

La Demenza Vascolare

Luca ROZZINI

Dementia is the clinical syndrome characterised by acquired losses of cognitive and emotional abilities severe enough to interfere with daily functioning and the quality of life.

DS Geldmacher, PJ Whitehouse

N Engl J Med, 335:330-336, 1996

Criteria diagnostici per la Demenza

A. Dimostrazione obiettiva della compromissione della memoria a breve e a lungo termine. Il deficit della memoria a breve termine (incapacità di apprendere nuove informazioni) può essere indicato dalla incapacità a ricordare tre oggetti dopo cinque minuti. Il difetto della memoria a lungo termine (incapacità di ricordare informazioni conosciute in passato) può essere indicato dalla incapacità di ricordare notizie personali passate (p.e. cosa è accaduto ieri, il luogo di nascita, l'occupazione), o fatti di comune conoscenza (p.e. ex-Presidenti, date storiche).

B. Almeno uno dei seguenti elementi:

- 1) deficit del pensiero astratto, riscontrabile nell'incapacità a cogliere somiglianze e differenze fra parole correlate, nella difficoltà a definire parole e concetti, ed in altre prove simili;
- 2) deficit di giudizio critico, riscontrabile nella incapacità di fare progetti ragionevoli per affrontare problemi o questioni interpersonali, familiari, o collegate con il lavoro;
- 3) altre turbe delle funzioni corticali superiori, come afasia (disturbo del linguaggio), aprassia (incapacità di eseguire attività motorie nonostante l'integrità della comprensione e della motricità), agnosia (incapacità di riconoscere o identificare oggetti nonostante l'integrità delle funzioni sensitive), "aprassia costruttiva" (per esempio, incapacità a ricopiare figure tridimensionali e a mettere insieme dei blocchi, o a ordinare dei bastoncini secondo schemi prestabiliti);
- 4) modificazioni di personalità, come, per esempio, alterazione o accentuazione di tratti premorbose.

C. Il disturbo in A e B interferisce significativamente con il lavoro, o con le attività sociali usuali, o con le relazioni interpersonali.

D. Non si verifica esclusivamente nel corso di Delirium.

E. Uno dei seguenti elementi:

- 1) dimostrazione fondata sull'anamnesi, sull'esame clinico, sugli esami di laboratorio, di un fattore (o fattori) specifico eziologicamente correlato al disturbo;
- 2) presunzione, in assenza di tale dimostrazione, di un fattore eziologico organico se il disturbo non può essere attribuito ad alcun disturbo mentale non-organico p.e. Depressione Maggiore responsabile di deficit cognitivo.

I criteri diagnostici della demenza (DSM-IV)

- Presenza di **deficit cognitivi multipli** caratterizzati da:
 - 1) Compromissione **mnesica** (deficit dell'abilità ad apprendere nuove informazioni o a richiamare informazioni precedentemente apprese) e almeno
 - 2) uno o più deficit cognitivi: **afasia** (disturbo del linguaggio); **aprassia** (incapacità ad eseguire attività motorie nonostante l'integrità della comprensione e della motricità); **agnosia** (incapacità a riconoscere o identificare oggetti in assenza di deficit sensoriali); **deficit del pensiero astratto e della capacità critica**
- I deficit cognitivi interferiscono significativamente nel lavoro, nelle attività sociali, nelle relazioni con gli altri, e determinano un peggioramento significativo rispetto al precedente livello funzionale

The ICD-10 Classification of Mental and Behavioural Disorders

World Health Organization, Geneva, 1992

- Dementia is a syndrome due to disease of the brain, **usually of a chronic or progressive nature**, in which there is disturbance of multiple higher cortical functions, **including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgment**. Consciousness is not clouded. Impairments of cognitive function are commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behaviour, or motivation. This syndrome occurs in Alzheimer's disease, in cerebrovascular disease, and in other conditions primarily or secondarily affecting the brain.
- Dementia produces **an appreciable decline in intellectual functioning, and usually some interference with personal activities of daily living, such as washing, dressing, eating, personal hygiene, excretory and toilet activities**. How such a decline manifests itself will depend largely on the social and cultural setting in which the patient lives. Changes in role performance, such as lowered ability to keep or find a job, should not be used as criteria of dementia because of the large cross-cultural differences that exist in what is appropriate, and because there may be frequent, externally imposed changes in the availability of work within

Revised Criteria for Mild Cognitive Impairment: Validation within a Longitudinal Population Study

Sylvaine Artero^a Ronald Petersen^c Jacques Touchon^b Karen Ritchie^a

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The criteria for MCI are those previously proposed by Petersen et al.

- (i) presence of a subjective memory complaint;
- (ii) Preserved general intellectual functioning (as estimated in this study by performance on a vocabulary test);
- (iii) demonstration of a memory impairment by cognitive testing;
- (iv) intact ability to perform activities of daily living;
- (v) absence of dementia.

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- (i) presence of a cognitive complaint from either the subject and/or a family member;
- (ii) absence of dementia;
- (iii) change from normal functioning;
- (iv) decline in any area of cognitive functioning;
- (v) preserved overall general functioning but possibly with increasing difficulty in the performance of activities of daily living.

La Demenza Vascolare

Vascular dementia: Diagnostic criteria for research studies

Report of the NINDS-AIREN International Workshop*

G.C. Román, MD; T.K. Tatemichi, MD; T. Erkinjuntti, MD; J.L. Cummings, MD; J.C. Masdeu, MD; J.H. Garcia, MD; L. Amaducci, MD; J.-M. Orgogozo, MD; A. Brun, MD; A. Hofman, MD, PhD; D.M. Moody, MD; M.D. O'Brien, MD; T. Yamaguchi, MD; J. Grafman, PhD; B.P. Drayer, MD; D.A. Bennett, MD; M. Fisher, MD; J. Ogata, MD; E. Kokmen, MD; F. Bermejo, MD; P.A. Wolf, MD; P.B. Gorelick, MD; K.L. Bick, PhD; A.K. Pajean, MD; M.A. Bell, DPhil; C. DeCarli, MD; A. Culebras, MD; A.D. Korczyn, MD; J. Bogousslavsky, MD; A. Hartmann, MD; and P. Scheinberg, MD

...In the Italian study VaD was more prevalent than AD in subjects 70 years old and older.

Rocca et al.

DSM-III criteria for the diagnosis of multi-infarcts dementia

- A. Demenza
- B. Deterioramento a gradini (cioè non uniformemente progressivo) con distribuzione dei deficit a scacchiera (cioè con interessamento di certe funzioni ma non di altre) all'inizio del decorso
- C. Sintomi e segni neurologici focali (per esempio aumento dei riflessi tendinei profondi, Babinski, paralisi pseudobulbare, alterazioni della marcia, debolezza di un arto ecc.)
- D. Dimostrazione, fondata sull'anamnesi, sull'esame clinico, o sugli esami di laboratorio, di una vasculopatia cerebrale eziologicamente correlata al disturbo.

DSM-IV-R criteria for the diagnosis of vascular dementia

A. The development of multiple cognitive deficits manifested by both:

1. Memory impairment (impaired ability to learn new information or to recall previously learned information)
2. One or more of the following cognitive disturbances:
 - (a) aphasia (language disturbance)
 - (b) apraxia (impaired ability to carry out motor activities despite intact motor function)
 - (c) agnosia (failure to recognize or identify objects despite intact sensory function)
 - (d) disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)

DSM-IV criteria for the diagnosis of vascular dementia

- B. The cognitive deficits in criteria A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.
- C. Focal neurological signs and symptoms (e.g., exaggeration of deep tendon reflexes, extensor plantar response, pseudobulbar palsy, gait abnormalities, weakness of an extremity) or laboratory evidence indicative of cerebrovascular disease (e.g., multiple infarctions involving cortex and underlying white matter) that are judged to be etiologically related to the disturbance.
- D. The deficits do not occur exclusively during the course of a delirium.

Criteria OMS per la diagnosi di demenza vascolare

(Classificazione Internazionale delle Malattie, ICD-10)

- deficit della memoria soprattutto quella a breve termine presente da almeno sei mesi;
- capacità di giudizio e ideazione relativamente conservate;
- relativa conservazione della personalità e dello stato di coscienza;
- storia di ipertensione arteriosa;
- danno cerebrale focale (in particolare, nelle forme sottocorticali, a livello della sostanza bianca sottocorticale degli emisferi cerebrali)

NEUROLOGY

**Vascular dementia: Diagnostic criteria for research studies: Report of the
NINDS-AIREN International Workshop**

G. C. Román, T. K. Tatemichi, T. Erkinjuntti, J. L. Cummings, J. C. Masdeu, J. H. Garcia, L. Amaducci, J.-M. Orgogozo, A. Brun, A. Hofman, D. M. Moody, M. D. O'Brien, T. Yamaguchi, J. Grafman, B. P. Drayer, D. A. Bennett, M. Fisher, J. Ogata, E. Kokmen, F. Bermejo, P. A. Wolf, P. B. Gorelick, K. L. Bick, A. K. Pajeau, M. A. Bell, C. DeCarli, A. Culebras, A. D. Korczyn, J. Bogousslavsky, A. Hartmann and P. Scheinberg
Neurology 1993;43;250-

Dementia syndrome

It was decided to adopt here the definition of dementia from the 10th revision of *The Neurological Adaptation of the International Classification of Diseases* (ICD-10 NA).

Diagnosis of dementia requires the presence of a decline in memory and intellectual abilities that causes impaired functioning in daily living.

“Impaired functioning in daily living” was accepted as a criterion for epidemiologic studies of VaD because it would ensure that the changes are more than incidental and would increase specificity. Chui et al. also included “interference with the conduct of the patient’s customary affairs of life” as a requirement for the diagnosis of ischemic VaD.

The impairment should be due to cognitive deficits and not to physical handicaps produced by stroke.

Dementia syndrome

For the diagnosis of VaD, cognitive decline should be demonstrated by **loss of memory and deficits in at least two other domains**, including orientation, attention, language-verbal skills, visuospatial abilities, calculations, executive functions, motor control, praxis, abstraction, and judgment.

The criteria for the clinical diagnosis of **probable** vascular dementia include **all** of the following:

1. *Dementia* defined by cognitive decline from a

previously higher level of functioning and manifested by impairment of memory and of **two or more cognitive domains** (orientation, attention, language, visuospatial functions, executive functions, motor control, and praxis), preferably established by clinical examination and documented by neuropsychological testing; deficits should be severe enough to interfere with activities of daily living not due to physical effects of stroke alone.

2. Cerebrovascular disease, defined by the presence of focal signs on neurologic examination, such as hemiparesis, lower facial weakness, Babinski sign, sensory deficit, hemianopia, and dysarthria consistent with stroke (with or without history of stroke), and

evidence of relevant CVD by brain imaging (CT or MRI) including multiple large-vessel infarcts or a single strategically placed infarct (angular gyrus, thalamus, basal forebrain, or PCA or ACA territories), as well as multiple basal ganglia and white matter lacunes or extensive periventricular white matter lesions, or combinations thereof.

Table 1. Brain imaging lesions associated with vascular dementia

I. Topography

Radiologic lesions associated with dementia include ANY of the following or combinations thereof:

1. Large-vessel strokes in the following territories:

Bilateral anterior cerebral artery

Posterior cerebral artery, including paramedian thalamic infarctions, inferior medial temporal lobe lesions

Association areas: parietotemporal, temporo-occipital territories (including angular gyrus)

Watershed carotid territories: superior frontal, parietal regions

2. Small-vessel disease:

Basal ganglia and frontal white matter lacunes

Extensive periventricular white matter lesions

Bilateral thalamic lesions

II. Severity

In addition to the above, relevant radiologic lesions associated with dementia include:

Large-vessel lesions of the dominant hemisphere

Bilateral large-vessel hemispheric strokes

Leukoencephalopathy involving at least $\frac{1}{4}$ of the total white matter

Although volume of lesion is weakly related to dementia, an additive effect may be present. White matter changes observed only on T₂ MRI but not on T₁ MRI or CT may not be significant. Absence of vascular lesions on brain CT/MRI *rules out* probable vascular dementia.

3. A relationship between the above two disorders, manifested or inferred by the presence of one or more of the following:

(a) onset of dementia within 3 months following a recognized **stroke**;

(b) abrupt deterioration in cognitive functions; or fluctuating, stepwise progression of cognitive deficits.

Clinical features consistent with the diagnosis of **probable** vascular dementia include the following:

- (a) Early presence of a gait disturbance (small step gait or marche a petits pas, or magnetic, apraxic-ataxic or parkinsonian gait);
- (b) history of unsteadiness and frequent, unprovoked falls;
- (c) early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease;
- (d) pseudobulbar palsy; and
- (e) personality and mood changes, abulia, depression, emotional incontinence, or other subcortical deficits including psychomotor retardation and abnormal executive function.

Clinical diagnosis of **possible** vascular dementia may be made in the presence of dementia with focal neurologic signs in patients in whom brain imaging studies to confirm **definite CVD are missing**; or in the absence of clear temporal relationship between dementia and stroke; or in patients with subtle onset and variable course (plateau or improvement) of cognitive deficits and evidence of relevant CVD.

NEUROLOGY

Criteria for the diagnosis of ischemic vascular dementia proposed by the State of California Alzheimer's Disease Diagnostic and Treatment Centers
H. C. Chui, J. I. Victoroff, D. Margolin, W. Jagust, R. Shankle and R. Katzman
Neurology 1992;42:473-

Dementia is a deterioration from a known or estimated prior level of intellectual function sufficient to **interfere broadly with the conduct of the patient's customary affairs of life**, which is not isolated to a single narrow category of intellectual performance, and which is independent of level of consciousness.

This deterioration should be supported by historical evidence and documented by either bedside mental status testing or ideally by more detailed neuropsychological examination, using tests that are quantifiable, reproducible, and for which normative data are available.

Probable IVD

A. The criteria for the clinical diagnosis of PROBABLE IVD include ALL of the following:

1. Dementia;
2. Evidence of two or more ischemic strokes by history, neurologic signs, and/or neuroimaging studies (CT or T₁-weighted MRI);

or

Occurrence of a single stroke with a clearly documented temporal relationship to the onset of dementia;

3. Evidence of at least one infarct outside the cerebellum by CT or T₁-weighted MRI.

Probable IVD

B. The diagnosis of PROBABLE IVD is supported by

1. Evidence of multiple infarcts in brain regions known to affect cognition;
2. A history of multiple transient ischemic attacks;
3. History of vascular risk factors (eg, hypertension, heart disease, diabetes mellitus);
4. Elevated Hachinski Ischemia Scale (original or modified version).

Table 1. Hachinski Ischemia Score

Abrupt onset*	2
Stepwise progression*†	1
Fluctuating course†‡	2
Nocturnal confusion‡	1
Relative preservation of personality†	1
Depression	1
Somatic complaints*	1
Emotional incontinence*†	1
History of hypertension*	1
History of strokes*†	2
Evidence of associated atherosclerosis	1
Focal neurologic symptoms*†‡	2
Focal neurologic signs*	2

* Items significantly more common in MID than AD.⁴¹

† Items significantly more common in MID than AD.⁴²

‡ Items that explained a significance portion of the variance in logistic regression.⁴²

C. Clinical features that are thought to be associated with IVD, but **await further research, include**

1. Relatively early appearance of gait disturbance and urinary incontinence;
2. Periventricular and deep white matter changes on T₂-weighted MRI that are excessive for age;
3. Focal changes in electrophysiologic studies (eg, EEG, evoked potentials) or physiologic neuroimaging studies (eg, SPECT, PET, NMR spectroscopy).

D. Other clinical features that do not constitute strong evidence either for or against a diagnosis of PROBABLE IVD include

1. Periods of slowly progressive symptoms;
2. Illusions, psychosis, hallucinations, delusions;
3. Seizures.

Possible IVD

A clinical diagnosis of POSSIBLE IVD may be made when there is

1. Dementia; and one or more of the following:

2a. A history or evidence of a single stroke (but not multiple strokes) without a clearly documented temporal relationship to the onset of dementia;

Or

2b. Binswanger's syndrome (without multiple strokes) that includes all of the following:

i. Early-onset urinary incontinence not explained by urologic disease, or gait disturbance (eg, parkinsonian, magnetic, apraxic, or "senile" gait) not explained by peripheral cause,

ii. Vascular risk factors, and

iii. Extensive white matter changes on neuroimaging.

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**Comparison of Different Clinical Criteria (DSM-III, ADDTC, ICD-10,
NINDS-AIREN, DSM-IV) for the Diagnosis of Vascular Dementia**

T. Pohjasvaara, R. Mäntylä, R. Ylikoski, M. Kaste and T. Erkinjuntti

Stroke 2000;31:2952-2957

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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Conclusions—Current criteria of VaD identify different frequencies and clusters of patients and are **not interchangeable**. Optimally, prospective studies with clinicopathological correlation could identify new criteria. Meanwhile, focus on more homogeneous subtypes (eg, small-vessel subcortical VaD) and detailed neuroimaging criteria could improve the diagnostics.

NEUROLOGY

Classification of vascular dementia in the Cardiovascular Health Study Cognition Study

O. L. Lopez, L. H. Kuller, J. T. Becker, W. J. Jagust, S. T. DeKosky, A. Fitzpatrick, J. Breitner, C. Lyketsos, C. Kawas and M. Carlson
Neurology 2005;64:1539-1547

DOI: 10.1212/01.WNL.0000159860.19413.C4

Conclusions: None of the clinical criteria for VaD identified the same group of subjects. The diagnosis of vascular dementia is difficult in epidemiologic studies because poststroke dementia can be due to Alzheimer disease (AD) and evidence of vascular disease can be found in the MRI of dementia cases without clinical strokes. Whether the clinical progression is related to AD pathology or vascular disease is difficult to establish.

Clinicopathological Validation Study of Four Sets of Clinical Criteria for Vascular Dementia

Gold et al.

Am J Psychiatry 2002; 159:82–87

Conclusions: Clinical criteria for vascular dementia are not interchangeable. The ADDTC criteria for possible vascular dementia are the most sensitive for the detection of vascular dementia; however, the DSM-IV criteria for vascular dementia and the NINDS-AIREN criteria for possible vascular dementia may be more effective in excluding mixed dementia. Given their inability to detect the vast majority of cases of vascular dementia, the ICD-10 criteria for vascular dementia and the ADDTC and NINDS-AIREN criteria for probable vascular dementia should be revised.

NEUROLOGY

Classification of vascular dementia in the Cardiovascular Health Study Cognition Study

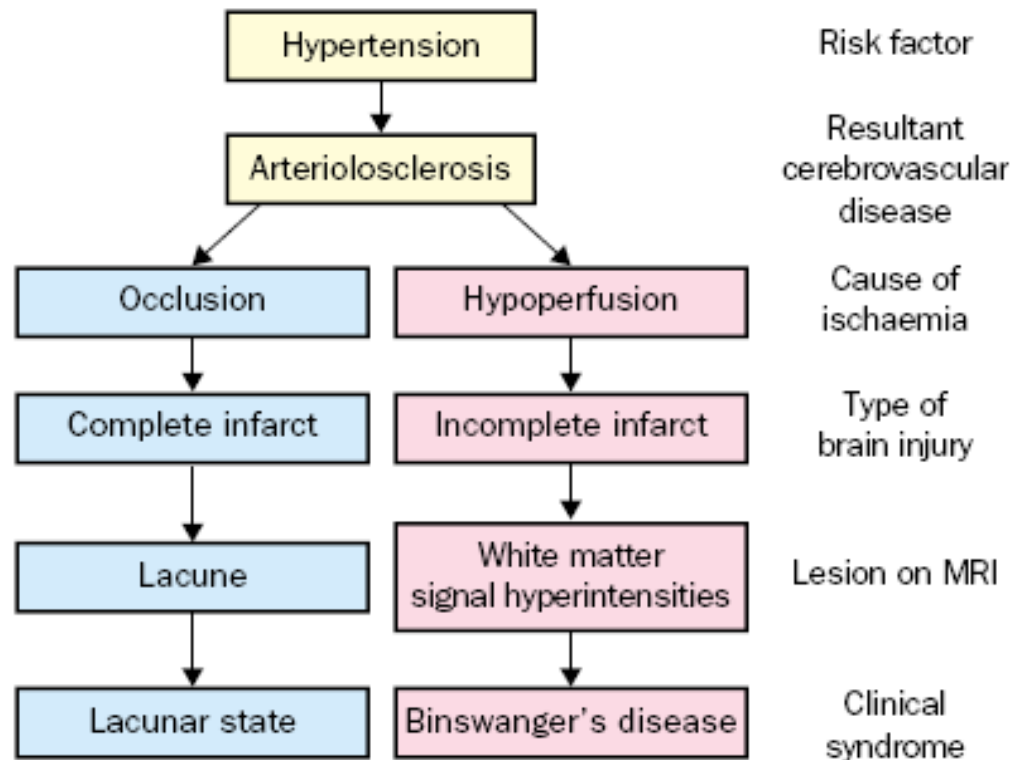
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Neurology 2005;64;1539-1547

...about a quarter of 3660 participants aged 65 or older had one or more lacunes on magnetic resonance imaging (MRI)...

...According to several population-based studies, the prevalence of cerebral white-matter hyperintensities on MRI in elderly people is in the range of 62–95%...

Subcortical ischaemic vascular dementia

Gustavo C Román, Timo Erkinjuntti, Anders Wallin, Leonardo Pantoni, and Helena C Chui
Lancet Neurology 2002;1:426-436



Subcortical ischaemic vascular dementia

Gustavo C Román, Timo Erkinjuntti, Anders Wallin, Leonardo Pantoni, and Helena C Chui

The criteria for the clinical diagnosis include all of the following:

Cognitive syndrome

Dysexecutive syndrome —impairment in goal formulation, initiation, planning, organising, sequencing, executing, set-shifting and maintenance, abstracting

Memory deficit —impaired recall, relatively intact recognition, moderate forgetfulness, and benefit from cues; may be mild
Deterioration from a previous higher level of functioning, interference with **complex (executive) occupational and social activities** not due to physical effects of cerebrovascular disease alone

Subcortical ischaemic vascular dementia

Gustavo C Román, Timo Erkinjuntti, Anders Wallin, Leonardo Pantoni, and Helena C Chui

Cerebrovascular disease

Evidence of relevant cerebrovascular disease by brain imaging
Presence or history of neurological signs consistent with subcortical cerebrovascular disease (such as hemiparesis, lower facial weakness, Babinski sign, sensory deficit, dysarthria, gait disorder, and extrapyramidal signs)

Subcortical ischaemic vascular dementia

Gustavo C Román, Timo Erkinjuntti, Anders Wallin, Leonardo Pantoni, and Helena C Chui

Clinical features supporting the diagnosis of SIVD include the following:

- Episodes of mild upper motor-neuron involvement such as drift, reflex asymmetry, and incoordination
- Early presence of a gait disturbance (small-step gait or marche à petits pas magnetic, apraxic-ataxic, or Parkinsonian gait)
- History of unsteadiness and frequent, unprovoked falls
- Early urinary frequency, urgency, and other urinary symptoms not explained by urological disease
- Dysarthria, dysphagia, extrapyramidal signs (hypokinesia, rigidity)
- Behavioural and psychological symptoms such as depression, personality change, emotional incontinence, and psychomotor retardation

Subcortical ischaemic vascular dementia

Gustavo C Román, Timo Erkinjuntti, Anders Wallin, Leonardo Pantoni, and Helena C Chui

Features that make the diagnosis of SIVD uncertain or unlikely include:

Early onset of memory deficit and progressive worsening of memory and other cognitive cortical functions, such as language (transcortical sensory aphasia), motor skills (apraxia), and perception (agnosia), in the absence of corresponding focal lesions on brain imaging.

Absence of relevant cerebrovascular disease lesions on brain CT scan or MRI.

Subcortical ischaemic vascular dementia

Gustavo C Román, Timo Erkinjuntti, Anders Wallin, Leonardo Pantoni, and Helena C Chui

CT

Extensive periventricular and deep white-matter lesions: patchy or diffuse symmetrical areas of low attenuation, of intermediate density between normal white matter and CSF, with ill-defined margins extending to the centrum semiovale, and at least one lacunar infarct

MRI

Binswanger-type white matter lesions: hyperintensities extending into periventricular and deep white matter; extending caps (>10 mm as measured parallel to ventricle) or irregular halo (>10 mm with broad, irregular margins and extending into deep white matter); and diffusely confluent hyperintensities (>25 mm, irregular shape) or extensive white matter change (diffuse hyperintensity without focal lesions); and lacune(s) in the deep grey matter

OR

Lacunar cases: **multiple lacunes (>5)** in the deep grey matter and at least moderate white-matter lesions; extending caps, irregular halo, diffusely confluent hyperintensities, or extensive white-matter changes

AND

Absence of haemorrhages, cortical and/or corticosubcortical non-lacunar territorial infarcts and watershed infarcts; signs of normal pressure hydrocephalus; and specific causes of white-matter lesions (eg, multiple sclerosis, sarcoidosis, and brain irradiation)

Neuropathology Lessons in Vascular Dementia

Helena Chui, MD

(Alzheimer Dis Assoc Disord 2005;19:45–52)

The hippocampus is the key enabler of episodic memory.

Hippocampal sclerosis (HS) refers to selective neuronal loss in the absence of cystic cavitation or neurofibrillary degeneration. HS is most prominent in the CA-1 sector of the hippocampus, extending into the subiculum. It has been reported to be a common neuropathologic finding in persons with dementia who are very old (80+ yrs),⁹ among 12% of elderly persons with dementia¹⁰ or with cardiac disease.¹¹ The pathogenesis of HS is still disputed, but systemic hypoxia ischemia¹² and ischemia due to intrinsic cerebrovascular disease are hypothesized, as CA-1 neurons have a relatively high metabolic rate but relatively poor vascular supply

Stroke

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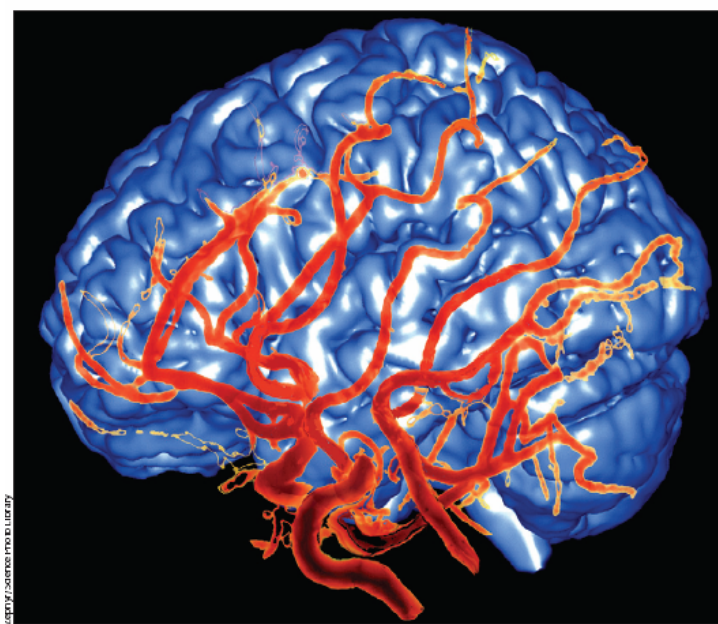
White Matter Lesions Are Associated With Progression of Medial Temporal Lobe Atrophy in Alzheimer Disease

Frank-Erik de Leeuw, Esther Korf, Frederik Barkhof and Philip Scheltens
Stroke 2006;37;2248-2252; originally published online Aug 10, 2006;

Conclusions—Our findings suggest that the presence and the progression of WML are associated with progression of Medial temporal lobe atrophy in AD. WML may be a predictor of the course of the disease and a potential treatment target in AD.

Caratteristiche socio demografiche di un campione di 442 pazienti consecutivamente valutati presso UVA Spedali Civili di Brescia

	SIVD N=71			AD N=371		
	Media	DS	%	Media	DS	
Età	78,6	7,0		74,9	7,2	
Sesso			47			71
Scolarità	6,2	3,1		6,4	3,4	
CDR	1,1	0,8		1,8	15,9	
MMSE	22,0	5,6		21,0	4,4	
ADAS	12,1	6,9		17,4	9,2	
GDS	5,3	3,7		4,2	3,2	
IADL	4,3	2,3		5,1	2,2	
BADL	5,0	1,4		5,3	1,1	
NPI	16,8	14,9		16,4	12,5	
APOE 4			39			53
Ipertensione			75			47
Diabete			17			11
Colesterolo	225,8	41,8		208,7	45,7	
Albumina gr	4,2	0,4		4,2	0,4	



Although small, the mechanism of action of cholinesterase inhibitors in vascular dementia is still worth investigating. Vascular lesions, particularly those that affect subcortical areas, might disrupt the cholinergic pathways to the cortex, and this might explain why cholinesterase inhibitors are also effective in vascular disease.

Amos D Korczyn

The Lancet Neurology 6 September 2007