WHAT ARE SUBJECTIVE MEMORY COMPLAINTS AND WHAT IS THEIR SIGNIFICANCE

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Subjective cognitive decline

Historical aspects of subjective cognitive symptoms

- Patients with Alzheimer's disease were supposed not to be aware of their disorder
- Thought to be useless in the diagnosis of dementia
- Often symptom of depression
- In the 1990s included in the MCI criteria
- Recently associated with biological markers and risk of dementia in individuals free from depression

Factors associated with subjective cognitive decline

- Preclinical AD
- Biological markers of AD (CSF, brain imaging)
- Depression
- Anxiety
- Physical health problems, chronic diseases
- Personality

Measurement of subjective cognitive decline

- Comparisons between 19 study groups
- Large heterogeneity across studies
- 75% of methods only used by one study
- Most common: memory (60%), executive function (16%), attention (11%)
- This makes comparisons between studies difficult
- Frequency differs widely between studies
- No single accepted standards or criteria

Rabin et al, and the Subjective Cognitive Decline Initiative (SCD-I) Working Group. J Alzheimer Dis 2015 Sep 24;48 Suppl 1:S63-86

MCI CRITERIA 1999

Petersen et al. Arch. Neurol.

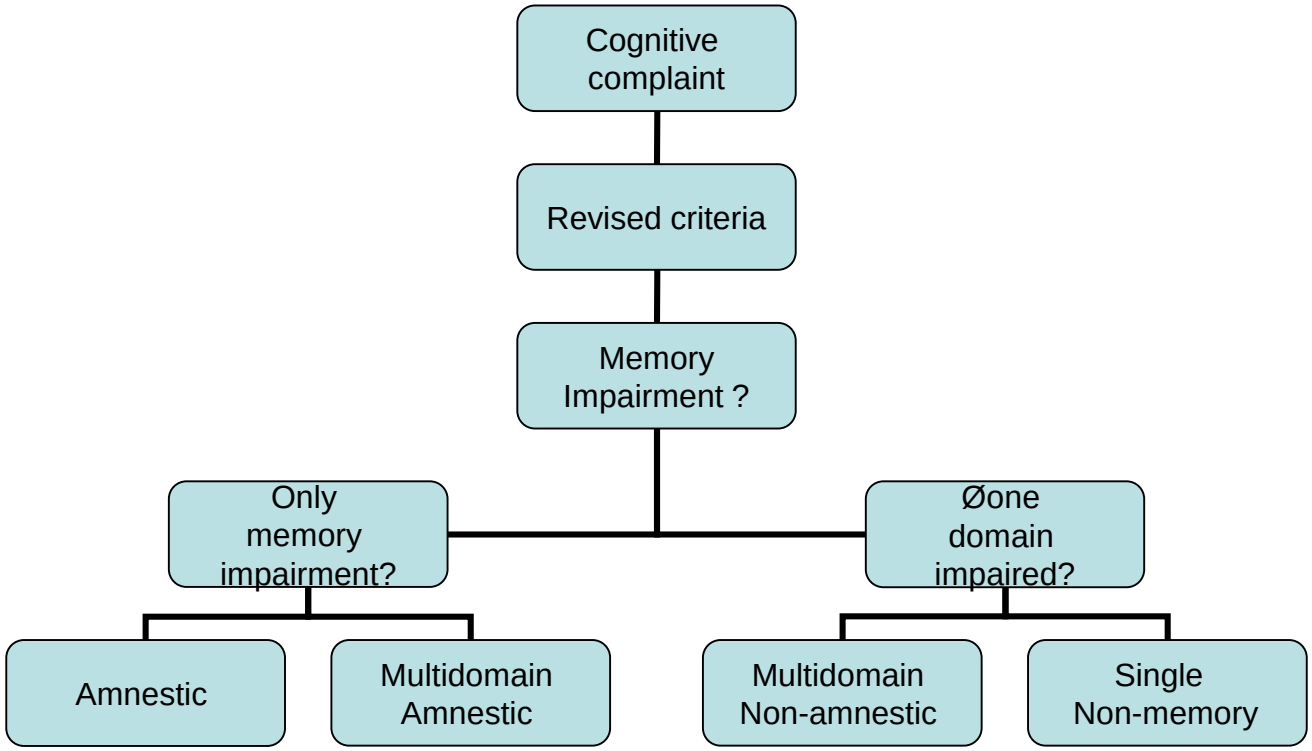
- not demented
- memory complaint

- normal ADL
- normal general cognitive function
- abnormal memory for age

REVISED MCI CRITERIA 2004

Winblad et al. J Intern Med

- not demented (DSM IV, ICD10)
- cognitive complaint or evidence of decline
- normal/ minimal loss ADL
- normal general cognitive function
- impairment objective cognitive tasks



Adapted from Winblad et al. J Intern Med 2004

POPULATION-BASED VALIDATION STUDIES

- Subjective memory impairment should not be included

as a mandatory criterion (Ritchie et al. Neurology, 2001; Fisk et al. Neurology, 2003)

DSM-5

NEUROPSYCHIATRIC EPIDEMIOLOGY THE GOTHENBURG STUDIES

- H70-study
- H85-study
- The 95+ Study

- The Prospective Population Study of Women (PPSW)

H70

Ålder	70	75	79	81	83	85	88	90	92	95	97	99	100	10
1901-02	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1906-07	+	+	+											
1911-12	+	+												
1922	+		+			+	+							
1930	+	+	+				2015							
1944	2014													

H85 GÖTEBORG

Ålder	85	88	90	92	95	97	99
1901-02	+	+	+	+	+	+	+
1923-24	+	+	+				
1930	2015						

95+ STUDY
GOTHENBURG, SWEDEN

	70	75	79	81	83	85	88	90	92	95	97	99	100	101-109
1901-02	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1903										+	+	+	+	+
1904												+	+	+
1905-06	+		+							+	+	+	+	+
1907-09											+	+	+	+
1910-12													+	+

General examinations

- Neuropsychiatric examination
- Key informant interview
- Medical examination (somatic disorders, alcohol, smoking)
- Functional ability (ADL, iADL, transportation)
- Anthropometry (length, weight etc)
- Social interview, social network, physical, social and cultural activities, life events, working life etc)
- Psychometric testings
- Personality (Eysenck, Five Factor, KASAM)
- Gender
- Blood, serum, plasma
- Genetic analyses
- ECG, blood pressure
- Lung function
- Physical function (walking speed, hand grip, balance, chair stand etc)
- Audiology
- Ophtalmology
- Dietary examination, DEXA (bone, muscle, fat)
- CT and MRI of brain
- Lumbar puncture/ Neurochemistry

The prevalence of subjective cognitive decline

Criteria for subjective cognitive decline

- Memory. Scale from 0-6. 4-6 are persistent troublesome symptoms
- Executive. Scale from 0-6. 4-6 are persistent troublesome symptoms

Sacuiu et al. Neurology 2005;65:1894-1900

Prevalence subjective memory complaints among individuals without dementia

Age	Birth year	%
70 (N=562)	1930	7
75 (N=778)	1930	3
79 (N=580)	1930	4
85 (N=435)	1923-24	7

No difference between sexes

Skoog, et al 2016

Relation to different measures

Association between subjective memory complaints and global measures of cognitive function and depression

Age	Mean MMSE score		Mean MADRS score	
	Subjective memory complaints		Subjective memory complaints	
	No	Yes	No	Yes
70 (N=562)	28.1	27.9	4.4	6.9**
75 (N=778)	27.5	27.0	6.2	11.2***
79 (N=580)	28.2	25.4***	5.4	11.7***
85 (N=435)	27.7	27.0	6.4	9.0*

MADRS = Mongomery-Åsberg Depression Scale,
MMSE = Mini Mental State Examination
*=p<0.05, **=p<0.01, ***=p<0.001

Skoog, et al 2016

Subjective memory impairment and CSF-markers of AD

Skoog, Kern et al 2016

Relation to development of dementia

Subjective cognitive decline among 85-year-olds without dementia in relation to incidence dementia during 3 years follow-up

Baseline	Development during 3 year follow-up		
Self-reported problem	Dementia	AD	VaD
Memory	1.9 (1.0-3.8)	3.0 (1.2-7.4)	1.4 (0.6-3.8)
Executive	1.1 (0.6-2.1)	1.3 (0.5-3.2)	0.9 (0.4-2.3)

Sacuiu et al. Neurology 2005;65:1894-1900

Subjective cognitive decline among 85-year-olds without dementia in relation to incidence dementia during 3 years follow-up

Self-reported problem	Sensitivity	Specificity	PPV	NPV
Memory	27.6	83.5	27.6	83.5
Executive	29.3	72.5	19.5	81.9

Sacuiu et al. Neurology 2005;65:1894-1900

Memory complaints and risk of cognitive impairment after nearly 2 decades among older women

Years before MCI/dementia	OR (95%-CI)
4	3.0 [1.8-5.0]
10	1.9 [1.1-3.1]
14	1.6 [0.9-2.7
18	1.7 [1.1-2.9

Kaup et al. Neurology. 2015;85:1852-8

The validity of cognitive complaints may vary depending on different factors

- Population (clinic versus population)
- Educational level
- Age
- Personality
- Presence of other pathology

Subjective cognitive decline and brain imaging findings

Baseline characteristics OF non-demented ELDERLY by participation to brain CT examination

Characteristics US2000 + H85	No brain CT	Brain CT	
	n = 508	n = 762	P-values
Age mean (SD)	79.6 (6.3)	75.5 (6.4)	**< 0.001**
Women n (%)	407 (80.0%)	536 (70.3%)	**< 0.001**
Education (> 6 yrs education) n (%)	149 (31.4%)	283 (37.9%)	**0.011**
MADRS mean score (SD)	6.5 (7.7)	5.2 (6.0)	**< 0.001**
APOE4 prevalence n (%)	125 (28.5%)	227 (31.4%)	0.323
Dementia incidence n (%)	130 (25.5%)	153 (20.1%)	**0.019**
Person years-at-risk mean (SD)	6.9 (4.1)	8.4 (3.7)	**< 0.001**

ANOVA was used to test the differences in age, MADRS score and person years-at-risk. Fisher's exact test was used to test differences in proportions.

Sacuiu er al 2016

SUBJECTIVE SYMPTOMS ASSOCIATED WITH CT-BRAIN CHANGES

	Self-reported impaired function OR (95% Confidence Interval)			
	Memory		***Executive function***	
	Unadjusted	Adjusted	Unadjusted	Adjusted
WML	**1.3 (1.0 -1.6)***	1.3 (1.0 - 1.6)	1.1 (0.9 – 1.3)	1.1 (0.8 – 1.4)
Cortical atrophy				
Frontal	1.1 (0.8 – 1.6)	1.1 (0.8 - 1.5)	**1.4 (1.0 – 2.0)***	1.2 (0.8 – 1.6)
Temporal	1.0 (0.6 - 1.4)	1.1 (0.8 – 1.5)	1.1 (0.8 – 1.6)	1.0 (0.7 – 1.4)
Parietal	1.3 (0.9 – 2.0)	1.4 (1.0 - 2.1)	0.9 (0.6 – 1.3)	1.0 (0.7 – 1.5)
Occipital	0.9 (0.6 -1.4)	1.3 (0.9 – 2.0)	0.9 (0.5 – 1.4)	1.2 (0.8 – 1.9)

Logistic regression models were adjusted for age, sex, education, APOE4 and MADRS score. *P-value < 0.05

NOTE: Confounding effect of MADRS, APOE4 & AGE on the relation SRM-WML (beta estimates show opposite direction of associations)

SUBJECTIVE SYMPTOMS ASSOCIATED WITH CT-BRAIN CHANGES in POPULATION STRATA

1.6 (1.2 – 2.2)** in APOE4 -

0.99 (0.6 – 1.6) in APOE4 +

Self-reported memory problems

OR (95% Confidence Interval)

	MADRS 0-8	**MADRS > 8**
WML	**1.4 (1.0 – 1.8)***	0.9 (0.6 – 1.5)
Cortical atrophy		
Frontal	1.1 (0.8 – 1.6)	1.2 (0.7 – 2.1)
Temporal	1.0 (0.7 – 1.5)	1.2 (0.7 – 2.3)
Parietal	1.2 (0.7 – 1.8)	**2.3 (1.1 – 4.8)***
Occipital	1.1 (0.7 – 1.9)	1.2 (0.5 – 2.7)

No effect of APOE4

Logistic regression models univariate and with covariates age, sex, education and APOE4.
*P-value < 0.05, **P-value>0.01

Also confounding effect of AGE on the relation SRM-WML: age 70-79 OR 1.4 (1.1-1.9)*
(beta estimates show opposite direction of assoc) age 80-92 OR 0.99 (0.6 -1.6)
TEST INTERACTIONS AGE * APOE4/ APOE4*MADRS/ AGE*MADRS

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SUBJECTIVE SYMPTOMS ASSOCIATED WITH CT-BRAIN CHANGES in POPULATION STRATA

1.8 (1.21– 2.9)* in APOE4 -

0.8 (0.4 – 1.8) in APOE4 +

	Self-reported executive problems OR (95% Confidence Interval)	
	MADRS 0-8	MADRS > 8
WML	1.1 (0.8 – 1.5)	1.0 (0.6 – 1.5)
Cortical atrophy		
Frontal	1.4 (1.0 – 2.2)	1.0 (0.5 – 1.6)
Temporal	1.2 (0.8 – 1.8)	1.0 (0.6 – 1.7)
Parietal	1.2 (0.7 – 1.8)	0.6 (0.3 – 1.2)
Occipital	1.5 (0.9 – 2.5)	0.5 (0.2 – 1.1)

Logistic regression models univariate and with covariates age, sex, education and APOE4.
*P-value < 0.05

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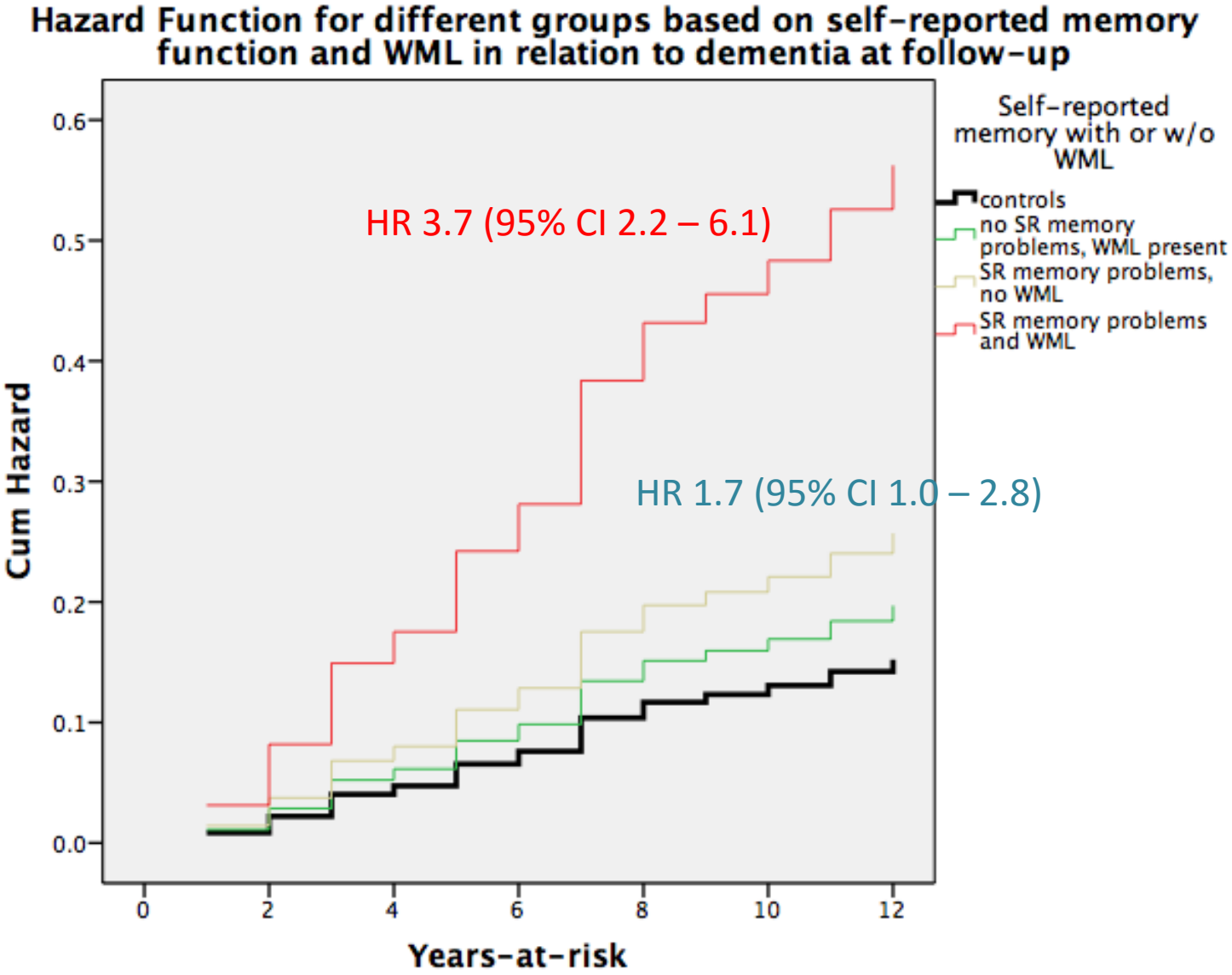

Cox regression model adjusted for age, sex, education, APOE4 and MADRS

Sacuiu er al 2016

Conclusion

- Subjective cognitive decline is common
- At least memory complaints are associated with later development of AD
- However, very low sensitivity and specificity
- Not useful as a single screening for AD
- Maybe better in combination with biological markers or objective signs of cognitive dysfunction
- Its use in MCI criteria underestimates this condition in epidemiological studies

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