

Mild Cognitive Impairment Due to Alzheimer's Disease



심 용 수

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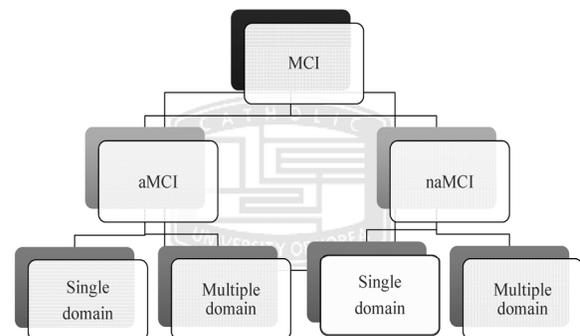
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Criteria for *Amnesic* MCI

- Cognitive concern
- Objective impairment in memory
- Relative preservation of nonmemory cognitive functions
- Preservation of activities of daily living
- Non demented

Archives of Neurology, 1999

MCI & subtypes



Journal of Internal Medicine, 2004

Cases

Case 1

- F/ 74 (Right handedness)
- 초등학교 졸업
- 60세까지 분식점 운영



Chief Complaint

- 2014. 11.
- 기억력 저하



Present illness

- 기억력 저하 (over 1yr)
 - 보고 들은 것 잘 기억 못한다.
 - 물건 맡겨두고 잊어 버린다.
 - 길 잃은 적은 없으나 가끔 헤매기는 했다.
 - 집안일, 정리정돈을 예전에 비해 귀찮아 하신다.
 - 냉장고 정리 잘하시며, 돈 관리와 은행일 직접 스스로 하신다.
 - 대중교통 이용하여 모임에도 한 달에 한번 나가신다.

Others

- No!
Hypertension, DM, Dyslipidemia, Cardiac disease, smoking
- FHx: demented mother



Neurological Exam &

- No focal signs
- Hachinski Ischemic Scale: 0점



K-MMSE

	21 / 30 (0.09 %ile)		
시간지남력	4 / 5	장소지남력	5 / 5
기억등록	3 / 3	주의집중 및 계산	2 / 5
기억회상	0 / 3	언어 및 시공간구성	7 / 9

1) day: +1
2) 93, 86, 77, 60, 63
3) unable even after cue
4) 명령시행

S-IADL

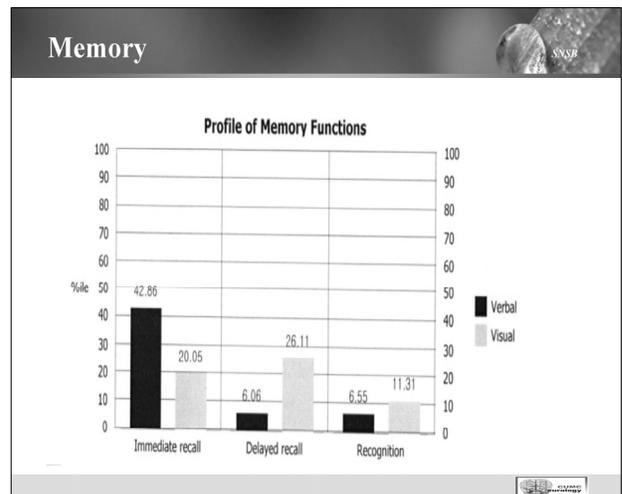
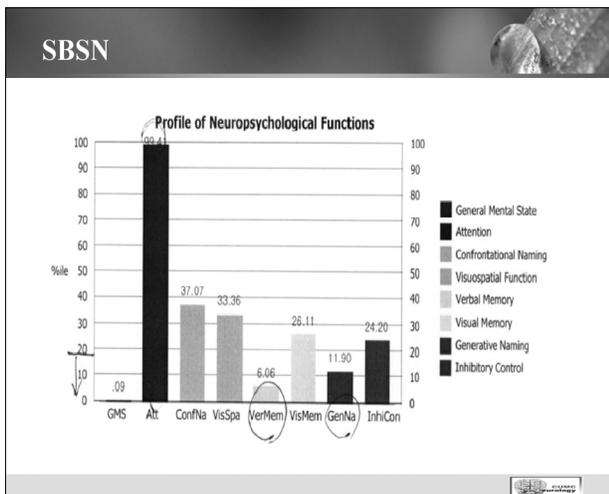
S-IADL													총점		
전화사용	물건사기	음식준비	집안일	대중교통이용	근거리외출	약먹기	돈관리	몸단장및치장	가전제품이용	소지품관리	문단속	약속지키기		최근일이야기	여가취미
1	0	0	0	1	0	0	0	0	0	0	0	0	2	0	4

CDR &

CDR 0.5			
기억력	1	지남력	1
판단력과 문제해결능력	0	사회활동	0
집안생활과 취미	0.5	위생과 몸치장	0
GDS (Geriatric Depression Scale)		12/30	

NPI

NPI												
	망상	환각	초조/공격성	우울/낙담	불안	다행감/들뜬 기분	무감동/무관심	탈연채	과민/불안정	비정상적 반복 행동	수면/야간행동	식욕/식습관
Y or N	N	N	N	N	N	N	N	N	N	N	N	N



Language & related Functions

Spontaneous speech: Fluency	Non-fluent		
Contents	Normal		
Comprehension	Abnormal		
Repetition	15	≥16	
Naming: Korean-Boston Naming Test (K-BNT)	38	37.07	-0.33
Short version of the K-BNT (S-K-BNT): form	N/A	N/A	N/A
score			
Reading	Normal		
Writing	Normal		
Finger Naming	Borderline		
Right-left orientation	Normal		
Body part identification	Normal		
Calculation: Addition (+)	3	≥16	
Subtraction (-)	3	≥16	
Multiplication (*)	3	≥16	
Division (/)	3	≥16	
total score	12	≥16	
Praxis: Ideomotor	4	≥16	
Buccofacial	N/A		

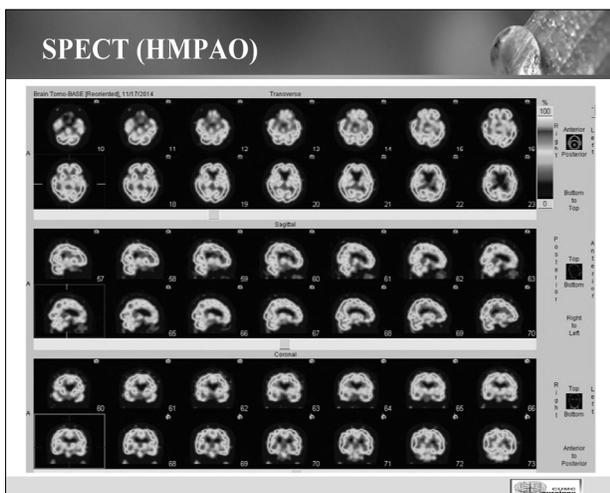
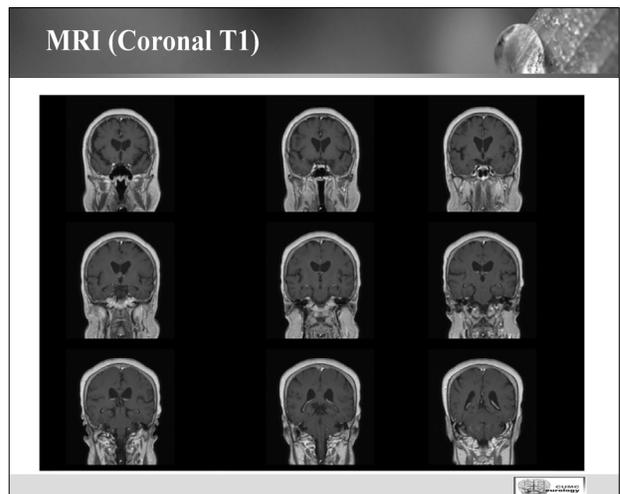
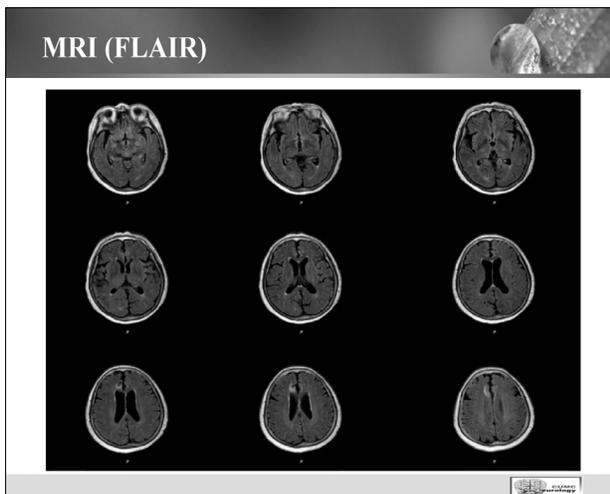
Frontal/ Executive Function

Motor Impersistence	Normal		
Contrasting program	20	≥14	
Go-No-Go	20	≥14	
Fist-edge-palm	Normal		
Alternating hand movement	Normal		
Alternating square & triangle	Normal		
Luria loop	PSV		
Controlled Oral Word Association Test (COUAT)			
Animal	7	2.91	-1.91
Supermarket	8	12.51	-1.15
~	2	14.23	-1.07
∞	3	17.35	-0.94
^	4	24.83	-0.68
Phonemic total score	9	11.9	-1.18
Korean-Color Word Stroop Test (K-CWST)			
Word reading: Number of correct response	111	≥16	
Number of error	1	<16	
Response time (sec)	104		
Correct response rate	0.99	<16	
Time-per-item	0.93	42.07	-0.2
Color reading: Number of correct response	64	24.2	-0.7
Number of error	0	81.33	0.89
Response time (sec)	120		
Correct response rate	1	74.86	0.67
Time-per-item	1.88	21.77	-0.78
Interference score	0.95	25.78	-0.65
			14.46

Others

Attention			
Digit span: Forward	8	99.41	2.52
Backward	4	69.85	0.52
Forward-Backward	4	0.96	-2.34
Letter Cancellation	Normal		
Neglect side	N/A		
Visuospatial Functions			
K-MMSE: Drawing	1	216	
Rey Complex Figure Test (RCFT): copy score	29	33.36	-0.43 28.1
time (sec)	244	77.34	0.75 84.85

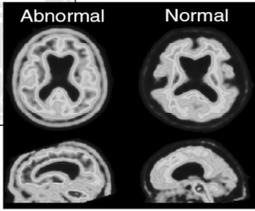
- ### LAB (Blood)
- CBC
 - Chemistry (LFT, Glucose, BUN/Cr, Na/K, Ca, etc.)
 - VDRL
 - TFT
 - Vitamins B12, Folate
 - Homocystein
 - Apo E genotype: E3/E3
- 



CREDOS Criteria of Cognitive Decline on SNSB

영역	검사 종목	평가 항목	기준
Memory	SVLT Rey figure	Delayed recall	16%이하만
Language	K-BNT		16%이하만
Visuospatial function	Rey figure copy		
Frontal function	Motor (이 중 3개 이상일 때 인정)	Contrasting program Go - No go Flat-edge-palm Alternating hand movement Alternative square and triangle Luria loop	세 가지 중에서 두 가지 이상이 abnormal 이면 전두엽 기능 장애
	COWAT (이 중 1개 이상일 때 인정)	Animal Supermarket Phonemic total (7-7-7-7)	
	Stroop	Color reading, correct response number	

[18F]flutemetamol PET



Acta Neuropathologica Communications, 2014

Case 2

- F/ 63 (Right handedness)
- 초등학교 졸업
- 3-4년 전까지 회사원으로 일함

Chief Complaint

- 2014. 12.
- 기억력 저하

Present illness

- 기억력 저하 (over 18 months)
- ✓ 자꾸 잊는다. (전화로 약속하고 잊는 경우 많음)
- ✓ 했던 말 반복한다.
- ✓ 불면증

Others

- Hypertension (160/102 mmHg), but no medication
- No! DM, Dyslipidemia, Cardiac disease, smoking
- FHx: demented sister

Neurological Exam &

- No focal signs
- Hachinski Ischemic Scale: 1점 (hypertension)

K-MMSE

28 / 30 (62.53 %ile)			
시간지남력	5 / 5	장소지남력	5 / 5
기억등록	3 / 3	주의집중 및 계산	5 / 5
기억회상	1 / 3	언어 및 시공간구성	9 / 9

SBSN

Memory

Seoul Verbal Learning Test-Elderly's version (SVLT-E)

Immediate recalls: Trial 1	5			
Trial 2	5			
Trial 3	4			
Total score	14	10.89	-1.23	6.86
Delayed recall	1	1.05	-2.31	0.35
Recognition: True positive	10	43.32	-0.17	39.48
False positive	5	0.39	-2.66	0.43
Recognition score	17	3.17	-1.86	2.42
Recognition discriminability index	70.83	3.32	-1.84	2.52
Rey Complex Figure Test (RCFT)				
Immediate recall	2.5	4.38	-1.71	5.12
Delayed recall	1.5	2.42	-1.97	2.75
Recognition: True positive	10	53.17	0.08	53.50
False positive	4	12.54	-1.15	
Recognition score	18	18.70	-0.89	19.38
Recognition discriminability index	75.00	18.74	-0.89	19.38

SBSN

Language & Related Functions

Spontaneous speech: Fluency				
Contents	Fluent	Normal		
Comprehension	Normal	Normal		
Repetition	15	15s		
Korean-Boston Naming Test (K-BNT)				
Short form of the K-BNT	9	8.66	-1.36	11.31
Reading	Normal	Normal		
Writing	Normal	Normal		
Finger naming				
Right-left orientation				
Body-part identification				
Calculation: Addition (+)				
Subtraction (-)				
Multiplication (x)				
Division (/)				
Total score				
Praxis: Ideomotor	4	15s		
Buccofacial				

SBSN

Frontal / Executive Functions

Motor impersistence				
Contrasting program				
Go-No go				
Fast-Edge-Palm: Right		Normal		
Left		Normal		
Alternating hand movement				
Alternating square & triangle		Normal		
Luria loop				
Controlled Oral Word Association Test (COWAT):				
Animal	12	23.86	-0.71	25.68
Supermarket	7	3.50	-1.81	1.66
o	8	63.12	0.34	
o	8	66.19	0.42	
^	10	82.00	0.92	83.36
Phonemic total score	26	74.44	0.66	
Animal + ^	20	37.98	-0.31	40.14
Korean-Color Word Stroop Test (K-CWST):				
Word Reading (WR): Number of correct response	112	15s		
Number of error response	0	15s		
Response time (sec)	70			
Correct response rate	1.00	15s		
Time-per-item	0.63	70.25	0.53	
Color Reading (CR): Number of correct response	58	9.04	-1.34	7.04
Number of error response	1	15s		
Response time (sec)	120			
Correct response rate	0.98	15s		
Time-per-item	2.03	8.53	-1.37	6.97
Interference score	1.41	4.06	-1.74	2.78

SBSN

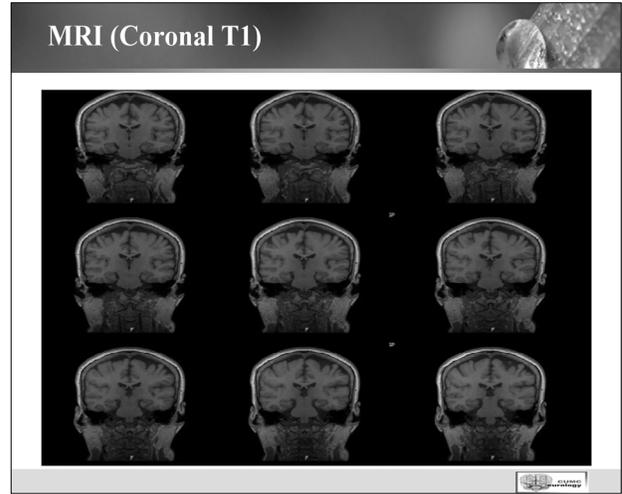
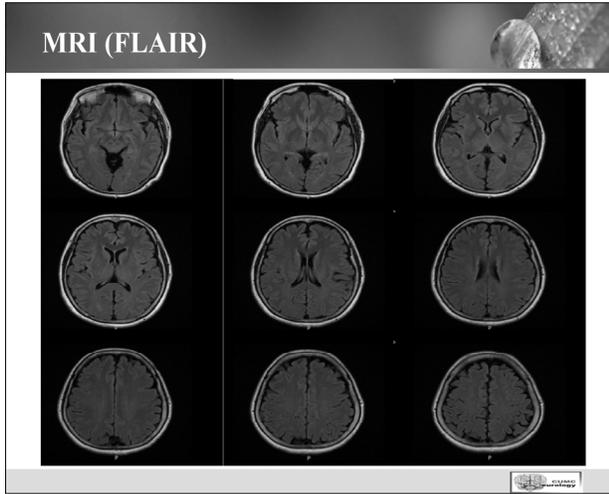
Visuospatial Functions

Clock Drawing Test (CDT): Contour				
Numbers	1			
Time setting	1			
Total score	3	15s		
Rey Complex Figure Test (RCFT): Copy score	32	54.54	0.11	51.71
Copy time (sec)	270	27.87	-0.59	32.00
Attention				
Vigilance test				
Digit Span Test: Forward	6	63.33	0.34	68.34
Backward				
Forward-Backward				
Letter cancellation				
Neglected side				
Cognitive Domain Scores				
Cognitive Domain	Raw Score	%ile Score	Z Score	T Score
Attention	0.13	63.79	0.35	53.53
Language	0.29	63.68	0.35	53.50
Visuospatial Function	-1.33	0.48	-2.59	24.14
Memory	-0.38	25.53	-0.60	43.43
Frontal / Executive Function				26.86

LAB (Blood)

- CBC
- Chemistry (LFT, Glucose, BUN/Cr, Na/K, Ca, etc.)
- VDRL
- TFT
- Vitamin B12, Folate
- Homocystein





CSF

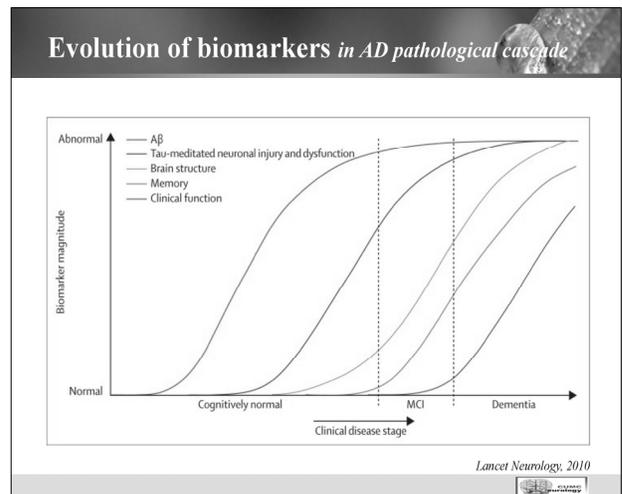
- Aβ 42: 336 pg/mL
- total tau: 326 pg/mL
- p-tau: 47 pg/mL



Table 4. Receiver operating characteristic (ROC) curve parameters

	Aβ42 (pg/mL)	pTau181 (pg/mL)	tTau (pg/mL)	pTau181/Aβ42	tTau/Aβ42
Test accuracy	84.00%	86.20%	86.20%	96.60%	96.60%
Positive predictive value	88.20%	93.30%	93.30%	100.00%	100.00%
Negative predictive value	83.30%	78.60%	78.60%	92.30%	92.30%
ROC AUC	0.917	0.868	0.922	0.941	0.995
Cut-off value (pg/mL or ratio)	450	>54.297	>320737	>0.163	>0.758
Sensitivity	88.20%	82.40%	82.40%	94.10%	94.10%
Specificity	83.30%	91.70%	100%	100%	100%

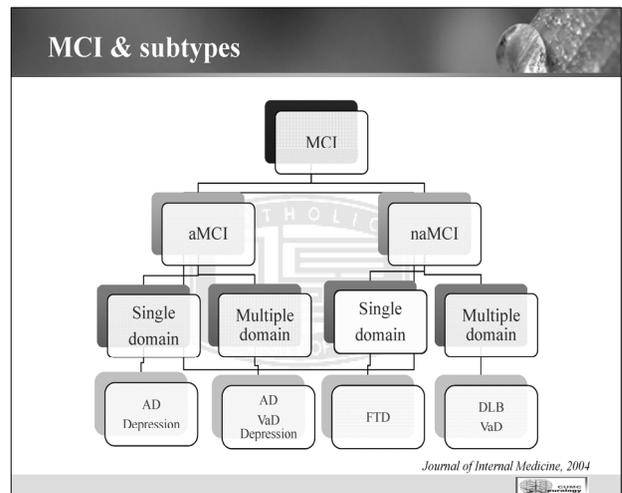
ROC, receiver operating characteristic; AUC, area under the curve. *DND, 2013; JCN, 2015*



Use of biomarkers for the diagnosis of MCI

Diagnostic Category	Biomarker Probability of AD etiology	Aβ (PET or CSF)	Neuronal Injury (tau, FDG, sMRI)
MCI	Uninformative	Conflicting/indeterminant/untested	
MCI d/t AD -intermediate likelihood	Intermediate	Positive Untested	Untested Positive
MCI d/t AD -high likelihood	Highest	Positive	Positive
MCI -unlikely d/t AD	Lowest	Negative	Negative

Alzheimer Dementia, 2011

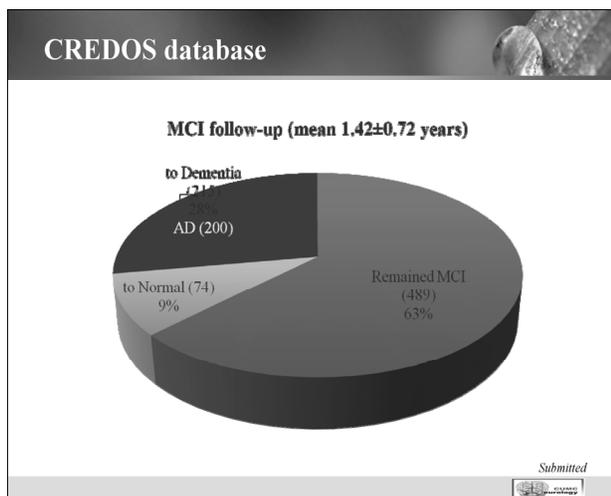


Possible Predictors of Progression in MCI

- Severity of clinical impairment
- Apolipoprotein E4 carrier
- Biomarkers
 - MRI: atrophy of MTL structures
 - FDG PET: evidence of parietotemporal hypometabolism
 - Amyloid imaging: positive for the presence of amyloid
 - CSF: lower Abeta 42 & elevated tau
- Positive family history of dementia

Archives of General Psychiatry, 2007

Clinical Predictors for MCI progression in a Korean cohort (CREDOS)



CREDOS database

Cox Proportional Hazard models

	HR	95% CI	P value
Age (years)	1.362	1.277 1.451	<0.001*
Education (years)	0.921	0.893 0.95	<0.001
<u>Sx duration (months)</u>	1.938	1.575 2.381	<0.001
amnesia	2.101	1.277 3.46	0.004
APOE ε 4	2.883	2.013 4.127	<0.001*
K-MMSE	0.871	0.839 0.904	<0.001*
CDR-SOB	1.329	1.134 1.557	<0.001*
S-IADL	1.038	1.015 1.063	0.002*
BMI (kg/m ²)	0.91	0.87 0.952	<0.001
GDS	0.969	0.936 1.003	0.078
Change of GDS	1.066	1.036 1.092	<0.001
ChEIs prescribed during the follow-up	3.546	2.481 5.076	<0.001

Submitted