

Supplementary table 1. Clinical profile

a) Demographic and clinical assessments

Demographic variables	MCI (n = 455)		AD (n = 153)	
	Mean	SD	Mean	SD
Age (years)	72.69	7.73	75.33	7.75
Education (years)	16.09	2.73	16.07	2.63
MMSE score	28.00	1.77	22.49	3.32
GDS score	1.85	1.56	2.03	2.18
NPI-D score	0.67	1.41	0.80	1.28
FAQ score	2.75	3.74	14.22	6.93
CDRSB score	1.49	0.99	5.10	2.30

b) Beta-amyloid deposition

Regions of Interest	MCI (n = 455)		AD (n = 153)	
	Mean	SD	Mean	SD
Frontal	1.39	0.29	1.57	0.29
Cingulate	1.46	0.29	1.63	0.28
Parietal	1.38	0.29	1.57	0.29
Temporal	1.30	0.26	1.46	0.27
Global	1.20	0.22	1.37	0.22

c) GDS score

Group	n	# with score of 0 ([%])	# with GDS score of >5 ([%])	# with GDS score of >10 ([%])
MCI	455	94 (20.66)	28 (6.15)	0 (0)
AD	153	29 (18.95)	17 (11.11)	3 (1.96)

d) NPI-D score

Group	n	# with score of 0 ([%])	# with score 1 or above ([%])
MCI	455	318 (69.89)	137 (30.11)
AD	153	96 (62.75)	57 (37.25)

(Abbreviations: AD = Alzheimer's disease; CDRSB = Clinical Dementia Rating Sum of Boxes score; FAQ = Functional Activities Questionnaire; GDS = Geriatric Depression Scale; MCI = mild cognitive impairment; MMSE = Mini-mental State Examination; SD = standard deviation)

Supplementary table 2. Demographic and clinical profile of high depressed and low depressed MCI patients

a) First pair

Demographic variables	Low depressed (n =28)		High depressed (n =28)		p-value
	Mean	SD	Mean	SD	
GDS score	1.36	1.37	5.54	1.11	<0.01*
Age (years)	75.01	8.91	73.11	9.01	0.43
Education years	15.89	2.96	16.04	2.50	0.85
MMSE score	28.21	1.29	28.00	1.68	0.59
MOCA score	22.93	5.49	22.86	3.39	0.95
FAQ score	1.89	1.99	4.18	5.11	0.03*
CDRSB score	1.43	0.96	1.98	1.32	0.08
Packs/day	0.50	0.67	0.61	0.69	0.54
Years of smoking	8.00	9.98	12.46	15.79	0.21
NPI total score	2.82	4.00	8.32	7.72	<0.01*
	Number (Frequency[%])		Number (Frequency[%])		p-value
Females	16 (57.14)		16 (57.14)		1.00
White	26 (92.86)		25 (89.29)		0.80
Never married	3 (10.71)		3 (10.71)		0.64
ApoE4 0 allele	18 (64.29)		19 (67.86)		0.96
ApoE4 1 allele	9 (32.14)		8 (28.57)		0.96
ApoE4 2 alleles	1 (3.57)		1 (3.57)		0.96
LMD	6 (21.43)		7 (25.00)		1.00
ND	16 (57.14)		11 (39.29)		0.29
CVD	19 (67.86)		22 (78.57)		0.55
MD	13 (46.43)		15 (53.57)		0.79
Alcohol abuse	3 (10.71)		3 (10.71)		1.00
Drug abuse	2 (7.14)		0 (0)		0.49
PD	12 (42.86)		18 (64.29)		0.18
History of smoking	14 (50.00)		15 (53.57)		1.00
Current smoking	0 (0)		1 (3.57)		1.00

b) Second pair

Demographic variables	Low depressed (n =28)		High depressed (n =28)		p-value
	Mean	SD	Mean	SD	
GDS score	1.50	1.40	5.54	1.11	<0.01*
Age (years)	76.84	7.84	73.11	9.01	0.10
Education years	16.11	2.64	16.04	2.50	0.92
MMSE score	27.71	1.86	28.00	1.68	0.55
MOCA score	23.25	3.11	22.86	3.39	0.65
FAQ score	2.54	3.51	4.18	5.11	0.17
CDRSB score	1.45	0.89	1.98	1.32	0.08
Packs/day	0.68	1.87	0.61	0.69	0.86
Years of smoking	11.89	16.63	12.46	15.79	0.90
NPI score	6.14	8.27	8.32	7.72	0.31

	Number(Frequency[%])	Number(Frequency[%])	p-value
Females	16 (57.14)	16 (57.14)	1.00
White	28 (100.00)	25 (89.29)	0.37
Never married	4 (14.29)	3 (10.71)	0.72
ApoE4 0 allele	19 (67.86)	19 (67.86)	1.00
ApoE4 1 allele	8 (28.57)	8 (28.57)	1.00
ApoE4 2 alleles	1 (3.57)	1 (3.57)	1.00
LMD	2 (7.14)	7 (25.00)	0.14
ND	12 (42.86)	11 (39.29)	1.00
CVD	20 (71.43)	22 (78.57)	0.76
MD	10 (35.71)	15 (53.57)	0.28
Alcohol abuse	1 (3.57)	3 (10.71)	0.61
Drug abuse	0 (0)	0 (0)	1.00
PD	8 (28.57)	18 (64.29)	0.02*
History of smoking	14 (50.00)	15 (53.57)	1.00
Current smoking	2 (7.14)	1 (3.57)	1.00

c) Third pair

Demographic variables	Low depressed (n=28)		High depressed (n=28)		p-value
	Mean	SD	Mean	SD	
GDS score	2.00	1.56	5.54	1.11	<0.01*
Age (years)	73.70	6.51	73.11	9.01	0.78
Education years	16.21	2.85	16.04	2.50	0.80
MMSE score	28.36	2.04	28.00	1.68	0.48
MOCA score	24.54	3.36	22.86	3.39	0.07
FAQ score	2.50	3.28	4.18	5.11	0.15
CDRSB score	1.25	0.80	1.98	1.32	0.02*
Packs/day	0.75	0.91	0.61	0.69	0.51
Years of smoking	10.71	14.38	12.46	15.79	0.67
NPI total score	4.64	7.12	8.32	7.72	0.07
	Number(Frequency[%])		Number(Frequency[%])		p-value
Females	16 (57.14)		16 (57.14)		1.00
White	27 (96.43)		25 (89.29)		0.40
Never married	4 (14.29)		3 (10.71)		0.72
ApoE4 0 allele	19 (67.86)		19 (67.86)		1.00
ApoE4 1 allele	8 (28.57)		8 (28.57)		1.00
ApoE4 2 alleles	1 (3.57)		1 (3.57)		1.00
LMD	3 (10.71)		7 (25.00)		0.30
ND	8 (28.57)		11 (39.29)		0.57
CVD	21 (75.00)		22 (78.57)		1.00
MD	18 (64.29)		15 (53.57)		0.59
Alcohol abuse	2 (7.14)		3 (10.71)		1.00
Drug abuse	0 (0)		0 (0)		1.00
PD	11 (39.29)		18 (64.29)		0.11
History of smoking	14 (50.00)		15 (53.57)		1.00
Current smoking	1 (3.57)		1 (3.57)		1.00

(Abbreviations: ApoE4 0 allele = 0 apolipoprotein E4 allele; ApoE4 1 allele = 1 apolipoprotein E4 allele; ApoE4 2 alleles = 2 apolipoprotein E4 alleles; CDRSB = Clinical Dementia Rating Scale Sum of Boxes; CVD = history of cardiovascular diseases; FAQ = Functional Activities Questionnaire; GDS = Geriatric Depression Scale; LMD = history of major depression; MCI = mild cognitive impairment; MD = history of metabolic disorders; MMSE = Mini Mental State Examination score; MOCA = Montreal Cognitive Assessment; ND = history of neurological disorders; NPI = Neuropsychiatric Inventory; PD = history of psychiatric disorders; SD = standard deviation)

Supplementary table 3. Demographic and clinical profile of low depressed and high depressed AD patients

a) First pair

Demographic variables	Low depressed AD (n=17)		High depressed AD (n=17)		p-value
	Mean	SD	Mean	SD	
GDS score	0.71	1.37	6.88	2.40	<0.01*
Age (years)	76.55	8.71	78.44	5.79	0.46
Education years	16.65	2.23	15.59	3.74	0.33
MMSE score	20.82	4.93	21.35	5.16	0.76
MOCA score	15.82	6.88	16.47	6.28	0.78
FAQ score	13.12	8.35	13.59	6.71	0.86
CDRSB score	5.53	3.57	4.62	1.32	0.34
Packs/day	0.35	0.61	0.68	0.79	0.19
Years of smoking	7.94	14.04	8.06	10.81	0.98
NPI total score	6.18	7.36	11.23	8.28	0.07
	Number(Frequency[%])		Number(Frequency[%])		p-value
Females	7 (41.18)		7 (41.18)		1.00
White	16 (94.12)		17 (100.00)		1.00
Never married	0 (0)		2 (11.76)		0.44
ApoE4 0 allele	9 (52.94)		9 (52.94)		1.00
ApoE4 1 allele	7 (41.18)		7 (41.18)		1.00
ApoE4 2 alleles	1 (5.88)		1 (5.88)		1.00
LMD	1 (5.88)		3 (17.65)		0.60
ND	7 (41.18)		5 (29.41)		0.72
CVD	7 (41.18)		12 (70.59)		0.17
MD	7 (41.18)		6 (35.29)		1.00
Alcohol abuse	0 (0)		1 (5.88)		1.00
Drug abuse	0 (0)		0 (0)		1.00
PD	8 (47.06)		10 (58.82)		0.73
History of smoking	5 (29.41)		9 (52.94)		0.30
Current smoking	1 (5.88)		0 (0)		1.00

b) Second pair

Demographic variables	Low depressed AD (n=17)		High depressed AD (n=17)		p-value
	Mean	SD	Mean	SD	
GDS score	0.71	1.37	6.88	2.40	<0.01*
Age (years)	76.55	8.71	78.44	5.79	0.46
Education years	16.65	2.23	15.59	3.74	0.33
MMSE score	22.00	2.83	21.35	5.16	0.65
FAQ score	18.00	6.85	13.59	6.71	0.07
CDRSB score	5.91	2.08	4.62	1.32	0.04*
Packs/day	0.68	0.90	0.68	0.79	1.00
Years of smoking	10.47	13.81	8.06	10.81	0.58
NPI total score	8.11	10.26	11.23	8.28	0.34

	Number(Frequency[%])	Number(Frequency[%])	p-value
Females	7 (41.18)	7 (41.18)	1.00
White	16 (94.11)	17 (100.00)	1.00
Never married	0 (0)	2 (11.76)	0.44
ApoE4 0 allele	9 (52.94)	9 (52.94)	1.00
ApoE4 1 allele	7 (41.18)	7 (41.18)	1.00
ApoE4 2 alleles	1 (5.88)	1 (5.88)	1.00
LMD	1 (5.88)	3 (17.65)	0.60
ND	3 (17.65)	5 (29.41)	0.69
CVD	9 (52.94)	12 (70.59)	0.48
MD	11 (64.71)	6 (35.29)	0.17
Alcohol abuse	0 (0)	1 (5.88)	1.00
Drug abuse	0 (0)	0 (0)	1.00
PD	7 (41.18)	10 (58.82)	0.39
History of smoking	9 (52.94)	9 (52.94)	1.00
Current smoking	1 (5.88)	0 (0)	1.00

c) Third pair

Demographic variables	Low depressed AD (n=17)		High depressed AD (n=17)		p-value
	Mean	SD	Mean	SD	
GDS score	0.88	0.60	6.88	2.40	<0.01*
Age (years)	76.24	8.61	78.44	5.79	0.39
Education years	15.71	2.29	15.59	3.74	0.91
MMSE score	22.82	1.98	21.35	5.16	0.29
MOCA score	17.00	4.43	16.47	6.28	0.78
FAQ score	13.76	7.22	13.59	6.71	0.94
CDRSB score	4.76	1.66	4.62	1.32	0.78
Packs/day	0.65	0.88	0.68	0.79	0.92
Years of smoking	11.35	14.90	8.06	10.81	0.47
NPI total score	7.00	9.70	11.23	8.28	0.18
	Number(Frequency[%])		Number(Frequency[%])		p-value
Females	7 (41.18)		7 (41.18)		1.00
White	16 (94.11)		17 (100.00)		1.00
Never married	0 (0)		2 (11.76)		0.44
ApoE4 0 allele	9 (52.94)		9 (52.94)		1.00
ApoE4 1 allele	7 (41.18)		7 (41.18)		1.00
ApoE4 2 alleles	1 (5.88)		1 (5.88)		1.00
LMD	2 (11.76)		3 (17.65)		1.00
ND	4 (23.53)		5 (29.41)		1.00
CVD	9 (52.94)		12 (70.59)		0.48
MD	12 (70.59)		6 (35.29)		0.08
Alcohol abuse	3 (17.65)		1 (5.88)		0.60
Drug abuse	1 (5.88)		0 (0)		1.00
PD	5 (29.41)		10 (58.82)		0.17
History of smoking	8 (47.06)		9 (52.94)		1.00
Current smoking	1 (5.88)		0 (0)		1.00

(Abbreviations: ApoE4 0 allele = 0 apolipoprotein E4 allele; ApoE4 1 allele = 1 apolipoprotein E4 allele; ApoE4 2 alleles = 2 apolipoprotein E4 alleles; CDRSB = Clinical Dementia Rating Scale Sum of Boxes; CVD = history of cardiovascular diseases; FAQ = Functional Activities Questionnaire; GDS = Geriatric Depression Scale; LMD = history of major depression; MCI = mild cognitive impairment; MD = history of metabolic disorders; MMSE = Mini Mental State Examination; MOCA = Montreal Cognitive Assessment; ND = history of neurological disorders; NPI = Neuropsychiatric Inventory; PD= history of psychiatric disorders; SD = standard deviation)

Supplementary table 4. Demographic and clinical assessments between not depressed and depressed patients with MCI (a) and AD (b)

a)

Demographic variables	Not Depressed MCI (n=80)		Depressed MCI (n=80)		p-value
	Mean	SD	Mean	SD	
GDS score	0	0	3.50	1.63	<0.01*
NPI-D score	0	0	2.46	1.94	<0.01*
Age (years)	75.11	7.11	73.19	9.15	0.14
Education years	16.01	2.69	15.59	2.86	0.33
MMSE score	28.26	1.48	28.24	1.63	0.92
MOCA score	24.01	3.18	23.58	3.36	0.40
FAQ score	2.04	2.80	4.28	4.72	<0.01*
CDRSB score	1.33	0.80	1.98	1.19	<0.01*
Packs/day	0.42	0.75	0.59	0.72	0.17
Years of smoking	8.29	14.42	11.90	15.55	0.13
NPI total score	2.91	4.81	11.09	8.45	<0.01*

	Number(Frequency[%])	Number(Frequency[%])	p-value
Females	34 (42.50)	33 (41.25)	1.00
White	76 (95.00)	80 (100)	0.13
Never married	2 (2.50)	2 (2.50)	0.91
ApoE4 0 allele	47 (58.75)	45 (56.25)	0.85
ApoE4 1 allele	27 (33.75)	27 (33.75)	0.85
ApoE4 2 alleles	6 (7.50)	8 (10.00)	0.85
LMD	8 (10.00)	18 (64.29)	0.05
ND	22 (27.50)	25 (31.25)	0.73
CVD	61 (76.25)	54 (67.50)	0.29
MD	32 (40.00)	36 (45.00)	0.63
Alcohol abuse	3 (3.75)	6 (7.50)	0.50
Drug abuse	1 (1.25)	0 (0)	1.00
PD	21 (26.25)	48 (60.00)	<0.01*
History of smoking	29 (36.25)	41 (51.25)	0.08
Current smoking	2 (2.50)	3 (3.75)	1.00

b)

Demographic variables	Not Depressed AD (n=22)		Depressed AD (n=22)		p-value
	Mean	SD	Mean	SD	
GDS score	0	0	2.95	3.09	<0.01*
NPI-D score	0	0	2.09	1.31	<0.01*
Age (years)	75.80	7.53	72.85	8.09	0.22
Education years	16.36	2.19	16.59	2.38	0.74
MMSE score	21.45	4.31	22.55	3.10	0.34
MOCA score	15.14	5.48	17.10	5.06	0.23
FAQ score	14.18	9.06	16.05	4.91	0.40
CDRSB score	6.23	3.84	5.11	1.81	0.23
Packs/day	0.48	0.76	0.41	0.68	0.76
Years of smoking	7.14	10.53	8.09	14.66	0.81
NPI total score	4.18	5.76	13.45	12.37	<0.01*

	Number(Frequency[%])	Number(Frequency[%])	p-value
Females	9 (40.91)	9 (40.91)	1.00
White	19 (86.36)	20 (90.91)	0.24
Married	22 (100.00)	19 (86.36)	0.11
ApoE4 0 allele	10 (45.45)	10 (45.45)	1.00
ApoE4 1 allele	8 (36.36)	8 (36.36)	1.00
ApoE4 2 alleles	4 (18.18)	4 (18.18)	1.00
LMD	1 (4.55)	6 (27.27)	0.10
ND	7 (31.82)	6 (27.27)	1.00
CVD	14 (63.64)	11 (50.00)	0.54
MD	9 (40.91)	13 (59.09)	0.37
Alcohol abuse	1 (4.55)	0 (0)	1.00
Drug abuse	0 (0)	0 (0)	1.00
PD	6 (27.27)	13 (59.09)	0.07
History of smoking	9 (40.91)	7 (31.82)	0.76
Current smoking	1 (4.55)	1 (4.55)	1.00

Supplementary table 5.

a) Partial correlation between depressive symptoms and A β levels in frontal, parietal, cingulate and temporal regions in MCI due to AD (n = 91)

Clinical assessments	Region of interest			
	Frontal	Cingulate	Parietal	Temporal
GDS score	r = -0.12, p = 0.33	r = -0.01, p = 0.96	r < -0.01, p = 0.98	r = -0.22, p = 0.08
NPI-D score	r = -0.11, p = 0.39	r = -0.06, p = 0.66	r = -0.06, p = 0.64	r = -0.13, p = 0.28

b) Partial correlation between depressive symptoms and A β levels in frontal, parietal, cingulate and temporal regions in MCI not due to AD (n=281)

Clinical assessments	Region of interest			
	Frontal	Cingulate	Parietal	Temporal
GDS score	r = 0.03, p = 0.66	r = 0.05, p = 0.43	r = 0.11, p = 0.08	r = 0.13, p = 0.04
NPI-D score	r < 0.01, p = 0.99	r = 0.05, p = 0.46	r = 0.07, p = 0.24	r = 0.04, p = 0.49