Kista, Sept 15, 2016

Why should white matter changes be taken into account; the clinical dementia perspective

Anders Wallin MD, PhD, Prof,
Institute of Neuroscience and Physiology at Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
Memory Clinic at Deparment of Neuropsychiatry, Sahlgrenska University Hospital, Gothenburg, Sweden
anders.wallin@neuro.gu.se

UNIVERSITY OF GOTHENBURG

The global impact of dementia

Year	Number of subjects with dementia (millions)	
2015	47	
2030	75	
2050	131	

M Prince, A Wimo, M Guerchet, GC Ali, Y Wu, AM Prina. World Alzheimer Report 2015: The global impact of dementia. An analysis of prevalence, incidence, costs and trends, Alzheimer's Disease International, London (2015)

AD - Increased biochemical knowledge but no treatment breakthrough WHY?

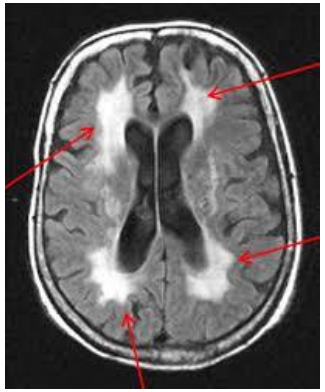
- trials being performed too late?
- too short duration
- inclusion of heterogeneous groups of patients?
- insufficient knowledge about both the specific clinical features or crucial comorbidities, such as vascular disease?
- crucial pathogenic pathways unknown?

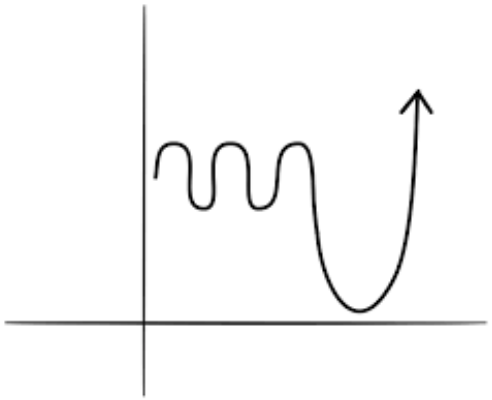
Vascular cognitive impairment (VCI) is potentially treatable BUT

- only limited number of trials
- no positive effect
- focus on stroke
- in VCI few trials on subcortical small vessel disease

Subcortical small vessel disease

- a common, fairly homogeneous type of VCI
- 50% of cases with vascular dementia
- speed/attention and executive impairments
- may appear with and without AD pathology
- arteriolosclerosis; cerebral amyloid angiopathy
- white matter rarefaction, microinfarcts, lacunar infarcts





a roller coaster journey

Review

Cerebrovascular Diseases

Cerebrovasc Dis 2011;32:577–588
DOI: 10.1159/000334498

Received: September 21, 2011
Accepted: October 18, 2011
Published online: December 1, 2011

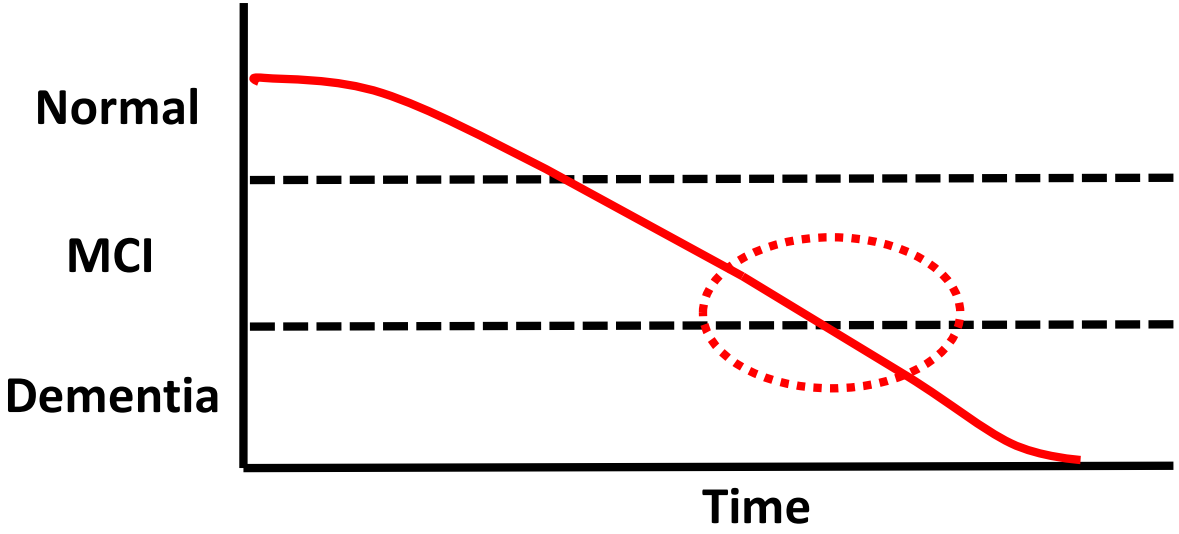
2001–2011: A Decade of the LADIS (Leukoaraiosis And DISability) Study: What Have We Learned about White Matter Changes and Small-Vessel Disease?

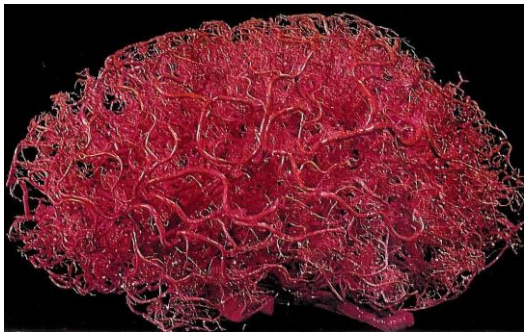
The LADIS Study Group[1]

Gothenburg MCI study 1999-

Healthy → MCI → Dementia

Alzheimer's disease (AD) and subcortical small vessel disease (SSVD) in a memory clinic setting





DIAGNOSTICS

+

Speed and attention
Memory and learning
Spatial function
Language
Executive function

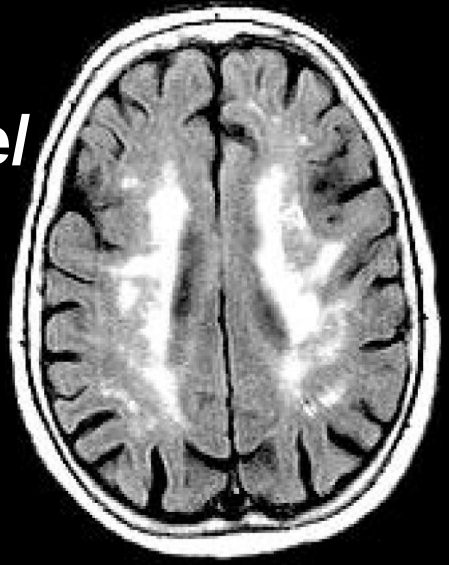
No/mild MRI white matter changes

= Alzheimer’s disease

DIAGNOSTICS

+

Mild/ moderate/ severe white matter changes



Speed and attention
Memory and learning
Spatial function
Language
Executive function

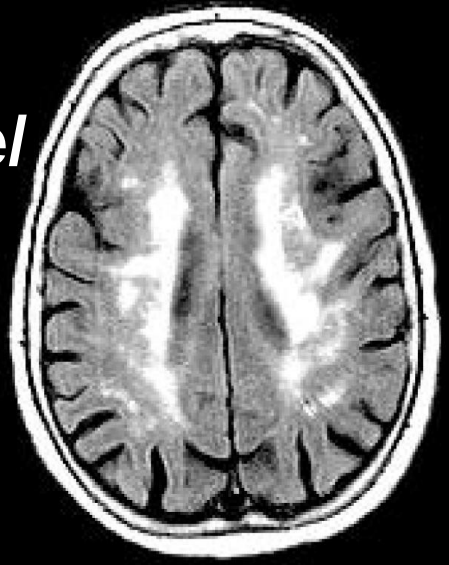
= **Subcortical small vessel disease**

DIAGNOSTICS

+

Speed and attention
Memory and learning
Spatial function
Language
Executive function

Moderate/ severe white matter changes



= Mixed type disease (AD/SSVD)

Table 3. Baseline syndromal and etiological diagnoses of the Gothenburg MCI study

Baseline	Healthy	SCI	MCI	Dementia	All patients
N	-	195	274	195	664
Male/female	-	82/113	110/164	83/112	275/389
Mean age (SD)	-	61.8 (7.6)	65.2 (7.7)	67.3 (7.4)	64.8 (7.9)
Mean years of education (SD)	-	13.6 (3.6)	11.8 (3.5)	11.0 (3.5)	12.1 (3.7)
Mean MMSE (SD)	-	29.1 (0.9)	28.0 (1.5)	24.8 (2.7)	27.4 (2.5)
AD	-	-	-	81	-
SVD	-	-	-	27	-
Mix	-	-	-	41	-
Other	-	-	-	46	-

Table 7. Conversion after 6 years for patients with SCI or MCI at baseline

Year 6	N 469	%	SCI at base-line N 195	%	MCI at base-line N 274	%
Total conversion n (%)	69	23.6%	6	5.3%	63	35.2%
To AD N (%)	29	9.9%	2	1.8%	27	15.1%
To SVD N (%)	16	5.5%	4	3.5%	12	6.7%
To Mix N (%)	15	5.1%	0	0.0%	15	8.4%
To other N (%)	8	2.7%	0	0.0%	8	4.5%

Neuropathological assessment in subjects with dementia

	Vascular lesions	Mixed pathology	Alzheimer's pathology	
Honolulu-Asia Aging study	24%	45%	20%	Petrovitch et al., 2005
Vienna	8%	24%	46%	Jellinger & Neumayer, 1964
Hisayama study	29.5%	4.7%	45.1%	Matsui et al., 2009

From H. Tomimoto / Neuroscience Research 71 (2011) 193–199

Gothenburg MCI study
DESIGN and 6 YEAR FOLLOW-UP

Review Article

JCBFM

Journal of Cerebral Blood Flow & Metabolism
2016, Vol. 36(1) 114–131

DOI: 10.1038/jcbfm.2015.147
jcbfm.sagepub.com
SAGE

The Gothenburg MCI study: Design and distribution of Alzheimer's disease and subcortical vascular disease diagnoses from baseline to 6-year follow-up

Anders Wallin[1], Arto Nordlund[1], Michael Jonsson[1], Karin Lind[1], Åke Edman[1], Mattias Göthlin[1], Jacob Stålhammar[1], Marie Eckerström[1], Silke Kern[1], Anne Börjesson-Hanson[1], Mårten Carlsson[1], Erik Olsson[1], Henrik Zetterberg[1,2], Kaj Blennow[1,3], Johan Svensson[4], Annika Öhrfelt[1], Maria Bjerke[1], Sindre Rolstad[1] and Carl Eckerström[1]

Gothenburg MCI and dementia studies
OVERVIEW of RESULTS

Review Article

JCBFM

Journal of Cerebral Blood Flow & Metabolism
2016, Vol. 36(1) 95–113

DOI: 10.1038/jcbfm.2015.148
jcbfm.sagepub.com

SAGE

Alzheimer's disease—subcortical vascular disease spectrum in a hospital-based setting: Overview of results from the Gothenburg MCI and dementia studies

Anders Wallin[1], Arto Nordlund[1], Michael Jonsson[1], Kaj Blennow[1,2], Henrik Zetterberg[1,3], Annika Öhrfelt[1], Jacob Stålhammar[1], Marie Eckerström[1], Mårten Carlsson[1], Erik Olsson[1], Mattias Göthlin[1], Johan Svensson[4], Sindre Rolstad[1], Carl Eckerström[1] and Maria Bjerke[1]

Gothenburg MCI study: Conclusion and Impact

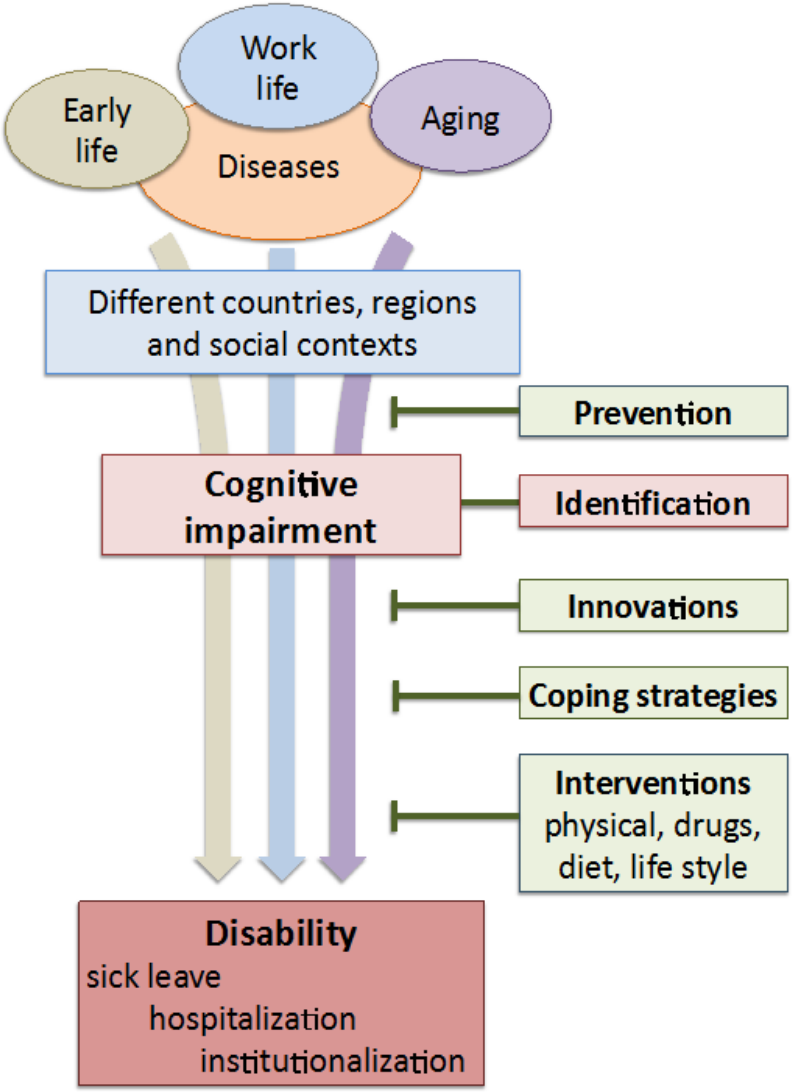
- It is possible to identify SSVD in a memory clinic setting
- The number of patients with SSVD is not insignificant
- MCI may precede not only AD dementia but also SSVD dementia
- Neuropsychological and neurochemical differences have been found between SSVD and AD
- Although the results need to be replicated they should already now be taken into account in the design of clinical trials and clinical practice

DEBATT

De är dags att se värdet av patientnära forskning

http://www.lakartidningen.se/Opinion/Debatt/2016/06/Det-ar-dags-att-se-vardet-av-patientnara-forskning/

The Center of Cognitive Medicine Inititative: Sustaining cognition in a changing society



Svensk förening för
Kognitiv Medicin

www.kognitivmedicin.se

- Anmäl dig till fjärde nationella konferensen i kognitiv medicin! Tema: **ADHD/ autism-spektrumtillstånd senare i livet**
- Plats: Wallenbergssalen, Göteborg
- Tid: 24 november 2016, 10:00 – 16:00

Thanks for your attention!

/Anders Wallin and his research group, about 25 people (postdocs, research students and others)

anders.wallin@neuro.gu.se