Appendix 1 to Sun Y, Hu N, Wang M, et al. Hippocampal subfield alterations in schizophrenia and major depressive disorder: a systematic review and network meta-analysis of anatomic MRI studies. *J Psychiatry Neurosci* 2023. doi: 10.1503/jpn.220086.

SUPPLEMENTARY MATERIALS

CONTENTS

tail volume reduction in SCZ versus HC

Appendix 1 to Sun Y, Hu N, Wang M, et al. Hippocampal subfield alterations in schizophrenia and major depressive disorder: a systematic review and network meta-analysis of anatomic MRI studies. *J Psychiatry Neurosci* 2023. doi: 10.1503/jpn.220086.

Supplementary Methods

1. Search strategy

We used the following keywords to search for hippocampal subfield volume studies of patients with schizophrenia: (1) hippocampal subfields, hippocampal subfield, hippocampal subregions, hippocampal subregion, cornu ammonis, CA, CA1, CA2, CA23, CA2/3, CA2-3, CA3, CA4, dentate gyrus, DG, DGL, DG/CA4 and subiculum; (2) magnetic resonance imaging, MRI and volume; (3) schizophrenia, schizophrenias, schizophrenic disorder, schizophrenic disorders, SCZ and psychosis. Similarly, the following keywords were used for hippocampal subfield volume studies of patients with major depressive disorder: (1) hippocampal subfields, hippocampal subfield, hippocampal subregions, hippocampal subregion, cornu ammonis, CA, CA1, CA2, CA23, CA2/3, CA2-3, CA3, CA4, dentate gyrus, DG, DGL, DG/CA4 and subiculum; (2) magnetic resonance imaging, MRI and volume; (3) major depressive disorder, major depressive disorders, major depression, unipolar depression, and MDD. In the above search, keywords (1), (2) and (3) were both combined with "AND" in PubMed and Embase.

2. Examples of inconsistencies in the study selection

(1) Some original studies included patients with psychosis, some of whom were patients with schizophrenia[1, 2]. The two authors initially disagreed on whether to include these

studies. After a joint discussion, the authors decided to exclude these studies on the basis of precision.

(2) Three studies[3-5] that harnessed FreeSurfer v5.3 were initially excluded by one reviewer, but were included by another reviewer. After finding this inconsistency, the three articles were read again and discussed by two reviewers. They were eventually included in the network meta-analysis because they used the the atlas of Iglesias et al[6] which is the same as FreeSurfer v6.0.

3. Study quality assessment

Based on the recommendation of the Cochrane Handbook (https://training.cochrane.org/handbook), we employed the Newcastle–Ottawa Scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) to assess the quality of the eligible studies. This scale was used to assess the risk of bias of individual studies based on three fundamental features: study selection (0–4 points), comparability (0–2 points), and exposure (0–3 points). A total score of 7–9 points is considered high quality.

4. Mathematical formula for combing groups according to the cochrane handbook

$$M = (N1M1 + N2M2)/(N1 + N2)$$

$$SD = \sqrt{\frac{(N_1 - 1){SD_1}^2 + (N_2 - 1){SD_2}^2 + \frac{N_1 N_2}{N_1 + N_2}({M_1}^2 + {M_2}^2 - 2M_1 M_2)}{N_1 + N_2 - 1}}$$

5. Direct cross-sectional comparisons between the SCZ and MDD (for 7 studies that reported ICV)

For individual study, the ICV-corrected volume of each hippocampal subfield was defined as absolute volume / mean of ICV. ICV is measured in liters. The mean of the ICV-corrected volume is mean volume / Mean of ICV and the SD of the ICV-corrected volume is mean SD / Mean of ICV. According to the following formula (see Supplementary Methods, point 4), the ICV-corrected volume (mean ± SD) of the same hippocampal subfield from multiple studies were pooled. When there are more than two groups to combine, the strategy is to apply the above formula sequentially. The Z test was used for volumetric comparisons. The false discovery rate method was used for multiple comparisons. We analysed 10 hippocampal subfields and the whole hippocampus for each hemisphere, and the number of tests for each analysis was 11.

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Supplementary Results

Table S1. PRISMA NMA checklist of items to include when reporting a systematic review involving a network meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	*p. 1*
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	p. 3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, *including mention of why a network meta-analysis has been conducted.*	*p. 6*

Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	p. 6
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	p. 7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).*	p. 7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	p. 7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary Materials p. 3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	p. 8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	p. 8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	p. 8-9
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	*p. 9-10*

Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	p. 8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	p. 8-9
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	p. 9-10
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	NA
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	**p. 11**
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	*p. 10*
RESULTS[†]			

Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	p. 11-12
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	***None***
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	*p. 14*
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1 and Table 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	Table S2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	Table 3, Table 4 and Table 5
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.* If additional summary measures were explored (such as treatment rankings), these should also be presented.	p. 14-15
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	*NA*
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	Table S8

Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, *alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses*, and so forth).	*p. 15-16*
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	p. 17-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	p. 21-22
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	p. 22-23
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	*p. 23*

PICOS = population, intervention, comparators, outcomes, study design; NA, not available.

[*]Text in italics indicates wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.

[†]Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

Table S2. Newcastle–Ottawa quality assessment of individual studies

Authors, year	Selection				Comparability		Exposure			Sum
	1	2	3	4	1	2	1	2	(3)	
Ho et al, 2017[3]	◆DSM-IV		◆	◆	◆	◆	◆	◆		7
Zheng et al, 2019[7]	◆DSM-IV			◆	◆	◆	◆	◆		6
du Plessis et al, 2020[8]	◆DSM-IV		◆	◆	◆	◆	◆	◆		7
Nakahara et al, 2020[9]	◆DSM-IV			◆	◆	◆	◆	◆		6
Ohi et al, 2021[10]	◆DSM-V		◆	◆	◆	◆	◆	◆		7
Sasabayashi et al, 2021[11]	◆DSM-IV+DSM-V		◆	◆	◆	◆	◆	◆		7
Xiu et al, 2021[4]	◆DSM-IV		◆	◆	◆	◆	◆	◆		7
Cao et al, 2017[5]	◆DSM-IV		◆	◆	◆	◆	◆	◆		7
Doolin et al, 2018[12]	◆DSM-IV		◆	◆	◆	◆	◆	◆		7
Maller et al, 2018[13]	◆DSM-IV			◆	◆	◆	◆	◆		6
Na et al, 2018[14]	◆DSM-IV			◆	◆	◆	◆	◆		6
Xu et al, 2018[15]	◆ICD-10		◆	◆	◆	◆	◆	◆		7
Han et al, 2019[16]	◆DSM-IV		◆	◆	◆	◆	◆	◆		7
Roddy et al, 2019[17]	◆DSM-IV			◆	◆	◆	◆	◆		6
Yuan et al, 2020[18]	◆DSM-IV			◆	◆	◆	◆	◆		6

DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Diseases; Sum = summary.

Table S3. Direct volume comparisons between SCZ patients and HC. This network meta-analysis analyzed 7 studies that reported ICV.

Regions of interest	MD	Lower CI	Upper CI	$P_{adjusted}$	*I-squared*	Number of studies	SCZ	HC
Left whole hippocampus*	-172.658	-288.097	-57.219	0.01	2%	3	454	385
Left CA1*	-27.256	-47.601	-6.910	0.02	0%	3	454	385
Left CA3	-7.921	-15.373	-0.468	0.054	57%	3	454	385
Left CA4*	-11.260	-18.457	-4.062	0.01	9%	3	454	385
Left GC/DG*	-13.157	-22.020	-4.295	0.01	41%	3	454	385
Left subiculum*	-15.920	-26.852	-4.988	0.01	0%	3	454	385
Left presubiculum	-11.289	-26.734	4.156	0.15	0%	2	253	260
Left parasubiculum	-3.321	-6.642	0.000	0.07	46%	2	253	260
Left molecular layer*	-22.757	-39.766	-5.749	0.02	0%	3	454	385
Left hippocampal tail*	-34.715	-58.863	-10.567	0.01	53%	3	454	385
Left fimbria	-3.112	-6.689	0.465	0.10	0%	2	253	260
Left hippocampal fissure*	4.947	0.501	9.392	0.047	0%	2	253	260
Left HATA	-2.273	-4.915	0.369	0.10	63%	2	253	260
Right whole hippocampus*	-153.469	-274.220	-32.719	0.03	24%	3	454	385

Right CA1*	-24.553	-47.564	-1.542	0.04	0%	3	454	385
Right CA3*	-6.592	-12.501	-0.682	0.04	32%	3	454	385
Right CA4*	-9.807	-15.932	-3.682	0.006	0%	3	454	385
Right GC/DG*	-11.413	-18.472	-4.353	0.006	0%	3	454	385
Right subiculum*	-14.111	-27.285	-0.936	0.04	3%	3	454	385
Right presubiculum	-9.936	-26.765	6.893	0.25	0%	2	253	260
Right parasubiculum*	-3.462	-6.609	-0.316	0.04	0%	2	253	260
Right molecular layer*	-20.831	-37.467	-4.195	0.03	0%	3	454	385
Right hippocampal tail	-25.071	-51.842	1.701	0.07	36%	3	454	385
Right fimbria*	-4.542	-8.211	-0.874	0.03	0%	2	253	260
Right hippocampal fissure*	9.789	5.313	14.264	<0.001	0%	2	253	260
Right HATA*	-2.761	-4.388	-1.134	0.006	0%	2	253	260

SCZ = schizophrenia; HC = healthy controls; MD = mean difference; CI = confidence interval; CA = cornu ammonis; GC/DG = granule cell layer of the dentate gyrus; HATA = hippocampus–amygdala transition area.

Statistical significance is indicated by *. The unit of mean difference is cubic millimeters.

Table S4. Direct volume comparisons between MDD patients and HC. This network meta-analysis analyzed 7 studies that reported ICV.

Regions of interest	MD	Lower CI	Upper CI	$P_{adjusted}$	*I-squared*	Number of studies	MDD	HC
Left whole hippocampus	-31.646	-165.724	102.433	0.95	91%	3	331	233
Left CA1	-5.726	-27.303	15.851	0.95	84%	4	372	277
Left CA3	-4.348	-12.195	3.499	0.95	73%	4	372	277
Left CA4	-6.911	-15.486	1.664	0.95	82%	3	331	233
Left GC/DG	-5.926	-15.197	3.346	0.95	79%	4	372	277
Left subiculum	-2.332	-13.727	9.063	0.95	75%	4	372	277
Left presubiculum	0.361	-12.416	13.138	0.96	85%	3	331	233
Left parasubiculum	-0.198	-3.230	2.834	0.96	59%	3	270	142
Left molecular layer	-8.899	-29.039	11.241	0.95	89%	3	331	233
Left hippocampal tail	3.824	-29.374	37.022	0.96	95%	2	284	203
Left fimbria	/	/	/	/	/	/	/	/
Left hippocampal fissure	/	/	/	/	/	/	/	/
Left HATA	1.010	-2.629	4.649	0.95	/	1	182	68
Right whole hippocampus	-21.822	-159.795	116.152	0.92	91%	3	331	233
Right CA1	-7.203	-30.809	16.403	0.92	86%	4	372	277
Right CA3	-2.604	-8.870	3.661	0.92	38%	4	372	277

Right CA4	-4.170	-11.224	2.885	0.90	70%	3	331	233
Right GC/DG	-5.441	-12.698	1.815	0.78	64%	4	372	277
Right subiculum	-2.826	-16.710	11.059	0.92	84%	4	372	277
Right presubiculum	0.524	-13.223	14.271	0.94	89%	3	331	233
Right parasubiculum	0.220	-2.673	3.112	0.94	69%	3	270	142
Right molecular layer	-6.816	-26.164	12.532	0.92	88%	3	331	233
Right hippocampal tail	9.003	-27.860	45.866	0.92	96%	2	284	203
Right fimbria	/	/	/	/	/	/	/	/
Right hippocampal fissure	/	/	/	/	/	/	/	/
Right HATA*	2.950	1.241	4.659	0.008	/	1	182	68

MDD = major depressive disorder; HC = healthy controls; MD = mean difference; CI = confidence interval; CA = cornu ammonis; GC/DG = granule cell layer of the dentate gyrus; HATA = hippocampus–amygdala transition area; NA, not available.

Statistical significance is indicated by *. The unit of mean difference is cubic millimeters.

Table S5. Indirect volume comparisons between SCZ and MDD patients. This network meta-analysis analyzed 7 studies that reported ICV.

Regions of interest	MD	Lower CI	Upper CI	$P_{adjusted}$
Left whole hippocampus	-141.012	-317.939	35.915	0.32
Left CA1	-21.530	-51.186	8.127	0.32
Left CA3	-3.573	-14.395	7.249	0.52
Left CA4	-4.349	-15.544	6.846	0.49
Left GC/DG	-7.232	-20.058	5.595	0.37
Left subiculum	-13.588	-29.379	2.203	0.32
Left presubiculum	-11.650	-31.695	8.395	0.37
Left parasubiculum	-3.123	-7.620	1.374	0.32
Left molecular layer	-13.858	-40.219	12.503	0.37
Left hippocampal tail	-38.539	-79.590	2.513	0.32
Left fimbria	/	/	/	/
Left hippocampal fissure	/	/	/	/
Left HATA	-3.283	-7.779	1.214	0.32
Right whole hippocampus	-131.648	-314.998	51.703	0.36
Right CA1	-17.350	-50.316	15.615	0.36
Right CA3	-3.987	-12.600	4.625	0.36
Right CA4	-5.638	-14.980	3.705	0.36
Right GC/DG	-5.972	-16.096	4.152	0.36
Right subiculum	-11.285	-30.425	7.855	0.36
Right presubiculum	-10.460	-32.190	11.270	0.36
Right parasubiculum	-3.682	-7.956	0.592	0.36
Right molecular layer	-14.015	-39.532	11.502	0.36
Right hippocampal tail	-34.074	-79.632	11.485	0.36
Right fimbria	/	/	/	/
Right hippocampal fissure	/	/	/	/

Right HATA*	-5.711	-8.070	-3.351	<0.001

SCZ = schizophrenia; MDD = major depressive disorder; MD = mean difference; CI = confidence interval; CA = cornu ammonis; GC/DG = granule cell layer of the dentate gyrus; HATA = hippocampus–amygdala transition area.

Statistical significance is indicated by *. The unit of mean difference is cubic millimeters.

Table S6. Direct cross-sectional volume comparisons between SCZ and MDD patients (for 7 studies that reported ICV)

Regions of interest	SCZ			MDD			Z	$P_{adjusted}$
	n	mean	SD	n	mean	SD		
Left								
whole hippocampus	454	2523.40	485.00	331	2220.01	207.11	11.92	5.07E-32
CA1	454	450.68	79.54	372	413.91	49.82	8.10	7.58E-16
CA3	454	164.52	51.55	372	137.52	20.14	10.25	4.55E-24
CA4	454	186.59	40.04	331	167.83	19.91	8.63	9.99E-18
GC/DG	454	214.37	40.66	372	194.83	21.67	8.82	2.09E-18
subiculum	454	308.40	48.19	372	274.85	28.64	12.40	2.97E-34
presubiculum	253	203.45	27.37	331	184.71	20.83	9.07	2.71E-19
parasubiculum	253	40.16	7.33	270	36.86	6.96	5.27	1.53E-07
molecular layer	454	386.01	49.37	331	366.65	36.47	6.32	3.21E-10
hippocampal tail	454	401.77	93.92	284	353.16	47.66	9.28	4.62E-20
fimbria	/	/	/	/	/	/	/	/
hippocampal fissure	/	/	/	/	/	/	/	/
HATA	253	38.89	6.13	182	39.92	4.85	-1.96	0.0497
Right								
whole hippocampus	454	2610.27	511.52	331	2243.57	218.08	13.67	8.86E-42
CA1	454	469.74	80.73	372	422.24	51.12	10.27	1.73E-24
CA3	454	176.61	54.40	372	144.58	21.42	11.51	4.55E-30
CA4	454	195.96	44.65	331	173.18	19.85	9.64	8.25E-22
GC/DG	454	224.05	43.94	372	198.46	22.06	10.85	4.29E-27
subiculum	454	310.88	49.43	372	272.06	31.40	13.70	8.86E-42

presubiculum	253	195.49	25.56	331	177.24	19.13	9.50	2.79E-21
parasubiculum	253	38.20	6.81	270	35.00	6.55	5.47	4.39E-08
molecular layer	454	401.04	52.28	331	372.05	36.55	9.14	7.36E-20
hippocampal tail	454	423.31	97.11	284	363.50	49.73	11.02	8.77E-28
fimbria	/	/	/	/	/	/	/	/
hippocampal fissure	/	/	/	/	/	/	/	/
HATA	253	40.06	6.29	182	36.93	4.25	6.19	6.51E-10

SCZ = schizophrenia; MDD = major depressive disorder; SD = standard deviation; CA = cornu ammonis; GC/DG = granule cell layer of the dentate gyrus; HATA = hippocampus–amygdala transition area.

Table S7. Univariate meta-regression to identify potential sources of heterogeneity in direct volume comparisons between SCZ patients and HC and between MDD patients and HC

Regions of interest	Dependent variable	Independent variable	Number of comparisons	Coefficient	95% CI	*P*	$P_{adjusted}$
SCZ versus HC							
Left hippocampal tail	Mean Difference	age at onset	7	-0.912	-1.586, -0.237	0.008*	0.01*
Left hippocampal tail	Mean Difference	age at study	8	-0.700	-1.122, -0.278	0.001*	0.002*
Left hippocampal tail	Mean Difference	illness duration	7	-1.775	-3.272, -0.279	0.02*	0.02*
Left hippocampal tail	Mean Difference	PANSS	6	-0.379	-0.620, -0.208	< 0.001*	< 0.001*
MDD versus HC							
Left CA1	Mean Difference	age at onset	6	-0.445	-1.145, 0.255	0.21	0.52
Left CA1	Mean Difference	age at study	8	-0.340	-0.914, 0.234	0.25	0.56
Left CA1	Mean Difference	illness duration	6	-0.344	-2.994, 2.306	0.80	0.95
Left CA1	Mean Difference	HDRS	7	-0.970	-2.204, 0.265	0.12	0.43
Left CA3	Mean Difference	age at onset	6	-0.236	-0.446, -0.026	0.03*	0.27
Left CA3	Mean Difference	age at study	8	-0.208	-0.386, -0.030	0.02*	0.27

Left CA3	Mean Difference	illness duration	6	-0.112	-1.089, 0.866	0.82	0.96
Left CA3	Mean Difference	HDRS	7	-0.444	-0.841, -0.047	0.03*	0.27
Left CA4	Mean Difference	age at onset	5	-0.234	-0.456, -0.012	0.04*	0.27
Left CA4	Mean Difference	age at study	7	-0.225	-0.406, -0.043	0.02*	0.27
Left CA4	Mean Difference	illness duration	5	-0.412	-1.830, 1.006	0.57	0.92
Left CA4	Mean Difference	HDRS	6	-0.455	-0.859, -0.051	0.03*	0.27
Left GC/DG	Mean Difference	age at onset	6	-0.261	-0.502, -0.020	0.03*	0.27
Left GC/DG	Mean Difference	age at study	6	-0.182	-0.400, 0.036	0.10	0.41
Left GC/DG	Mean Difference	illness duration	6	-0.225	-1.330, 0.880	0.69	0.95
Left GC/DG	Mean Difference	HDRS	6	-0.358	-0.855, 0.140	0.16	0.50
Left subiculum	Mean Difference	age at onset	6	-0.185	-0.565, 0.194	0.34	0.65
Left subiculum	Mean Difference	age at study	8	-0.196	-0.482, 0.089	0.18	0.52
Left subiculum	Mean Difference	illness duration	6	-0.178	-1.561, 1.204	0.80	0.95
Left subiculum	Mean Difference	HDRS	7	-0.387	-0.982, 0.209	0.20	0.52
Left presubiculum	Mean Difference	age at onset	5	0.008	-0.262, 0.277	0.96	1.00
Left presubiculum	Mean Difference	age at study	5	0.015	-0.214, 0.242	0.90	0.99
Left presubiculum	Mean Difference	illness duration	5	0.268	-0.936, 1.471	0.66	0.95

Left presubiculum	Mean Difference	HDRS	5	0.083	-0.405, 0.571	0.74	0.95
Left molecular layer	Mean Difference	age at onset	5	-0.137	-0.710, 0.437	0.64	0.95
Left molecular layer	Mean Difference	age at study	5	-0.097	-0.591, 0.397	0.70	0.95
Left molecular layer	Mean Difference	illness duration	5	-0.003	-2.797, 2.790	1.00	1.00
Left molecular layer	Mean Difference	HDRS	5	0.004	-1.124, 1.132	0.99	1.00
Right CA1	Mean Difference	age at onset	6	-0.307	-0.915, 0.301	0.32	0.65
Right CA1	Mean Difference	age at study	8	-0.251	-0.685, 0.184	0.26	0.56
Right CA1	Mean Difference	illness duration	6	-0.074	-2.291, 2.142	0.95	1.00
Right CA1	Mean Difference	HDRS	7	-0.452	-1.416, 0.512	0.36	0.67
Right CA3	Mean Difference	age at onset	6	-0.112	-0.304, 0.080	0.25	0.56
Right CA3	Mean Difference	age at study	8	-0.112	-0.288, 0.065	0.21	0.52
Right CA3	Mean Difference	illness duration	6	0.009	-0.747, 0.766	0.98	1.00
Right CA3	Mean Difference	HDRS	7	-0.346	-0.684, -0.008	0.04*	0.28
Right CA4	Mean Difference	age at onset	5	-0.153	-0.352, 0.045	0.13	0.43
Right CA4	Mean Difference	age at study	7	-0.185	-0.376, 0.007	0.06	0.30
Right CA4	Mean Difference	illness duration	5	-0.227	-1.379, 0.925	0.70	0.95
Right CA4	Mean Difference	HDRS	6	-0.428	-0.796, -0.060	0.02*	0.27
Right GC/DG	Mean Difference	age at onset	6	-0.209	-0.420, 0.003	0.05	0.30
Right GC/DG	Mean Difference	age at study	6	-0.155	-0.340, 0.031	0.10	0.41

Right GC/DG	Mean Difference	illness duration	6	-0.331	-1.286, 0.623	0.50	0.84
Right GC/DG	Mean Difference	HDRS	6	-0.356	-0.749, 0.0380	0.08	0.36
Right subiculum	Mean Difference	age at onset	6	-0.208	-0.597, 0.182	0.30	0.61
Right subiculum	Mean Difference	age at study	8	-0.239	-0.544, 0.066	0.12	0.43
Right subiculum	Mean Difference	illness duration	6	-0.230	-1.697, 1.237	0.76	0.95
Right subiculum	Mean Difference	HDRS	7	-0.415	-1.054, 0.223	0.20	0.52
Right presubiculum	Mean Difference	age at onset	5	0.054	-0.232, 0.342	0.71	0.95
Right presubiculum	Mean Difference	age at study	5	0.056	-0.184, 0.296	0.65	0.95
Right presubiculum	Mean Difference	illness duration	5	0.491	-0.725, 1.708	0.43	0.75
Right presubiculum	Mean Difference	HDRS	5	0.205	-0.292, 0.701	0.42	0.75
Right molecular layer	Mean Difference	age at onset	5	0.049	-0.619, 0.716	0.89	0.99
Right molecular layer	Mean Difference	age at study	5	0.049	-0.518, 0.615	0.87	0.99
Right molecular layer	Mean Difference	illness duration	5	0.396	-2.678, 3.470	0.81	0.95
Right molecular layer	Mean Difference	HDRS	5	0.354	-0.891, 1.560	0.58	0.92

SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CI = confidence interval; CA = cornu ammonis; GC/DG = granule cell layer of the dentate gyrus; PANSS = Positive and Negative Syndrome Scale; HDRS = Hamilton Depression Rating Scale.

Statistical significance is indicated by *.

Table S8. Egger's linear regression test

SCZ VS HC		MDD VS HC	
Region of interests	$P_{adjusted}$	**Region of interests**	$P_{adjusted}$
Left whole hippocampus	0.96	Left whole hippocampus	0.95
Left CA1	0.96	Left CA1	0.95
Left CA3	0.96	Left CA3	0.95
Left CA4	0.96	Left CA4	0.95
Left GC/DG	0.96	Left GC/DG	0.95
Left subiculum	0.96	Left subiculum	0.95
Left presubiculum	0.96	Left presubiculum	0.95
Left parasubiculum	0.96	Left parasubiculum	0.95
Left molecular layer	0.96	Left molecular layer	0.95
Left hippocampal tail	0.96	Left hippocampal tail	0.95
Left fimbria	0.96	Left fimbria	NA
Left hippocampal fissure	0.96	Left hippocampal fissure	NA
Left HATA	0.96	Left HATA	NA
Right Whole hippocampus	0.94	Right whole hippocampus	0.92
Right CA1	0.94	Right CA1	0.92
Right CA3	0.94	Right CA3	0.92
Right CA4	0.94	Right CA4	0.92
Right GC/DG	0.94	Right GC/DG	0.92
Right subiculum	0.94	Right subiculum	0.92
Right presubiculum	0.94	Right presubiculum	0.92
Right parasubiculum	0.94	Right parasubiculum	0.92
Right molecular layer	0.94	Right molecular layer	0.92
Right hippocampal tail	0.94	Right hippocampal tail	0.92
Right fimbria	0.94	Right fimbria	NA
Right hippocampal fissure	0.65	Right hippocampal fissure	NA
Right HATA	0.039	Right HATA	NA

SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CA = cornu ammonis; GC/DG = granule cell layer of the dentate gyrus; HATA =

hippocampus–amygdala transition area; NA = Not available, the number of included studies is too small to be tested for publication bias.

Statistical significance is indicated by *.

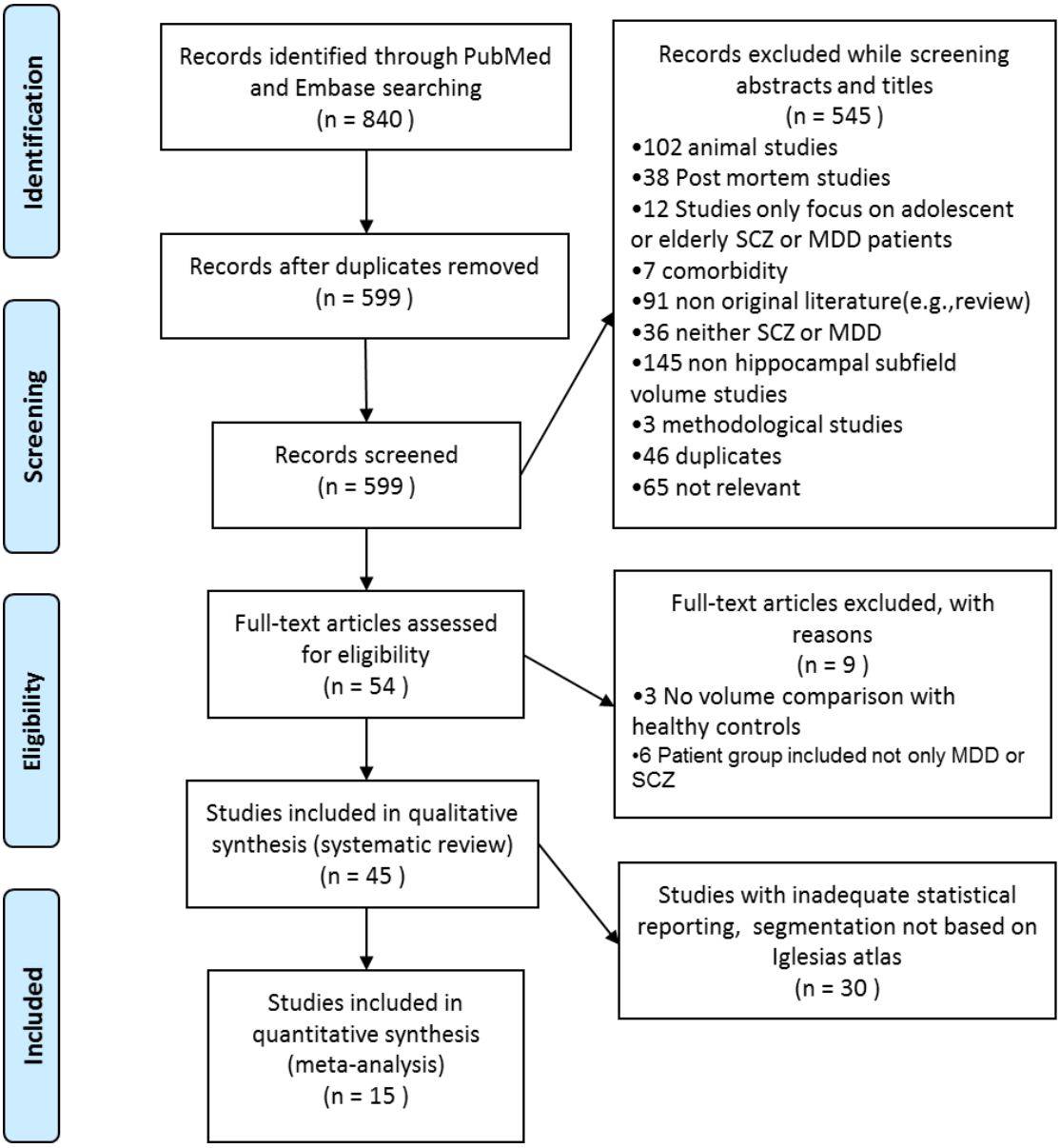
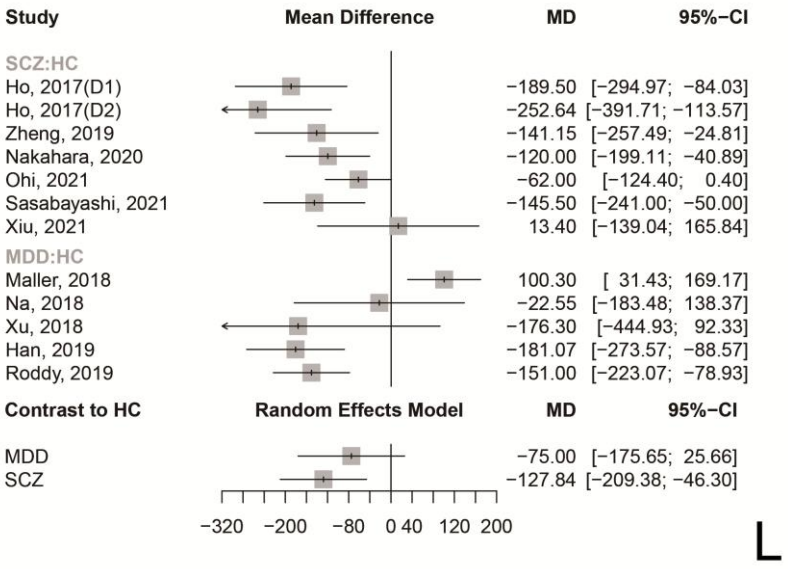


Fig. S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart. SCZ = schizophrenia; MDD = major depressive disorder.



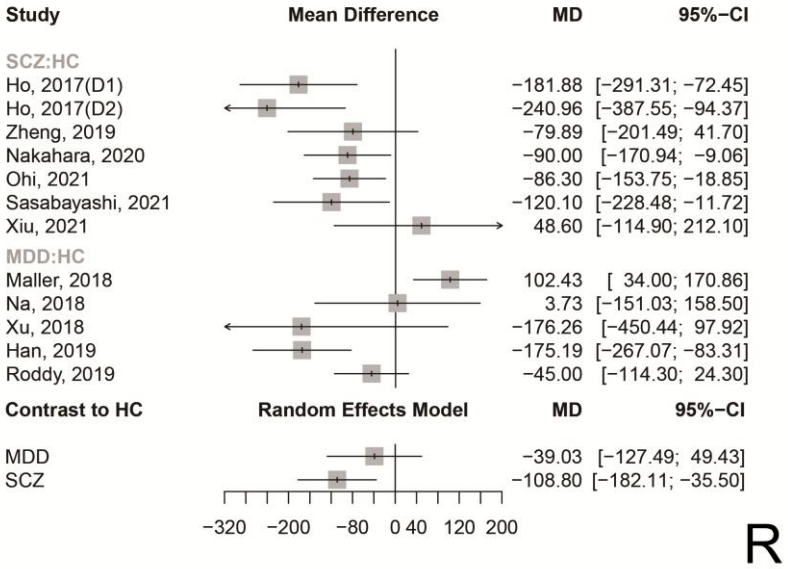
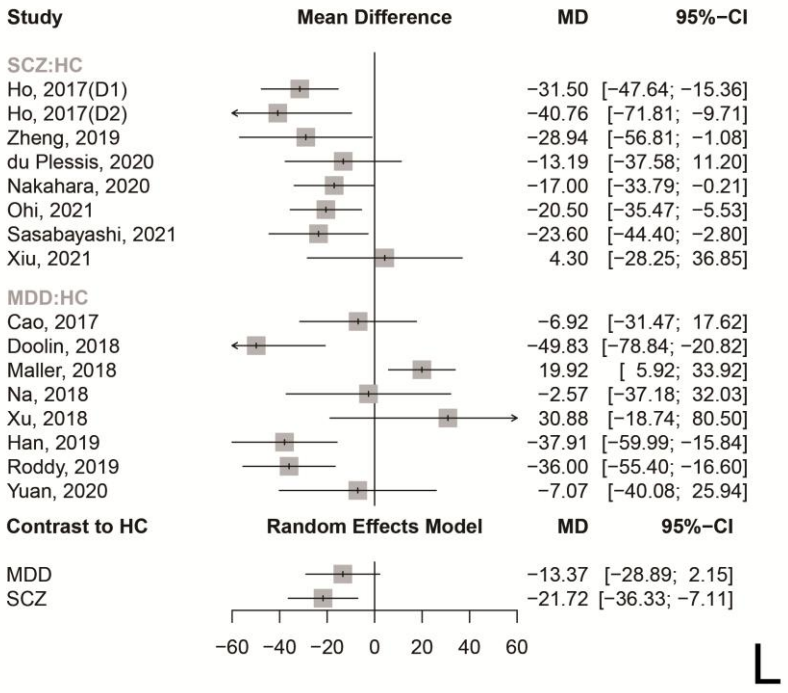


Fig. S2-1. Forest plots for the whole hippocampus. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CI = confidence interval; MD = mean difference; L = left; R = right.



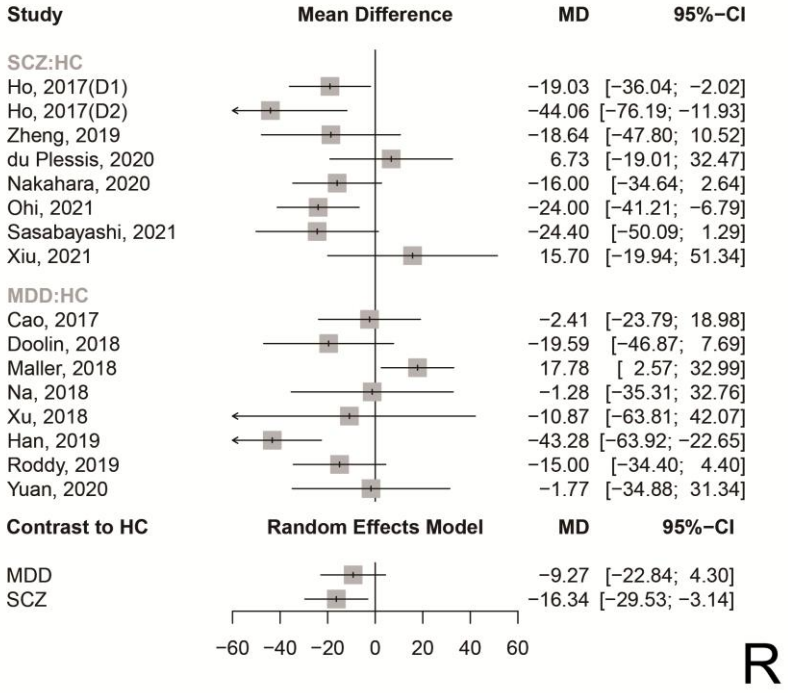
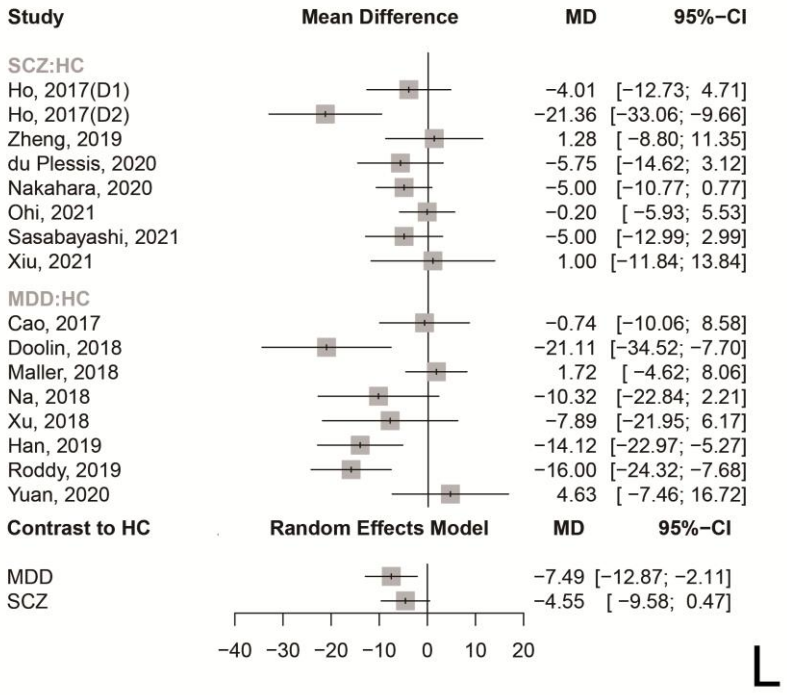


Fig. S2-2. Forest plots for the CA1. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CA = cornu ammonis; CI = confidence interval; L = left; R = right.



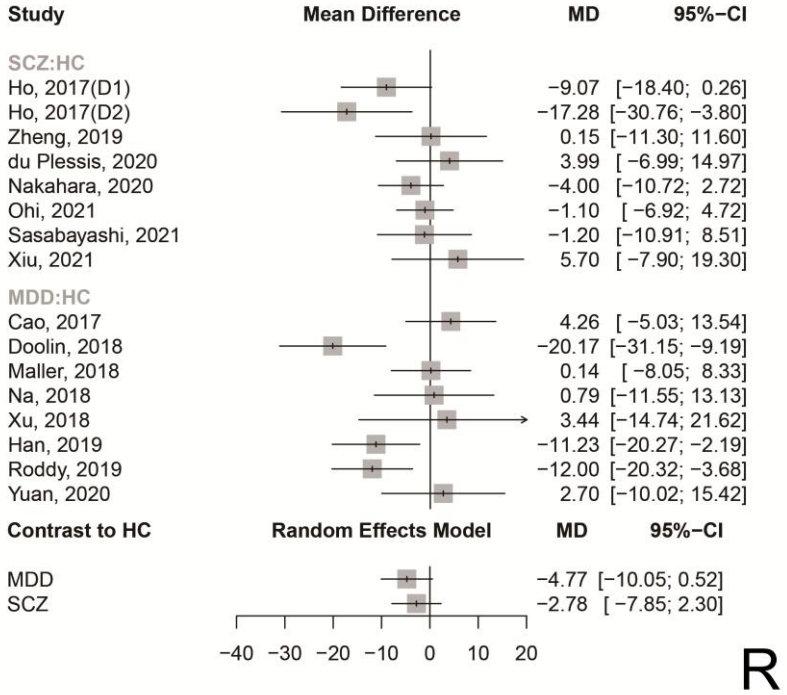
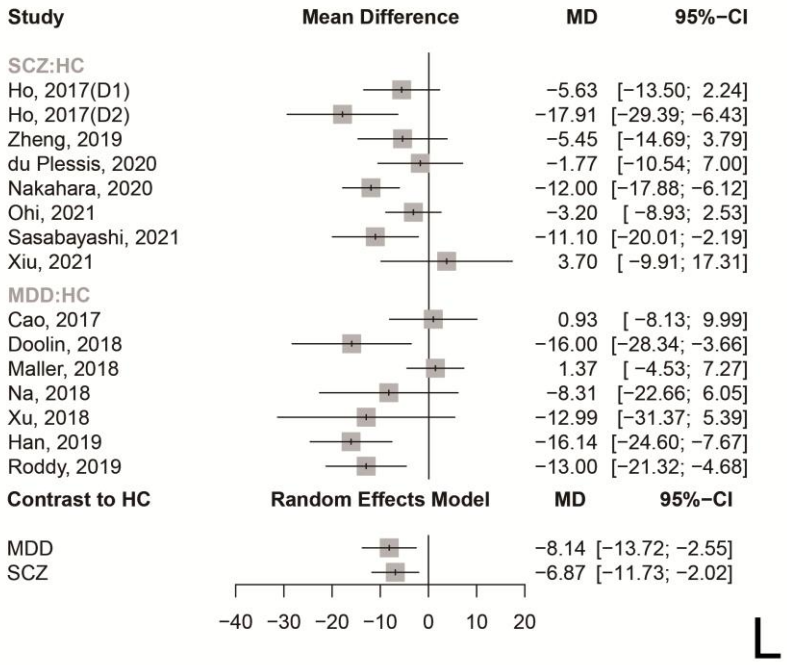


Fig. S2-3. Forest plots for the CA3. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CA = cornu ammonis; CI = confidence interval; L = left; R = right.



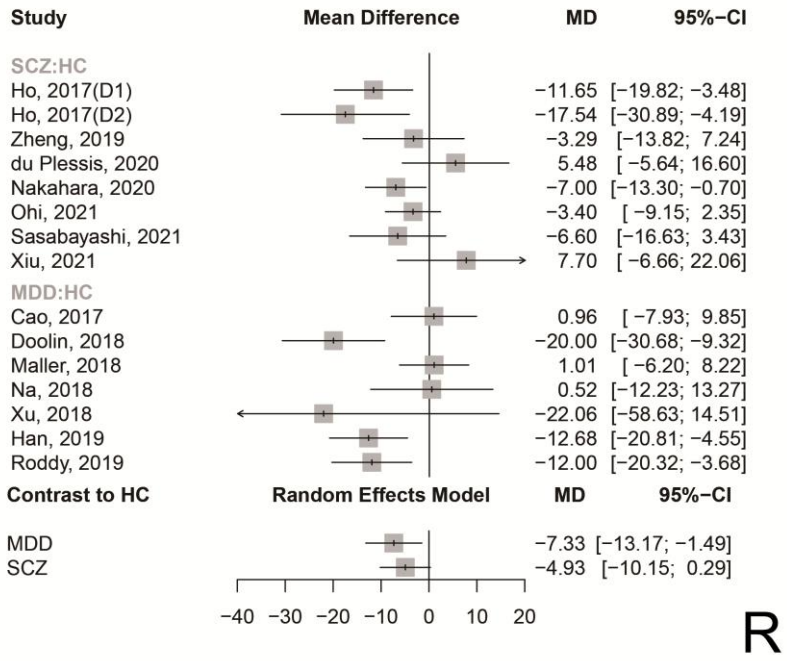
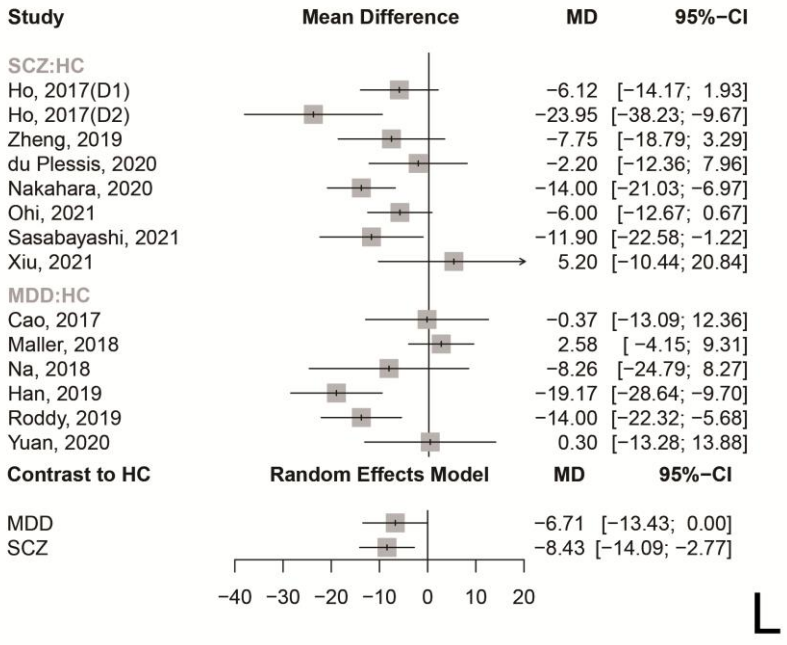


Fig. S2-4. Forest plots for the CA4. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CA = cornu ammonis; CI = confidence interval; L = left; R = right.



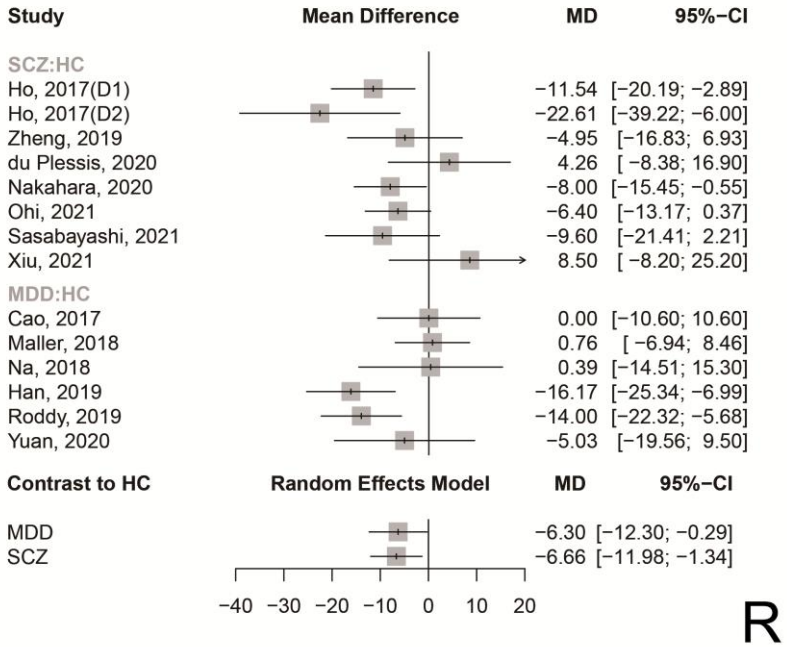
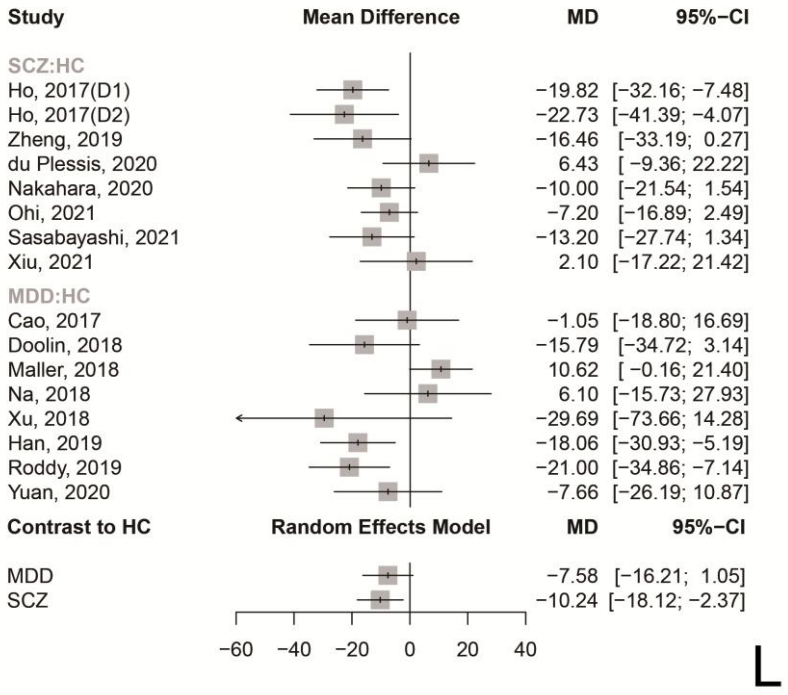


Fig. S2-5. Forest plots for the GC/DG. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; GC/DG = granule cell layer of the dentate gyrus; CI = confidence interval; L = left; R = right.



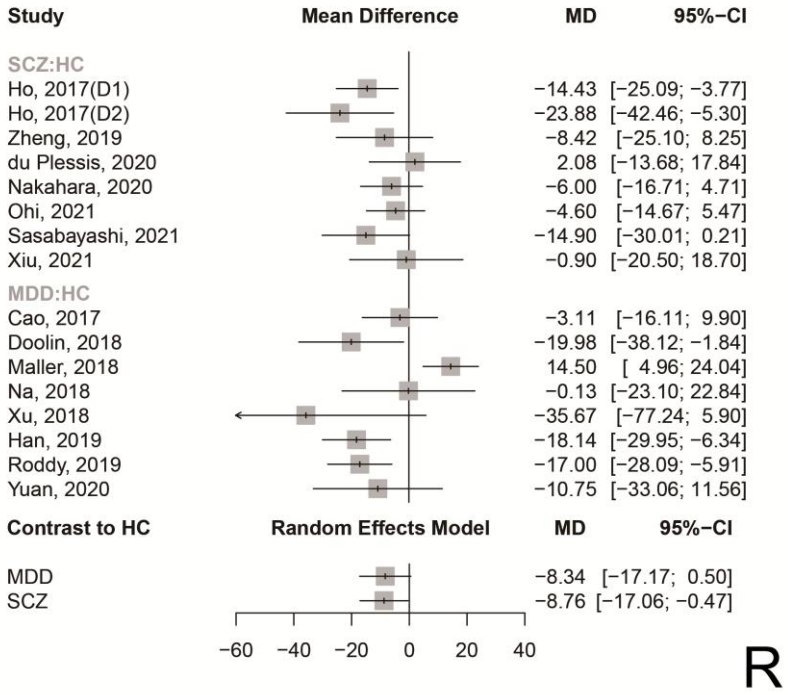
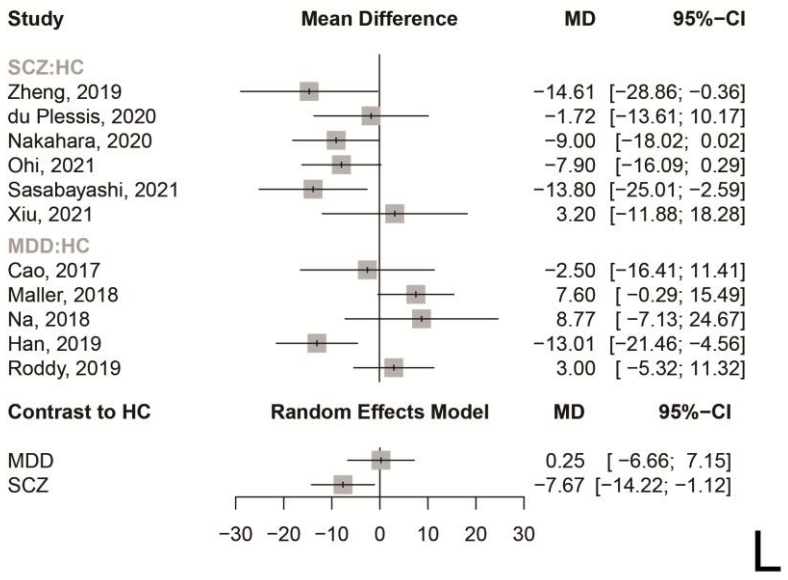


Fig. S2-6. Forest plots for the subiculum. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CI = confidence interval; L = left; R = right.



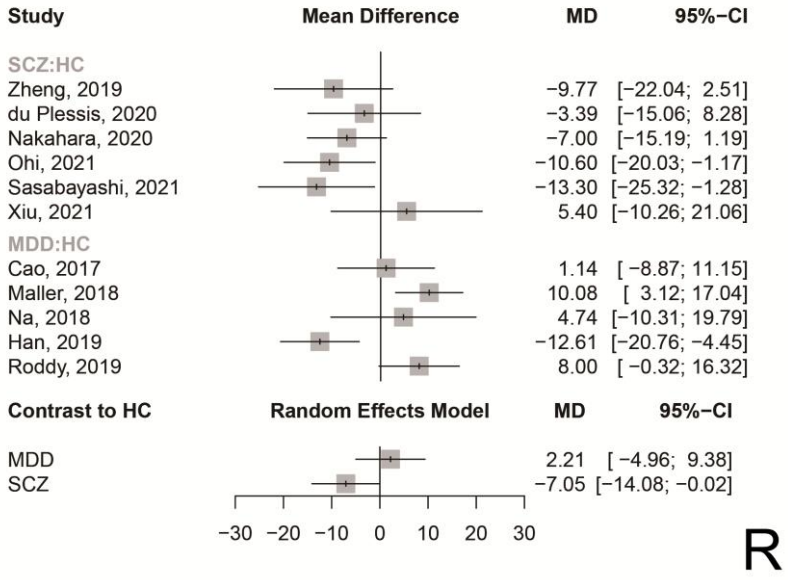
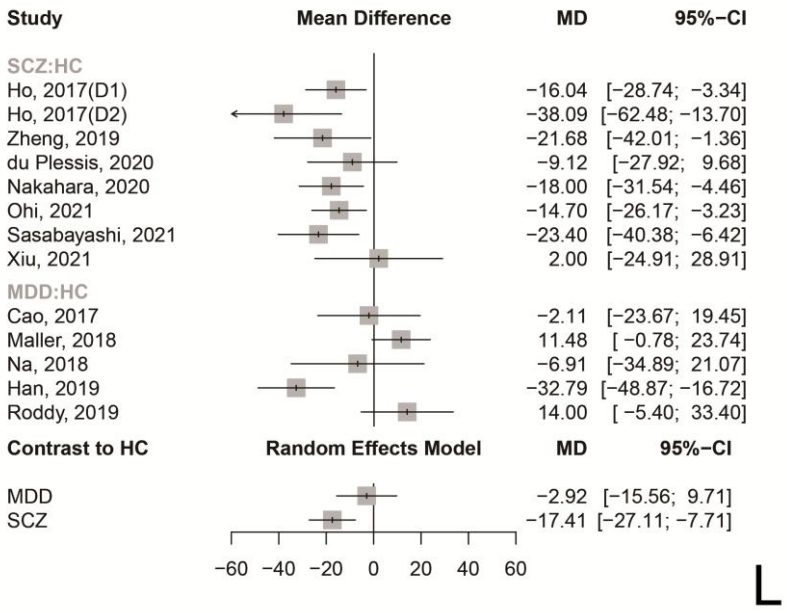


Fig. S2-7. Forest plots for the presubiculum. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CI = confidence interval; L = left; R = right.



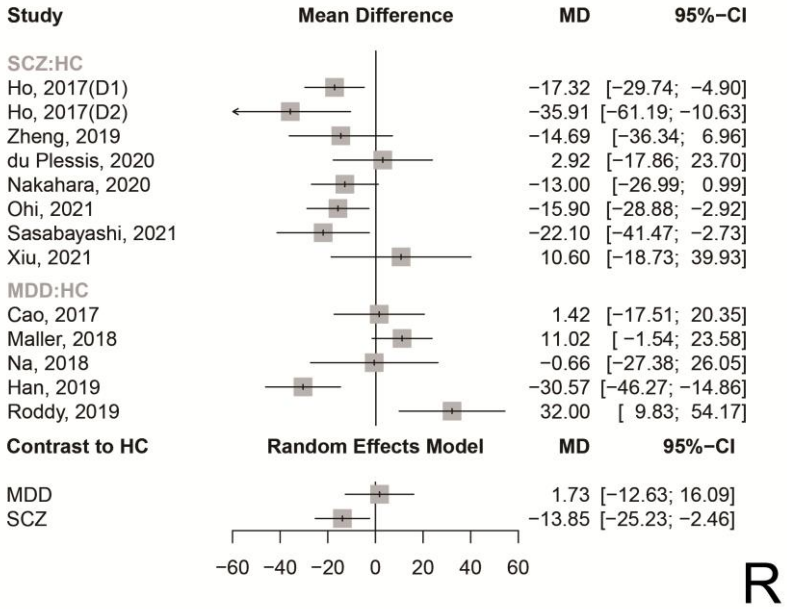
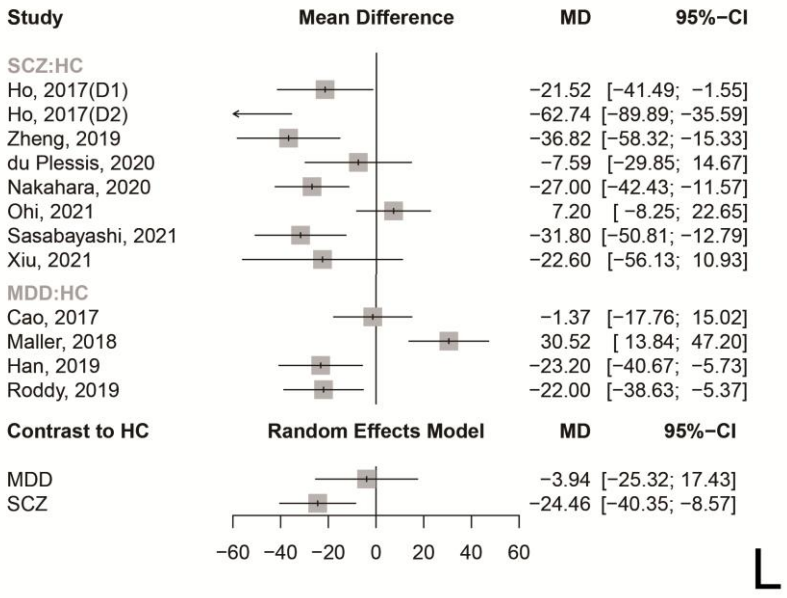


Fig. S2-8. Forest plots for the molecular layer. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CI = confidence interval; L = left; R = right.



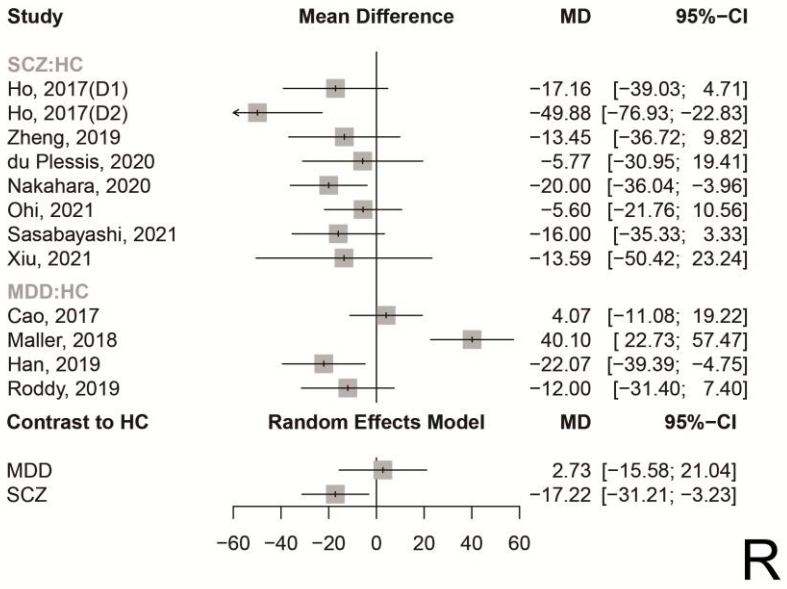
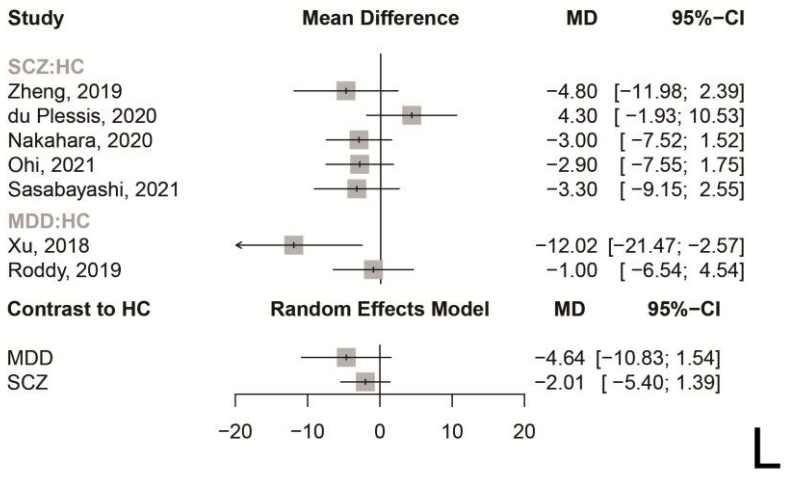


Fig. S2-9. Forest plots for the hippocampal tail. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CI = confidence interval; L = left; R = right.



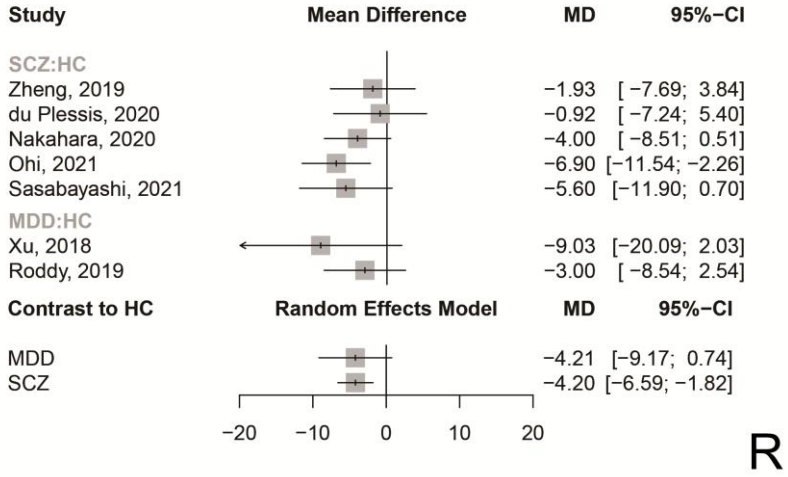
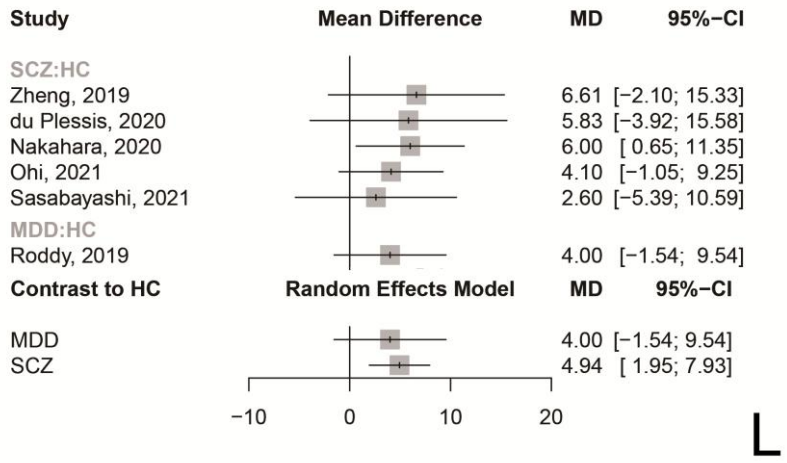


Fig. S2-10. Forest plots for the fimbria. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CI = confidence interval; L = left; R = right.



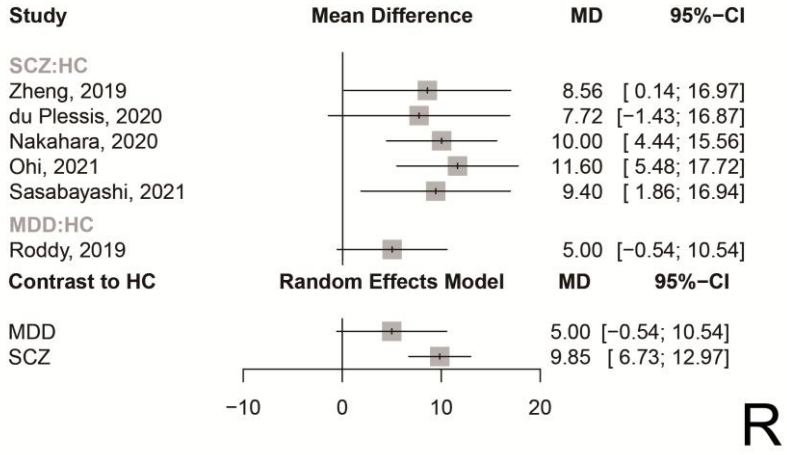


Fig. S2-11. Forest plots for the hippocampal fissure. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; CI = confidence interval; L = left; R = right.

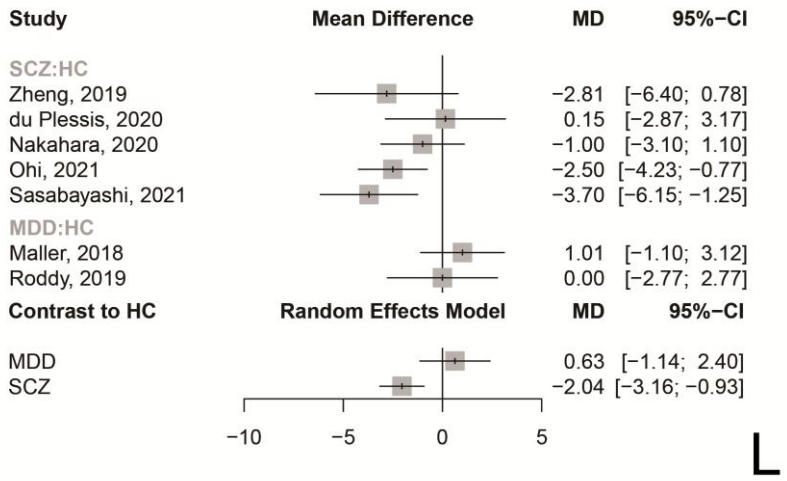
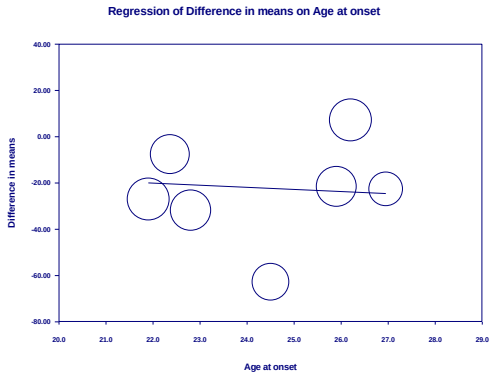
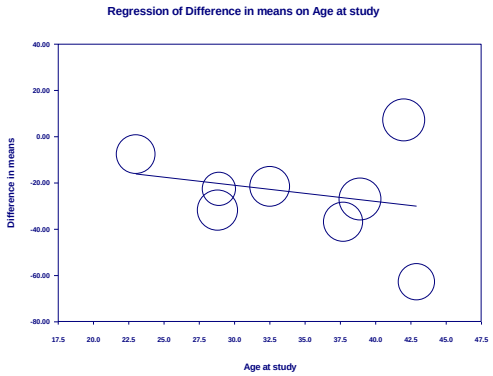


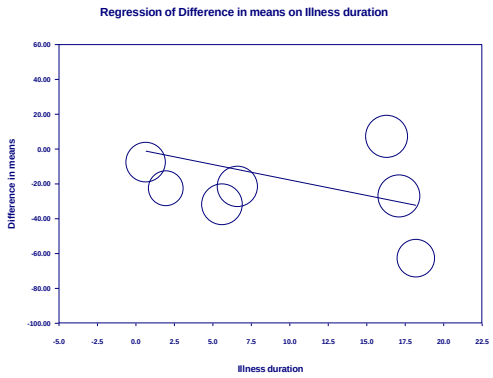
Fig. S2-12. Forest plot for the left HATA. SCZ = schizophrenia; MDD = major depressive disorder; HC = healthy controls; HATA = hippocampus–amygdala transition area; CI = confidence interval; L = left.



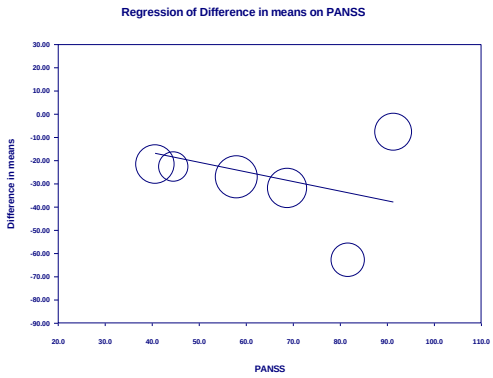
（z = -2.65, $p_{adjusted}$ = 0.01）



（z = -3.25, $p_{adjusted}$= 0.002）



（z = -2.33, $p_{adjusted}$ = 0.02）



（z = -3.94, $p_{adjusted}$ = 0.000）

Fig. S3. Meta-regression graph: the moderating effect of age at onset, age at study, illness duration and PANSS on the effect size (MD) of left hippocampal tail volume reduction in SCZ versus HC. Each circle represents an individual study, and the size of the circle is proportional to the study weight.

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