Vascular Dementia or Dementia with Cerebro-Vascular Disease : Changes in Concepts

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Current concepts on dementia

Excessive emphasis on memory disturbances :

- Based on the cortico-hippocampic type (AD)
- Not applicable to the sub-cortical and fronto-temporal types, more frequents in VaD

The DSM-IV definition is loose :

- 1) memory loss + 2) cognitive impairment x and y (+ z…) = dementia if (and only if) there is 3) a functional loss
- Executive dysfunction is often prominent in VaD : alternative to memory loss as first criterion? It drives the early functional loss…

WHO ICD-10 : Dementia is not only a dysmnesia

Definition of VaD

VaD is an etiological category of dementia in ICD-10

- Includes dementia resulting from cerebral ischemia or hemorrhage (post-stroke dementia)
- Much rarer : dementia from global hypoperfusion (post-CABG or post-CHF)
- BUT: the definition of ***dementia*** needs to be clarified: phenocopy of AD or broader definition?

Diagnosis of VaD: NINDS-AIREN criteria

Dementia
- Impaired memory (?)
- ≥2 other cognitive domains impaired

+ Cerebrovascular disease
- History of CVD (3-month)
- Neurological examination
- Neuroimaging

Probable/Possible diagnosis
- Temporal relationship between CVD and dementia
- Abrupt onset/stepwise progression
- Absence of disorders that could account for deficits (eg, AD)

Diagnosis of VaD

Román GC et al. Neurology. 1993;43:250-60

Alternative Definitions

Vascular cognitive disorder (VCD): a diagnostic category that includes any degree of cognitive impairment resulting from cerebrovascular disease [CVD]. Includes :

Vascular cognitive impairment (VCI): isolated cognitive dysfunction, not qualifying as dementia, and

Vascular Dementia (VaD): cognitive impairment causing dementia, both resulting from ischemic or hemorrhagic CVD (post-stroke dementia); or from hypoperfusion (hypotension, post coronary artery bypass graft [CABG] or post congestive heart failure [CHF])

•*Roman et al, J Neurol Sci, 2004*

Executive Control Functions

- "Command and control" of complex goal-directed action
- Examples include initiation, sequencing and monitoring of complex behavior
- Executive dysfunction is expressed as disorganized thought, behavior, or emotions
- ECF was added to the DSM-IV definition of dementia in 1994

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th edition (1994).

Executive dysfunction in vascular dementia

Is a characteristic feature of VaD[1] although not mandatory in current criteria

Includes difficulties in planning, organization, problem-solving, conceptualization, mental flexibility

Leads to difficulties in performing instrumental activities of daily living (IADL)[2] Such as managing finances, phoning, transportation, medication, engaging in hobbies[3]

[1]Román GC, Royall DR. Alzheimer Dis Assoc Disord. 1999;13:S69-80
[2]Pohjasvaara T, et al. Eur J Neurol. 2002;9:269-75
[3]Dartigues et al, PAQUID Study, 1994

Key differentiating factors

Alzheimer's disease	Vascular dementia
Insidious onset	Sudden onset
Progressively deteriorating course	Fluctuating, stepwise course with plateaus
No early focal neurological signs	Early focal neurological symptoms & signs
No vascular damage on brain imaging	Evidence of relevant vascular brain damage

Moroney et al. Neurology 1997; 49: 1096–105

Epidemiology: Prevalence of AD + CVD in the elderly

	Year	Population (%)
Rochester[1]	1987	9
Appiganano[2]	1990	13
Gothenburg[3]	1993	8.2
Canadian IVIC[4]	2000	7.5
Canadian SHA1 (VCI/AD)[5]	2000	8
Campo Grande[6]	2002	37
Cardiovascular Health Study[7]	2003	16

Overall: 10–20%

1. Schoenberg et al. Ann Neurol 1987; 2. Rocca et al. Neurology 1990; 3. Skoog et al. N Engl J Med 1993; 4. Rockwood et al. Ann N Y Acad Sci 2000; 5. Rockwood et al. Neurology 2000; 6. Yamada et al. Psychiatry Clin Neurosci 2002; 7. Lopez et al. Neuroepidemiology 2003;

Stroke and VaD

Worldwide, stroke has affected ≈31 million people[1]

↓

25% to 41% may develop VaD[2]

↓

≈8 to 13 million people with VaD caused by stroke

[1]Murray & Lopez. WHO global health statistics. 1996; [2]Román. J Neurol Sci. 2002

Poststroke Dementia Prevalence

Helsinki: 6% to 25.5%

New York City: 27% to 41%

USA: 1 million cases

Europe: 800,000 VaD cases

Global prevalence of VaD in Europe:

- 16/1000 after age 65
- 52/1000 after age 90

EURODEM. Neurology. 2000; 54 (suppl 5).

Poststroke Dementia Incidence

United States: 150,000 new cases/y

1/3 of the 360,000 incident cases of AD

Europe: 134,000 new cases/y

Incident stroke cases: → 536,000/y

EURODEM. Neurology. 2000; 54 (suppl 5).

VaD Is More Than MID…

Strategic single strokes: thalamic dementia, inferior genu lacune, caudate stroke

White matter incomplete ischemia: Binswanger's disease, CADASIL*

Subcortical Ischemic Vascular Dementia: small-vessel disease with multiple lacunar strokes

CADASIL=cerebral autosomal dominant arteriopathy + subcortical infarcts & leukoencephalopathy.

1) Large-Vessel Disease

=> Large ischaemic areas

Discrete infarcts in strategic locations

Frontal lobe	Hippocampus, basal forebrain	Gyrus angularis	Parietal-occipital lobes
Aphasia, apraxia, disinhibition, apathy	Amnesia	Constructional problems	Alexia, agraphia,apraxia

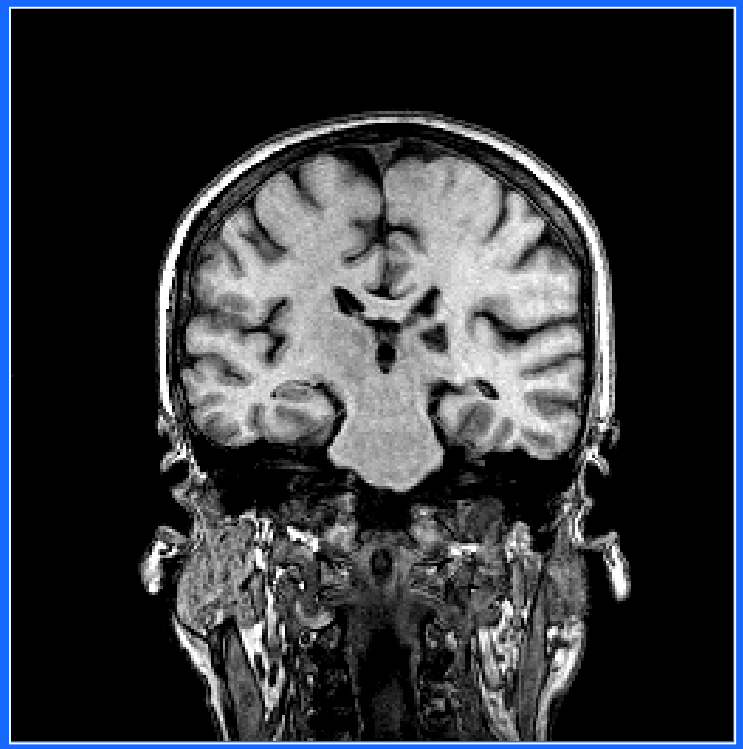
Cortical type of dementia - MID

Large vessel infarctions

Cortical VaD

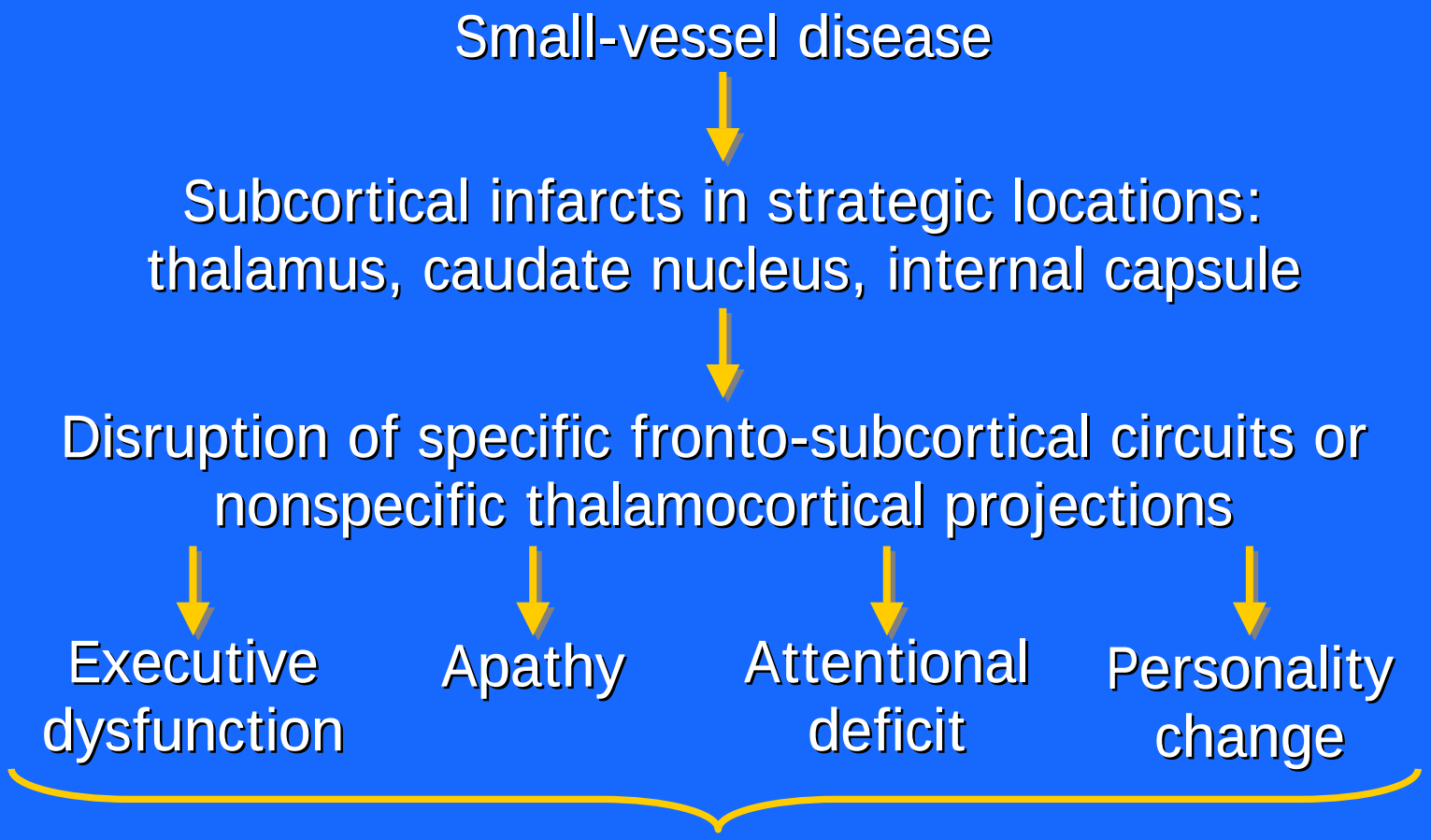
Left cortico-subcortical occipito-temporal infarct

Soubcortical VaD



Left thalamic infarct

Disruption of Cortico-Subcortical Circuits



Thalamic VaD

Bilateral medial thalamic ischemic strokes

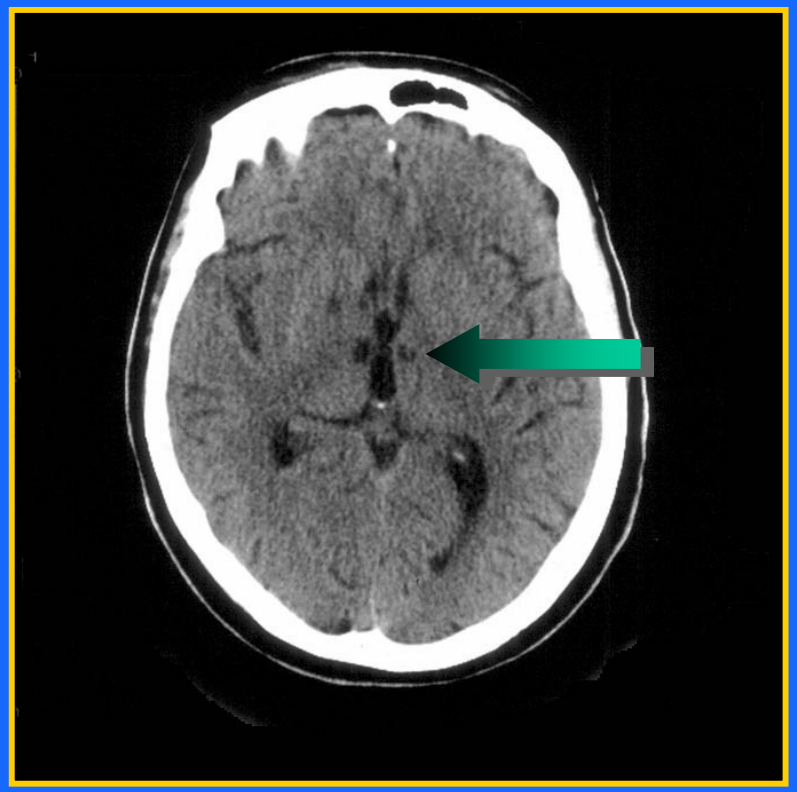
(L) anterior thalamus - polar thalamic from PCoA

Medial and central thalamus: CM nucleus - mamillothalamic tract - paramedian thalamic artery from basilar-PCA occlusion

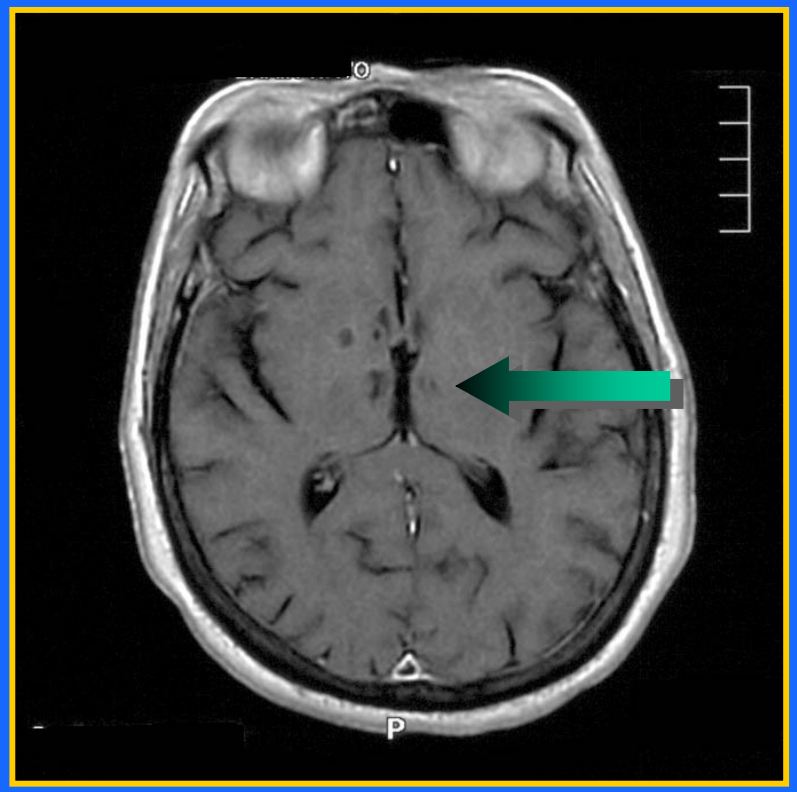
The critical lesion in thalamic amnesia is damage of the mamillothalamic tract, which projects into the anterior nuclei of the thalamus, and then to the cingulate cortex

PCoA = posterior communicating artery. PCA = posterior cerebral artery

Thalamic VaD Imaging



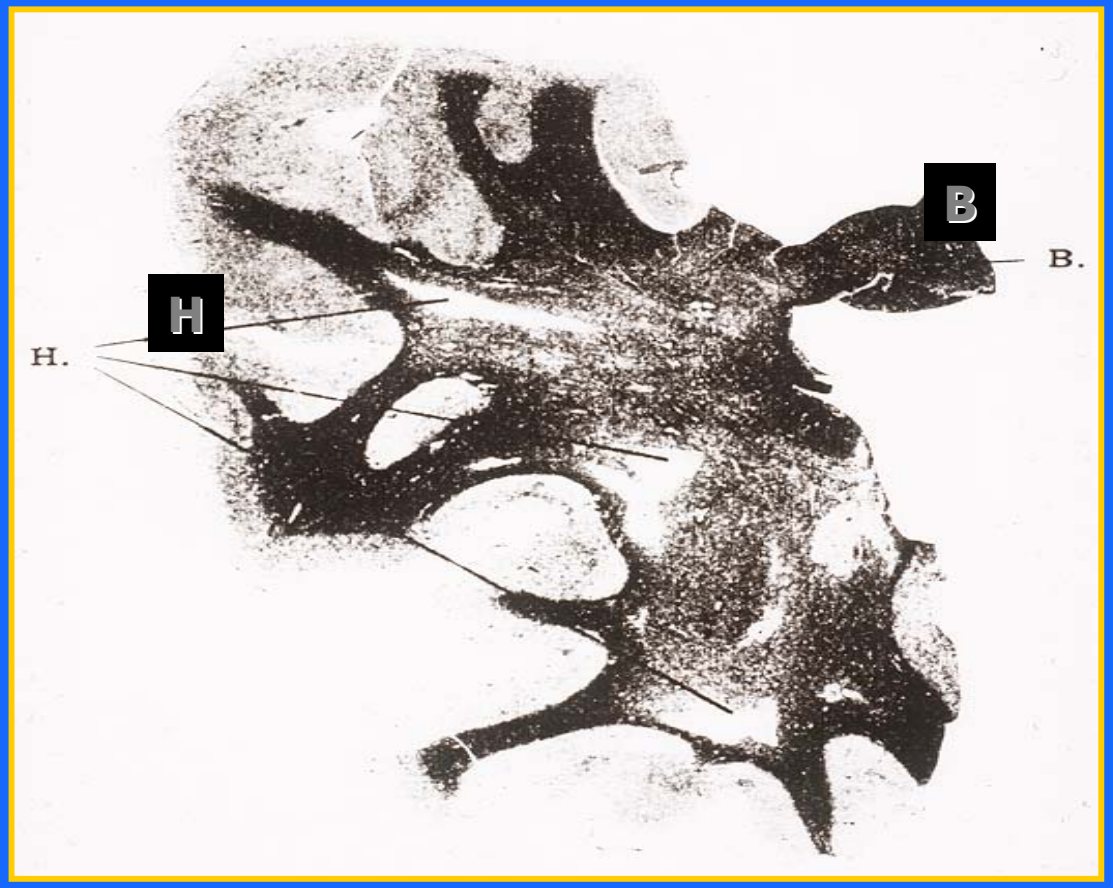
CT



MRI

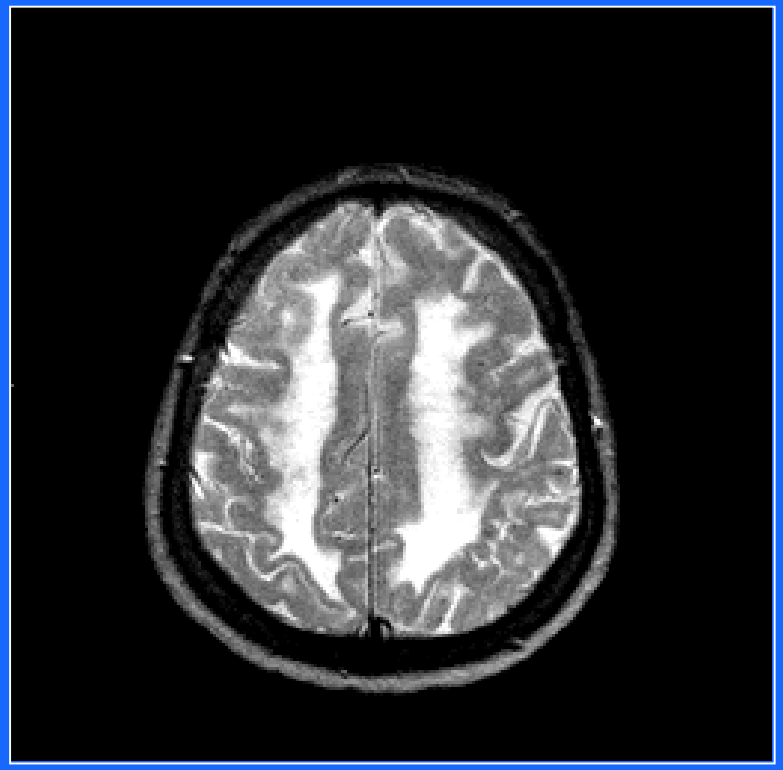
Binswanger's Disease

(Illustrated in Kraepelin's *Psychiatrie* 1910)

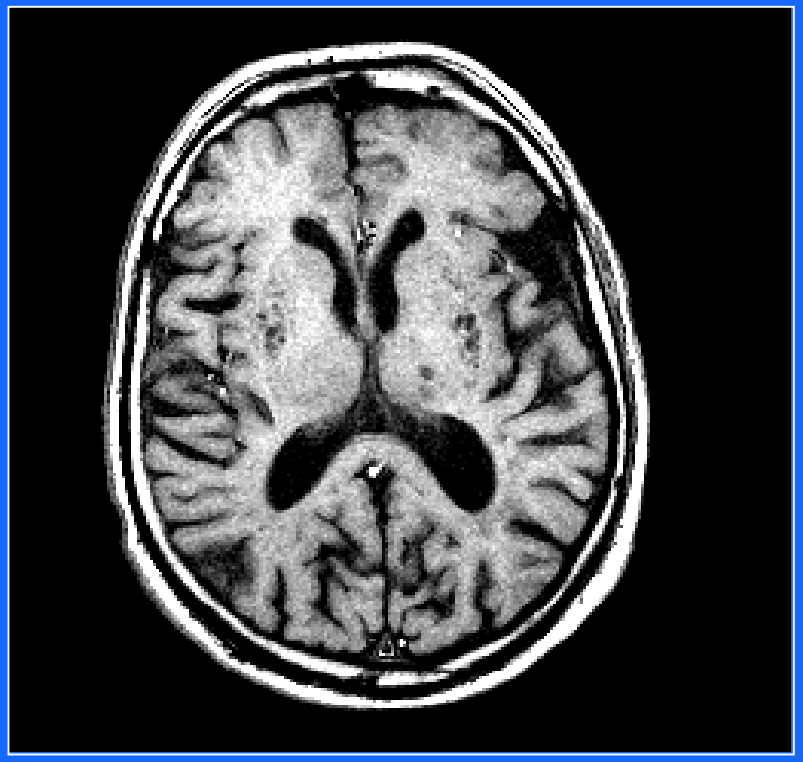


Figur 127. Subkortikale Encephalitis.
B=Balken; H=Herdartige Markatrophie.

Sub-cortical VaD at MRI



White matter lesions predominance



Lacunar infarct predominance

Lacunes Are *Not* Benign Lesions

Silent lacunes, particularly in the thalamus, more than double the risk of dementia [HR=2.26; 95% CI, 1.09-4.70]

5-year mortality in patients with lacunes reaches 27.4%

One or more silent lacunes occurred in about one fourth of 3660 participants in the Cardiovascular Health Study (CHS), age ≥65

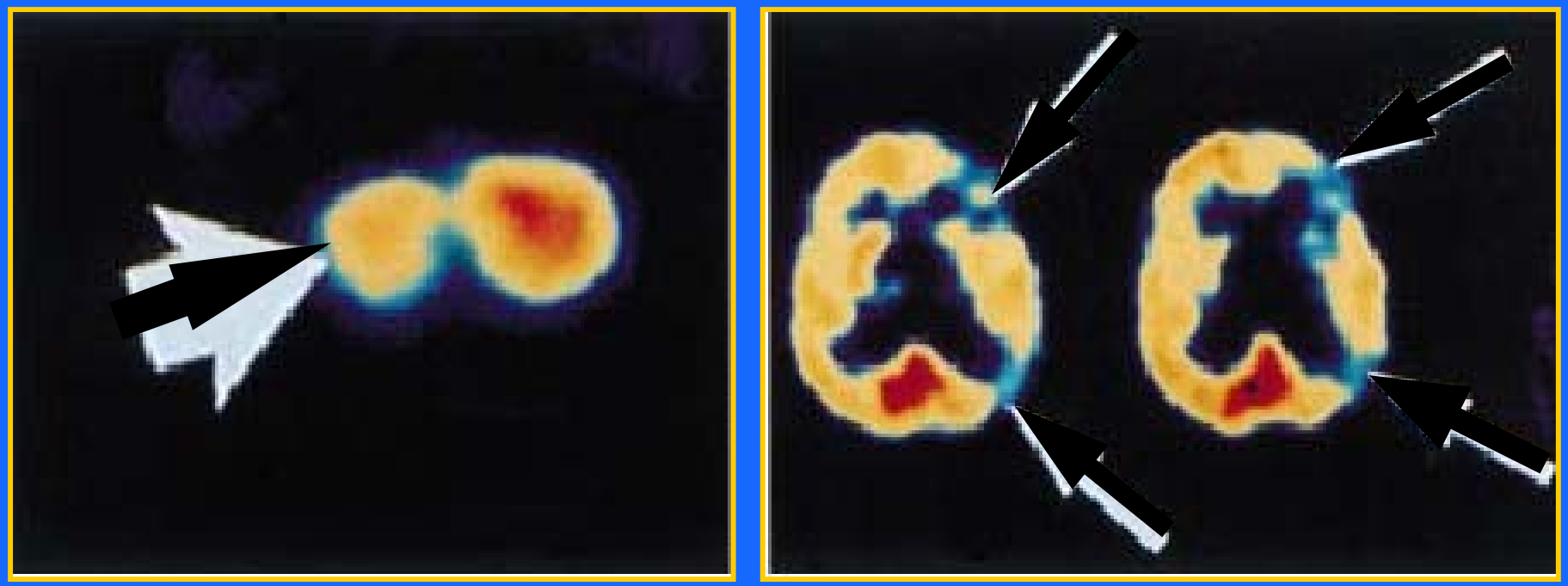
Vermeer et al. N Engl J Med. 2003;348:1215-1222; Norrving. Lancet Neurol. 2003; 2: 238-245; Longstreth et al. Arch Neurol. 1998; 55: 1217-1225.

Extensive Metabolic and Neuropsychological Abnormalities Associated With Discrete Infarction of the Genu of the Internal Capsule

MRI scan

Chukwudelunzu et al. J Neurol Neurosurg Psychiatry. 2001; 71: 658-662.

PET Abnormalities with Infarction of the Genu of the Internal Capsule



On 18FDG positron emission tomography (PET) images of the brain; decreased metabolic activity is apparent in the *left* temporal lobe (long arrows), occipito-temporal lobe (long arrows), and *right* cerebellar hemisphere (short arrow) 2 weeks after stroke.

Chukwudelunzu et al. J Neurol Neurosurg Psychiatry. 2001;71:658-662.

AD and CVD

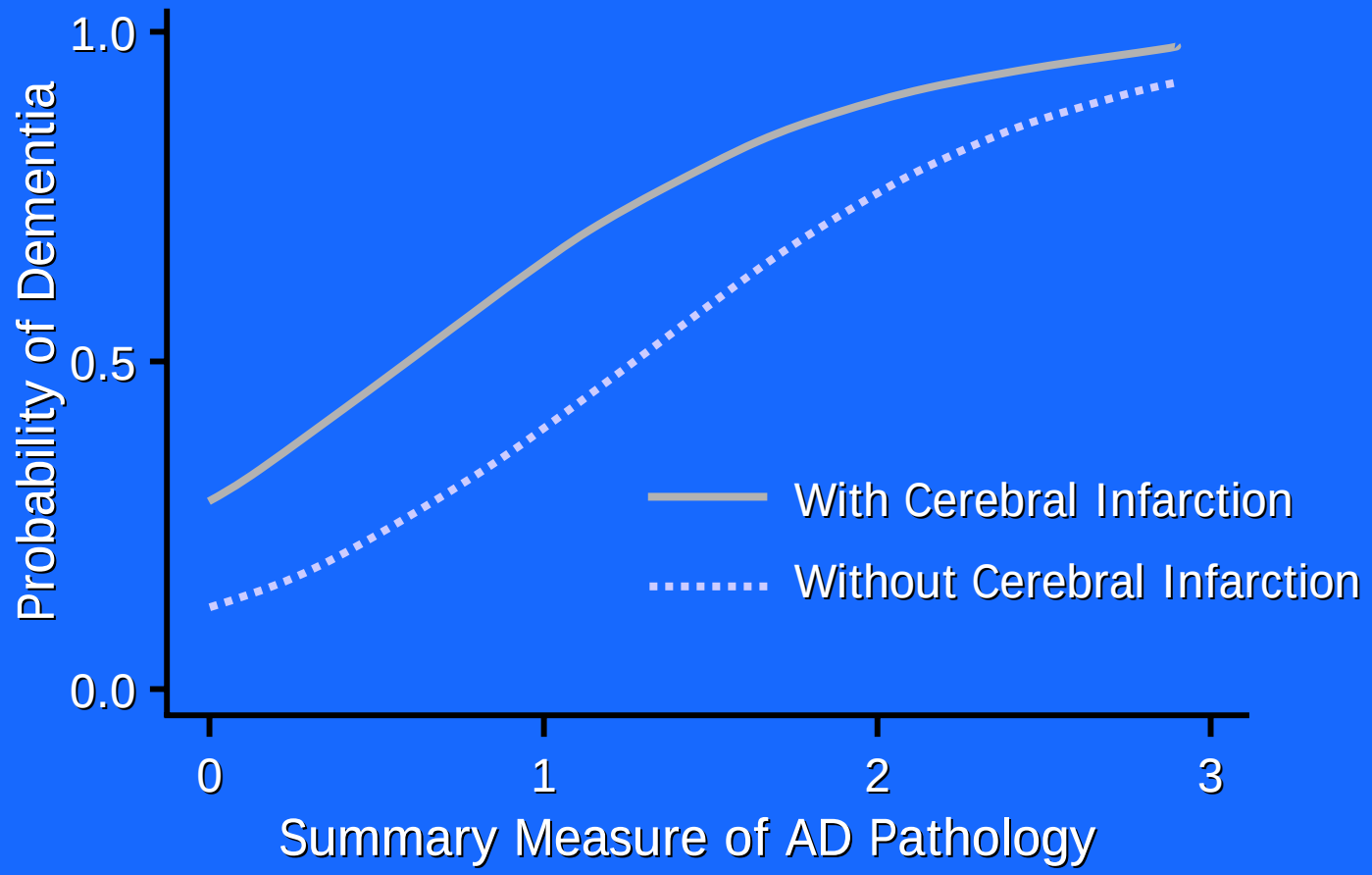
- Comorbid AD + CVD is frequent in autopsy series in the old-old
- Vascular risk factors increase AD risk (?)
- Pure AD, without CVD, occurs in only 20% of postmortem studies in patients with dementia
- There is a significant inverse relationship between severity of CVD and Braak & Braak's stages of AD => interaction?

AD + CVD

- CVD may exteriorise preclinical AD to "Alzheimer's dementia"
- Many patients with "AD" actually have low Braak's lesions + CVD
- Many cases diagnosed as "AD" are in fact cases of VaD
- Treatment of vascular risk factors may therefore prevent dementia onset and progression

AD : Alzheimer's disease; CVD : cerebrovascular disease; VaD : vascular dementia.

Probability of Clinically Diagnosed Dementia as a Function of AD Pathology



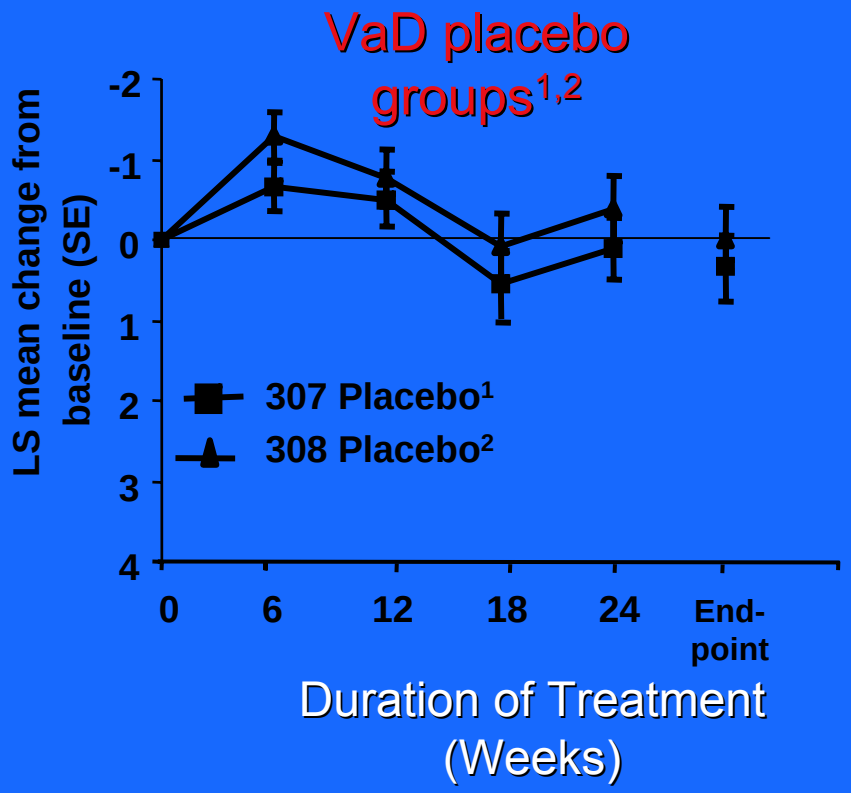
Schneider et. al., Neurology. 2003;60:1082-1088

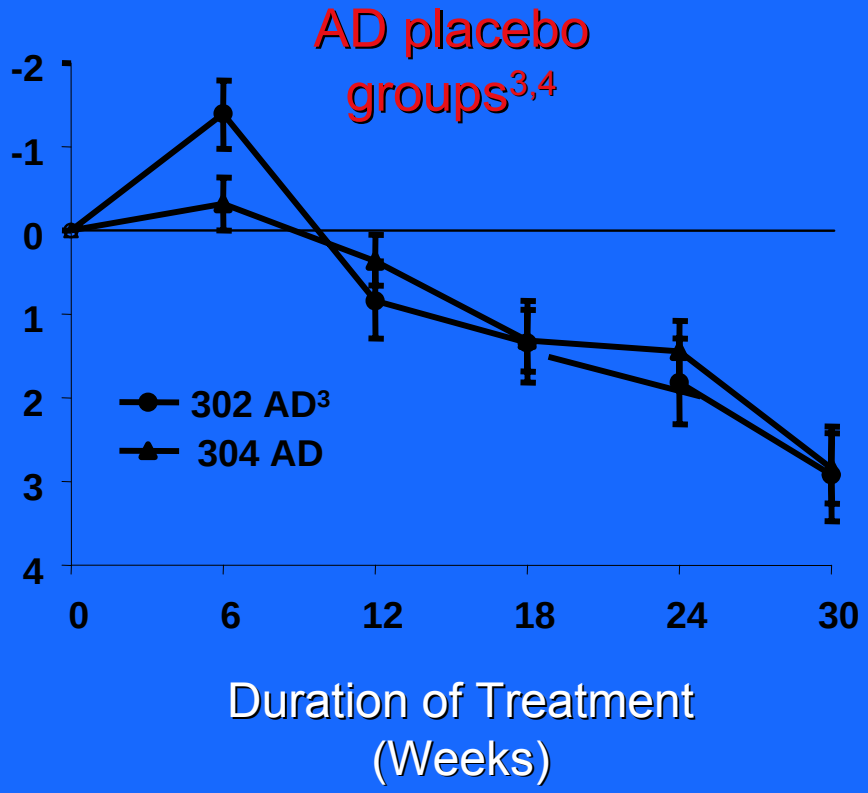
AD vs VaD : difference in course

Prospective results from clinical trials

Placebo group progressions in VaD and AD: ADAS-cog in donepezil trials

Historical comparisons from pivotal studies

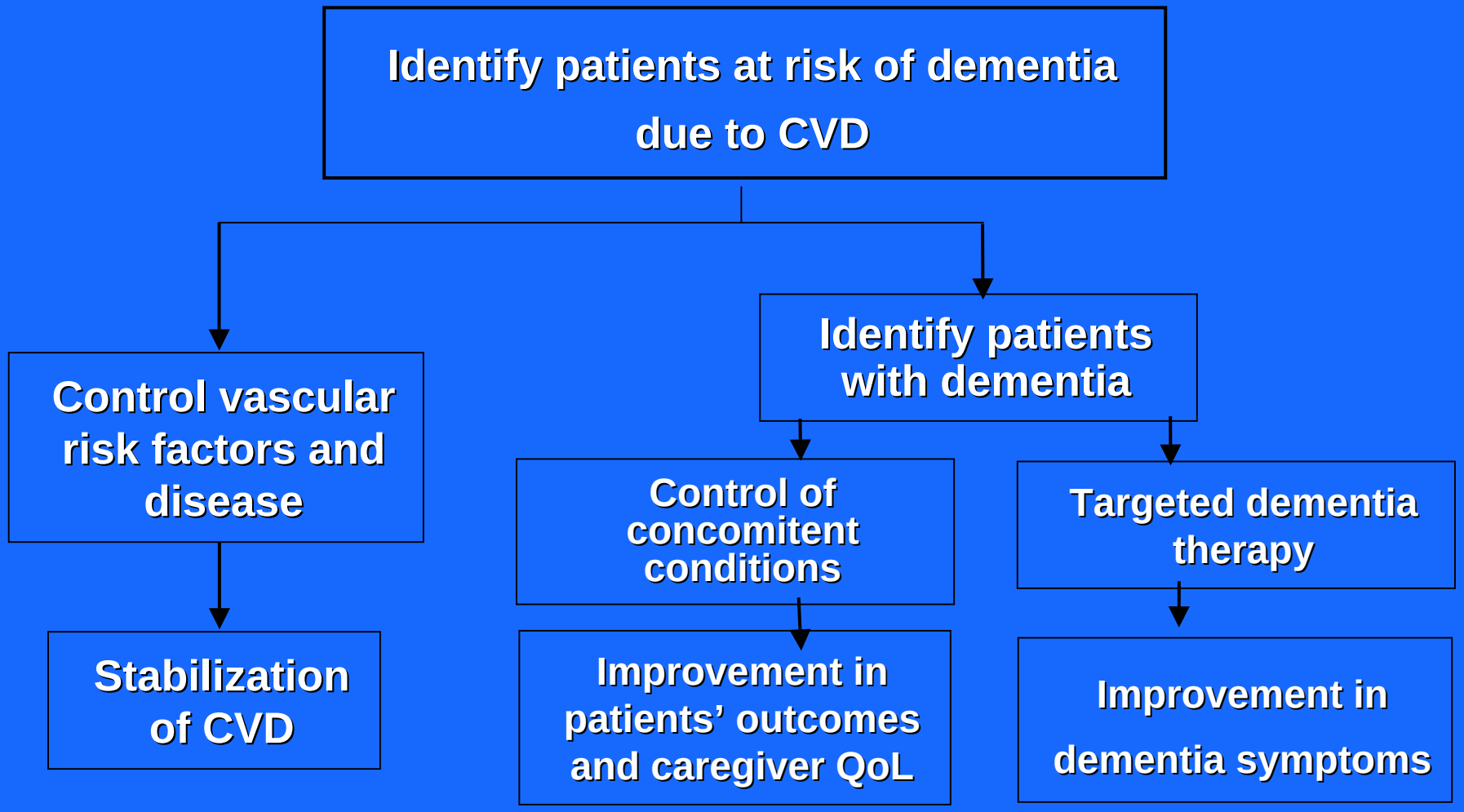




[1]Black et al. Stroke. 2003; [2]Wilkinson et al. Neurology. 2003;

[3]Rogers et al. Neurology. 1998; [4]Burns et al. Dement Geriatr Cogn Disord. 1999

Management of VaD



Sachdev et al. 1999; Nyhenuis and Gorelick, 1998

Primary Prevention of VaD

- Target
  - Brain at risk of CVD
- Action (treatment of risk factors)
  - Arterial hypertension
  - Cardiac abnormality
  - Lipid abnormality: DIET, statins
  - Diabetes mellitus
  - Homocysteine

O'Brien et al. Lancet Neurol. 2003; 2 : 89-98

Secondary Prevention of VaD

Target

- CVD brain at risk of VCI/VaD

Action

- Treatment of acute stroke (tPa)
- Prevention of stroke recurrence
- Slow progression of VaD related changes
- Treatment of vascular risk factors
- Neuroprotection ?

VCI=vascular cognitive impairment.

O'Brien et al. Lancet Neurol. 2002, 2: 89-98

Diagnostic criteria for Dementia

A1 : Memory impairment

Impaired ability to learn new information or to recall previously learned information (1)

(1) From DSM IV-TR

Diagnostic criteria for Dementia

A2 : Disturbance in executive functioning

Planning, organizing, sequencing, abstracting (1)

(1) From DSM IV-TR

Diagnostic criteria for Dementia

A3: One (or more) cognitive disturbances:

(a) Impairment in abstract thinking, as indicated by inability to find similarities and differences between related words, difficulty in defining words and concept, and other similar tasks (2)

(b) Impaired judgment, as indicated by inability to make reasonable plans to deal with interpersonal, family, and job-related problems and issues (2)

(c) Aphasia (language disturbance) (1)

(1) From DSM IV-TR (2) From DSM III-R

Diagnostic criteria for Dementia

A3 : One (or more) cognitive disturbances:

(d) Apraxia (impaired ability to carry out motor activities despite intact motor function) (1)

(e) Agnosia (failure to recognize or identify objects despite intact sensory function) (1 & 2)

(f) Constructional difficulty (e.g., inability to copy three-dimensional figures, assemble blocks, or arrange sticks in specific designs) (2)

(1) From DSM IV-TR (2) From DSM III-R

Dementia with new relevant Cerebro-vascular lesion(s) - Definition

Dementia

Occurring within 3 months after a recurrent stroke

and/or

With at least 1 out of 3 types of new lesions on brain imaging:

Strategic stroke > 1.5 cm diameter

More than 2 supratentorial lacunes

More than 25% ischaemic white matter changes

Conclusion

VaD and vascular cognitive impairment may become the most common cause of cognitive loss and behavioral changes in the elderly, particulaly in the older-old, causing a major public health problem.