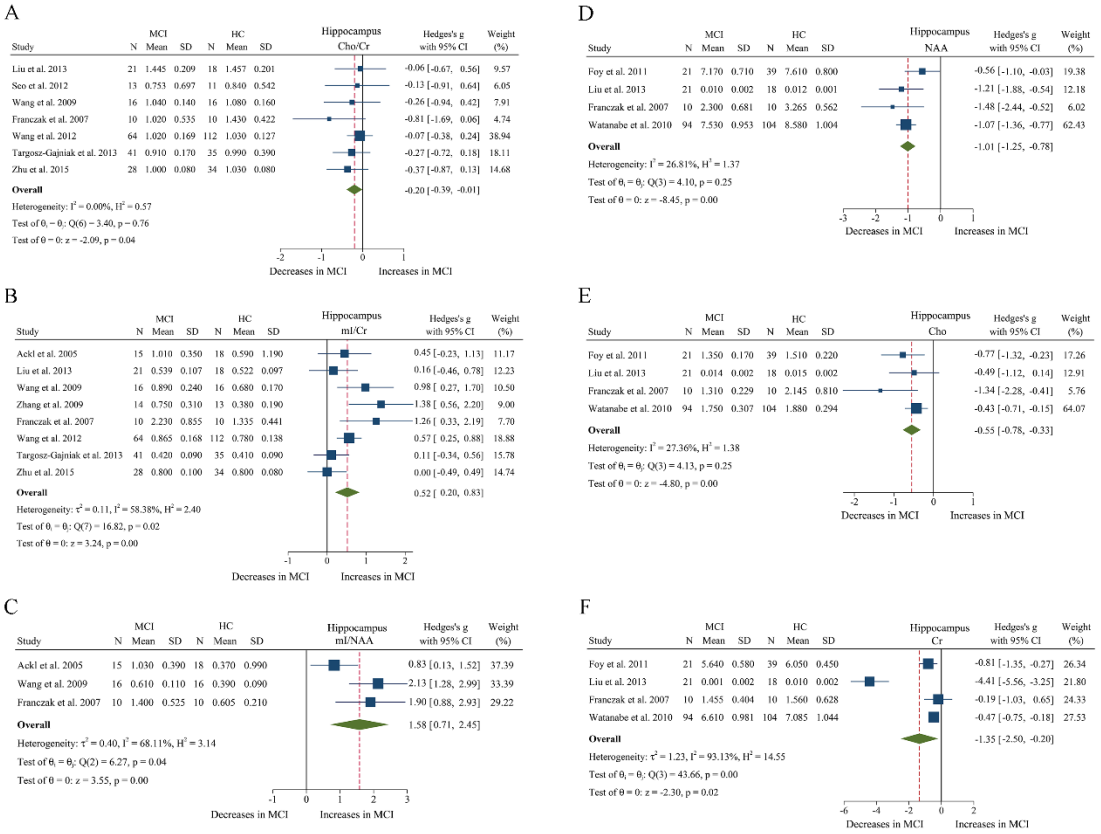
Supplementary Table 1 results of meta-analysis

Region	Subjects	Metabolites	No. of Studies	I^2	H^2	Z	P	SMD	95%CI
Hippocampus	MCI Vs HC	mI	4	58.99%	2.44	1.08	0.28	0.23	-0.19 to 0.65
		Glx/Cr	3	86.62%	7.47	-1.44	0.15	-0.76	-1.81 to 0.28
	AD Vs MCI	mI/Cr	4	29.18%	1.41	1.92	0.06	0.25	-0.01 to 0.50
	MCI-converter Vs MCI-stable	Cho/Cr	2	0.00%	0.03	-1.91	0.06	-0.47	-0.94 to 0.01
		NAA/Cr	2	17.31%	1.21	-0.72	0.47	-0.17	-0.65 to 0.30
PC	MCI Vs HC	mI/NAA	3	76.15%	4.19	0.04	0.97	0.02	-0.79 to 0.82
		Cho/Cr	17	89.01%	9.10	1.96	0.05	0.34	-0.00 to 0.69
		NAA/Cho	4	58.33%	2.40	-1.80	0.07	-0.35	-0.72 to 0.03
	AD Vs HC	Cr	4	73.18%	3.73	-1.71	0.09	-0.37	-0.80 to 0.05
		Cho	6	50.97%	2.04	1.81	0.07	0.23	-0.02 to 0.48
	AD Vs MCI	Cho/Cr	9	56.41%	2.29	0.79	0.43	0.10	-0.15 to 0.35
		mI	4	0.00%	0.37	-0.69	0.49	-0.07	-0.28 to 0.13
		Cho	3	76.46%	4.25	-0.17	0.87	-0.05	-0.57 to 0.48
	MCI-converter Vs MCI-stable	NAA/Cr	2	0.00%	0.07	0.68	0.50	0.17	-0.33 to 0.67
		Cho/Cr	2	0.00%	0.64	0.44	0.66	0.11	-0.39 to 0.61
Temporal lobe	MCI Vs HC	NAA/Cr	3	0.00%	0.30	-0.81	0.42	-0.12	-0.40 to 0.17
	AD Vs HC	Cho/Cr	3	19.57%	1.24	1.91	0.06	0.35	-0.01 to 0.71
		mI/Cr	4	0.00%	0.50	-1.87	0.06	-0.27	-0.57 to 0.01
Parietal lobe	MCI Vs HC	NAA/Cr	3	0.00%	0.41	0.16	0.88	0.02	-0.2 to 0.24
	MCI-converter Vs MCI-stable	Cho/Cr	2	35.30%	1.55	0.82	0.41	0.15	-0.21 to 0.50
		NAA/mI	2	81.64%	5.45	-0.18	0.85	-0.08	-0.92 to 0.76
Occipital lobe	AD Vs HC	NAA/Cr	3	0.00%	0.47	-1.69	0.09	-0.22	-0.47 to 0.04
		Cho/Cr	3	54.88%	2.22	1.08	0.28	0.22	-0.18 to 0.63

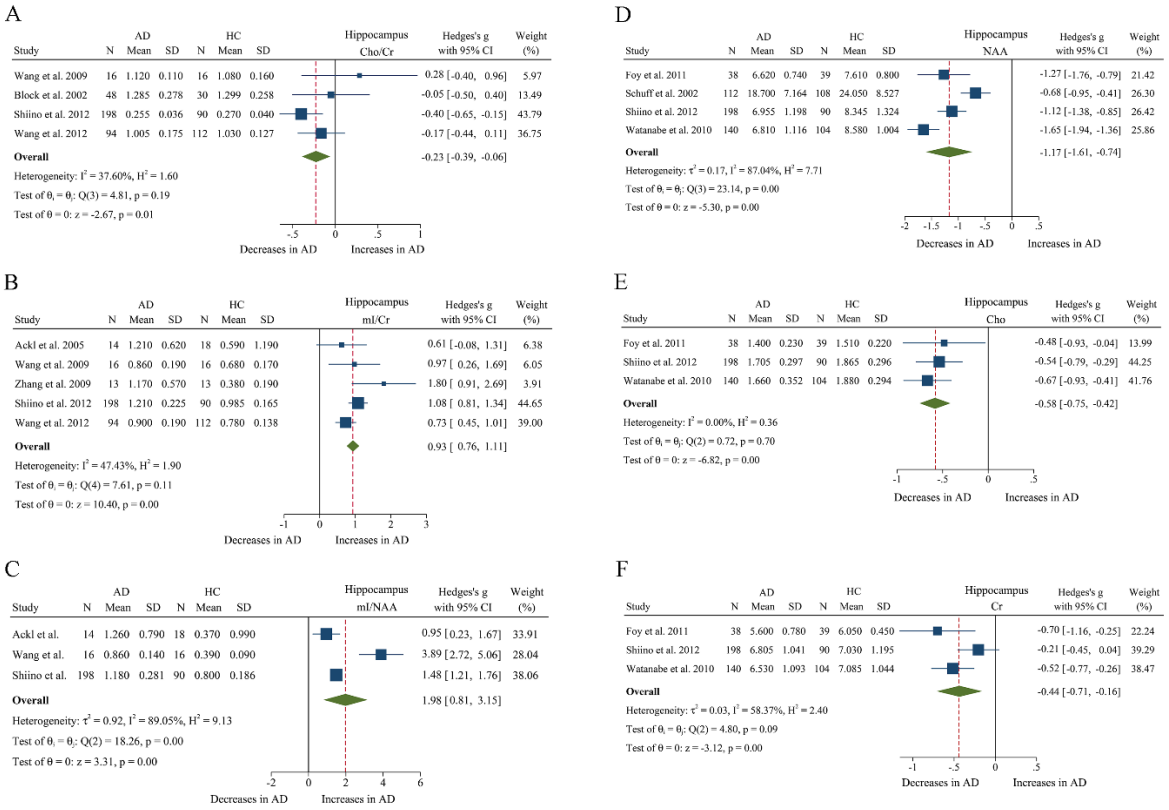
Region	Subjects	Metabolites	No. of Studies	I^2	H^2	Z	P	SMD	95%CI
Occipital lobe	AD Vs HC	Cho	3	43.21%	1.76	-0.80	0.42	-0.11	-0.40 to 0.17
		Cr	3	28.62%	1.40	-1.45	0.15	-0.21	-0.49 to 0.07
		mI	3	96.34%	27.29	1.09	0.28	1.09	-0.87 to 3.05
	MCI-converter Vs MCI-stable	NAA/Cr	3	83.86	6.20	-1.93	0.05	-0.98	-1.98 to 0.02
		mI/Cr	2	0.00%	0.68	-0.09	0.93	-0.02	-0.37 to 0.34
		NAA/mI	2	86.41%	7.36	-0.87	0.38	-0.44	-1.44 to 0.56
AC	MCI Vs HC	NAA/Cr	3	50.97%	2.04	-0.80	0.42	-0.20	-0.68 to 0.29
	AD Vs MCI	NAA/Cr	3	73.20%	3.73	-1.10	0.45	-0.25	-0.88 to 0.39
temporo-parietal lobe	AD Vs HC	NAA	3	32.36%	1.48	-0.93	0.35	-0.17	-0.51 to 0.18
		Cho	3	88.49%	8.69	0.89	0.37	0.51	-0.61 to 1.62
		Cr	3	0.00%	0.56	-0.55	0.59	-0.10	-0.44 to 0.25
Frontal WM	AD Vs HC	mI	3	68.55%	3.18	1.80	0.07%	0.64	-0.06 to 1.34
		NAA	3	47.43%	1.90	-0.80	0.42%	-0.15	-0.50 to 0.21
PWM	MCI Vs HC	Cho/Cr	3	0.00%	0.54	-0.01	0.99%	0.00	-0.26 to 0.25

HC: healthy controls, AD: Alzheimer's disease, MCI: Mild Cognitive Impairment, SMD: standardized mean difference, PC: posterior cingulate cortex, PWM: paratrigonal white matter, AC: anterior cingulate cortex, WM: white matter, NAA: N-Acetyl Aspartate, mI: myo-inositol, Cho: Choline, Cr: Creatine, Glx: glutamate + glutamine.

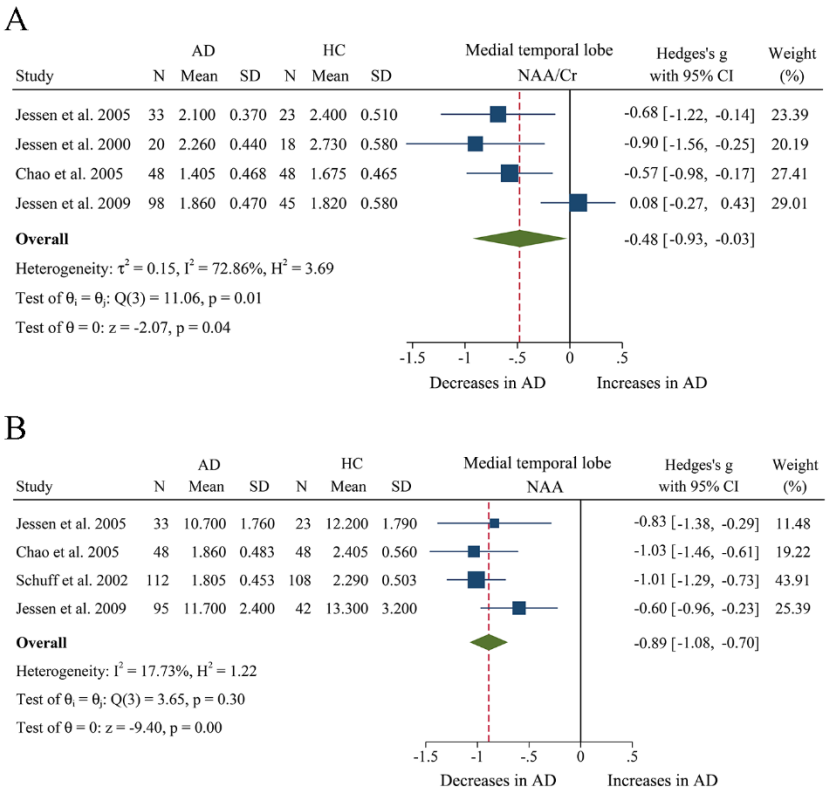
Supplementary Figure S1 Forest plots show the change of neurochemicals in hippocampus between MCI patients and HC subjects. **(A)** Data include 429 individuals from 7 studies for meta-analysis of Cho/Cr levels between MCI and HC. **(B)** Data include 465 individuals from 8 studies for meta-analysis mI/Cr levels between MCI and HC. **(C)** Data include 85 individuals from 3 studies for meta-analysis of mI/NAA levels between MCI and HC. **(D)** Data include 317 individuals from 4 studies for meta-analysis of NAA levels between MCI and HC. **(E)** Data include 317 individuals from 4 studies for meta-analysis of Cho levels between MCI and HC. **(F)** Data include 317 individuals from 4 studies for meta-analysis of Cr levels between MCI and HC.



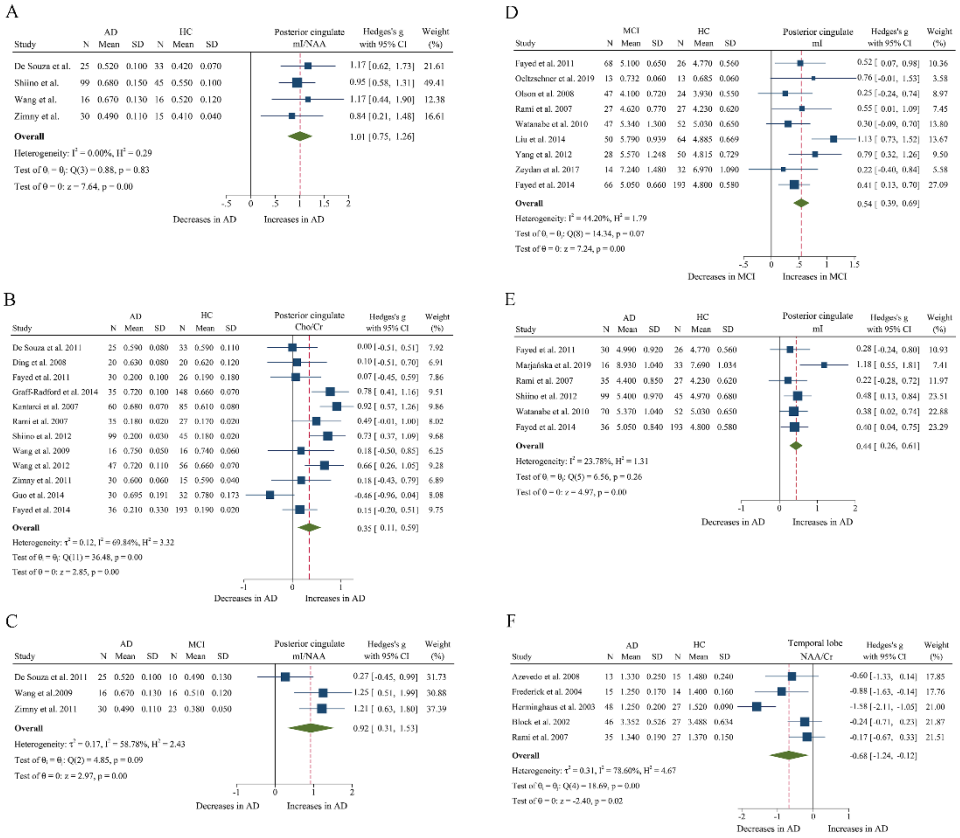
Supplementary Figure S2 Forest plots show the change of neurochemicals in hippocampus between AD patients and HC subjects. **(A)** Data include 604 individuals from 4 studies for meta-analysis of Cho/Cr levels between AD and HC. **(B)** Data include 584 individuals from 5 studies for meta-analysis mI/Cr levels between AD and HC. (**C)** Data include 352 individuals from 3 studies for meta-analysis of mI/NAA levels between AD and HC. **(D**) Data include 829 individuals from 4 studies for meta-analysis of NAA levels between AD and HC. **(E)** Data include 609 individuals from 3 studies for meta-analysis of Cho levels between AD and HC. **(F)** Data include 609 individuals from 3 studies for meta-analysis of Cr levels between AD and HC.



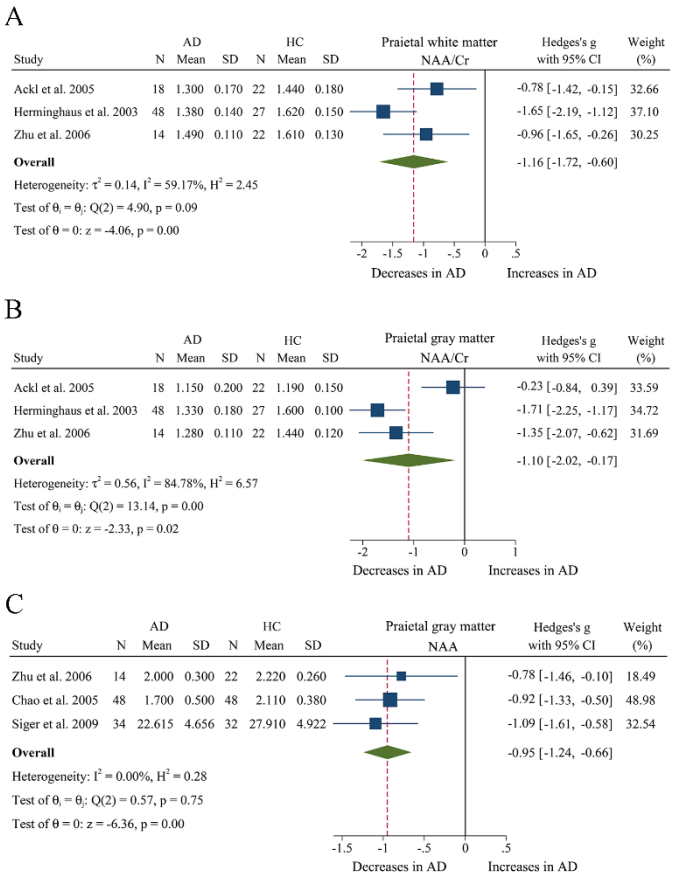
Supplementary Figure S3 Forest plots show the changes of NAA/Cr and NAA in medial temporal lobe between AD patients and HC subjects. **(A)** Data include 333 individuals from 4 studies for meta-analysis of NAA/Cr levels between AD and HC. **(B)** Data include 509 individuals from 4 studies for meta-analysis NAA levels between AD and HC.



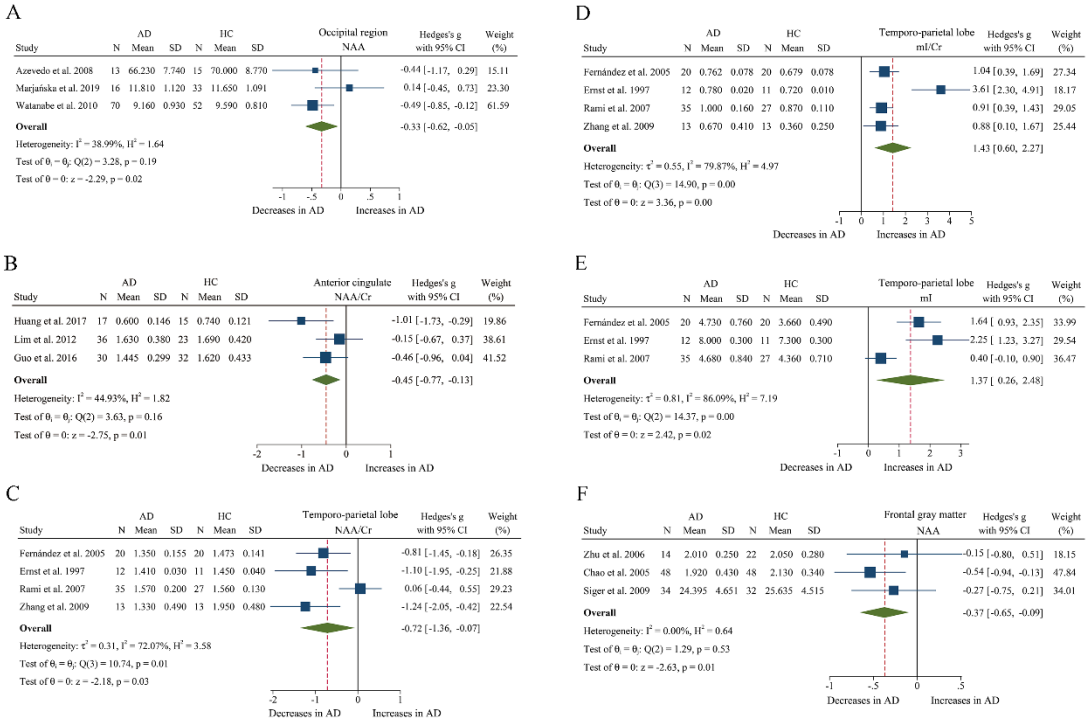
Supplementary Figure S4 Forest plots show the change of neurochemicals in posterior cingulate and temporal lobe between MCI, AD patients and HC subjects. **(A)** Data include 279 individuals from 4 studies for meta-analysis of mI/NAA levels between AD and HC. **(B)** Data include 1159 individuals from 12 studies for meta-analysis Cho/Cr levels between AD and HC. **(C)** Data include 120 individuals from 3 studies for meta-analysis of mI/NAA levels between AD and MCI. **(D**) Data include 841 individuals from 9 studies for meta-analysis of mI levels between MCI and HC. **(E)** Data include 662 individuals from 6 studies for meta-analysis of mI levels between AD and HC. **(F)** Data include 267 individuals from 5 studies for meta-analysis of NAA/Cr levels in temporal lobe between AD and HC.



Supplementary Figure S5 Forest plots show the change of NAA/Cr and NAA in parietal lobe between AD patients and HC subjects. **(A)** Data include 151 individuals from 3 studies for meta-analysis of NAA/Cr levels in the Parietal WM between AD and HC. **(B)** Data include 151 individuals from 3 studies for meta-analysis NAA/Cr levels in Parietal GM between AD and HC. **(C)** Data include 198 individuals from 3 studies for meta-analysis of NAA levels in the Parietal GM between AD and HC.



Supplementary Figure S6 Forest plots show the change of NAA and NAA/Cr in occipital lobe, anterior cingulate, temporo-parietal lobe and frontal region between AD patients and HC subjects. **(A)** Data include 199 individuals from 3 studies for meta-analysis of NAA levels in occipital lobe between AD and HC. **(B)** Data include 136 individuals from 3 studies for meta-analysis NAA/Cr levels in the anterior cingulate between AD and HC. (C) Data include 151 individuals from 4 studies for meta-analysis of NAA/Cr levels in temporo-parietal lobe between AD and HC. **(D)** Data include 151 individuals from 4 studies for meta-analysis of mI/Cr levels in temporo-parietal lobe between AD and HC. **(E)** Data include 125 individuals from 3 studies for meta-analysis of mI levels in temporo-parietal lobe between AD and HC. **(F)** Data include 198 individuals from 3 studies for meta-analysis of NAA levels in frontal GM between AD and HC.



Supplementary Figure S7 Forest plots show the change of NAA/Cr and mI/Cr in paratrigonal white matter lobe between MCI patients and HC subjects. **(A)** Data include 266 individuals from 3 studies for meta-analysis of NAA/Cr levels between MCI and HC. **(B)** Data include 266 individuals from 3 studies for meta-analysis mI/Cr levels in anterior cingulate cortex between AD and HC.