Démences vasculaires

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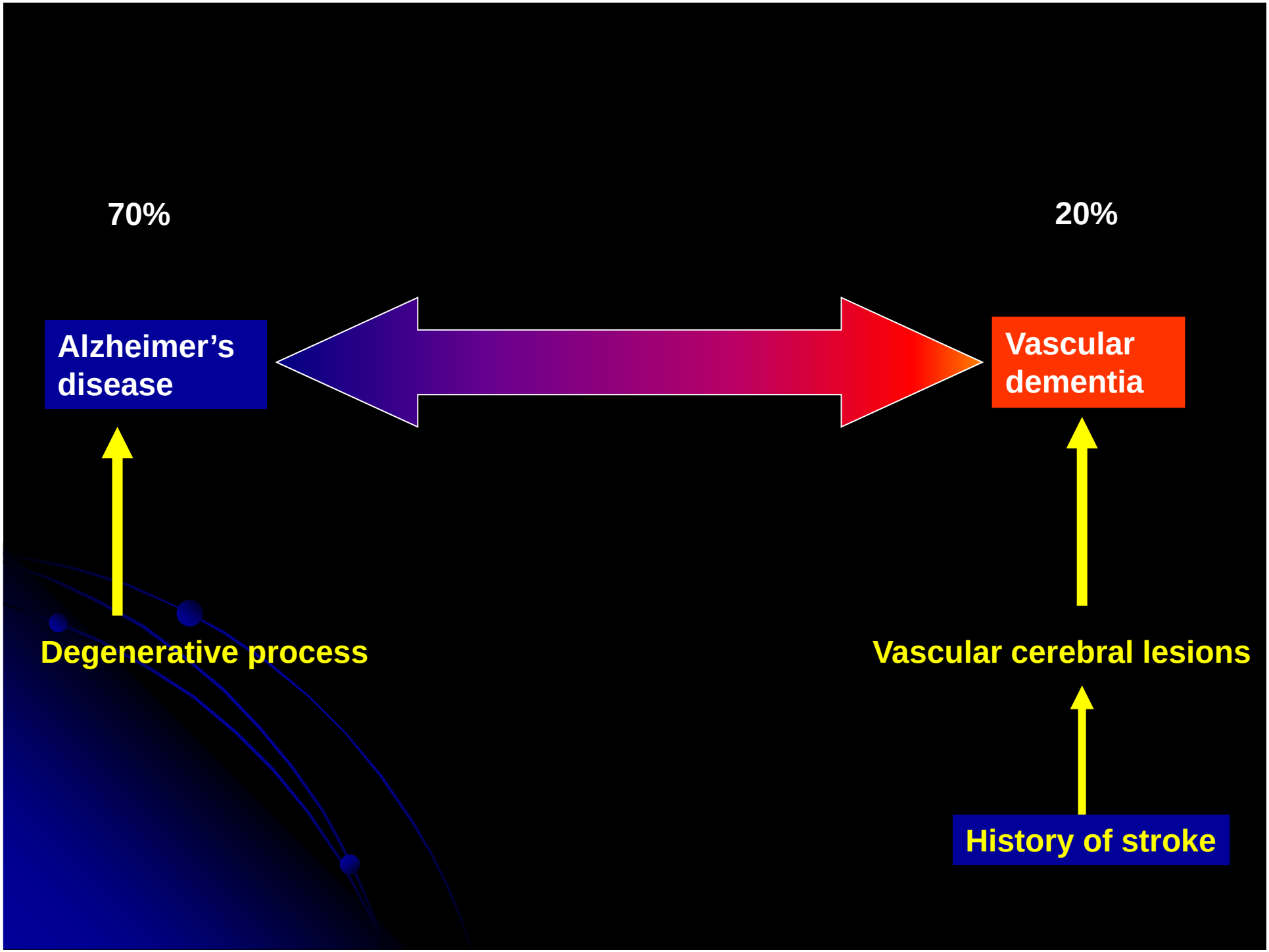
DSM IV criteria of dementia

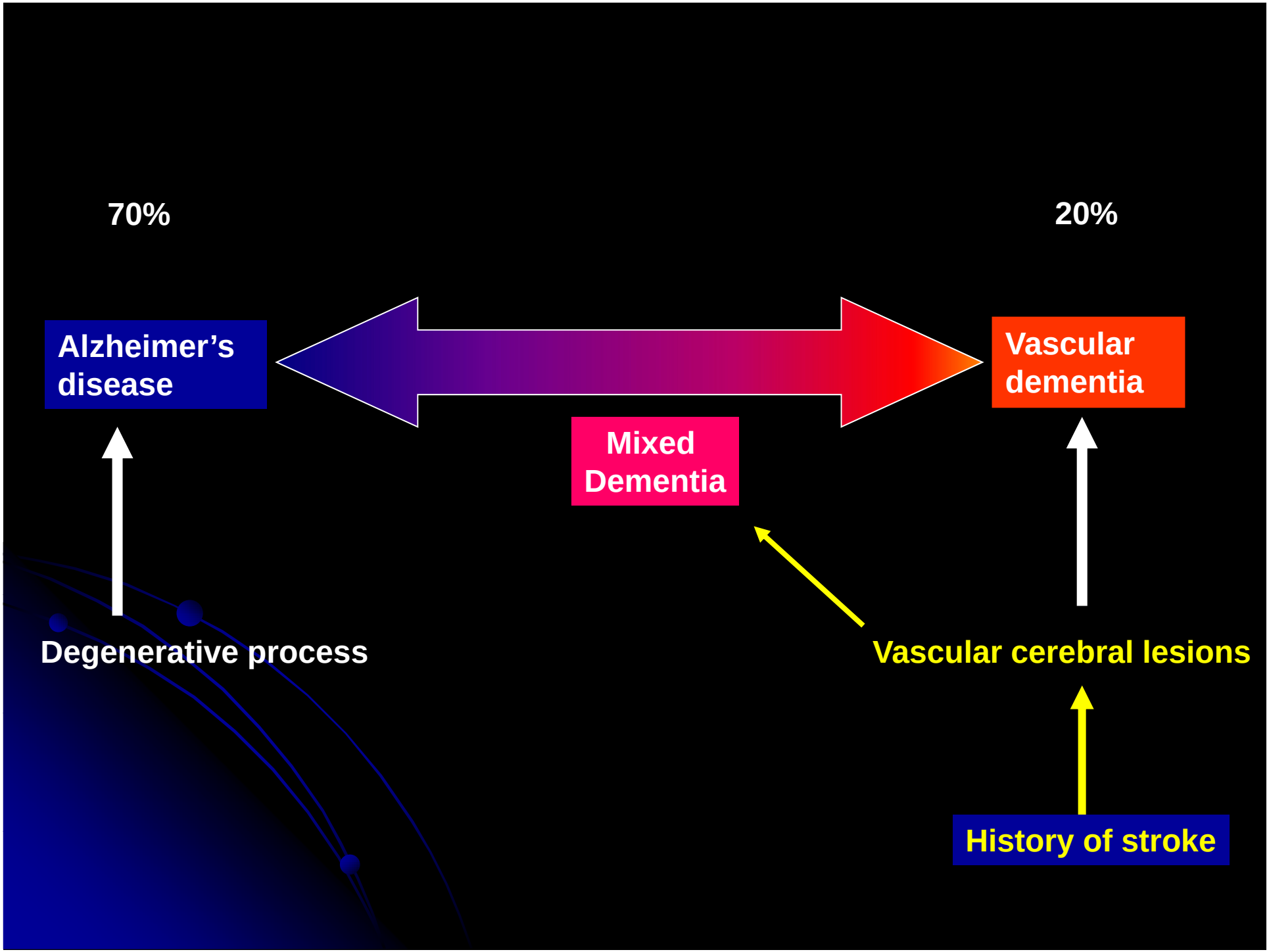
A1. Memory impairment

A2. One or more of the following cognitive disturbances

a. Aphasia
b. Apraxia
c. Agnosia
d. Disturbance in executive functioning

B. Significant impairment in social or occupational functioning and significant decline from a previous level of functioning


70%
20%
Alzheimer's disease
Vascular dementia
Degenerative process
Vascular cerebral lesions
History of stroke


70%
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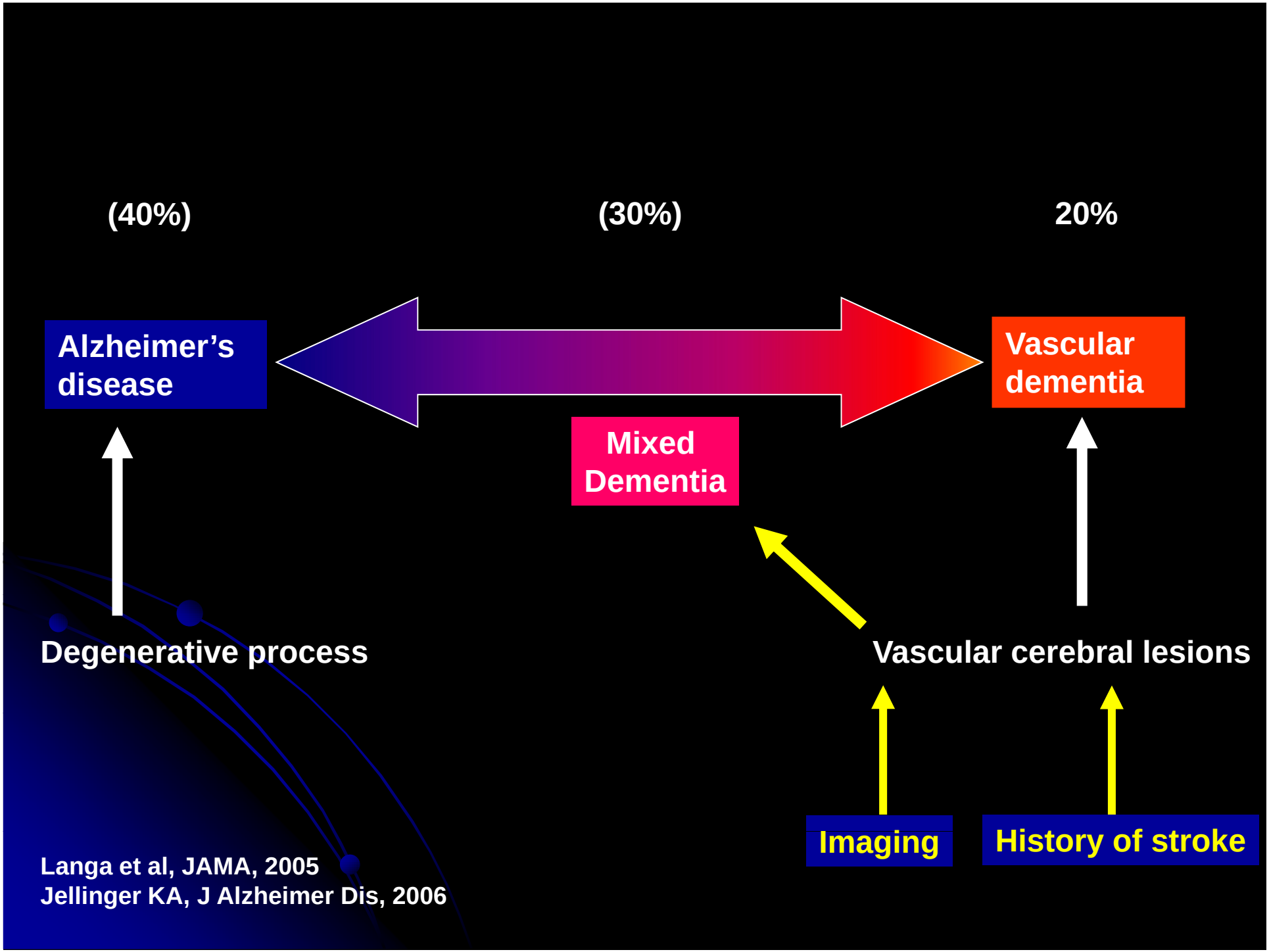
Alzheimer's disease
Vascular dementia
Mixed Dementia
Degenerative process
Vascular cerebral lesions
History of stroke

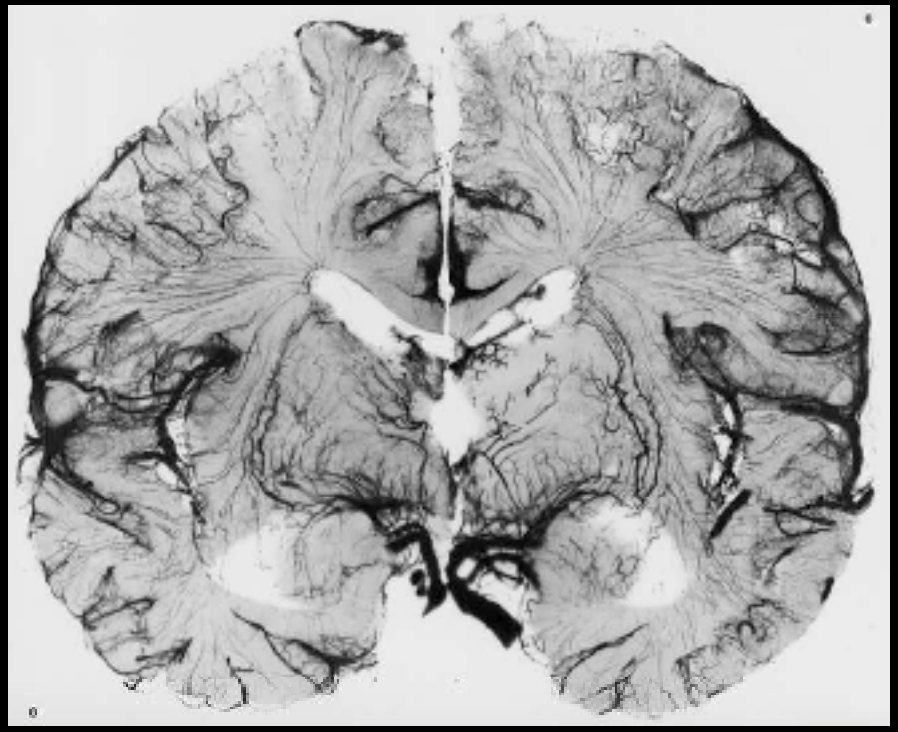

(40%)
(30%)
20%
Alzheimer's disease
Vascular dementia
Mixed Dementia
Degenerative process
Vascular cerebral lesions
Imaging
History of stroke
Langa et al, JAMA, 2005
Jellinger KA, J Alzheimer Dis, 2006

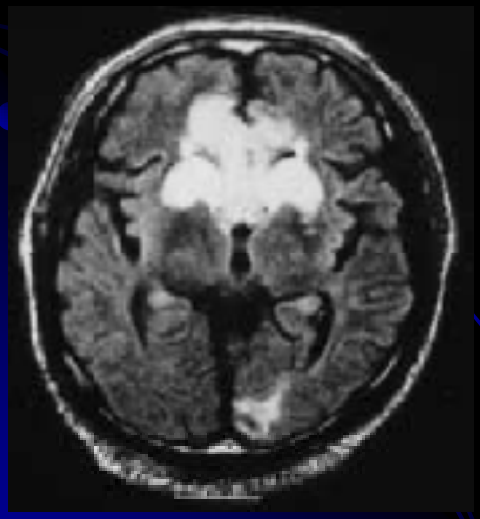
Vascular dementia

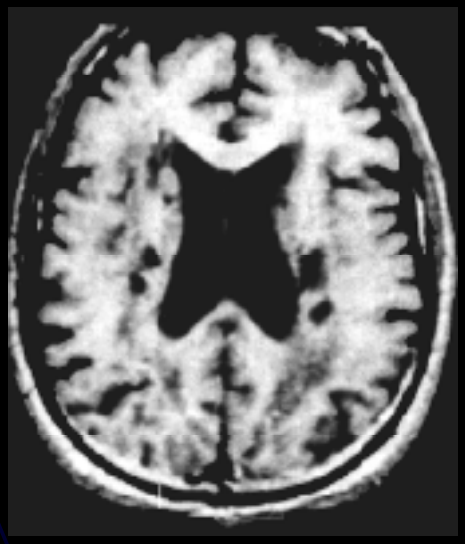
- A clinico-radiological syndrome
- Various definitions
- More of less specific criteria
- Most specific: NINDS-AIREN criteria
  - based on presence of
    1. Dementia
    2. Cerebrovascular disease (focal signs of stroke and neuroimaging evidence)
    3. Temporal relationship between 1 and 2
    4. Clinical features consistent with the diagnosis of VaD
    5. Clinical features not suggestive of Alz D
  - conservative for diagnosis, specificity 91%
  - miss classify 9% AD, 29% Mixed D (Chui et al, 2000)

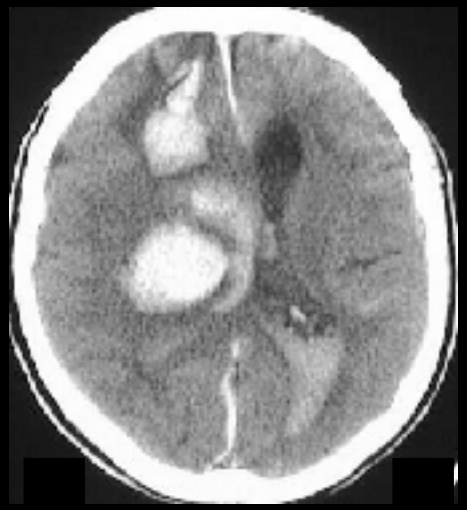
All causes of stroke can lead to VaD

Main causes of stroke	Percent
Primary hemorrhage	**15**
Ischemic stroke	**85**
Atherothromboembolism	20
Intracranial small-vessel diseases	25
Cardiac source of embolism	20
Cerebral venous thrombosis	0.5
Miscellaneous unusual causes (e.g. dissection, arteritis, drug abuse)	5
Undetermined cause	30





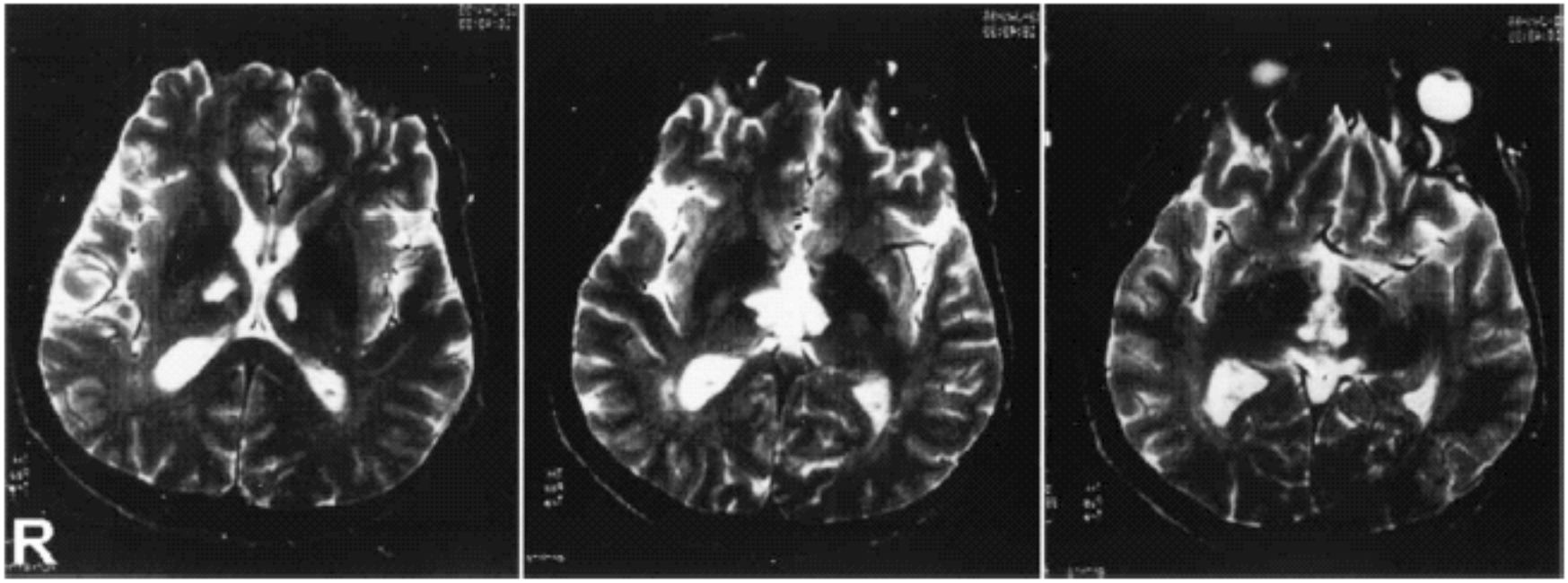




Can a single stroke cause dementia ?

Bithalamic infarction

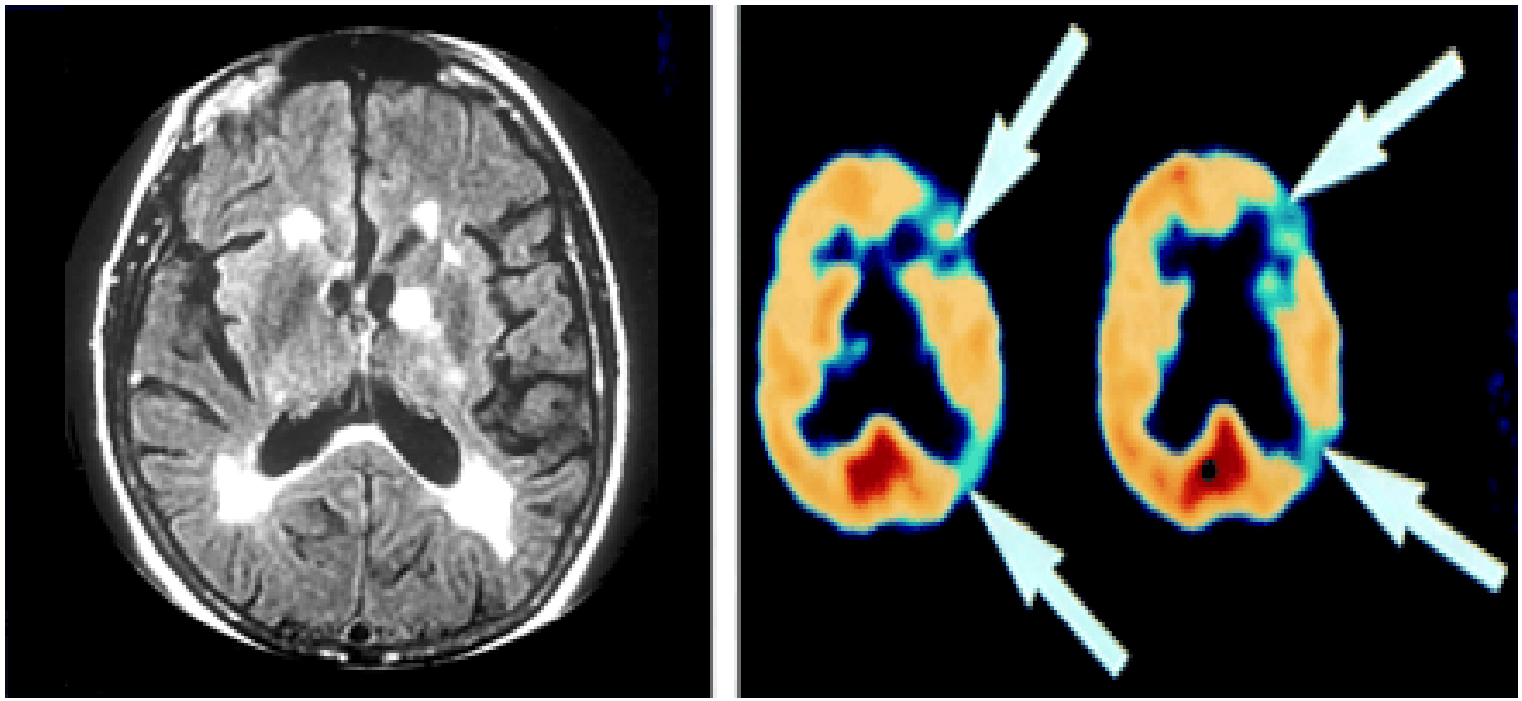
(paramedian arteries)



Clinically: Acute stupor > apathy, loss of psychic self activation, memory disturbances (korsakoff type)

Extensive metabolic and neuropsychological abnormalities associated with discrete infarction of the genu of the internal capsule

Chukwudelunzu FE et al, JNNP, 2001; 71: 658-662



- Improvement with time: acute disorientation, memory loss, language impairment, and behavioral changes (Madureira et al, 1999)
- Persisting symptoms: associated ischemic lesions (Pantoni et al , 2001)

Single stroke dementia

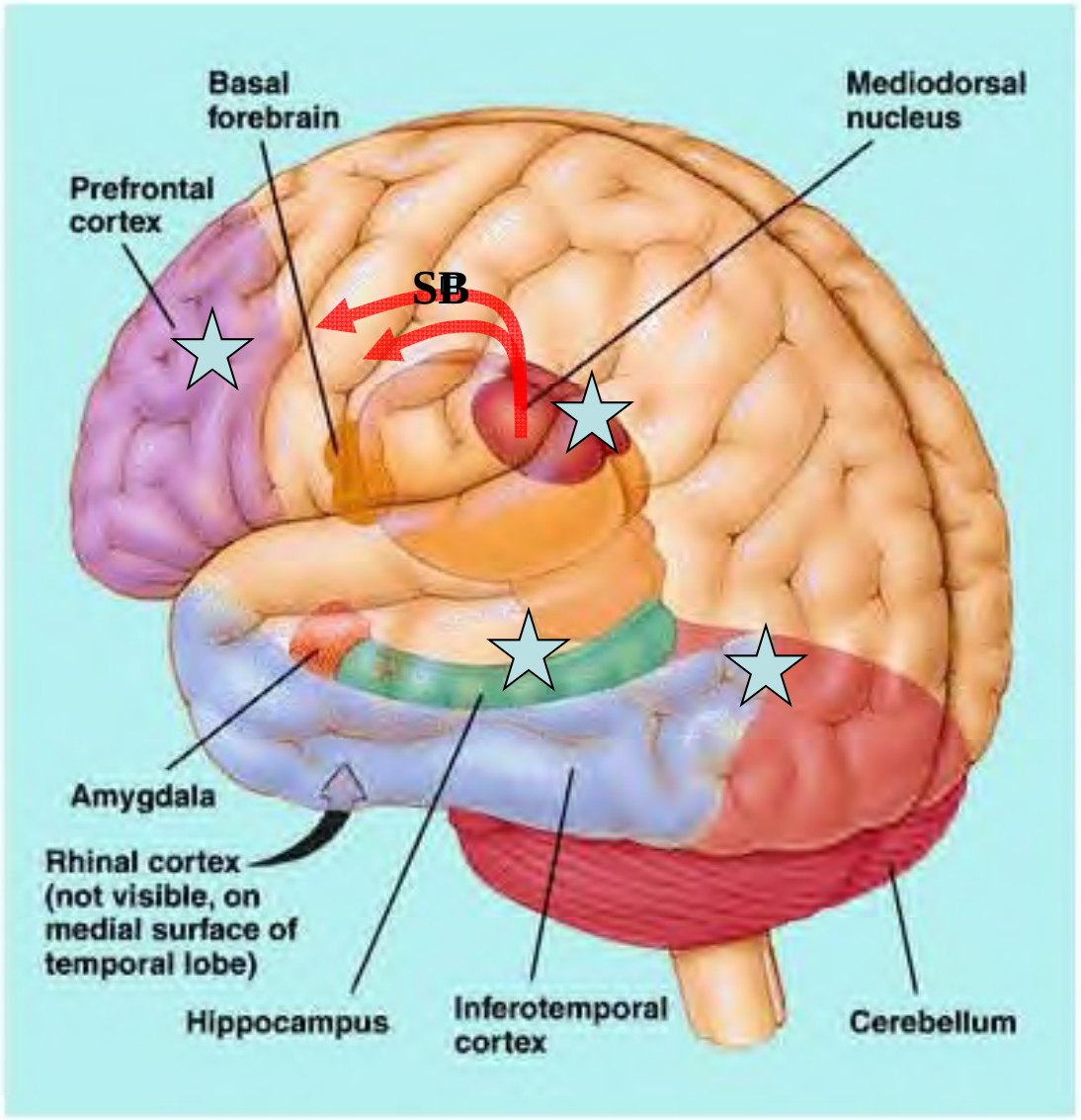
Demographic and clinical features of 12 patients with single stroke dementia

Age (years)	Gender	Hemisphere	Stroke location	Stroke mechanism	Neuropsychology (impaired domains)
61	F	Left	thalamus	lacune	VsM, VC
80	M	Left	thalamus	lacune	VbM, VsM, VC
72	M	Left	thalamus	hemorrhage	A, L, VsM, VC
69	M	Left	thalamus + hypothalamus	lacune	L, VsM
85	F	Left	thalamus + subthalamus + IC(pl)	lacune	VsM, VC
59	M	Left	subcortical frontal lobe including minor forceps	giant lacune	L, VbM, VsM, VC
82	F	Left	angular gyrus	MCA embolism	A, L, VbM, VsM
54	M	Left	anterior corpus callosum	ACA thrombosis	VbM, VsM, VC
86	M	Left	anterior CC + basal forebrain + medial frontal lobe	ACA thrombosis	A, L, VsM
58	F	Left	thalamus + occipital lobe	PCA embolism	L, VsM, VC
54	F	Left	thalamus + hippo + splenium + IC(pl)	PCA embolism	L, VbM, VsM, VC
68	M	Right	thalamus + hippo + splenium + occipital lobe	PCA embolism	VbM, VsM, VC

IC(pl) = internal capsule, posterior limb; CC = corpus callosum; hippo = hippocampus; MCA = middle cerebral artery; ACA = anterior cerebral artery; PCA = posterior cerebral artery; A = attention; L = language; VbM = verbal memory; VsM = visual memory; VC = visuoconstruction.

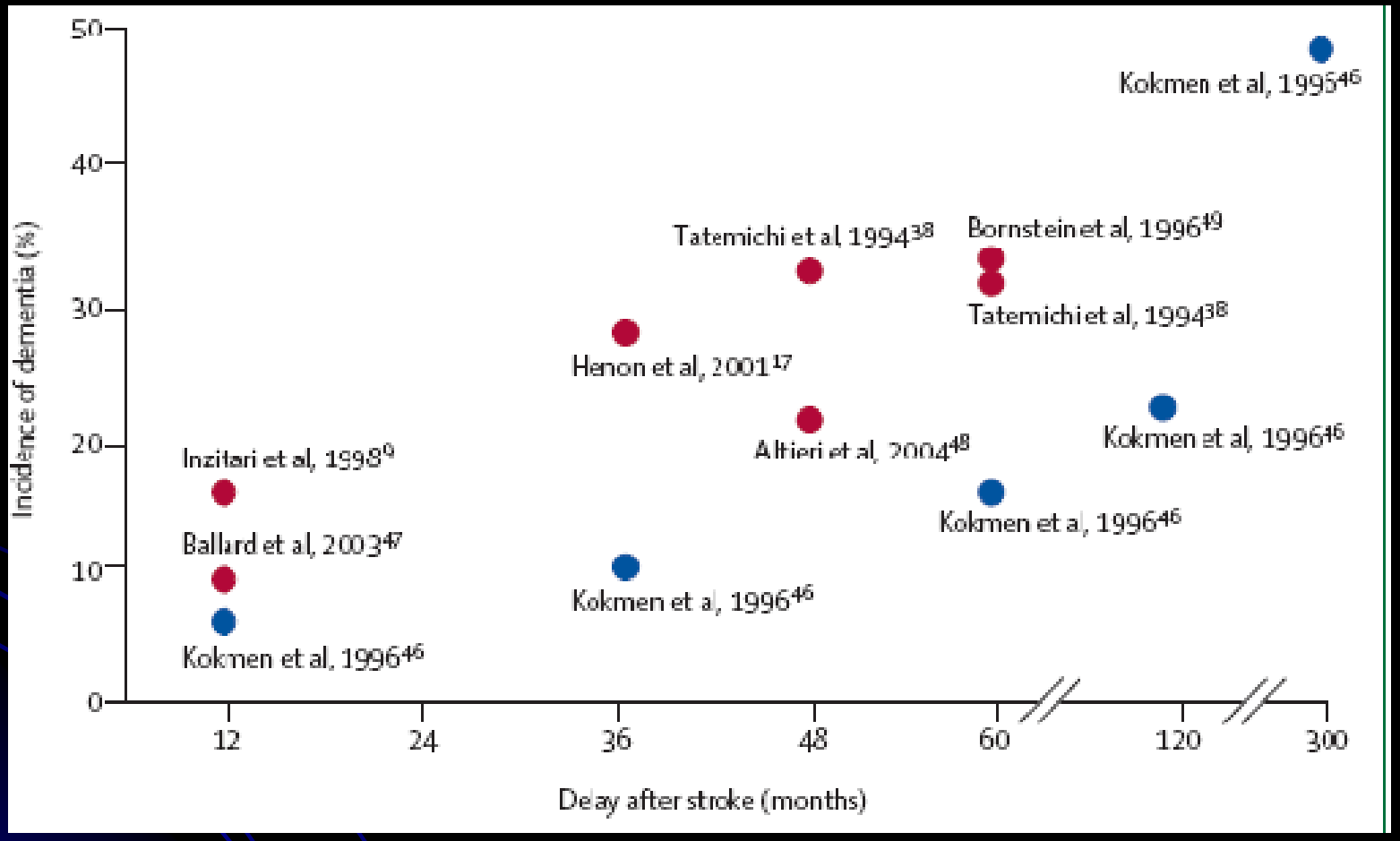
Single stroke dementia: Insights from 12 cases in Singapore. Auchus et al. *Journal of the Neurological Sciences 203– 204 (2002) 85–89*

► Structures of the Brain That Play a Role in Memory



★ **strategic location**

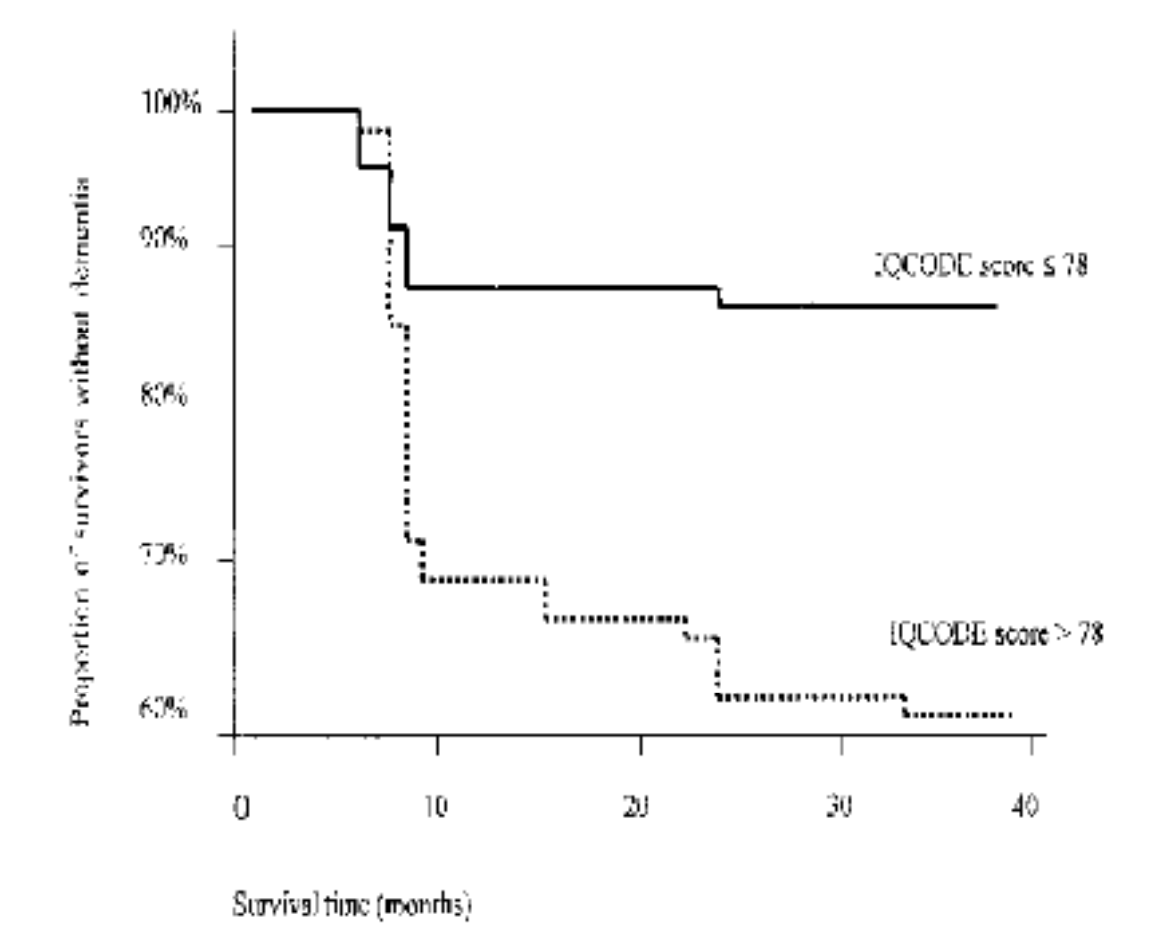
Incidence of post-stroke dementia



Leys et al, Lancet Neurol, 2005

Role of previous cognitive status

3 year incidence of post-stroke dementia in 202 patients



Independent predictors PSD
- **Age**
- **Preexisting cognitive decline**
- **Severity of deficit**
- **Diabetes**
- **Silent infarcts**

Presumed etiology > AD 1/3 VaD 2/3

Henon et al, Neurology, 2001

Risk factors associated with dementia after stroke in the Framingham study

TABLE 2. Relative Risk of Dementia in Subjects With Stroke as Compared to Controls: Crude Risks and Risks After Adjustment for Age, Sex, Education, ApoE Genotype, Stroke Recurrence, and Stroke Risk Factors

Variable Adjusted for:	Dementia/N*	RR	95% CI	*P*
None: crude risk	158/1272	2.2	1.5–3.1	<0.001
Age, sex, and education	153/1239	2.0	1.4–2.9	<0.001
ApoE ε4 genotype†	92/801	2.8	1.7–4.4	<0.001
Stroke type† (hemisphere, ABI/CE)	153/1239	2.0	1.4–2.9	<0.001
Second stroke†	153/1239	2.0	1.4–2.9	<0.001
Second stroke and stroke risk factors† (hypertension, diabetes, atrial fibrillation, current smoking)	114/844	2.4	1.6–3.7	<0.001

RR indicates relative risk; CI, confidence interval; apoE, apolipoprotein E; ABI, atherothrombotic brain infarcts; CE, cardioembolic.

*N represents total number of cases plus controls with information available regarding status of each vascular risk factor within 3 years of entry (stroke for cases and match year for controls).

†Adjusted for age, sex, and education in addition to listed variable.

Ivan et al, Stroke, 2004

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Ivan et al, Stroke, 2004

Imaging markers increase the risk of VaD

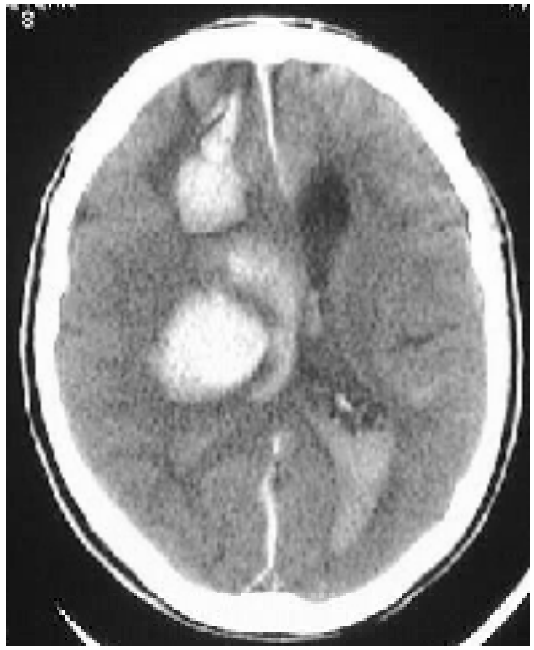
Cardiovascular Health Cognition Study: Cox models for incident VaD

	VaD		Mixed D	
Variables in the Model	HR	95% CI	HR	95% CI
Age at MRI	1.1	1.03–1.14	1.2	1.12–1.19
Female	0.7	0.39–1.24	1.2	0.84–1.76
Race (nonwhite)	2.5	1.16–5.41	1.9	1.06–3.27
3MSE at MRI	0.9	0.87–0.94	0.9	0.9–0.94
$ApoE_4$ (yes)	0.8	0.42–1.67	2.4	1.64–3.58
White matter grade 3+	3.8	1.99 7.2	2.2	1.47 3.21
Ventricular grade 5+	1.6	0.87–2.93	1.9	1.28–2.85
Large infarcts (present)	2.3	1.28–4.22	4.0	2.66–6.0
Stroke before MRI	2.4	1.23–4.85	1.5	0.88–2.59
Education < grade 12	0.5	0.10–2.14	0.5	0.20–1.39
Diabetes by ADA	0.6	0.24–1.41	1.5	0.95–2.52
Hypertension	1.8	1.00–3.20	1.0	0.66–1.39
MI before MRI	1.1	0.50–2.41	0.9	0.48–1.61
Angina before MRI	2.1	1.05–4.01	1.4	0.90–2.21

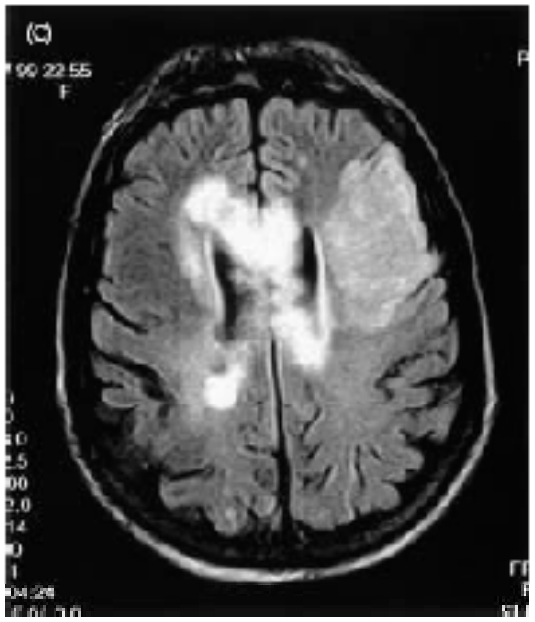
Kuller et al Neurology, 2006

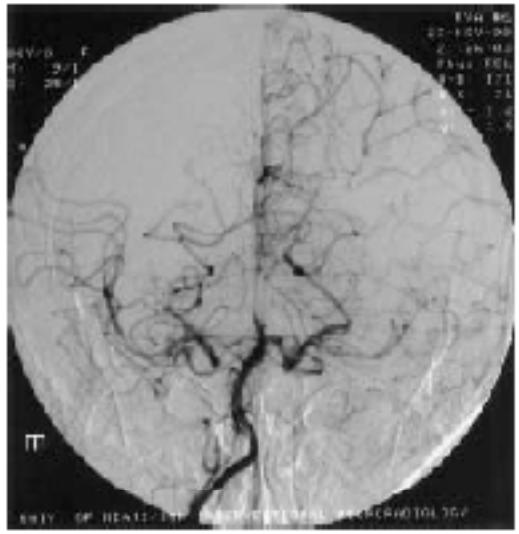
Multiple cortical vascular lesions: volume or location ?

Amyloid angiopathy



Bilateral carotid occlusion
(Rabinstein et al, 2004)





Vascular dementia: location of lesions >>> volume of lesions

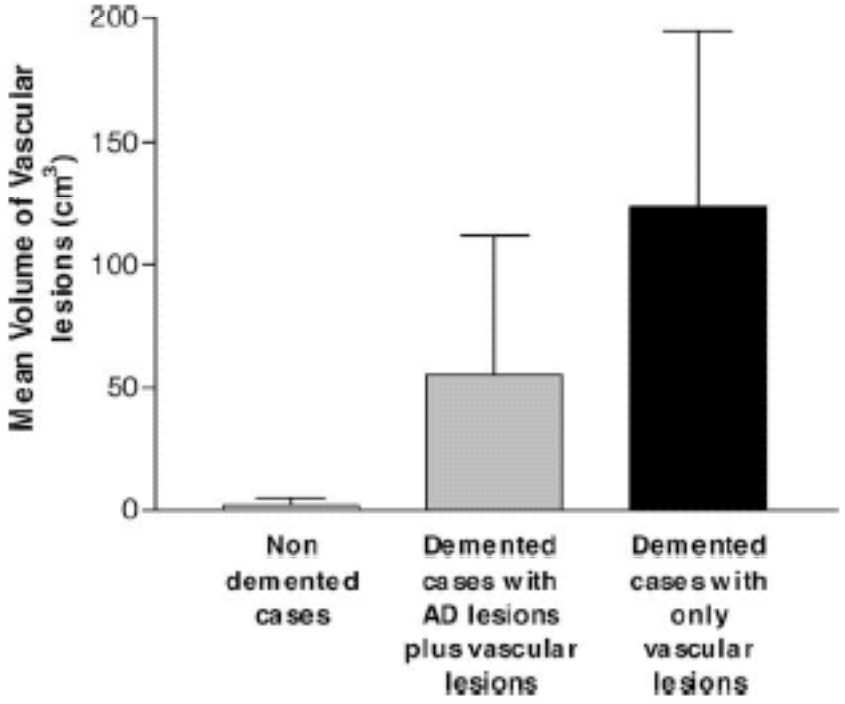


Fig. 1. Mean volume of the vascular lesions (cm^3). The clinically demented patients were divided into two groups according to neuropathological examination: cases with vascular lesions alone and cases with AD lesions plus vascular lesions.

Volume of ischemic lesions >

0,1% MMSE variability

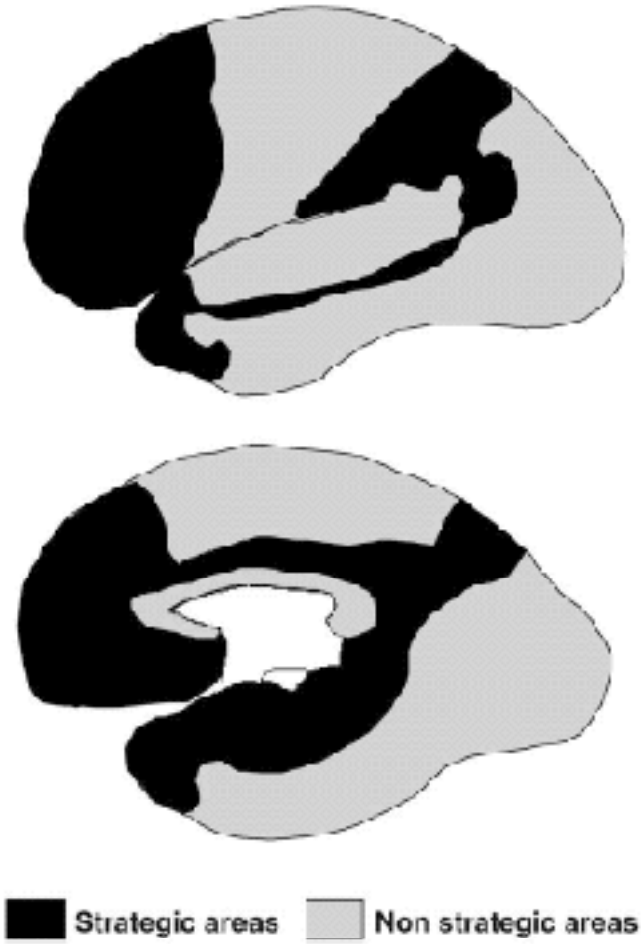


Fig. 2. The simple map (external and internal sides), redrawn from the Mesulam's human brain map showing the "strategic areas" demonstrated by this study (limbic and heteromodal association cortical areas shown in black). The white matter was also found to be "strategic."

Location in strategic areas >

47.4% MMSE variability

D. Zekry et al. / Neurobiology of Aging 24 (2003) 213–219

Multiple subcortical vascular lesions,
weight and significance of visible lesions ?

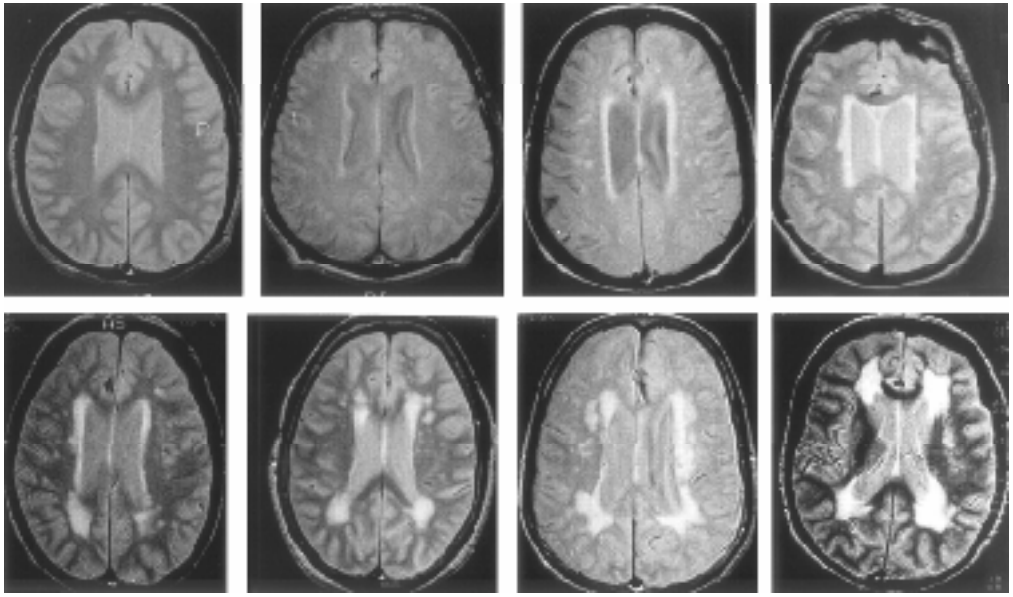
Subcortical ischemic vascular dementia

- **Revised NINDS-AIREN criteria (Erkinkuntti et al, 2000)**
  - Dementia
    - Memory deficit
    - Dysexecutive syndrome
    - Impaired activities of daily life
  - Focal signs: hemiparesis, pyramidal signs, sensory deficit, dysarthria, gait disorders, extrapyramidal signs
  - Extensive WML and ≥ I lacune in deep gray matter **or** multiple deep gray matter lacunar infarcts

White-matter T2 hyperintensities, which role ?

WM T2-hyperintensities are frequent and appear most often silent

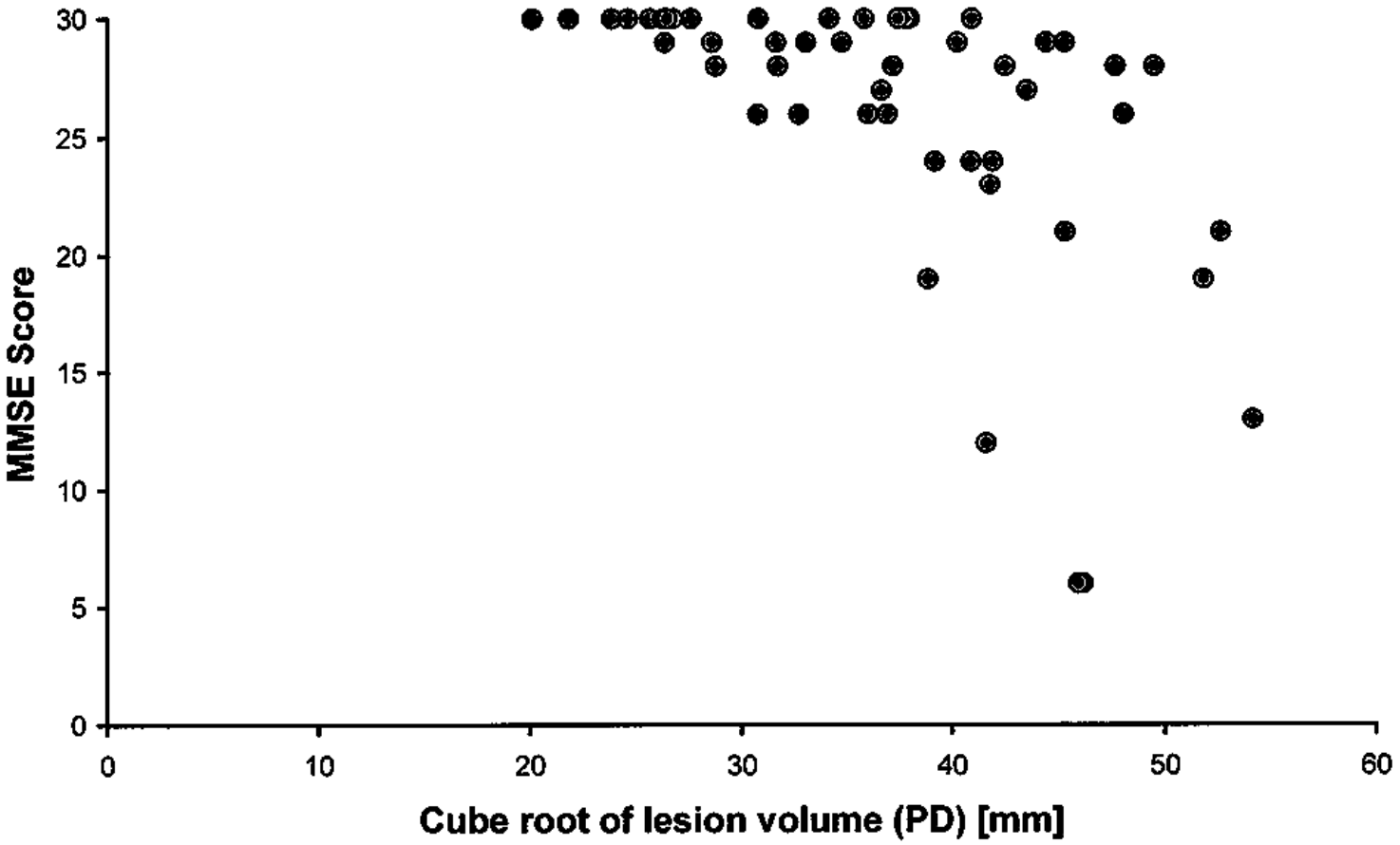
- SVD responsible for « silent » WM hyperintensities
  - WM high intensity lesions (WML) w suggestive topographic distribution (previously so-called « leukoaraïosis »)
  - Cardiovascular Health Study: population based, no dementia or severe disability, age > 65 years, 3301 pts with MRI, **95% with WML** (Longstreth et al, Stroke, 1997)



Factors > severity of WML

-Age, hypertension (systolic), silent infarcts, poor income

Correlation of MRI with cognitive performances



Dichgans et al, Neurology, 1999

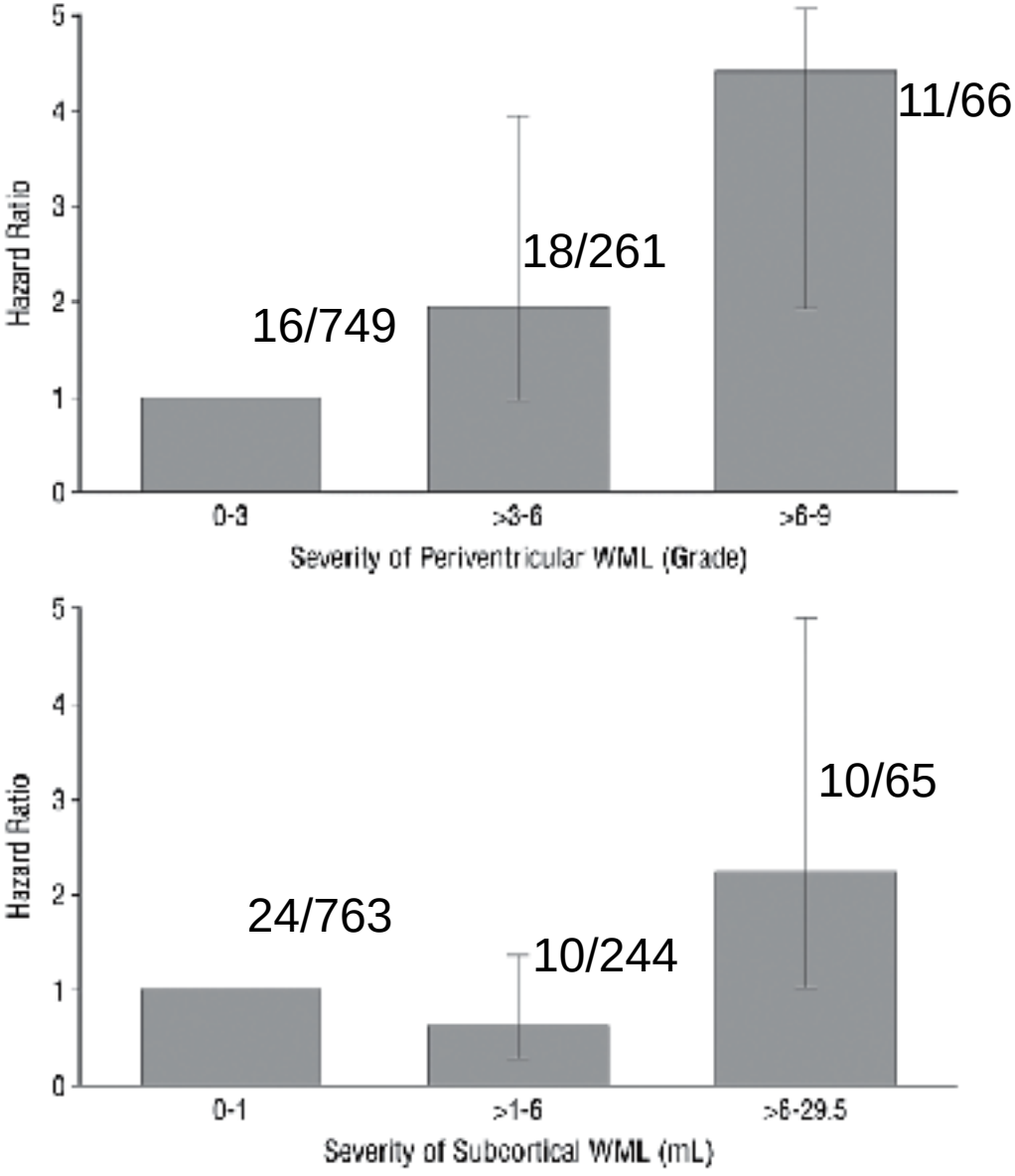
Volume of WM lesions and cognitive performances

	age-matched	> 0.5% volume IC
Nb	17	5
Age	69 ± 6	74 ± 14
WMHI	0.19 ± 0.11	0.80 ± 0.24
Cerebrum	79 ± 3	77 ± 2
Central CSF	2.1 ± 0.8	3.4 ±1
General IQ	135 ± 14	124 ± 20
WAIS Verbal	85 ± 9	20 ± 3
WAIS Performance	50 ± 9	47 ± 14
Wechsler Immediate verbal memory	19 ± 5	17 ± 2
Wechsler Visual memory	10 ± 2	6 ± 5
Wechsler Delayed Visual memory	9 ± 3	6 ± 5
WAIS Digit Symbol	53 ± 9	46 ± 11
Porteus Maze	14 ± 3	15 ± 2
FAS Word List	46 ± 9	15 ± 2
Trail Making A time (sec)	38 ± 9	66 ± 29
Trail Making B time (sec)	75 ± 26	153 ± 70
Cmrglu		
Global grey matter	7.8 ± 0.8	6.9 ± 0.3
Frontal	8.4 ± 1.0	7.3 ± 0.5
Parietal	8.0 ± 0.9	7.2 ± 0.4
Temporal	6.87 ± 0.9	5.99 ± 0.7

De Carli et al, Neurology, 1995

The Rotteram study: risk of dementia

5572 person-years of follow-up (mean per person, 5.2 years)

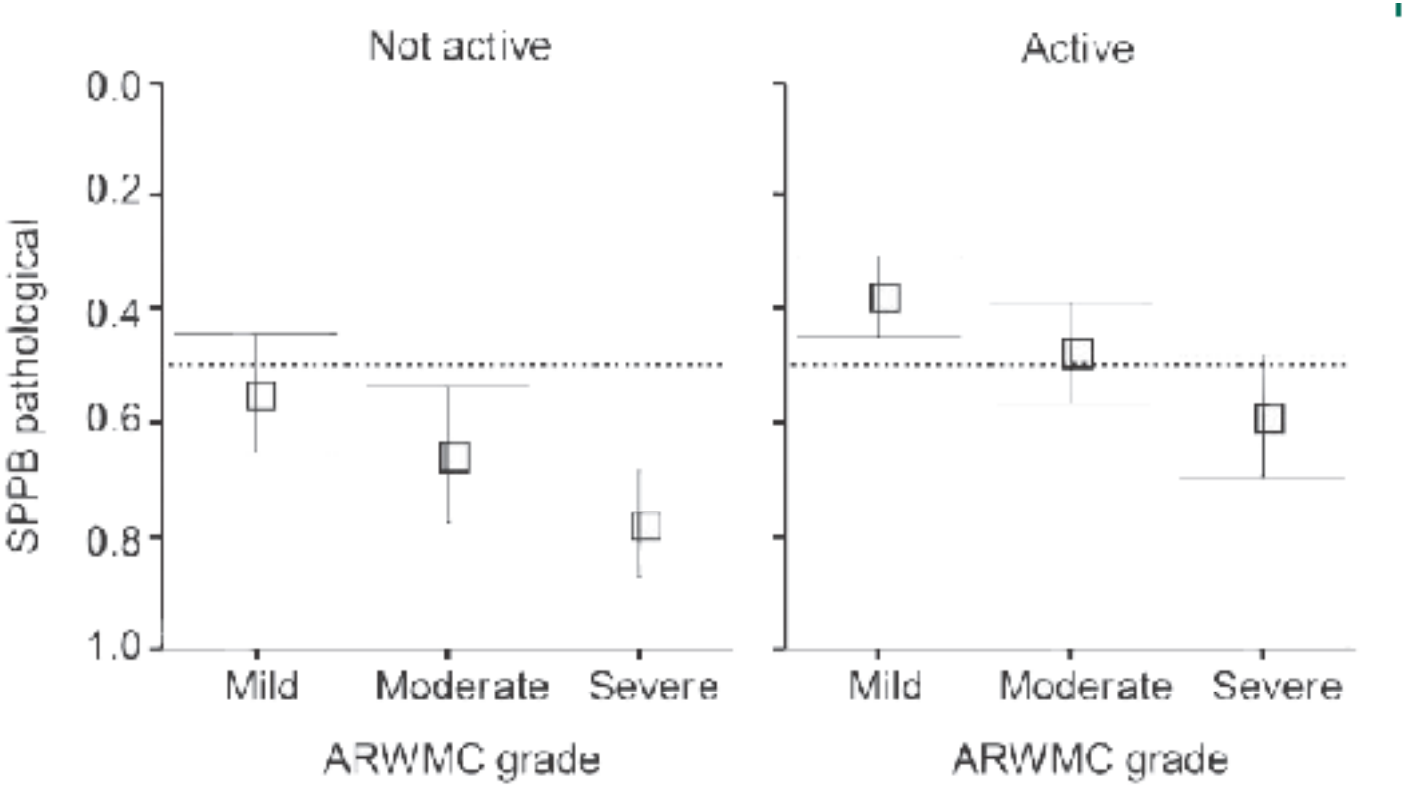


RR: 1.50 after adjustement 95% CI, 1.04-2.16 for stroke and exclusion pf pts w MMS <25 at onset

No adjustment for silent infarcts

Prins et al, Arch Neurol. 2004;61:1531-1534

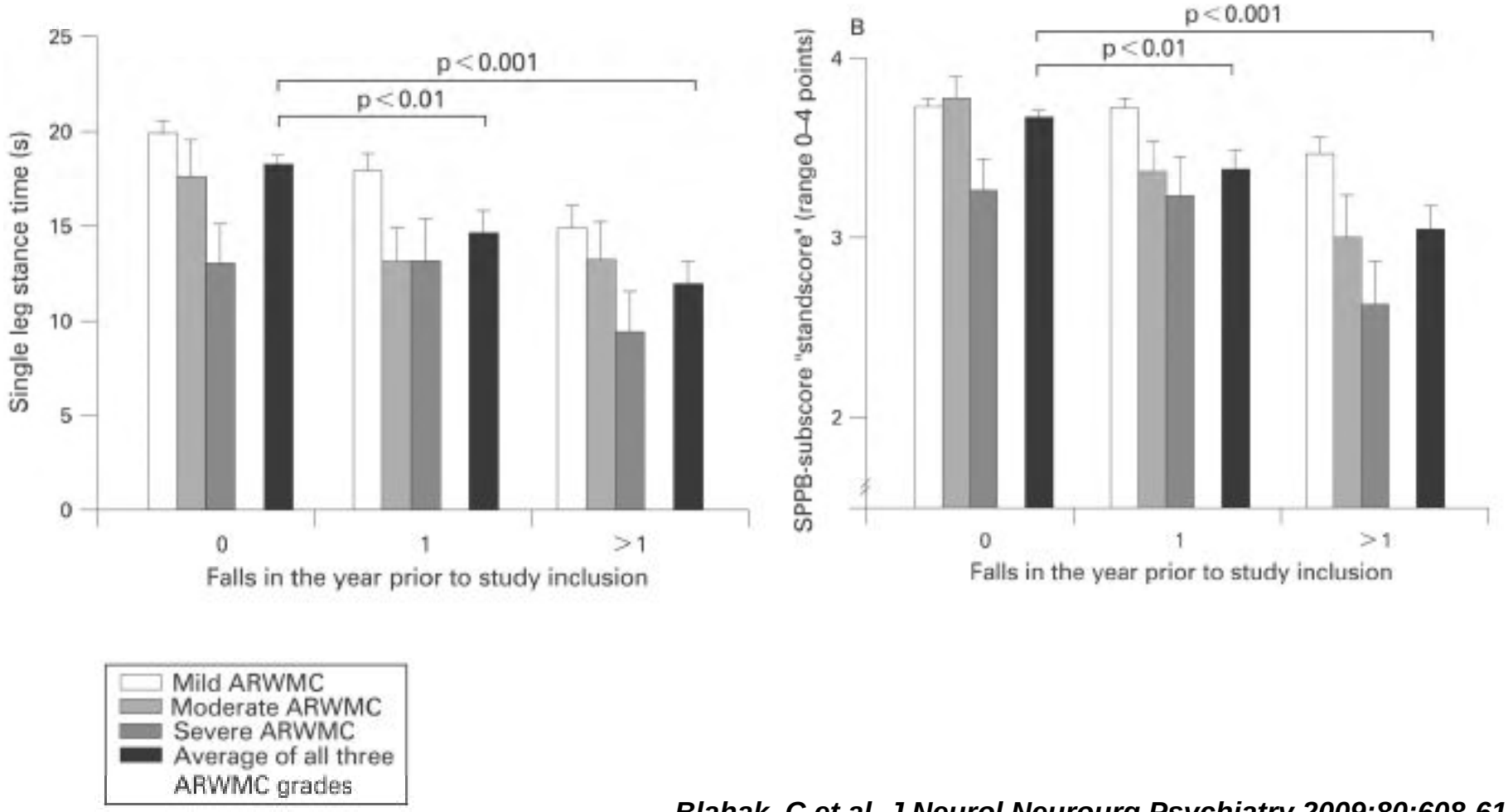
Short physical performance battery and WMH
Ladis study



Stand score (0-4), walk score (0-4), chair stands (0-4): total 12

Baezner et al, Neurology, 2008

Mean single leg stance time (A) and the standing balance subscore of the Short Physical Performance Battery (SPPB) (B), dependent on the rate of falls in the year prior to study inclusion.



Blahak, C et al. J Neurol Neurourg Psychiatry 2009;80:608-613

Plaintes urinaires et étendue des lésions de la SB
Etude LADIS

Table 4. Association Between Urinary Complaints and Age-Related White Matter Change (ARWMC) Severity (Fazekas Scale) Adjusting for Age, Sex, Lacunar and Nonlacunar Infarcts, Diabetes Mellitus, and Use of Diuretics (Logistic Regression Analysis)

	Any Urinary Complaint	Frequency	Nocturia	Incontinence	Urgency
ARWMC	Odds Ratio (95% Confidence Interval)				
Moderate versus mild	0.86 (0.57–1.23)	0.87 (0.54–1.42)	0.83 (0.56–1.22)	0.83 (0.51–1.34)	1.13 (0.68–1.87)
Severe versus mild	1.22 (0.76–1.94)	1.20 (0.73–1.99)	0.83 (0.54–1.28)	0.90 (0.53–1.53)	1.74 (1.04–2.90)

Urinary complaints (nocturia, urinary frequency, urgency, incontinence) were recorded based on patients' answers to four questions.

Poggesi et al, JAGS, 2008

Miction impérieuse ou urgences urinaires et lésions de la SB: étude LADIS

Urinary Urgency	Severe Versus Mild ARWMC Odds Ratio (95% Confidence Interval)
Univariate	1.75 (1.09–2.83)
Adjusted for age, sex	1.79 (1.10–2.91)
Adjusted for age, sex, memory disturbances	1.80 (1.11–2.93)
Adjusted for age, sex, gait disturbances	1.76 (1.10–2.87)
Adjusted for age, sex, history of depression	1.79 (1.10–2.91)
Adjusted for age, sex, memory, or gait disturbances	1.79 (1.09–2.93)
Adjusted for age, sex, memory, or history of depression	1.80 (1.11–2.93)
Adjusted for age, sex, memory, gait disturbances, or history of depression	1.78 (1.08–2.91)

Poggesi et al, JAGS, 2008

Volume of WMH and risk of major depression (3C study)

	Lifetime Major Depression[a]				
	No		Yes		
	Mean	SE	Mean	SE	p^b
N	(*n* = 1417;85.5%)		(*n* = 241;14.5%)		
Mean WML Volume	6.8	.50	7.5	.54	.03
Mean WML Volume by Type					
Periventricular	5.5	.44	6.1	.49	.05
Deep	1.3	.09	1.5	.10	.02
Mean WML Volume by Lobe					
Frontal	3.1	.28	3.5	.30	.01
Occipital	.7	.03	.7	.04	.48
Parietal	1.4	.13	1.5	.14	.12
Temporal	1.6	.13	1.7	.14	.25

SE, standard error.

[a]Lifetime major depression episode measured by the Mini-International Neuropsychiatric Interview or use of antidepressive medication.

[b]Analysis of covariance adjusting for sex, age, hypertension, history of cardiovascular disease, alcohol and tobacco consumption, physical impairment, and brain white matter volume.

Godin et al, Biop Psych, 2008

Risk of incident depression according to WML (3C Study)

Table 4. Relation between Baseline White Matter Lesion (WML) Volume and the Risk of Incident Depression[a] in Subjects with No Depression[b] at Baseline ($n = 956$)

WML Volume Percentile	*N*	OR (95% CI)[c]
< 25th	242	1
25th–50th	251	1.2 (.6–2.3)
50th–75th	237	1.5 (.8–2.9)
≥75th	226	2.4 (1.3–4.6)

[a]Defined as high depressive symptomatology or antidepressive intake.

[b]That is, no antidepressant, no high depressive symptomatology, and no MDE at baseline.

[c]Adjusted for sex, age, hypertension, history of cardiovascular disease, alcohol and tobacco consumption, baseline Center for Epidemiological Studies—Depression scale score, physical impairment, and brain white matter volume.

Godin et al, Biop Psych, 2008

Silent infarcts, which role ?

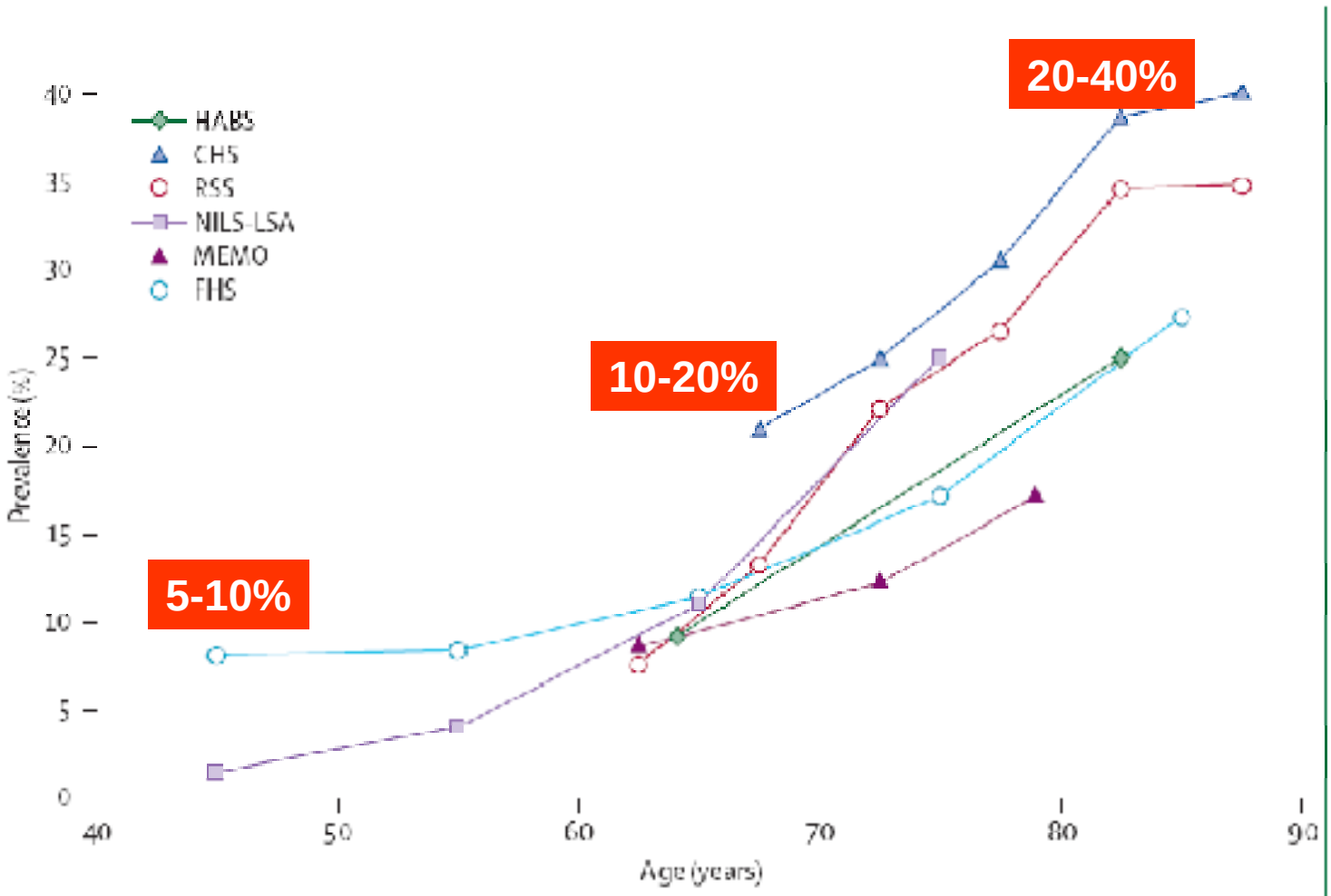
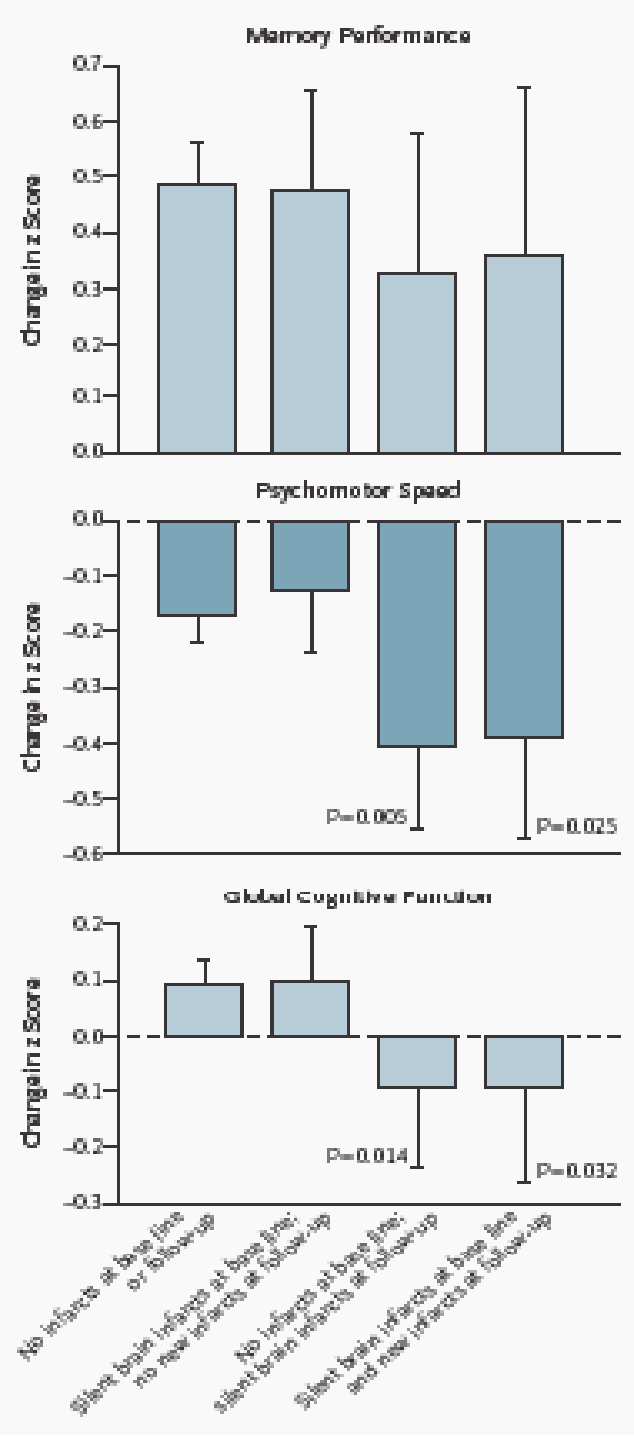


Figure 2: **Prevalence of silent brain infarcts with increasing age, as reported in six population-based studies**
HABS, Helsinki (Finland) Aging Brain Study;[9] CHS, Cardiovascular Health Study;[10] RSS, Rotterdam Scan Study;[11] NILS-LSA, National Institute for Longevity Sciences-Longitudinal Study of Aging;[12] MEMO, Memory and Morbidity in Augsburg Elderly study;[13] and FHS, Framingham Heart Study.[14]

Vermeer et al, Lancet Neurol, 2007

Silent infarcts: risk of dementia

- <u>The Rotterdam scan study</u>
  - 1015 pts, 60-90 years w MRI 1995-96 / 1999-2000
  - **Risk of dementia in pts with occurrence of silent infarcts**
    - No WM lesions: < 0.6% / year
    - <u>Silent infarcts</u>: **risk x 2.26** [1.09-4.70]



Silent infarcts: risk of cognitive decline

Table 3. Association between the Presence of Silent Brain Infarcts on Magnetic Resonance Imaging in 1995–1996 and Subsequent Cognitive Decline.*

Variable	Silent Brain Infarcts		
	All	Thalamic	Nonthalamic
	decline in z score (95% CI)		
Memory performance	–0.01 (–0.16 to 0.15)	–0.50 (–0.87 to –0.13)	0.06 (–0.10 to 0.23)
Psychomotor speed	–0.19 (–0.34 to –0.04)	–0.11 (–0.36 to 0.13)	–0.20 (–0.36 to –0.05)
Global cognitive function	–0.15 (–0.27 to –0.02)	–0.28 (–0.50 to –0.06)	–0.13 (–0.26 to 0.001)

* Values are the mean differences in the z scores between follow-up and base line, with 95 percent confidence intervals (CIs) between those with and those without silent brain infarcts, adjusted for age, sex, level of education, and interval between neuropsychological tests. A positive value indicates an increase in the z score.

Table 2. Relation between the Presence of Silent Brain Infarcts at Base Line, the Severity of Periventricular and Subcortical White-Matter Lesions, and the Risk of Dementia.

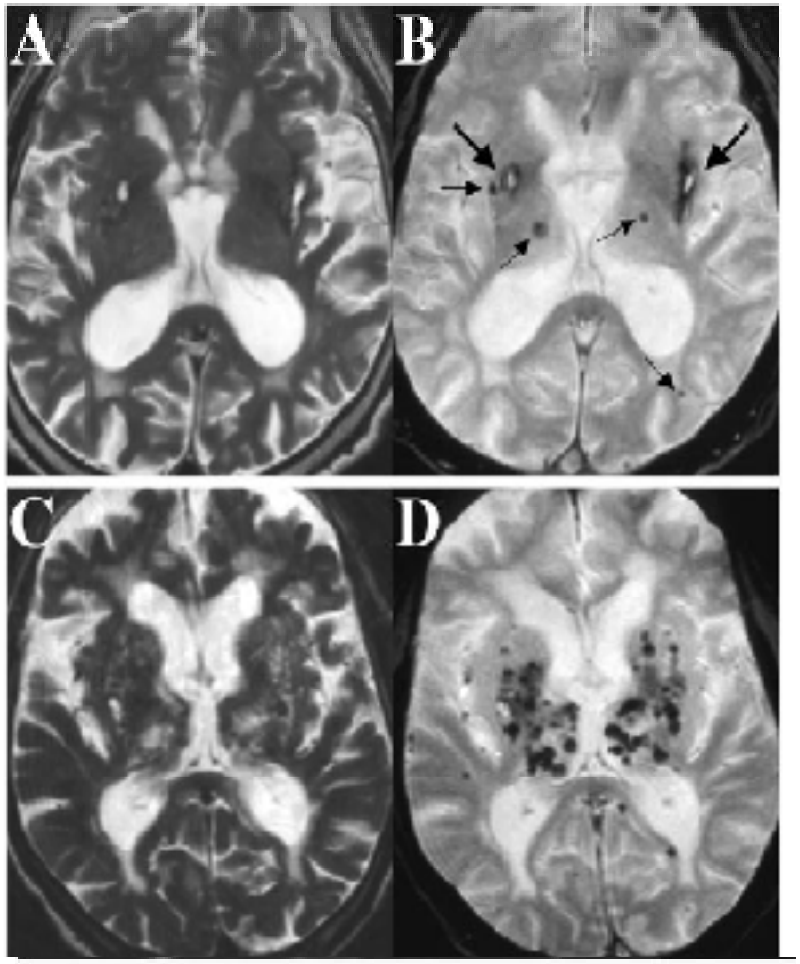
Variable	Hazard Ratio (95% Confidence Interval)	
	Adjusted for Age, Sex, and Level of Education	Adjusted for Age, Sex, Level of Education, and MRI Measures*
Silent brain infarcts (yes vs. no)	2.26 (1.09–4.70)	2.03 (0.91–4.55)
Severity of periventricular white-matter lesions (per SD increase)	1.59 (1.13–2.25)	1.47 (0.92–2.35)
Severity of subcortical white-matter lesions (per SD increase)	1.21 (0.96–1.53)	0.92 (0.65–1.29)

* The magnetic resonance imaging (MRI) measures adjusted for were presence or absence of silent brain infarcts, severity of periventricular and subcortical white-matter lesions, and severity of subcortical brain atrophy.

Vermeer et al, NEJM, 2003, 348, 1215-

Microbleeds, which role ?

Microbleeds are associated with other markers of severity in SVD



Kato et al, Stroke, 2002

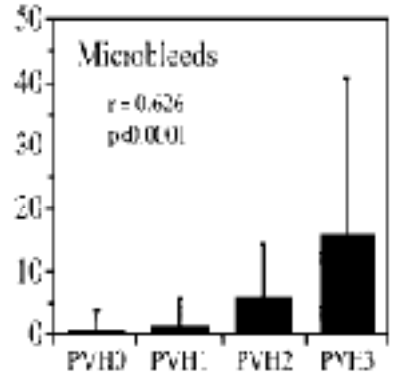


Figure 2. There was a significant correlation between the number of microbleeds and the severity of periventricular hyperintensities (PVHs) graded as 0 (none, n=54), 1 (mild, n=77), 2 (moderate, n=55), and 3 (severe, n=27). The stroke patients with different subtypes and controls (a total of 213) were examined all together.

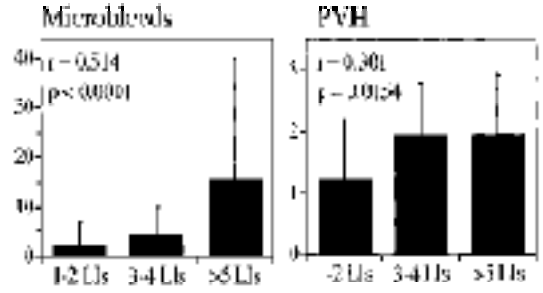
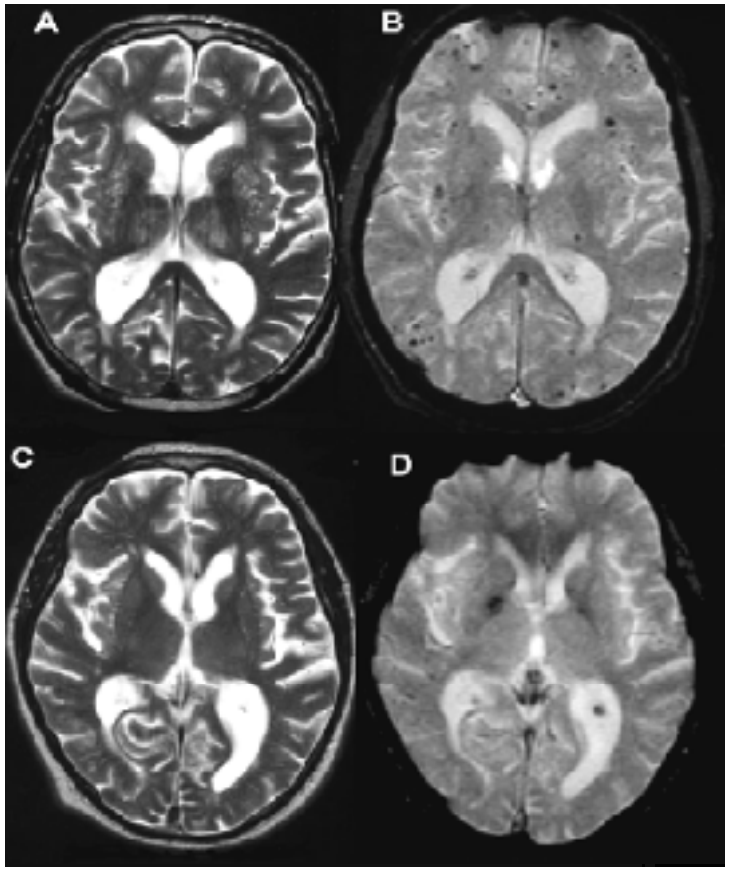
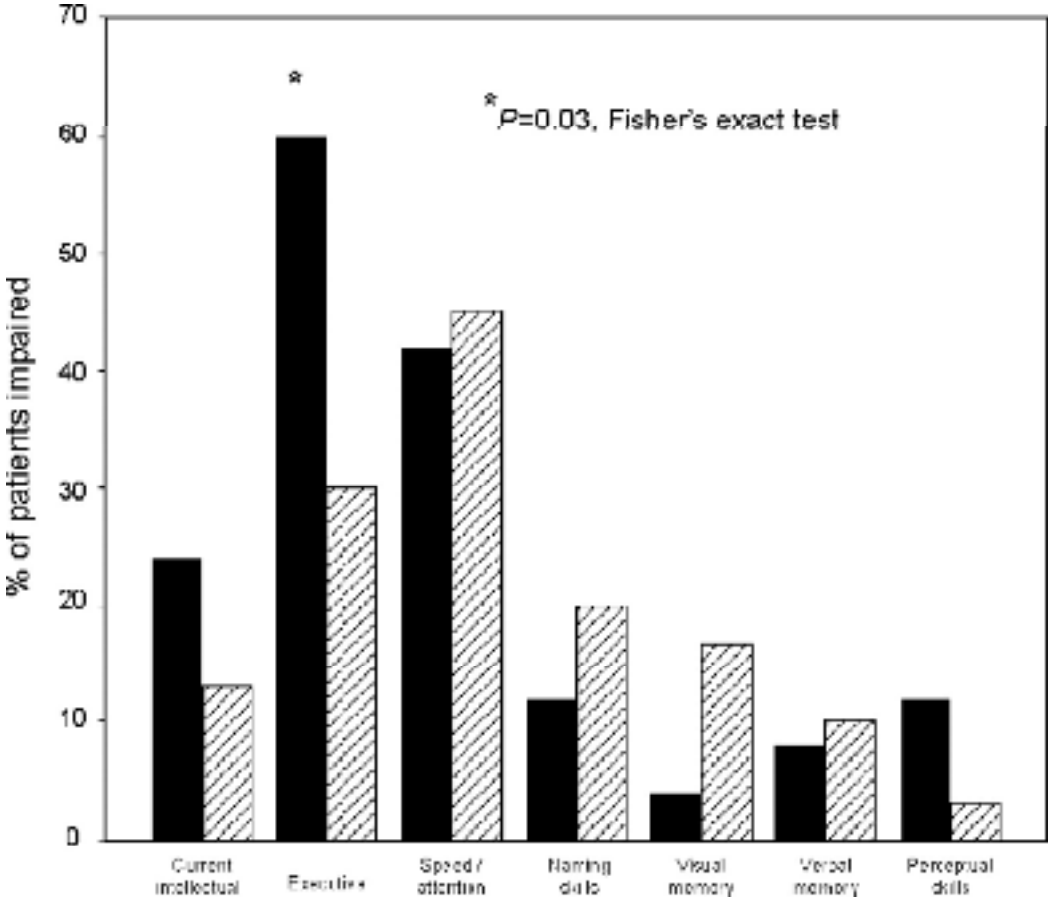


Figure 4. There was a significant correlation between the number of lacunar infarcts (LIs) and the number of microbleeds or the severity of periventricular hyperintensities (PVHs) graded from 0 (none) through 3 (severe). A total of 66 patients with lacunar infarction were divided into 3 subgroups: 1 to 2 infarcts (n=22), 3 to 4 infarcts (n=21), and >5 infarcts (n=23).





Werring et al, Brain, 2004

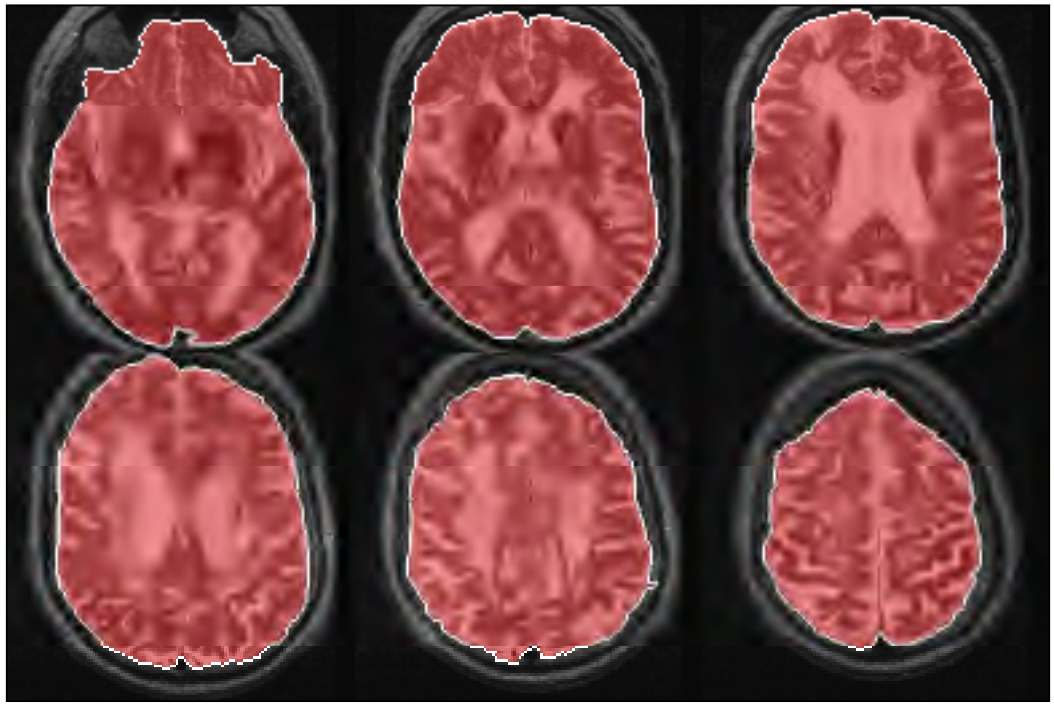
Table 3 Analysis of factors of poor outcome in CADASIL patients

Characteristic	mRS < 3 [*n* (%)]	mRS ⩾ 3 [*n* (%)]	*P*-value
Male	45 (41)	18 (53)	0.22
Age (years ± SD)	49.8 ± 11.0	59.5 ± 8.0	<0.0001
History of hypertension	18 (16)	9 (26)	0.19
Dementia	4 (17)	19 (83)	<0.0001
Past or current smoker	56 (51)	14 (41)	0.32
Diabetes mellitus	3 (3)	1 (3)	1.00
History of hypercholesterolaemia	52 (47)	21 (62)	0.14
Anticoagulant use	3 (3)	4 (12)	0.05
Antithrombotic use	75 (68)	28 (82)	0.11
Any alcohol consumption	63 (62.4)	14 (42.4)	0.04
Total cholesterol	5.58 ± 1.01	5.24 ± 1.25	0.11
LDL	3.51 ± 0.90	3.36 ± 0.96	0.42
HDL	1.52 ± 0.42	1.27 ± 0.32	0.002
HbA1c	5.5 ± 0.44	5.3 ± 0.37	0.04
Blood glucose (mmol/l ± SD)	5.3 ± 0.75	5.3 ± 0.58	0.49
SBP (mmHg ± SD)	126 ± 14	136 ± 21	0.03
DBP (mmHg ± SD)	75 ± 10	77 ± 12	0.28
nWMH	7.13 ± 4.82	9.61 ± 4.94	0.005
nLV	0.58 ± 0.72	1.82 ± 2.7	<0.0001
Number of microhaemorrhages	0.97 ± 2.5	13.5 ± 30.4	<0.0001

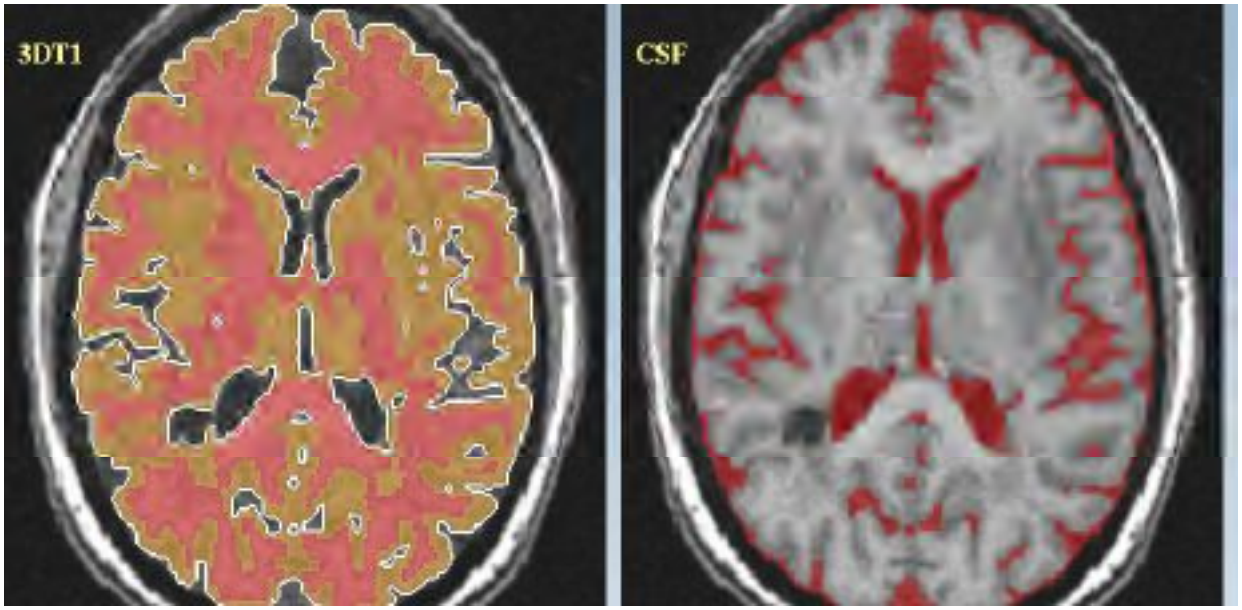
LDL = low-density lipoprotein; HDL = high-density lipoprotein; HbA1c = haemoglobin A1c; SBP = systolic blood pressure; DBP = diastolic blood pressure; nWMH = normalized white matter hyperintensity volume; nLV = normalized lacunar infarct volume.

Viswanathan et al, Brain 2006

Cerebral volume



Intracranial cavity segmentation



CSF segmentation

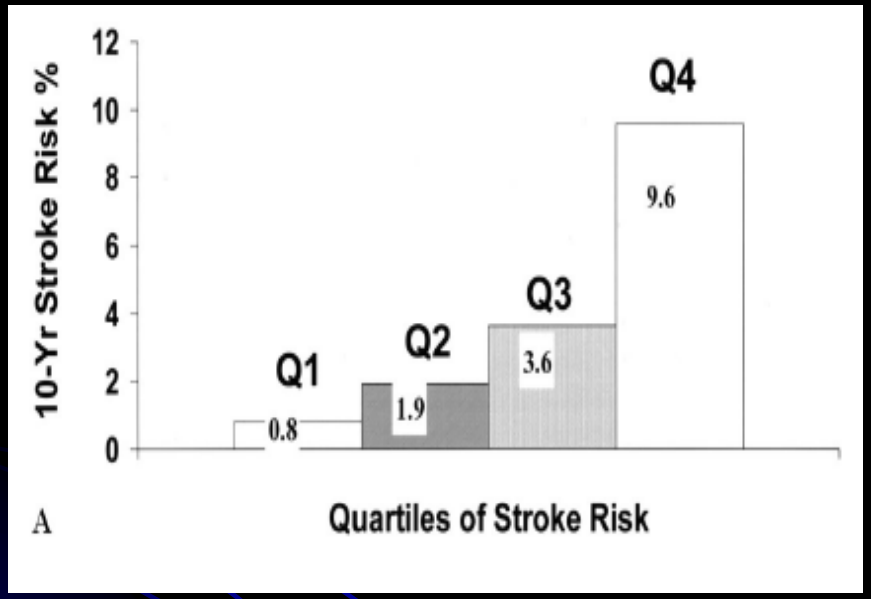
The framingham stroke risk profile is associated with cerebral atrophy and cognitive decline

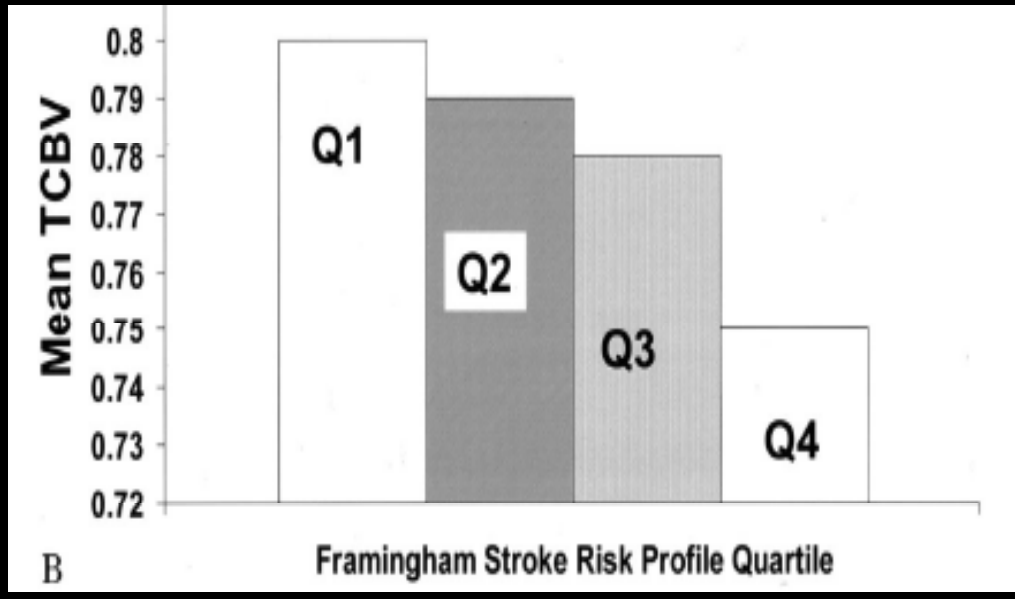
Framingham stroke risk profile

	Points										
	0	+1	+2	+3	+4	+5	+6	+7	+8	+9	+10
Men											
Age, y	54–56	57–59	60–62	63–65	66–68	69–72	73–75	76–78	79–81	82–84	85
Untreated systolic blood pressure, mm Hg	97–105	106–115	116–125	126–135	136–145	146–155	156–165	166–175	176–185	186–195	196–205
Treated systolic blood pressure, mm Hg	97–105	106–112	113–117	118–123	124–129	130–135	136–142	143–150	151–161	162–176	177–205
History of diabetes	No		Yes								
Cigarette smoking	No			Yes							
Cardiovascular disease	No				Yes						
Atrial fibrillation	No				Yes						
Left ventricular hypertrophy on electrocardiogram	No					Yes					

AGA Stroke Council, Circulation, 2006

The framingham stroke risk profile is correlated to cerebral atrophy and cognitive decline





Seshadri et al, Neurology, 2004

Correlated to performances in
- attention
- executive
- visuospatial functions

Decreased volume of cortical gray matter in subcortical ischemic vascular dementia

Diagnosis	cGM	sGM	WM	sCSF	vCSF	WMSH
Control	503 ± 28*	18 ± 3	459 ± 31*	267 ± 43	46 ± 14*	5 ± 6*
AD	458 ± 40	17 ± 5	419 ± 37	319 ± 52	66 ± 22‡	8 ± 7†
Percent change	−10	−6	−9	19	43	60
SIVD	438 ± 42*	15 ± 4	426 ± 36*	286 ± 65	85 ± 24*‡	45 ± 39*†
Percent change	−13	−17	−7	7	85	800

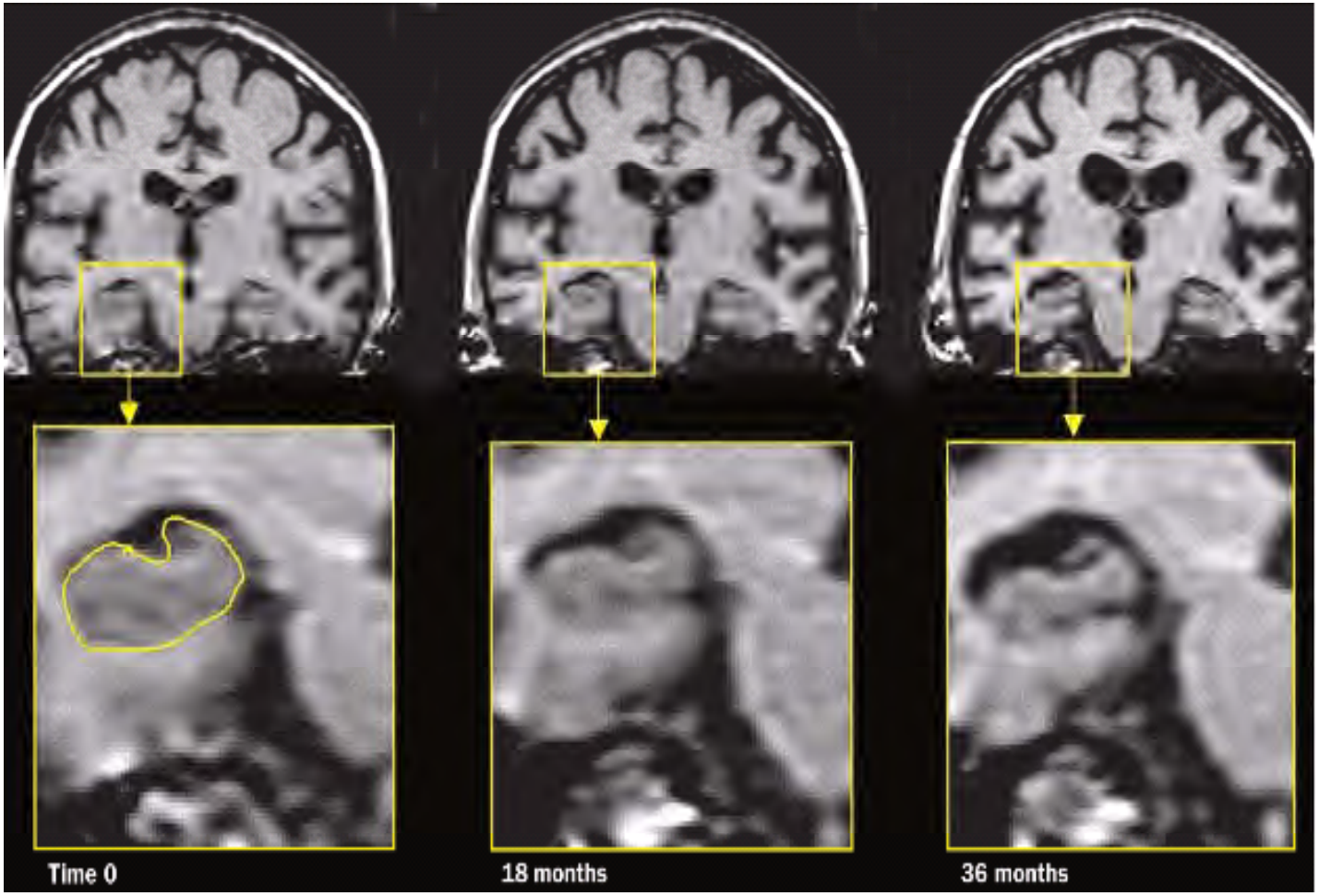
Data represented as mean ± SD in units of cm^3. Percent change compared with cognitively normal subjects.

* $p < 0.01$ subjects with SIVD vs cognitively normal subjects.
† $p < 0.01$, ‡ $p < 0.05$ subjects with SIVD vs subjects with AD.

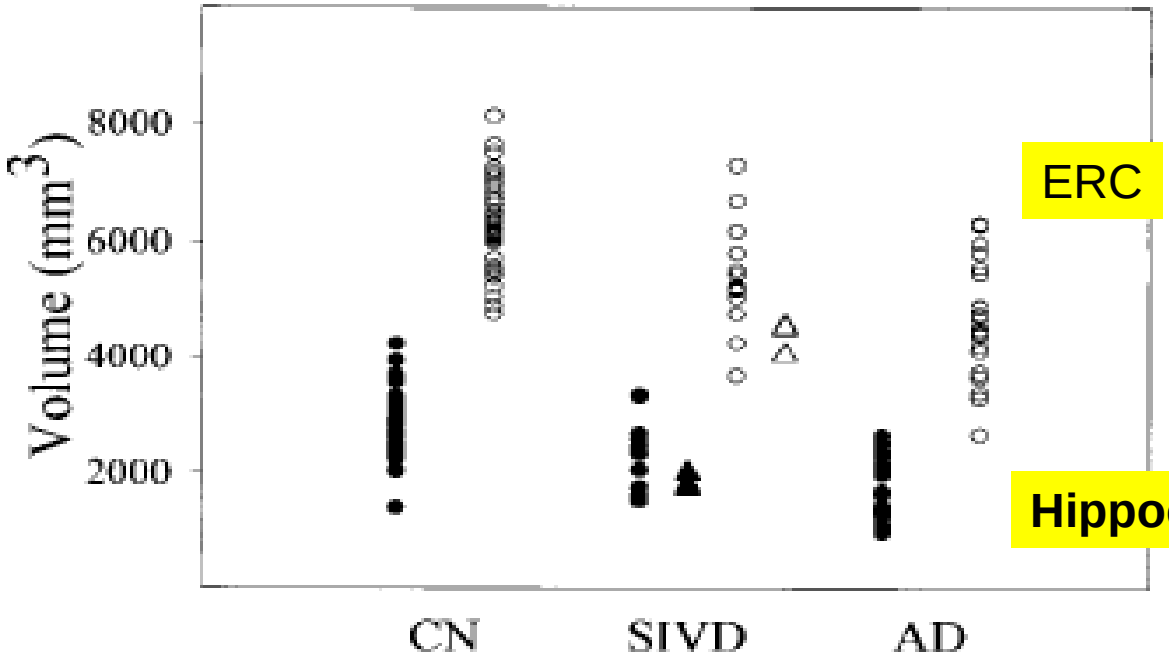
cGM = cortical gray matter; sGM = subcortical gray matter; WM = white matter; sCSF = sulcal CSF; vCSF = ventricular CSF; WMSH = white matter signal hyperintensities; SIVD = subcortical ischemic vascular dementia.

From Du et al, Neurology, 2002

Visual assessment of hippocampus atrophy in Alzheimer’s disease



Atrophy of hippocampus and entorhinal cortex in VaD



ERC

Hippocampe

Figure 1. Plot of volumes of entorhinal cortex (ERC) and hippocampus in cognitively normal (CN) subjects, subjects with subcortical ischemic vascular dementia (SIVD) and AD. Black circles = ERC; open circles = hippocampus; black triangles = ERC of confirmed SIVD; open triangles = hippocampus of confirmed SIVD.

Du et al, Neurology, 2002

Medial temporal cortex in AD and in SIVD

Demographics	Cognitively normal subjects	Patients with AD	Patients with SIVD
No. (% F)	38 (47)	22 (55)	18 (33)
Age, y	75.0 ± 4.3	76.7 ± 4.7	74.2 ± 8.3
Mini-Mental State Examination	28.9 ± 0.9	19.5 ± 4.7*	19.9 ± 4.7*
Hachinski Ischemic Score	1.2 ± 2.0	1.0 ± 0.5	7.7 ± 3.7*‡
List Recall Test	9.9 ± 2.4	0.5 ± 1.3*	3.1 ± 3.5*‡
Delayed List Recall Test	10.8 ± 1.7	0.6 ± 1.4*	3.8 ± 3.5*‡
Mattis Dementia Rating Scale	8.0 ± 0.2	6.8 ± 1.8*	5.1 ± 2.7*§
Letter Verbal Fluency Test	15.7 ± 4.8	12.0 ± 5.6*	4.5 ± 3.7*‡

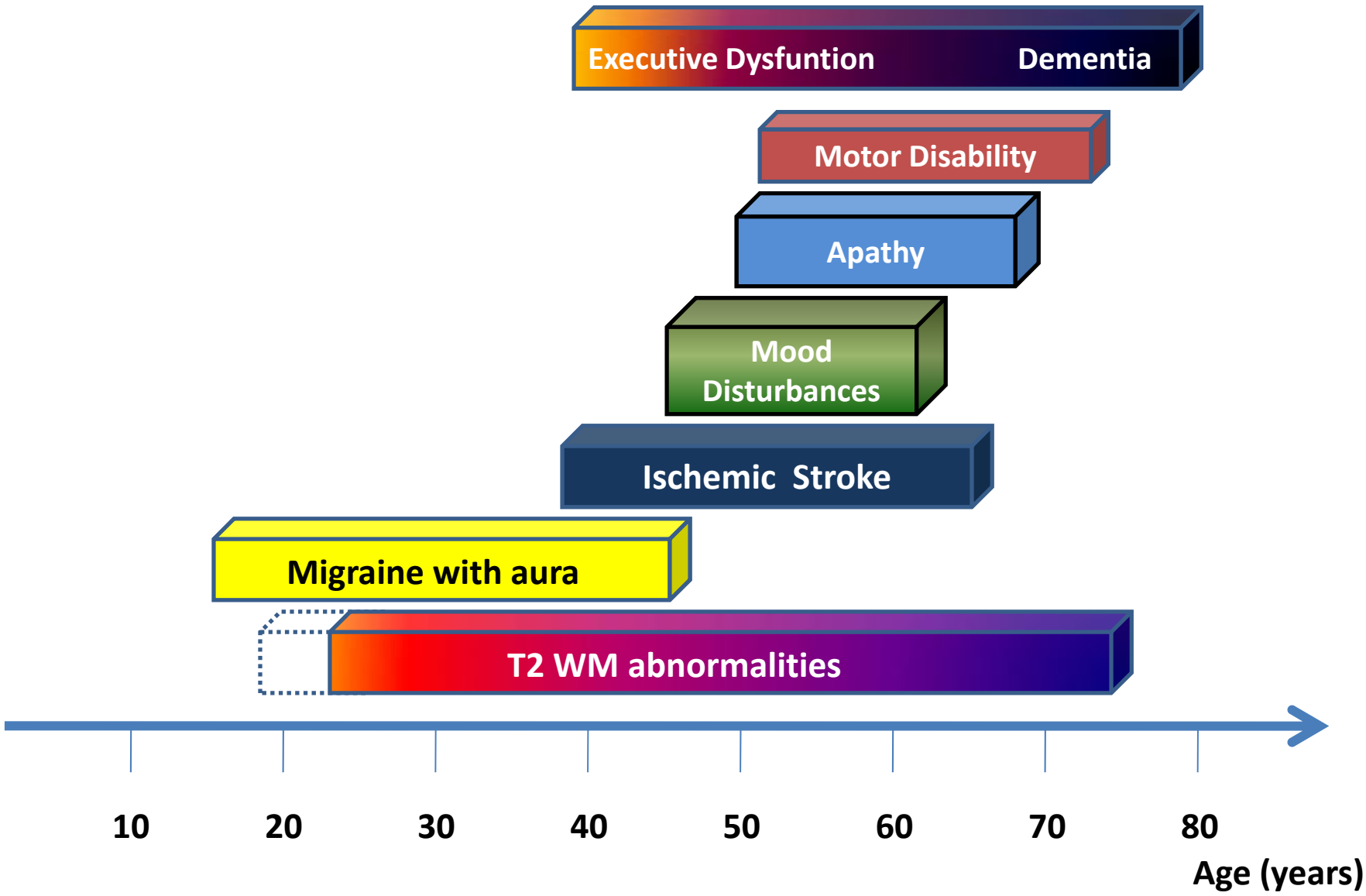
Diagnosis	Entorhinal cortex	Hippocampus
Cognitively normal subjects	2,787 ± 582	6,307 ± 817
AD	1,649 ± 503	4,587 ± 997
Percent change vs cognitively normal subjects	40.8	27.3
SIVD	2,183 ± 543*†	5,162 ± 915*‡
Percent change vs cognitively normal subjects	−21.7	−18.2

Data represented as mean ± SD in units of mm^3.

* $p < 0.01$, SIVD compared with cognitively normal subjects.
† $p < 0.01$, ‡ $p < 0.05$, subjects with SIVD compared with subjects with AD.

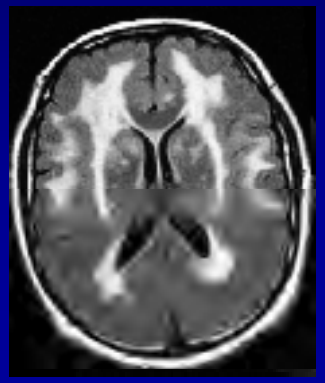
Du et al, Neurology, 2002

Natural History of CADASIL

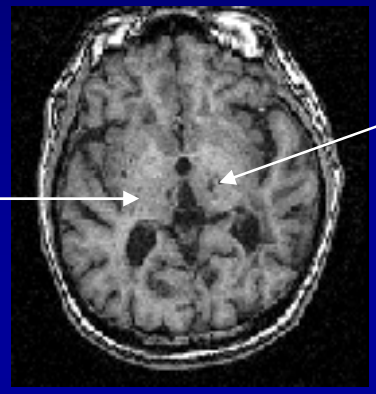


Weight of MRI lesions in CADASIL

White Matter Hyperintensities (WMH)

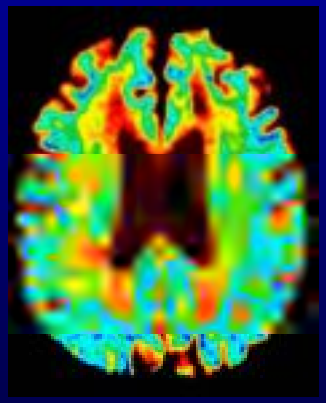


Lacunar Lesions

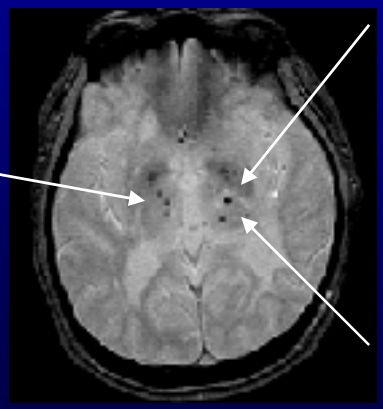


Cognitive impairment
&
Disablity

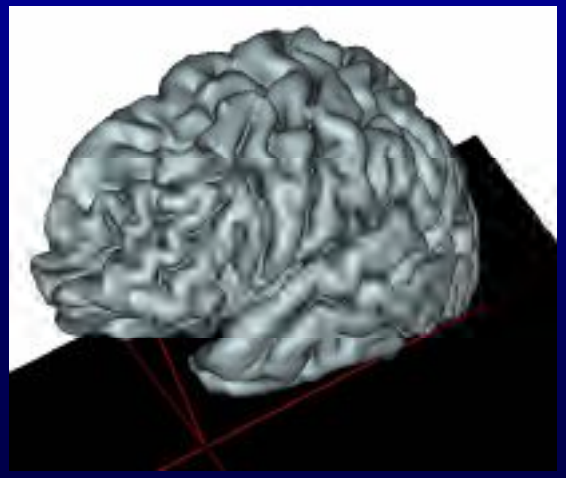
Diffusion Changes



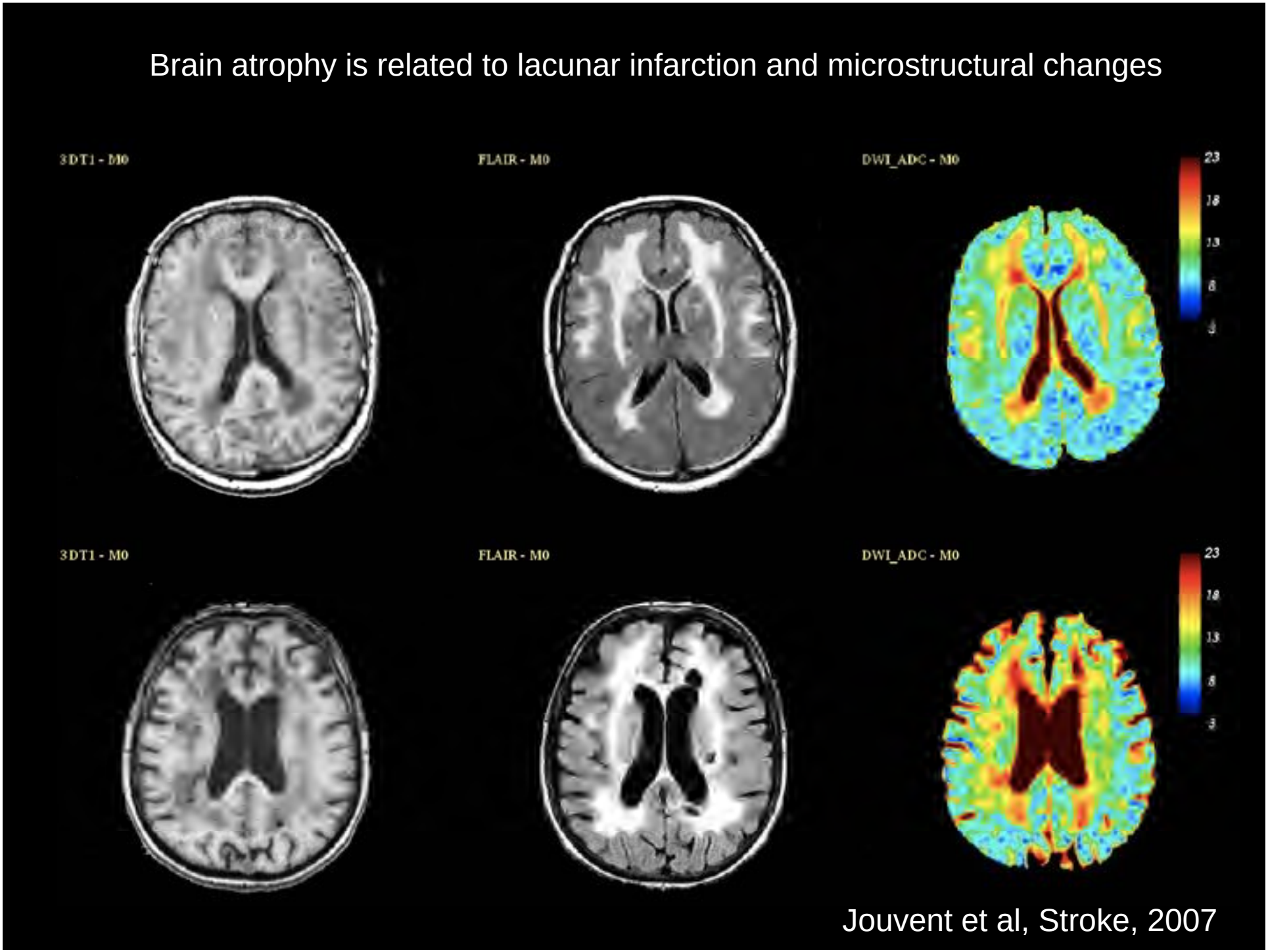
Microhemorrhages



Brain Atrophy



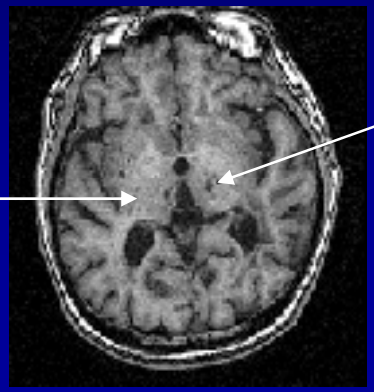
Brain atrophy is related to lacunar infarction and microstructural changes



Jouvent et al, Stroke, 2007

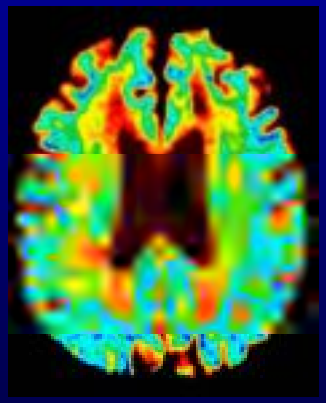
Weight of MRI lesions in CADASIL

Lacunar Lesions

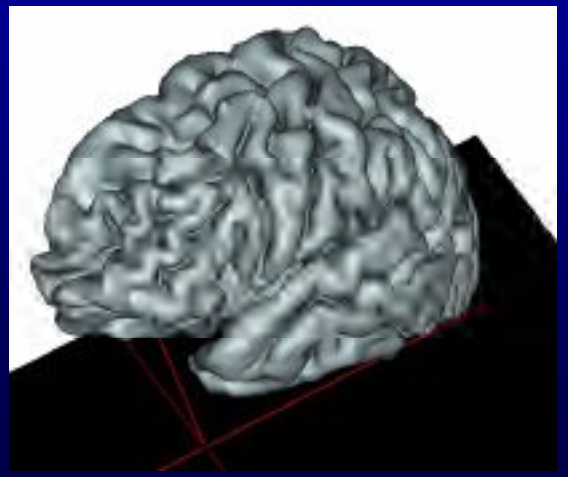


Cognitive impairment

Diffusion Changes



Brain Atrophy



Total explained variance: 45%

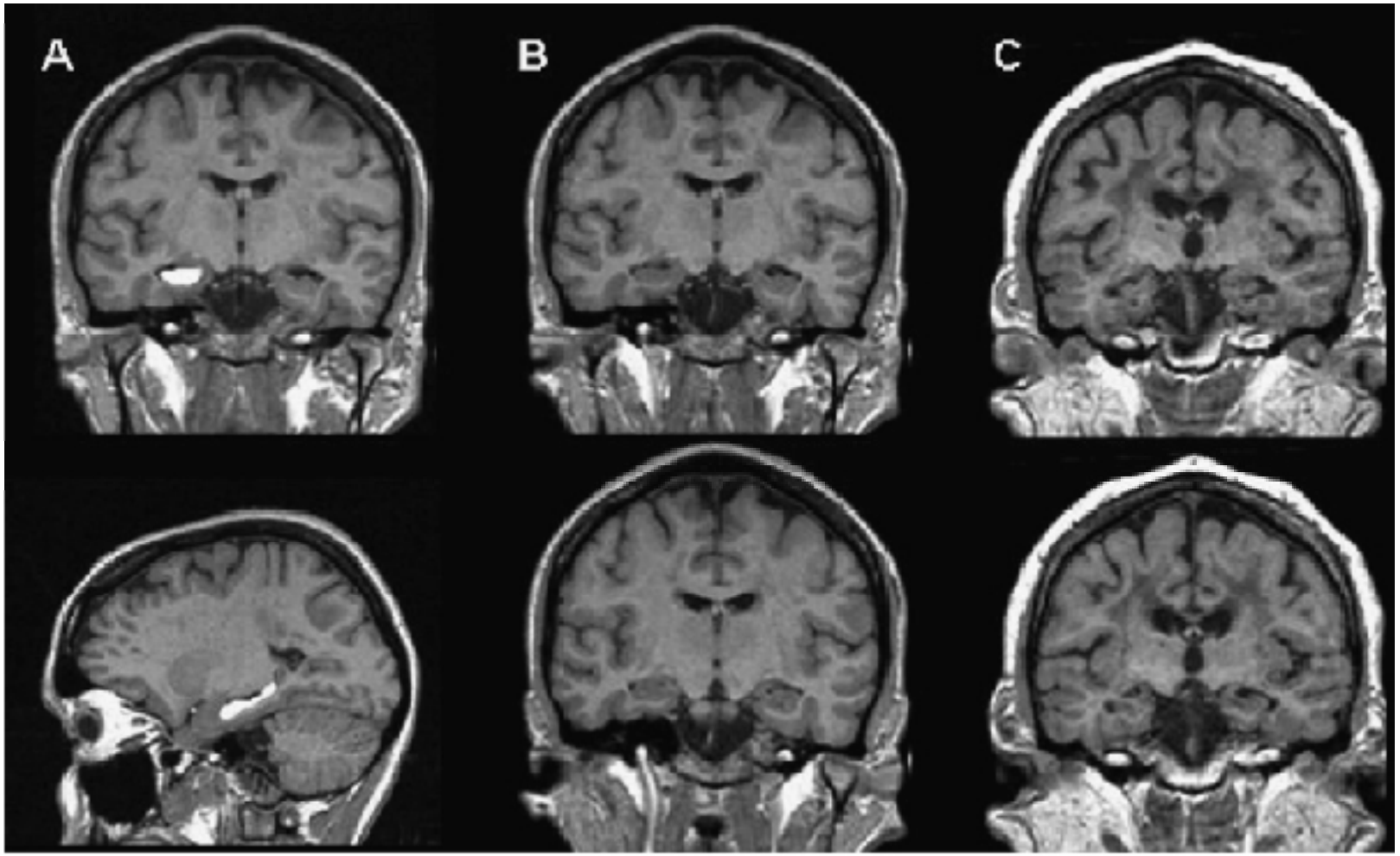
Viswanathan et al, Biol Aging, 2008

Hippocampal volume is an independent predictor of cognitive performance in CADASIL

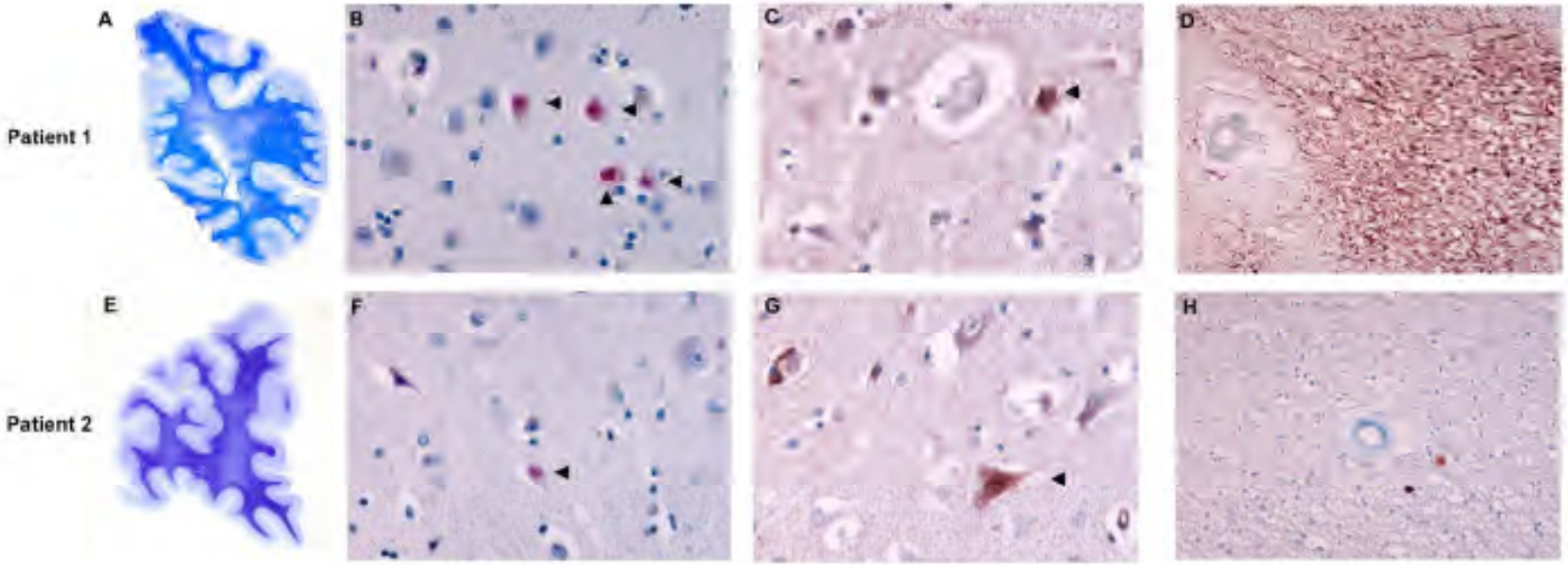
Mike O'Sullivan[a,*], Elmar Ngo[a], Anand Viswanathan[b,c], Eric Jouvent[b], Andreas Gschwendtner[a], Philipp G. Saemann[d], Marco Duering[a], Chahin Pachai[e], Marie-Germaine Bousser[b], Hugues Chabriat[b], Martin Dichgans[a]

NEUROBIOLOGY OF AGING

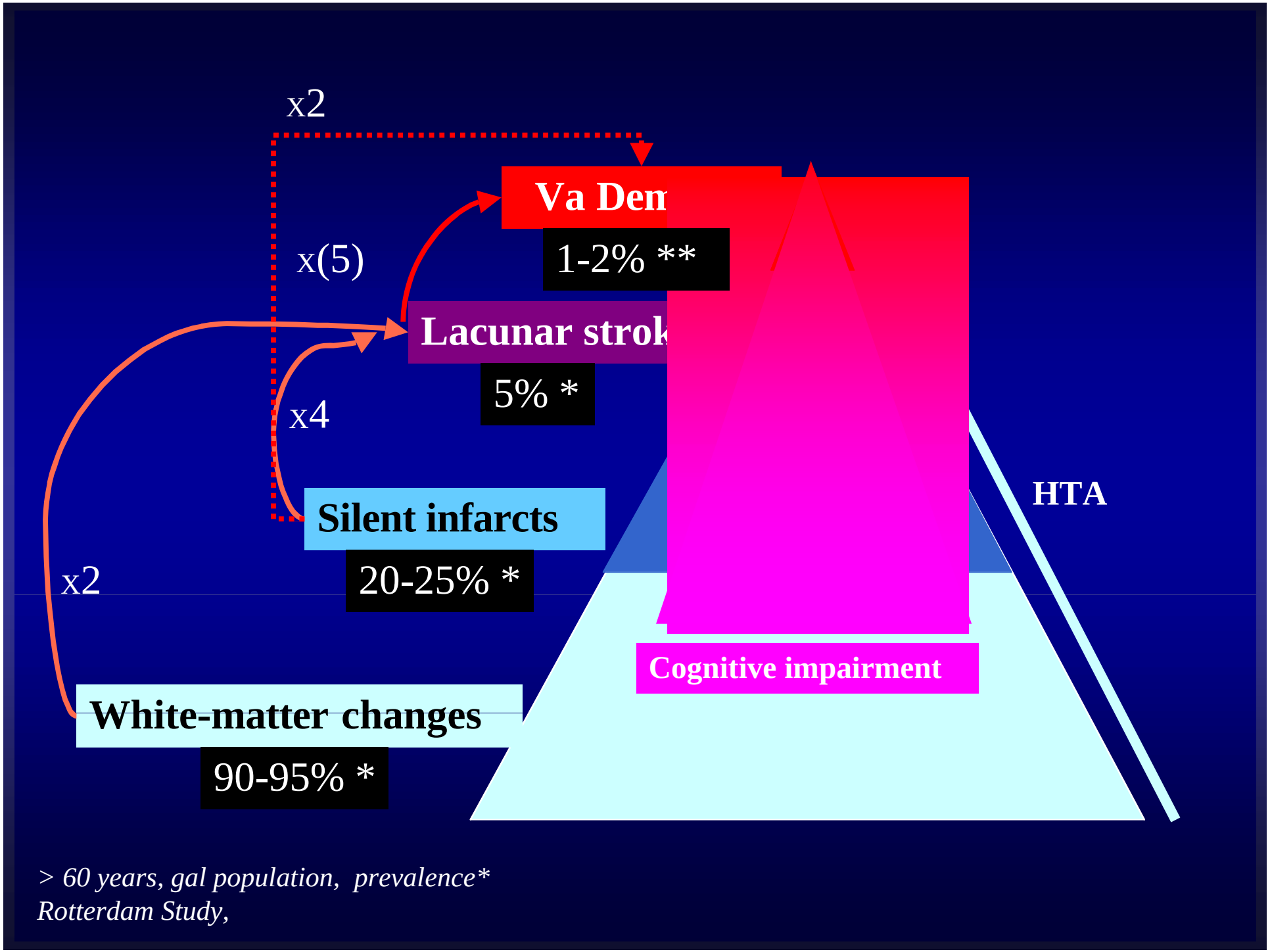
www.elsevier.com/locate/neuaging



Apoptose neuronale corticale dans CADASIL



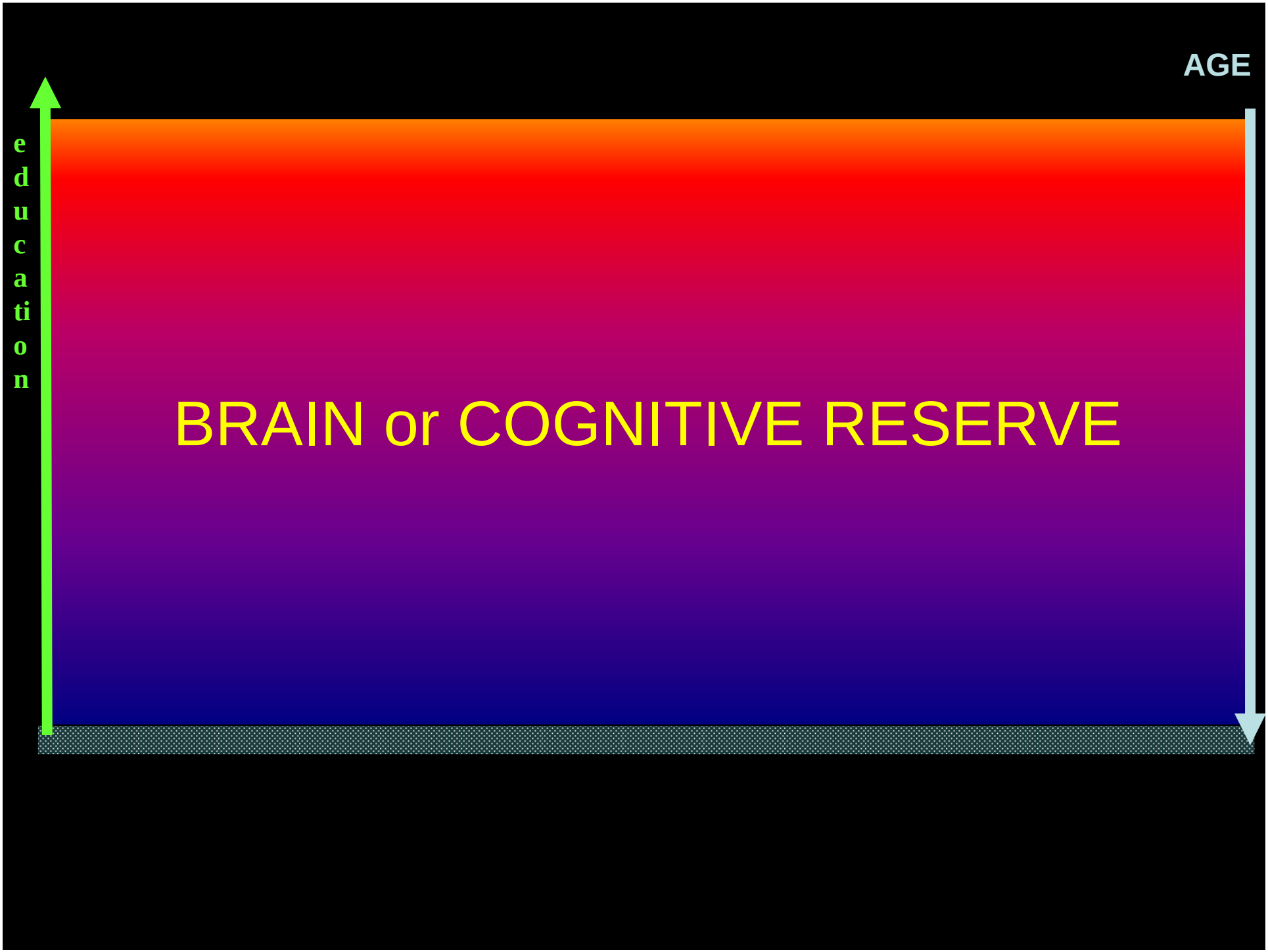
Viswanathan et al, Stroke, 2007

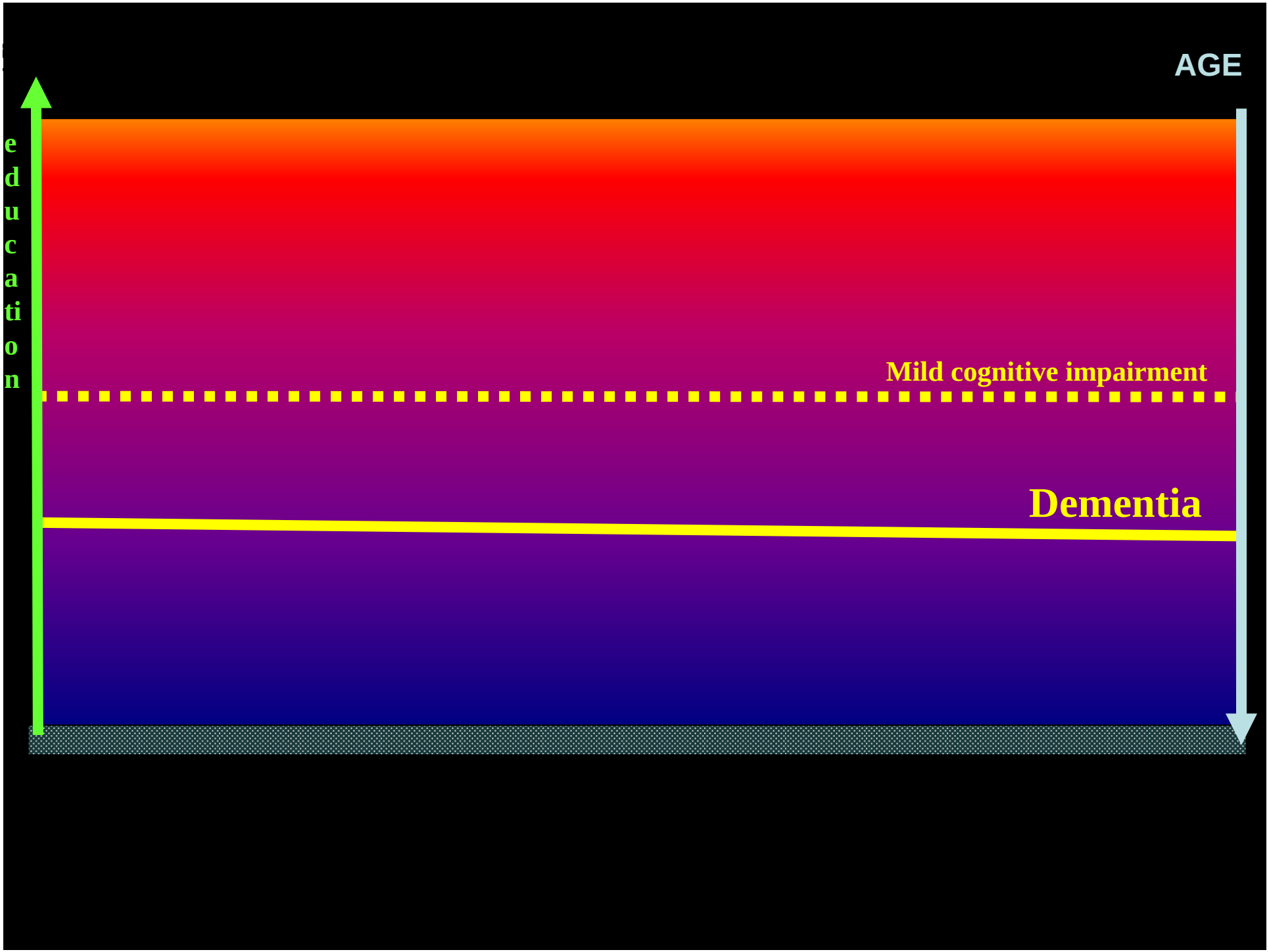


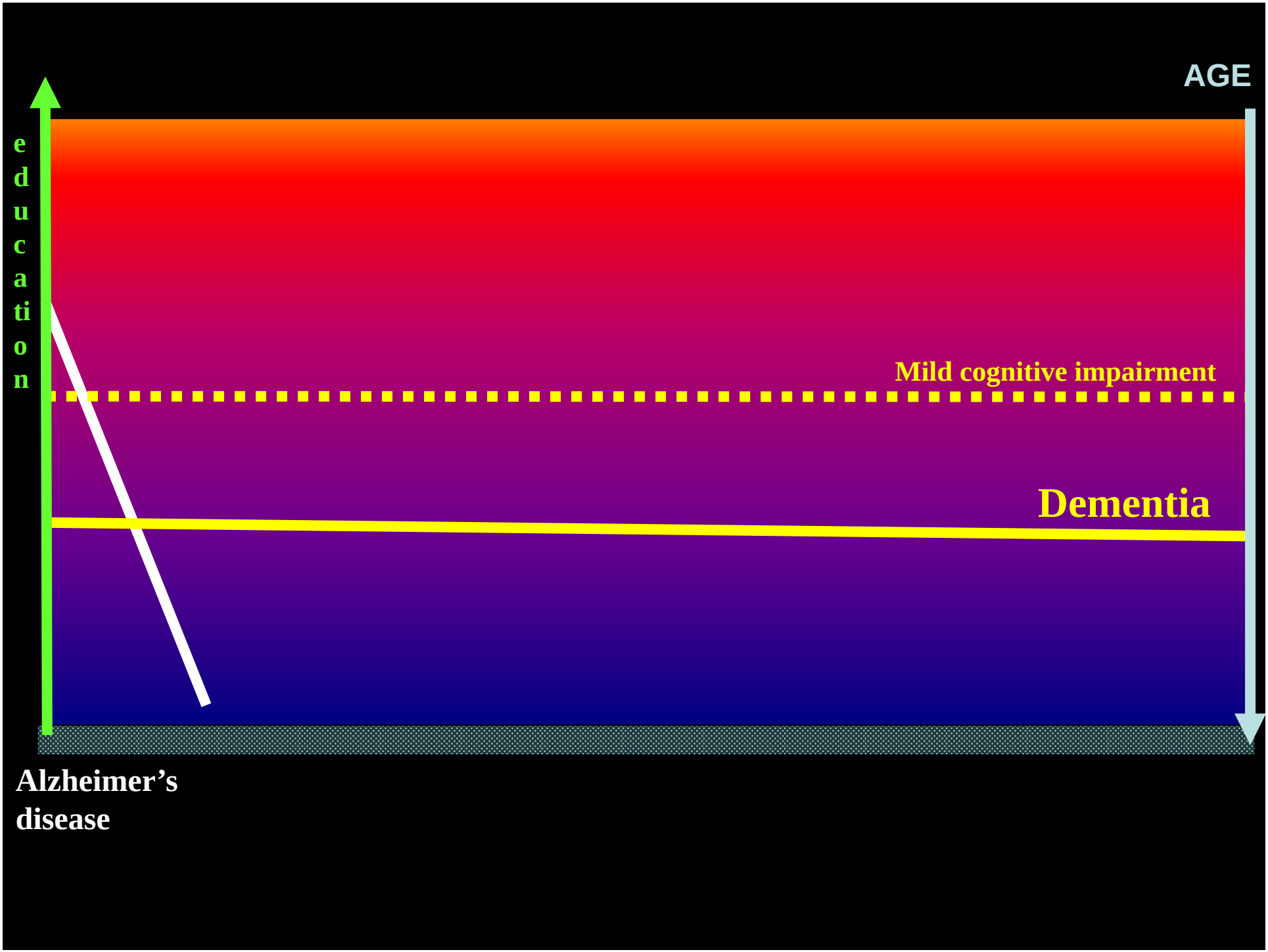
*> 60 years, gal population, prevalence**
Rotterdam Study,

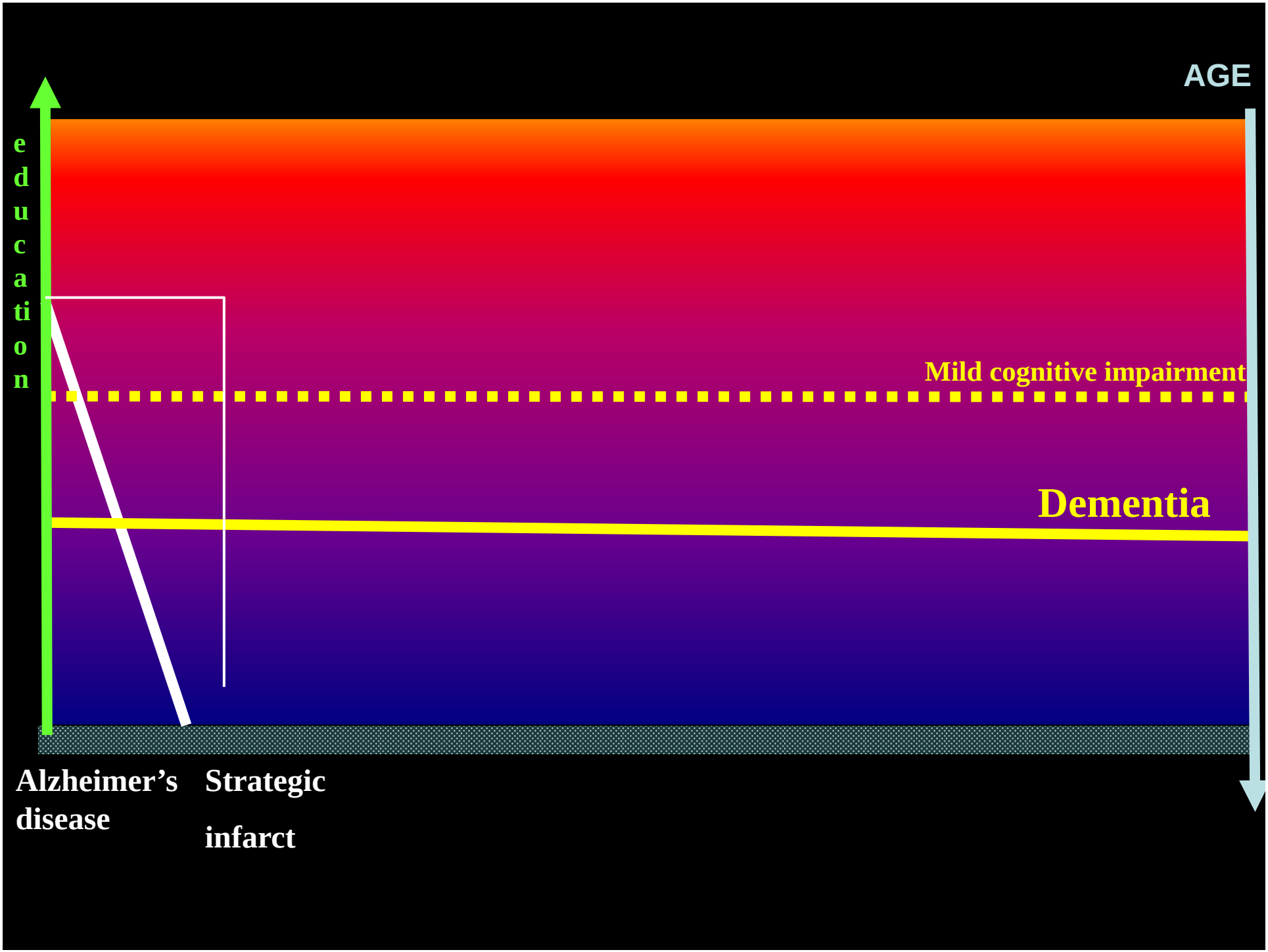
Conclusion

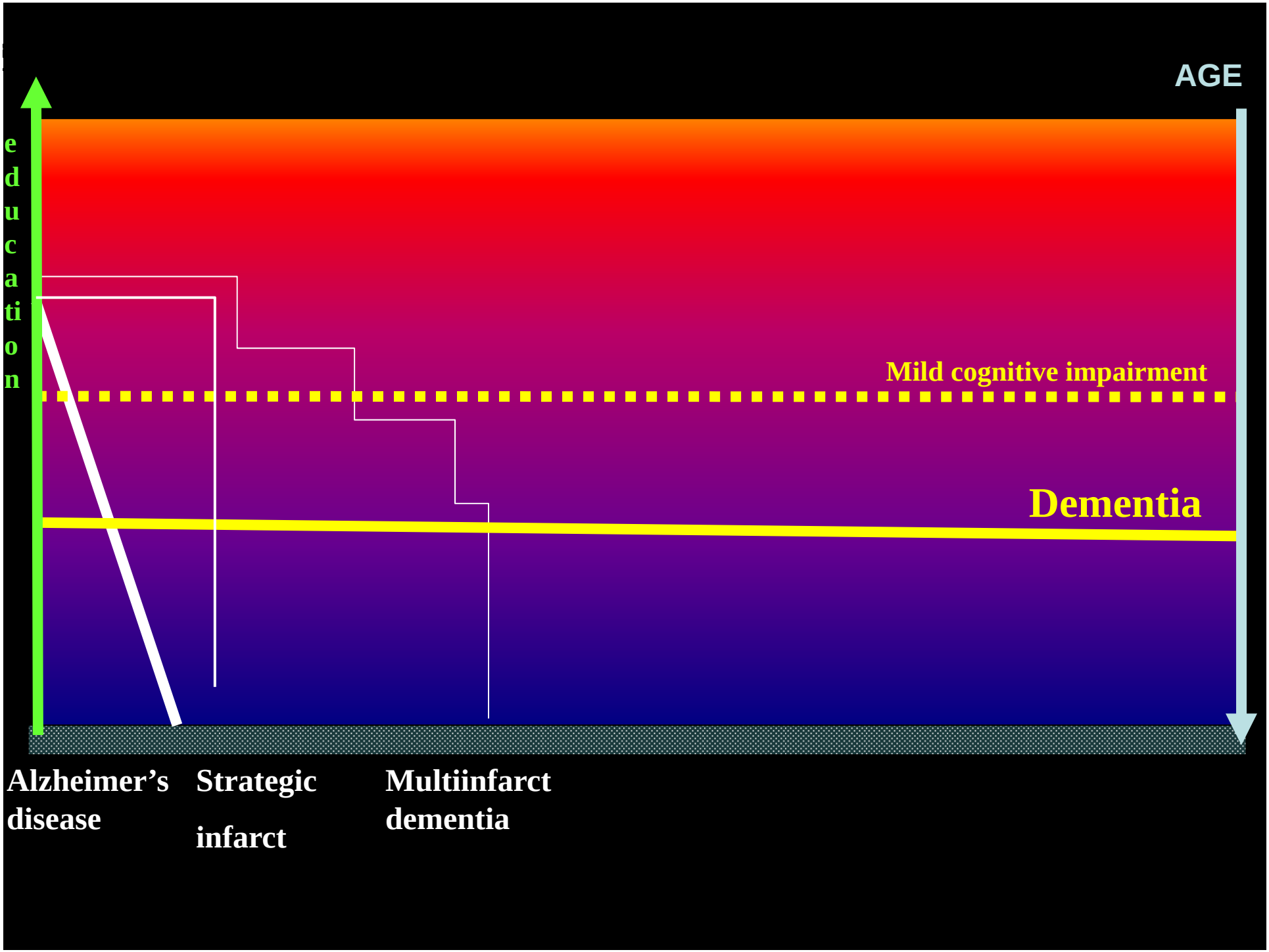
- **Les démences vasculaires correspondent à un syndrome clinico-radiologique et non à une maladie**
- **Les démences vasculaires « pures » sont en rapport avec des lésions d'origine vasculaire interrompant les réseaux neuronaux qui sous-tendent les fonctions cognitives altérées définissant la « démence »**
- **Les hypersignaux de la SB lorsqu'ils sont étendus et diffus sont responsables d'une atteinte des fonctions exécutives mais ne sont pas responsables lorsqu'ils sont isolés d'une démence**
- **Le stade de démence est en rapport avec des lésions destructives du tissu cérébral associées aux hypersignaux de la SB: infarctus lacunaires, altérations microstructurales tissulaires, réduction du volume cérébral, atrophie hippocampique**
- **TOUTES les lésions du tissu cérébral d'origine vasculaire peuvent réduire la « réserve cérébrale cognitive » et modifier le seuil d'apparition de la démence comme l'âge, le niveau d'éducation, l'apoE4 ou des lésions dégénératives**

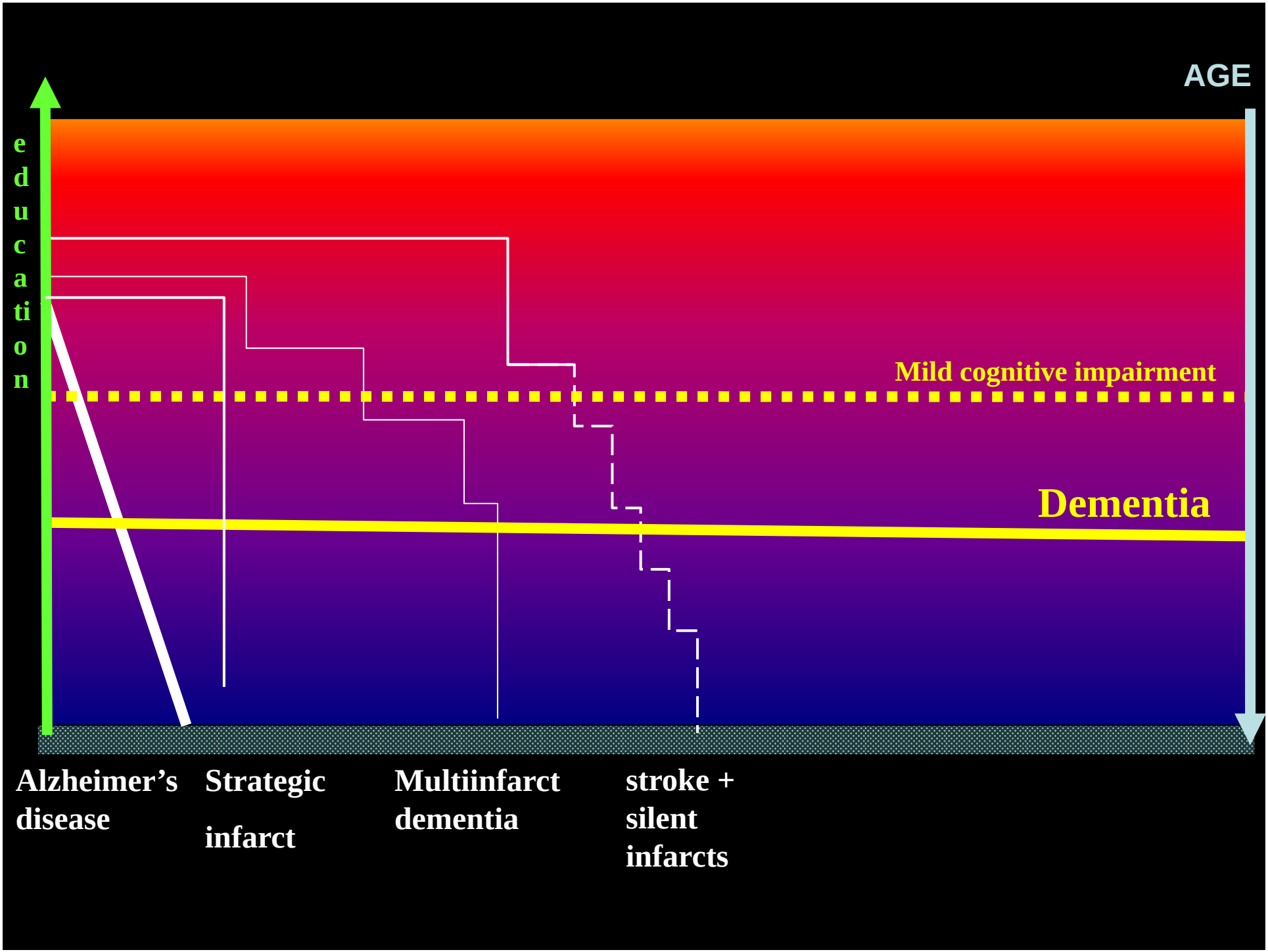

AGE
education
BRAIN or COGNITIVE RESERVE

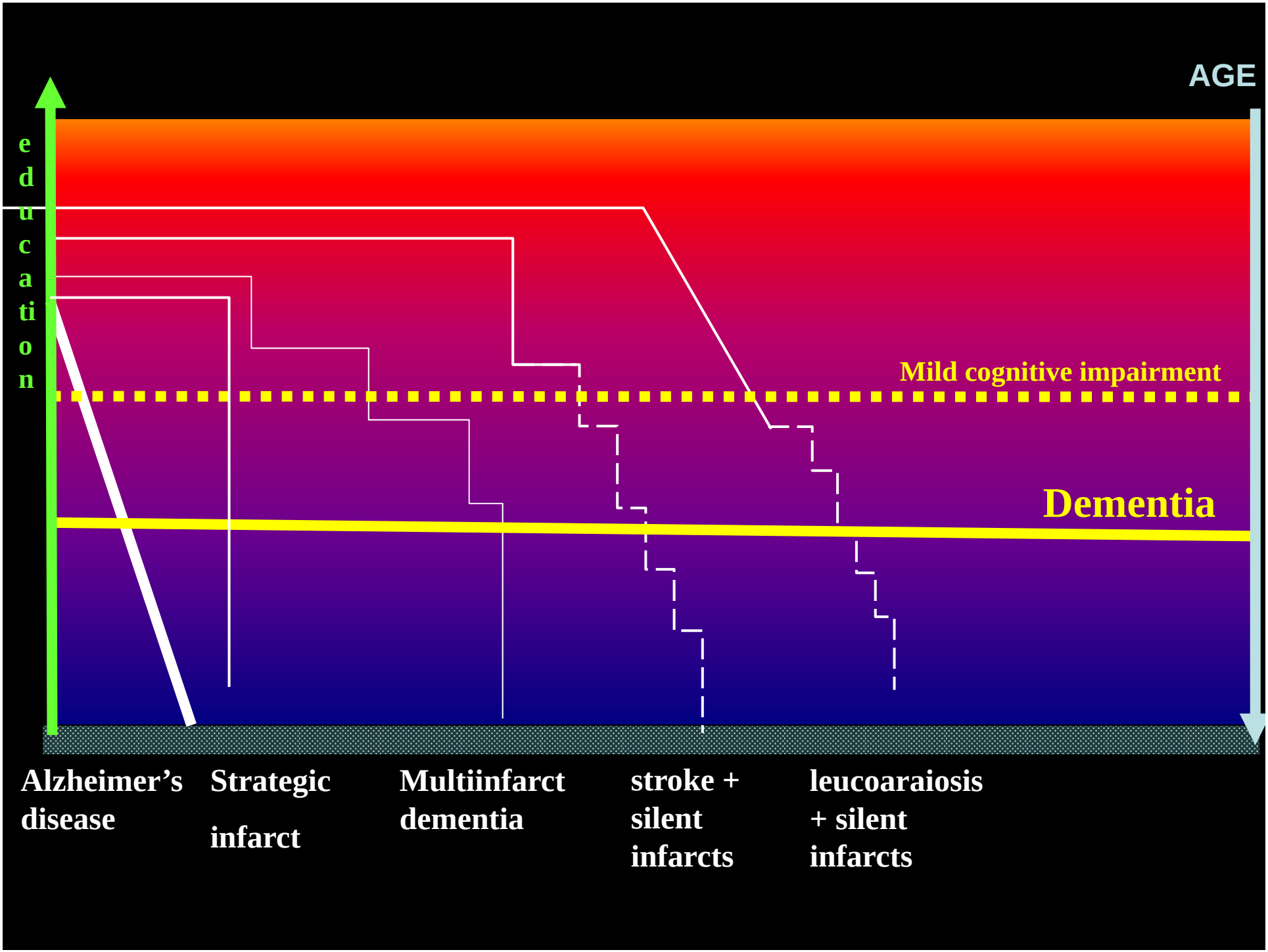

AGE
education
Mild cognitive impairment
Dementia

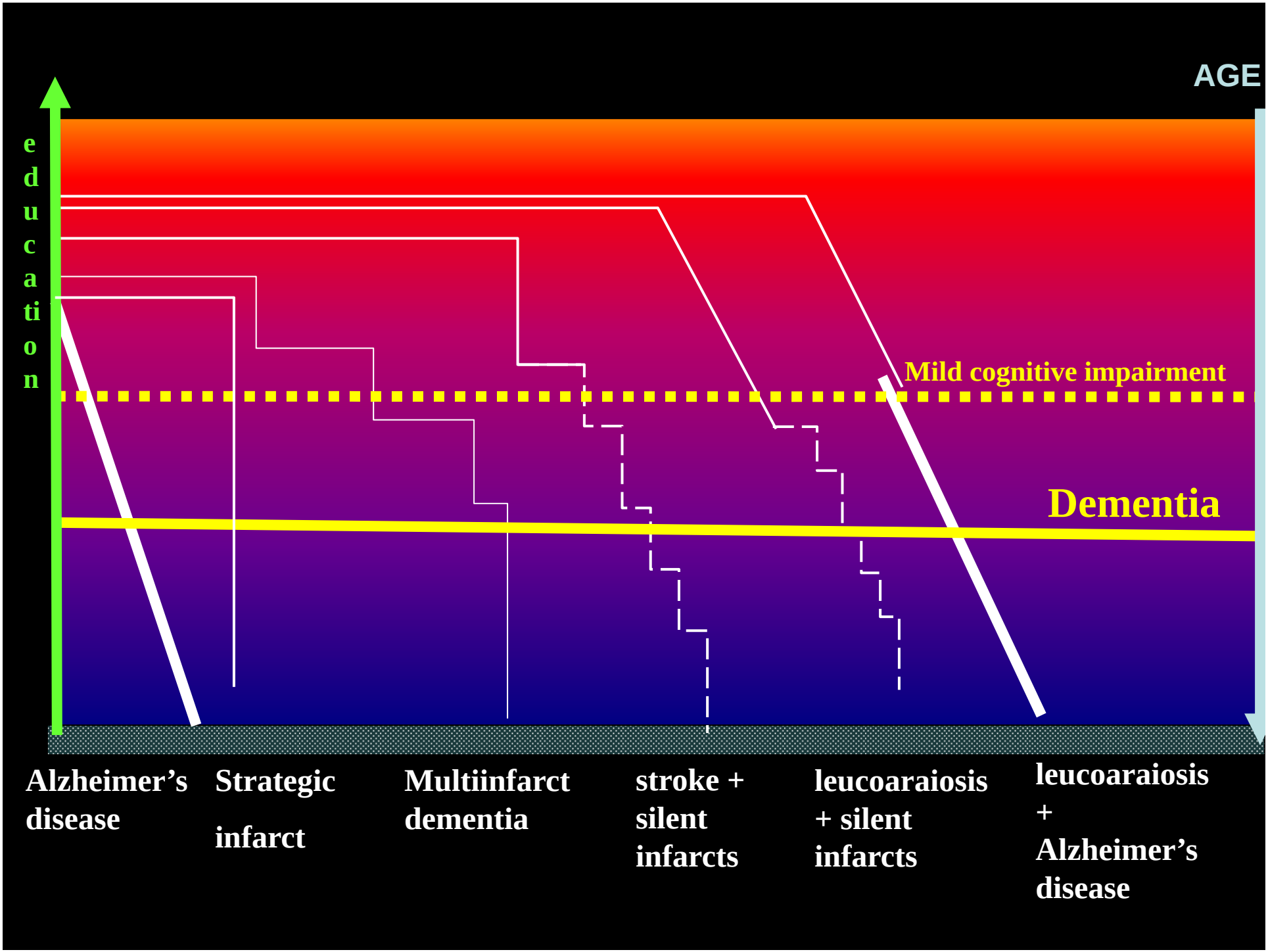

AGE
education
Mild cognitive impairment
Dementia
Alzheimer's disease

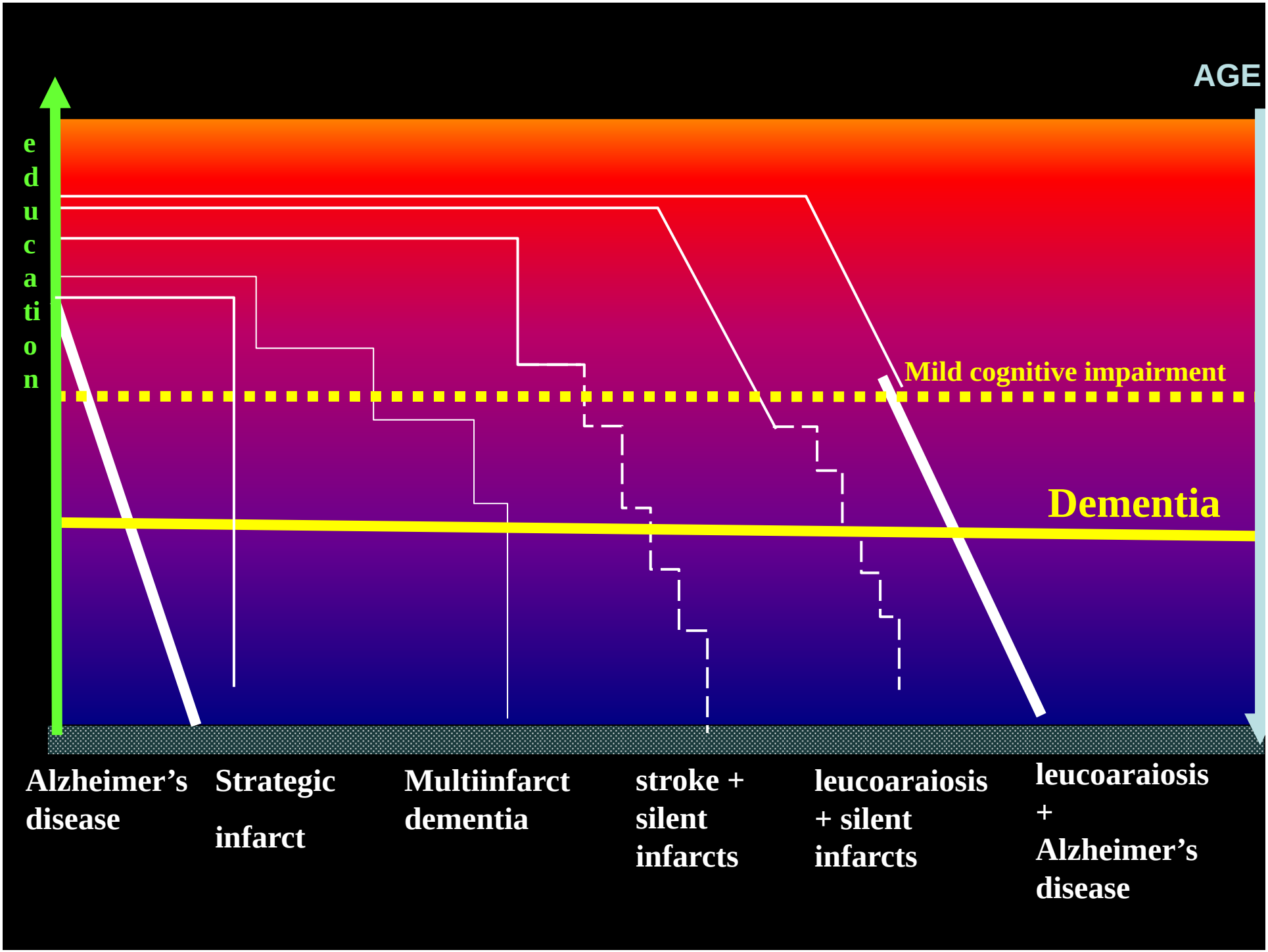

AGE
education
Mild cognitive impairment
Dementia
Alzheimer's disease
Strategic infarct

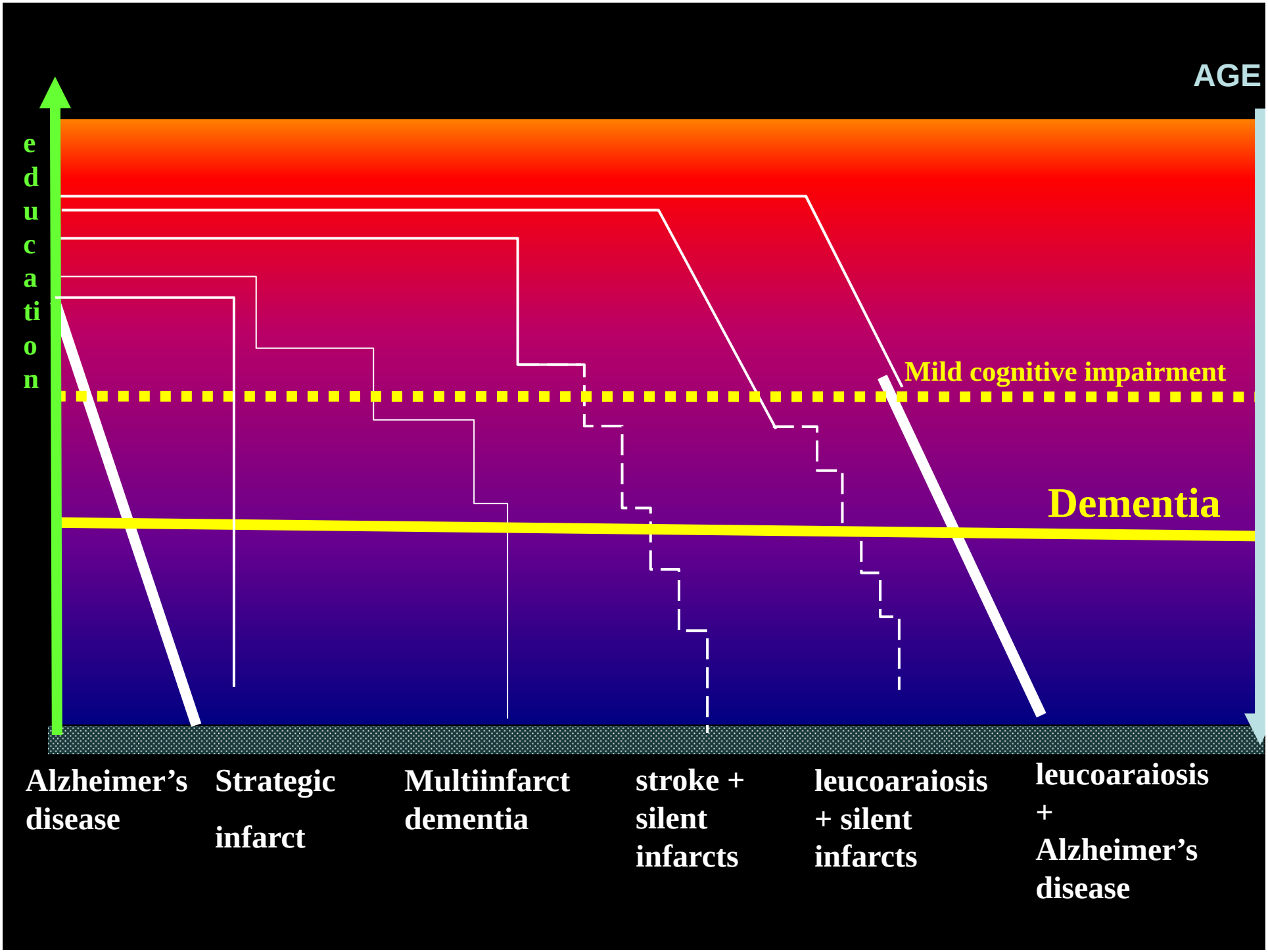

AGE
education
Mild cognitive impairment
Dementia
Alzheimer's disease
Strategic infarct
Multiinfarct dementia


AGE
education
Mild cognitive impairment
Dementia
Alzheimer's disease
Strategic infarct
Multiinfarct dementia
stroke + silent infarcts


AGE
education
Mild cognitive impairment
Dementia
Alzheimer's disease
Strategic infarct
Multiinfarct dementia
stroke + silent infarcts
leucoaraiosis + silent infarcts


AGE
education
Mild cognitive impairment
Dementia
Alzheimer's disease
Strategic infarct
Multiinfarct dementia
stroke + silent infarcts
leucoaraiosis + silent infarcts
leucoaraiosis + Alzheimer's disease


AGE
education
Mild cognitive impairment
Dementia
Alzheimer's disease
Strategic infarct
Multiinfarct dementia
stroke + silent infarcts
leucoaraiosis + silent infarcts
leucoaraiosis + Alzheimer's disease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Mild cognitive impairment
Dementia
Alzheimer's disease
Strategic infarct
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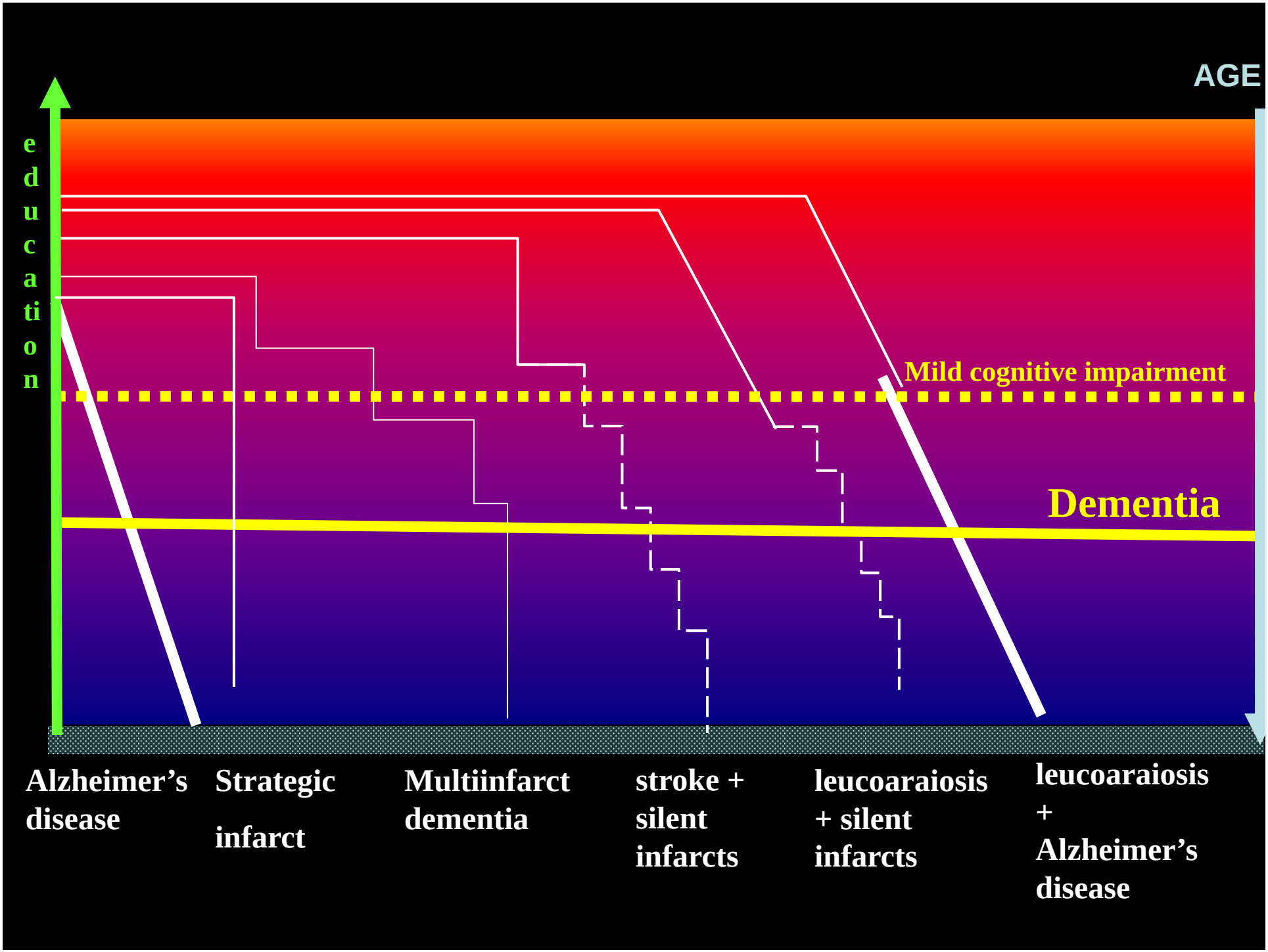
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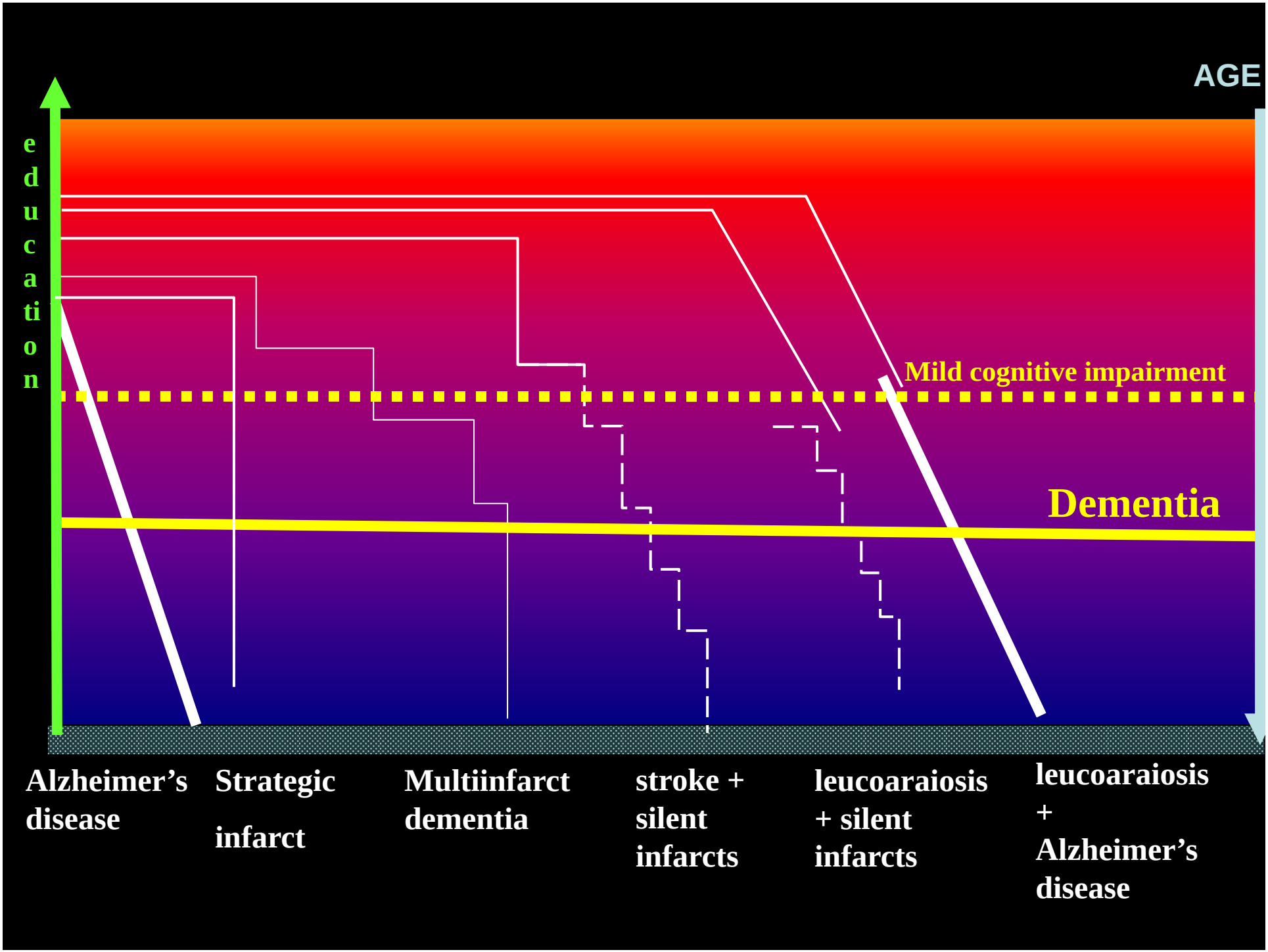
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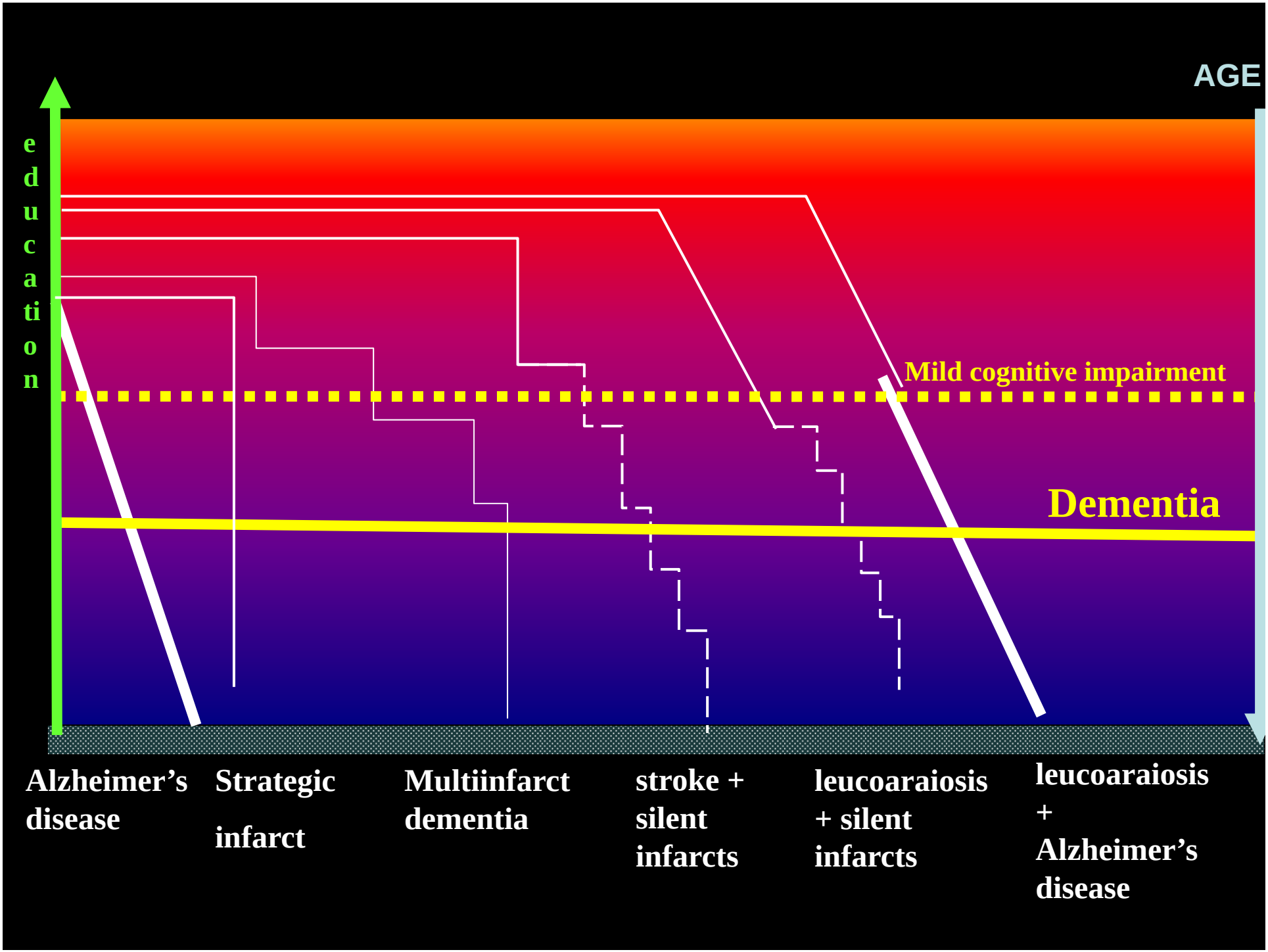
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