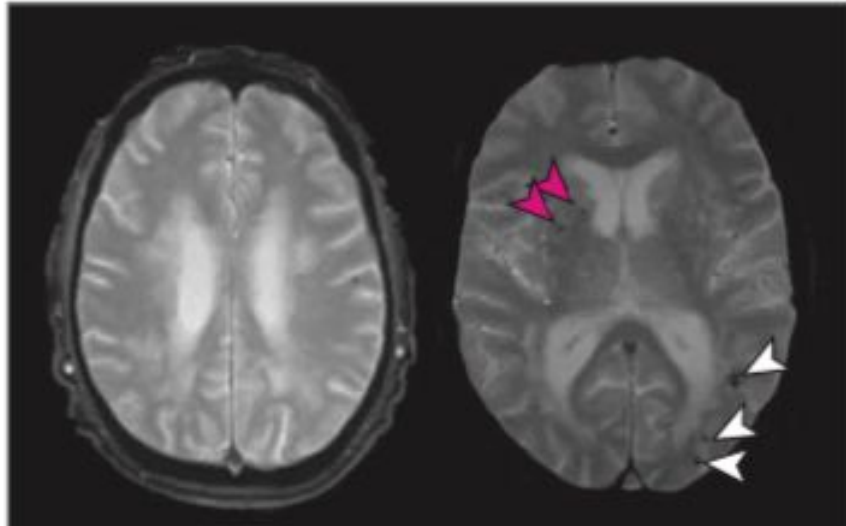
White matter hyperintensities



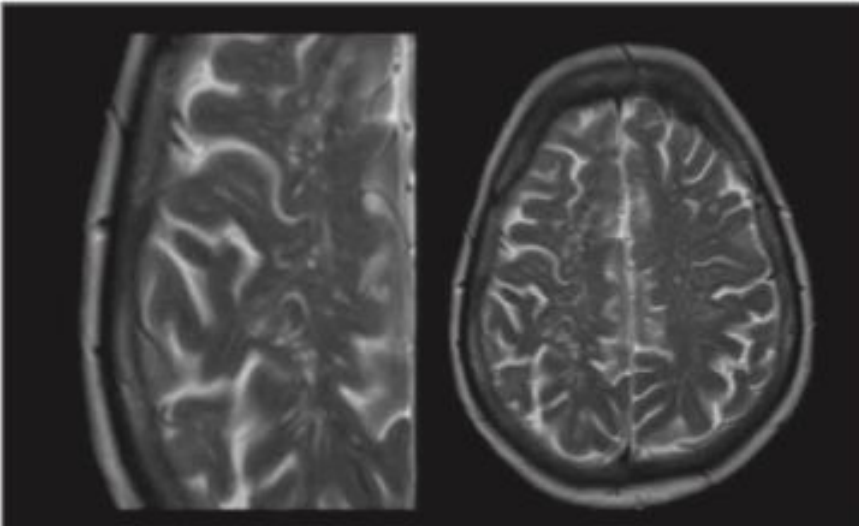
Brain infarcts



Cerebral microbleeds



Perivascular spaces

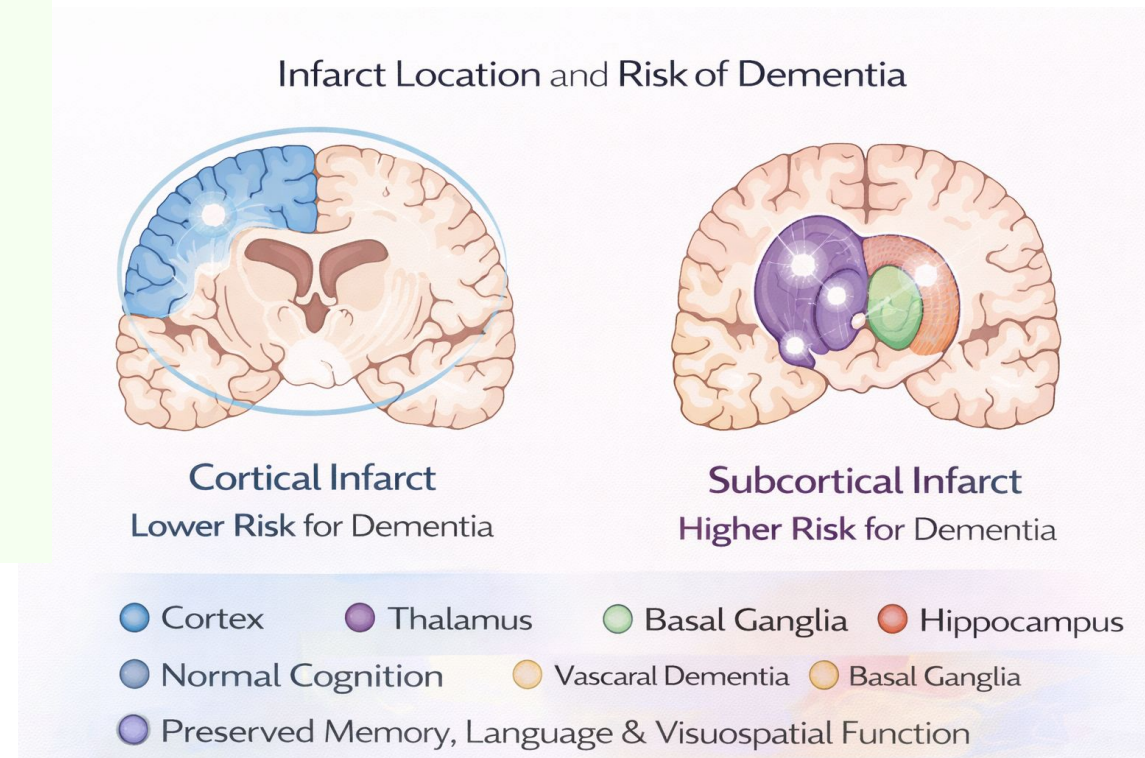


MRI markers

MRI marker	Pathophysiologic substrate	Stroke risk	Dementia risk	Mortality risk	Key clinical implication
White matter hyperintensities (WMH)	Chronic cerebral small vessel ischemia with demyelination and axonal loss	↑↑ Ischemic stroke and intracerebral hemorrhage	↑ All-cause dementia and Alzheimer disease	↑↑	Strongest imaging predictor of future stroke, cognitive decline, and death
MRI-defined covert brain infarcts (BI)	Silent subcortical or cortical infarction	↑↑ Ischemic stroke and intracerebral hemorrhage	↑ (modest)	↑	Identifies high vascular risk despite absence of clinical stroke
Cerebral microbleeds (CMB)	Hemorrhagic small vessel arteriopathy (hypertensive or amyloid-related)	↑ Ischemic and hemorrhagic stroke	No consistent association	↑	Signals combined ischemic–hemorrhagic risk
Perivascular spaces (PVS)	Small vessel disease with impaired	↑ (limited evidence)	↑ (emerging evidence)	↑ (vascular death)	Emerging biomarker requiring further validation

Stroke Subtype and Clinical Outcomes at 9 Years After Lacunar or Mild Cortical Ischemic Stroke

Garcia DJ: Neurology 2025
20;105(5):e214018.



Predictor	Odds ratio	95% CI	<i>p</i> Value
Dementia diagnosis			
Stroke subtype (lacunar)	0.85	0.352–2.080	0.73
Age	1.08	1.030–1.130	0.001

Cox Proportional Hazards Model Results for 25-year Incident Dementia by Infarct Group

Sullivan K, J Alzheimers Dis. 2023;91(2):543–549.

	Hazards Ratio	p
Infarct-Free	-	-
Smaller Infarcts Only <3 mm	1.22	0.479
Single Larger Infarct $\geq 3\text{mm}$ but <20mm	1.22	0.306
Multiple Larger Infarcts	1.40	0.232
Smaller Infarcts + Single Larger Infarcts	2.60	0.006
Smaller Infarcts + Multiple Larger Infarcts	2.62	0.099

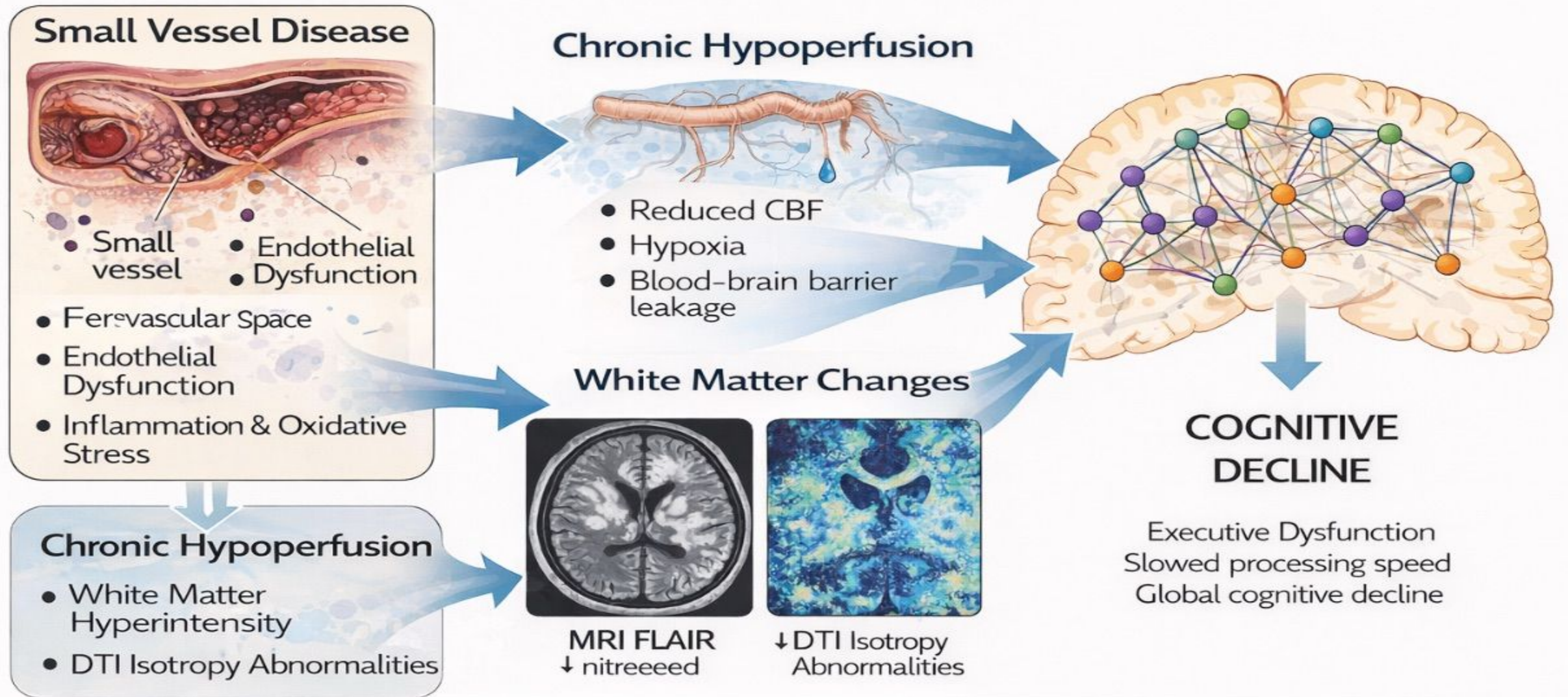
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Is infarction simply a marker?

Role of **Chronic Hypoperfusion** in **Small Vessel Disease** on **White Matter Changes** and **Cognition**



Chronic hypoperfusion due to small vessel disease induces white matter damage that disrupts network connections and impairs cognitive function.

Grading of severity of white matter lesions (Fazekas grades)

Periventricular White Matter Hyperintensities (PVWMH)

- **Grade 0**

No periventricular hyperintensities

- **Grade 1**

Caps or thin *pencil-like lining* around the ventricles

- **Grade 2**

Smooth *halo* of hyperintensity surrounding the ventricles

- **Grade 3**

Irregular periventricular hyperintensities extending into the deep white matter

Deep White Matter Hyperintensities (DWMH)

- **Grade 0**

No deep white matter lesions

- **Grade 1**

Punctate (small, focal) lesions

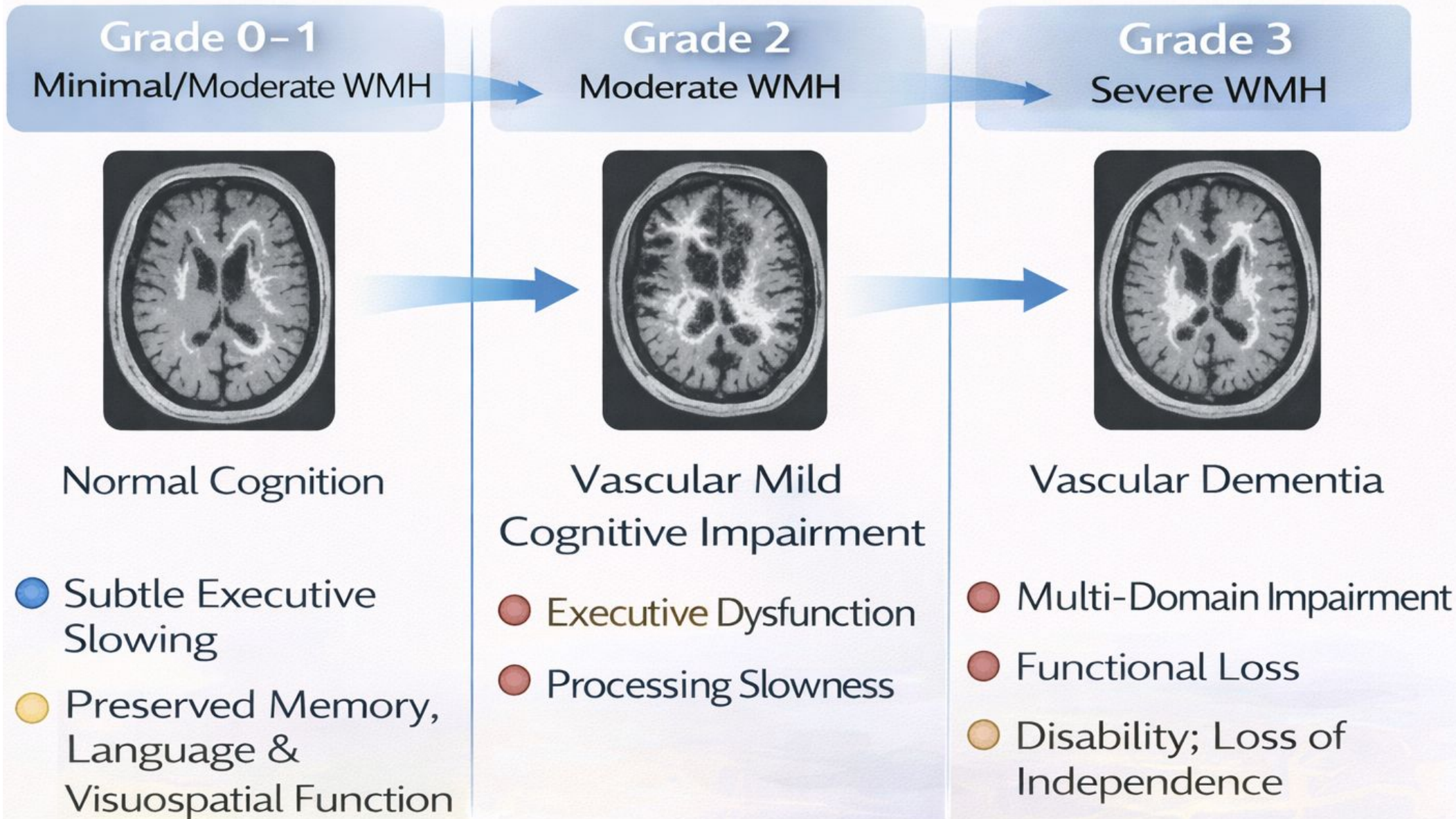
- **Grade 2**

Beginning confluence of lesions

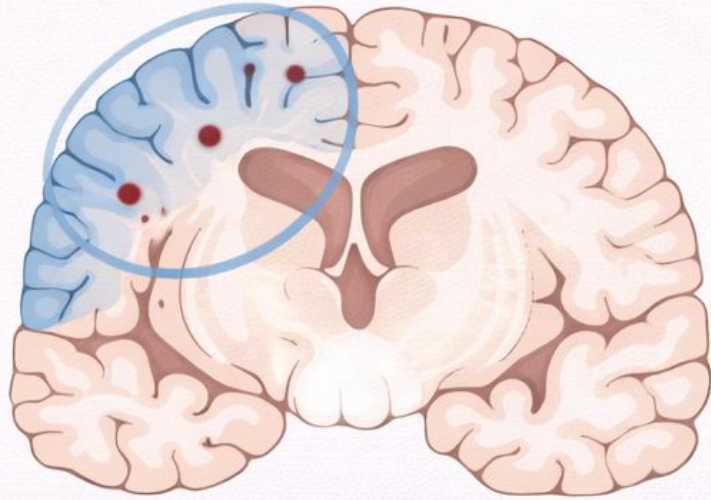
- **Grade 3**

Large confluent areas of hyperintensity

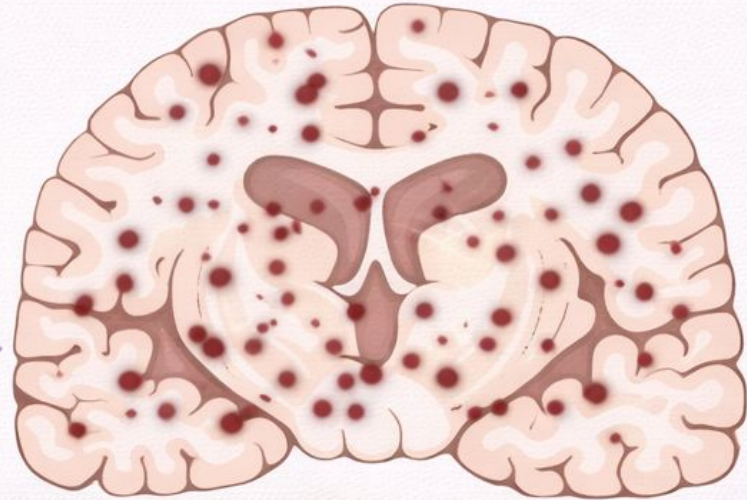
WMH Fazekas Grades and Cognitive Deficits



Cerebral Microbleeds and Risk of Vascular Cognitive Impairment and Dementia



Small Number
of Microbleeds
Lower Risk of VCI/VD



Numerous Microbleeds
Higher Risk of VCI/VD

● Cortic–Subcortical (Lobar)

● Deep Subcortical (Lacunar) Microbleeds

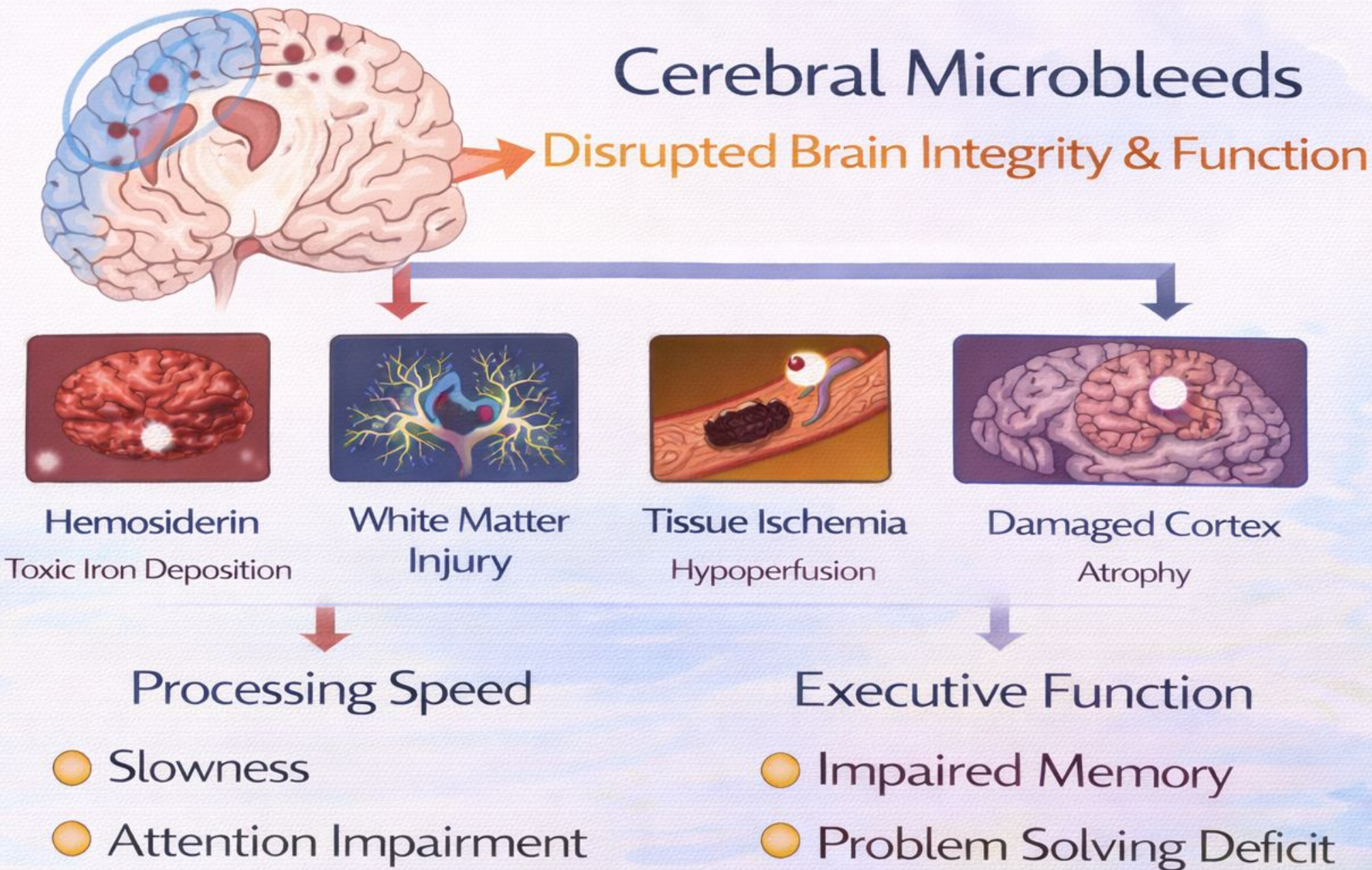
● Vascular Mild Cognitive Impairment

● Vascular Dementia

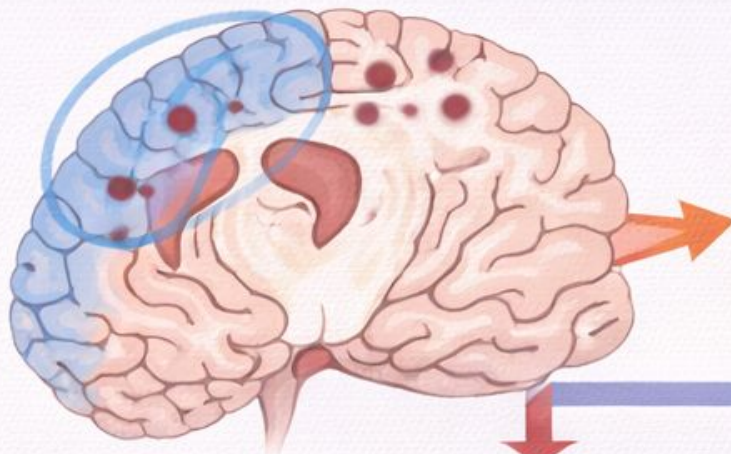
● Executive Dysfunction

● Processing Slowness

Cerebral Microbleeds and Cognitive Deficits

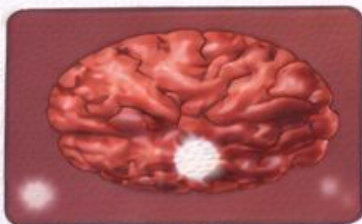


Cerebral Microbleeds and Cognitive Deficits



Cerebral Microbleeds

Disrupted Brain Integrity & Function



Hemosiderin

Toxic Iron Depo



White Matter



Tissue Ischemia



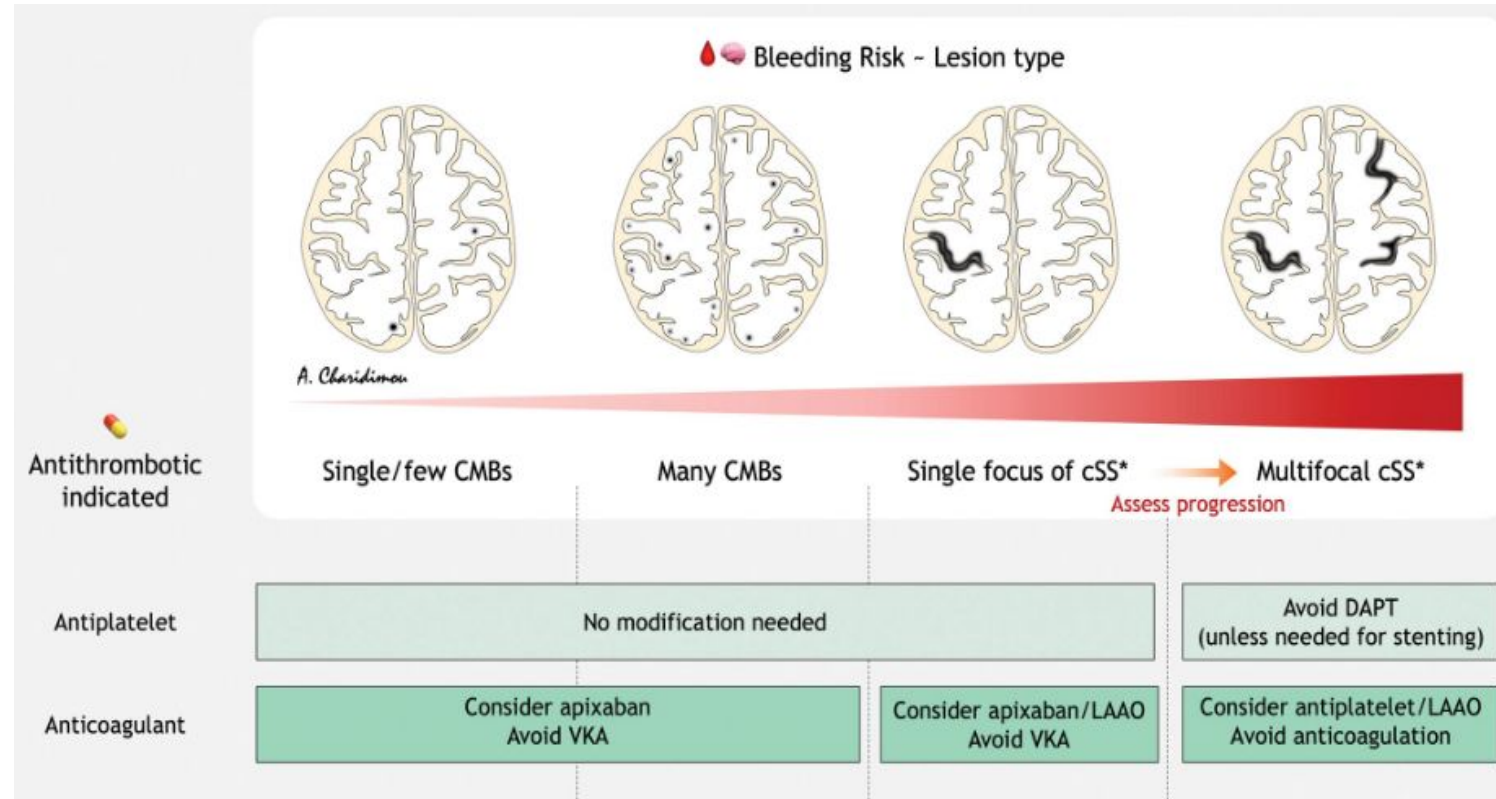
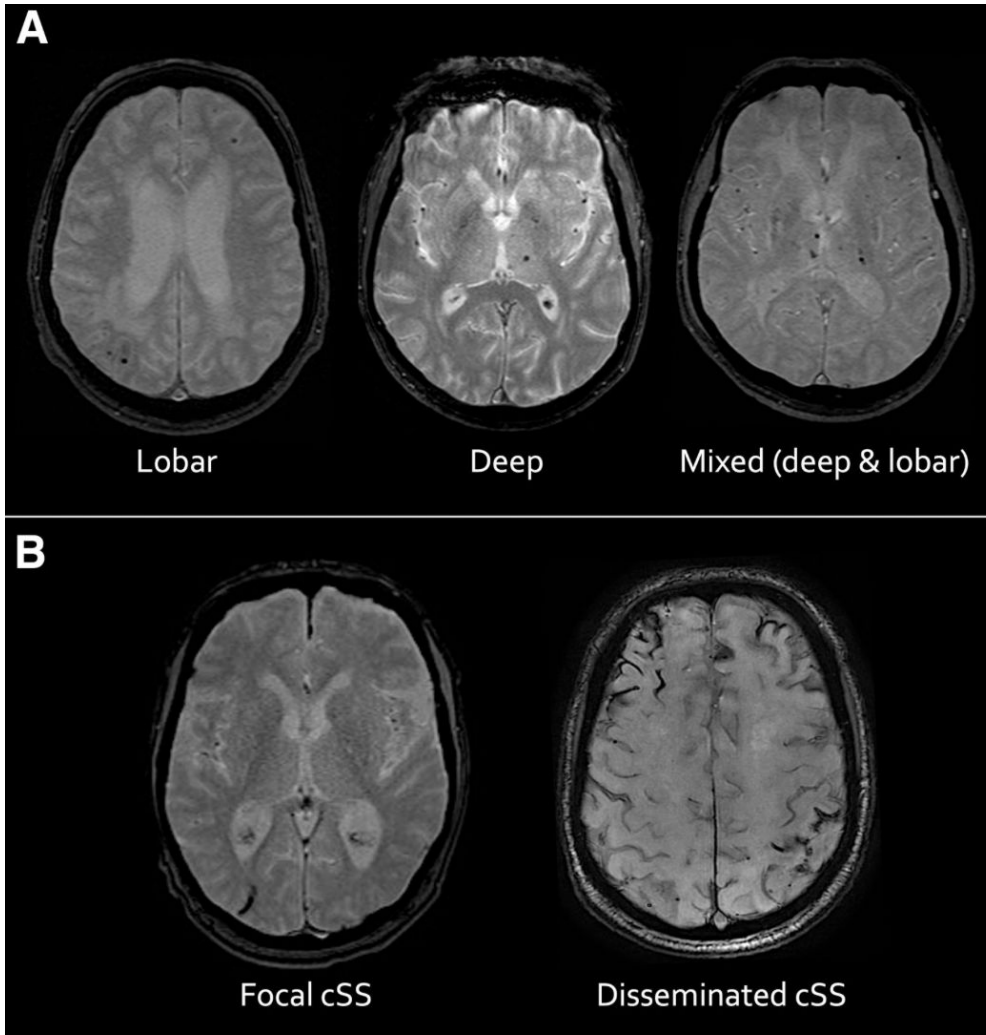
Damaged Cortex

Caution regarding antithrombotic medication

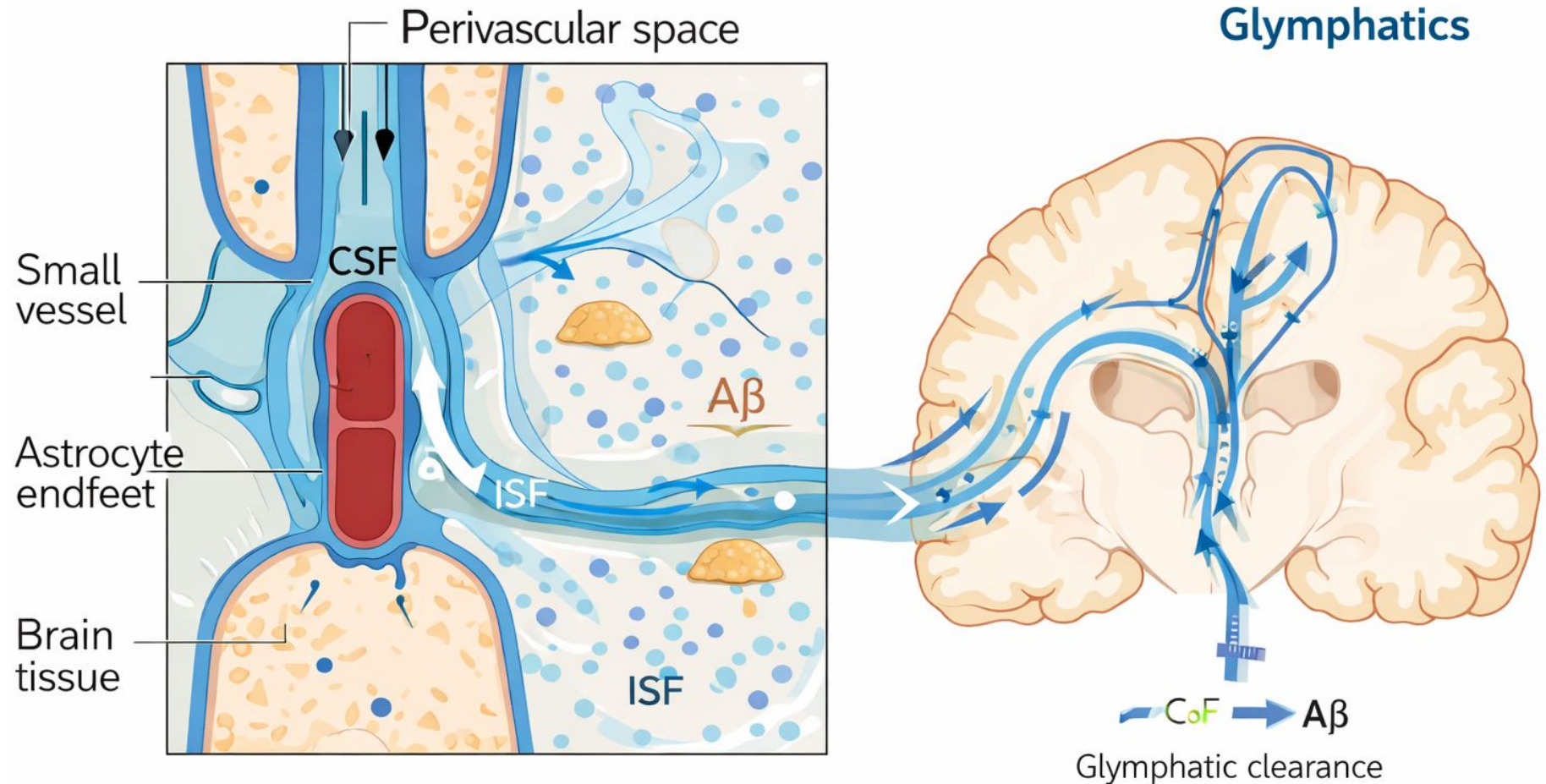
Proo

- Slowness
- Attention Impairment
- Impaired Memory
- Problem Solving Deficit

Antithrombotic treatment in patients with cerebral microbleeds (role of cortical superficial siderosis)



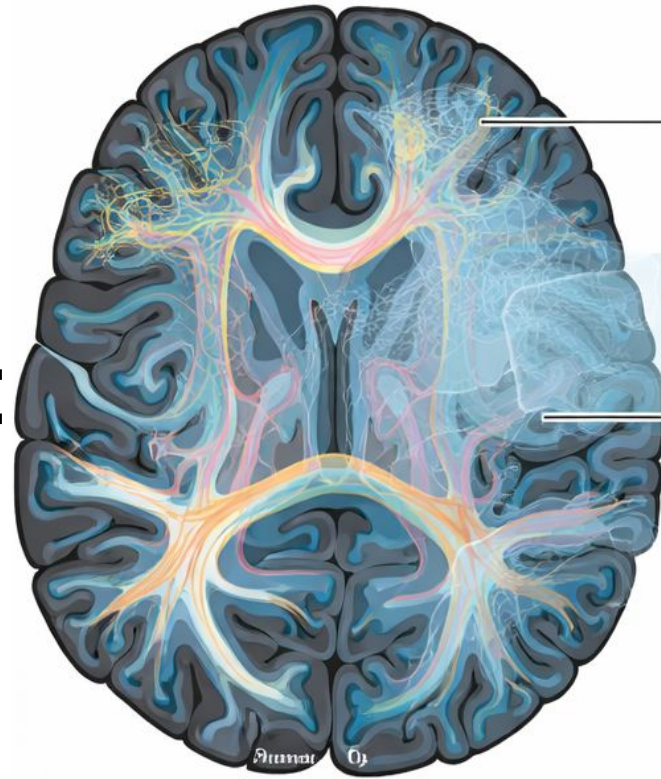
Perivascular space dilation may not be vascular related



Perivascular space-glymphatic clearance

DTI Abnormalities and Cognition

Diffusion tensor imaging abnormalities: the normal MRI VCI/VCD



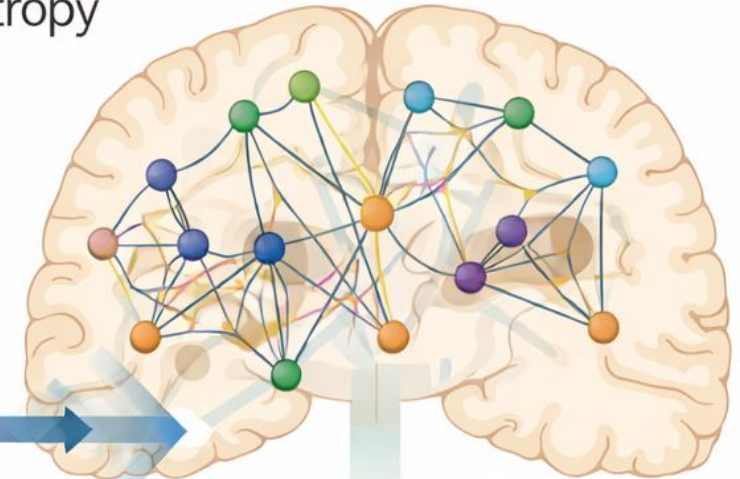
Reduced Fractional Anisotropy
↓ FA

Increased Mean Diffusivity
↑ MD

↑ ↓ water diffusion directionality

↑ ↓ isotropic water diffusion
increased extracellular water

White Matter Network Disconnection



COGNITIVE DECLINE

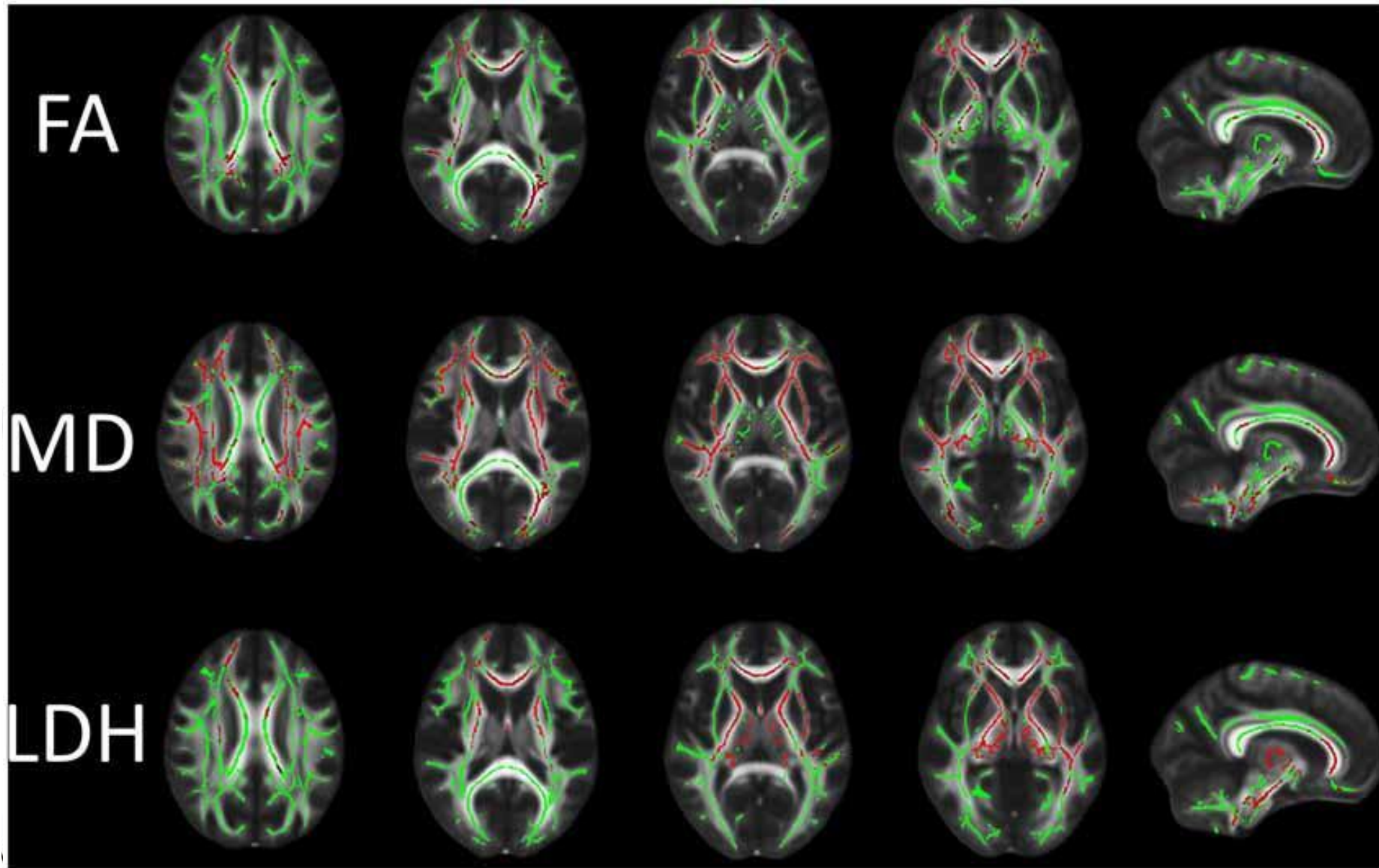
executive dysfunction
slowed processing speed
global cognitive decline

Network disconnection – not lesion count – is key to cognitive impairment in cerebral small vessel disease

Diffusion tensor imaging abnormalities the normal MRI VCI/VCD

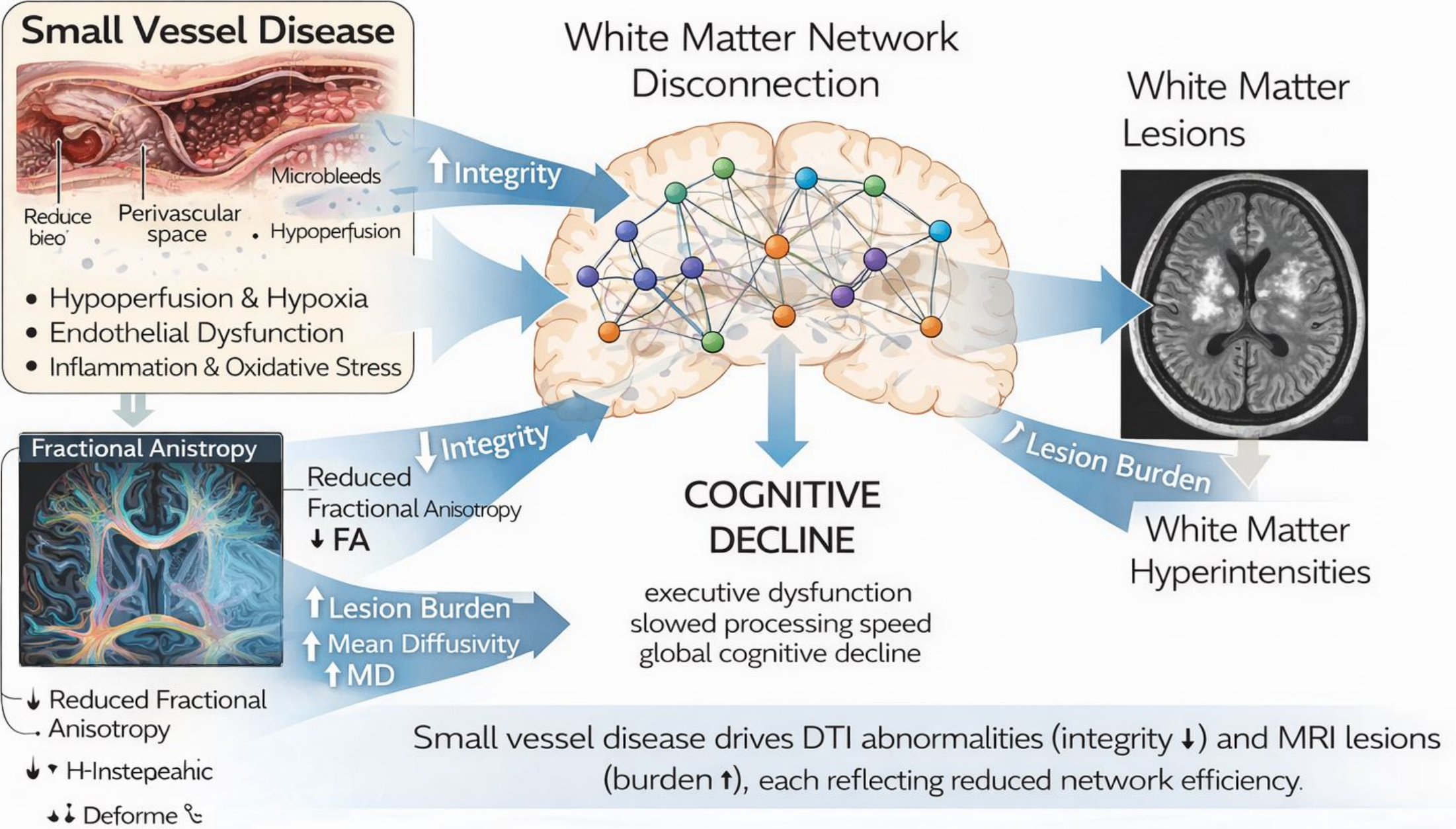
Green indicates the FA skeleton with a threshold of 0.2, which highlights the tracts used in the comparison. Red indicates the regions with decreased FA and LDH values and increased MD values in the VCIND group.

DTI Abnormalities and Cognition



vessel disease

Small Vessel Disease, DTI Abnormalities, and White Matter Lesions

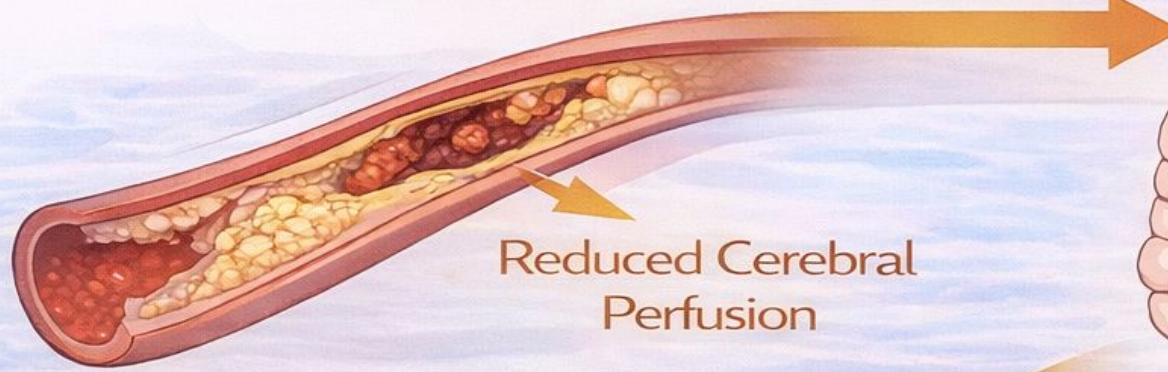


Cerebral Atherosclerosis and Alzheimer's Disease Progression

Mixed pathology

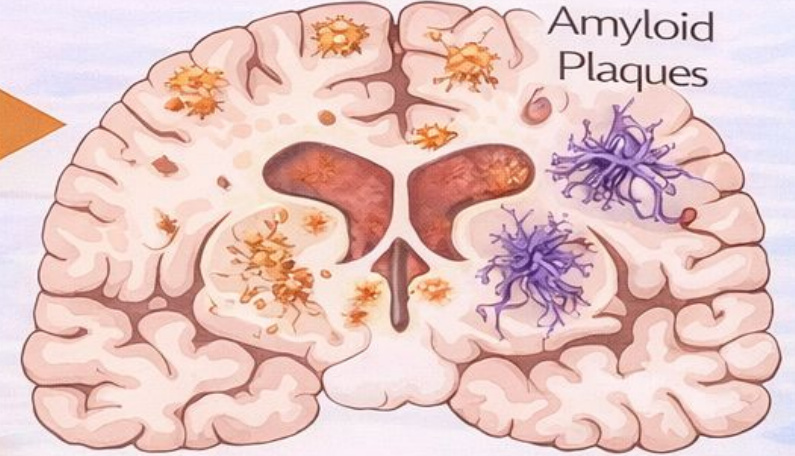
Cerebral Atherosclerosis

Reduced Cerebral Perfusion



Cerebral Atherosclerosis

- Atherosclerotic Plaque
- Carotid Stenosis
- Small Vessel Occlusion
- Endothelial Dysfunction



Alzheimer's-Type Pathology

- Amyloid Accumulation & Deposition
- Tau Phosphorylation & Tangles
- Neurodegeneration

Vascular Pathology

- Cerebral Atherosclerosis
- Carotid Stenosis
- Small Vessel Occlusion

Alzheimer's-Type Pathology

- Amyloid Accumulation & Deposition
- Tau Phosphorylation & Tangles
- Neurodegeneration

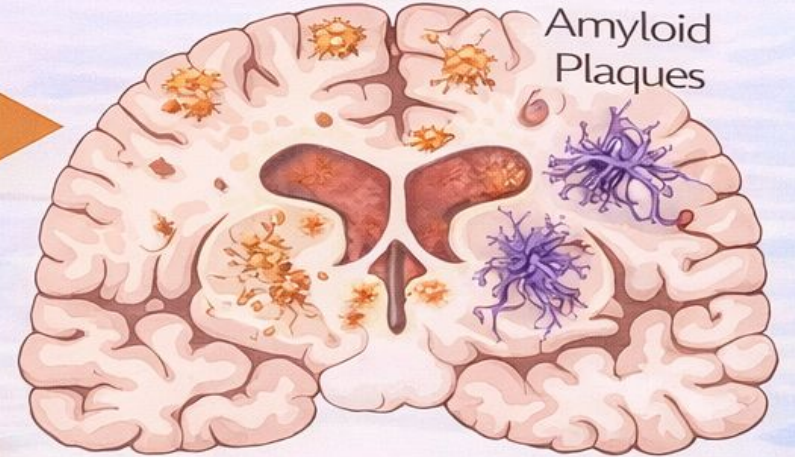
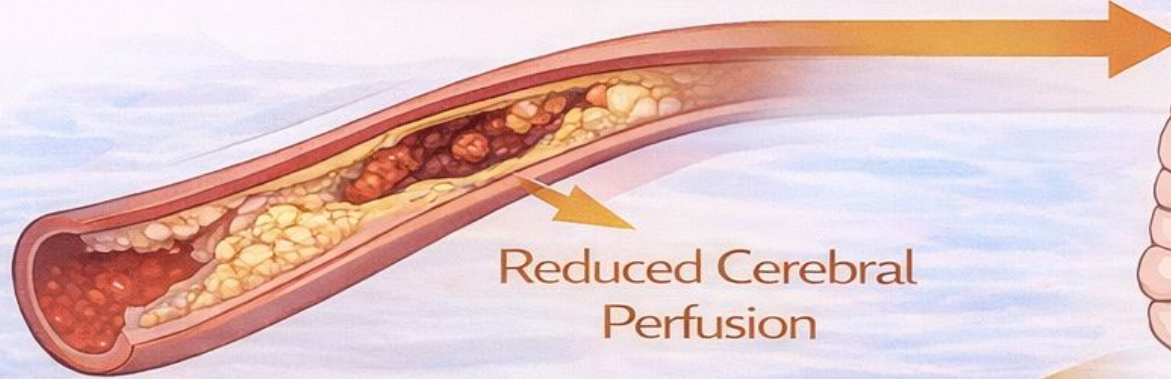
Cognitive Decline & Dementia

Cerebral Atherosclerosis and Alzheimer's Disease Progression

Mixed pathology

Cerebral Atherosclerosis

Reduced Cerebral Perfusion



Cerebral Atherosclerosis

- Atherosclerotic Plaque
- Carotid Stenosis
- Small Vessel Occlusion
- Embolism

Alzheimer's-Type Pathology

- Amyloid Accumulation & Deposition
- Tau Phosphorylation & Tangles
- Neurodegeneration

Cholinergic medication may have role

Vascular

- Cerebral Atherosclerosis
- Carotid Stenosis
- Small Vessel Occlusion

Pathology

- Amyloid Accumulation & Deposition
- Tau Phosphorylation & Tangles
- Neurodegeneration

Cognitive Decline & Dementia

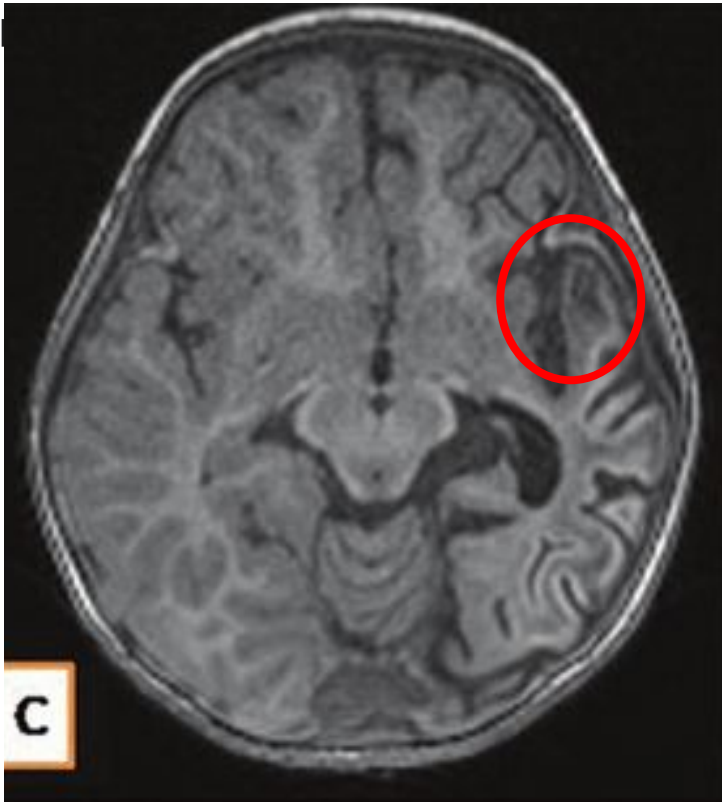


Neuroanatomical correlates of atrial fibrillation

Qureshi AI. J Vasc Int Neurol. 2014 Dec;7(5):18–23.

Patients with atrial fibrillation have an increased risk of cognitive decline in the absence of ischemic stroke

Patients with atrial fibrillation have an increased risk of cognitive decline in the absence of ischemic stroke. 157–63.



Entorhinal Cortex ↓
Right: $p = 0.01$
Left: $p = 0.01$

MMSE Correlation:
Left $r^2 = 0.50$ ($p = 0.001$)
Right $r^2 = 0.30$ ($p = 0.05$)

Middle Temporal Lobe ↓
Right: $p = 0.04$
Left: $p = 0.001$

MMSE Correlation:
Left $r^2 = 0.10$ ($p = 0.50$)
Right $r^2 = 0.20$ ($p = 0.20$)
Not significant

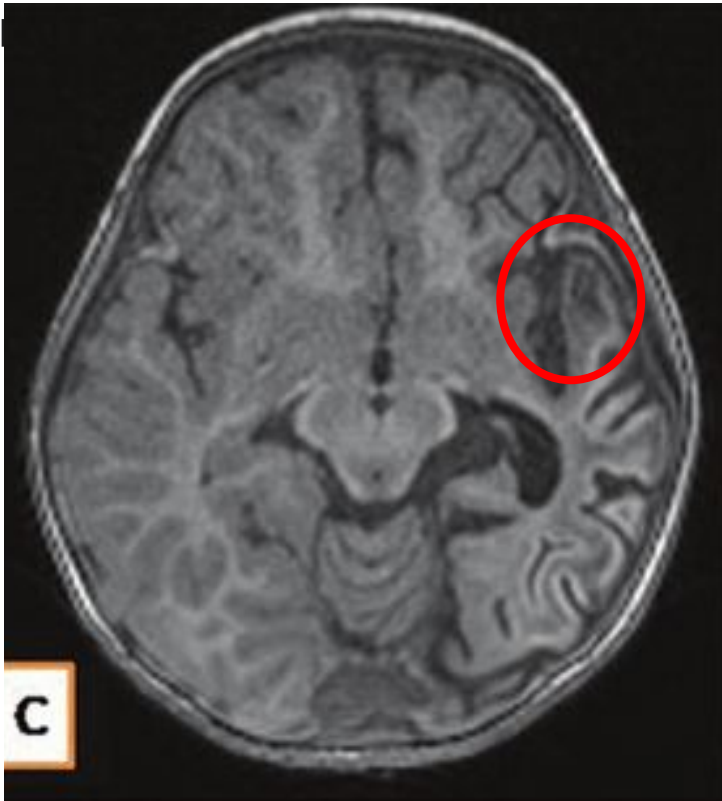
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Is atrial fibrillation a brain disease?

Patients with atrial fibrillation have an increased risk of cognitive decline in the absence of ischemic stroke. 157–63.



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Left $r^2 = 0.10$ ($p = 0.50$)
Right $r^2 = 0.20$ ($p = 0.20$)
Not significant

Conclusions

- ❑ Increasing emphasis on executive function deficits as early markers (precedes memory deficits).
- ❑ Increasing emphasis on infarct independent subcortical dysfunction.
- ❑ Some of these dysfunctions are not visible on routine MRIs (require diffusion tensor imaging).
- ❑ Overlapping mechanisms some of which are not vascular.
- ❑ New treatment strategies would have to address the new pathophysiologic and diagnostic paradigms.

Thank you ! Zeenat Qureshi Stroke Institutes 2025

Turkish National Stroke
Thrombectomy Registry



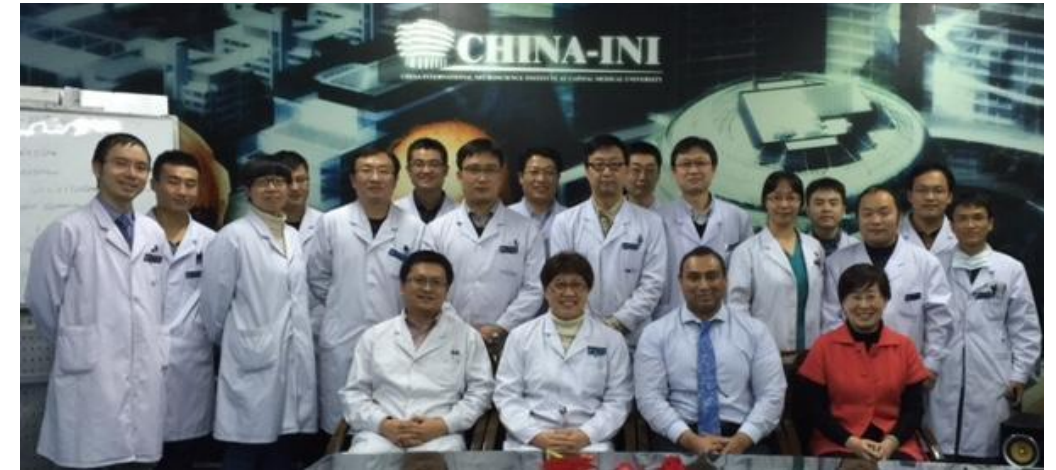
St. Cloud, Minnesota, USA



Firat University, Elazig, Turkey



**Donka National Hosp, Conakry,
Guinea**



Xuan Wu Hosp, Beijing, China

Neurocognitive Recovery Following Revascularization

Evidence for Hemodynamic Restoration in Intracranial and Carotid
Artery Stenotic Disease

ASN Annual Meeting, Puerto Rico, Jan 2026

Rami Fakhri, MD
Neuroendovascular Surgery
Centra Medical Group
Lynchburg, VA

Pathophysiological Basis

The Hemodynamic-Cognitive Axis

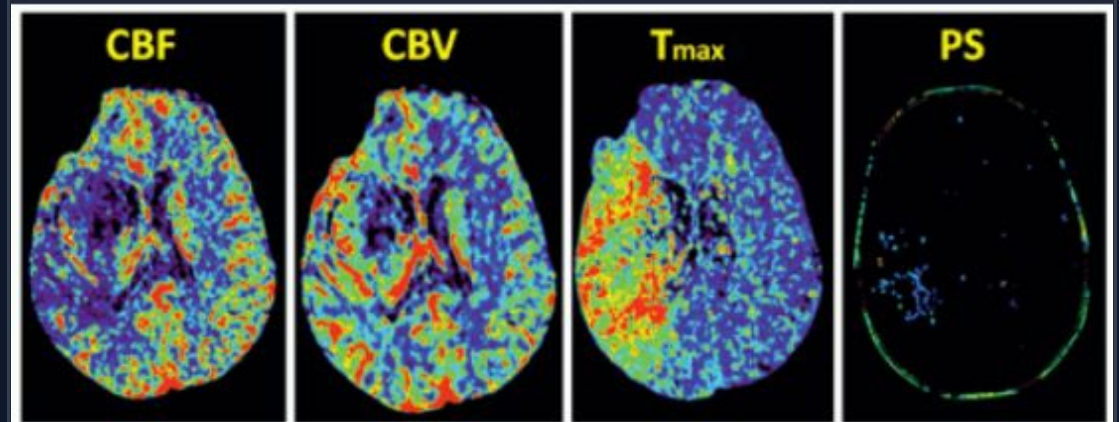
HEMODYNAMICS & COGNITION

Chronic Hypoperfusion

Reduced Cerebral Blood Flow (CBF) drives neurocognitive decline, independent of infarct.

Functional Dormancy: Neurons remain viable but lack the metabolic energy for complex network participation.

Restoration of flow via recanalization acts as a metabolic "re-awakening".



MECHANISMS OF COGNITIVE RECOVERY



Metabolic

Enhancement of glucose and oxygen delivery to the neurovascular unit, restoring ATP levels.



Anti-Inflammatory

Reperfusion reduces chronic microglial activation and neuroinflammatory cytokine signaling.



Connectivity

Stabilization of the Default Mode Network (DMN) and increased connectivity

ICAD and ECAD

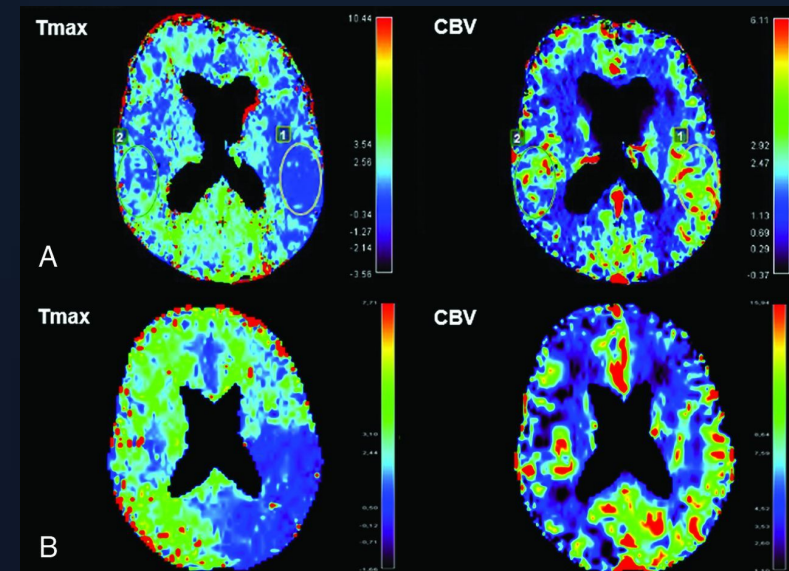
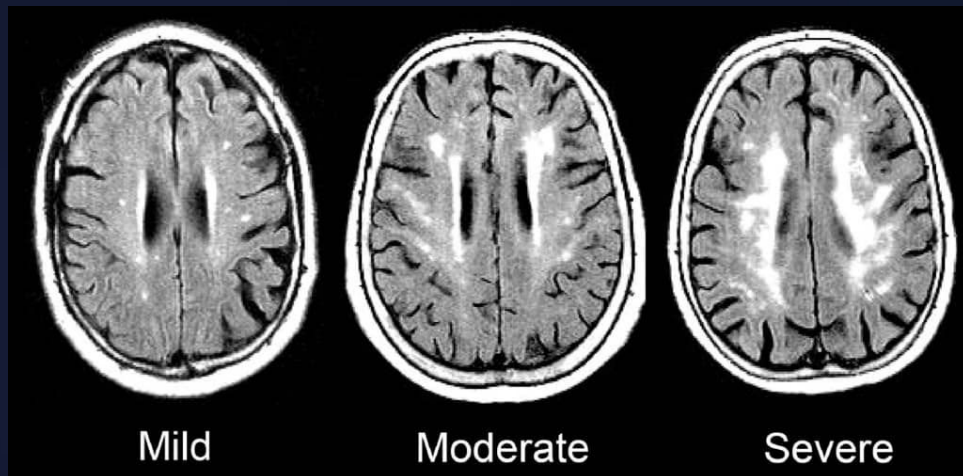
The Cognitive Burden

THE BURDEN OF ICAD

- Natural history of patients with ICAD: transient ischemic attack (TIA), recurrent ischemic stroke, **chronic hypoperfusion** (causing cumulative white matter disease and gradual cognitive worsening).
- Even without history of stroke, patients with high-grade stenosis (70-99%) perform significantly lower on standard memory tests than age-matched controls (*Yin et al, Brain Behav, 2024*).
- Cerebral hypoperfusion affects cognitive domains requiring **high metabolic demand**: executive function, processing speed, memory, and attention (*Xie et al, Neuroreport, 2021*).

THE BURDEN OF ICAD

- Patients with **decreased cerebral perfusion** showed significant **impairment in global cognition**, memory, psychomotor speed, executive function, and frontal lobe function. **Anterior circulation** stenosis and **moderate-to-severe stenosis** similarly impaired these domains (*Xie et al., Neuroreport, 2021*).



| SAMMPRIS TRIAL (2011)

- The Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS): 30-day stroke or death rate of 14.7% in the stenting group versus 5.8% in the medical group (P=0.002).
- A recent post-hoc analysis evaluated long-term cognitive outcomes using the MoCA test.
 - The stenting group showed reduced odds of achieving a normal MoCA score (≥ 26) compared to the medical group (OR 0.54, 95% CI 0.29 to 1.00, P=0.050).
 - The stenting group's cognitive trajectory was hindered by periprocedural micro-infarcts and perforator occlusions. (*Jaro et*

| Carotid Artery Revascularization

- Quantitative flow MRI studies show that post-CAS **flow can be 60% higher** than pre-CAS levels in patients with $\geq 90\%$ stenosis ($p < 0.050$). Cognitive responses correlated with these flow increases (*Kaur et al, Medicina, 2025*)
- A systematic review identified 7 studies (661 participants) examining cognition and CBF (*Kwok et. al, Clinical Therapeutic, 2023*) .
 - Demonstrated **improvement in cognitive domains** following revascularization, improvement in CBF, and correlation between CBF changes and cognitive improvement. The strongest benefits occurred in patients with the most significant baseline perfusion deficits.

| Carotid Artery Revascularization

- A 2025 retrospective cohort study analyzed approx 500K patients with asymptomatic carotid stenosis from U.S. insurance claims (*Vitali et. al, Alzheimer's and Dementia, 2025*)

- After propensity score matching, CEA was associated with **significantly lower Alzheimer's disease risk** (RR=0.93, p0.05) and similar trends for non-AD dementia. Notably, CAS showed no significant protective effect, possibly related to higher microembolization rates.

Imaging Correlates of Cognitive Improvement

Imaging Modality	Finding Pre-Revascularization	Finding Post-Revascularization
CTP	Prolonged MTT and Tmax	Normalization of MTT/Tmax; Improved CBF
Quantitative Flow MRI	Reduced absolute flow in target vessel	60% increase in flow (if stenosis $\geq 90\%$)
PET / MRI	Reduced FDG uptake; impaired white matter integrity	Improved energy metabolism and white matter structure

THE "ASYMPTOMATIC" MYTH







Silent Cognitive Decay

Patients labeled "asymptomatic" due to absence of stroke frequently suffer from high-grade hemodynamic deficits.

Clinical Finding. CAS significantly increases attention scores at 3 months post-op. Revascularization targets the white matter tract integrity that is compromised by chronic low-flow states.

DOMAIN SPECIFIC CHANGES


-  **Processing Speed:** Significant improvements seen in CAS patients, linked to stabilization of white matter tracts in the corona radiata.
-  **Delayed Recall:** Selective improvements in symptomatic cohorts, likely due to restoration of perfusion to hippocampal afferents.
-  **Visuospatial:** Improvements noted in both CAS and CEA, primarily in patients with baseline impairment.
-  **Executive Function:** Dependent on hemodynamic reserve; highest gains seen in patients with pre-op steal phenomenon.

VERTEBROBASILAR Angioplasty and Stenting

Metric	Pre-Surgery	1-Month Post	12-Month Post
Total MoCA	24.92 ± 3.06	26.54 ± 2.45	27.81 ± 1.90
Visuospatial	Impaired	Improved	Marked Gain
Delayed Recall	Impaired	Moderate Gain	Significant Gain

CONCLUSION: PRACTICAL ALGORITHM

Screen	Image	Treat	Monitor
● MoCA for all >70% stenosis Even if "asymptomatic"	● CTP/Tmax identifying hypoperfusion Prioritize treatment for patients with highest hypoperfusion deficits	● Submaximal Angioplasty / Stenting + BMM Delay treatment 2 weeks Aggressive MM	● 12m Cognitive Follow-up.



"We are entering an era of Functional Neurointervention, where success is measured by the quality of a life saved, not just the absence of a stroke."