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Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis

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Supplemental Methods

Supplemental Results

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Supplemental Methods

Data extraction

Data extracted included sample size, age, gender, and brain volumes for all studies. When provided, years of education, Mini-Mental State Examination (MMSE)[1] score, field strength, and segmentation type were also extracted. Further information was extracted for participants with depression including diagnostic method (i.e., Diagnostic and Statistical Manual of Mental Disorders (DSM)/International Classification of Diseases and Related Health Problems (ICD)), depressive and anxious symptomatology, depression status, number of previous episodes, onset and duration of illness, family history of depression, medication status (if in medication, medicines taken), and treatment resistance.

Data on depression status and explicit classification from reports were used to categorize depression subgroups at data extraction. No *a priori* subgroups were established, and categorisation was driven by the retrieved studies. These groups included current (Cur) or remitted (Rem) depression, subtype of depression (melancholic (Mel), psychotic (Psy), or atypical (Aty)), first (FE) or multiple (ME) episodes of depression, age of onset of depression (paediatric (PO), adult (AO), early (EO), or late (LO)), family history (FH) of depression, intake of antidepressants (Med/noMed), treatment resistance (TR), comorbidity with anxiety disorders (Anx), suicide attempt/ideation (Sui), and physical/sexual abuse (Abu). Heterogeneous samples and samples that could not be included in the above groups due to lack of information were merged into a mixed group (Mix), in an effort to reduce some of the heterogeneity in main analyses. In many instances, the Mix group represented the combined effect of subgroups, such as EO/LO, FE/ME, or Cur/Rem. If more than one category was suitable, other homogeneous subgroups were given precedence over Cur and Rem to prioritize other clinical features. Similarly, Cur and Rem subgroups were given precedence over Mix group.

Quality assessment

Quality of studies was assessed at study level with the Newcastle-Ottawa scale (NOS)[2], modified based on validated items included in previous reviews[3,4]. Modifications were developed in consultation with senior author, and agreed by all authors. Studies were rated using a star-system and were judged based on the selection of healthy controls (HC) and depressed participants (DEP), on the comparability of these groups, on the ascertainment of depression assessment, and on non-response rates. A maximum of ten starts could be awarded to a study (**Supplemental Table S1**).

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Missing data

If total volume measures were not reported, mean and standard deviation (SD) were derived from right and left volume measures according to the following formula:

$$mean_{Total} = mean_{Right} + mean_{Left} \qquad SD_{Total} = \sqrt{SD_{Right}^2 + SD_{Left}^2}$$

Sample selection in meta-analyses

A number of studies reported brain measures on multiple depression subgroups. Studies reporting on multiple independent subgroups were included in main analyses as separate samples, and then independently investigated in subgroup analyses. Studies reporting on multiple subgroups that were not independent were selected based on sample size: the largest subgroup was selected for main analyses, and then all subgroups were independently investigated in subgroup analyses. However, if sample size was identical between dependent subgroups, homogenous subgroups were selected for main analyses, and then all subgroups were independently investigated in subgroup analyses. Sensitivity analyses were conducted on the selection of homogeneous groups. Please refer to **Assessment of subgroup selection** and **Supplemental Tables S6 and S7**.

Meta-regression

Analyses first investigated the influence of age and sex as independent demographic variables of cohorts, that is, mean age/gender of HC and mean age/gender of DEP separately, and then combined into single measures of these demographics. While there were no substantial differences in age between cohorts, the number of females varied greatly between HC and DEP in some studies (visual inspection) and, thus, sex was further investigated as the difference in percent female between cohorts. Two models were used based on these observations: model A, with mean age of HC and DEP, and percent female of HC and DEP; and model B, with mean age of HC and DEP, and the difference in percent female between HC and DEP. In hippocampus volume (HcV), segmentation procedure, depressive symptoms, and medication status were investigated individually; with only segmentation procedure investigated within models due to power constraints.

Supplemental Results

Included studies

The online search identified 13,637 references. Once duplicates were removed, 9,229 unique references were screened by title. Title screening excluded 8,669 irrelevant entries, leaving 560 abstracts to be screened. Abstract

screening excluded a further 205 entries that failed inclusion/exclusion criteria, leaving 355 articles to be screened by full-text. Full-text screening excluded a further 43 articles that failed inclusion/exclusion criteria, leaving 312 articles for inclusion in review. After accounting for population studies, voxel-based morphometry (VBM), multiple reports of the same sample, white matter hyperintensity (WMH) studies and brain structures not included in the review due to insufficient studies, 105 articles from the online search were included in analyses.

19 studies were obtained through manual search, five[5-9] of which were from bibliographies while the remaining [10-24] were from previous reviews[25-27]. Four studies[20,21,23,24] that failed inclusion/exclusion criteria were excluded by full-text screening, leaving 15 articles for inclusion in review. After accounting for population studies, VBM, multiple reports of the same sample, WMH and brain structures not included in the review, seven studies[5,6,10-12,15,16] from manual search were included in the review. Ultimately, 112 studies were included in analyses comprising 105 records from online search and seven records from manual search. Detailed demographics of HC and DEP included can be found in **Supplemental Table S2**.

Quality assessment

Detailed description of scores can be found in **Supplemental Table S3**. Studies were rated out of 10 stars. The lowest score was 4.5/10 stars in three studies[28-30], while the highest score was 8.5/10 stars in 19 studies[31-49]. The three studies with low score were included in large meta-analyses for ICV, TBV, hippocampus, amygdala, putamen, and caudate where exclusion was unlikely to influence effect sizes. A sensitivity analysis on the moderating effect of NOS scores in total HcV found no significant results (k=61, QM-p=0.1871).

Meta-analyses

Management of duplicate samples was specific to brain region, and thus excluded studies have been specified for each analysis. In total 11 regions were investigated given minimum requirements: four global measures (GMV, WMV, TBV, and ICV), and seven subcortical measures (hippocampus, amygdala, caudate, pallidum, putamen, thalamus, and nucleus accumbens). Although there were enough studies to investigate some cortical regions such as frontal lobe[50-52], orbitofrontal cortex[53-55], anterior cingulate cortex (ACC[53,56,57]), and subgenual ACC[57-59], tracing methods varied greatly and could not be pooled into meta-analyses. Furthermore, in the case of subgenual ACC, both tracing methods and naming differed among studies.

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TBV

Excluded studies

15 studies[52,60-73] were identified as duplicates and were excluded from analyses according to Methods. Two studies[74,75] were excluded since neither age or gender could be established. One study[17] was excluded since age of HC could not be established. Two studies[76,77] were excluded due to the large variance in TBV measures. One study[78] was identified as an outlier in DEP main analyses and was excluded from these analyses.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S1.**

Results

31 studies[5,12,15,29,31,32,36,38,39,41,46,50,51,54,78-94] reporting differences in TBV were included (n=3,095, age=54.8 years, 66.7% female). No significant differences were found. Significant heterogeneity was found with DEP-LO (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

15 studies[29,31,39,50,51,54,78,79,82-85,87,91,95] were excluded since no clear information on anxiety comorbidity could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S2.**

Anxiety exclusion results

12 studies[5,32,36,38,80,81,86,88-90,92,93] reporting differences in TBV excluding anxiety disorders were included (n=1,565, age=59.7 years, 66.5% female). No significant volumetric differences were found between HC and DEP, or in subgroup analyses (**Supplemental Table S5**).

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Anxiety comorbidity results

Four studies[12,15,41,46] with comorbid anxiety disorders were included (n=458, age=36.1 years 64.8% female). No significant differences were found between HC and DEP (**Supplemental Table S5**).

GMV

Excluded studies

No duplicates were found, except for multiple groups of DEP in one study[96]. The groups reported included DEP-Mix, DEP-PO and DEP-AO, and first-episode (FE) and multiple-episodes (ME) of depression. DEP-Mix, DEP-PO and DEP-AO groups were segregated according to comorbidity with anxiety disorders; whereas DEP-FE and DEP-ME presented comorbidity. Given sample size, DEP-Mix with and without comorbidity were selected for main analysis as per Methods, while homogeneous groups were selected for subgroup analyses. One study[77] was excluded due to large variance in GMV measures.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S3.**

Anxiety comorbidity assessment

Excluded studies

Three studies[16,84,87] were excluded since no clear information on anxiety comorbidity could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S4.**

Anxiety comorbidity results

Five studies[41,96-99] with comorbid anxiety disorders were included (n=742, age=37.6 years, 62.1% female). No significant volumetric differences were found between HC and DEP (**Supplemental Table S5**).

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Hippocampus volume

Total hippocampus volume

Excluded studies

13 studies[28,31,32,44,54,64,78,100-105] reported differences in total hippocampal volume (THcV), four of which[32,44,54,100] also reported right (RHcV) and left (LHcV) volumes. 47 studies[10,18,30,33,37,39,40,43,46,49,68,71,77,80,86,88,92,93,106-134] reported differences in RHcV and LHcV, from which THcV was derived according to Supplemental Methods. Nine studies[18,64,68,71,112,115,124,126,134] were identified as duplicates and were excluded from analyses according to Methods. Five studies[43,44,92,116,131] belonged to the same research group and reported volumes for DEP-Mix[131], DEP-EO DEP-LO[44], DEP-Mel and DEP-Aty[116], DEP-Rem[43], and DEP-Cur[92]. Given sample size, DEP-Cur was selected for DEP main analyses, while all others were for subgroup analyses. However, not enough studies were available to conduct DEP-Mel/DEP-Aty analyses and, therefore, this study[116] was not included. One study[10] reported volumes using manual and automated segmentation, with manual segmentation selected for analyses. Three studies[74,75,135] were excluded since neither age or gender of samples could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S5**.

Anxiety comorbidity assessment

Excluded studies

11 studies[10,28,30,31,39,54,78,101,105,108,128] were excluded since no clear information on anxiety comorbidity could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S6**.

Anxiety comorbidity results

Ten studies[46,100,102,114,120,122,123,129,130,132] with comorbid anxiety disorders were included (n=1,049, age=36.7 years, 58.2% female). No significant volumetric differences were found between HC and DEP, or in subgroup analysis. Significant heterogeneity was found in all analyses (**Supplemental Table S5**).

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Right hippocampus volume

Excluded studies

Eight studies[18,68,71,112,115,124,126,134] were identified as duplicates and were excluded form analyses according to Methods. Five studies[43,44,92,116,131] belonged to the same research group and reported volumes for DEP-Mix[131], DEP-EO and DEP-LO[44], DEP-Mel and DEP-Aty[116], DEP-Rem[43], and DEP-Cur[92]. Given sample size, DEP-Cur was selected for DEP main analyses, while all others were selected for subgroup analyses. However, not enough studies were available to conduct DEP-Mel/DEP-Aty analyses and, therefore, this study[116] was not included. One study[10] reported volumes using manual and automated segmentation, with manual segmentation selected for analyses. Three studies[74,75,135] were excluded since neither age or gender could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S7**.

Anxiety comorbidity assessment

Excluded studies

Six studies[10,30,39,54,108,128] were excluded since no clear information on anxiety comorbidity could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S8.**

Anxiety comorbidity results

Nine studies[46,100,114,120,122,123,129,130,132] with comorbid anxiety disorders were included (n=1,006, age=36.8 years, 58.1% female). No significant volumetric differences were found between HC and DEP, or in subgroup analyses. Significant heterogeneity was found in all analyses (**Supplemental Table S5**).

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Left hippocampus volume

Excluded studies

Eight studies[18,68,71,112,115,124,126,134] were identified as duplicates and were excluded form analyses according to Methods. Five studies[43,44,92,116,131] belonged to the same research group and reported volumes for DEP-Mix[131], DEP-EO and DEP-LO[44], DEP-Mel and DEP-Aty[116], DEP-Rem[43], and DEP-Cur[92]. Given sample size, DEP-Cur was selected for DEP main analyses, while all others were selected for subgroup analyses. However, not enough studies were available to conduct DEP-Mel/DEP-Aty analyses and, therefore, this study[116] was not included. One study[10] reported volumes using manual and automated segmentation, with manual segmentation selected for analyses. Three studies[74,75,135] were excluded since neither age or gender could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S9**.

Anxiety comorbidity assessment

Excluded studies

Six studies[10,30,39,54,108,128] were excluded since no clear information on anxiety comorbidity could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S10**.

Anxiety comorbidity results

Nine studies[46,100,114,120,122,123,129,130,133] with comorbid anxiety disorders were included (n=1,006, age=36.8 years, 58.1% female). No significant volumetric differences were found between HC and DEP, or in subgroup analyses. Significant heterogeneity was found in all analyses (**Supplemental Table S5**).

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Amygdala volume

Total amygdala volume

Excluded studies

Three studies[28,101,136] reported differences in total amygdala volume (TAV), one of which[136] also reported right (RAV) and left (LAV) volumes. 17 studies[5,6,37,46,47,69,73,81,93,110,111,113,114,120,133,137,138] reported differences in RAV and LAV, from which TAV was derived according to Supplemental Methods. Two studies[5,113] were identified as duplicates and were excluded from analyses according to Methods. One study[136] was excluded since age of DEP sample could not be established. One study[138] was excluded since accurate number of males and females in DEP could not be established. One study[135] was excluded since neither age or gender of samples could be established. The same research group reported measures for DEP-Mix and DEP-Rem and DEP-Cur[111], and DEP-FE and DEP-ME[6]. Given sample size, DEP-FE and DEP-ME were selected for main analysis as per Methods.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S11**.

Results

16 studies[6,28,37,46,47,69,73,81,93,101,110,111,114,120,133,137] reporting differences in TAV (n=1,241, age=46.7 years, 61.6% female) were included. No significant differences were found. Most analyses showed significant heterogeneity (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

Two studies[28,101] were excluded since no clear information on anxiety comorbidity could be established. The same research group reported measures for DEP-Mix and DEP-Rem and DEP-Cur[111], and DEP-FE and DEP-ME[6] excluding anxiety disorders. Given sample size, DEP-FE and DEP-ME were selected for main analysis as per Methods.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S12**.

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Anxiety exclusion results

Ten studies[6,37,47,69,81,93,110,111,133,137] reporting differences in TAV excluding anxiety disorders were included (n=765, age=51.9 years, 64.1% female). No significant volumetric differences were found between HC and DEP, on in subgroup analyses. However, a trend was found in DEP analysis. Significant heterogeneity was found in all analyses (**Supplemental Table S5**).

Right amygdala volume

Excluded studies

Two studies[5,113] were identified as duplicates and were removed from analyses according to Methods. One study[136] was excluded since age of DEP sample could not be established. One study[138] was excluded since accurate number of males and females could not be established. One study[135] was excluded since neither age or gender of samples could be established. The same research group reported measures for DEP-Mix and DEP-Rem and DEP-Cur[111], and DEP-FE and DEP-ME[6]. Given sample size, DEP-FE and DEP-ME were selected for main analysis as per Methods.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S13**.

Results

14 studies[6,37,46,47,69,73,81,93,110,111,114,120,133,137] reporting differences in RAV were included (n=1,131, age=46.8 years, 61.2% female). No significant differences were found. Most analyses showed significant heterogeneity (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

All included studies had information on anxiety comorbidity. The same research group reported measures for DEP-Mix and DEP-Rem and DEP-Cur[111], and DEP-FE and DEP-ME[6] excluding anxiety disorders. Given sample size, DEP-FE and DEP-ME were selected for main analysis as per Methods.

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Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S14**.

Anxiety exclusion results

Ten studies[6,37,47,69,81,93,110,111,133,137] reporting differences in RAV excluding anxiety disorders (n= 765, age= 51.9 years, 64.1% female) were included. No significant volumetric differences were found between HC and DEP, or in subgroup analyses. Significant heterogeneity was found in DEP and DEP-FE analyses (**Supplemental Table S5**).

Anxiety comorbidity results

Four studies[46,73,114,120] with comorbid anxiety disorders were included (n=366, age=36.2 years, 55.2% female). No significant volumetric differences were found between HC and DEP (**Supplemental Table S5**).

Left amygdala volume

Excluded studies

Two studies[5,113] were identified as duplicates and were removed from analyses according to Methods. One study[136] was excluded since age of DEP sample could not be established. One study[138] was excluded since accurate number of males and females could not be established. One study[135] was excluded since neither age or gender of samples could be established. The same research group reported measures for DEP-Mix and DEP-Rem and DEP-Cur[111], and DEP-FE and DEP-ME[6]. Given sample size, DEP-FE and DEP-ME were selected for main analysis as per Methods.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S15**.

Results

14 studies[6,37,46,47,69,73,81,93,110,111,114,120,133,137] reporting differences in LAV were included (n=1,131, age=46.8 years, 61.2% female). No significant differences were found. Most analyses showed significant heterogeneity (**Supplemental Table S4**).

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Anxiety comorbidity assessment

Excluded studies

All included studies had information on anxiety comorbidity. The same research group reported measures for DEP-mix and DEP-Rem and DEP-Cur[111], and DEP-FE and DEP-ME[6] excluding anxiety disorders. Given sample size, DEP-FE and DEP-ME were selected for main analysis as per Methods.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S16**.

Anxiety exclusion results

Ten studies[6,37,47,69,81,93,110,111,133,137] reporting differences in LAV excluding anxiety disorders (n=765, age=51.9 years, 64.1% female) were included. No significant volumetric differences were found between HC and DEP, or in subgroup analyses. However, a trend was found in DEP analysis. Except for DEP-Mix, significant heterogeneity was found in all analyses (**Supplemental Table S5**).

Putamen volume

Total putamen volume

Excluded studies

Seven studies[14,28,52,95,139-141] reported differences in total putamen volume (TPuV), one of which[139] also reported right (RPuV) and left (LPuV) volumes. Nine studies[37,38,114,122,128,133,137,142,143] reported differences in RPuV and LPuV, from which TPuV was derived according to Supplemental Methods. Two studies[14,52] were identified as a duplicates and were excluded from analyses according to Methods. One study[139] was excluded since number males and females could not be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S17**.

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Anxiety comorbidity assessment

Excluded studies

Three studies[28,128,140] were excluded since no clear information on anxiety comorbidity could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S18**.

Anxiety comorbidity results

Four studies[95,114,122,141] reporting differences in TPuV including anxiety disorders were included (n=836, age=38.1 years, 58.9% female). No significant differences were found between HC and DEP. Significant heterogeneity was found (**Supplemental Table S5**).

Right putamen volume

Excluded studies

No duplicates were found. One study[139] was excluded since the number of males and females could not be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S19**.

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established. The analysis with anxiety comorbidity was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S20**.

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Left putamen volume

Excluded studies

No duplicates were found. One study[139] was excluded since the number of males and females could not be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S21**.

Results

Nine studies[37,38,114,122,128,133,137,142,143] reporting differences in LPuV were included (n=1,248, age=47.8 years, 59.3% female). No significant differences were found in (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established. The analysis with anxiety comorbidity was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S22**.

Caudate volume

Total caudate volume

Excluded studies

Eight studies[13,14,28,52,62,65,140,141] reported differences in total caudate volume (TCV), one of which[62] also reported right (RCV) and left (LCV) volumes. Five studies[37,95,114,122,128,133,142-144] reported differences in RCV and LCV, from which TCV was derived according to Supplemental Methods. Three studies[14,52,65] were identified as duplicates and were excluded from analyses according to Methods. Two studies[13,62] belonged to the same research

group and reported volumes for DEP-Mix, DEP-EO and DEP-LO[13]; and DEP-Mix[62]. Given sample size, DEP-Mix in[62] was selected for DEP analyses, while DEP-EO and DEP-LO in[13] were selected for subgroup analyses. However, not enough studies were available to conduct DEP-EO/DEP-LO analyses and, therefore, this study[13] was not included. One study[135] was excluded since neither age or gender of samples could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S23**.

Results

13 studies[28,37,62,95,114,122,128,133,137,140-143] reporting differences in TCV were included (n=1,686, age=46.1 years, 62.4% female). No significant differences were found. Significant heterogeneity was found with DEP (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

Three studies[28,128,140] were excluded since no clear information on anxiety comorbidity could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S24**.

Anxiety exclusion results

Six studies[37,62,133,137,142,143] reporting differences in TCV excluding anxiety disorders were included (n=600, age=60.2 years, 66.5% female). No significant volumetric differences were found between HC and DEP, or in subgroup analysis. Significant heterogeneity was only found in DEP-Mix analysis (**Supplemental Table S5**).

Anxiety comorbidity results

Four studies[95,114,122,141] reporting differences in TCV comorbid with anxiety disorders were included (n=836, age=38.1 years, 58.9% female). No significant differences were found between HC and DEP. Significant heterogeneity was found (**Supplemental Table S5**).

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Right caudate volume

Excluded studies

No duplicates were found. One study[135] was excluded since neither age or gender of samples could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S25**.

Results

Nine studies[37,62,114,122,128,133,137,142,143] reporting differences in RCV were included (n=1,241, age=47.8 years, 59.4% female). No significant differences were found (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established. The analysis with anxiety comorbidity was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S26**.

Anxiety exclusion results

Six studies[37,62,133,137,142,143] reporting differences in RCV excluding anxiety disorders were included (n=600, age=60.2 years, 66.5% female). No significant volumetric differences were found between HC and DEP, or in subgroup analysis (**Supplemental Table S5**).

Left caudate volume

Excluded studies

No duplicates were found. One study[135] was excluded since neither age or gender of samples could be established.

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Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S27**.

Results

Nine studies[37,62,114,122,128,133,137,142,143] reporting differences in LCV were included (n=1,241, age=47.8 years, 59.4% female). No significant differences were found (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established. The analysis with anxiety comorbidity was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S28**.

Anxiety exclusion results

Six studies[37,62,133,137,142,143] reporting differences in LCV excluding anxiety disorders were included (n=600, age=60.2 years, 66.5% female). No significant volumetric differences were found between HC and DEP, or in subgroup analysis (**Supplemental Table S5**).

Pallidum volume

Total pallidum volume

Excluded studies

Two studies[95,141] reported differences in total pallidum volume (TPaV). Seven studies[37,114,122,128,133,137,142] reported differences in right (RPaV) and left (LPaV) volumes, from which TPaV was derived according to Supplemental Methods. No duplicates were found.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S29**.

Results

Nine studies[37,95,114,122,128,133,137,141,142] reporting differences in TPaV were included (n=1,231, age=41.6 years, 58.8% female). No significant differences were found. Significant heterogeneity was found with DEP (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S30**.

Anxiety exclusion results

Four studies[37,133,142,144] reporting differences in TPaV excluding anxiety disorders were included (n=306, age=53.3 years, 59.2% female). No significant differences were found between HC and DEP (**Supplemental Table S5**).

Anxiety comorbidity results

Four studies[95,114,122,141] reporting differences in TPaV comorbid with anxiety were included (n=836, age=38.1 years, 58.9% female). No significant differences were found between HC and DEP. Significant heterogeneity was found (**Supplemental Table S5**).

Right pallidum volume

Excluded studies

No duplicates were found.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S31**.

Results

Seven studies[37,114,122,128,133,137,142] reporting differences in RPaV were included (n=947, age=41.8 years, 54.8% female). No significant differences were found. Significant heterogeneity was found with DEP (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established. The analysis with anxiety comorbidity was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plot of main analysis is shown in **Supplemental Figure S32**.

Left pallidum volume

Excluded studies

No duplicates were found.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S33**.

Results

Seven studies[37,114,122,128,133,137,142] reporting differences in LPaV were included (n=947, age=41.8 years, 54.8% female). No significant differences were found (**Supplemental Table S4**).

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established. The analysis with anxiety comorbidity was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plot of main analysis is shown in **Supplemental Figure S34**.

Anxiety exclusion results

Four studies[37,133,137,142] reporting differences in LPaV excluding anxiety disorders were included (n=306, age=53.3 years, 59.2% female). No significant volumetric differences were found between HC and DEP (**Supplemental Table S5**).

Thalamus volume

Total thalamus volume

Excluded studies

Three studies[13,14,52] reported differences in total thalamus volume (TTV). Six studies[37,114,122,128,133,137] reported differences in right (RTV) and left (LTV) volumes, from which TTV was derived according to Supplemental Methods. One study[14] was identified as a duplicate and was excluded according to Methods. Two studies[13,52] belonged to the same group and reported multiple volumes for DEP-Mix, DEP-EO, and DEP-LO[13], and separately for DEP-Mix[52]. Given sample size, DEP-Mix in[52] was selected for main analysis while DEP-EO and DEP-LO in[13] were selected for subgroup analysis. However, DEP-EO/DEP-LO analyses were not conducted due to low number of studies and, thus this study[13] was not included in TTV analyses.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S35**.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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Anxiety comorbidity assessment

Excluded studies

Three studies[13,52,128] were excluded since no clear information on anxiety comorbidity could be established. The analysis with anxiety comorbidity was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plot of main analysis is shown in **Supplemental Figure S36**.

Right thalamus volume

Excluded studies

No duplicates were found.

Forest plots

Individual forest plot of main analysis is shown in **Supplemental Figure S37**.

Results

Six studies[37,114,122,128,133,144] reporting differences in RTV were included (n=874, age=42.1 years, 55.6% female). No significant differences were found (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established. The analysis comorbid with anxiety was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plot of main analysis is shown in **Supplemental Figure S38**.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

Left thalamus volume

Excluded studies

No duplicates were found.

Forest plots

Individual forest plot of main analysis is shown in **Supplemental Figure S39**.

Results

Six studies[37,114,122,128,133,144] reporting differences in LTV were included (n=874, age=42.1 years, 55.6% female). No significant differences were found (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

One study[128] was excluded since no clear information on anxiety comorbidity could be established. The analysis comorbid with anxiety was not conducted since only two studies[114,122] were available.

Forest plots

Individual forest plot of main analysis is shown in **Supplemental Figure S40**.

Accumbens volume

Total accumbens volume

Excluded studies

Two studies[95,140] reported differences in total accumbens volume (TAcV). Two studies[19,114] reported differences in right (RAcV) and left (LAcV) volumes, from which TAcV was derived according to Supplemental Methods. No duplicates were found. No analyses for RAcV and LAcV were conducted since only two studies[19,114] were available.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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Forest plots

Individual forest plot of main analysis is shown in **Supplemental Figure S41**.

Results

Four studies[19,95,114,140] reporting differences in TAcV were included (n=563, age=36.5 years, 61.1% female). No significant differences were found. Significant heterogeneity was found (**Supplemental Table S4**).

Anxiety comorbidity assessment

Excluded studies

Two studies[19,140] were excluded since no clear information on anxiety comorbidity could be established. The anxiety comorbidity assessment analyses were not conducted since only two studies two studies[95,114] were available.

WMV

Excluded studies

One study[37] in which total WMV could be estimated from right and left volumes was included. No duplicates were found, except for the multiple groups of DEP in one study[96]. The groups reported included DEP-Mix, DEP-PO and DEP-AO, and DEP-FE and DEP-ME. DEP-Mix, DEP-PO, and DEP-AO groups were segregated according to comorbidity with anxiety disorders; whereas DEP-FE and DEP-ME presented comorbidity. Given sample size, DEP-Mix with and without comorbidity were selected for main analysis as per Methods, while homogeneous groups were selected for subgroup analyses. One study[77] was excluded due to large variance in WMV measures.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S42**.

Results

Ten studies[5,37,41,84,87,88,93,96,145,146] reporting differences in WMV were included (n=1,245, age=44.5 years, 57.1% female). No significant differences were found (**Supplemental Table S4**).

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

Anxiety comorbidity assessment

Excluded studies

Two studies[84,87] were excluded since no clear information on anxiety comorbidity could be established. The analysis with anxiety comorbidity was not conducted since only two studies[41,96] were available.

Forest plots

Individual forest plot of main is shown in **Supplemental Figure S43**.

Anxiety exclusion results

Seven studies[5,37,88,93,96,145,146] reporting differences in WMV excluding anxiety disorders were included (n=779, age=46.9 years, 57.8% female). No significant volumetric differences were found between HC and DEP (**Supplemental Table S5**).

ICV

Excluded studies

12 studies[15,18,73,124,131,134,147-152] were identified as duplicates and were excluded from analyses according to Methods. One study[153] was excluded since age of HC could not be established. One study[136] was excluded since age of DEP could not be established. One study[85] included both major (MDD) and minor depression disorder groups, but only MDD group was selected. Two studies[76,77] were excluded due to large variance of ICV measures. DEP-Cur in one study[15] was excluded due to large variance of ICV measures.

Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S44**.

Anxiety comorbidity assessment

Excluded studies

11 studies[28,30,48,54,83,85,101,105,108,154,155] were excluded since no clear information on anxiety comorbidity could be established.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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Forest plots

Individual forest plots of main and subgroup analyses are shown in **Supplemental Figure S45**.

Anxiety comorbidity results

Nine studies[46,58,102,114,123,129,130,156,157] with comorbid anxiety disorders were included (n=654, age=39.1 years, 61.9% female). No significant volumetric differences were found between HC and DEP, or in subgroup analyses (**Supplemental Table S5**).

Sensitivity analyses

Assessment of subgroup selection

A number of studies reported volumes for both DEP-Mix and homogeneous groups of depressives. Following exclusion of duplicates according to Methods, homogeneous groups were selected in DEP meta-analyses to provide an accurate representation of volumetric differences. The following analyses assess the effect of DEP-Mix exclusion in DEP meta-analyses in TBV, HcV, and ICV.

TBV

DEP analysis

Two studies[80,86] reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. No significant volumetric difference was found. Furthermore, no significant differences were found between main and sensitivity analysis (**Supplemental Table S6**).

DEP no ANX analysis

Two studies[80,86] excluding anxiety disorders reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. No significant volumetric difference was found. Furthermore, no significant differences were found between main and sensitivity analysis (**Supplemental Table S7**).

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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Total hippocampus volume

DEP analysis

Two studies[80,86] reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. Two studies[49,107] reported volumes for DEP-Mix, and separately for DEP-FE and DEP-ME. One study[103] reported volumes for DEP-Mix, and separately for DEP-TR and DEP-noTR. One study[105] reported volumes for DEP-Cur, and separately for DEP-Med and DEP-noMed. Significant volumetric differences were found, similar to main analysis. Furthermore, no significant differences were found between main and sensitivity analyses (**Supplemental Table S6**).

DEP no ANX analysis

Two studies[80,86] reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. Two studies[49,107] reported volumes for DEP-Mix, and separately for DEP-FE and DEP-ME. One study[103] reported volumes for DEP-Mix, and separately for DEP-TR and DEP-noTR. Significant volumetric differences were found, similar to main analysis. Furthermore, no significant differences were found between main and sensitivity analyses (**Supplemental Table S7**).

Right hippocampus volume

DEP analysis

Two studies[80,86] reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. Two studies[49,107] reported volumes for DEP-Mix, and separately for DEP-FE and DEP-ME. Significant volumetric differences were found, similar to main analysis. Furthermore, no significant differences were found between main and sensitivity analyses (**Supplemental Table S6**).

DEP no ANX analysis

Two studies[80,86] reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. Two studies[49,107] reported volumes for DEP-Mix, and separately for DEP-FE and DEP-ME. Significant volumetric differences were found, similar to main analysis. Furthermore, no significant differences were found between main and sensitivity analyses (**Supplemental Table S7**).

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Left hippocampus volume

DEP analysis

Two studies[80,86] reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. Two studies[49,107] reported volumes for DEP-Mix, and separately for DEP-FE and DEP-ME. Significant volumetric differences were found, similar to main analysis. Furthermore, no significant differences were found between main and sensitivity analyses (**Supplemental Table S6**).

DEP no ANX analysis

Two studies[80,86] reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. Two studies[49,107] reported volumes for DEP-Mix, and separately for DEP-FE and DEP-ME. Significant volumetric differences were found, similar to main analysis. Furthermore, no significant differences were found between main and sensitivity analyses (**Supplemental Table S7**).

ICV

DEP analysis

One study[86] reported volumes for DEP-Mix, and separately for DEP-EO and DEP-LO. Two studies[49,107] reported volumes for DEP-Mix and separately for DEP-FE and DEP-ME. One study[156] reported volumes for DEP-Mix, and separately for DEP-Rem and DEP-Cur. One study[158] reported volumes for DEP-Mix, and separately and for DEP-noMed and DEP-Med. One study[105] reported volumes for DEP-Cur, and separately for DEP-noMed and DEP-Med. No significant volumetric difference was found. Furthermore, no significant differences were found between main and sensitivity analysis (**Supplemental Table S6**).

DEP no ANX analysis

One study[86] reported volumes for DEP-Mix and separately for DEP-EO and DEP-LO. Two studies[49,107] reported volumes for DEP-Mix and separately for DEP-FE and DEP-ME. One study[158] reported volumes for DEP-Mix and separately and for DEP-noMed and DEP-Med. A trend found. However, no significant differences were found between main and sensitivity analysis (**Supplemental Table S7**).

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DEP ANX analysis

One study[156] reported volumes for DEP-Mix and separately for DEP-Rem and DEP-Cur. No significant volumetric difference was found. Furthermore, no significant differences were found between main and sensitivity analysis (**Supplemental Table S7**).

Study influence assessment

Disproportionate study influence in reported estimates was investigated using the leave-one-out method. Assessment was conducted in analyses that included more than ten studies in order to limit intrinsic effects in analyses with fewer included studies. Study influence only affected the significance of estimates in ICV analyses.

TBV

Evidence of influence was found in two analyses. In DEP analysis (k=37, studies=27), four studies[41,79,84,92] were identified; however, exclusion did not change significance of results. In DEP-Mix analysis (k=13, studies=12), two studies[41,79] were identified; however, exclusion did not change significance of results (**Supplemental Table S8**).

GMV

Evidence of influence was found in DEP analysis (k=19, studies=15). One study[99] (DEP-FE) was identified; however, exclusion did not change significance of results (**Supplemental Table S8**).

Right hippocampus volume

Evidence of influence was found in DEP no ANX analysis (k=25, studies=20). One study[88] was identified; however, exclusion did not change significance of results (**Supplemental Table S8**).

Left hippocampus volume

Evidence of influence was found in two analyses. In DEP analysis (k=50, studies=34), one study[129] was identified; however, exclusion did not change significance of results. In DEP no ANX analysis (k=25, studies=20), one study[88] was identified; however, exclusion did not change significance of results (**Supplemental Table S8**).

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Total amygdala volume

Evidence of influence was found in DEP analysis (k=25, studies=15). One study[81] (DEP-LO) was identified; however, exclusion did not change significance of results (**Supplemental Table S8**).

Right amygdala volume

Evidence of influence was found in DEP analysis (k=23, studies=13), One study[81] (DEP-LO) was identified; however, exclusion did not change significance of results (**Supplemental Table S8**).

Left amygdala volume

Evidence of influence was found in DEP analysis (k=23, studies=13), One study[81] (DEP-LO) was identified; however, exclusion did not change significance of results (**Supplemental Table S8**).

ICV

Evidence of influence was found in four analyses. In DEP analysis (k=59, studies=42), three studies[42,49,129] were identified; however, exclusions did not change the significance of results. In DEP-Mix analysis (k=25, studies=25) three studies[42,49,129] were identified, with individual exclusions varying the significance of results and exclusion of all identified studies showing no significant volumetric differences. In DEP no ANX analysis (k=30, studies=23) two studies[42,49] (DEP-Mix) were identified, with individual exclusions varying the significance of results and exclusion of all identified studies showing significant volumetric differences. In DEP-Mix no ANX analysis (k=15, studies=15) two studies[42,49] (DEP-Mix) were identified, with individual exclusions varying the significance of results and exclusion of all identified studies showing non-significant volumetric differences (**Supplemental Table S8**).

Bias assessment

TBV

Six out of a total of 11 meta-analyses in TBV presented bias (54.5%). From the six main meta-analyses, three presented bias; while from the five meta-analyses assessing anxiety comorbidity, three presented bias. Using the fill-and-trim method, two analyses changed the significance of the presented results. Unlike initial results,

significant volumetric differences were found in the analysis with DEP-LO and DEP no ANX (**Supplemental Table S9**).

GMV

One out of a total of seven meta-analyses in GMV presented bias (14.3%). From the four main meta-analyses, one presented bias; while none of the three meta-analyses assessing anxiety comorbidity presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

Total hippocampus volume

Ten out of a total of 18 meta-analyses in THcV presented bias (55.6%). From the ten main meta-analyses, five presented bias; while from the eight meta-analyses assessing anxiety comorbidity, five presented bias. Using the trim-and-fill method, two analyses changed the significance of the presented results. Unlike initial results, significant volumetric differences were found with DEP-EO no ANX and DEP ANX (**Supplemental Table S9**).

Right hippocampus volume

Eight out of a total of 16 meta-analyses in RHcV presented bias (50.0%). From the eight main meta-analyses, four presented bias; while from the eight meta-analyses assessing anxiety comorbidity, four presented bias. In one of these analyses (DEP-Mix ANX), bias was only present in Egger test. Using the trim-and-fill method, two analyses changed the significance of the presented results. Unlike initial results, significant volumetric differences were found with DEP-Cur and DEP-EO no ANX, and a trend with DEP ANX (**Supplemental Table S9**).

Left hippocampus volume

Eight out of a total of 16 meta-analyses in LHcV presented bias (50.0%). From the eight main meta-analyses, four presented bias; while from the eight meta-analyses assessing anxiety comorbidity, four presented bias. Using the trim-and-fill method, only analysis changed the significance of the presented results. Unlike initial results, significant volumetric differences were found with DEP ANX (**Supplemental Table S9**).

Total amygdala volume

Three out of a total of ten meta-analyses in TAV presented bias (30.0%). From the five main meta-analyses, two presented bias; while from the five meta-analyses assessing anxiety comorbidity, one presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

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Right amygdala volume

Five out of a total of ten meta-analyses in RAV presented bias (50.0%). From the five main meta-analyses, four presented bias; while from the five meta-analyses assessing anxiety comorbidity, one presented bias. Using the trim-and-fill method, one analysis changed the significance of the presented results. Unlike initial results, significant volumetric differences were found with DEP no ANX (**Supplemental Table S9**).

Left amygdala volume

Two out of a total of ten meta-analyses in LAV presented bias (20.0%). From the five main meta-analyses, two presented bias; while none of the meta-analyses assessing anxiety comorbidity presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

Total putamen volume

Two out of a total of five meta-analyses in TPuV presented bias (40.0%). From the two main meta-analyses, one presented bias; while from the three meta-analyses assessing anxiety comorbidity, one presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

Right putamen volume

Two out of a total of four meta-analyses in RPuV presented bias (50.0%). From the two main meta-analyses, none presented bias; while both meta-analyses assessing anxiety comorbidity presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

Left putamen volume

Three out of a total of four meta-analyses in LPuV presented bias (75.0%). From the two main meta-analyses, one presented bias; while both meta-analyses assessing anxiety comorbidity presented bias. Using the trim-and-fill method, one analysis changed the significance of the presented results. Unlike initial results, no significant volumetric differences were found with DEP no ANX (**Supplemental Table S9**).

Total caudate volume

Two out of a total of five meta-analyses in TCV presented bias (40.0%). From the two main meta-analyses, one presented bias; while from the three meta-analyses assessing anxiety comorbidity, one presented bias. Using the

trim-and-fill method, one analysis changed the significance of the presented results. Unlike initial results, significant volumetric differences were found with DEP-Mix (**Supplemental Table S9**).

Right caudate volume

Three out of a total of four meta-analyses in RCV presented bias (75.0%). From the two main meta-analyses, one presented bias; while both meta-analyses assessing anxiety comorbidity presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

Left caudate volume

Three out of a total of four meta-analyses in LCV presented bias (75.0%). From the two main meta-analyses, one presented bias; while both meta-analyses assessing anxiety comorbidity presented bias. Using the trim-and-fill method, one analysis changed the significance of the presented results. Unlike initial results, significant volumetric differences were found with DEP no ANX (**Supplemental Table S9**).

Total pallidum volume

Three out of a total of four meta-analyses in TPaV presented bias (75.0%). Both main meta-analyses presented bias; while from the two meta-analyses assessing anxiety comorbidity, one presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

Right pallidum volume

All meta-analyses in RPaV presented bias (100.0%). Using the trim-and-fill method, one analysis changed the significance of the presented results. Unlike initial result, significant differences were found with DEP-Mix (**Supplemental Table S9**).

Left pallidum volume

All meta-analyses in LPaV presented bias (100.0%). Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

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Right thalamus volume

One out of a total of two meta-analyses in RTV presented bias (50.0%). The only meta-analysis assessing anxiety comorbidity presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

Total accumbens volume

The only meta-analysis in TAcV presented bias (100.0%). Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

WMV

Three out of a total of four meta-analyses in WMV presented bias (75.0%). From the three main meta-analyses, two presented bias; while the only meta-analysis assessing anxiety comorbidity presented bias. Using the trim-and-fill method, the significance of results remained unchanged (**Supplemental Table S9**).

ICV

Nine out of a total of 18 meta-analyses in ICV presented bias (50.0%). From the 11 main meta-analyses, seven presented bias; while from the seven meta-analyses assessing anxiety comorbidity, two presented bias. Using the trim-and-fill method, one analysis changed the significance of the presented results. Unlike initial results, significant volumetric differences were found with DEP-Mix no ANX, and a trend with DEP-Rem (**Supplemental Table S9**).

Meta-regression

Although a trend was reported with age in RHcV, neither variable in isolation or as part of a model could significantly account for the observed heterogeneity in TBV, and HcV analyses (QMp>0.05). Similar results were found with segmentation procedure, depressive symptoms, and medication status in HcV. Furthermore, the test for residual heterogeneity in these meta-regressions suggested that other moderators may influence observed outcomes measures (QE-p<0.0001) (**Supplemental Table S10**).

The effect of gender, as the difference between the percent female in HC and DEP, was found to be significant in ICV. The effect of gender accounted for 22.4% of the observed variance in ICV (QMp=0.0325), with no evidence of other moderators influencing this measure (QEp>0.05) (**Supplemental Table S10**).

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Supplemental Table S1. Modified Newcastle-Ottawa scale

Detailed description of items included in the assessment of study quality using a modified version of the Newcastle-Ottawa scale (NOS). Items that grant a star are indicated with (★). A study can be awarded a maximum of one star in each item, except for 2a and 3b were two stars can be assigned. A maximum of ten stars can be awarded to a single study.

1. Selection	2. Comparability	3. Exposure
a. Is the case definition adequate? i. yes, independent validation based on diagnostic criteria (DSM or ICD)★ ii. yes, based on self-report with no reference to diagnostic criteria iii. no description b. Representativeness of the cases i. consecutive or representative series of cases within hospital/clinic★ ii. not stated, but description of source(s) of cases½★ iii. potential for selection biases or not stated c. Selection of Controls i. community controls from the same area as cases★ ii. hospital controls or controls attending clinic iii. no description d. Definition of Controls i. no history of depression or any other psychiatric disorder★ ii. no history of depression, but other psychiatric disorders may be present iii. no description	a. Comparability of cases and controls on the basis of the design or analysis i. study controls for age and gender★ (½★ if one) ii. study controls for neurological disease or dementia (or < 60yo)★ iii. sample ≥60yo with no mention of control for neurological disease or dementia	a. Same method of ascertainment for cases and controls i. yes★ ii. no iii. not stated b. Ascertainment of depression i. psychiatric/clinical assessment record★ ii. structured interview blind to case/control status★ iii. interview not blinded to case/control status iv. written self-report or medical record only v. no description c. Non-Response rate i. same rate for both groups (if no exclusions stated, assign star)★ ii. non respondents described iii. rate different or no designation

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Supplemental Table S2. Detailed demographic data of included studies

n: total number of participants, HC: healthy controls, DEP: depressed participants, M: males, F: female/number of females, %F: percent female, SD: standard deviation, Scanner: scanner strength in Tesla (T), Mix: heterogeneous group of depressed, EO: early-onset depression, LO: late-onset depression, FE: first episode, ME: multiple episodes, noMed: not taking antidepressants, Med: taking antidepressants, TR: treatment-resistant depression, Psy: psychotic depression, Mel: melancholic depression, Rem: depression in remission, Cur: currently in depression, Sui: suicide attempt/ideation, FH: family history of depression, Abu: physical/sexual abuse, Anx: depression comorbid with anxiety.
*Data provided by authors

†HC and DEP-Rem used in HcV analyses.

			HC						DEP			DEP subgroups						
				Age (years)			Age (years)			Age (years)			Age (years)			Age (years)			
Reference	n	%F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	DEP subgroups	Scanner
Abdallah et al., 2015	59	40.7	26	37.3 (13.3)	14	--	--	--	--	--	--	19	39.6 (10.9)	6	14	43.9 (12.3)	4	noTR/TR	3.0 T
Abdallah et al., 2017	60	58.3	26	37.4 (15.3)	12	--	--	--	--	--	--	34	41.7 (11.7)	23	--	--	--	Cur	3.0 T
Abe et al., 2010	63	47.6	42	48.0 (13.2)	20	--	--	--	21	48.1 (13.5)	10	--	--	--	--	--	--	Mix	1.5 T
Ahdidan et al., 2013 (M)*	13	0.0	9	35.6 (10.3)	0	--	--	--	4	32.0 (3.5)	0	--	--	--	--	--	--	Mix	1.5 T
Ahdidan et al., 2013 (F)*	43	100.0	24	37.0 (11.6)	24	--	--	--	19	41.0 (13.0)	19	--	--	--	--	--	--	Mix	1.5 T
Almeida et al., 2003	88	77.3	37	72.9 (6.6)	27	--	--	--	--	--	--	24	72.8 (6.6)	23	27	75.5 (5.8)	18	EO/LO	1.0 T
Andreescu et al., 2008	103	64.1	32	71.0 (6.7)	17	--	--	--	71	72.2 (6.2)	49	--	--	--	--	--	--	Mix	1.5 T
Arnone et al., 2013	130	71.5	66	32.1 (9.3)	46	--	--	--	--	--	--	25	34.5 (11.0)	20	39	36.3 (8.8)	27	Rem/Cur	1.5 T
Ashtari et al., 1999	86	65.1	46	71.4 (0.3)	28	--	--	--	40	74.3 (6.0)	28	--	--	--	--	--	--	Mix	1.0 T
Ballmaier et al., 2008	80	66.3	34	72.4 (6.9)	19	--	--	--	46	71.1 (7.66)	34	24	68.0 (5.8)	20	22	74.5 (8.1)	14	Mix/EO/LO	1.5 T
Bearden et al., 2009	62	77.4	31	36.7 (10.7)	24	--	--	--	31	39.2 (11.9)	24	--	--	--	--	--	--	Mix	1.5 T

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			HC						DEP			DEP subgroups						
				Age (years)			Age (years)			Age (years)			Age (years)			Age (years)			
Reference	n	%F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	DEP subgroups	Scanner
Bergouigan et al., 2009	42	73.8	21	28.2 (5.5)	14	--	--	--	--	--	--	21	33.2 (9.6)	17	--	--	--	LO	1.5 T
Bijanki et al., 2014	40	65.0	20	45.4 (9.9)	13	--	--	--	--	--	--	20	46.0 (9.5)	13	--	--	--	Psy	1.5 T
Burke et al., 2011	122	60.7	31	68.8 (6.0)	21	--	--	--	--	--	--	54	66.1 (6.0)	34	37	70.1 (6.6)	19	EO/LO	1.5 T
Caetano et al., 2004	62	77.4	31	36.7 (10.7)	24	--	--	--	31	39.2 (11.9)	24	--	--	--	--	--	--	Mix	1.5 T
Carceller-Sindreu et al., 2015	95	75.8	34	47.9 (8.1)	24	--	--	--	21	44.4 (6.7)	14	20	47.1 (8.2)	18	20	48.6 (8.0)	16	FE/ME/TR	3.0 T
Cardoner et al., 2007	105	46.7	72	30.1 (10.2)	32	--	--	--	--	--	--	33	30.1 (10.2)	17	--	--	--	Anx	1.5 T
Cohen et al., 2013	61	54.1	22	32.2 (11.5)	11	--	--	--	19	37.3 (11.7)	13	20	36.4 (13.4)	9	--	--	--	Mix/Psy	3.0 T
Cole et al., 2010	74	75.7	37	42.2 (9.0)	28	--	--	--	37	41.9 (8.9)	28	13	38.1 (7.9)	11	24	44.0 (9.4)	17	Mix/FE/ME	1.5 T
Cole et al., 2011	195	57.9	111	33.0 (9.2)	56	--	--	--	--	--	--	84	48.8 (8.9)	57	--	--	--	ME	1.5 T
Colloby et al., 2011	68	69.1	30	74.4 (6.4)	20	--	--	--	38	74.1 (6.1)	27	--	--	--	--	--	--	Mix	3.0 T
Devantier et al., 2016	56	46.4	27	59.5 (5.0)	13	--	--	--	--	--	--	29	59.8 (4.5)	13	--	--	--	LO	3.0 T
De Winter et al., 2017	100	70.0	52	72.4 (6.4)	37	--	--	--	48	74.1 (7.51)	33	--	--	--	--	--	--	Mix	3.0 T
Dombrovsky et al., 2012*	52	57.7	19	70.5 (7.5)	12	--	--	--	20	67.7 (7.0)	13	13	66.0 (6.4)	5	--	--	--	Mix/Sui	3.0 T
Eker et al., 2010	47	74.5	22	29.7 (6.4)	17	--	--	--	--	--	--	25	32.1 (9.3)	18	--	--	--	FE	1.5 T
Eker et al., 2011	87	69.0	43	30.4 (6.7)	27	--	--	--	44	33.6 (9.5)	33	--	--	--	--	--	--	Mix	1.5 T
Elderkin-Thompson et al., 2008	84	63.1	41	72.2 (7.3)	20	--	--	--	--	--	--	18	67.4 (5.9)	15	25	73.0 (8.2)	18	EO/LO	1.5 T
Emsell et al., 2017	107	72.0	52	72.7 (6.5)	38	--	--	--	55	73.6 (7.4)	39	--	--	--	--	--	--	Cur	3.0 T
Exner et al., 2009	52	73.1	26	33.0 (8.9)	18	--	--	--	--	--	--	26	35.0 (10.5)	20	--	--	--	Mel	1.5 T
Frodl et al., 2002	60	56.7	30	40.6 (12.5)	17	--	--	--	--	--	--	30	40.3 (12.6)	17	--	--	--	FE	1.5 T
Frodl et al., 2003	114	52.6	30	40.6 (12.5)	17	27	46.3 (11.3)	13	--	--	--	30	40.3 (12.6)	17	27	49.1 (10.5)	13	FE/ME	1.5 T
Frodl et al., 2004	48	60.4	30	45.7 (12.9)	18	--	--	--	--	--	--	18	46.4 (15.4)	11	--	--	--	Rem	1.5 T
Frodl et al., 2008†	60	63.3	30	43.6 (13.1)	19	--	--	--	30	45.0 (11.1)	19	17	42.7 (10.5)	12	13	48.1 (11.7)	7	Mix/Rem/Cur	1.5 T
Frodl et al., 2012	83	59.0	43	37.0 (13.7)	25	--	--	--	40	41.4 (10.9)	24	--	--	--	--	--	--	Mix	3.0 T
Fung et al., 2015	48	60.4	29	27.1 (8.4)	18	--	--	--	19	30.0 (8.9)	11	--	--	--	--	--	--	Mix	3.0 T
Gifuni et al., 2016 (Sample 1)*	44	0.0	12	41.5 (11.1)	0	--	--	--	--	--	--	14	43.9 (10.5)	0	18	33.6 (10.9)	0	Rem/Sui	1.5 T
Gifuni et al., 2016 (Sample 2 M)*	64	0.0	7	42.2 (8.5)	0	--	--	--	--	--	--	13	39.0 (9.7)	0	44	40.2 (6.3)	0	Rem/Sui	1.5 T
Gifuni et al., 2016 (Sample 2 F)*	63	100.0	18	37.1 (10.4)	18	--	--	--	--	--	--	25	36.7 (7.8)	25	20	36.1 (7.0)	20	Rem/Sui	1.5 T
Han et al., 2014	42	71.4	22	43.7 (12.3)	15	--	--	--	--	--	--	20	42.7 (12.4)	15	--	--	--	FE	3.0 T

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			HC						DEP			DEP subgroups							
				Age (years)			Age (years)			Age (years)			Age (years)			Age (years)			
Reference	n	%F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	DEP subgroups	Scanner
Han et al., 2016	41	100.0	21	42.3 (10.2)	21	--	--	--	--	--	--	20	42.3 (13.7)	20	--	--	--	noMed	1.5 T
Han et al., 2017	227	75.3	101	40.6 (13.8)	70	--	--	--	126	43.8 (11.6)	101	--	--	--	--	--	--	Mix	3.0 T
Hannestad et al., 2006	246	69.1	64	70.0 (7.7)	41	--	--	--	182	70.2 (5.8)	129	--	--	--	--	--	--	Mix	1.5 T
Hickie et al., 2007	61	63.9	16	55.8 (10.3)	9	--	--	--	45	52.0 (12.8)	30	--	--	--	--	--	--	Mix	1.5 T
Huang et al., 2013	47	61.7	27	32.8 (9.9)	19	--	--	--	20	35.0 (10.5)	10	9	32.7 (11.6)	4	11	36.9 (9.6)	6	Mix/noMed/Med	4.7 T
Hviid et al., 2010	69	69.6	38	47.7 (11.2)	28	--	--	--	--	--	--	31	47.5 (11.9)	20	--	--	--	Rem	1.5 T
Janssen et al., 2004	69	100.0	41	62.4 (11.4)	41	--	--	--	--	--	--	28	64.0 (10.9)	28	--	--	--	EO	1.5 T
Janssen et al., 2007	37	100.0	22	71.1 (7.5)	22	--	--	--	--	--	--	15	72.7 (6.7)	15	--	--	--	LO	1.5 T
Kanellopoulos et al., 2010*	56	62.5	23	70.7 (5.7)	14	--	--	--	33	72.3 (6.8)	21	--	--	--	--	--	--	Mix	1.5 T
Keller et al., 2008	64	53.1	22	32.2 (11.5)	11	--	--	--	--	--	--	19	36.6 (11.9)	12	23	36.5 (13.2)	11	Cur/Psy	3.0 T
Klauser et al., 2015	89	68.5	33	34.7 (9.9)	21	--	--	--	56	34.0 (9.0)	40	27	35.0 (9.7)	18	29	33.1 (8.3)	22	Mix/Rem/Cur	1.5 T
Kronmuller et al., 2009 (M)	35	0.0	11	42.0 (11.3)	0	--	--	--	--	--	--	13	38.1 (11.9)	0	11	48.3 (8.7)	0	FE/ME	1.5 T
Kronmuller et al., 2009 (F)	52	100.0	19	42.7 (14.0)	19	--	--	--	--	--	--	13	41.5 (16.6)	13	20	45.9 (11.8)	20	FE/ME	1.5 T
Kumar et al., 1998	65	73.8	30	69.4 (6.1)	23	--	--	--	--	--	--	35	74.6 (6.9)	25	--	--	--	LO	1.5 T
Kumar et al., 2000	81	72.8	30	69.4 (6.1)	23	--	--	--	51	74.3 (6.6)	36	--	--	--	--	--	--	Mix	1.5 T
Lacerda et al., 2003	73	45.2	48	35.1 (10.0)	29	--	--	--	25	41.2 (11.0)	4	--	--	--	--	--	--	Mix	1.5 T
Lavretsky et al., 2005	82	63.4	41	72.2 (7.3)	20	--	--	--	--	--	--	30	71.7 (7.8)	25	11	67.4 (6.1)	7	noMed/Med	1.5 T
Lavretsky et al., 2007	84	63.1	41	72.2 (7.3)	20	--	--	--	43	70.7 (7.8)	33	--	--	--	--	--	--	Mix	1.5 T
Lenze et al., 1999	48	100.0	24	53.0 (??)	24	--	--	--	24	53.0 (??)	24	--	--	--	--	--	--	Mix	1.5 T
Lenze et al., 2008	55	100.0	24	46.0 (14.0)	24	--	--	--	--	--	--	31	50.0 (15.0)	31	--	--	--	Rem	1.5 T
Lim et al., 2012a	60	51.7	30	72.4 (4.5)	16	--	--	--	30	73.7 (6.4)	15	--	--	--	--	--	--	Mix	3.0 T
Lim et al., 2012b	95	77.9	47	70.7 (4.4)	38	--	--	--	--	--	--	48	71.8 (4.8)	36	--	--	--	LO	3.0 T
Lloyd et al., 2004	90	77.8	39	73.1 (6.7)	29	--	--	--	51	74.0 (6.3)	41	23	72.7 (6.7)	22	28	75.1 (5.8)	19	Mix/EO/LO	1.0 T
Lorenzetti et al., 2009	89	68.5	33	34.0 (9.9)	21	--	--	--	--	--	--	27	35.1 (10.0)	18	29	32.5 (8.3)	22	Rem/Cur	1.5 T
Lorenzetti et al., 2010	87	70.1	31	34.7 (9.9)	21	--	--	--	--	--	--	27	35.1 (10.0)	18	29	32.5 (8.3)	22	Rem/Cur	1.5 T
Machino et al., 2014	58	44.8	29	38.7 (8.4)	13	--	--	--	--	--	--	29	39.6 (8.3)	13	--	--	--	TR	1.5 T
Maller et al., 2007 (M)	35	0.0	13	39.3 (12.7)	0	--	--	--	22	37.3 (8.8)	0	--	--	--	--	--	--	Mix	1.5 T
Maller et al., 2007 (F)	40	100.0	17	35.8 (11.0)	17	--	--	--	23	37.5 (13.0)	23	--	--	--	--	--	--	Mix	1.5 T

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			HC						DEP			DEP subgroups							
				Age (years)			Age (years)			Age (years)			Age (years)			Age (years)			
Reference	n	%F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	DEP subgroups	Scanner
Maller et al., 2012	258	47.7	76	35.0 (9.8)	35	--	--	--	--	--	--	182	42.2 (14.0)	88	--	--	--	TR	1.5 T
Malykhin et al., 2010	73	76.7	34	33.5 (8.1)	27	--	--	--	--	--	--	23	35.7 (8.5)	15	16	32.2 (7.8)	14	noMed/Med	1.5 T
Meisenzahl et al., 2010	230	46.5	138	33.3 (12.2)	60	--	--	--	92	44.6 (12.3)	47	47	41.8 (13.5)	26	45	45.5 (11.1)	21	Mix/FE/ME	1.5 T
Naismith et al., 2002	67	65.7	20	56.1 (9.8)	12	--	--	--	47	51.8 (12.4)	32	--	--	--	--	--	--	Mix	*NA*
Nugent et al., 2013	381	58.8	169	34.0 (9.3)	98	--	--	--	--	--	--	71	38.0 (12.1)	50	141	36.0 (11.1)	76	Rem/Cur	3.0 T
Ota et al., 2017	71	46.5	35	38.9 (13.4)	16	--	--	--	36	38.4 (11.3)	17	19	35.7 (11.7)	10	17	41.3 (10.3)	7	Rem/noMed/Med	3.0 T
Ozalay et al., 2013	69	73.9	33	31.4 (7.8)	23	--	--	--	--	--	--	36	31.6 (8.0)	28	--	--	--	noMed	1.5 T
Ozalay et al., 2016	48	100.0	24	47.3 (5.6)	24	--	--	--	--	--	--	24	46.2 (3.9)	24	--	--	--	FH	3.0 T
Pan et al., 2009	253	68.4	83	69.8 (5.6)	61	--	--	--	170	69.4 (7.5)	112	--	--	--	--	--	--	Mix	1.5 T
Parashos et al., 1998	64	56.3	32	53.8 (17.7)	18	--	--	--	32	54.2 (17.6)	18	--	--	--	--	--	--	Mix	1.5 T
Penttila et al., 2009	105	54.3	70	42.8 (11.5)	33	--	--	--	--	--	--	35	47.2 (8.8)	24	--	--	--	TR	1.5 T
Phillips et al., 2015	54	66.7	28	45.7 (10.6)\	18	--	--	--	--	--	--	26	46.0 (10.4)	18	--	--	--	TR	1.5 T
Posener et al., 2003	69	55.1	42	33.2 (10.8)	23	--	--	--	--	--	--	27	33.0 (10.7)	15	--	--	--	Cur	1.5 T
Ribeiz et al., 2013	52	76.9	22	70.4 (7.6)	17	--	--	--	30	70.7 (6.6)	23	--	--	--	--	--	--	Mix	1.5 T
Rodriguez-Cano et al., 2014	96	60.4	64	46.0 (9.8)	38	--	--	--	32	48.7 (13.0)	20	--	--	--	--	--	--	Mix	1.5 T
Rusch et al., 2001	40	57.5	15	37.4 (14.4)	9	--	--	--	25	33.2 (9.5)	14	--	--	--	--	--	--	Mix	1.5 T
Sacchet et al., 2017*	232	75.4	116	33.7 (10.5)	84	--	--	--	116	36.5 (11.6)	91	--	--	--	--	--	--	Mix	3.0 T
Savitz et al., 2011	134	62.7	74	37.1 (11.9)	45	--	--	--	--	--	--	32	41.3 (13.3)	24	28	43.9 (11.5)	15	Rem/Cur	3.0 T
Savitz et al., 2015a	100	71.0	47	34.3 (11.4)	29	--	--	--	--	--	--	53	34.6 (9.8)	42	--	--	--	noMed	3.0 T
Savitz et al., 2015b	49	69.4	20	35.0 (10.9)	10	--	--	--	--	--	--	29	36.4 (10.0)	24	--	--	--	Cur	3.0 T
Sawyer et al., 2012	384	68.8	146	70.4 (6.3)	103	--	--	--	--	--	--	238	70.0 (7.5)	161	--	--	--	Cur	1.5 T
Saylam et al., 2006	48	75.0	24	30.2 (6.1)	18	--	--	--	24	33.4 (9.3)	18	--	--	--	--	--	--	Mix	1.5 T
Schmidt et al., 2017	60	61.7	20	36.5 (13.2)	12	--	--	--	--	--	--	20	36.2 (12.8)	12	20	40.6 (12.1)	13	noMed/Med	7.0 T
Sexton et al., 2012	61	65.6	25	71.8 (7.3)	16	--	--	--	36	71.8 (7.7)	24	--	--	--	--	--	--	Mix	3.0 T
Sheline et al., 1998	40	100.0	20	53.0 (17.0)	20	--	--	--	--	--	--	20	54.0 (18.0)	20	--	--	--	Rem	1.5 T
Sivakumar et al., 2015	45	48.9	20	65.4 (5.7)	7	--	--	--	--	--	--	25	65.3 (5.7)	15	--	--	--	LO	3.0 T
Soriano-Mas et al., 2011	110	58.2	40	59.2 (7.1)	23	--	--	--	--	--	--	70	61.6 (9.7)	41	--	--	--	Mel	1.5 T
Stratmann et al., 2014	264	56.8	132	37.8 (11.4)	74	--	--	--	132	37.9 (11.9)	76	--	--	--	--	--	--	Mix	3.0 T

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			HC						DEP			DEP subgroups							
				Age (years)			Age (years)			Age (years)			Age (years)			Age (years)			
Reference	n	%F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	n	mean (SD)	F	DEP subgroups	Scanner
Tae et al., 2011	42	100.0	21	42.3 (10.2)	21	--	--	--	21	41.7 (11.0)	21	--	--	--	--	--	--	Mix	1.5 T
Taylor et al., 2005	218	70.6	83	69.4 (6.3)	64	--	--	--	--	--	--	72	68.7 (6.4)	51	63	71.5 (7.9)	39	EO/LO	1.5 T
Taylor et al., 2007	370	67.6	144	70.3 (6.5)	100	--	--	--	226	70.0 (7.4)	150	--	--	--	--	--	--	Mix	1.5 T
Taylor et al., 2014	144	69.4	70	69.7 (6.2)	57	--	--	--	--	--	--	47	69.3 (6.5)	28	27	72.1 (7.3)	15	Rem/Cur	1.5 T
Taylor et al., 2015	144	67.4	91	29.9 (9.1)	56	--	--	--	--	--	--	53	37.5 (8.9)	41	--	--	--	EO	*NA*
Turner et al., 2012*	89	57.3	44	33.6 (9.7)	24	--	--	--	45	36.7 (9.6)	27	--	--	--	--	--	--	Mix	3.0 T
Ueda et al., 2016	78	33.3	48	41.2 (11.4)	13	--	--	--	--	--	--	30	44.3 (13.0)	13	--	--	--	FE	3.0 T
van Eijndhoven et al., 2009	60	66.7	20	37.3 (12.7)	13	--	--	--	--	--	--	20	35.8 (11.7)	14	20	34.1 (11.6)	13	Rem/FE	1.5 T
van Tol et al., 2010	221	65.2	65	40.5 (9.7)	41	58	38.9 (9.0)	37	68	37.2 (10.2)	44	88	37.3 (10.6)	59	68	37.4 (10.1)	41	Mix/Anx/FE	3.0 T
Vasic et al., 2015	72	61.1	29	34.5 (10.7)	18	--	--	--	43	37.1 (10.9)	26	--	--	--	--	--	--	Mix	3.0 T
Vassilopoulou et al., 2013	57	73.7	18	46.6 (7.5)	13	--	--	--	--	--	--	22	52.1 (8.2)	17	17	52.9 (10.8)	12	Mel/Psy	1.5 T
Vythilingam et al., 2002	46	100.0	14	27.0 (5.0)	14	--	--	--	11	34.0 (8.0)	11	21	33.0 (6.0)	21	--	--	--	Mix/Abu	1.5 T
Vythilingam et al., 2004	71	62.0	33	34.0 (10.0)	21	--	--	--	38	41.0 (11.0)	23	--	--	--	--	--	--	Mix	1.5 T
Weber et al., 2010	100	79.0	62	71.1 (7.3)	48	--	--	--	--	--	--	38	66.1 (6.2)	31	--	--	--	EO	3.0 T
Weniger et al., 2006	44	100.0	23	32.0 (7.0)	23	--	--	--	21	34.0 (9.0)	21	--	--	--	--	--	--	Mix	1.5 T
Wisse et al., 2015	47	61.7	34	62.0 (11.0)	23	--	--	--	13	54.0 (7.0)	6	--	--	--	--	--	--	Mix	1.5 T
Wolkowitz et al., 2015	43	62.8	18	37.8 (12.0)	12	--	--	--	--	--	--	25	34.9 (9.6)	15	--	--	--	noMed	4.0 T
Yang et al., 2017	168	72.6	68	29.8 (6.5)	49	16	32.9 (7.6)	12	--	--	--	43	30.1 (7.5)	31	41	31.7 (8.0)	30	FE/Abu	3.0 T
Zannas et al., 2013	159	69.8	70	69.1 (6.0)	56	--	--	--	89	69.9 (6.9)	55	--	--	--	--	--	--	Mix	1.5 T
Zavorotnyy et al., 2018	53	77.4	30	49.6 (14.6)	23	--	--	--	23	48.7 (13.7)	18	--	--	--	--	--	--	Mix	3.0 T
Zhao et al., 2017a	88	46.6	43	31.3 (7.8)	21	--	--	--	45	32.7 (7.9)	20	--	--	--	--	--	--	Mix	3.0 T
Zhao et al., 2017b	77	44.2	41	30.8 (7.3)	18	--	--	--	--	--	--	36	32.8 (8.0)	16	--	--	--	FE	3.0 T

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Supplemental Table S3. Detailed NOS scores

Detailed description of scores in each item of the modified NOS. 0= no star, 0.5= ½★, 1= ★.

		Selection				Comparability		Exposure				
Reference	**Rater**	**1a**	**1b**	**1c**	**1d**	**2a (age/gender)**	**2a (neuro/dem)**	**3a**	**3b (record)**	**3b (interview)**	**3c**	**Score**
Abdallah et al., 2017	KA	1	0	0	1	0.5	1	0	1	0	1	**5.5**
	DEO	1	0	0	1	0.5	1	0	1	0	1	**5.5**
Abdallah et al., 2015	KA	1	0	0	1	1	1	0	1	0	1	**6.0**
	DEO	1	0	0	1	1	1	0	1	0	1	**6.0**
Abe et al., 2010	KA	1	0	0	1	1	1	0	1	0	1	**6.0**
	DEO	1	0	0	1	1	1	0	1	0	1	**6.0**
Ahdidan et al., 2013	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Almeida et al., 2003	KA	1	0.5	0	0	1	1	0	1	0	1	**5.5**
	DEO	1	0.5	0	0	1	1	0	1	0	1	**5.5**
Andreescu et al., 2008	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Arnone et al., 2013	KA	1	0	0	1	1	1	1	1	0	1	**7.0**
	DEO	1	0	0	1	1	1	1	1	0	1	**7.0**
Ashtari et al., 1999	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Ballmaier et al., 2008	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Bearden et al., 2009	KA	1	0	1	1	1	1	0	1	0	1	**7.0**
	DEO	1	0	1	1	1	1	0	1	0	1	**7.0**
Bergouigan et al., 2009	KA	1	0.5	1	1	1	1	1	1	0	0	**7.5**
	DEO	1	0.5	1	1	1	1	1	1	0	0	**7.5**
Bijanki et al., 2014	KA	1	0.5	1	1	1	1	0	0	0	0	**5.5**
	DEO	1	0.5	1	1	1	1	0	0	0	0	**5.5**
Burke et al., 2011	KA	1	0.5	1	1	1	1	0	1	0	0	**6.5**
	DEO	1	0.5	1	1	1	1	0	1	0	0	**6.5**
Caetano et al., 2004	KA	1	0	0	1	1	1	0	1	0	1	**6.0**
	DEO	1	0	0	1	1	1	0	1	0	1	**6.0**
Carceller-Sindreu et al., 2015	KA	1	0.5	0	1	1	1	1	0	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	1	0	0	1	**6.5**

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		Selection				Comparability		Exposure				
Reference	**Rater**	**1a**	**1b**	**1c**	**1d**	**2a (age/gender)**	**2a (neuro/dem)**	**3a**	**3b (record)**	**3b (interview)**	**3c**	**Score**
Cardoner et al., 2007	KA	1	1	1	1	1	1	0	1	0	1	**8.0**
	DEO	1	1	1	1	1	1	0	1	0	1	**8.0**
Cohen et al., 2013	KA	1	0.5	0.5	1	1	0	0	1	0	1	**6.0**
	DEO	1	0.5	0.5	1	1	0	0	1	0	1	**6.0**
Cole et al., 2010	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Cole et al., 2011	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Colloby et al., 2011	KA	1	0.5	1	1	0.5	1	1	0	0	1	**7.0**
	DEO	1	0.5	1	1	0.5	1	1	0	0	1	**7.0**
Devantier et al., 2016	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	1	1	0	0	**7.5**
De Winter et al., 2017	KA	1	1	0	1	1	1	1	1	0	0	**7.0**
	DEO	1	1	0	1	1	1	1	1	0	0	**7.0**
Dombrovsky et al., 2012	KA	1	0.5	0	1	0.5	1	1	1	0	1	**7.0**
	DEO	1	0.5	0	1	0.5	1	1	1	0	1	**7.0**
Eker et al., 2010	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Eker et al., 2011	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Elderkin-Thompson et al., 2008	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Emsell et al., 2017	KA	1	0.5	1	1	1	1	1	1	0	0	**7.5**
	DEO	1	0.5	1	1	1	1	1	1	0	0	**7.5**
Exner et al., 2009	KA	1	1	1	1	0	1	0	1	0	0	**6.0**
	DEO	1	1	1	1	0	1	0	1	0	0	**6.0**
Frodl et al., 2012	KA	1	0.5	1	0	0	1	0	1	0	1	**5.5**
	DEO	1	0.5	1	0	0	1	0	1	0	1	**5.5**
Frodl et al., 2008	KA	1	0.5	1	1	1	1	0	1	0	0	**6.5**
	DEO	1	0.5	1	1	1	1	0	1	0	0	**6.5**
Frodl et al., 2002	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Frodl et al., 2003	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Frodl et al., 2004a	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Fung et al., 2015	KA	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**
	DEO	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**

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		Selection				Comparability		Exposure				
Reference	**Rater**	**1a**	**1b**	**1c**	**1d**	**2a (age/gender)**	**2a (neuro/dem)**	**3a**	**3b (record)**	**3b (interview)**	**3c**	**Score**
Gifuni et al., 2016	KA	1	0.5	1	1	0.5	1	0	1	0	0	**6.0**
	DEO	1	0.5	1	1	0.5	1	0	1	0	0	**6.0**
Han et al., 2014	KA	1	0.5	1	1	1	0	0	1	0	1	**6.5**
	DEO	1	0.5	1	1	1	0	0	1	0	1	**6.5**
Han et al., 2016	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Han et al., 2017	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Hannestad et al., 2006	KA	1	0.5	1	0	1	1	0	0	0	1	**5.5**
	DEO	1	0.5	1	0	1	1	0	0	0	1	**5.5**
Hickie et al., 2007	KA	1	0.5	1	0	0	1	0	0	0	1	**4.5**
	DEO	1	0.5	1	0	0	1	0	0	0	1	**4.5**
Huang et al., 2013	KA	1	0	0	1	0	1	0	1	0	1	**5.0**
	DEO	1	0	0	1	0	1	0	1	0	1	**5.0**
Hviid et al., 2010	KA	1	1	0	1	0	1	0	1	0	0	**5.0**
	DEO	1	1	0	1	0	1	0	1	0	0	**5.0**
Janssen et al., 2007	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Janssen et al., 2004	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Kanellopoulos et al., 2010	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Keller et al., 2008	KA	1	0.5	0	1	1	0	1	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	0	1	1	0	1	**6.5**
Klauser et al., 2015	KA	1	0.5	1	1	1	1	1	1	0	0	**7.5**
	DEO	1	0.5	1	1	1	1	1	1	0	0	**7.5**
Kronmuller et al., 2009	KA	1	1	0	1	1	1	1	1	0	0	**7.0**
	DEO	1	1	0	1	1	1	1	1	0	0	**7.0**
Kumar et al., 2000	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Kumar et al., 1998	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Lacerda et al., 2003	KA	1	0	0	1	0.5	1	0	1	0	1	**5.5**
	DEO	1	0	0	1	0.5	1	0	1	0	1	**5.5**
Lavretsky et al., 2007	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Lavretsky et al., 2005	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**

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		Selection				Comparability		Exposure				
Reference	**Rater**	**1a**	**1b**	**1c**	**1d**	**2a (age/gender)**	**2a (neuro/dem)**	**3a**	**3b (record)**	**3b (interview)**	**3c**	**Score**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Lenze et al., 1999	KA	1	0.5	1	0	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	1	0	1	1	0	1	0	1	**6.5**
Lenze et al., 2008	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Lim et al., 2012a	KA	1	0	0	1	1	1	0	1	0	1	**6.0**
	DEO	1	0	0	1	1	1	0	1	0	1	**6.0**
Lim et al., 2012b	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Lloyd et al., 2004	KA	1	0.5	1	1	0	1	0	0	0	1	**5.5**
	DEO	1	0.5	1	1	0	1	0	0	0	1	**5.5**
Lorenzetti et al., 2009	KA	1	0.5	0	1	1	1	1	1	0	0	**6.5**
	DEO	1	0.5	0	1	1	1	1	1	0	0	**6.5**
Lorenzetti et al., 2010	KA	1	0.5	0	1	0.5	1	1	1	0	0	**6.0**
	DEO	1	0.5	0	1	0.5	1	1	1	0	0	**6.0**
Machino et al., 2014	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Maller et al., 2007	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Maller et al., 2012	KA	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**
	DEO	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**
Malykhin et al., 2010	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Meisenzahl et al., 2010	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Naismith et al., 2002	KA	1	0.5	1	0	0	1	0	0	0	1	**4.5**
	DEO	1	0.5	1	0	0	1	0	0	0	1	**4.5**
Nugent et al., 2013	KA	1	0.5	0	1	1	0	0	1	0	1	**5.5**
	DEO	1	0.5	0	1	1	0	0	1	0	1	**5.5**
Ota et al., 2017	KA	1	0	0	1	1	1	1	1	0	0	**6.0**
	DEO	1	0	0	1	1	1	1	1	0	0	**6.0**
Ozalay et al., 2013	KA	1	0	0	1	1	1	0	1	0	1	**6.0**
	DEO	1	0	0	1	1	1	0	1	0	1	**6.0**
Ozalay et al., 2016	KA	1	0.5	1	1	1	1	0	1	0	0	**6.5**
	DEO	1	0.5	1	1	1	1	0	1	0	0	**6.5**
Pan et al., 2009	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**

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Reference	**Rater**	**1a**	**1b**	**1c**	**1d**	**2a (age/gender)**	**2a (neuro/dem)**	**3a**	**3b (record)**	**3b (interview)**	**3c**	**Score**
Parashos et al., 1998	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Penttila et al., 2009	KA	1	1	1	1	1	1	0	1	0	1	**8.0**
	DEO	1	1	1	1	1	1	0	1	0	1	**8.0**
Phillips et al., 2015	KA	1	0.5	1	1	1	1	0	1	0	0	**6.5**
	DEO	1	0.5	1	1	1	1	0	1	0	0	**6.5**
Posener et al., 2003	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Ribeiz et al., 2013	KA	1	0.5	1	1	0	1	0	1	0	1	**6.5**
	DEO	1	0.5	1	1	0	1	0	1	0	1	**6.5**
Rodriguez-Cano et al., 2014	KA	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**
	DEO	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**
Rusch et al., 2001	KA	1	0.5	1	1	0	0	0	1	0	1	**5.5**
	DEO	1	0.5	1	1	0	0	0	1	0	1	**5.5**
Sacchet et al., 2017	KA	1	0	0	1	1	1	0	1	0	1	**6.0**
	DEO	1	0	0	1	1	1	0	1	0	1	**6.0**
Savitz et al., 2015a	KA	1	0	0	1	1	1	0	1	0	1	**6.0**
	DEO	1	0	0	1	1	1	0	1	0	1	**6.0**
Savitz et al., 2015b	KA	1	0	0	1	1	1	0	1	0	0	**5.0**
	DEO	1	0	0	1	1	1	0	1	0	0	**5.0**
Savitz et al., 2011	KA	1	0	0	1	0	1	0	1	0	1	**5.0**
	DEO	1	0	0	1	0	1	0	1	0	1	**5.0**
Sawyer et al., 2012	KA	1	0.5	1	1	0.5	1	1	1	0	1	**8.0**
	DEO	1	0.5	1	1	0.5	1	1	1	0	1	**8.0**
Saylam et al., 2006	KA	1	0	0	1	0.5	1	0	0	0	1	**4.5**
	DEO	1	0	0	1	0.5	1	0	0	0	1	**4.5**
Schmidt et al., 2017	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Sexton et al., 2012	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Sheline et al., 1998	KA	1	0.5	1	1	1	1	1	1	0	0	**7.5**
	DEO	1	0.5	1	1	1	1	1	1	0	0	**7.5**
Sivakumar et al., 2015	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Soriano-Mas et al., 2011	KA	1	1	1	1	1	1	0	1	0	1	**8.0**
	DEO	1	1	1	1	1	1	0	1	0	1	**8.0**
Stratmann et al., 2014	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**

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	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Tae et al., 2011	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Taylor et al., 2015	KA	1	0.5	0	1	1	1	0	1	0	0	**5.5**
	DEO	1	0.5	0	1	1	1	0	1	0	0	**5.5**
Taylor et al., 2007	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Taylor et al., 2014	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Taylor et al., 2005	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Turner et al., 2012	KA	1	0	0	1	0.5	1	1	1	0	1	**6.5**
	DEO	1	0	0	1	0.5	1	1	1	0	1	**6.5**
Ueda et al., 2016	KA	1	0.5	1	0	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	1	0	1	1	0	1	0	1	**6.5**
van Eijndhoven et al., 2009	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
van Tol et al., 2010	KA	1	1	1	1	1	1	0	1	0	0	**7.0**
	DEO	1	1	1	1	1	1	0	1	0	0	**7.0**
Vasic et al., 2015	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Vassilopoulou et al., 2013	KA	1	0.5	1	0	0.5	1	0	1	0	0	**5.0**
	DEO	1	0.5	1	0	0.5	1	0	1	0	0	**5.0**
Vythilingam et al., 2002	KA	1	0.5	1	1	1	1	0	1	0	1	**7.5**
	DEO	1	0.5	1	1	1	1	0	1	0	1	**7.5**
Vythilingam et al., 2004	KA	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**
	DEO	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**
Weber et al., 2010	KA	1	0.5	1	1	1	1	1	1	0	0	**7.5**
	DEO	1	0.5	1	1	1	1	1	1	0	0	**7.5**
Weniger et al., 2006	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Wisse et al., 2015	KA	1	1	0	0	1	0	1	1	0	0	**5.0**
	DEO	1	1	0	0	1	0	1	1	0	0	**5.0**
Wolkowitz et al., 2015	KA	1	0.5	0.5	1	1	0	1	1	0	1	**7.0**
	DEO	1	0.5	0.5	1	1	0	1	1	0	1	**7.0**
Yang et al., 2017	KA	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**
	DEO	1	0.5	1	1	0.5	1	0	1	0	1	**7.0**

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Reference	**Rater**	**1a**	**1b**	**1c**	**1d**	**2a (age/gender)**	**2a (neuro/dem)**	**3a**	**3b (record)**	**3b (interview)**	**3c**	**Score**
Zannas et al., 2013	KA	1	0.5	1	1	1	1	1	1	0	0	**7.5**
	DEO	1	0.5	1	1	1	1	1	1	0	0	**7.5**
Zavorotnyy et al., 2018	KA	1	0.5	1	1	1	1	1	1	0	1	**8.5**
	DEO	1	0.5	1	1	1	1	1	1	0	1	**8.5**
Zhao et al., 2017a	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**
Zhao et al., 2017b	KA	1	0.5	0	1	1	1	0	1	0	1	**6.5**
	DEO	1	0.5	0	1	1	1	0	1	0	1	**6.5**

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Supplemental Table S4. Meta-analysis results per brain region

k: number of samples or subsamples, n: total number of participants, HC: healthy controls, DEP: depressed participants, M: males, F: females, MD: mean difference, SE: standard error, CI: confidence interval, Qp: Q-statistic p-value, τ^2: variance of true effects, I^2: proportion real differences between studies, TBV: total brain, GMV: grey matter, WMV: white matter, ICV: intracranial, THcV: total hippocampus, RHcV: right hippocampus, LHcV: left hippocampus, TAV: total amygdala, RAV: right amygdala, LAV: left amygdala, TPuV: total putamen, RPuV: right putamen, LPuV: left putamen, TCV: total caudate, RCV: right caudate, LCV: left caudate, TPaV: total pallidum, RPaV: right pallidum, LPaV: left pallidum, TTV: total thalamus, RTV: right thalamus, LTV: left thalamus, TAcV: total accumbens volumes, Mix: heterogeneous group of depressed, EO: early-onset depression, LO: late-onset depression, FE: first episode, ME: multiple episodes, noMed: not taking antidepressants, Med: taking antidepressants, TR: treatment-resistant depression, Rem: depression in remission, Cur: currently in depression. Bold font indicates significance at $p \leq 0.05$ and $I^2 > 50\%$.

				Number of subjects			Age (years)		Meta-analysis results							
Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
TBV	HC vs DEP	27	37	2618	1123 (M: 391, F: 732)	1495 (M: 496, F: 999)	50.73	53.19	-1.506	4.127	-9.595	6.583	0.715	0.279	0.000	0.00%
	HC vs DEP-Mix	12	13	1233	524 (M: 183, F: 341)	709 (M: 221, F: 488)	56.76	61.08	8.375	6.116	-3.612	20.361	0.171	0.183	0.000	0.00%
	HC vs DEP-EO	6	6	370	208 (M: 53, F: 155)	162 (M: 31, F: 131)	65.18	66.12	2.201	11.192	-19.734	24.136	0.844	0.849	0.000	0.00%
	HC vs DEP-LO	7	7	413	220 (M: 66, F: 154)	193 (M: 70, F: 123)	69.97	71.55	16.391	12.855	-8.805	41.587	0.202	**<0.0001**	688.646	**71.95%**
	HC vs DEP-Rem	4	4	261	151 (M: 48, F: 103)	110 (M: 23, F: 87)	37.87	41.22	7.234	16.222	-24.561	39.029	0.656	0.926	0.000	0.00%
	HC vs DEP-Cur	4	4	617	295	322	52.70	61.27	-7.031	10.479	-27.570	13.508	0.502	0.938	0.000	0.00%

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Region	Analysis	Studies	k	Number of subjects			Age (years)		Meta-analysis results							
				Total	HC	DEP	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2
					(M: 103, F: 192)	(M: 109, F: 213)										
GMV	**HC vs DEP**	15	19	1788	823	965	39.77	41.72	5.541	2.437	0.765	10.318	**0.023**	0.276	0.000	0.00%
					(M: 372, F: 451)	(M: 392, F: 573)										
GMV	HC vs DEP-Mix	4	4	512	261	251	42.88	42.46	1.999	5.425	-8.633	12.632	0.712	0.607	0.000	0.00%
					(M: 109, F: 152)	(M: 98, F: 153)										
	HC vs DEP-FE	5	5	415	224	191	36.72	36.94	6.125	4.440	-2.578	14.827	0.168	0.546	0.000	0.00%
					(M: 95, F: 129)	(M: 76, F: 115)										
	HC vs DEP-TR	3	3	421	175	246	38.73	42.59	10.666	8.021	-5.054	26.387	0.184	0.136	93.016	47.89%
					(M: 94, F: 81)	(M: 121, F: 125)										
WMV	HC vs DEP	10	12	1245	508	737	44.66	44.42	-2.351	3.377	-8.969	4.267	0.486	0.217	12.782	9.34%
					(M: 221, F: 287)	(M: 313, F: 424)										
	HC vs DEP-Mix	3	3	460	239	221	40.35	38.62	-0.346	5.599	-11.320	10.628	0.951	0.687	0.000	0.00%
					(M: 104, F: 135)	(M: 91, F: 130)										
	HC vs DEP-FE	3	3	226	108	118	39.08	37.56	6.645	9.677	-12.323	25.612	0.492	0.237	75.471	25.98%
					(M: 41, F: 67)	(M: 47, F: 71)										
ICV	HC vs DEP	42	59	3775	1728	2047	48.86	51.07	5.806	4.516	-3.045	14.658	0.199	0.069	220.756	21.38%
					(M: 618, F: 1110)	(M: 691, F: 1356)										
	HC vs DEP-Mix	25	25	2235	1080	1155	50.51	54.79	11.731	5.838	0.288	23.173	**0.045**	0.278	121.417	**15.50%**
					(M: 383, F: 697)	(M: 364, F: 791)										
	HC vs DEP-EO	5	5	434	274	160	56.56	57.37	5.162	18.859	-31.800	42.125	0.784	0.106	839.154	48.09%
					(M: 80, F: 194)	(M: 23, F: 137)										
	HC vs DEP-LO	3	3	198	110	88	71.76	74.29	13.652	18.797	-23.189	50.492	0.468	0.542	0.000	0.00%
					(M: 38, F: 72)	(M: 26, F: 62)										
	HC vs DEP-FE	4	4	337	231	106	36.53	39.57	8.328	18.012	-26.975	43.631	0.644	0.268	327.309	23.99%

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Region	Analysis	Studies	k	Number of subjects			Age (years)		Meta-analysis results							
				Total	HC	DEP	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2
					(M: 102, F: 129)	(M: 37, F: 69)										
	HC vs DEP-ME	4	4	493	320	173	35.78	47.09	22.036	20.536	-18.214	62.286	0.283	0.062	919.847	**56.87%**
					(M: 152, F: 168)	(M: 60, F: 113)										
	HC vs DEP-noMed	6	6	302	176	126	44.98	44.94	-18.519	16.384	-50.630	13.592	0.258	0.666	0.000	0.00%
					(M: 61, F: 115)	(M: 37, F: 89)										
ICV	HC vs DEP-Med	4	4	192	137	55	46.32	42.99	-0.831	23.732	-47.345	45.683	0.972	0.977	0.000	0.00%
					(M: 55, F: 82)	(M: 21, F: 34)										
	HC vs DEP-TR	3	3	366	138	228	40.36	43.18	-0.749	18.685	-37.371	35.874	0.968	0.987	0.000	0.00%
					(M: 61, F: 77)	(M: 106, F: 122)										
	HC vs DEP-Rem	3	5	266	140	126	53.47	49.54	-14.587	14.135	-42.291	13.116	0.302	0.310	0.000	0.00%
					(M: 44, F: 96)	(M: 55, F: 71)										
	HC vs DEP-Cur	5	5	386	210	176	56.51	53.37	-6.795	19.324	-44.670	31.079	0.725	0.125	627.956	34.19%
					(M: 68, F: 142)	(M: 59, F: 117)										
THcV	**HC vs DEP**	42	61	3879	1737	2142	44.60	47.84	0.202	0.040	0.123	0.281	**<0.0001**	**<0.0001**	0.072	**86.58%**
					(M: 651, F: 1086)	(M: 788, F: 1354)										
	HC vs DEP-Mix	24	26	1826	881	945	46.13	50.79	0.267	0.059	0.150	0.383	**<0.0001**	**<0.0001**	0.071	**83.25%**
					(M: 324, F: 557)	(M: 334, F: 611)										
	HC vs DEP-EO	4	4	344	197	147	69.18	68.32	0.153	0.096	-0.035	0.340	0.111	0.087	0.019	**53.55%**
					(M: 44, F: 153)	(M: 26, F: 121)										
	HC vs DEP-LO	7	7	488	266	222	67.13	68.07	0.347	0.100	0.151	0.543	**0.001**	**<0.0001**	0.049	**77.86%**
					(M: 73, F: 193)	(M: 67, F: 155)										
	HC vs DEP-FE	7	8	497	310	187	35.66	37.50	0.105	0.108	-0.106	0.316	0.329	**0.001**	0.064	**73.46%**
					(M: 140, F: 170)	(M: 75, F: 112)										

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				Number of subjects			Age (years)		Meta-analysis results							
Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	τ^2	I^2
	HC vs DEP-ME	4	5	500	316 (M: 153, F: 163)	184 (M: 69, F: 115)	35.10	47.02	0.320	0.091	0.141	0.499	**0.001**	**0.011**	0.024	**68.43%**
	HC vs DEP-no Med	3	3	138	74 (M: 25, F: 49)	64 (M: 19, F: 45)	39.61	37.43	0.121	0.168	-0.209	0.451	0.471	0.084	0.049	**59.43%**
	HC vs DEP TR	3	3	352	130 (M: 63, F: 67)	222 (M: 112, F: 110)	37.77	42.74	0.546	0.284	-0.011	1.103	0.055	**<0.0001**	0.207	**96.82%**
	HC vs DEP-Rem	6	8	603	364 (M: 132, F: 232)	239 (M: 91, F: 148)	44.00	46.10	-0.022	0.050	-0.121	0.076	0.657	0.841	0.000	0.00%
THcV	HC vs DEP-Cur	7	7	967	464 (M: 184, F: 280)	503 (M: 191, F: 312)	46.34	52.47	0.108	0.078	-0.044	0.260	0.162	**0.010**	0.025	**64.83%**
RHcV	**HC vs DEP**	34	50	3447	1544 (M: 579, F: 965)	1903 (M: 700, F: 1203)	44.35	47.86	0.114	0.023	0.069	0.159	**<0.0001**	**<0.0001**	0.017	**76.61%**
	HC vs DEP-Mix	20	21	1594	783 (M: 287, F: 496)	811 (M: 280, F: 531)	45.91	50.55	0.137	0.031	0.075	0.198	**<0.0001**	**<0.0001**	0.013	**68.44%**
	HC vs DEP-EO	4	4	344	197 (M: 44, F: 153)	147 (M: 26, F: 121)	69.18	68.32	0.118	0.054	0.012	0.223	**0.029**	0.133	0.005	44.34%
	HC vs DEP-LO	6	6	451	244 (M: 73, F: 171)	207 (M: 67, F: 140)	66.78	67.73	0.204	0.061	0.085	0.323	**0.001**	**0.047**	0.011	**54.43%**
	HC vs DEP-FE	7	8	497	310 (M: 140, F: 170)	187 (M: 75, F: 112)	35.66	37.50	0.047	0.062	-0.074	0.168	0.444	**0.012**	0.017	**61.02%**
	HC vs DEP-ME	4	5	500	316 (M: 153, F: 163)	184 (M: 69, F: 115)	35.10	47.02	0.183	0.030	0.125	0.242	**<0.0001**	0.206	0.000	5.69%
	HC vs DEP-Rem	6	8	603	364 (M: 132, F: 232)	239 (M: 91, F: 148)	44.00	46.10	-0.020	0.033	-0.085	0.046	0.558	0.932	0.000	0.00%

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Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP-Cur	5	5	847	409 (M: 155, F: 254)	438 (M: 167, F: 271)	47.53	54.69	0.052	0.047	-0.040	0.144	0.268	0.137	0.004	40.92%
LHcV	**HC vs DEP**	34	50	3447	1544 (M: 579, F: 965)	1903 (M: 700, F: 1203)	44.35	47.86	0.105	0.023	0.060	0.150	**<0.0001**	**<0.0001**	0.017	**77.01%**
	HC vs DEP-Mix	20	21	1594	783 (M: 287, F: 496)	811 (M: 280, F: 531)	45.91	50.55	0.133	0.031	0.071	0.194	**<0.0001**	**<0.0001**	0.013	**67.97%**
	HC vs DEP-EO	4	4	344	197 (M: 44, F: 153)	147 (M: 26, F: 121)	69.18	68.32	0.051	0.041	-0.030	0.132	0.214	0.306	0.001	14.68%
	HC vs DEP-LO	6	6	451	244 (M: 73, F: 171)	207 (M: 67, F: 140)	66.78	67.73	0.176	0.049	0.081	0.271	**0.0003**	0.183	0.005	34.90%
LHcV	HC vs DEP-FE	7	8	497	310 (M: 140, F: 170)	187 (M: 75, F: 112)	35.66	37.50	0.068	0.052	-0.033	0.169	0.188	**0.040**	0.011	**52.77%**
	HC vs DEP-ME	4	5	500	316 (M: 153, F: 163)	184 (M: 69, F: 115)	35.10	47.02	0.121	0.054	0.015	0.227	**0.025**	**0.023**	0.008	**62.41%**
	HC vs DEP-Rem	6	8	603	364 (M: 132, F: 232)	239 (M: 91, F: 148)	44.00	46.10	-0.001	0.034	-0.067	0.065	0.981	0.789	0.000	0.00%
	HC vs DEP-Cur	5	5	847	409 (M: 155, F: 254)	438 (M: 167, F: 271)	47.53	54.69	0.042	0.048	-0.052	0.136	0.379	0.129	0.005	46.31%
TAV	HC vs DEP	15	25	1181	463 (M: 167, F: 296)	718 (M: 287, F: 431)	46.31	47.12	0.091	0.061	-0.029	0.211	0.139	**<0.0001**	0.081	**90.25%**
	HC vs DEP-Mix	6	6	362	167 (M: 52, F: 115)	195 (M: 59, F: 136)	46.77	50.08	0.018	0.087	-0.153	0.188	0.203	**0.001**	0.035	**78.81%**
	HC vs DEP-FE	3	3	177	91	86	35.46	35.72	-0.146	0.182	-0.503	0.211	0.424	**<0.0001**	0.087	**89.00%**

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Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
					(M: 43, F: 48)	(M: 40, F: 46)										
	HC vs DEP-Rem	5	7	274	138	136	40.95	40.50	-0.035	0.049	-0.131	0.060	0.470	0.075	0.007	42.17%
					(M: 47, F: 91)	(M: 47, F: 89)										
	HC vs DEP-Cur	4	4	193	103	90	36.81	36.88	-0.025	0.092	-0.204	0.155	0.788	0.122	0.017	**50.56%**
					(M: 42, F: 61)	(M: 25, F: 65)										
RAV	HC vs DEP	13	23	1071	427	644	46.48	47.26	0.044	0.029	-0.014	0.101	0.136	**<0.0001**	0.014	**77.75%**
					(M: 150, F: 277)	(M: 267, F: 377)										
	HC vs DEP-Mix	5	5	301	151	150	45.81	49.51	0.001	0.035	-0.067	0.069	0.985	0.191	0.002	31.11%
					(M: 45, F: 106)	(M: 44, F: 106)										
	HC vs DEP-FE	3	3	177	91	86	35.46	35.72	-0.074	0.087	-0.244	0.096	0.396	**0.017**	0.016	**73.80%**
					(M: 43, F: 48)	(M: 40, F: 46)										
	HC vs DEP-Rem	5	7	274	138	136	40.95	40.50	-0.016	0.024	-0.064	0.032	0.510	0.632	0.000	0.12%
					(M: 47, F: 91)	(M: 47, F: 89)										
RAV	HC vs DEP-Cur	3	3	144	83	61	37.25	37.11	-0.032	0.038	-0.106	0.043	0.402	0.830	0.000	0.00%
					(M: 32, F: 51)	(M: 20, F: 41)										
LAV	HC vs DEP	13	23	1071	427	644	46.48	47.26	0.026	0.035	-0.042	0.095	0.453	**<0.0001**	0.022	**84.24%**
					(M: 150, F: 277)	(M: 267, F: 377)										
	HC vs DEP-Mix	5	5	301	151	150	45.81	49.51	-0.013	0.053	-0.117	0.090	0.803	**0.008**	0.010	**72.34%**
					(M: 45, F: 106)	(M: 44, F: 106)										
	HC vs DEP-FE	3	3	177	91	86	35.46	35.72	-0.064	0.099	-0.257	0.130	0.521	**0.001**	0.024	**82.32%**
					(M: 43, F: 48)	(M: 40, F: 46)										
	HC vs DEP-Rem	5	7	274	138	136	40.95	40.50	-0.027	0.033	-0.091	0.038	0.418	0.118	0.003	36.44%
					(M: 47, F: 91)	(M: 47, F: 89)										

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				Total	HC	DEP	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2
	HC vs DEP-Cur	3	3	144	83 (M: 32, F: 51)	61 (M: 20, F: 41)	37.25	37.11	-0.059	0.037	-0.132	0.013	0.109	0.878	0.000	0.00%
TPuV	**HC vs DEP**	13	20	1693	716 (M: 256, F: 460)	977 (M: 382, F: 595)	44.09	47.59	0.212	0.075	0.065	0.359	**0.005**	**0.0001**	0.059	**59.70%**
	HC vs DEP-Mix	8	8	856	375 (M: 116, F: 259)	481 (M: 156, F: 325)	48.43	54.61	0.203	0.074	0.058	0.348	**0.006**	0.653	0.000	0.00%
RPuV	**HC vs DEP**	9	15	1248	518 (M: 192 F: 326)	730 (M: 316, F: 414)	45.97	49.14	0.088	0.044	0.002	0.175	**0.046**	0.085	0.010	37.43%
	HC vs DEP-Mix	5	5	524	224 (M: 70, F: 154)	300 (M: 109, F: 191)	53.66	61.13	0.094	0.062	-0.028	0.215	0.131	0.857	0.000	0.00%
LPuV	HC vs DEP	9	15	1248	518 (M: 192, F: 326)	730 (M: 316, F: 414)	45.97	49.14	0.081	0.047	-0.010	0.173	0.081	0.072	0.011	39.47%
	HC vs DEP-Mix	5	5	524	224 (M: 70, F: 154)	300 (M: 109, F: 191)	53.66	61.13	0.071	0.059	-0.044	0.187	0.226	0.734	0.000	0.00%
TCV	HC vs DEP	13	20	1686	697 (M: 257, F: 440)	989 (M: 377, F: 612)	43.41	48.00	0.031	0.059	-0.085	0.147	0.597	**0.005**	0.031	**51.88%**
TCV	HC vs DEP-Mix	8	8	849	356 (M: 117, F: 239)	493 (M: 151, F: 342)	47.33	55.26	0.140	0.086	-0.028	0.308	0.102	0.243	0.016	28.16%
RCV	HC vs DEP	9	15	1241	499 (M: 193, F: 306)	742 (M: 311, F: 431)	45.09	49.67	0.017	0.036	-0.053	0.086	0.635	0.106	0.006	33.31%
	HC vs DEP-Mix	5	5	517	205 (M: 71, F: 134)	312 (M: 104, F: 208)	52.23	61.91	0.060	0.051	-0.039	0.160	0.235	0.378	0.000	1.71%
LCV	HC vs DEP	9	15	1241	499 (M: 193, F: 306)	742 (M: 311, F: 431)	45.09	49.67	0.021	0.032	-0.041	0.083	0.507	0.129	0.004	25.39%

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Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP-Mix	5	5	517	205 (M: 71, F: 134)	312 (M: 104, F: 208)	52.23	61.91	0.080	0.053	-0.024	0.184	0.130	0.225	0.003	24.11%
TPaV	HC vs DEP	9	16	1231	546 (M: 209, F: 337)	685 (M: 298, F: 387)	40.29	42.70	0.051	0.028	-0.004	0.106	0.070	**0.0001**	0.008	**67.88%**
	HC vs DEP-Mix	5	5	494	252 (M: 87, F: 165)	242 (M: 83, F: 159)	40.49	44.86	0.044	0.038	-0.031	0.118	0.248	0.183	0.003	38.94%
RPaV	HC vs DEP	7	13	947	411 (M: 170, F: 241)	536 (M: 258, F: 278)	40.75	42.54	0.028	0.020	-0.012	0.068	0.165	**0.001**	0.003	**64.66%**
	HC vs DEP-Mix	3	3	223	117 (M: 48, F: 69)	106 (M: 51, F: 55)	42.35	49.70	0.054	0.033	-0.011	0.120	0.104	0.978	0.000	0.00%
LPaV	HC vs DEP	7	13	947	411 (M: 170, F: 241)	536 (M: 258, F: 278)	40.75	42.54	0.025	0.015	-0.004	0.054	0.095	0.144	0.001	19.16%
	HC vs DEP-Mix	3	3	223	117 (M: 48, F: 69)	106 (M: 51, F: 55)	42.35	49.70	0.018	0.038	-0.056	0.092	0.631	0.244	0.001	25.99%
TTV	HC vs DEP	7	13	938	395 (M: 165, F: 230)	543 (M: 251, F: 292)	42.50	43.29	0.140	0.194	-0.242	0.520	0.473	**<0.0001**	0.400	**87.36%**
	HC vs DEP-Mix	3	3	214	101 (M: 43, F: 58)	113 (M: 44, F: 69)	49.44	52.85	0.774	0.184	0.414	1.134	**<0.0001**	0.751	0.000	0.00%
RTV	HC vs DEP	6	12	874	363 (M: 151, F: 212)	511 (M: 237, F: 274)	41.50	42.61	0.091	0.097	-0.100	0.281	0.351	**<0.0001**	0.081	**76.54%**
LTV	HC vs DEP	6	12	874	363 (M: 151, F: 212)	511 (M: 237, F: 274)	41.50	42.61	0.036	0.098	-0.156	0.227	0.715	**<0.0001**	0.076	**73.60%**
TAcV	HC vs DEP	4	9	563	226 (M: 83, F: 143)	337 (M: 136, F: 201)	35.20	37.45	-0.018	0.025	-0.067	0.032	0.491	**0.001**	0.004	**69.57%**

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Supplemental Table S5. Assessment of anxiety comorbidity per brain region

k: number of samples or subsamples, n: total number of subjects, HC: healthy controls, DEP: depressed participants, M: males, F: females, MD: mean difference, SE: standard error, CI: confidence interval, Qp: Q-statistic p-value, τ^2: variance of true effects, I^2: proportion real differences between studies, TBV: total brain, GMV: grey matter, WMV: white matter, ICV: intracranial, THcV: total hippocampus, RHcV: right hippocampus, LHcV: left hippocampus, TAV: total amygdala, RAV: right amygdala, LAV: left amygdala, TPuV: total putamen, RPuV: right putamen, LPuV: left putamen, TCV: total caudate, RCV: right caudate, LCV: left caudate, TPaV: total pallidum, RPaV: right pallidum, LPaV: left pallidum, TTV: total thalamus, RTV: right thalamus, LTV: left thalamus volumes, Mix: heterogeneous group of depressed, EO: early-onset depression, LO: late-onset depression, FE: first episode, ME: multiple episodes, noMed: not taking antidepressants, Med: taking antidepressants, TR: treatment-resistant depression, Rem: depression in remission, Cur: currently in depression, no ANX: no comorbidity, ANX: comorbidity. Bold font indicates significance at $p \leq 0.05$ and $I^2 > 50\%$.

				Number of subjects			Age (years)		Meta-analysis results							
Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
TBV	HC vs DEP no ANX	10	13	1190	472 (M: 157, F: 315)	718 (M: 239, F: 479)	56.74	56.78	-7.371	6.963	-21.017	6.276	0.290	0.483	0.000	0.00%
	HC vs DEP-Mix no ANX	4	4	509	202 (M: 65, F: 137)	307 (M: 92, F: 215)	71.24	71.06	1.279	10.776	-19.841	22.400	0.906	0.860	0.000	0.00%
	HC vs DEP-EO no ANX	3	3	205	104 (M: 35, F: 69)	101 (M: 25, F: 76)	71.58	68.05	9.827	16.042	-21.615	41.269	0.540	0.638	0.000	0.00%
	HC vs DEP-LO no ANX	3	3	191	104 (M: 35, F: 69)	87 (M: 35, F: 52)	71.58	72.82	7.435	15.440	-22.828	37.697	0.630	0.463	0.000	0.00%
	HC vs DEP ANX	4	6	458	214 (M: 78, F: 136)	244 (M: 83, F: 161)	36.02	36.10	-1.866	10.281	-22.015	18.284	0.856	0.850	0.000	0.00%

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Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
GMV	**HC vs DEP no ANX**	8	10	892	387 (M: 179, F: 208)	505 (M: 218, F: 287)	40.68	43.04	11.005	4.810	1.578	20.432	**0.022**	0.547	22.880	9.86%
	HC vs DEP-FE no ANX	3	3	178	98 (M: 55, F: 43)	80 (M: 37, F: 43)	40.22	40.25	15.396	9.344	-2.919	33.710	0.099	0.439	0.000	0.00%
GMV	HC vs DEP ANX	5	6	742	375 (M: 150, F: 225)	367 (M: 131, F: 236)	37.06	38.11	3.559	3.513	-3.327	10.445	0.311	0.153	0.000	0.00%
WMV	HC vs DEP no ANX	7	8	779	320 (M: 133, F: 187)	459 (M: 196, F: 263)	46.78	47.01	3.662	4.126	-4.425	11.749	0.375	0.486	0.000	0.00%
ICV	**HC vs DEP no ANX**	23	30	2353	1083 (M: 391, F: 692)	1270 (M: 421, F: 849)	51.55	54.47	13.802	6.204	1.642	25.962	**0.026**	0.274	191.157	17.78%
	HC vs DEP-Mix no ANX	16	16	1686	809 (M: 299, F: 510)	877 (M: 282, F: 595)	52.24	57.60	12.765	7.932	-2.782	28.312	0.108	0.192	230.603	24.89%
	HC vs DEP-EO no ANX	4	4	365	233 (M: 80, F: 153)	132 (M: 23, F: 109)	55.54	55.95	21.650	15.926	-9.564	52.864	0.174	0.451	0.000	0.00%
	HC vs DEP-FE no ANX	3	3	282	197 (M: 92, F: 105)	85 (M: 30, F: 55)	34.57	38.38	20.913	16.023	-10.491	52.317	0.192	0.328	0.000	0.00%
	HC vs DEP-noMed no ANX	3	3	134	82 (M: 15, F: 67)	52 (M: 13, F: 39)	35.53	37.70	-37.443	23.304	-83.119	8.233	0.108	0.650	0.000	0.00%
	HC vs DEP ANX	9	16	654	270 (M: 92, F: 178)	384 (M: 157, F: 227)	39.47	38.87	-4.747	9.293	-22.961	13.467	0.610	**0.040**	411.763	38.08%
	HC vs DEP-Mix ANX	5	5	325	167 (M: 50, F: 117)	158 (M: 43, F: 115)	37.89	38.66	4.848	12.412	-19.479	29.175	0.696	0.175	206.245	25.43%
THcV	**HC vs DEP no ANX**	22	28	2121	952	1169	50.29	54.02	0.246	0.058	0.133	0.360	**<0.0001**	**<0.0001**	0.073	**83.74%**

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				Total	HC	DEP	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2
					(M: 360, F: 592)	(M: 422, F: 747)										
	HC vs DEP-Mix no ANX	16	17	1344	651	693	50.32	55.09	0.261	0.077	0.111	0.411	**0.001**	**<0.0001**	0.080	**85.31%**
					(M: 248, F: 403)	(M: 251, F: 442)										
	HC vs DEP-EO no ANX	3	3	275	156	119	70.97	69.33	0.107	0.109	-0.107	0.321	0.327	0.068	0.022	**62.09%**
					(M: 44, F: 112)	(M: 26, F: 93)										
THcV	**HC vs DEP-LO no ANX**	5	5	409	223	186	70.41	71.64	0.373	0.099	0.179	0.567	**0.0002**	**0.027**	0.032	**65.14%**
					(M: 66, F: 157)	(M: 63, F: 123)										
THcV	HC vs DEP-FE no ANX	6	6	441	280	161	34.93	37.14	0.065	0.119	-0.168	0.297	0.585	**0.001**	0.064	**77.13%**
					(M: 129, F: 151)	(M: 62, F: 99)										
	HC vs DEP-Rem no ANX	4	4	274	158	116	55.74	54.16	-0.020	0.068	-0.153	0.113	0.768	0.613	0.000	0.00%
					(M: 42, F: 116)	(M: 43, F: 73)										
	HC vs DEP ANX	10	21	1049	417	632	35.32	37.66	0.105	0.081	-0.054	0.264	0.197	**<0.0001**	0.104	**90.13%**
					(M: 162, F: 255)	(M: 276, F: 356)										
	HC vs DEP-Mix ANX	4	4	228	113	115	31.69	35.80	0.302	0.207	-0.104	0.708	0.145	**<0.0001**	0.154	**91.54%**
					(M: 34, F: 79)	(M: 40, F: 75)										
RHcV	**HC vs DEP no ANX**	20	25	2006	903	1103	50.14	53.85	0.134	0.030	0.075	0.193	**<0.0001**	**<0.0001**	0.015	**69.53%**
					(M: 339, F: 564)	(M: 387, F: 716)										
	HC vs DEP-Mix no ANX	14	15	1229	602	627	50.10	54.91	0.128	0.037	0.056	0.201	**0.001**	**0.0002**	0.013	**67.88%**
					(M: 227, F: 375)	(M: 216, F: 411)										
	HC vs DEP-EO no ANX	3	3	275	156	119	70.97	69.33	0.084	0.050	-0.015	0.183	0.094	0.271	0.002	28.16%
					(M: 44, F: 112)	(M: 26, F: 93)										
	HC vs DEP-LO no ANX	5	5	409	223	186	70.41	71.64	0.189	0.061	0.070	0.308	**0.002**	0.051	0.010	**57.59%**
					(M: 66, F: 157)	(M: 63, F: 123)										
	HC vs DEP-FE no ANX	6	6	441	280	161	34.93	37.14	0.032	0.072	-0.109	0.173	0.653	**0.007**	0.021	**68.74%**

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Region	Analysis	Studies	k	Number of subjects			Age (years)		Meta-analysis results							
				Total	HC	DEP	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2
					(M: 129, F: 151)	(M: 62, F: 99)										
	HC vs DEP-Rem no ANX	4	4	274	158	116	55.74	54.16	-0.007	0.044	-0.093	0.079	0.877	0.645	0.000	0.00%
					(M: 42, F: 116)	(M: 43, F: 73)										
	HC vs DEP ANX	9	20	1006	399	607	35.21	37.78	0.057	0.043	-0.027	0.140	0.182	**<0.0001**	0.023	**81.49%**
					(M: 156, F: 243)	(M: 266, F: 341)										
	HC vs DEP-Mix ANX	4	4	228	113	115	31.69	35.80	0.173	0.108	-0.038	0.384	0.107	**0.001**	0.037	**83.69%**
					(M: 34, F: 79)	(M: 40, F: 75)										
LHcV	**HC vs DEP no ANX**	20	25	2006	903	1103	50.14	53.85	0.124	0.029	0.067	0.180	**<0.0001**	**<0.0001**	0.013	**67.74%**
					(M: 339, F: 564)	(M: 387, F: 716)										
LHcV	**HC vs DEP-Mix no ANX**	14	15	1229	602	627	50.10	54.91	0.137	0.034	0.070	0.204	**<0.0001**	**0.001**	0.010	**62.22%**
					(M: 227, F: 375)	(M: 216, F: 411)										
	HC vs DEP-EO no ANX	3	3	275	156	119	70.97	69.33	0.036	0.053	-0.069	0.141	0.500	0.181	0.003	39.69%
					(M: 44, F: 112)	(M: 26, F: 93)										
	HC vs DEP-LO no ANX	5	5	409	223	186	70.41	71.64	0.167	0.049	0.071	0.264	**0.001**	0.172	0.005	38.87%
					(M: 66, F: 157)	(M: 63, F: 123)										
	HC vs DEP-FE no ANX	6	6	441	280	161	34.93	37.14	0.041	0.049	-0.055	0.137	0.406	0.165	0.005	34.46%
					(M: 129, F: 151)	(M: 62, F: 99)										
	HC vs DEP-Rem no ANX	4	4	274	158	116	55.74	54.16	-0.002	0.043	-0.086	0.082	0.962	0.533	0.000	0.00%
					(M: 42, F: 116)	(M: 43, F: 73)										
	HC vs DEP ANX	9	20	1006	399	607	35.21	37.78	0.073	0.044	-0.013	0.159	0.096	**<0.0001**	0.026	**83.45%**
					(M: 156, F: 243)	(M: 266, F: 341)										
	HC vs DEP-Mix ANX	4	4	228	113	115	31.69	35.80	0.111	0.107	-0.098	0.320	0.297	**<0.0001**	0.037	**83.78%**
					(M: 34, F: 79)	(M: 40, F: 75)										
TAV	HC vs DEP no ANX	9	12	705	314	391	50.53	54.13	0.199	0.109	-0.014	0.412	0.067	**<0.0001**	0.130	**93.25%**

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Region	Analysis	Studies	k	Number of subjects			Age (years)		Meta-analysis results							
				Total	HC	DEP	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2
					(M: 110, F: 204)	(M: 143, F: 248)										
	HC vs DEP-Mix no ANX	4	4	257	128	129	48.29	52.03	0.040	0.075	-0.108	0.188	0.600	**0.039**	0.015	**66.18%**
					(M: 45, F: 83)	(M: 44, F: 85)										
	HC vs DEP-FE no ANX	3	3	177	91	86	35.46	35.72	-0.146	0.182	-0.503	0.211	0.424	**<0.0001**	0.087	**89.00%**
					(M: 43, F: 48)	(M: 40, F: 46)										
TAV	HC vs DEP-Rem no ANX	3	3	127	70	57	44.49	44.24	0.061	0.157	-0.246	0.369	0.697	**0.012**	0.056	**76.19%**
					(M: 18, F: 52)	(M: 11, F: 46)										
	HC vs DEP ANX	4	11	366	113	253	35.23	36.65	-0.066	0.026	-0.116	-0.016	**0.010**	0.249	0.000	0.05%
					(M: 40, F: 73)	(M: 124, F: 129)										
RAV	HC vs DEP no ANX	9	12	705	314	391	50.53	54.13	0.094	0.052	-0.009	0.195	0.072	**<0.0001**	0.026	**84.76%**
					(M: 110, F: 204)	(M: 143, F: 248)										
RAV	HC vs DEP-Mix no ANX	4	4	257	128	129	48.29	52.03	0.022	0.030	-0.037	0.080	0.465	0.265	0.000	0.02%
					(M: 45, F: 83)	(M: 44, F: 85)										
	HC vs DEP-FE no ANX	3	3	177	91	86	35.46	35.72	-0.074	0.087	-0.244	0.096	0.396	**0.017**	0.016	**73.80%**
					(M: 43, F: 48)	(M: 40, F: 46)										
	HC vs DEP-Rem no ANX	3	3	127	70	57	44.49	44.24	-0.003	0.079	-0.158	0.152	0.971	0.141	0.009	48.99%
					(M: 18, F: 52)	(M: 11, F: 46)										
	HC vs DEP ANX	4	11	366	113	253	35.23	36.65	-0.013	0.018	-0.047	0.022	0.479	0.694	0.000	0.09%
					(M: 40, F: 73)	(M: 124, F: 129)										
LAV	HC vs DEP no ANX	9	4	705	314	391	50.53	54.13	0.105	0.056	-0.004	0.213	0.059	**<0.0001**	0.031	**87.46%**
					(M: 110, F: 204)	(M: 143, F: 248)										
	HC vs DEP-Mix no ANX	4	4	257	128	129	48.29	52.03	0.028	0.042	-0.053	0.110	0.497	0.119	0.003	49.46%
					(M: 45, F: 83)	(M: 44, F: 85)										
	HC vs DEP-FE no ANX	3	3	177	91	86	35.46	35.72	-0.064	0.099	-0.257	0.130	0.521	**0.001**	0.024	**82.32%**

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Region	Analysis	Studies	k	Number of subjects			Age (years)		Meta-analysis results							
				Total	HC	DEP	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2
	HC vs DEP-Rem no ANX	3	3	127	(M: 43, F: 48) 70 (M: 18, F: 52)	(M: 40, F: 46) 57 (M: 11, F: 46)	44.49	44.24	0.050	0.083	-0.113	0.212	0.549	0.063	0.013	**62.05%**
	HC vs DEP ANX	4	11	366	113 (M: 40, F: 73)	253 (M: 124, F: 129)	35.23	36.65	-0.062	0.019	-0.099	-0.025	**0.001**	0.605	0.000	0.00%
TPuV	**HC vs DEP no ANX**	6	6	607	268 (M: 82, F: 186)	339 (M: 123, F: 216)	56.45	62.87	0.335	0.124	0.092	0.578	**0.007**	0.029	0.053	**58.96%**
	HC vs DEP-Mix no ANX	4	4	435	180 (M: 50, F: 130)	255 (M: 91, F: 164)	58.57	65.43	0.148	0.096	-0.040	0.336	0.123	0.422	0.000	0.00%
	HC vs DEP ANX	4	11	836	341 (M: 129, F: 212)	495 (M: 215, F: 280)	36.53	39.10	0.100	0.115	-0.125	0.325	0.384	**0.002**	0.075	**63.52%**
RPuV	**HC vs DEP no ANX**	6	6	607	268 (M: 82, F: 186)	339 (M: 123, F: 216)	56.45	62.87	0.167	0.053	0.063	0.271	**0.002**	0.503	0.001	2.61%
RPuV	HC vs DEP-Mix no ANX	4	4	435	180 (M: 50, F: 130)	255 (M: 91, F: 164)	58.57	65.43	0.087	0.070	-0.049	0.223	0.211	0.733	0.000	0.00%
LPuV	**HC vs DEP no ANX**	6	6	607	268 (M: 82, F: 186)	339 (M: 123, F: 216)	56.45	62.87	0.171	0.076	0.022	0.321	**0.025**	0.120	0.015	44.32%
	HC vs DEP-Mix no ANX	4	4	435	180 (M: 50, F: 130)	255 (M: 91, F: 164)	58.57	65.43	0.059	0.066	-0.070	0.188	0.367	0.607	0.000	0.00%
TCV	HC vs DEP no ANX	6	6	600	249 (M: 83, F: 166)	351 (M: 118, F: 233)	55.48	63.51	0.118	0.083	-0.045	0.281	0.156	0.132	0.015	36.44%
	HC vs DEP-Mix no ANX	4	4	428	161 (M: 51, F: 110)	267 (M: 86, F: 181)	57.32	66.16	0.121	0.146	-0.166	0.407	0.409	**0.049**	0.052	**62.73%**
	HC vs DEP ANX	4	11	836	341	495	36.53	39.10	-0.059	0.089	-0.233	0.115	0.505	**0.002**	0.046	**62.56%**

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Region	Analysis	Studies	k	Number of subjects			Age (years)		Meta-analysis results							
				Total	HC	DEP	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2
					(M: 129, F: 212)	(M: 215, F: 280)										
RCV	HC vs DEP no ANX	6	6	600	249	351	55.48	63.51	0.044	0.042	-0.039	0.126	0.300	0.540	0.000	0.03%
					(M: 83, F: 166)	(M: 118, F: 233)										
	HC vs DEP-Mix no ANX	4	4	428	161	267	57.32	66.16	0.041	0.063	-0.083	0.164	0.519	0.299	0.002	14.86%
					(M: 51, F: 110)	(M: 86, F: 181)										
LCV	HC vs DEP no ANX	6	6	600	249	351	55.48	63.51	0.078	0.047	-0.015	0.170	0.099	0.336	0.002	11.50%
					(M: 83, F: 166)	(M: 118, F: 233)										
	HC vs DEP-Mix no ANX	4	4	428	161	267	57.32	66.16	0.091	0.073	-0.052	0.234	0.212	0.150	0.009	41.19%
					(M: 51, F: 110)	(M: 86, F: 181)										
TPaV	HC vs DEP no ANX	4	4	306	161	145	50.08	56.85	0.079	0.045	-0.009	0.168	0.080	0.278	0.002	29.36%
					(M: 60, F: 101)	(M: 65, F: 80)										
	HC vs DEP ANX	4	11	836	341	495	37.11	39.10	0.039	0.040	-0.039	0.116	0.328	**<0.0001**	0.013	**78.85%**
					(M: 129, F: 212)	(M: 215, F: 280)										
RPaV	**HC vs DEP no ANX**	4	4	306	161	145	50.08	56.85	0.050	0.024	0.003	0.097	**0.039**	0.911	0.000	0.00%
					(M: 60, F: 101)	(M: 65, F: 80)										
LPaV	HC vs DEP no ANX	4	4	306	161	145	50.08	56.85	0.028	0.037	-0.045	0.101	0.454	0.149	0.002	44.08%
					(M: 60, F: 101)	(M: 65, F: 80)										
TTV	**HC vs DEP no ANX**	3	3	233	113	120	56.46	60.11	0.433	0.140	0.158	0.708	**0.002**	0.629	0.000	0.00%
					(M: 41, F: 72)	(M: 44, F: 76)										
RTV	**HC vs DEP no ANX**	3	3	233	113	120	56.46	60.11	0.220	0.096	0.032	0.408	**0.022**	0.799	0.000	0.00%
					(M: 41, F: 72)	(M: 44, F: 76)										
LTV	**HC vs DEP no ANX**	3	3	233	113	120	56.46	60.11	0.217	0.102	0.016	0.418	**0.034**	0.783	0.000	0.00%
					(M: 41, F: 72)	(M: 44, F: 76)										

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Supplemental Table S6. Sensitivity analyses on selection of homogeneous groups

Meta-analyses contrasting homogenous group selection in main analyses (HC vs DEP) and heterogeneous group selection (DEP SEN) . k: number of samples or subsamples, n: total number of participants, HC: healthy controls, DEP: depressed participants, MD: mean difference, SE: standard error, CI: confidence interval, Qp: Q-statistic p-value, τ^2: variance of true effects, I^2: proportion real differences between studies, zp: z-statistic p-value, TBV: total brain, ICV: intracranial, THcV: total hippocampus, RHcV: right hippocampus, LHcV: left hippocampus volumes. Bold font indicates significance at $p \leq 0.05$ and $I^2 > 50\%$.

				Number of subjects			Age (years)		Meta-analysis results								Contrast to main model	
Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**	**z-value**	**zp**
TBV	HC vs DEP	27	37	2618	1123	1495	50.73	53.19	-1.506	4.127	-9.595	6.583	0.715	0.279	0.000	0.00%	-0.007	0.994
					(M: 391, F: 732)	(M: 496, F: 999)												
	DEP SEN	27	35	2618	1123	1495	50.73	53.19	-1.465	4.177	-9.651	6.722	0.726	0.246	0.000	0.00%		
					(M: 391, F: 732)	(M: 496, F: 999)												
ICV	HC vs DEP	42	59	3775	1728	2047	48.86	51.07	5.806	4.516	-3.045	14.658	0.199	0.069	220.756	21.38%	0.259	0.796
					(M: 618, F: 1110)	(M: 691, F: 1356)												
	DEP SEN	42	53	3775	1728	2047	48.86	51.12	4.117	4.709	-5.113	13.348	0.382	0.053	226.942	22.69%		
					(M: 618, F: 1110)	(M: 691, F: 1356)												
THcV	**HC vs DEP**	42	61	3879	1737	2142	44.60	47.84	0.202	0.040	0.123	0.281	**<0.0001**	**<0.0001**	0.072	**86.58%**	0.147	0.883
					(M: 651, F: 1086)	(M: 788, F: 1354)												
	DEP SEN	42	55	3879	1737	2142	44.60	47.89	0.193	0.043	0.110	0.277	**<0.0001**	**<0.0001**	0.074	**87.53%**		
					(M: 651, F: 1086)	(M: 788, F: 1354)												
RHcV	**HC vs DEP**	34	50	3447	1544	1903	44.35	47.86	0.114	0.023	0.069	0.159	**<0.0001**	**<0.0001**	0.017	**76.61%**	0.188	0.851

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				Number of subjects			Age (years)		Meta-analysis results							Contrast to main model	
Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**	**z-value**	**zp**
					(M: 579, F: 965)	(M: 700, F: 1203)												
	DEP SEN	34	46	3447	1544	1903	44.35	47.91	0.108	0.024	0.060	0.156	**<0.0001**	**<0.0001**	0.017	**77.90%**		
					(M: 579, F: 965)	(M: 700, F: 1203)												
LHcV	**HC vs DEP**	34	50	3447	1544	1903	44.35	47.86	0.105	0.023	0.060	0.150	**<0.0001**	**<0.0001**	0.017	**77.01%**	0.087	0.930
					(M: 579, F: 965)	(M: 700, F: 1203)												
	DEP SEN	34	46	3447	1544	1903	44.35	47.91	0.102	0.024	0.054	0.149	**<0.0001**	**<0.0001**	0.017	**78.15%**		
					(M: 579, F: 965)	(M: 700, F: 1203)												

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Supplemental Table S7. Sensitivity analyses on selection of homogeneous groups in anxiety comorbidity assessment

Meta-analyses contrasting homogenous group selection in main analyses (HC vs DEP) and heterogeneous group selection (DEP SEN), excluding anxiety comorbidity (no ANX) and comorbid with anxiety (ANX). k: number of samples or subsamples, n: total number of participants, HC: healthy controls, DEP: depressed participants, MD: mean difference, SE: standard error, CI: confidence interval, Qp: Q-statistic p-value, τ^2: variance of true effects, I^2: proportion real differences between studies, zp: z-statistic p-value, TBV: total brain, ICV: intracranial, THcV: total hippocampus, RHcV: right hippocampus, LHcV: left hippocampus volumes. Bold font indicates significance at $p \leq 0.05$ and $I^2 > 50\%$.

				Number of subjects			Age (years)		Meta-analysis results								Contrast to main model	
Region	**Analysis**	**Studies**	**k**	**Total**	**HC**	**DEP**	**HC**	**DEP**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**	**z-value**	**zp**
TBV	HC vs DEP no ANX	10	13	1190	472 (M: 157, F: 315)	718 (M: 239, F: 479)	56.74	56.78	-7.371	6.963	-21.017	6.276	0.290	0.483	0.000	0.00%	0.030	0.976
	DEP no ANX SEN	10	11	1190	472 (M: 157, F: 315)	718 (M: 239, F: 479)	56.74	56.77	-7.670	7.210	-21.801	6.461	0.287	0.415	0.000	0.00%		
ICV	HC vs DEP no ANX	23	30	2353	1083 (M: 391, F: 692)	1270 (M: 421, F: 849)	51.55	54.47	13.802	6.204	1.642	25.962	**0.026**	0.274	191.157	17.78%	0.198	0.843
	DEP no ANX SEN	23	26	2353	1083 (M: 391, F: 692)	1270 (M: 421, F: 849)	51.55	54.54	12.013	6.548	-0.820	24.846	*0.067*	0.297	184.854	17.88%		
	HC vs DEP ANX	9	16	654	270 (M: 92, F: 178)	384 (M: 157, F: 227)	39.47	38.87	-4.747	9.293	-22.961	13.467	0.610	**0.040**	411.763	38.08%	0.088	0.930
	DEP ANX SEN	9	15	654	270	384	39.47	38.87	-5.949	10.036	-25.619	13.721	0.553	**0.029**	529.084	45.14%		

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Region	Analysis	Studies	k	Number of subjects			Age (years)		Meta-analysis results								Contrast to main model	
				Total	HC (M: 92, F: 178)	DEP (M: 157, F: 227)	HC	DEP	MD	SE	95% CI		p	Qp	τ^2	I^2	z-value	zp
THcV	**HC vs DEP no ANX**	22	28	2121	952 (M: 360, F: 592)	1169 (M: 422, F: 747)	50.29	54.02	0.246	0.058	0.133	0.360	**<0.0001**	**<0.0001**	0.073	**83.74%**	0.190	0.850
	DEP no ANX SEN	22	23	2121	952 (M: 360, F: 592)	1169 (M: 422, F: 747)	50.29	54.10	0.230	0.065	0.103	0.356	**0.0004**	**<0.0001**	0.077	**85.39%**		
RHcV	**HC vs DEP no ANX**	20	25	2006	903 (M: 339, F: 564)	1103 (M: 387, F: 716)	50.14	53.85	0.134	0.030	0.075	0.193	**<0.0001**	**<0.0001**	0.015	**69.53%**	0.195	0.845
	DEP no ANX SEN	20	21	2006	903 (M: 339, F: 564)	1103 (M: 387, F: 716)	50.14	53.93	0.125	0.034	0.059	0.191	**0.0002**	**<0.0001**	0.016	**72.22%**		
LHcV	**HC vs DEP no ANX**	20	25	2006	903 (M: 339, F: 564)	1103 (M: 387, F: 716)	50.14	53.85	0.124	0.029	0.067	0.180	**<0.0001**	**<0.0001**	0.013	**67.74%**	0.054	0.957
	DEP no ANX SEN	20	21	2006	903 (M: 339, F: 564)	1103 (M: 387, F: 716)	50.14	53.93	0.122	0.032	0.059	0.184	**0.0001**	**<0.0001**	0.014	**69.90%**		

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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Supplemental Table S8. Assessment of study influence

Leave-one-out method results per brain region. Reported meta-analyses are shown first (underlined) to aid comparison with leave-one-out method (EXC Ref). Analyses excluding all identified studies in leave-one-out method (EXC all) are also reported. k: number of samples or subsamples, HC: healthy controls, DEP: depressed participants, MD: mean difference, SE: standard error, CI: confidence interval, Qp: Q-statistic p-value, τ^2: variance of true effects, I^2: proportion real differences between studies, TBV: total brain, ICV: intracranial, GMV: grey matter, RHcV: right hippocampus, LHcV: left hippocampus, TAV: total amygdala, RAV: right amygdala, LAV: left amygdala volumes, Mix: heterogeneous group of depressed, FE: first episode, ME: multiple episodes, Abu: physical/sexual abuse, no ANX: analysis excluding anxiety comorbidity. Bold font indicates significance at $p \leq 0.05$ and $I^2 > 50\%$.

				Leave-one-out meta-analysis results							
Region	**Analysis**	**Studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
TBV	DEP	27	37	-1.506	4.127	-9.595	6.583	0.715	0.279	0.000	0.00%
	EXC Andreescu (2008)	26	36	-0.968	4.582	-9.948	8.013	0.833	0.242	42.674	5.76%
	EXC Devantier (2016)	26	36	0.328	4.334	-8.165	8.822	0.940	0.312	0.000	0.00%
	EXC Sawyer (2012)	26	36	-0.511	4.492	-9.315	8.293	0.910	0.253	25.623	3.54%
	EXC Stratmann (2014)	26	36	-1.211	4.563	-10.155	7.732	0.791	0.241	39.549	5.37%
	EXC all	23	33	2.434	5.853	-9.037	13.905	0.678	0.219	172.910	15.75%
	HC vs DEP-Mix	12	13	8.375	6.116	-3.612	20.361	0.171	0.183	0.000	0.00%
	EXC Andreescu (2008)	11	12	12.942	8.033	-2.803	28.686	0.107	0.171	129.310	17.40%
	EXC Stratmann (2014)	11	12	12.813	8.366	-3.585	29.211	0.126	0.156	176.982	22.44%
	EXC all	10	11	16.934	9.861	-2.394	36.262	0.086	0.167	261.362	25.68%
ICV	HC vs DEP	42	59	5.806	4.516	-3.045	14.658	0.199	0.069	220.756	21.38%
	EXC Meisenzahl (2010) DEP-ME	42	58	3.693	4.050	-4.245	11.631	0.362	0.175	62.912	7.06%

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Region	Analysis	Studies	k	Leave-one-out meta-analysis results							
				MD	SE	95% CI		p	Qp	τ^2	I^2
	EXC Taylor (2007)	41	58	6.658	4.678	-2.510	15.827	0.155	0.073	236.425	21.50%
	EXC Vythilingam (2002) DEP-Mix	42	58	5.395	4.790	-3.994	14.784	0.260	0.063	273.071	23.41%
ICV	EXC Vythilingam (2002) DEP-Abu	42	58	6.582	4.749	-2.727	15.891	0.166	0.073	253.428	21.76%
	EXC all	39	55	5.087	4.961	-4.636	14.810	0.305	0.167	171.862	13.14%
	DEP-Mix	25	25	11.731	5.838	0.288	23.173	**0.045**	0.278	121.417	15.50%
	EXC Meisenzahl (2010) DEP-Mix	24	24	8.345	5.264	-1.972	18.662	0.113	0.447	0.000	0.00%
	EXC Taylor (2007)	24	24	15.295	5.403	4.706	25.884	**0.005**	0.381	0.000	0.00%
	EXC Vithilingnam (2002) DEP-Mix	24	24	11.480	6.654	-1.562	24.521	0.085	0.232	201.785	20.42%
	EXC all	22	22	11.384	6.696	-1.741	24.509	0.089	0.464	0.000	0.00%
	HC vs DEP no ANX	23	30	13.802	6.204	1.642	25.962	**0.026**	0.274	191.157	17.78%
	EXC Meisenzahl (2010) DEP-Mix	23	29	10.110	5.800	-1.258	21.478	0.081	0.511	45.443	4.69%
	EXC Taylor (2007)	22	29	17.282	6.157	5.214	29.350	**0.005**	0.395	79.675	7.35%
	EXC all	21	28	13.928	6.106	1.959	25.896	**0.023**	0.607	0.000	0.00%
	HC vs DEP-Mix no ANX	16	16	12.765	7.932	-2.782	28.312	0.108	0.192	230.603	24.89%
	EXC Meisenzahl (2010) DEP-Mix	15	15	7.488	7.542	-7.293	22.269	0.321	0.375	72.444	8.52%
	EXC Taylor (2007)	15	15	18.089	7.884	2.637	33.541	**0.022**	0.330	91.377	9.90%
	EXC all	14	14	12.993	8.163	-3.006	28.991	0.111	0.462	0.000	0.00%
GMV	**DEP**	15	19	5.541	2.437	0.765	10.318	**0.023**	0.276	0.000	0.00%
	EXC Yang (2017) DEP-FE	15	18	5.955	3.004	0.068	11.843	**0.047**	0.227	19.229	12.18%

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Region	Analysis	Studies	k	Leave-one-out meta-analysis results MD	SE	95% CI		p	Qp	τ^2	I^2
RHcV	**DEP no ANX**	20	25	0.134	0.030	0.075	0.193	**<0.0001**	**<0.0001**	0.015	**69.53%**
	EXC Maller (2012)	19	24	0.118	0.027	0.065	0.171	**<0.0001**	**0.0003**	0.009	**58.35%**
LHcV	**DEP**	34	50	0.105	0.023	0.060	0.150	**<0.0001**	**<0.0001**	0.017	**77.01%**
	EXC Vithilingnam (2002) DEP-Abu	34	49	0.094	0.021	0.053	0.135	**<0.0001**	**<0.0001**	0.012	**69.79%**
LHcV	**DEP no ANX**	20	25	0.124	0.029	0.067	0.180	**<0.0001**	**<0.0001**	0.013	**67.74%**
	EXC Maller (2012)	19	24	0.108	0.026	0.058	0.158	**<0.0001**	**0.001**	0.008	**55.00%**
TAV	DEP	15	25	0.091	0.061	-0.029	0.211	0.139	**<.0001**	0.081	**90.25%**
	EXC Burke (2011) DEP-LO	15	24	0.050	0.048	-0.045	0.145	0.300	**<0.0001**	0.044	**83.53%**
RAV	DEP	13	23	0.044	0.029	-0.014	0.101	0.136	**<0.0001**	0.014	**77.75%**
	EXC Burke (2011) DEP-LO	13	22	0.022	0.020	-0.016	0.061	0.253	**0.004**	0.004	48.50%
LAV	HC vs DEP	13	23	0.026	0.035	-0.042	0.095	0.453	**<0.0001**	0.022	**84.24%**
	EXC Burke (2011) DEP-LO	13	22	0.005	0.028	-0.051	0.060	0.867	**<0.0001**	0.012	**74.75%**

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Supplemental Table S9. Assessment of bias

Evidence of publication bias with Egger regression test and trim-and-fill method. t: t-statistic, df: degrees of freedom, k: number of samples or subsamples, HC: healthy controls, DEP: depressed participants, MD: mean difference, SE: standard error, CI: confidence interval, Qp: Q-statistic p-value, τ^2: variance of true effects, I^2: proportion real differences between studies, TBV: total brain, GMV: grey matter, WMV: white matter, ICV: intracranial, THcV: total hippocampus, RHcV: right hippocampus, LHcV: left hippocampus, TAV: total amygdala, RAV: right amygdala, LAV: left amygdala, TPuV: total putamen, RPuV: right putamen, LPuV: left putamen, TCV: total caudate, RCV: right caudate, LCV: left caudate, TPaV: total pallidum, RPaV: right pallidum, LPaV: left pallidum, TAcV: total accumbens volumes, Mix: heterogeneous group of depressed, EO: early-onset depression, LO: late-onset depression, FE: first episode, ME: multiple episodes, noMed: not taking antidepressants, TR: treatment-resistant depression, Rem: depression in remission, Cur: currently in depression, no ANX: analysis excluding anxiety comorbidity, ANX: analysis comorbid with anxiety. Bold font indicates significance at $p \leq 0.05$ ($p \leq 0.1$ for Egger test) and $I^2 > 50\%$.

*Change of significance once corrected for publication bias.

		Egger test			Trim-and-fill									
Region	**Analysis**	**t**	**df**	**p**	**Missing studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
TBV	HC vs DEP	0.764	35	0.450	7 left side	44	-8.563	5.306	-18.962	1.836	0.107	**0.012**	393.460	36.47%
	HC vs DEP-Mix	1.179	11	0.263	2 left side	15	6.394	7.302	-7.917	20.705	0.381	0.091	162.326	22.18%
	HC vs DEP-LO*	-2.037	5	**0.097**	3 right side	10	39.086	14.962	9.762	68.411	**0.009**	**<0.0001**	1701.546	**86.96%**

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		Egger test			Trim-and-fill									
Region	**Analysis**	**t**	**df**	**p**	**Missing studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP no ANX*	0.281	11	0.784	4 left side	17	-15.170	6.622	-28.149	-2.191	**0.022**	0.279	42.399	5.65%
	HC vs DEP-Mix no ANX	-3.553	2	**0.071**	1 right side	5	4.502	10.078	-15.252	24.255	0.655	0.832	0.000	0.00%
	HC vs DEP-EO no ANX	0.526	1	0.692	2 left side	5	-5.200	12.970	-30.621	20.221	0.689	0.470	0.000	0.00%
GMV	DEP-TR	-0.333	1	0.795	1 right side	4	16.127	9.181	-1.866	34.121	0.079	0.056	205.714	**63.64%**
WMV	HC vs DEP-Mix	17.716	1	**0.036**	2 left side	5	-4.080	4.723	-13.337	5.177	0.388	0.665	0.000	0.00%
	HC vs DEP-FE	14.989	1	**0.042**	2 left side	5	-5.660	10.749	-26.728	15.408	0.599	0.054	331.782	**59.09%**
	HC vs DEP no ANX	0.194	6	0.853	1 left side	9	2.391	4.043	-5.533	10.315	0.554	0.355	0.000	0.00%
ICV	HC vs DEP	-0.032	57	0.975	3 right side	62	7.879	4.654	-1.242	16.999	0.091	**0.019**	290.557	25.67%
	HC vs DEP-Mix	-0.519	23	0.609	4 right side	29	17.426	6.151	5.369	29.482	**0.005**	0.073	245.109	25.51%
	HC vs DEP-LO	3.496	1	0.177	2 left side	5	-6.600	15.464	-36.909	23.709	0.670	0.311	53.750	4.45%
	HC vs DEP-FE	-1.288	2	0.327	1 right side	5	16.984	16.571	-15.496	49.463	0.305	0.212	293.425	20.65%
	HC vs DEP-ME	-0.279	2	0.806	1 right side	5	30.373	19.002	-6.870	67.615	0.110	0.058	925.159	**54.04%**

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		Egger test			Trim-and-fill									
Region	**Analysis**	**t**	**df**	**p**	**Missing studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP-noMed	-2.153	4	**0.098**	2 right side	8	-10.196	15.157	-39.904	19.511	0.501	0.618	0.000	0.00%
	HC vs DEP-Rem	1.403	3	0.255	2 left side	7	-28.269	15.197	-58.054	1.515	0.063	0.117	375.580	23.61%
	DEP no ANX	-0.658	28	0.516	4 right side	34	18.398	6.212	6.223	30.573	**0.003**	0.112	251.639	20.95%
	HC vs DEP-Mix no ANX*	-0.397	14	0.697	3 right side	19	19.117	8.018	3.403	34.831	**0.017**	0.071	331.321	30.24%
THcV	HC vs DEP	0.685	59	0.496	2 right side	63	0.219	0.041	0.139	0.299	**<0.0001**	**<0.0001**	0.078	**87.23%**
	HC vs DEP-Mix	1.781	24	**0.088**	4 left side	30	0.195	0.065	0.068	0.323	**0.003**	**<0.0001**	0.102	**86.87%**
	HC vs DEP-LO	2.147	5	**0.085**	1 left side	8	0.313	0.101	0.114	0.511	**0.002**	**<0.0001**	0.053	**77.16%**
	HC vs DEP-noMed	-0.612	1	0.651	1 right side	4	0.195	0.152	-0.104	0.493	0.201	0.085	0.046	**52.86%**
	HC vs DEP-Cur	-0.184	5	0.861	1 right side	8	0.153	0.085	-0.014	0.320	0.073	**0.002**	0.038	**72.66%**
	HC vs DEP-Mix no ANX	0.696	15	0.497	3 left side	20	0.180	0.084	0.015	0.345	**0.033**	**<0.0001**	0.118	**88.53%**
	HC vs DEP-EO no ANX*	-9.174	1	**0.069**	2 right side	5	0.270	0.126	0.023	0.517	**0.032**	**0.002**	0.063	**81.21%**
	HC vs DEP-Rem no ANX	1.293	2	0.325	2 left side	6	-0.061	0.062	-0.182	0.060	0.325	0.540	0.000	0.00%

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		Egger test			Trim-and-fill									
Region	**Analysis**	**t**	**df**	**p**	**Missing studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP ANX*	-0.101	19	0.921	3 right side	24	0.170	0.080	0.013	0.326	**0.033**	**<0.0001**	0.116	**90.39%**
	HC vs DEP-Mix ANX	2.898	2	0.101	1 left side	5	0.157	0.221	-0.277	0.591	0.478	**<0.0001**	0.223	**93.21%**
RHcV	HC vs DEP	1.025	48	0.310	2 right side	52	0.123	0.023	0.077	0.169	**<0.0001**	**<0.0001**	0.018	**77.37%**
	HC vs DEP-Mix	2.151	19	**0.045**	4 left side	25	0.099	0.034	0.032	0.165	**0.004**	**<0.0001**	0.021	**75.51%**
	HC vs DEP-LO	1.159	4	0.311	1 left side	7	0.189	0.060	0.073	0.306	**0.002**	**0.045**	0.011	**50.43%**
RHcV	HC vs DEP-Cur*	-0.945	3	0.414	3 right side	8	0.133	0.057	0.021	0.245	**0.020**	**0.001**	0.017	**75.97%**
	HC vs DEP-Mix no ANX	0.835	13	0.419	2 left side	17	0.101	0.039	0.025	0.178	**0.009**	**<0.0001**	0.018	**73.22%**
	HC vs DEP-EO no ANX*	-1.069	1	0.479	2 right side	5	0.160	0.058	0.046	0.275	**0.006**	**0.027**	0.011	**64.56%**
	HC vs DEP ANX	0.097	18	0.924	2 right side	22	0.080	0.043	-0.004	0.163	0.063	**<0.0001**	0.026	**82.08%**
	HC vs DEP-Mix ANX	3.627	2	**0.068**	0 left side	NA	NA	NA	NA	NA	NA	NA	NA	NA
LHcV	HC vs DEP	0.606	48	0.547	5 right side	55	0.127	0.023	0.081	0.173	**<0.0001**	**<0.0001**	0.020	**79.39%**
	HC vs DEP-Mix	2.795	19	**0.012**	5 left side	26	0.085	0.035	0.017	0.153	**0.014**	**<0.0001**	0.022	**76.34%**

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		Egger test			Trim-and-fill									
Region	**Analysis**	**t**	**df**	**p**	**Missing studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP-LO	1.070	4	0.345	2 left side	8	0.141	0.047	0.049	0.233	**0.003**	0.102	0.006	39.19%
	HC vs DEP-Rem	-0.558	6	0.597	1 right side	9	0.005	0.033	-0.060	0.070	0.882	0.759	0.000	0.00%
	HC vs DEP-EO no ANX	-3.498	1	0.177	2 right side	5	0.110	0.062	-0.011	0.231	0.075	**0.020**	0.013	**69.97%**
	HC vs DEP-LO no ANX	0.595	3	0.594	1 left side	6	0.141	0.048	0.047	0.235	**0.003**	0.102	0.006	45.86%
	HC vs DEP-Rem no ANX	3.409	2	**0.076**	2 left side	6	-0.045	0.037	-0.117	0.028	0.226	0.294	0.000	0.04%
	HC vs DEP ANX*	0.018	18	0.986	4 right side	24	0.114	0.042	0.032	0.197	**0.007**	**<0.0001**	0.029	**84.51%**
TAV	HC vs DEP-Rem	1.720	5	0.146	1 left side	8	-0.059	0.060	-0.176	0.059	0.326	**0.019**	0.017	**62.68%**
	HC vs DEP-Cur	0.147	2	0.896	1 right side	5	-0.001	0.082	-0.163	0.160	0.989	0.146	0.014	43.05%
	HC vs DEP no ANX*	0.204	10	0.843	3 right side	15	0.334	0.115	0.109	0.559	**0.004**	**<0.0001**	0.184	**94.91%**
RAV	HC vs DEP-Mix	-0.971	3	0.403	1 right side	6	0.022	0.038	-0.053	0.096	0.574	0.081	0.004	49.62%
	HC vs DEP-FE	-2.294	1	0.262	2 right side	5	-0.020	0.035	-0.088	0.048	0.563	0.919	0.000	0.00%
	HC vs DEP-Rem	0.445	5	0.675	2 left side	9	-0.028	0.023	-0.073	0.018	0.233	0.542	0.000	0.08%

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		Egger test			Trim-and-fill									
Region	**Analysis**	**t**	**df**	**p**	**Missing studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP-Cur	-2.137	1	0.279	2 right side	5	-0.020	0.035	-0.088	0.048	0.563	0.919	0.000	0.00%
	HC vs DEP no ANX*	0.308	10	0.765	3 right side	15	0.153	0.054	0.046	0.259	**0.005**	**<0.0001**	0.037	**87.81%**
LAV	HC vs DEP-Rem	3.261	5	**0.022**	2 left side	9	-0.058	0.040	-0.136	0.021	0.151	**0.016**	0.008	**60.82%**
	HC vs DEP-Cur	-5.962	1	0.106	2 right side	5	-0.050	0.034	-0.116	0.016	0.138	0.958	0.000	0.00%
TPuV	HC vs DEP	0.927	18	0.366	1 left side	21	0.196	0.076	0.047	0.345	**0.010**	**<0.0001**	0.062	**60.02%**
	HC vs DEP-Mix no ANX	0.315	2	0.783	1 left side	5	0.079	0.108	-0.132	0.291	0.462	0.223	0.016	28.06%
RPuV	HC vs DEP no ANX	-0.636	4	0.560	2 right side	8	0.234	0.059	0.118	0.350	**<0.0001**	0.118	0.010	38.41%
RPuV	HC vs DEP-Mix no ANX	-0.042	2	0.970	1 right side	5	0.105	0.065	-0.022	0.232	0.106	0.768	0.000	0.00%
LPuV	HC vs DEP-Mix	0.793	3	0.486	2 left side	7	0.038	0.053	-0.066	0.143	0.472	0.713	0.000	0.00%
	HC vs DEP no ANX*	0.687	4	0.530	1 left side	7	0.127	0.077	-0.024	0.279	0.100	**0.048**	0.022	**54.17%**
	HC vs DEP-Mix no ANX	0.641	2	0.587	2 left side	6	0.010	0.058	-0.104	0.124	0.858	0.496	0.000	0.00%
TCV	HC vs DEP-Mix*	-0.911	6	0.398	2 right side	10	0.207	0.094	0.023	0.391	**0.028**	0.088	0.033	42.16%

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		Egger test			Trim-and-fill									
Region	**Analysis**	**t**	**df**	**p**	**Missing studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP no ANX	-1.487	4	0.211	1 right side	7	0.160	0.090	-0.017	0.336	0.076	0.056	0.026	47.68%
RCV	HC vs DEP	-1.578	13	0.139	3 right side	18	0.051	0.038	-0.023	0.126	0.174	**0.014**	0.010	44.80%
	HC vs DEP no ANX	-0.630	4	0.563	1 right side	7	0.057	0.041	-0.023	0.137	0.163	0.436	0.000	0.00%
	HC vs DEP-Mix no ANX	-0.375	2	0.744	1 right side	5	0.071	0.064	-0.055	0.197	0.266	0.213	0.005	23.97%
LCV	HC vs DEP	-2.201	13	**0.046**	4 right side	19	0.057	0.035	-0.011	0.125	0.099	**0.016**	0.008	40.67%
	HC vs DEP no ANX*	-1.043	4	0.356	1 right side	7	0.093	0.047	0.002	0.184	**0.046**	0.275	0.002	12.94%
	HC vs DEP-Mix no ANX	-0.730	2	0.542	1 right side	5	0.126	0.073	-0.018	0.269	0.086	0.101	0.011	44.17%
TPaV	HC vs DEP	0.662	14	0.519	2 left side	18	0.029	0.031	-0.031	0.089	0.344	**<0.0001**	0.012	**74.72%**
TPaV	HC vs DEP-Mix	0.917	3	0.427	1 left side	6	0.035	0.036	-0.035	0.105	0.330	0.215	0.002	33.04%
	HC vs DEP no ANX	0.099	2	0.930	1 left side	5	0.070	0.042	-0.011	0.152	0.092	0.357	0.002	22.26%
RPaV	HC vs DEP	0.376	11	0.714	1 left side	14	0.022	0.020	-0.018	0.062	0.279	**0.0004**	0.003	**65.28%**
	HC vs DEP-Mix*	-3.594	1	0.173	2 right side	5	0.060	0.028	0.006	0.115	**0.031**	0.997	0.000	0.00%

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		Egger test			Trim-and-fill									
Region	**Analysis**	**t**	**df**	**p**	**Missing studies**	**k**	**MD**	**SE**	**95% CI**		**p**	**Qp**	**τ^2**	**I^2**
	HC vs DEP no ANX	-0.269	2	0.813	2 right side	6	0.064	0.020	0.025	0.104	**0.002**	0.892	0.000	0.00%
LPaV	HC vs DEP	0.525	11	0.610	2 left side	15	0.019	0.015	-0.009	0.048	0.185	0.129	0.001	18.86%
	HC vs DEP-Mix	0.763	1	0.585	1 left side	4	0.002	0.036	-0.068	0.072	0.958	0.211	0.001	23.40%
	HC vs DEP no ANX	0.472	2	0.683	1 left side	5	0.015	0.035	-0.053	0.084	0.659	0.155	0.002	39.03%
RTV	HC vs DEP no ANX	0.491	1	0.710	1 left side	4	0.191	0.086	0.022	0.359	**0.027**	0.821	0.000	0.00%
TAcV	HC vs DEP	0.747	7	0.480	2 left side	11	-0.037	0.025	-0.086	0.013	0.149	**<0.0001**	0.005	**72.45%**

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Supplemental Table S10. Meta-regression results

k: number of samples or subsamples, mod: moderator, HC: healthy controls, DEP: depressed participants, %F: percent female, diff: difference, %Med: percent medicated, mod: moderator, Seg: segmentation, Man/Auto: manual/automated segmentation, HDS-17: 17-item Hamilton Depression Score, MD: mean difference, SE: standard error, CI: confidence interval, QEp: test for residual heterogeneity p-value, QMp: test of moderators p-value, τ^2: variance of true effects, I^2: residual heterogeneity unaccounted by model, R^2: heterogeneity accounted by model, TBV: total brain, THcV: total hippocampus, RHcV: right hippocampus, LHcV: left hippocampus, ICV: intracranial volumes. Model A: combined demographics of HC and DEP, Model B: combined age and %F diff of HC and DEP. Bold font indicates significance at $p \leq 0.05$ and $I^2/R^2 > 50\%$.

				Mixed-Effects Model										
Region	**Analysis**	**Moderator**	**k**		**MD**	**SE**	**95% CI**		**p**	**QEp**	**QMp**	**τ^2**	**I^2**	**R^2**
TBV	Gender	Total %F	37	intercept	-9.435	18.568	-45.827	26.958	0.611	0.248	0.661	0.000	0.00%	0.00%
				mod	0.120	0.273	-0.416	0.655	0.661					
		HC %F	37	intercept	-6.403	17.802	-41.293	28.487	0.719	0.244	0.777	0.000	0.00%	**74.27%**
				mod	0.076	0.269	-0.451	0.603	0.777					
		DEP %F	37	intercept	-11.083	17.258	-44.908	22.743	0.521	0.252	0.568	0.000	0.00%	0.00%
				mod	0.141	0.247	-0.342	0.624	0.568					
		HC/DEP %F	37	intercept	-8.833	18.216	-44.536	26.870	0.628	0.221	0.788	0.000	0.00%	16.08%
				HC %F	-0.197	0.511	-1.199	0.805	0.700					
				DEP %F	0.295	0.469	-0.624	1.213	0.529					
		%F diff	37	intercept	-2.487	4.451	-11.210	6.236	0.576	0.253	0.556	0.000	0.00%	14.28%
				mod	-0.274	0.465	-1.185	0.638	0.556					
	Age	Total Age	37	intercept	-4.010	7.782	-19.262	11.242	0.606	0.246	0.693	8.992	1.34%	0.00%

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Region	Analysis	Moderator	k	Mixed-Effects Model									
					MD	SE	95% CI		p	QEp	QMp	τ^2	I^2	R^2
				mod	0.102	0.258	-0.403	0.606	0.693					
		HC Age	37	intercept	-4.153	7.596	-19.041	10.735	0.585	0.247	0.664	10.566	1.57%	0.00%
				mod	0.111	0.255	-0.388	0.609	0.664					
		DEP Age	37	intercept	-3.982	7.936	-19.537	11.573	0.616	0.246	0.705	7.586	1.14%	0.00%
				mod	0.098	0.259	-0.410	0.606	0.705					
TBV	Age	HC/DEP Age	37	intercept	-2.853	8.600	-19.708	14.001	0.740	0.215	0.847	45.043	6.34%	0.00%
				HC age	0.733	1.764	-2.724	4.191	0.678					
				DEP age	-0.633	1.802	-4.166	2.900	0.726					
	Model	Model A	37	intercept	-9.872	19.252	-47.605	27.860	0.608	0.215	0.873	16.499	2.41%	0.00%
				%F	0.094	0.282	-0.459	0.648	0.738					
				age total	0.089	0.264	-0.429	0.606	0.738					
		Model B	37	intercept	-4.118	7.938	-19.676	11.441	0.604	0.219	0.821	28.136	4.00%	0.00%
				%F diff	-0.236	0.493	-1.202	0.730	0.632					
				age total	0.080	0.270	-0.449	0.609	0.767					
THcV	Gender	Total %F	61	intercept	0.108	0.110	-0.108	0.323	0.327	**<0.0001**	0.354	0.073	**86.56%**	0.00%
				mod	0.002	0.002	-0.002	0.005	0.354					
		HC %F	61	intercept	0.113	0.106	-0.095	0.321	0.288	**<0.0001**	0.366	0.073	**86.53%**	0.00%
				mod	0.001	0.002	-0.002	0.004	0.366					
		DEP %F	61	intercept	0.122	0.111	-0.095	0.338	0.272	**<0.0001**	0.434	0.073	**86.63%**	0.00%
				mod	0.001	0.002	-0.002	0.004	0.434					
		HC/DEP %F	61	intercept	0.119	0.111	-0.099	0.337	0.286	**<0.0001**	0.654	0.075	**86.66%**	0.00%
				HC %F	0.002	0.005	-0.007	0.011	0.623					
				DEP %F	-0.001	0.005	-0.010	0.008	0.844					
		%F diff	61	intercept	0.207	0.043	0.123	0.291	**<0.0001**	**<0.0001**	0.736	0.074	**86.63%**	0.00%

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					MD	SE	95% CI		p	QEp	QMp	τ^2	I^2	R^2
				mod	0.002	0.005	-0.007	0.010	0.736					
	Age	Total Age	61	intercept	0.197	0.059	0.081	0.312	**0.001**	**<0.0001**	0.902	0.074	**86.67%**	0.00%
				mod	0.000	0.003	0.123	-0.005	**0.006**					
		HC Age	61	intercept	0.209	0.057	0.098	0.320	**0.0002**	**<0.0001**	0.856	0.074	**86.64%**	0.00%
				mod	-0.001	0.003	-0.006	0.005	0.856					
		DEP Age	61	intercept	0.185	0.062	0.063	0.306	**0.003**	**<0.0001**	0.710	0.074	**86.66%**	0.00%
				mod	0.001	0.003	-0.005	0.007	0.710					
THcV	Age	HC/DEP Age	61	intercept	0.148	0.064	0.023	0.274	**0.020**	**<0.0001**	0.146	0.071	**85.48%**	1.86%
				HC age	-0.019	0.010	-0.037	0.000	0.054					
				DEP age	0.020	0.010	0.000	0.040	0.051					
	Segmentation	Man/Auto	61	intercept	0.119	0.064	-0.008	0.245	0.065	**<0.0001**	0.099	0.071	**84.92%**	2.45%
				mod	0.135	0.082	-0.025	0.296	0.099					
	Medication	%Med	33	intercept	0.128	0.087	-0.042	0.298	0.140	**<0.0001**	0.205	0.086	**87.34%**	0.00%
				%med	0.002	0.002	-0.001	0.005	0.205					
	Symptoms	HDS-17	22	intercept	0.240	0.268	-0.285	0.766	0.370	**<0.0001**	0.850	0.087	**84.76%**	0.00%
				HDS-17	0.003	0.014	-0.024	0.029	0.850					
	Model	Model A	61	intercept	0.107	0.115	-0.119	0.332	0.354	**<0.0001**	0.654	0.075	**86.65%**	0.00%
				%F	0.002	0.002	-0.002	0.005	0.361					
				age total	0.000	0.003	-0.006	0.006	0.986					
		Model B	61	intercept	0.199	0.060	0.082	0.317	**0.001**	**<0.0001**	0.930	0.075	**86.70%**	0.00%
				%F diff	0.002	0.005	-0.007	0.011	0.718					
				age total	0.001	0.003	-0.005	0.006	0.854					
	Model + Seg	Model A + Seg	61	intercept	0.069	0.117	-0.160	0.299	0.554	**<0.0001**	0.379	0.073	**84.96%**	0.00%

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					MD	SE	95% CI		p	QEp	QMp	τ^2	I^2	R^2
				%F	0.001	0.002	-0.002	0.004	0.539					
				age total	-0.001	0.003	-0.006	0.005	0.797					
				seg	0.129	0.087	-0.040	0.299	0.136					
		Model B + Seg	61	intercept	0.124	0.073	-0.019	0.267	0.090	**<0.0001**	0.360	0.073	**84.75%**	0.00%
				%F diff	0.003	0.005	-0.006	0.012	0.479					
				age total	0.000	0.003	-0.006	0.005	0.909					
				seg	0.151	0.087	-0.018	0.321	0.080					
RHcV	Gender	Total %F	50	intercept	0.065	0.066	-0.065	0.195	0.327	**<0.0001**	0.427	0.017	**77.00%**	0.00%
				mod	0.001	0.001	-0.001	0.003	0.427					
RHcV	Gender	HC %F	50	intercept	0.063	0.064	-0.062	0.188	0.320	**<0.0001**	0.393	0.017	**76.92%**	0.00%
				mod	0.001	0.001	-0.001	0.003	0.393					
		DEP %F	50	intercept	0.072	0.068	-0.061	0.205	0.289	**<0.0001**	0.509	0.017	**77.11%**	0.00%
				mod	0.001	0.001	-0.001	0.003	0.509					
		HC/DEP %F	50	intercept	0.074	0.068	-0.060	0.208	0.280	**<0.0001**	0.625	0.017	**77.20%**	0.00%
				HC mod	0.002	0.003	-0.004	0.008	0.479					
				DEP mod	-0.001	0.003	-0.007	0.004	0.645					
		%F diff	50	intercept	0.121	0.025	0.071	0.170	**<0.0001**	**<0.0001**	0.526	0.017	**76.73%**	0.00%
				mod	0.002	0.003	-0.004	0.007	0.526					
	Age	Total Age	50	intercept	0.090	0.033	0.025	0.155	**0.007**	**<0.0001**	0.317	0.017	**76.69%**	0.00%
				mod	0.002	0.002	-0.002	0.005	0.317					
		HC Age	50	intercept	0.101	0.032	0.038	0.163	**0.002**	**<0.0001**	0.534	0.017	**76.88%**	0.00%
				mod	0.001	0.002	-0.002	0.004	0.534					
		DEP Age	50	intercept	0.080	0.035	0.011	0.149	**0.022**	**<0.0001**	0.205	0.017	**76.46%**	0.17%
				mod	0.002	0.002	-0.001	0.005	0.205					

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					MD	SE	95% CI		p	QEp	QMp	τ^2	I^2	R^2
		HC/DEP Age	37	intercept	0.054	0.037	-0.019	0.126	0.146	**<0.0001**	0.056	0.015	**73.86%**	7.22%
				HC mod	-0.010	0.005	-0.020	0.000	**0.043**					
				DEP mod	0.013	0.006	0.002	0.024	**0.020**					
	Segmentation	Man/Auto	50	intercept	0.056	0.040	-0.023	0.135	0.165	**<0.0001**	0.077	0.016	**73.14%**	3.49%
				mod	0.086	0.049	-0.009	0.182	0.077					
	Medication	%Med	28	intercept	0.106	0.050	0.008	0.204	**0.035**	**<0.0001**	0.602	0.019	**76.68%**	0.00%
				%med	0.000	0.001	-0.001	0.002	0.602					
	Symptoms	HDS-17	19	intercept	0.162	0.143	-0.118	0.442	0.258	**<0.0001**	0.914	0.016	**70.54%**	0.00%
				HDS-17	-0.001	0.007	-0.015	0.013	0.914					
	Model	Model A	50	intercept	0.044	0.070	-0.093	0.181	0.527	**<0.0001**	0.460	0.017	**77.07%**	0.00%
				%F	0.001	0.001	-0.001	0.003	0.454					
				age total	0.002	0.002	-0.002	0.005	0.337					
		Model B	50	intercept	0.094	0.034	0.028	0.160	**0.005**	**<0.0001**	0.402	0.017	**76.55%**	0.00%
				%F diff	0.003	0.003	-0.003	0.009	0.364					
				age total	0.002	0.002	-0.001	0.005	0.234					
	Model + Seg	Model A + Seg	50	intercept	0.011	0.073	-0.131	0.154	0.878	**<0.0001**	0.265	0.017	**73.67%**	0.00%
				%F	0.001	0.001	-0.001	0.002	0.628					
				age total	0.001	0.002	-0.002	0.005	0.421					
				seg	0.078	0.051	-0.021	0.177	0.121					
		Model B + Seg	50	intercept	0.035	0.045	-0.053	0.124	0.434	**<0.0001**	0.133	0.016	**72.40%**	2.82%
				%F diff	0.004	0.003	-0.002	0.010	0.179					
				age total	0.002	0.002	-0.001	0.005	0.268					

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				Mixed-Effects Model										
Region	**Analysis**	**Moderator**	**k**		**MD**	**SE**	**95% CI**		**p**	**QEp**	**QMp**	**τ^2**	**I^2**	**R^2**
				seg	0.098	0.051	-0.001	0.197	0.053					
LHcV	Gender	Total %F	50	intercept	0.082	0.064	-0.044	0.208	0.203	**<0.0001**	0.709	0.017	**77.40%**	0.00%
				mod	0.000	0.001	-0.002	0.002	0.709					
		HC %F	50	intercept	0.080	0.062	-0.042	0.202	0.197	**<0.0001**	0.673	0.017	**77.34%**	0.00%
				mod	0.000	0.001	-0.001	0.002	0.673					
		DEP %F	50	intercept	0.090	0.066	-0.039	0.219	0.173	**<0.0001**	0.812	0.017	**77.44%**	0.00%
				mod	0.000	0.001	-0.002	0.002	0.812					
		HC/DEP %F	50	intercept	0.091	0.066	-0.039	0.221	0.168	**<0.0001**	0.800	0.018	**77.41%**	0.00%
				HC mod	0.002	0.003	-0.004	0.008	0.533					
				DEP mod	-0.002	0.003	-0.007	0.004	0.606					
LHcV	Gender	%F diff	50	intercept	0.111	0.025	0.061	0.160	**<0.0001**	**<0.0001**	0.548	0.017	**76.97%**	0.00%
				mod	0.002	0.003	-0.004	0.007	0.548					
	Age	Total Age	50	intercept	0.104	0.034	0.038	0.169	**0.002**	**<0.0001**	0.975	0.017	**77.35%**	0.00%
				mod	0.000	0.002	-0.003	0.003	0.975					
LHcV	Age	HC Age	50	intercept	0.108	0.032	0.046	0.171	**0.001**	**<0.0001**	0.855	0.017	**77.23%**	0.00%
				mod	0.000	0.002	-0.003	0.003	0.855					
		DEP Age	50	intercept	0.101	0.036	0.031	0.170	**0.005**	**<0.0001**	0.884	0.017	**77.39%**	0.00%
				mod	0.000	0.002	-0.003	0.004	0.884					
		HC/DEP Age	50	intercept	0.086	0.038	0.012	0.161	**0.024**	**<0.0001**	0.547	0.018	**76.35%**	0.00%
				HC mod	-0.006	0.005	-0.016	0.005	0.276					
				DEP mod	0.006	0.006	-0.005	0.017	0.279					
	Segmentation	Man/Auto	50	intercept	0.053	0.041	-0.027	0.132	0.195	**<0.0001**	0.119	0.017	**74.29%**	1.80%
				mod	0.076	0.049	-0.020	0.172	0.119					
	Medication	%Med	28	intercept	0.097	0.052	-0.005	0.198	0.061	**<0.0001**	0.720	0.022	**80.44%**	0.00%

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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Region	Analysis	Moderator	k	Mixed-Effects Model										
					MD	SE	95% CI		p	QEp	QMp	τ^2	I^2	R^2
				%med	0.000	0.001	-0.001	0.002	0.720					
	Symptoms	HDS-17	19	intercept	0.136	0.154	-0.166	0.437	0.378	**<0.0001**	0.940	0.026	**80.36%**	0.00%
				HDS-17	0.001	0.008	-0.015	0.016	0.940					
	Model	Model A	50	intercept	0.081	0.069	-0.053	0.215	0.237	**<0.0001**	0.931	0.018	**77.75%**	0.00%
				%F	0.000	0.001	-0.002	0.002	0.707					
				age total	0.000	0.002	-0.003	0.003	0.987					
		Model B	50	intercept	0.106	0.034	0.040	0.173	**0.002**	**<0.0001**	0.826	0.018	**77.27%**	0.00%
				%F diff	0.002	0.003	-0.004	0.008	0.536					
				age total	0.000	0.002	-0.003	0.004	0.855					
	Model + Seg	Model A + Seg	50	intercept	0.046	0.072	-0.096	0.187	0.529	**<0.0001**	0.493	0.018	**74.87%**	0.00%
				%F	0.000	0.001	-0.002	0.002	0.870					
				age total	0.000	0.002	-0.003	0.003	0.902					
				seg	0.076	0.051	-0.023	0.175	0.132					
LHcV	Model + Seg	Model B + Seg	50	intercept	0.052	0.046	-0.038	0.142	0.260	**<0.0001**	0.330	0.017	**73.91%**	0.00%
				%F diff	0.003	0.003	-0.003	0.009	0.312					
				age total	0.000	0.002	-0.003	0.004	0.910					
				seg	0.089	0.051	-0.011	0.189	0.082					
ICV	**Gender**	Total %F	59	intercept	21.086	14.643	-7.613	49.785	0.150	0.078	0.273	197.521	19.01%	10.53%
				mod	-0.218	0.199	-0.608	0.172	0.273					
		HC %F	59	intercept	24.749	13.922	-2.539	52.036	0.076	0.090	0.151	184.124	17.94%	16.59%
				mod	-0.275	0.192	-0.651	0.101	0.151					
		DEP %F	59	intercept	13.820	15.074	-15.725	43.364	0.359	0.066	0.577	221.715	20.93%	0.00%

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DOI: 10.1503/jpn.190156

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Region	Analysis	Moderator	k	Mixed-Effects Model										
					MD	SE	95% CI		p	QEp	QMp	τ^2	I^2	R^2
				mod	-0.112	0.201	-0.505	0.281	0.577					
		HC/DEP %F	59	intercept	15.668	14.692	-13.127	44.463	0.286	0.131	0.066	171.708	16.92%	22.22%
				HC %F	-1.087	0.483	-2.033	-0.141	**0.024**					
				DEP %F	0.903	0.494	-0.065	1.870	0.067					
		%F diff	59	intercept	2.606	4.619	-6.447	11.658	0.573	0.130	**0.033**	171.398	17.38%	22.36%
				mod	-1.020	0.477	-1.956	-0.085	**0.033**					
	Age	Total Age	59	intercept	2.939	6.992	-10.766	16.644	0.674	0.058	0.583	271.704	24.42%	0.00%
				mod	0.163	0.297	-0.419	0.745	0.583					
		HC Age	59	intercept	3.802	6.554	-9.042	16.647	0.562	0.058	0.665	268.213	24.12%	0.00%
				mod	0.121	0.281	-0.429	0.672	0.665					
		DEP Age	59	intercept	0.799	7.562	-14.022	15.620	0.916	0.061	0.401	273.527	24.57%	0.00%
				mod	0.264	0.314	-0.352	0.880	0.401					
		HC/DEP Age	59	intercept	-4.594	8.447	-21.149	11.961	0.587	0.079	0.271	244.846	22.40%	0.00%
				HC age	-1.417	1.019	-3.414	0.580	0.164					
				DEP age	1.778	1.138	-0.454	4.009	0.118					
	Model	Model A	59	intercept	17.827	16.393	-14.302	49.957	0.277	0.066	0.530	253.142	22.67%	0.00%
				%F	-0.206	0.207	-0.611	0.200	0.321					
				age total	0.131	0.295	-0.446	0.709	0.321					
ICV	Model	Model B	59	intercept	1.894	6.726	-11.289	15.077	0.778	0.112	0.107	208.772	19.81%	5.43%
				%F diff	-1.011	0.492	-1.976	-0.047	**0.040**					
				age total	0.042	0.289	-0.525	0.609	0.885					

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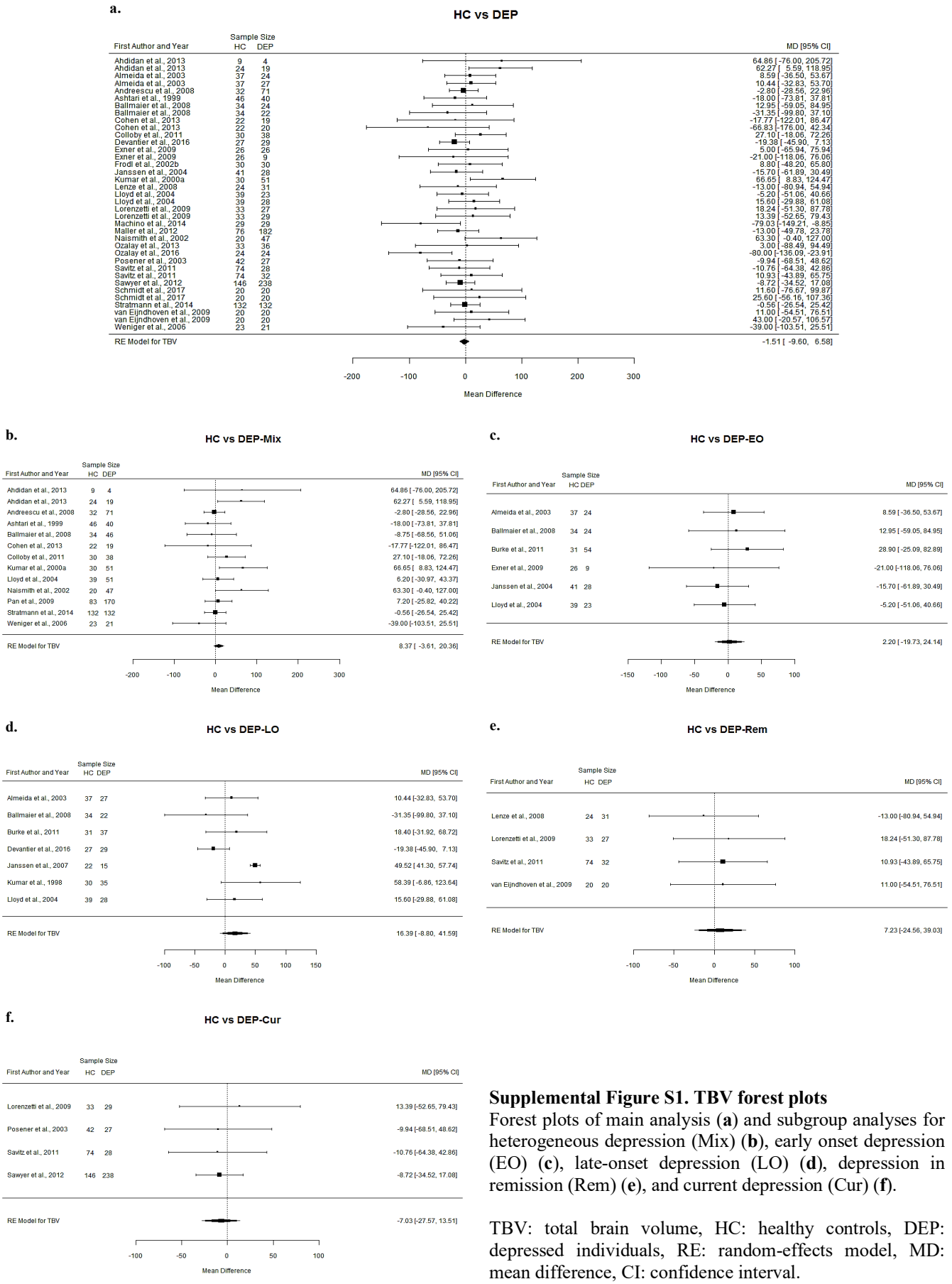

Supplemental Figure S1. TBV forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), early onset depression (EO) (**c**), late-onset depression (LO) (**d**), depression in remission (Rem) (**e**), and current depression (Cur) (**f**).

TBV: total brain volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

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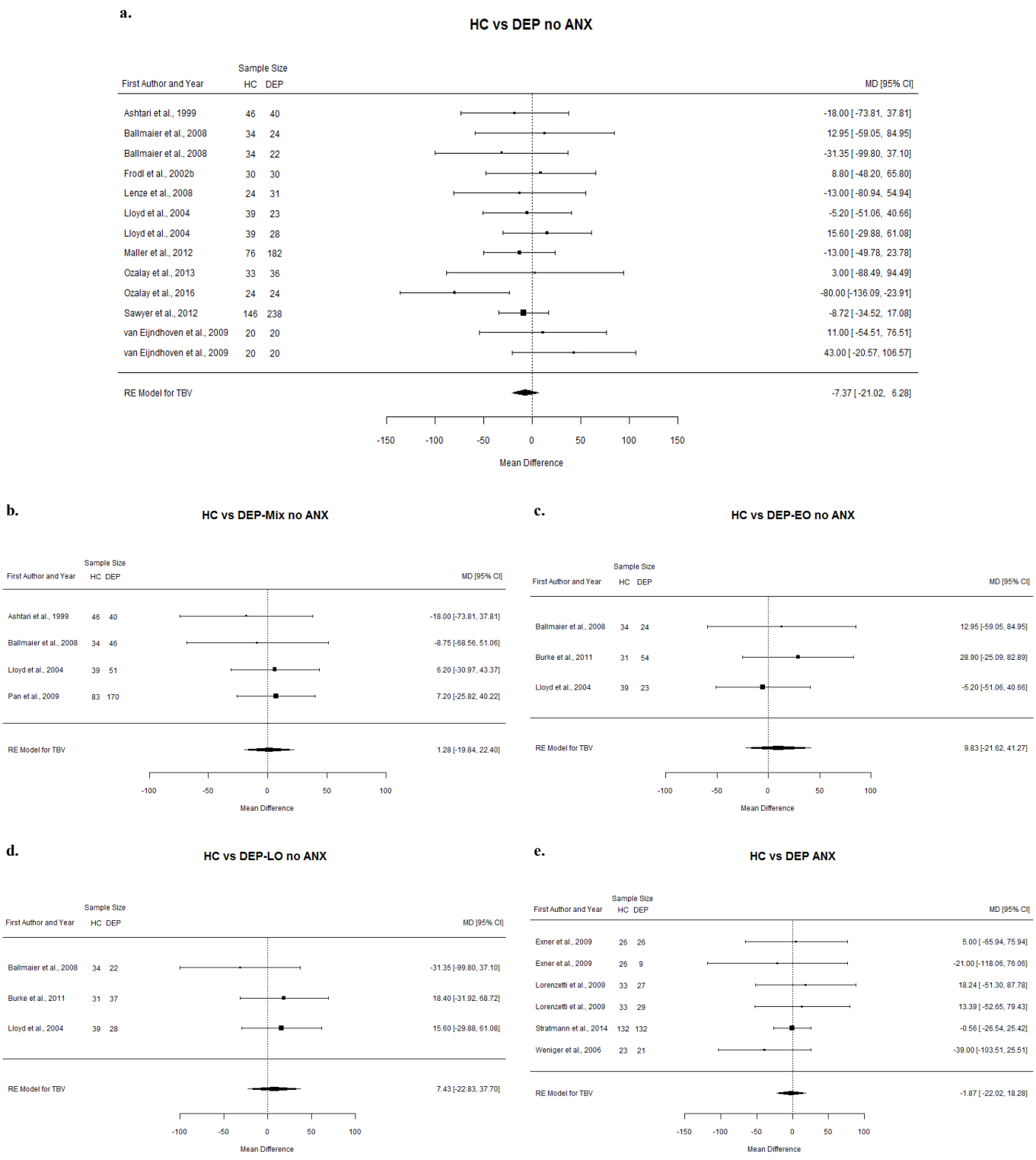

Supplemental Figure S2. TBV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), early-onset depression (EO) (**c**), and late-onset depression (LO) (**d**) excluding anxiety disorders (no ANX). Forest plot of main analysis comorbid with anxiety disorders (ANX) (**e**).

TBV: total brain volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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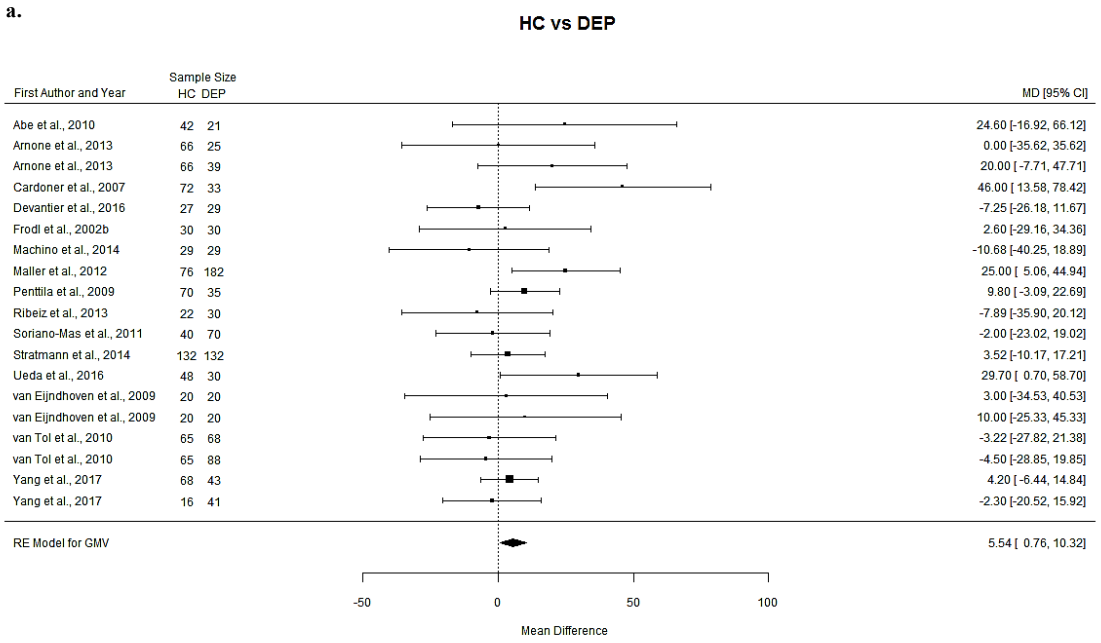

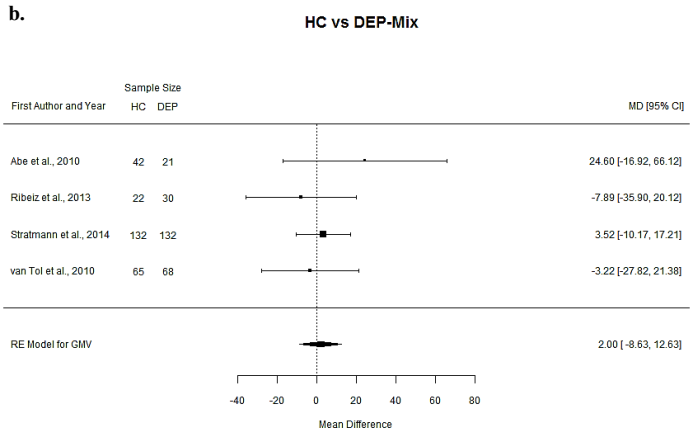

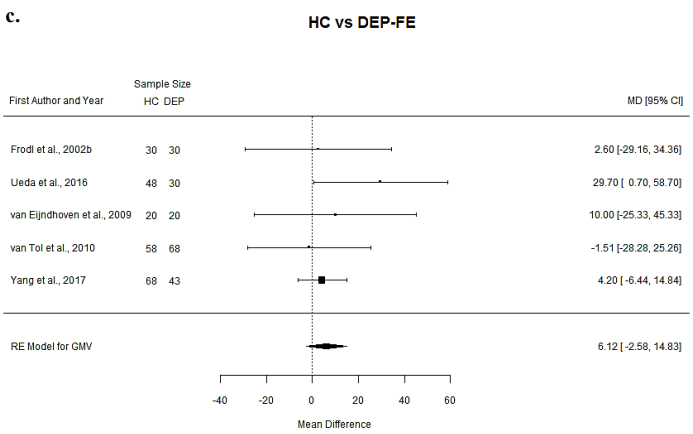

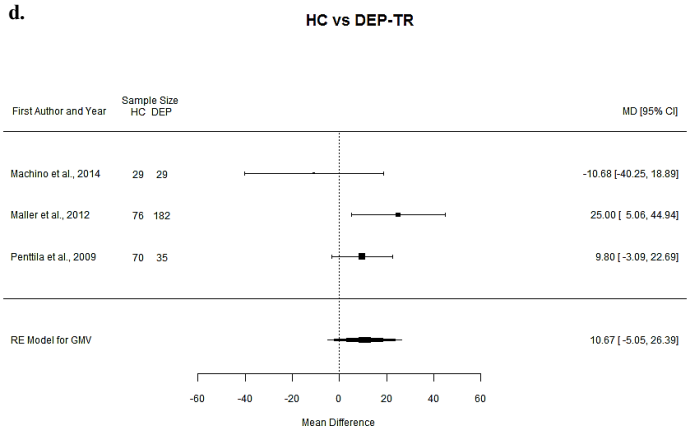

Supplemental Figure S3. GMV forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), first-episode of depression (FE) (**c**), and treatment-resistant depression (TR) (**d**).

GMV: grey matter volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

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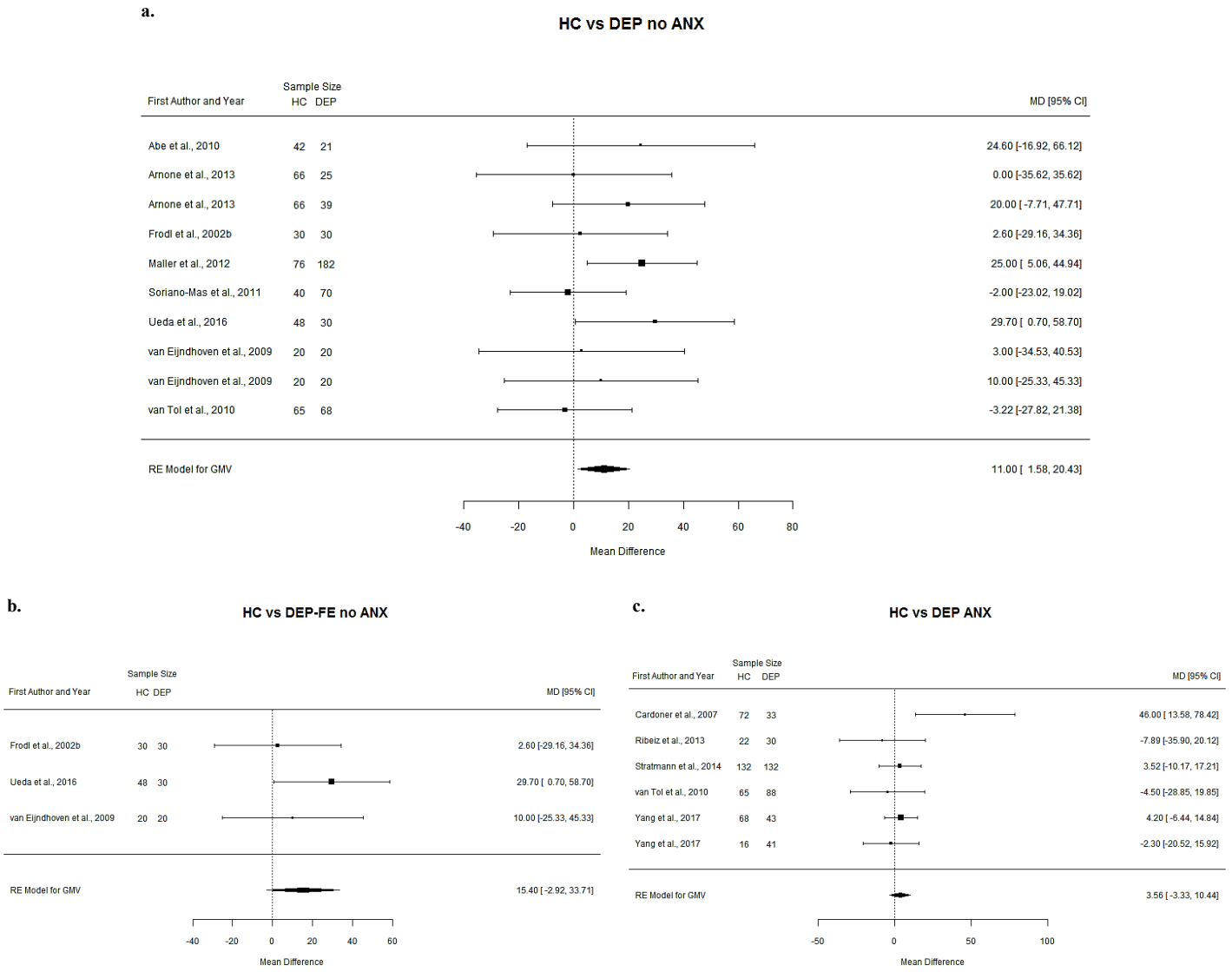

Supplemental Figure S4. GMV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**) and subgroup analysis for first-episode of depression (FE) (**b**) excluding anxiety disorders (no ANX). Forest plot of main analysis comorbid with anxiety disorders (ANX) (**c**).

GMV: grey mater volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.

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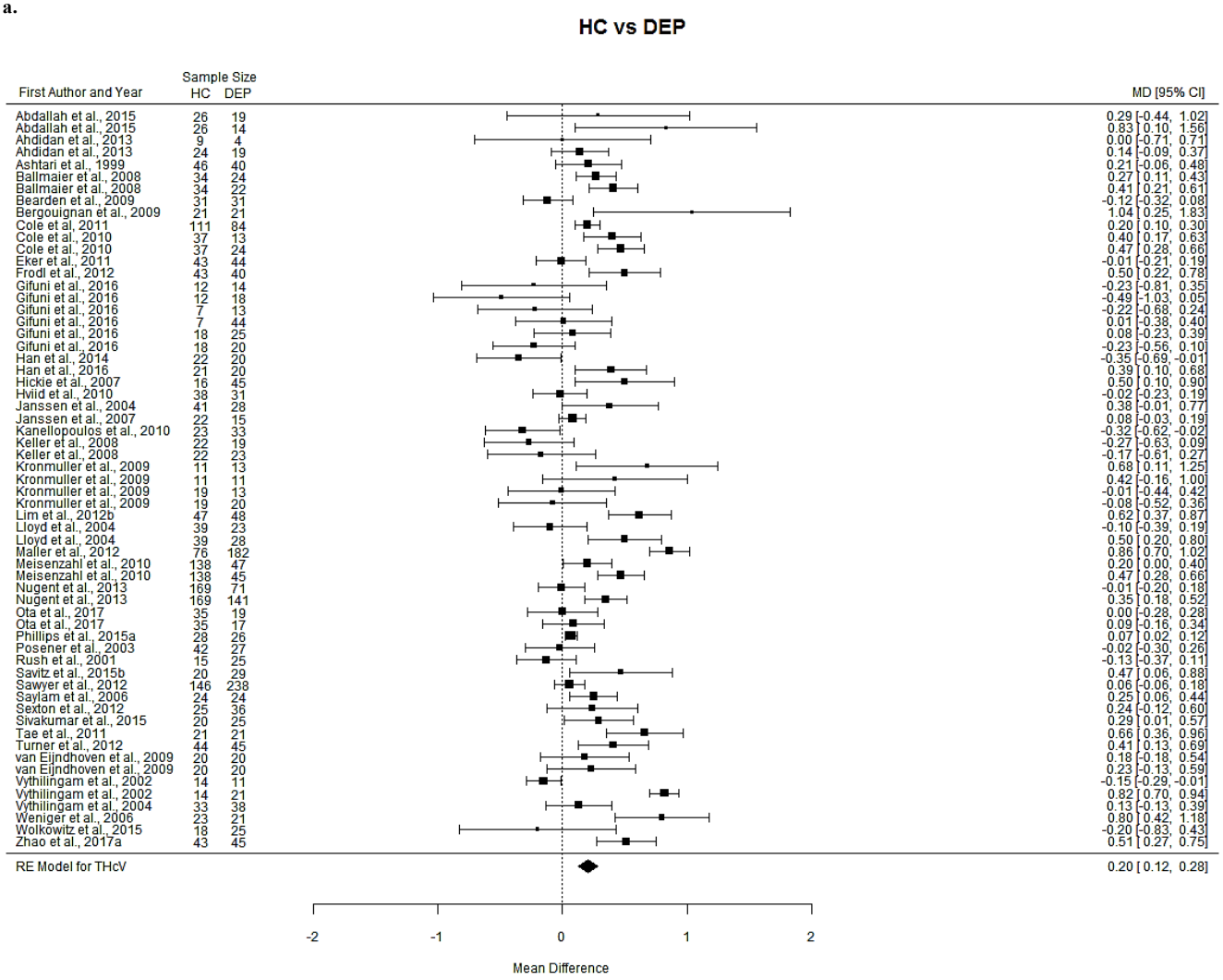

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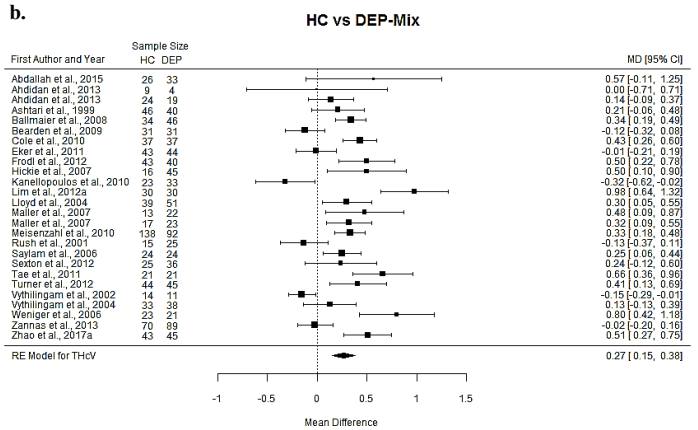

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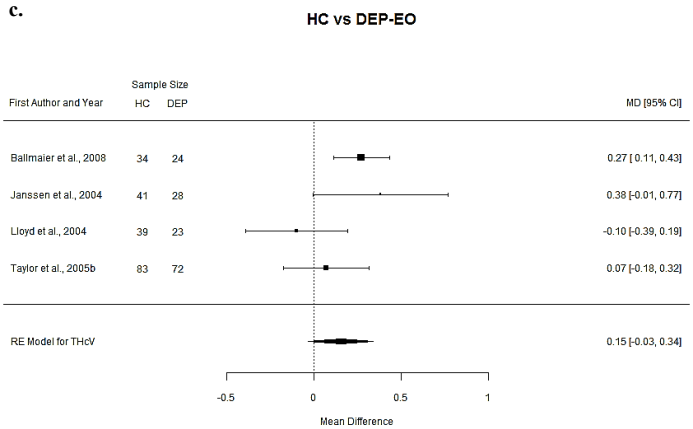

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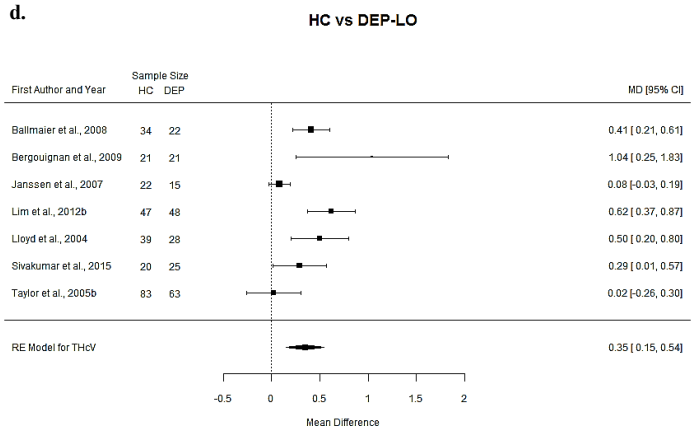

Supplemental Figure S5. THcV forest plots

Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), early-onset depression (EO) (**c**), and late-onset depression (LO) (**d**).

THcV: total hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

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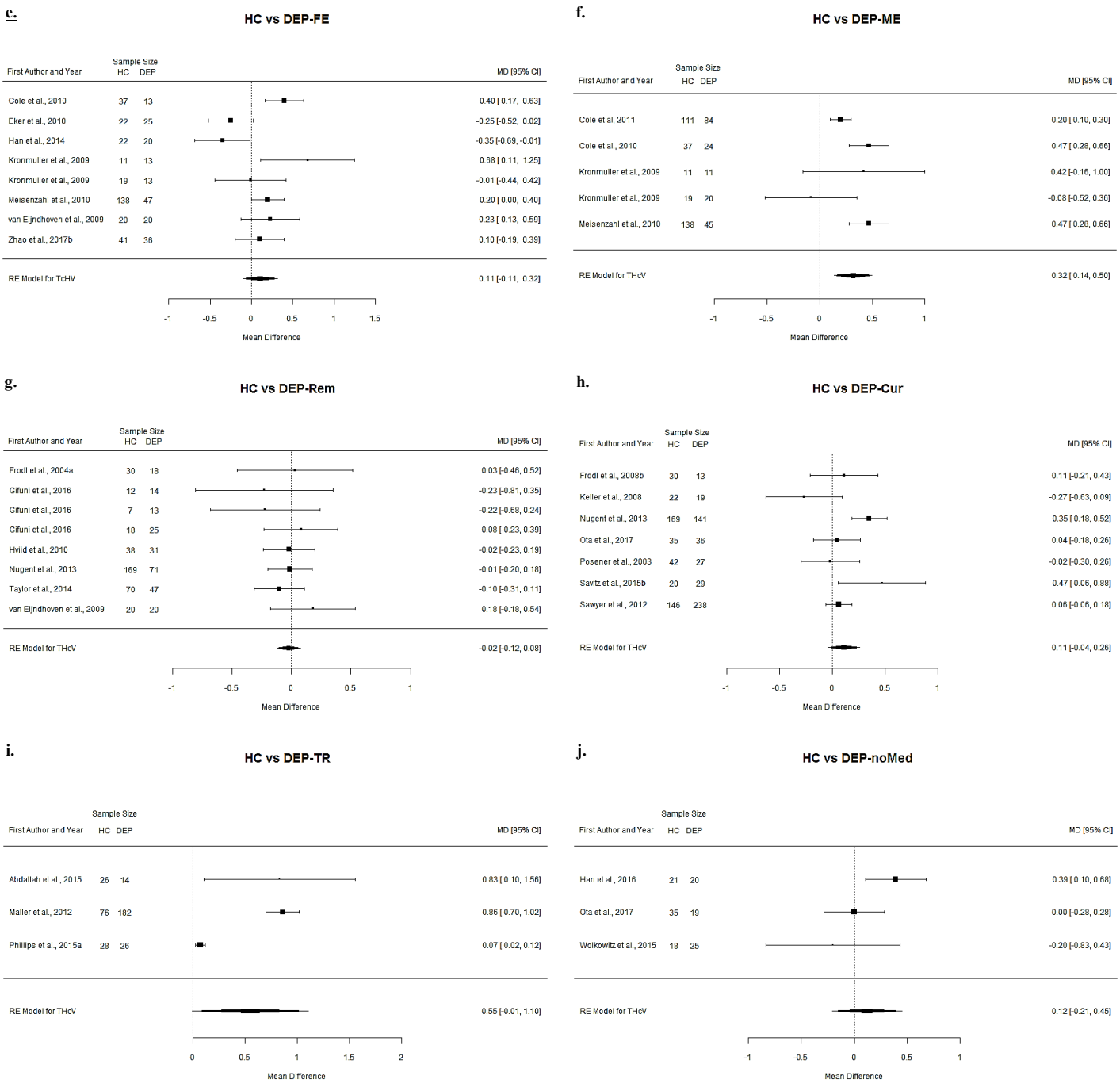

Supplemental Figure S5. THcV forest plots (continued)
Forest plots of subgroup analyses for first-episode of depression (FE) (**e**), multiple-episodes of depression (ME) (**f**), depression in remission (Rem) (**g**), current depression (Cur) (**h**), treatment-resistant depression (TR) (**i**), and non-medicated depression (noMED) (**j**).

THcV: total hippocampus volume, HC: healthy controls, DEP: depressed individuals, DEP-FE: first episode, RE: random-effects model, MD: mean difference, CI: confidence interval.

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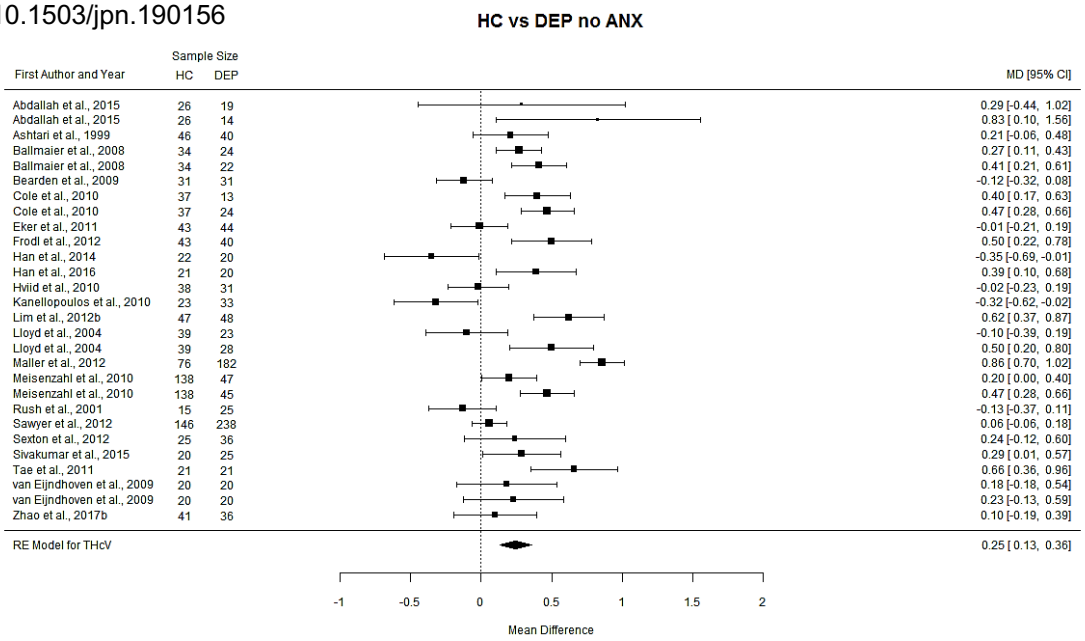

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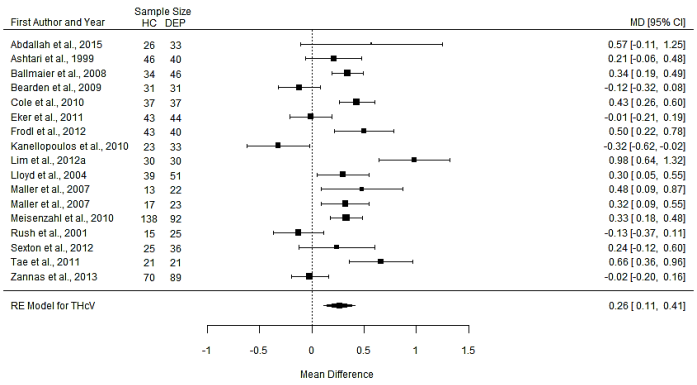

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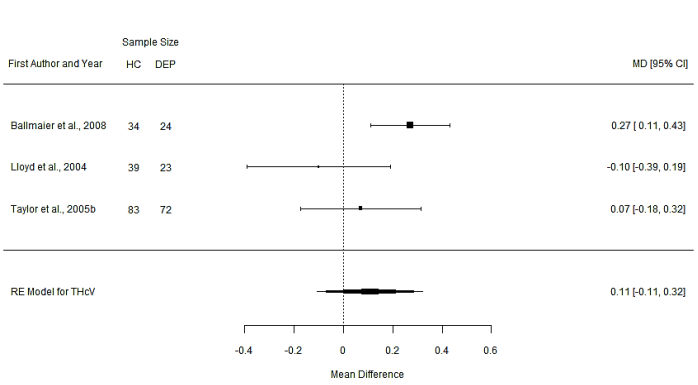

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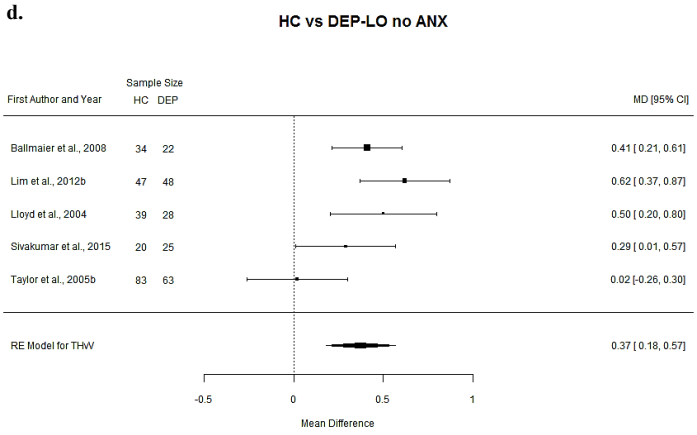

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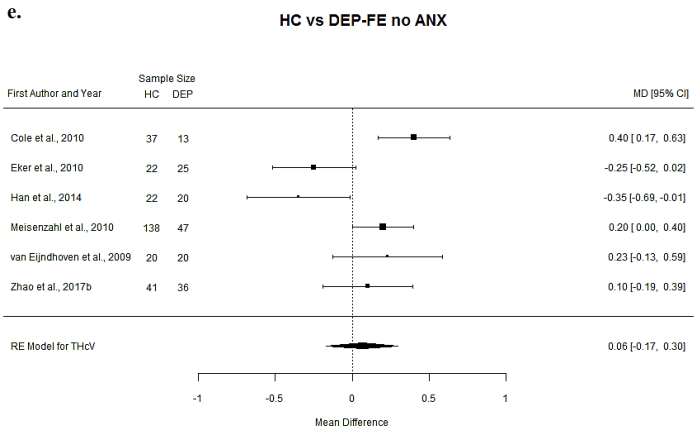

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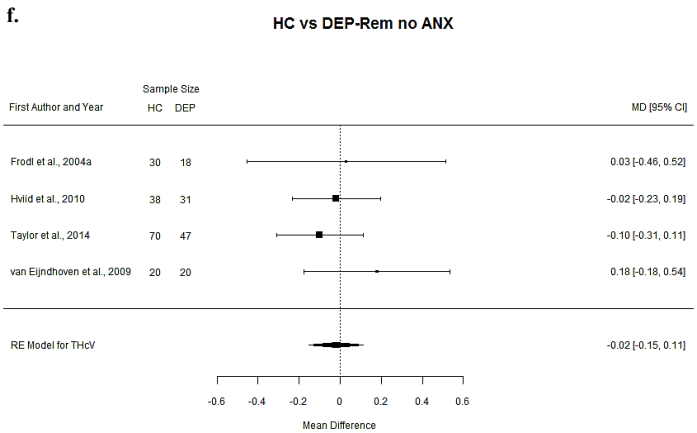

Supplemental Figure S6. THcV assessment of anxiety comorbidity forest plots

Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), early-onset depression (EO) (**c**), late-onset depression (LO) (**d**), first-episode of depression (FE) (**e**), and depression in remission (Rem) (**f**) excluding anxiety disorders (no ANX).

THcV: total hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

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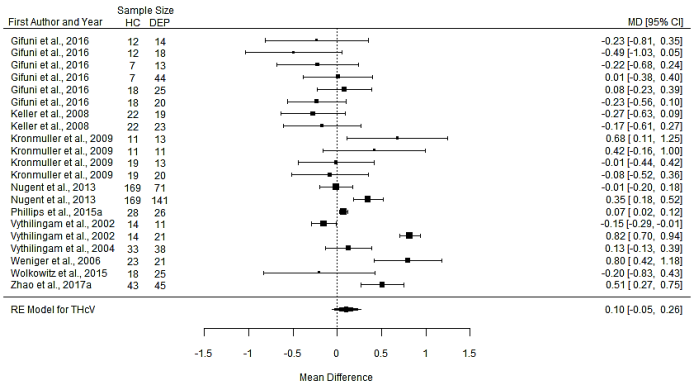
g.



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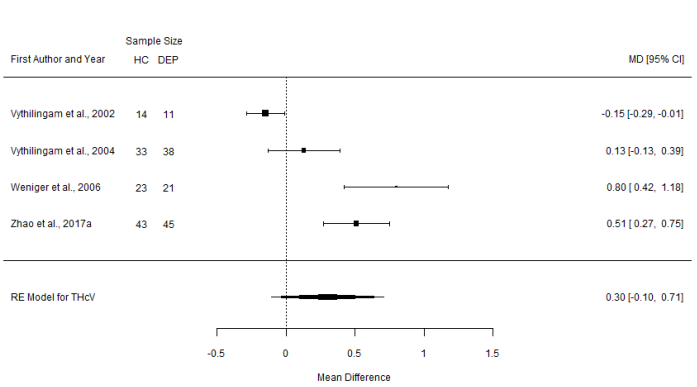

Supplemental Figure S6. THcV assessment of anxiety comorbidity forest plots (continued)
Forest plots of main analysis (**g**), and subgroup analysis for heterogeneous depression (Mix) (**h**) comorbid with anxiety disorders (ANX).

THcV: total hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

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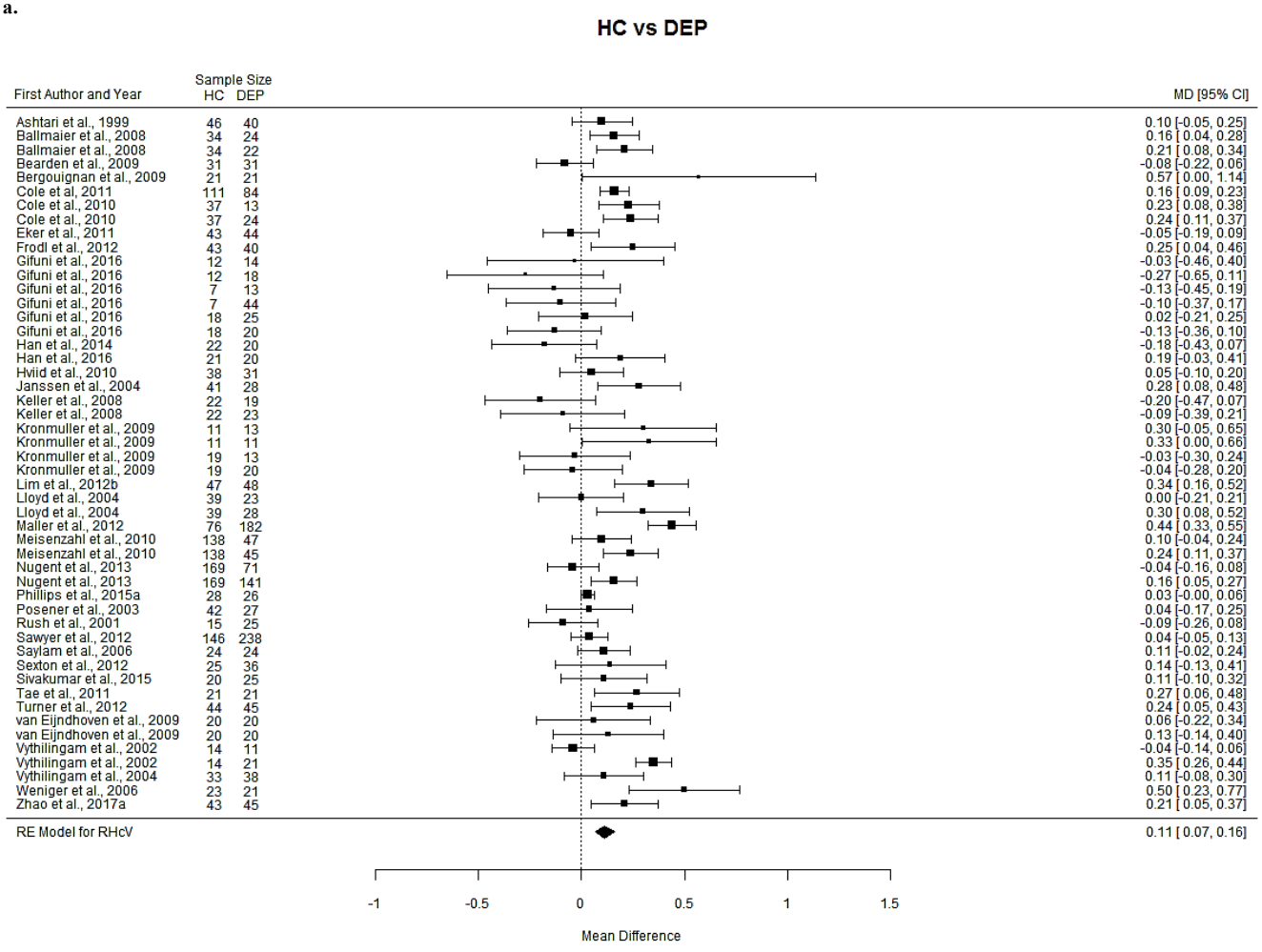

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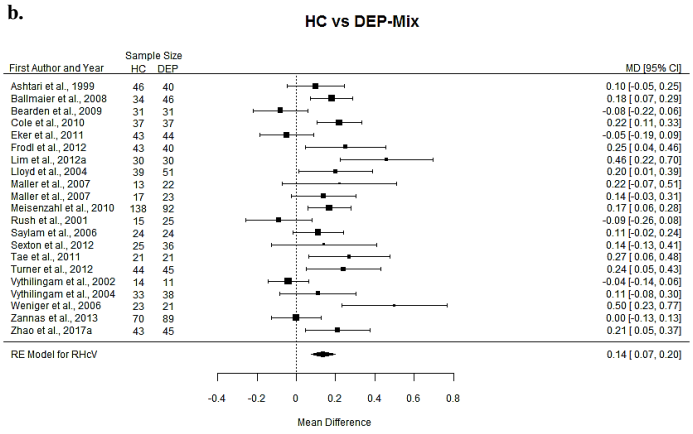

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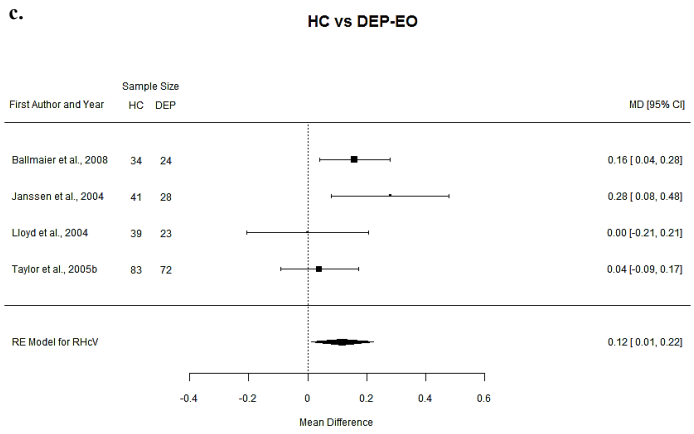

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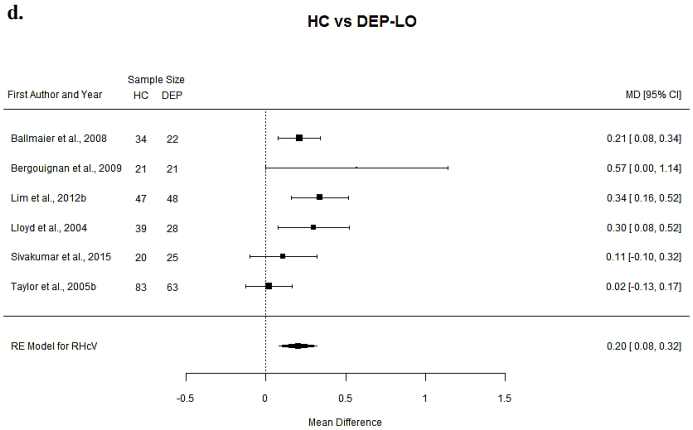

Supplemental Figure S7. RHcV forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), early-onset depression (EO) (**c**), and late-onset depression (LO) (**d**).

RHcV: right hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

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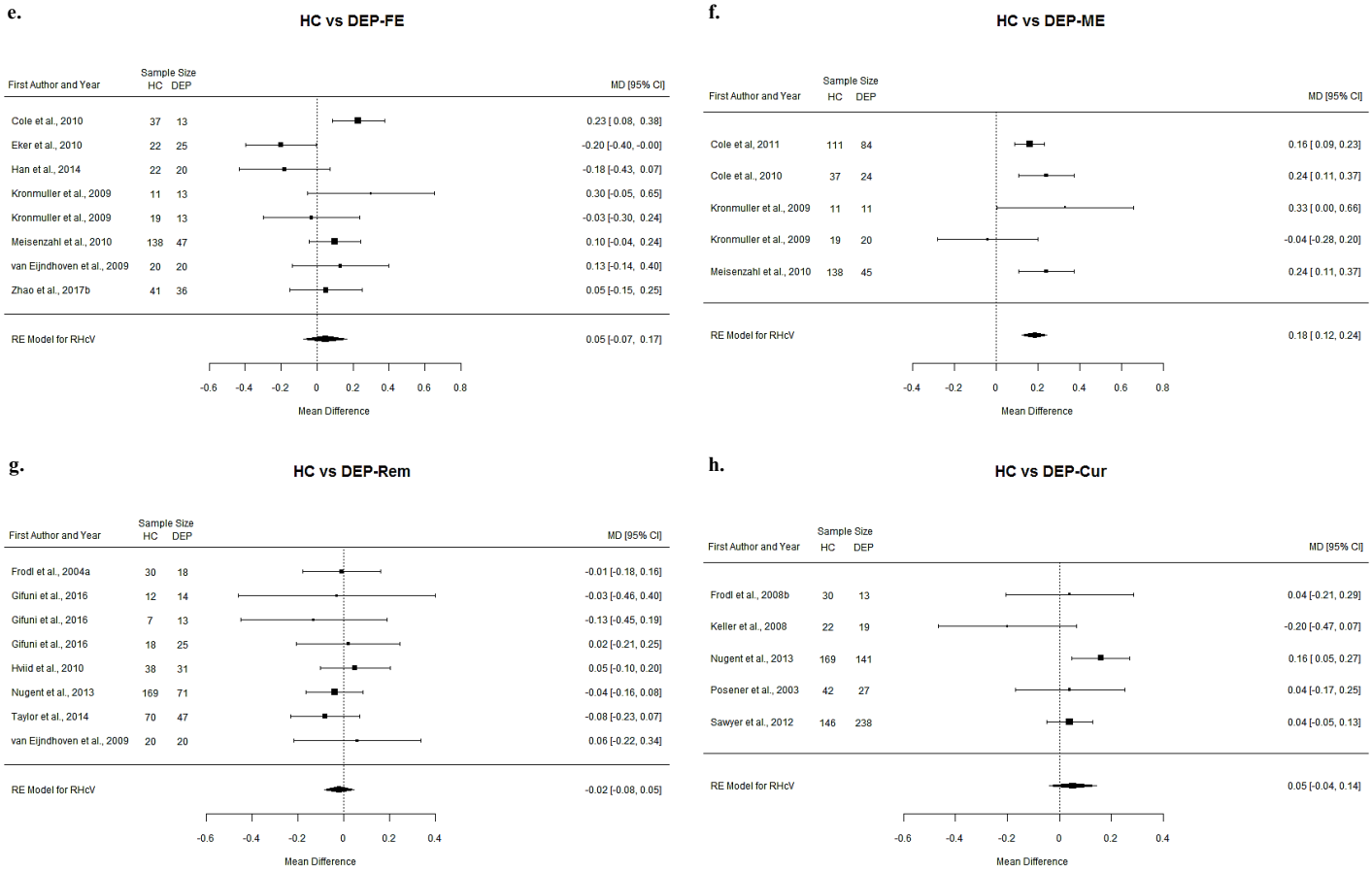

Supplemental Figure S7. RHcV forest plots (continued)
Forest plots of subgroup analyses for first-episode of depression (FE) (**e**), multiple-episodes of depression (ME) (**f**), depression in remission (Rem) (**g**), and current depression (Cur) (**h**).

RHcV: right hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

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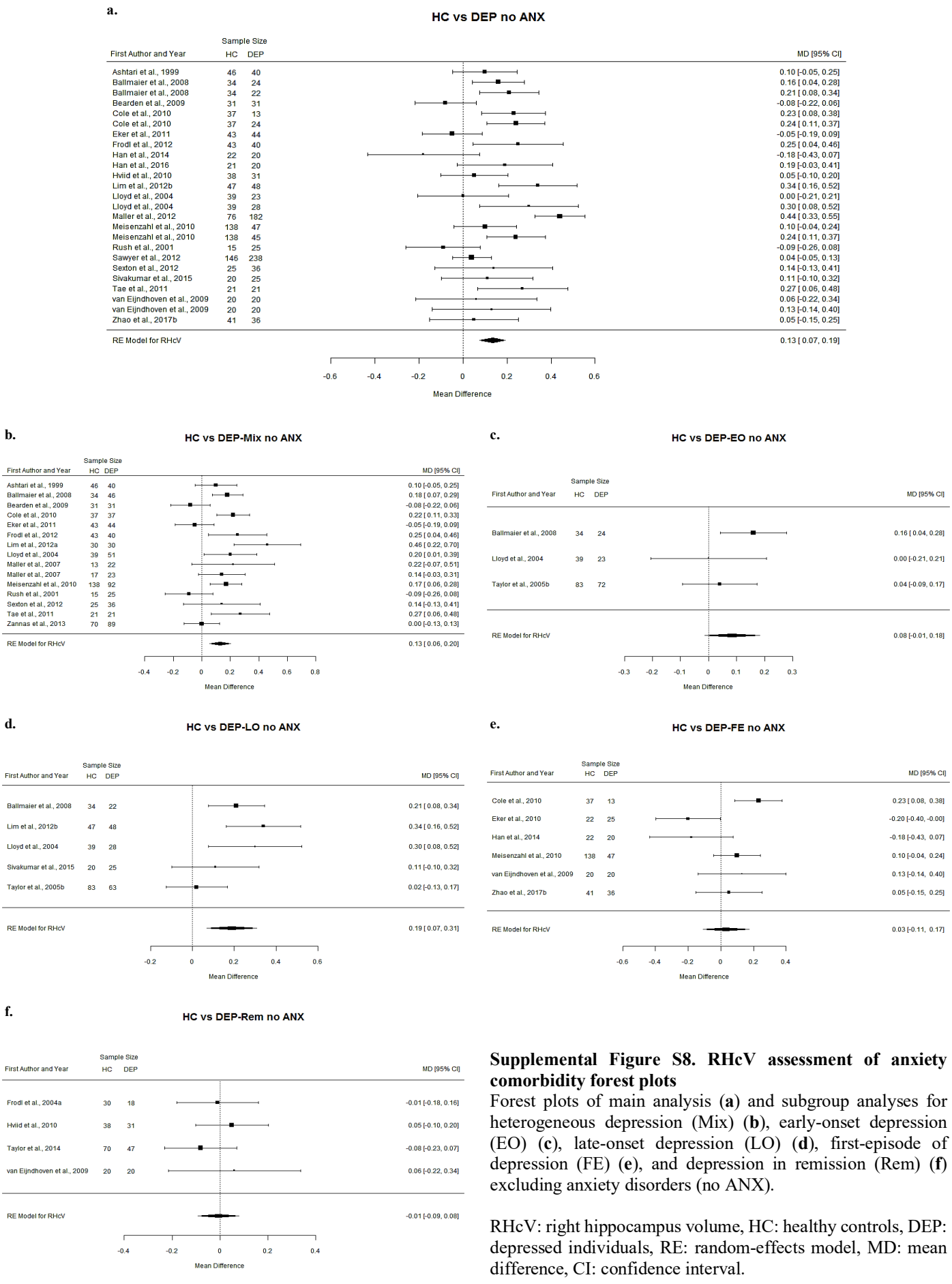

Supplemental Figure S8. RHcV assessment of anxiety comorbidity forest plots

Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), early-onset depression (EO) (**c**), late-onset depression (LO) (**d**), first-episode of depression (FE) (**e**), and depression in remission (Rem) (**f**) excluding anxiety disorders (no ANX).

RHcV: right hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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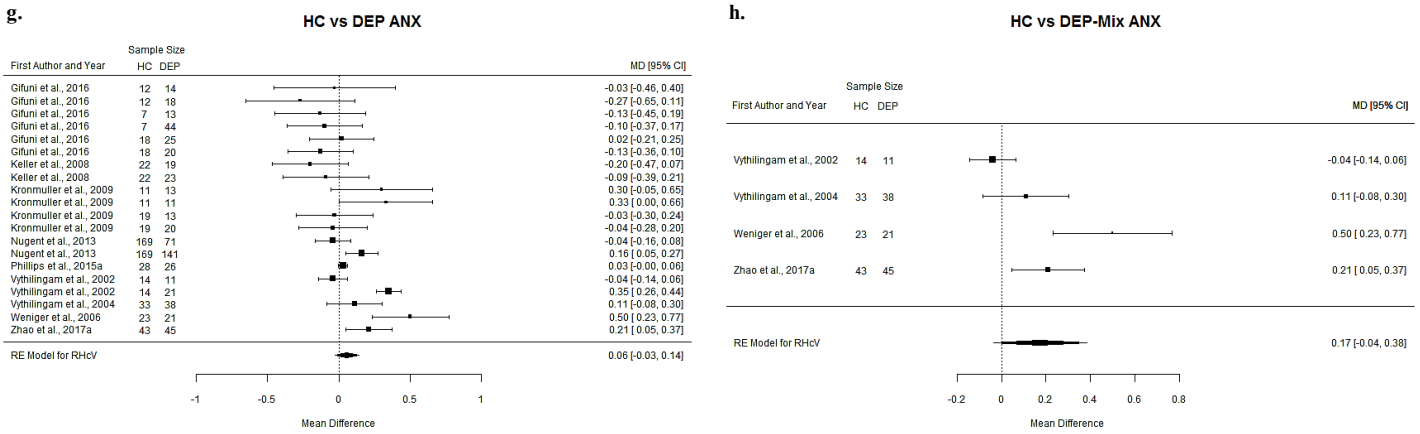

Supplemental Figure S8. RHcV assessment of anxiety comorbidity forest plots (continued)
Forest plots of main analysis (**g**), and subgroup analysis for heterogeneous depression (Mix) (**h**) comorbid with anxiety disorders (ANX).

RHcV: right hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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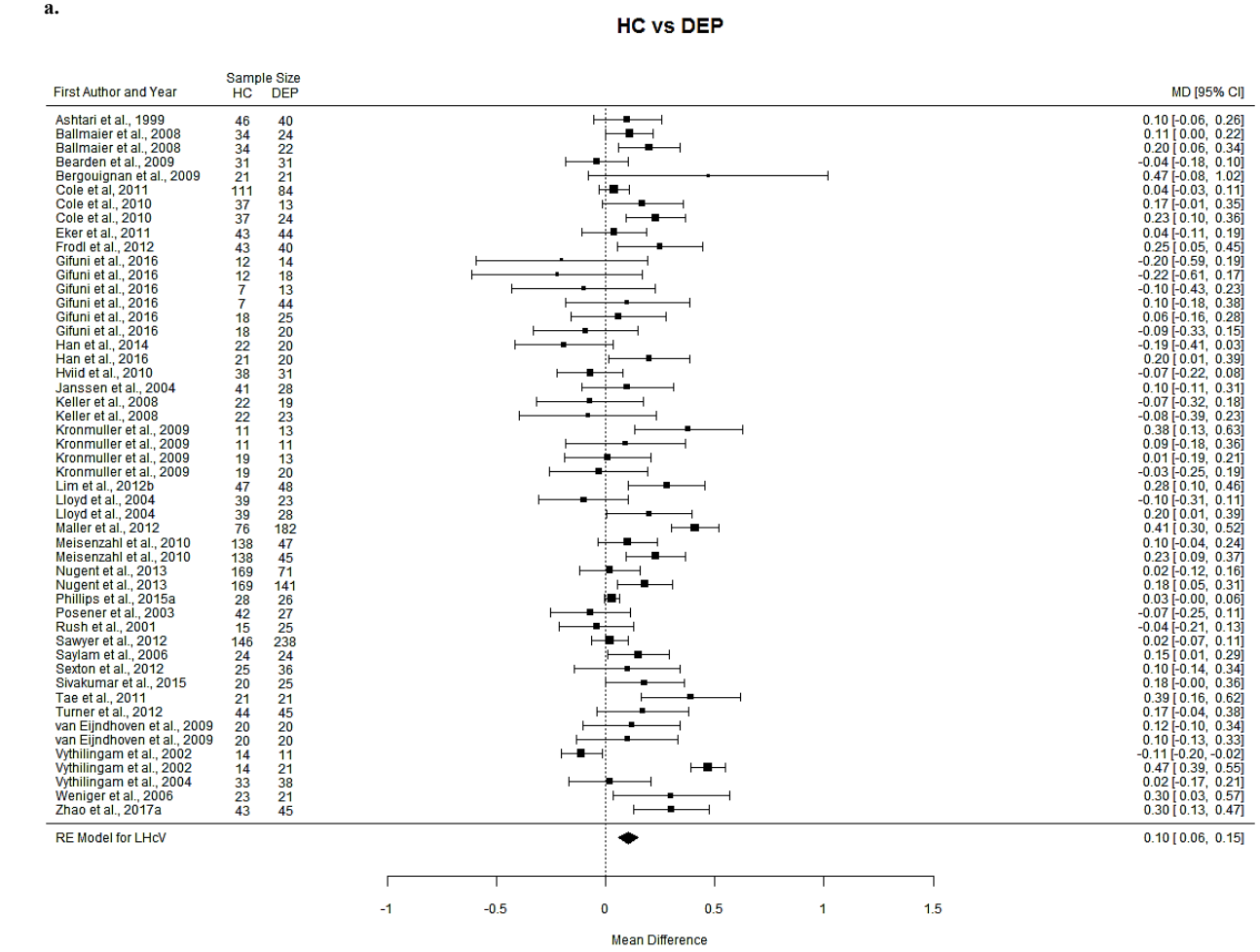

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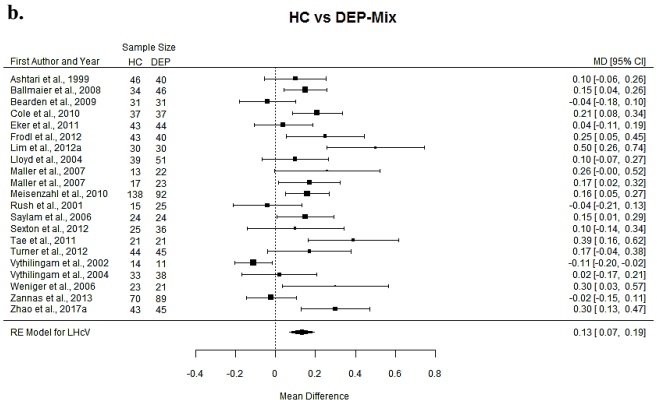

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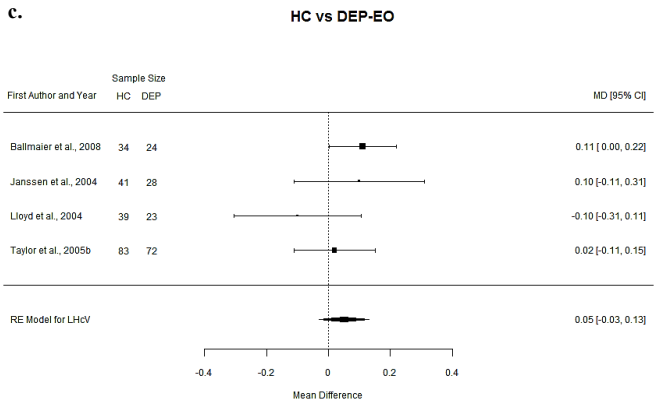

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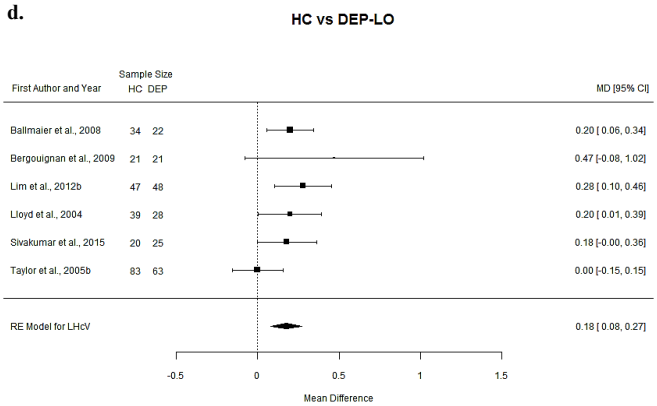

Supplemental Figure S9. LHcV forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), early-onset depression (EO) (**c**), and late-onset depression (LO) (**d**).

LHcV: left hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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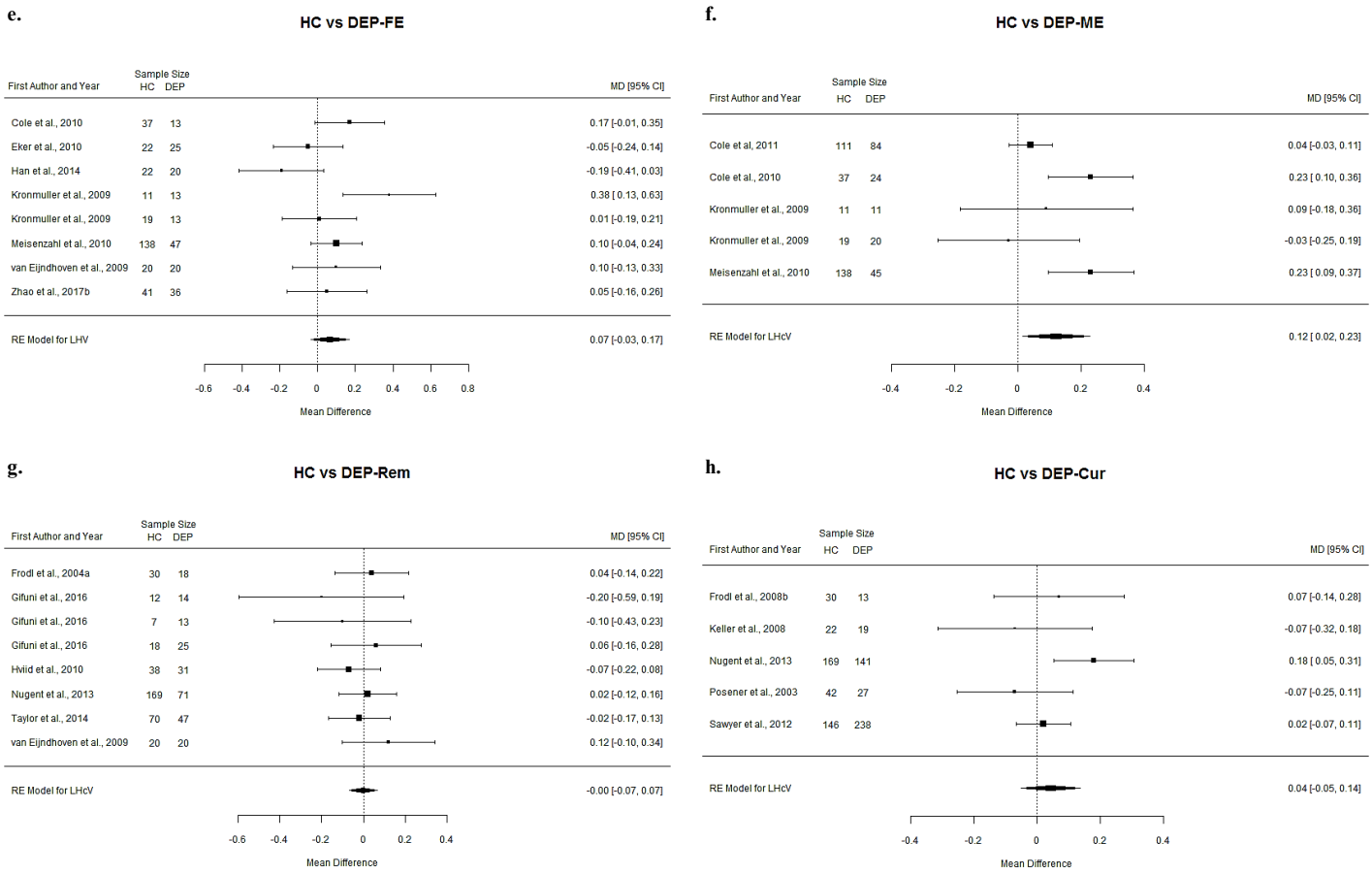

Supplemental Figure S9. LHcV forest plots (continued)
Forest plots of subgroup analyses for first-episode depression (FE) (**e**), multiple-episodes of depression (ME) (**f**), depression in remission (Rem) (**g**), and current depression (Cur) (**h**).

LHcV: left hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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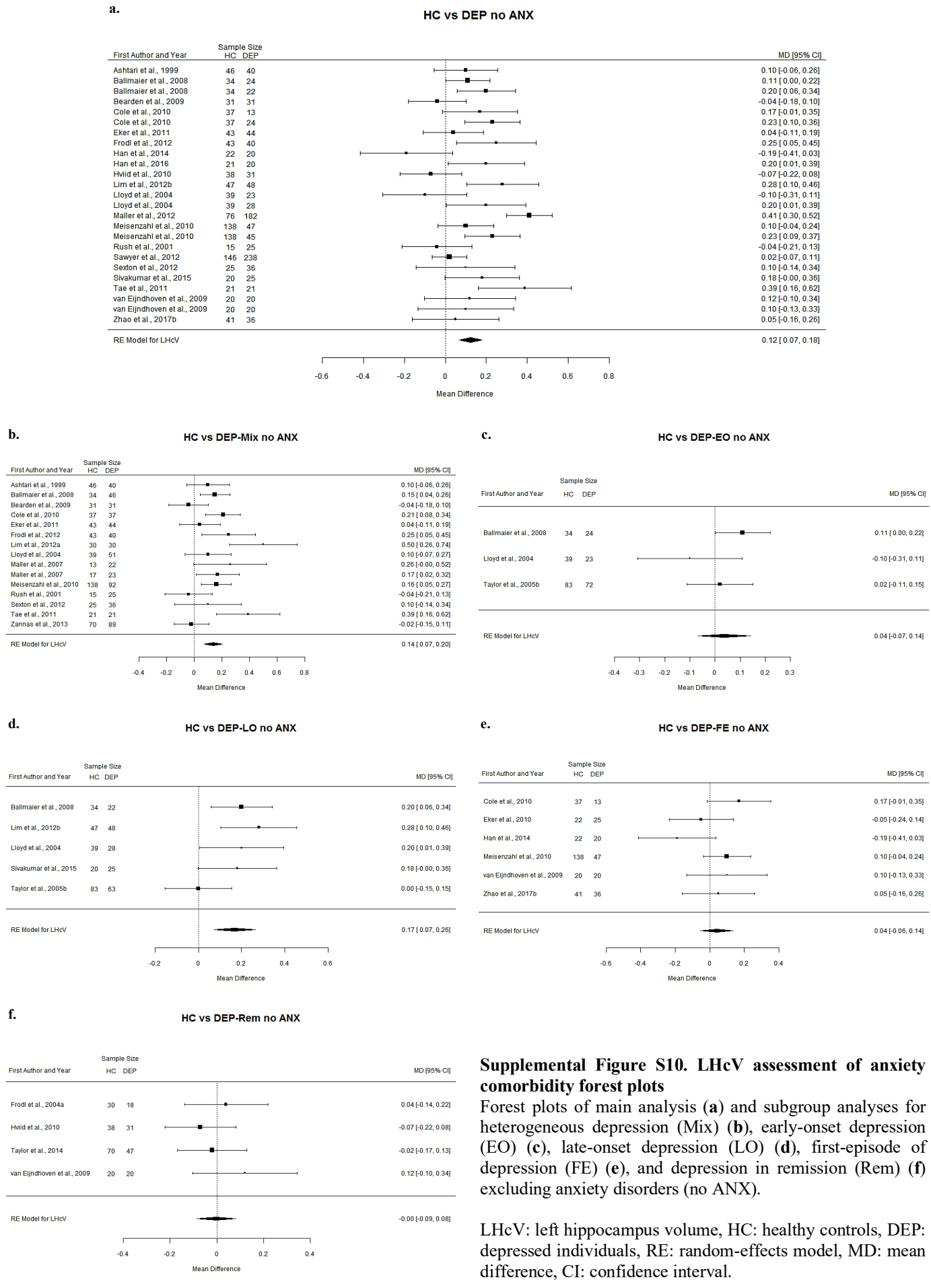

Supplemental Figure S10. LHcV assessment of anxiety comorbidity forest plots

Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), early-onset depression (EO) (**c**), late-onset depression (LO) (**d**), first-episode of depression (FE) (**e**), and depression in remission (Rem) (**f**) excluding anxiety disorders (no ANX).

LHcV: left hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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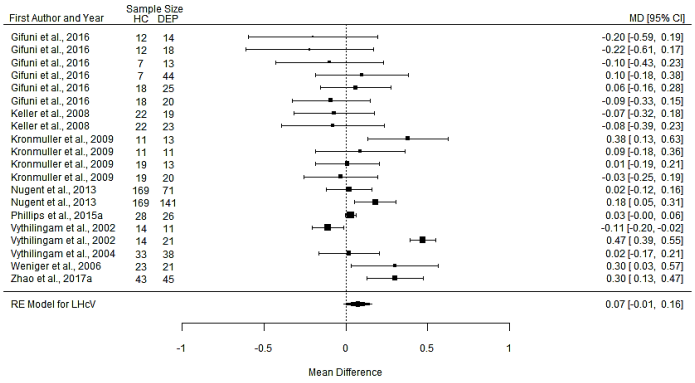
g.



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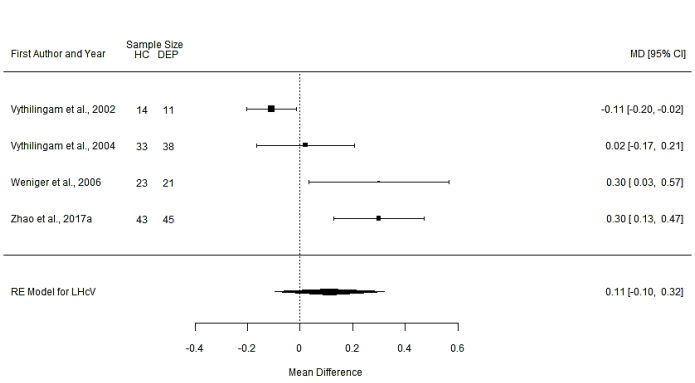

Supplemental Figure S10. LHcV assessment of anxiety comorbidity forest plots (continued)
Forest plots of main analysis (**g**), and subgroup analysis for heterogeneous depression (Mix) (**h**) comorbid with anxiety disorders (ANX).

LHcV: left hippocampus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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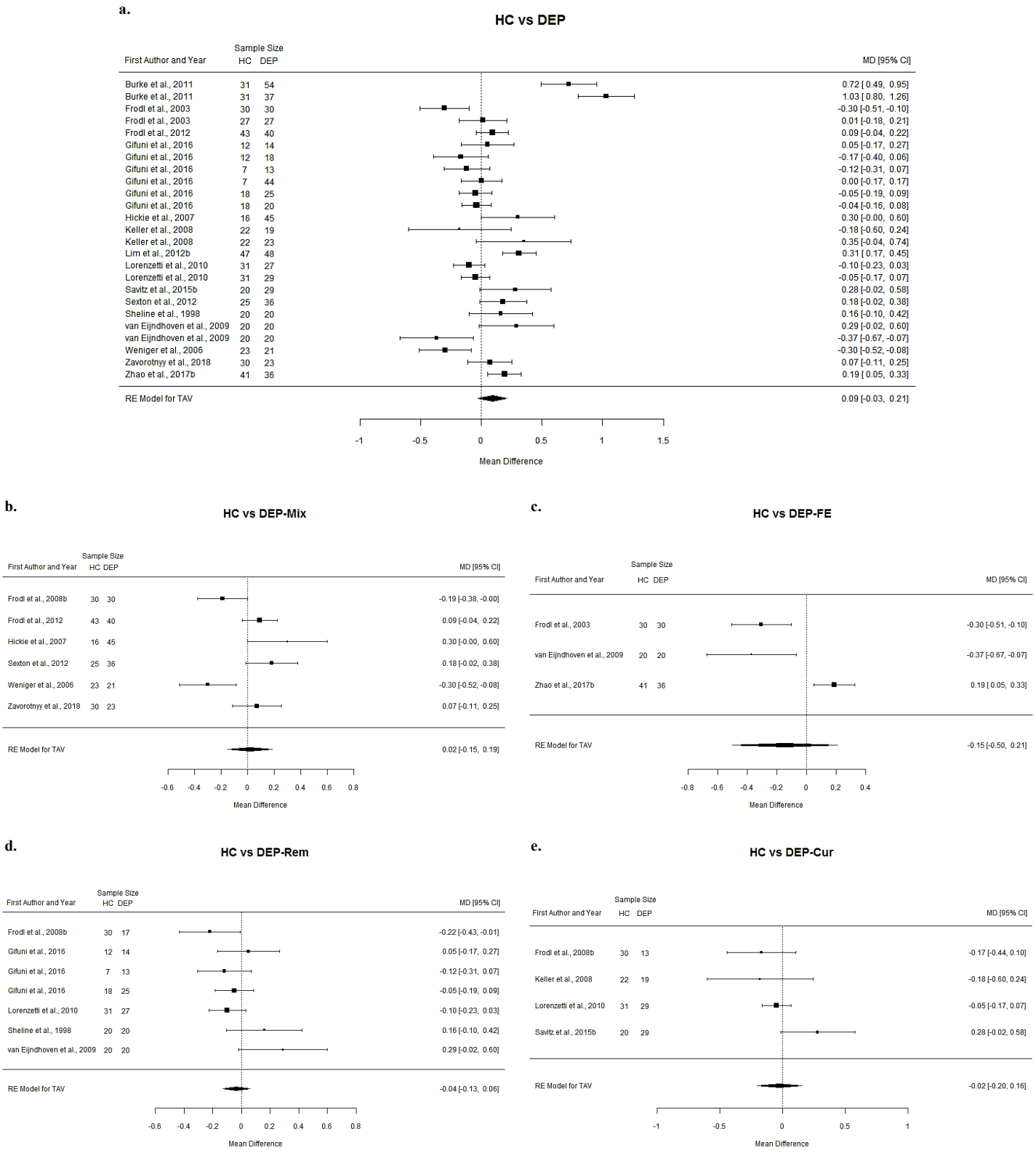

Supplemental Figure S11. TAV forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), first-episode of depression (FE) (**c**), depression in remission (Rem) (**d**), and current depression (Cur) (**e**).

TAV: total amygdala volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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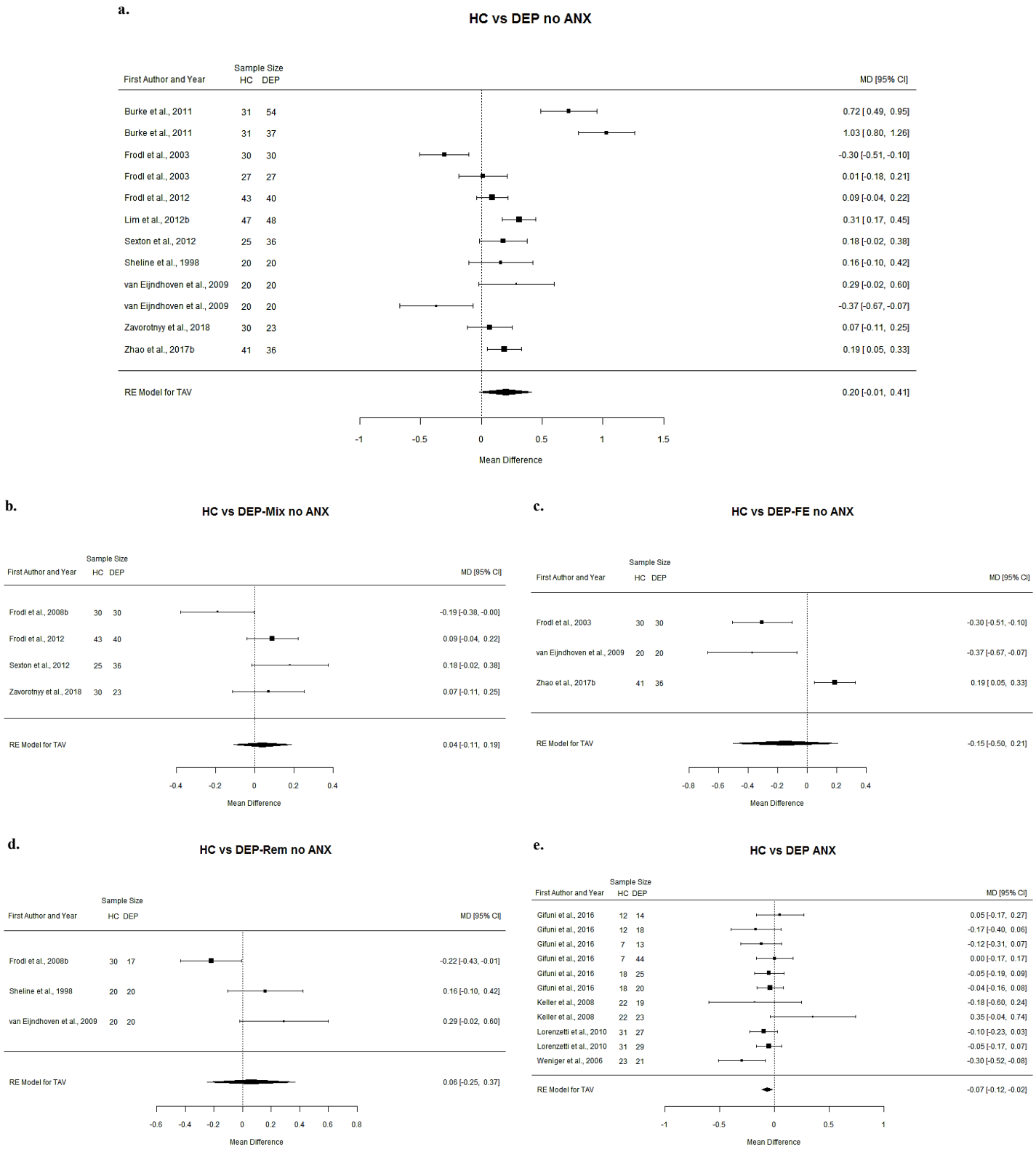

Supplemental Figure S12. TAV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), first-episode of depression (FE) (**c**), and depression in remission (Rem) (**d**) excluding anxiety disorders (no ANX). Forest plot of main analysis (**e**) comorbid with anxiety disorders (ANX).

TAV: total amygdala volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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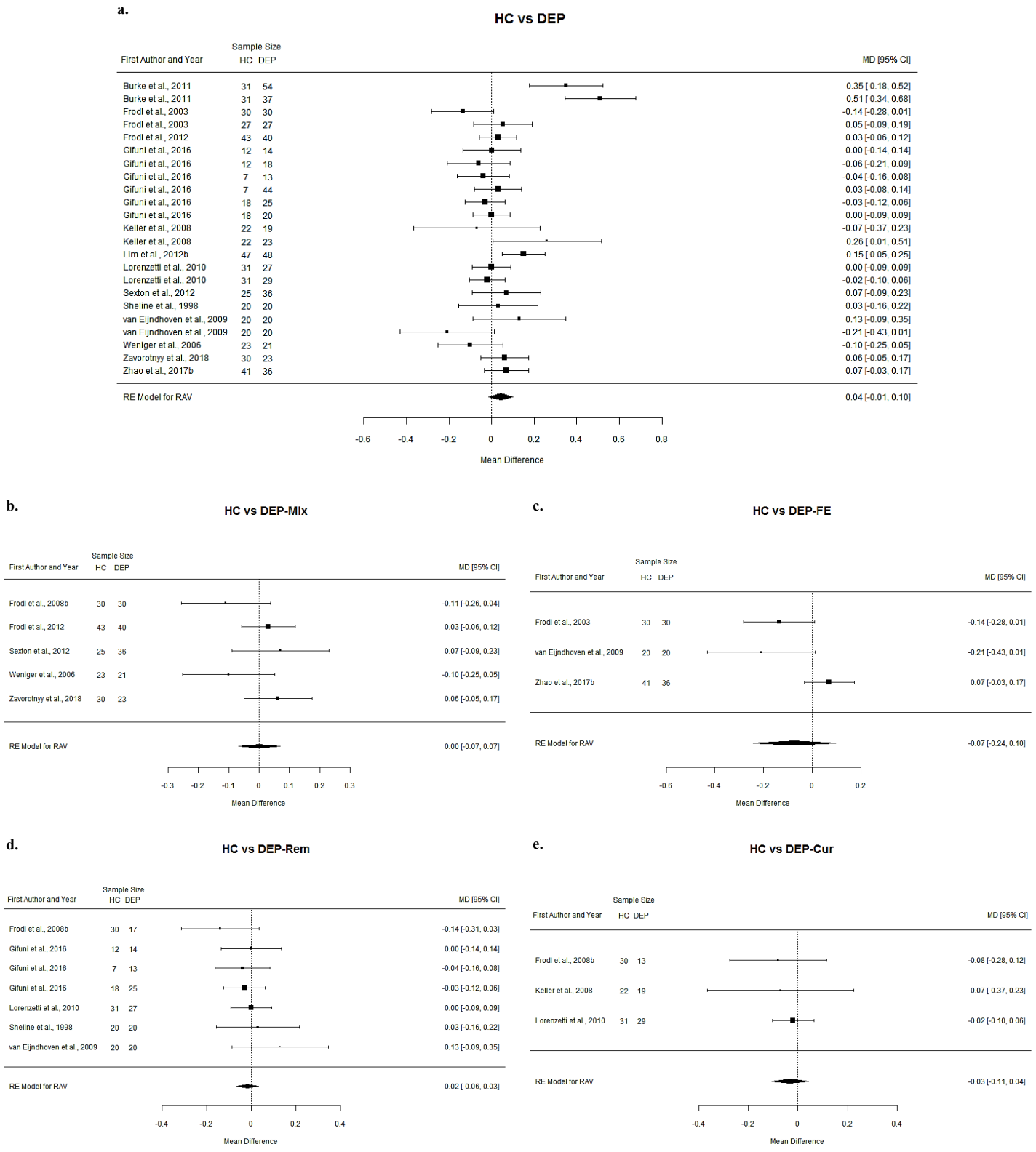

Supplemental Figure S13. RAV forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), first-episode of depression (FE) (**c**), depression in remission (Rem) (**d**), and current depression (Cur) (**e**).

RAV: right amygdala volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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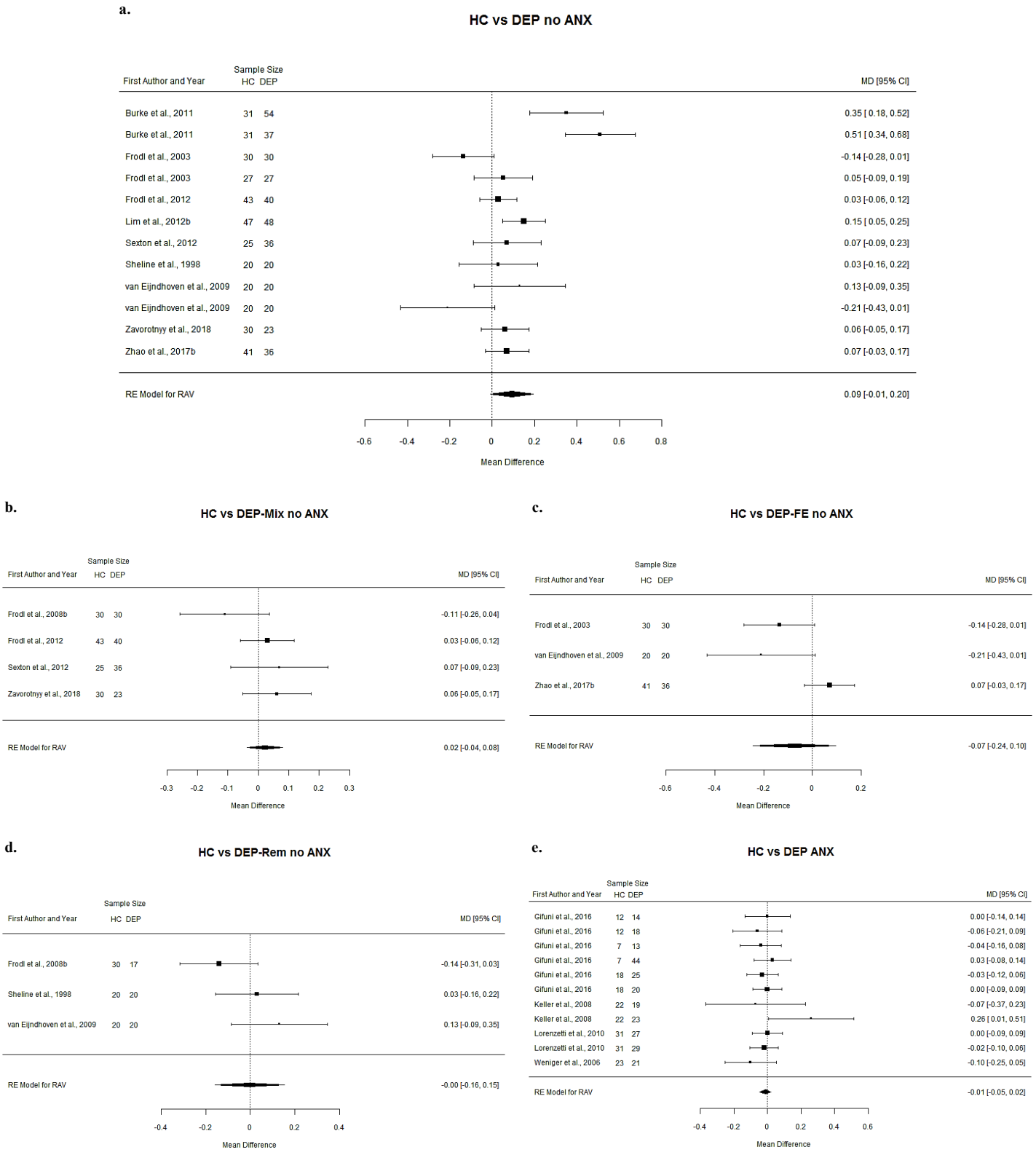

Supplemental Figure S14. RAV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), first-episode depression (FE) (**c**), and depression in remission (Rem) (**d**) excluding anxiety disorders (no ANX). Forest plot of main analysis (**e**) comorbid with anxiety disorders (ANX).

RAV: right amygdala volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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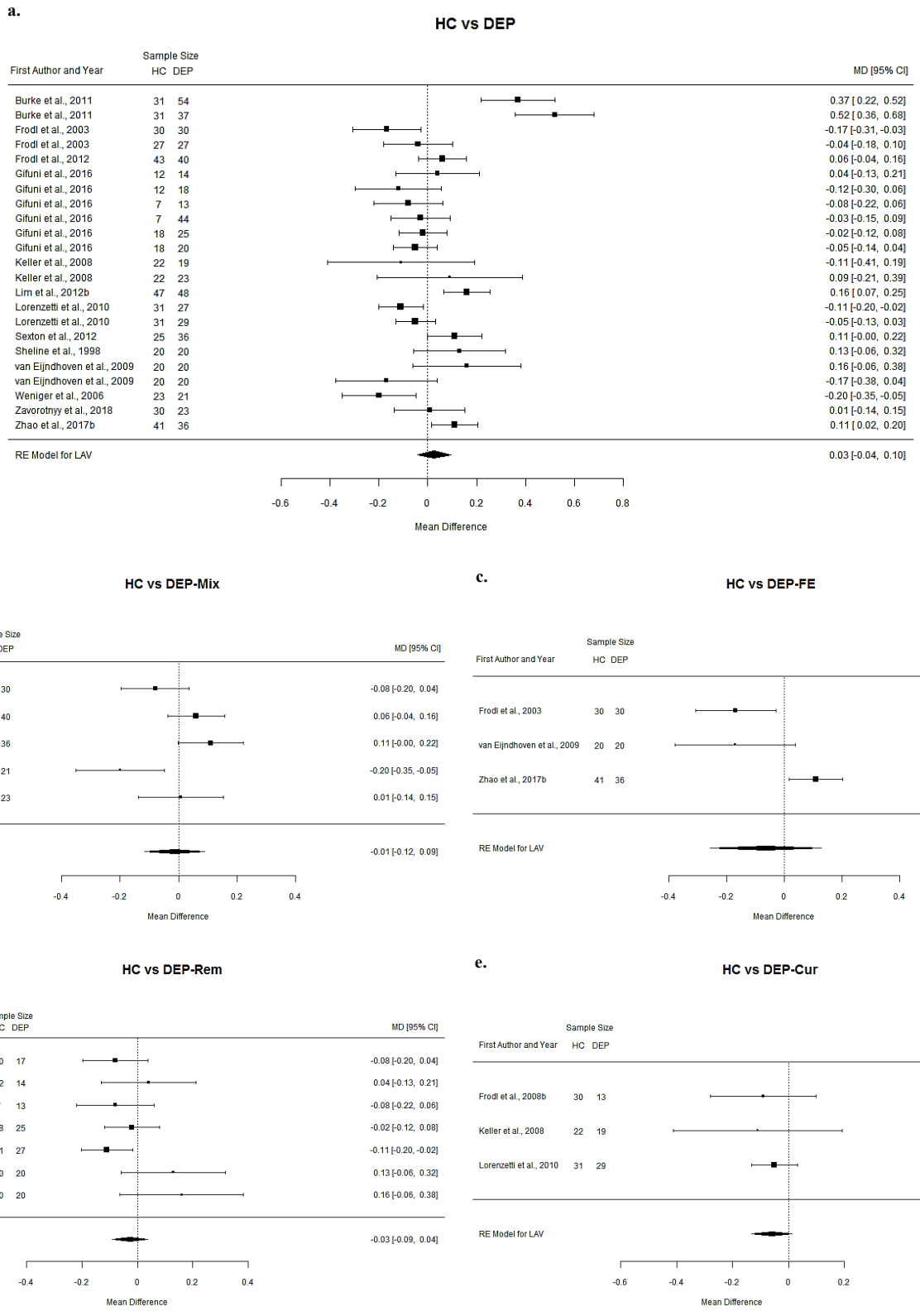

Supplemental Figure S15. LAV forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), first-episode depression (FE) (**c**), depression in remission (Rem) (**d**), and current depression (Cur) (**e**).

LAV: left amygdala volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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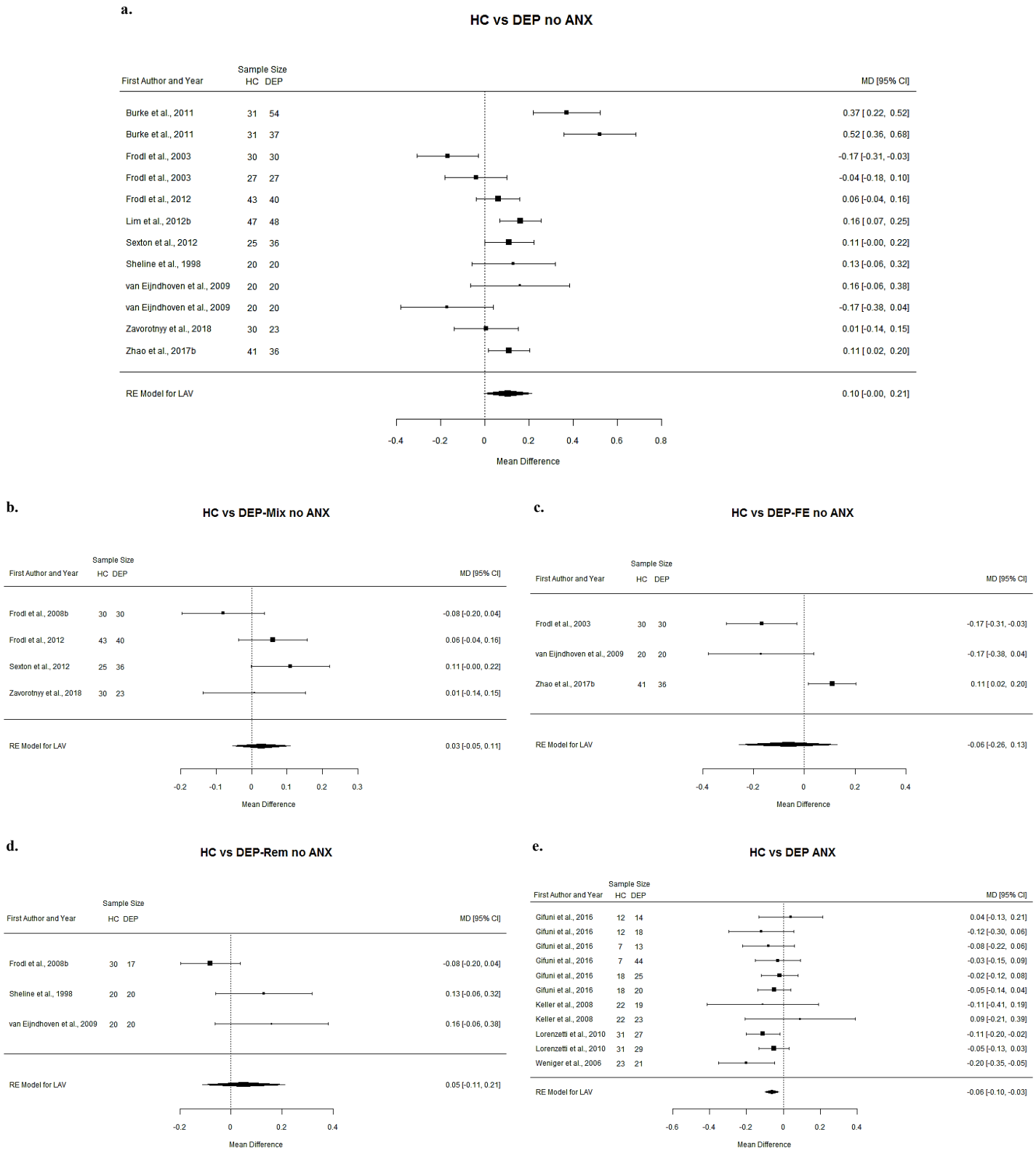

Supplemental Figure S16. LAV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**), first-episode depression (FE) (**c**), and depression in remission (Rem) (**d**) excluding anxiety disorders (no ANX). Forest plot of main analysis (**e**) comorbid with anxiety disorders (ANX).

LAV: left amygdala volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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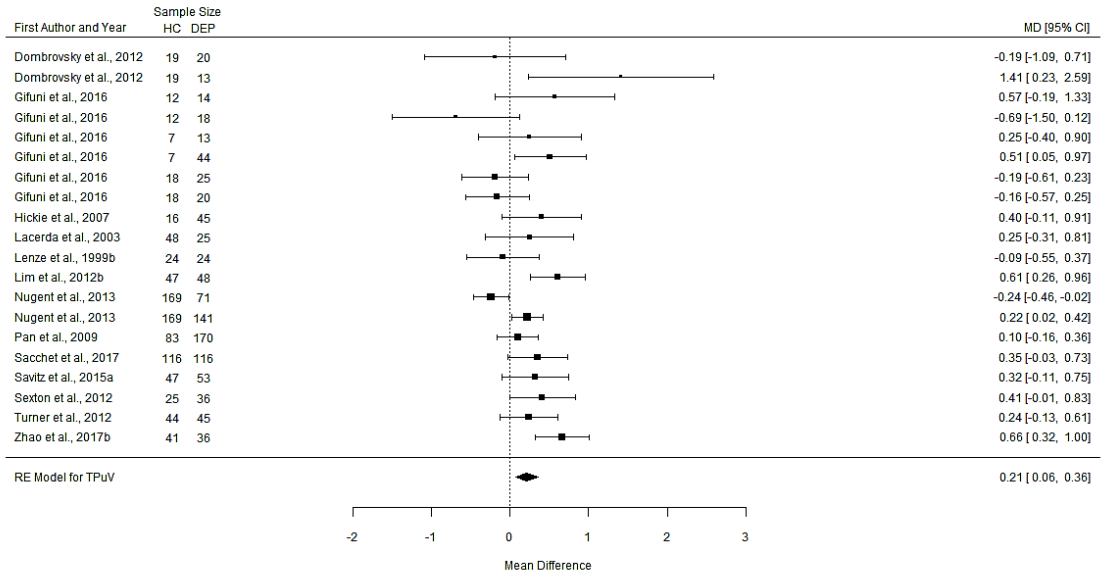

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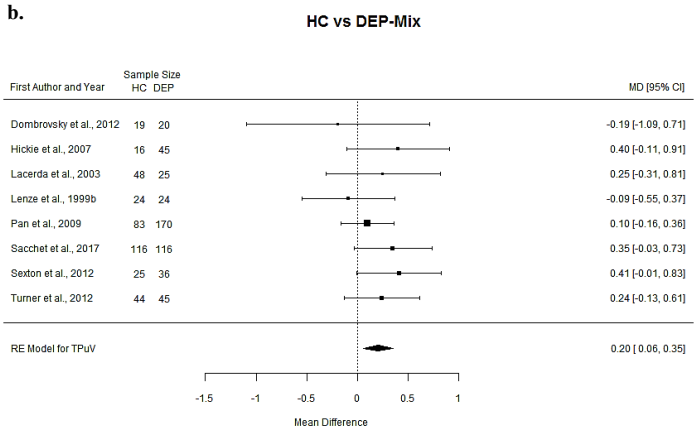

Supplemental Figure S17. TPuV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

TPuV: total putamen volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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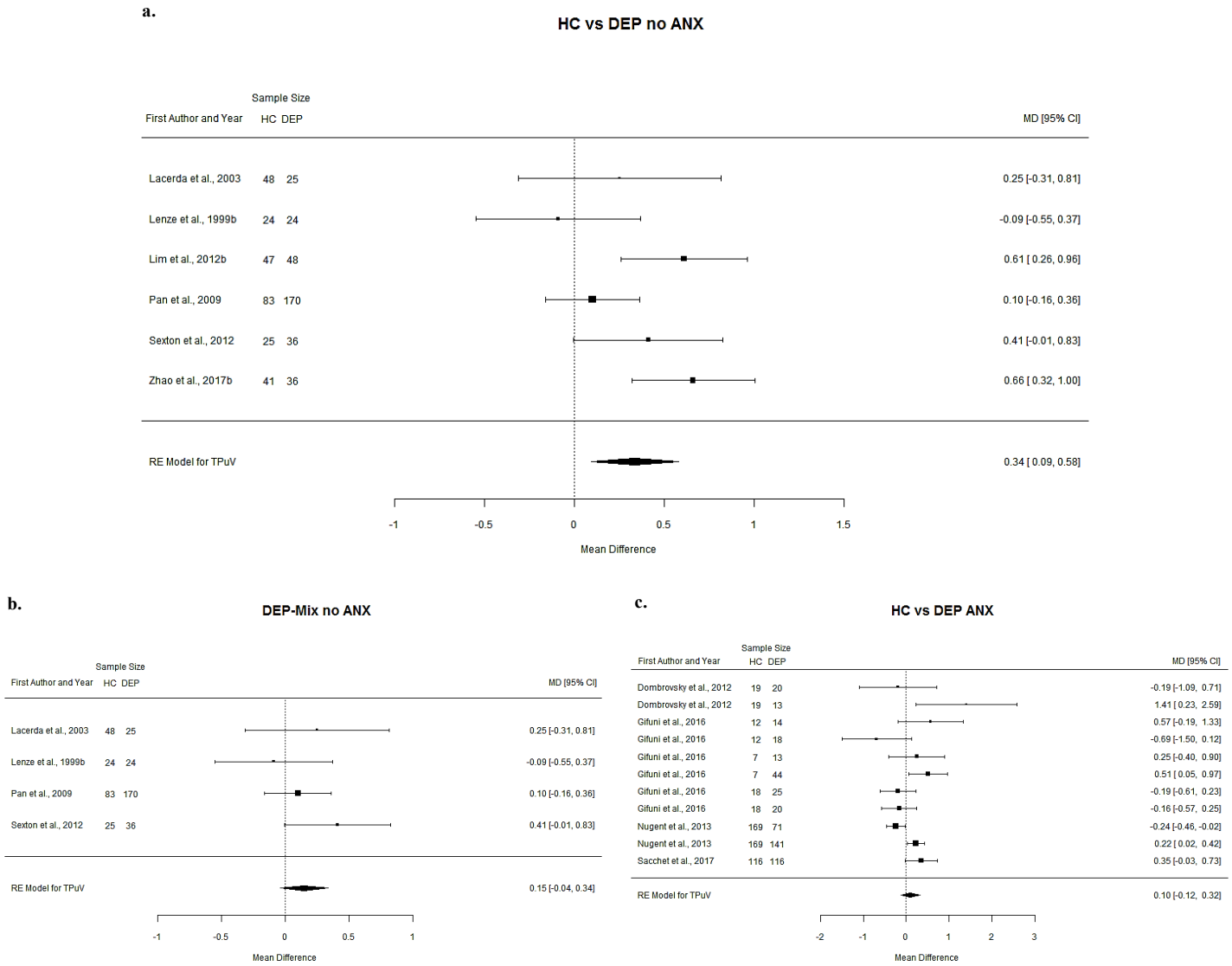

Supplemental Figure S18. TPuV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**) excluding anxiety disorders (no ANX). Forest plot of main analysis (**c**) comorbid with anxiety disorders ANX).

TPuV: total putamen volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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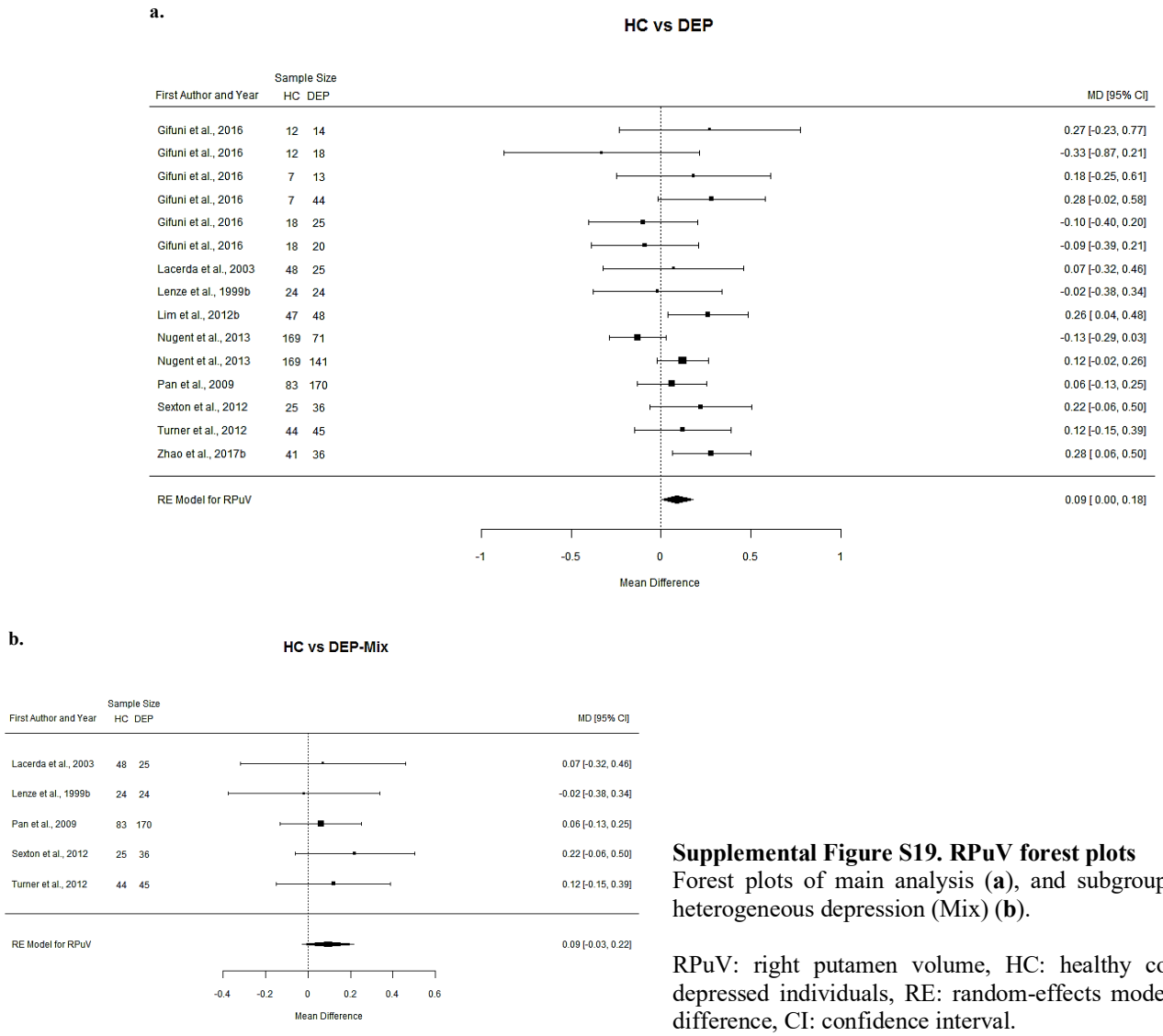

Supplemental Figure S19. RPuV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

RPuV: right putamen volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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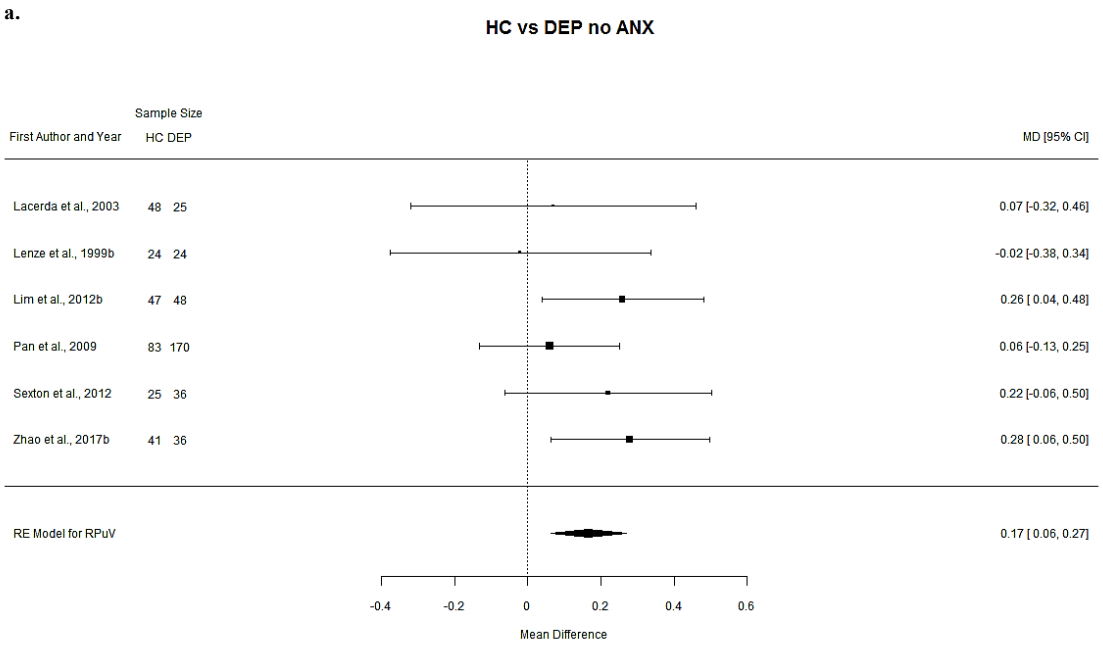

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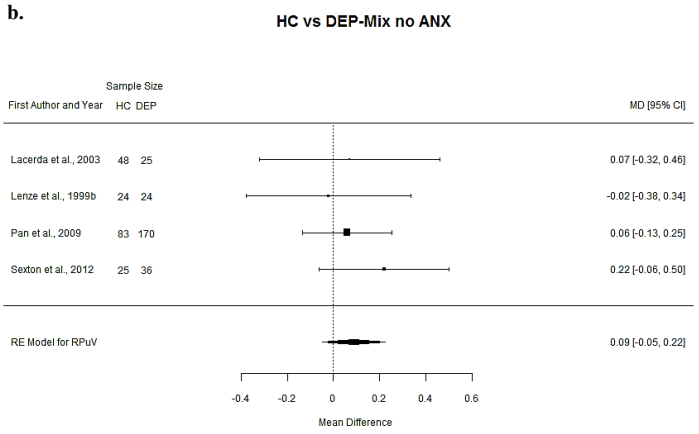

Supplemental Figure S20. RPuV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**) excluding anxiety disorders (no ANX).

RPuv: right putamen volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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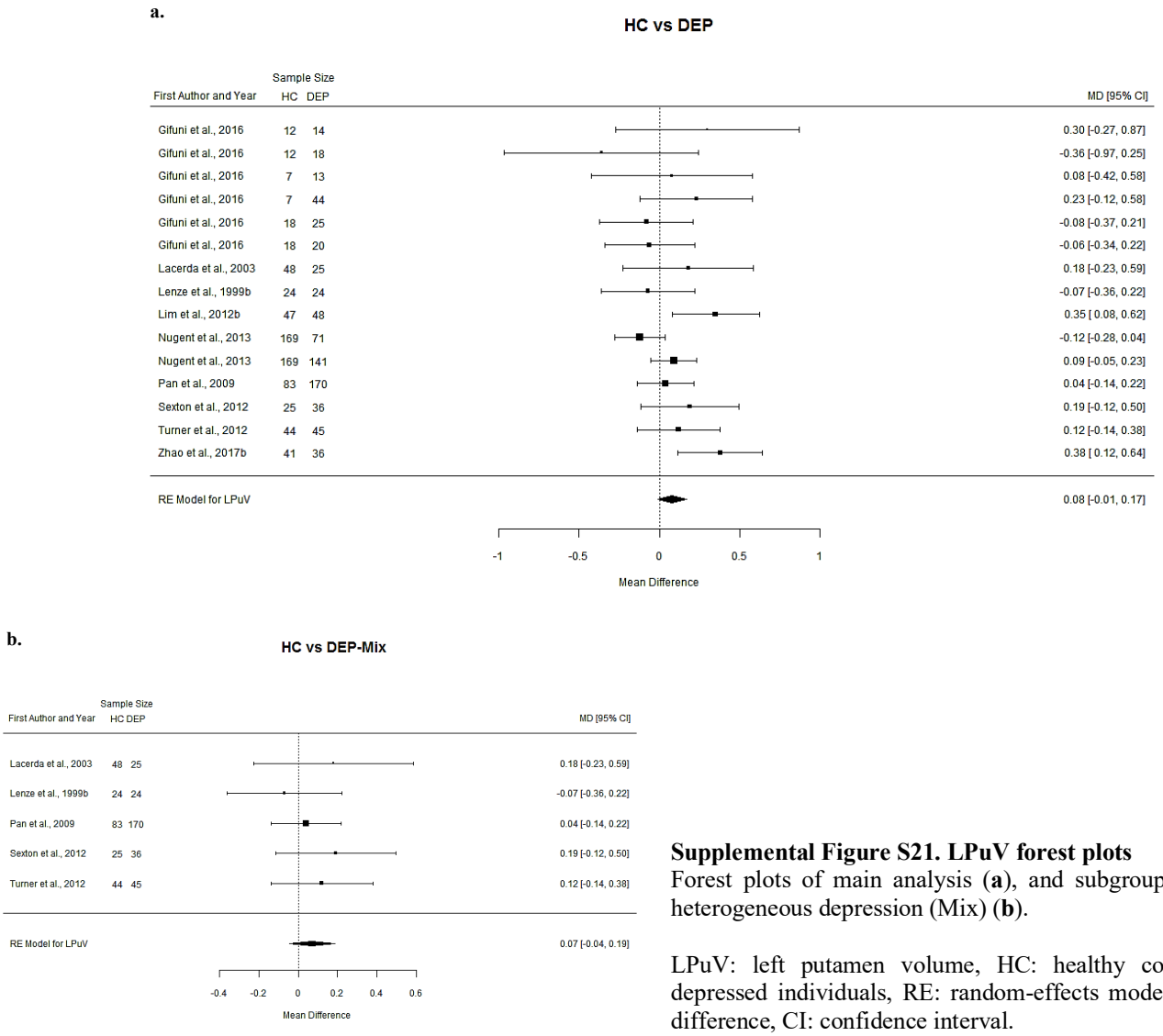

Supplemental Figure S21. LPuV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

LPuV: left putamen volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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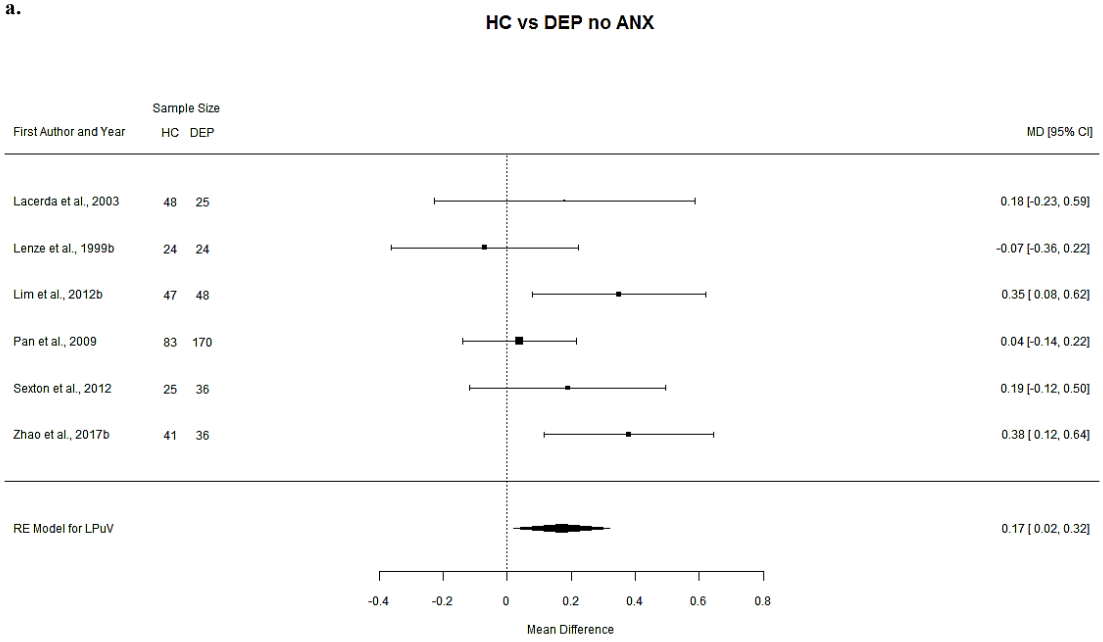

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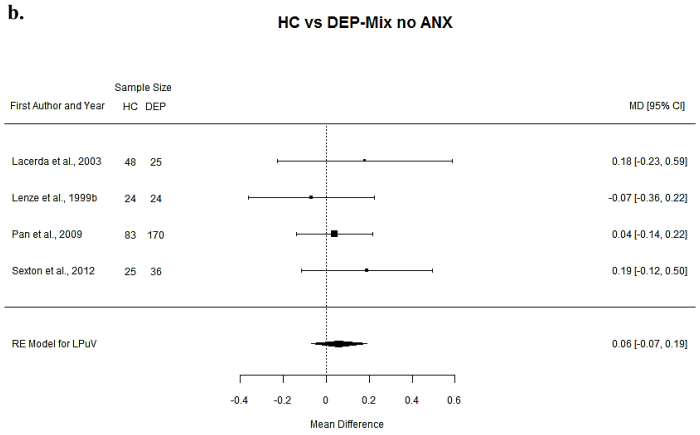

Supplemental Figure S22. LPuV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**) excluding anxiety disorders (no ANX).

LPuV: left putamen volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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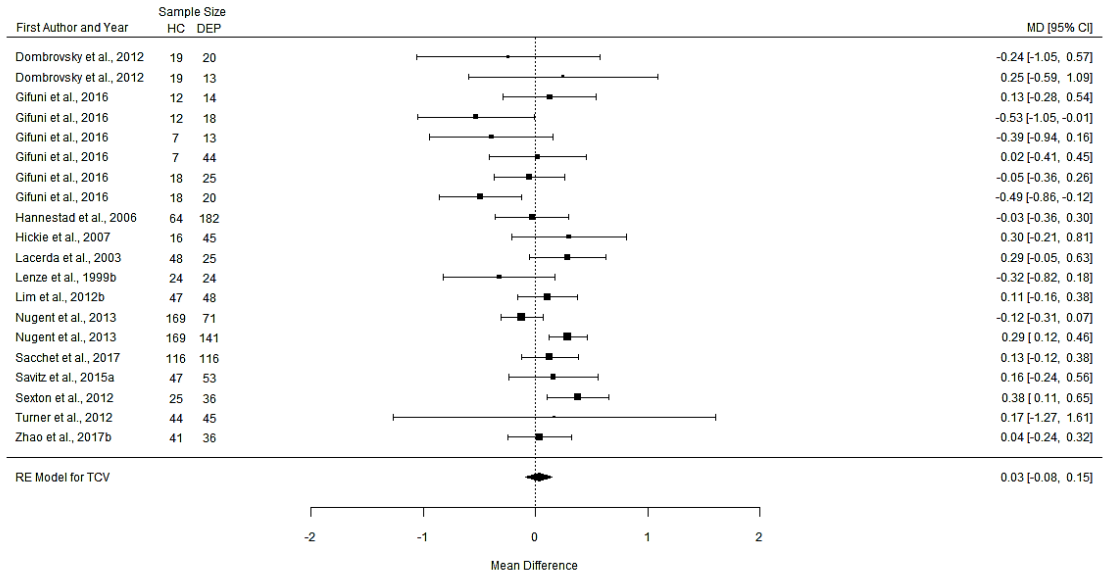

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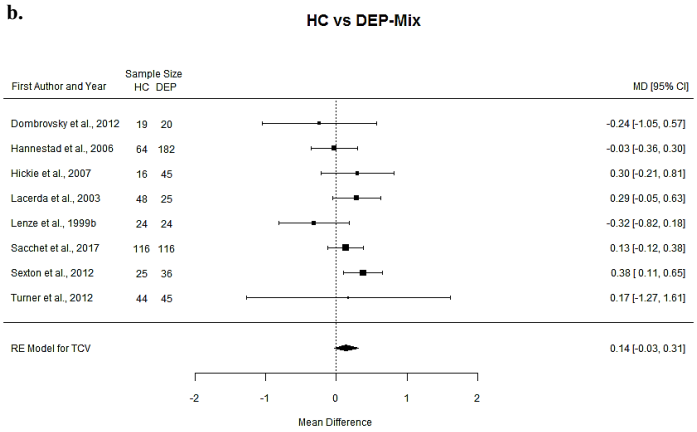

Supplemental Figure S23. TCV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

TCV: total caudate volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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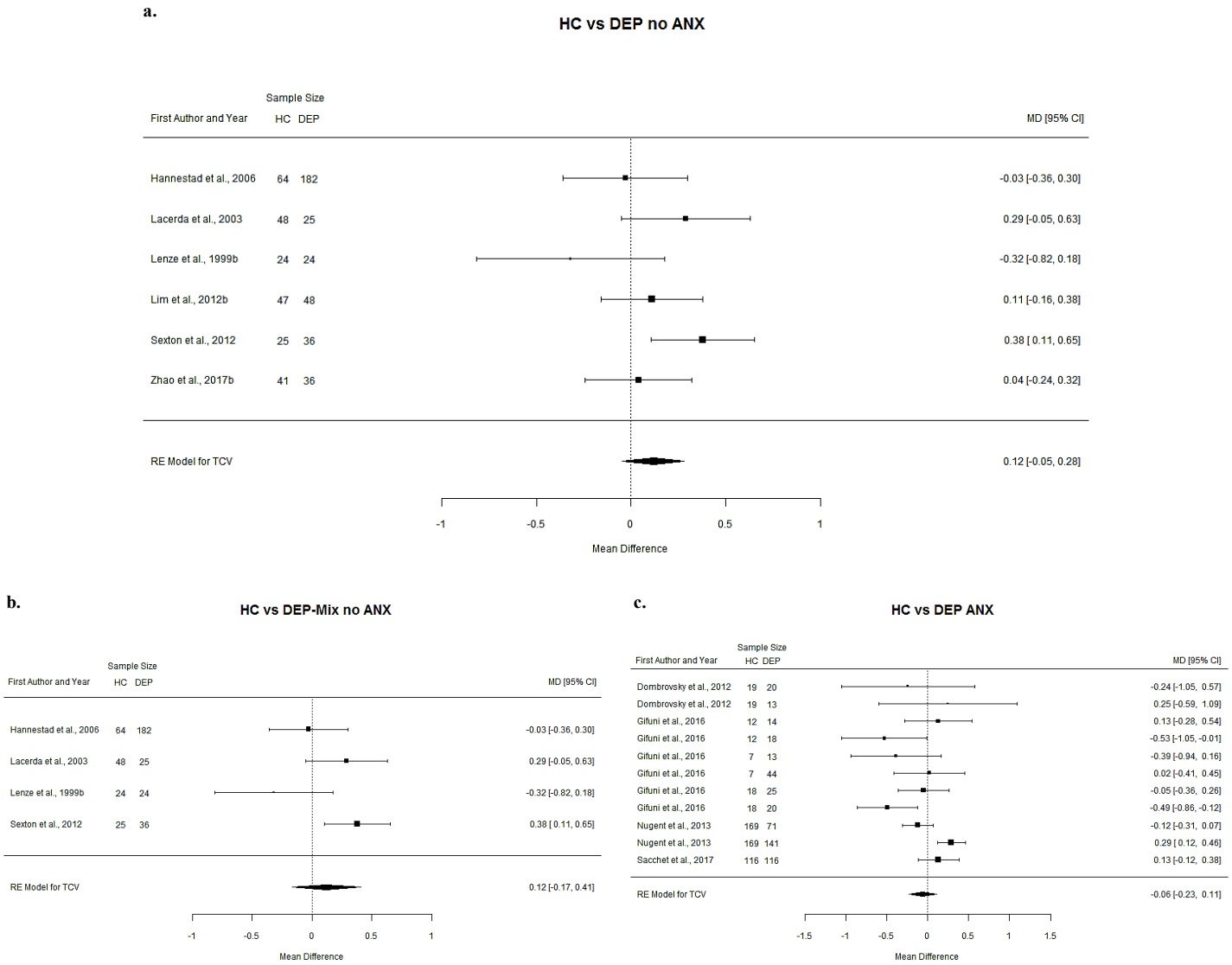

Supplemental Figure S24. TCV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**) excluding anxiety disorders (no ANX). Forest plot of main analysis (**c**) comorbid with anxiety disorders (ANX).

TCV: total caudate volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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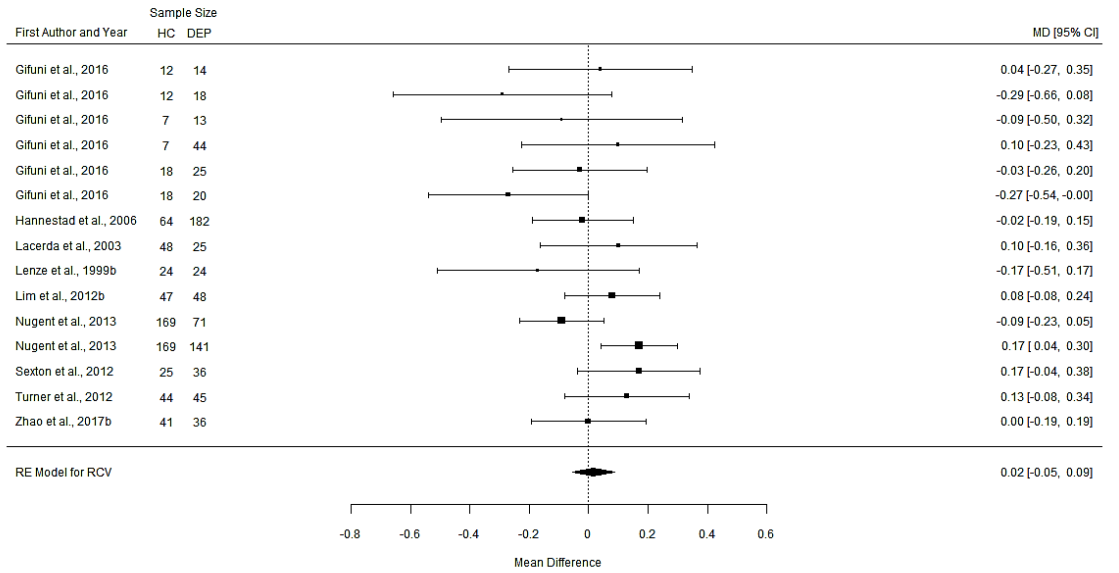

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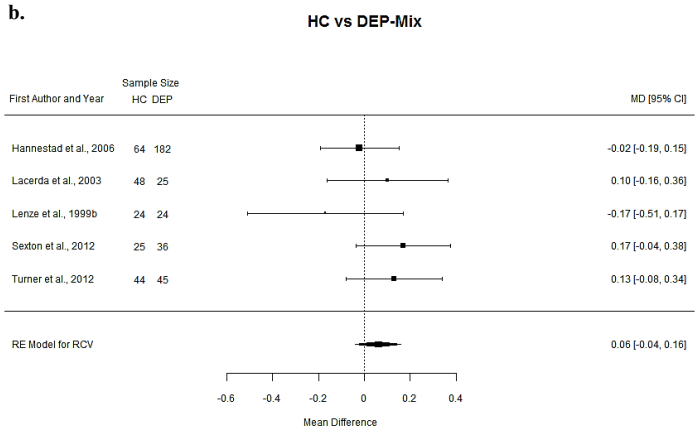

Supplemental Figure S25. RCV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

RCV: right caudate volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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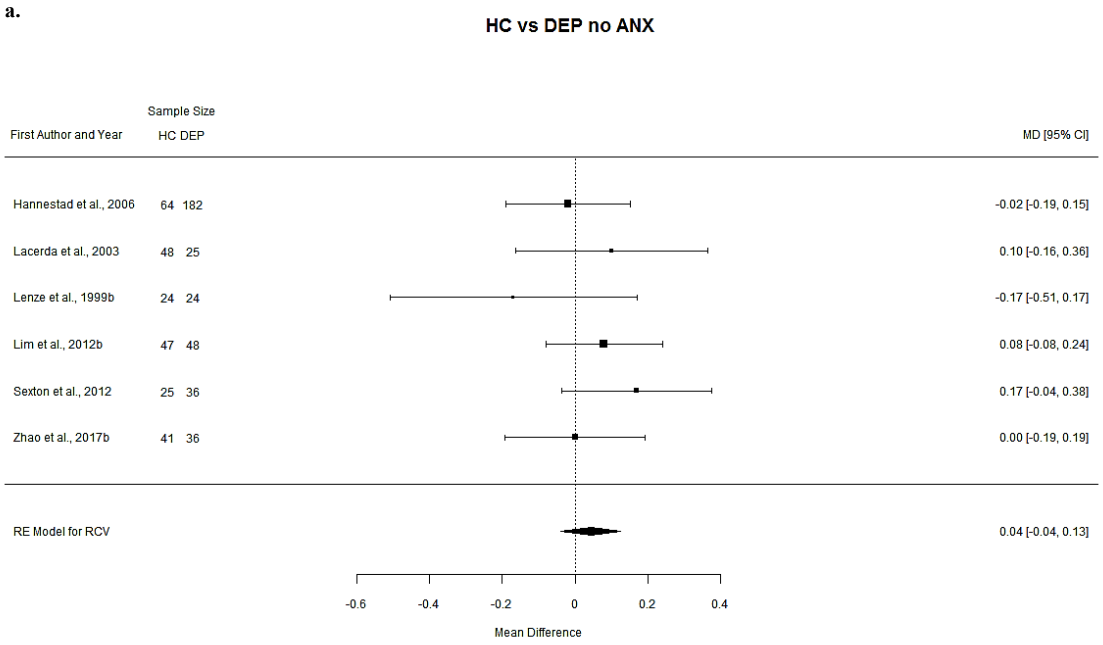
a.



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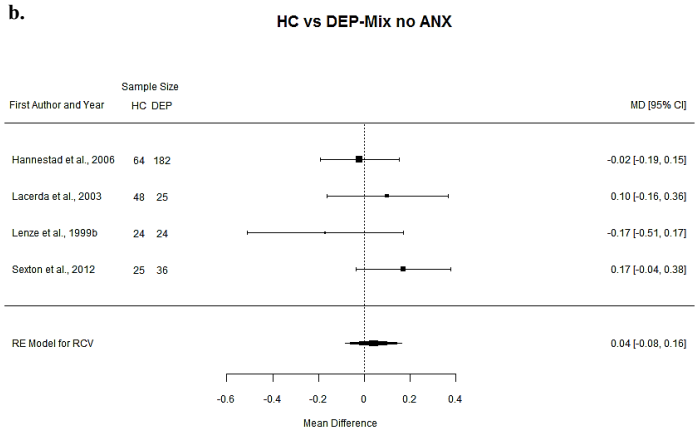

Supplemental Figure S26. RCV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**) excluding anxiety disorders (no ANX).

RCV: right caudate volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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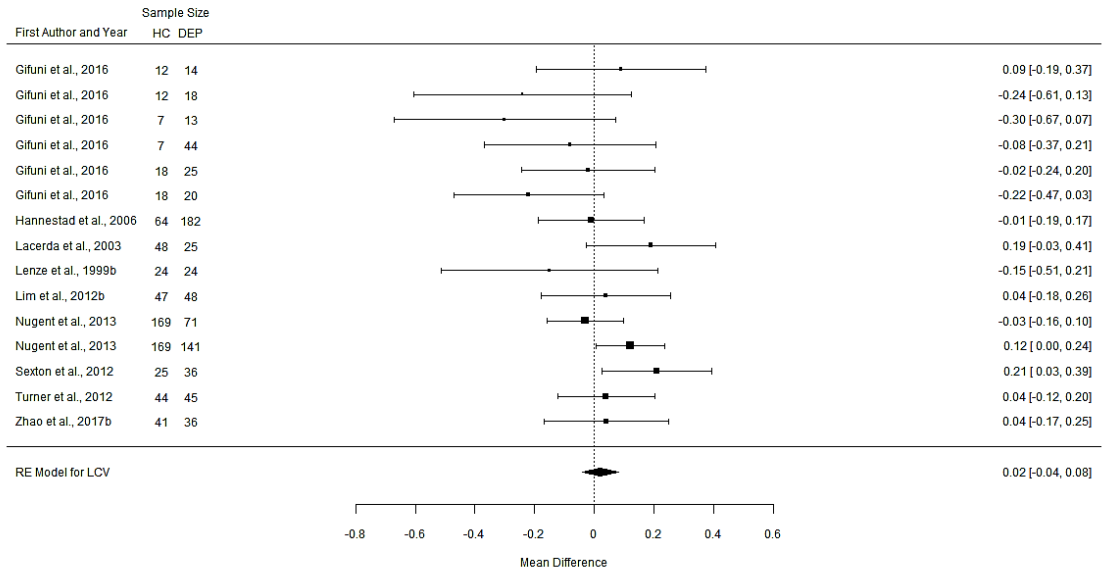
a.



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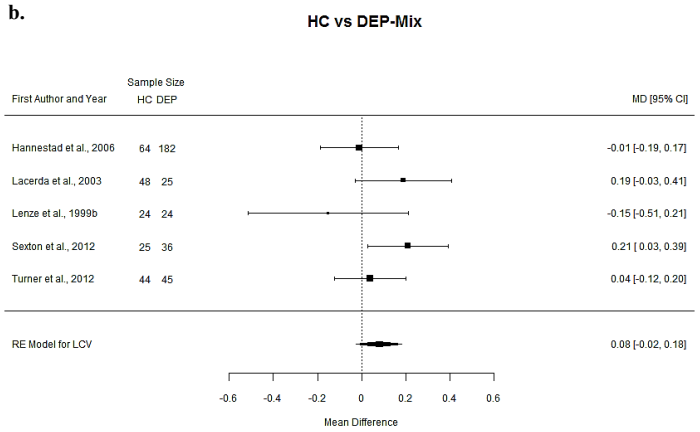

Supplemental Figure S27. LCV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

LCV: left caudate volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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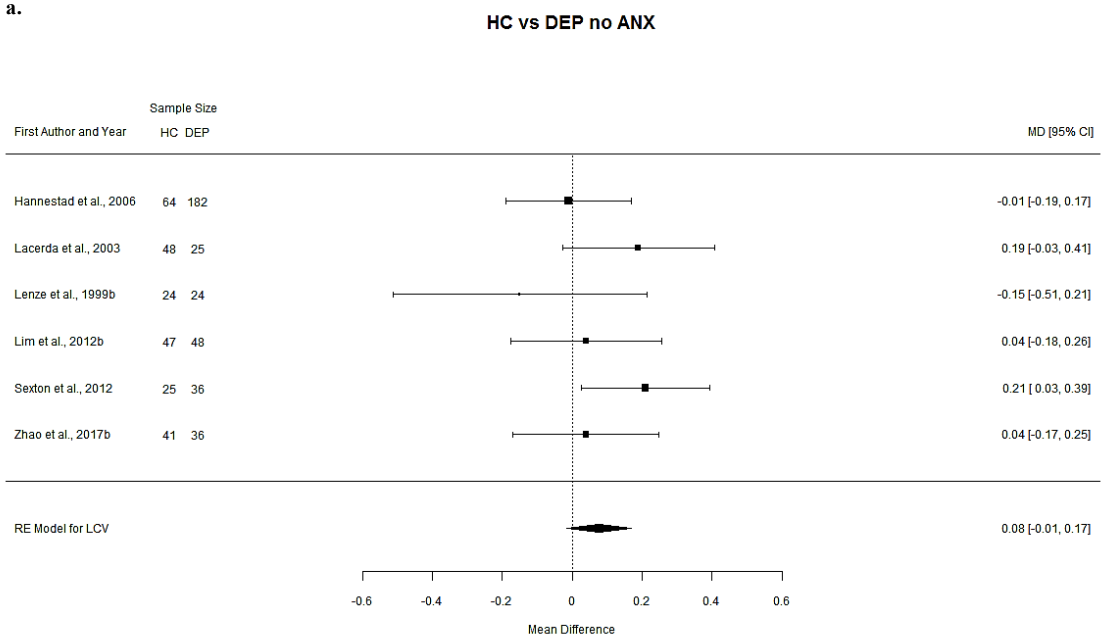

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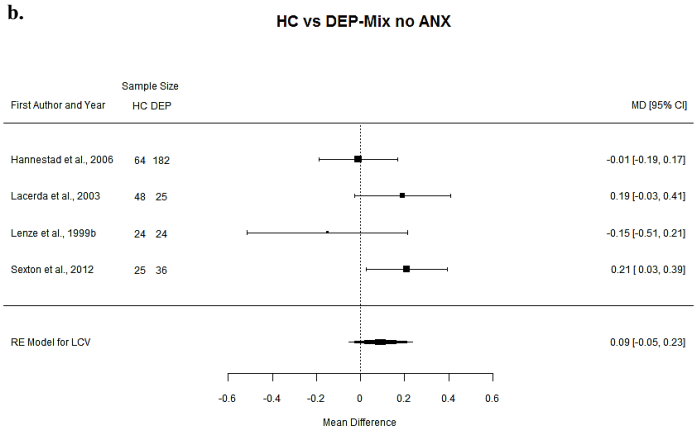

Supplemental Figure S28. LCV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**) excluding anxiety disorders (no ANX).

LCV: left caudate volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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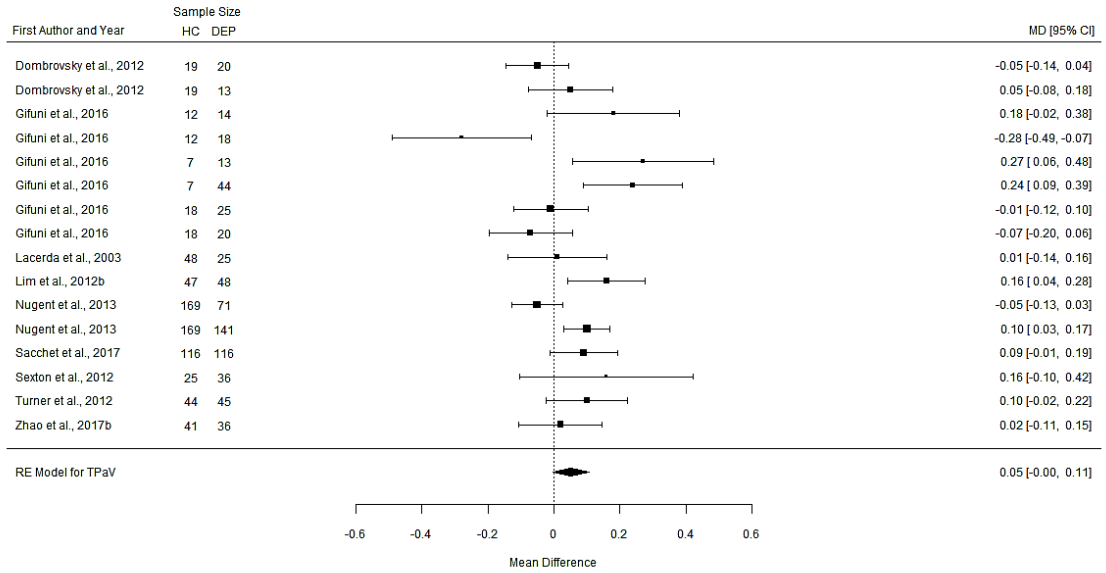

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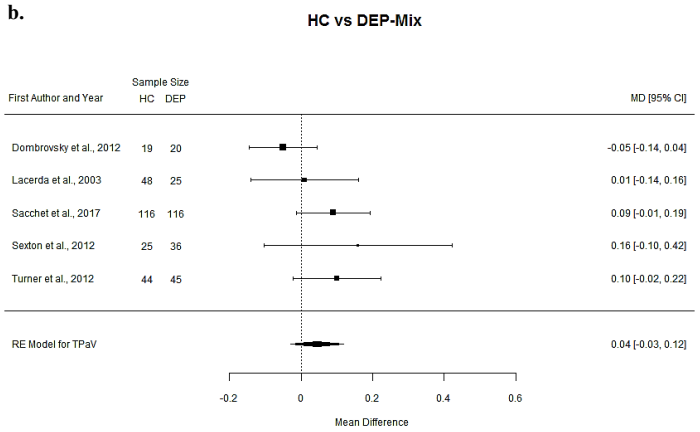

Supplemental Figure S29. TPaV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

TPaV: total pallidum volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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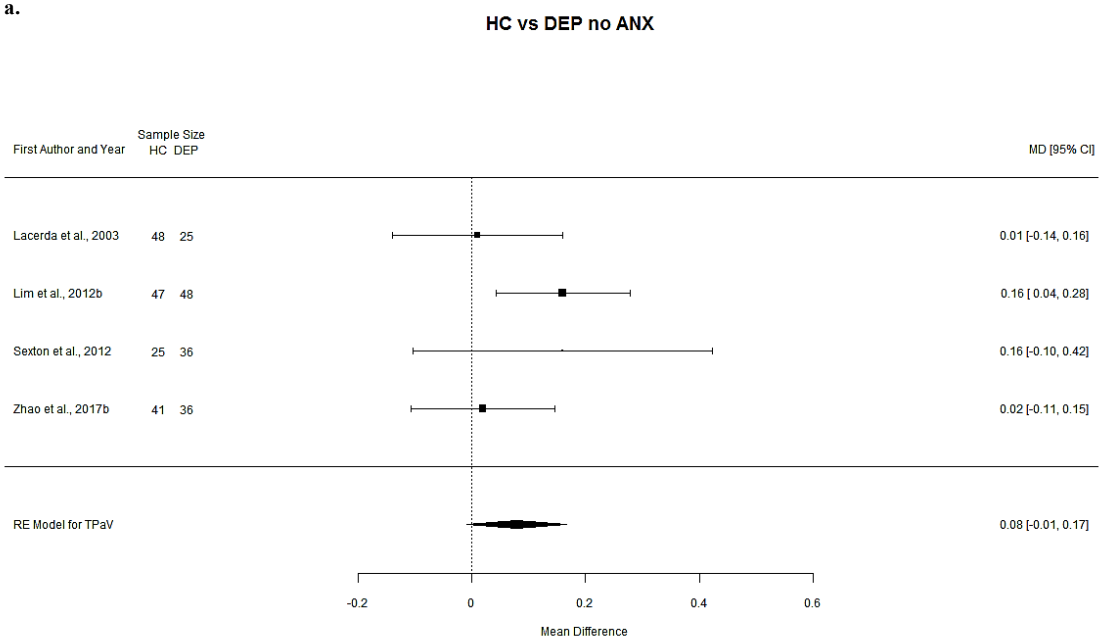

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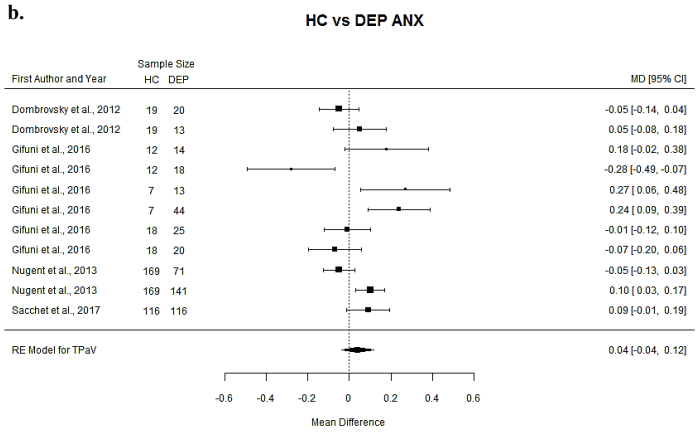

Supplemental Figure S30. TPaV assessment of anxiety comorbidity forest plots
Forest plot of main analysis (**a**) excluding anxiety disorders (no ANX). Forest plot of main analysis (**b**) comorbid with anxiety disorders (ANX).

TPaV: total pallidum volume, HC: healthy controls, DEP: depressed individuals RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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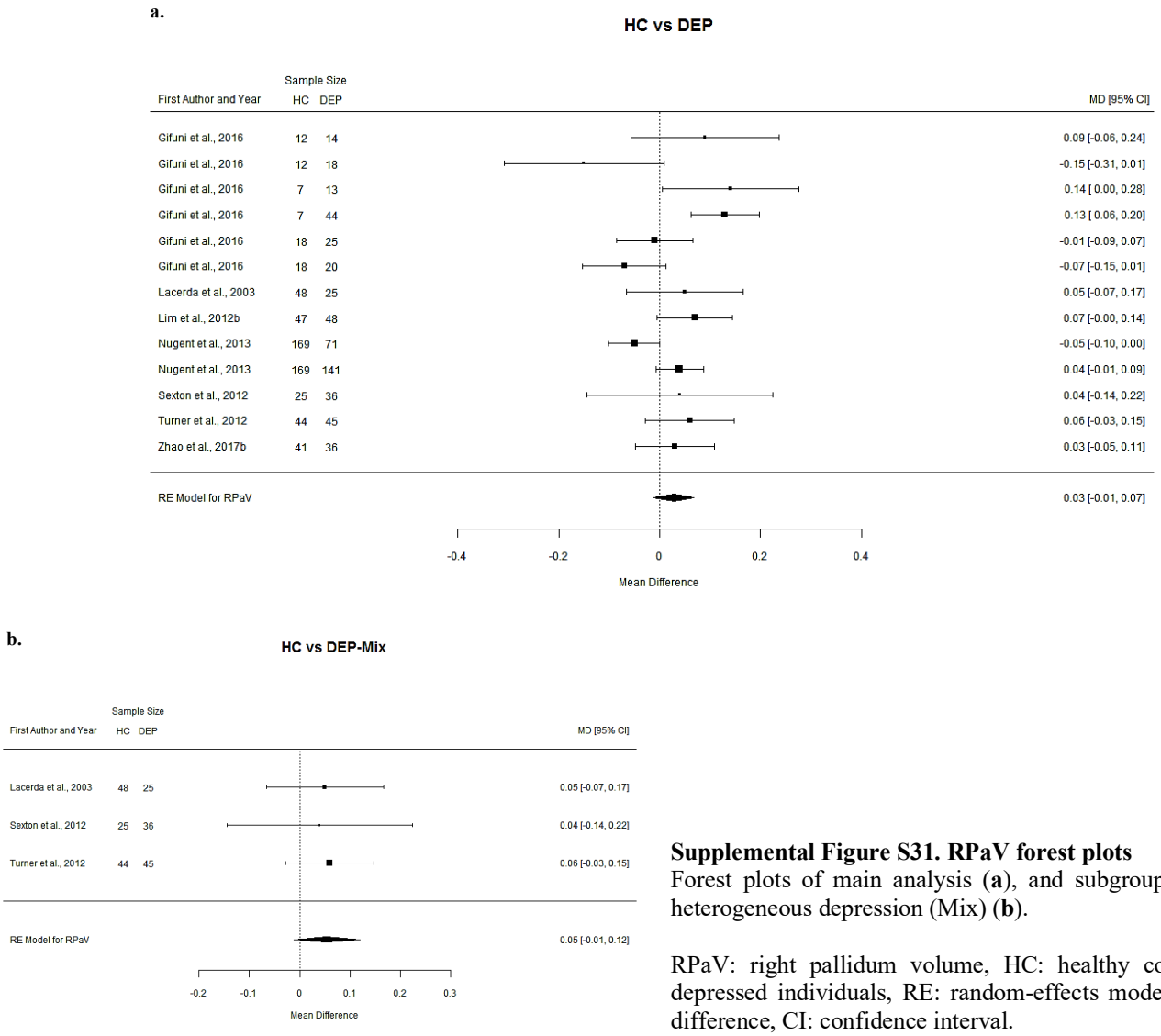

Supplemental Figure S31. RPaV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

RPaV: right pallidum volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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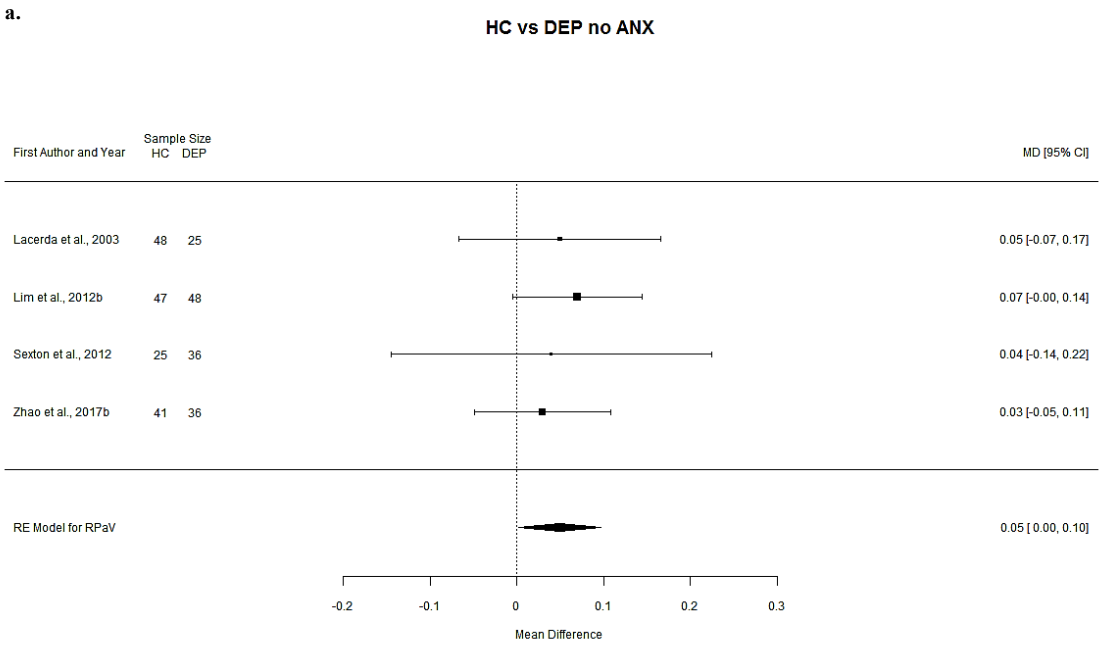

Supplemental Figure S32. RPaV assessment of anxiety comorbidity forest plot
Forest plot of main analysis (**a**) excluding anxiety disorders (no ANX).

RPaV: right pallidum volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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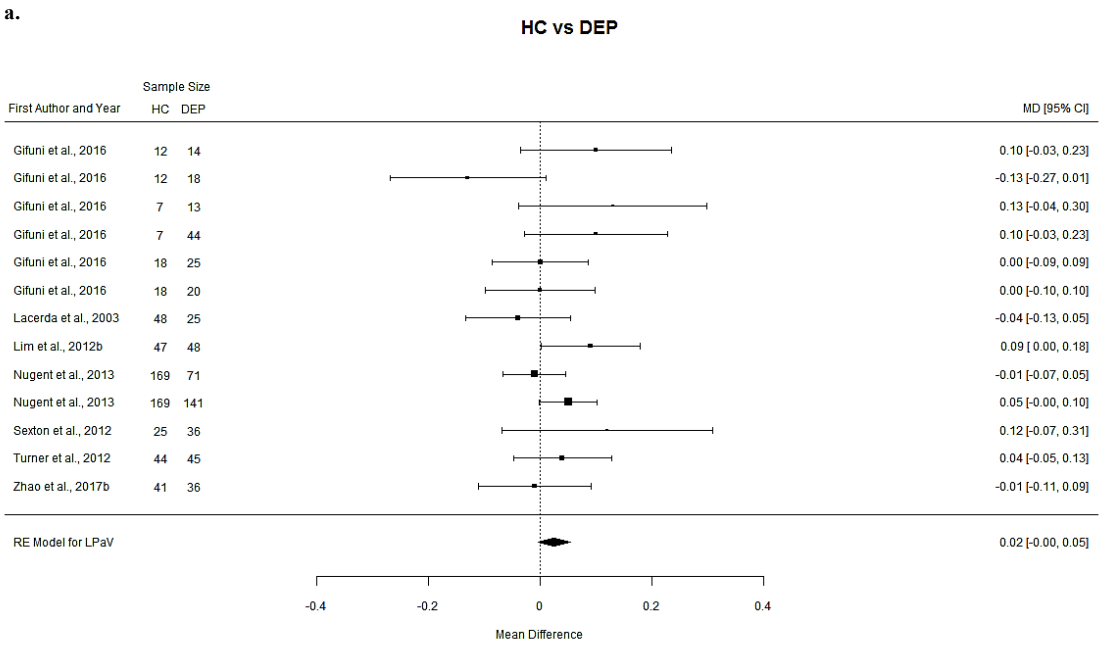

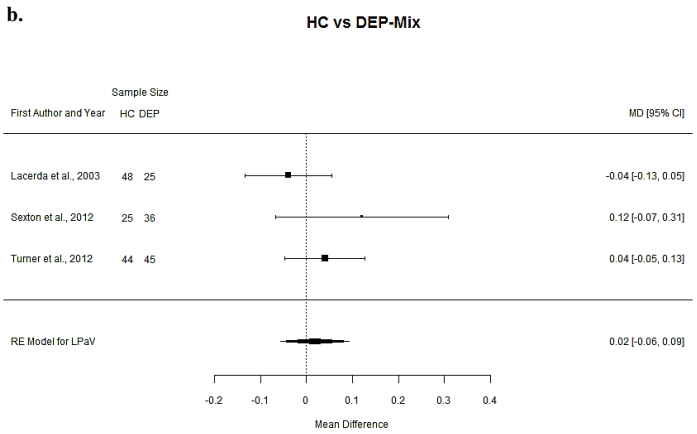

Supplemental Figure S33. LPaV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

LPaV: left pallidum volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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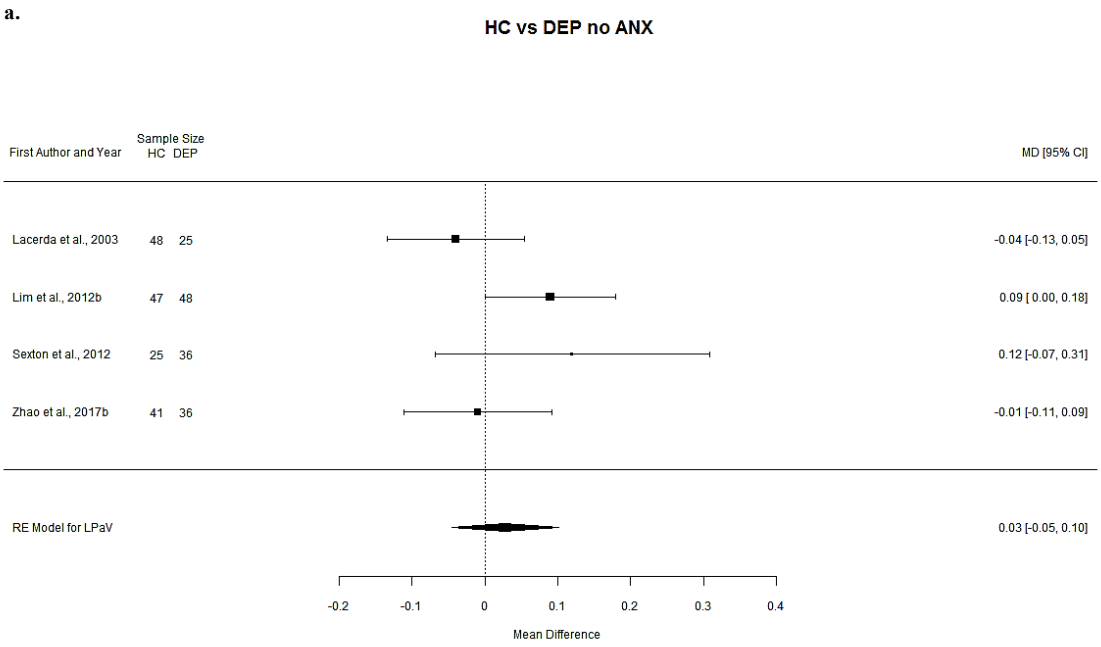

Supplemental Figure S34. LPaV assessment of anxiety comorbidity forest plot
Forest plot of main analysis (**a**) excluding anxiety disorders (no ANX).

LPaV: left pallidum volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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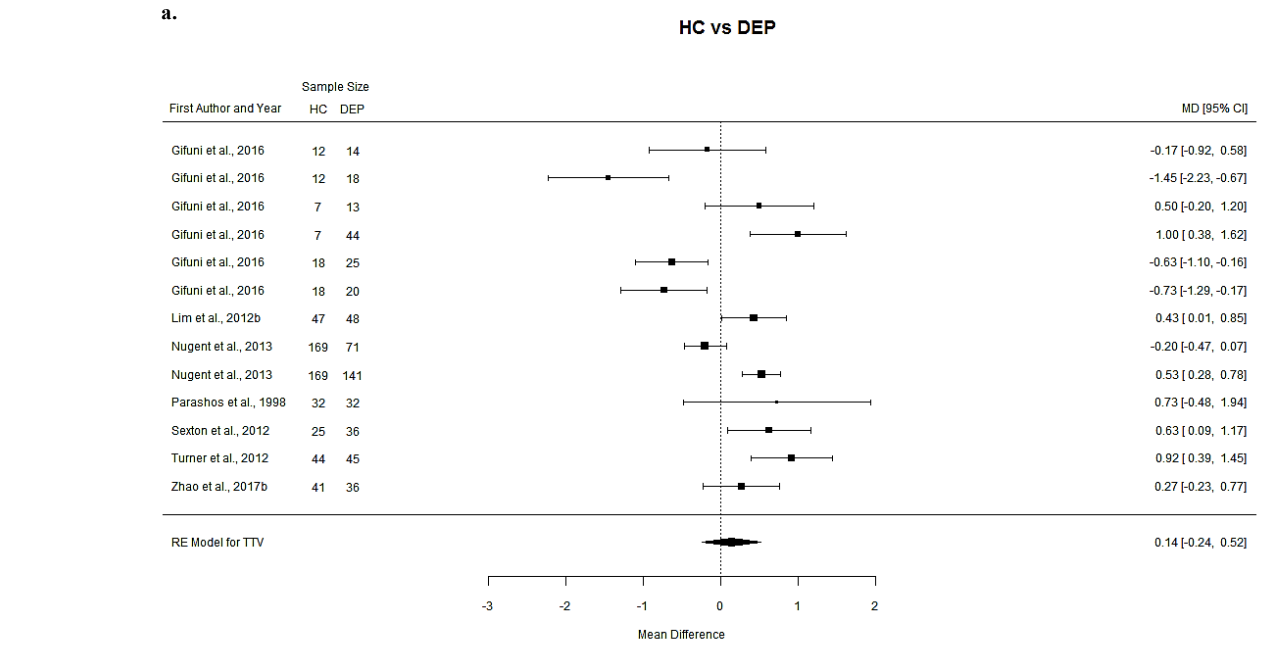

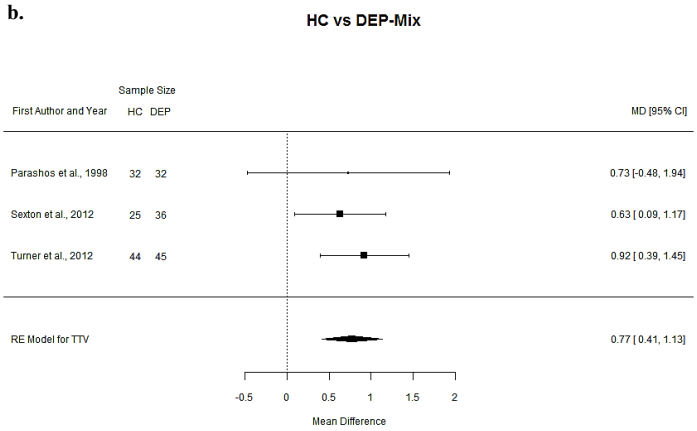

Supplemental Figure S35. TTV forest plots
Forest plots of main analysis (**a**), and subgroup analysis for heterogeneous depression (Mix) (**b**).

TTV: total thalamus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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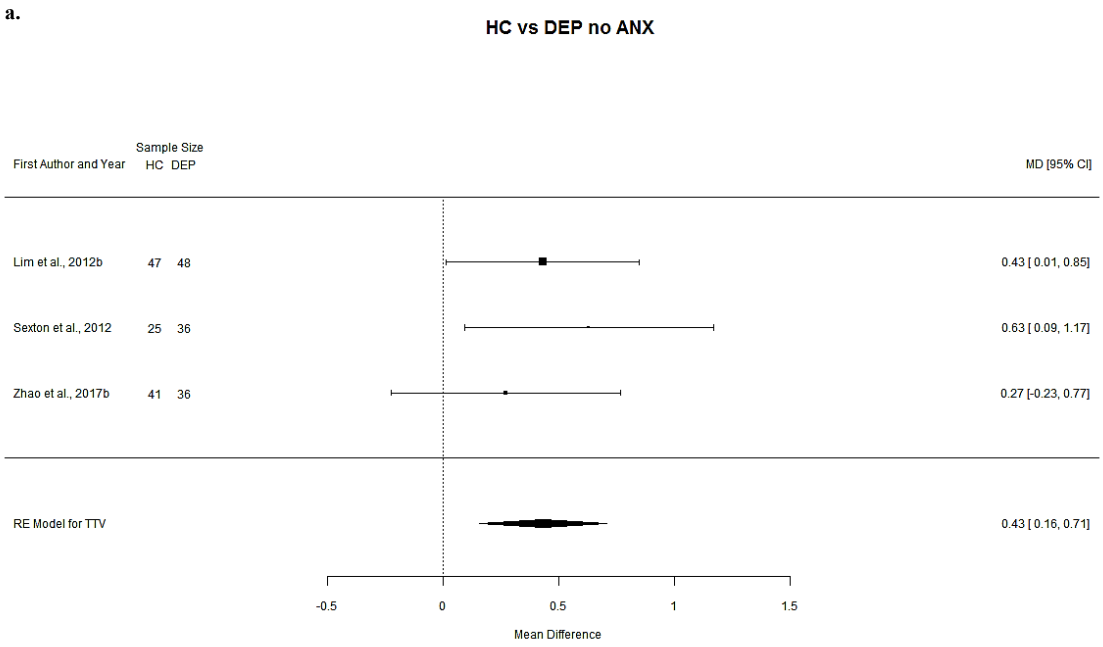

Supplemental Figure S36. TTV assessment of anxiety comorbidity forest plot
Forest plot of main analysis (**a**) excluding anxiety disorders (no ANX).

TTV: total thalamus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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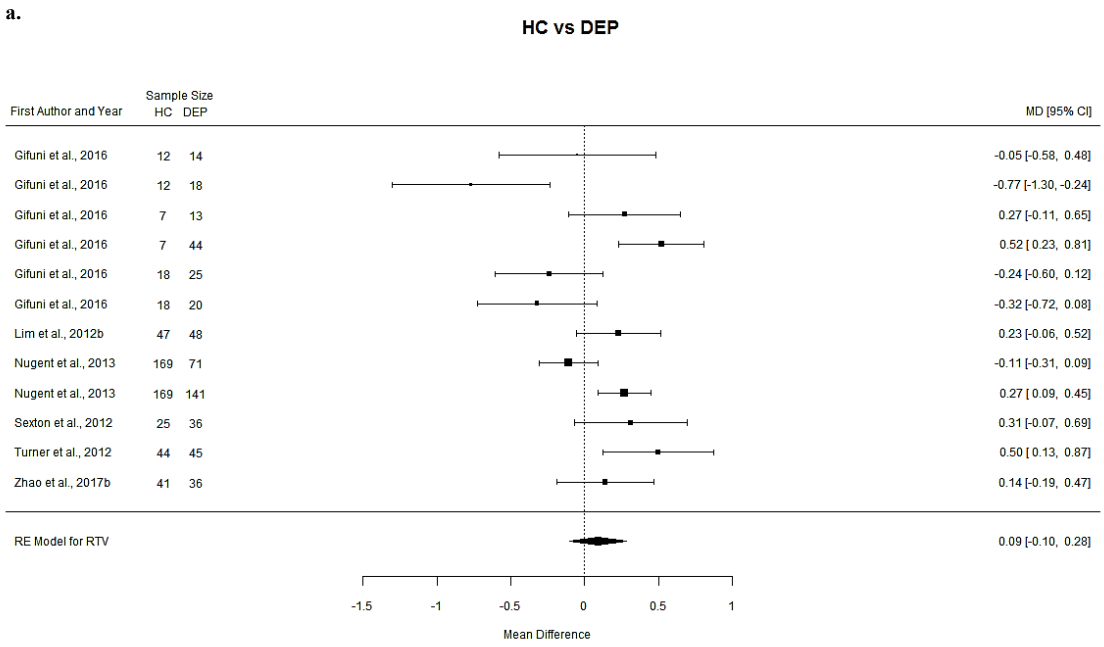

Supplemental Figure S37. RTV forest plot
Forest plot of main analysis (**a**).

RTV: right thalamus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
DOI: 10.1503/jpn.190156

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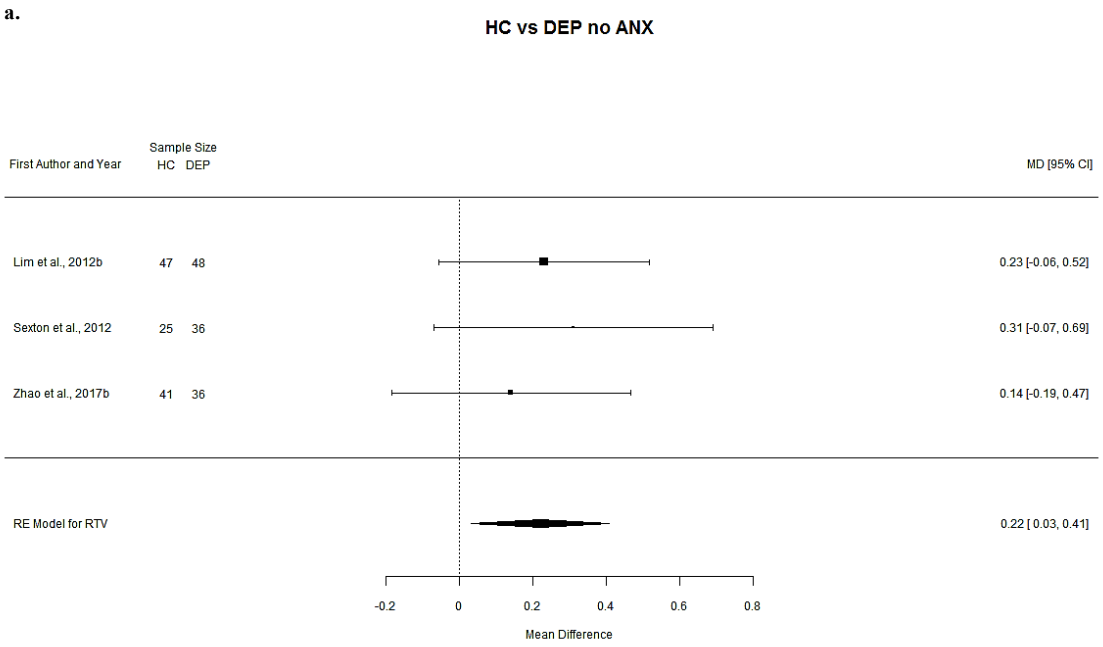

Supplemental Figure S38. RTV assessment of anxiety comorbidity forest plot
Forest plot of main analysis (**a**) excluding anxiety disorders (no ANX).

RTV: right thalamus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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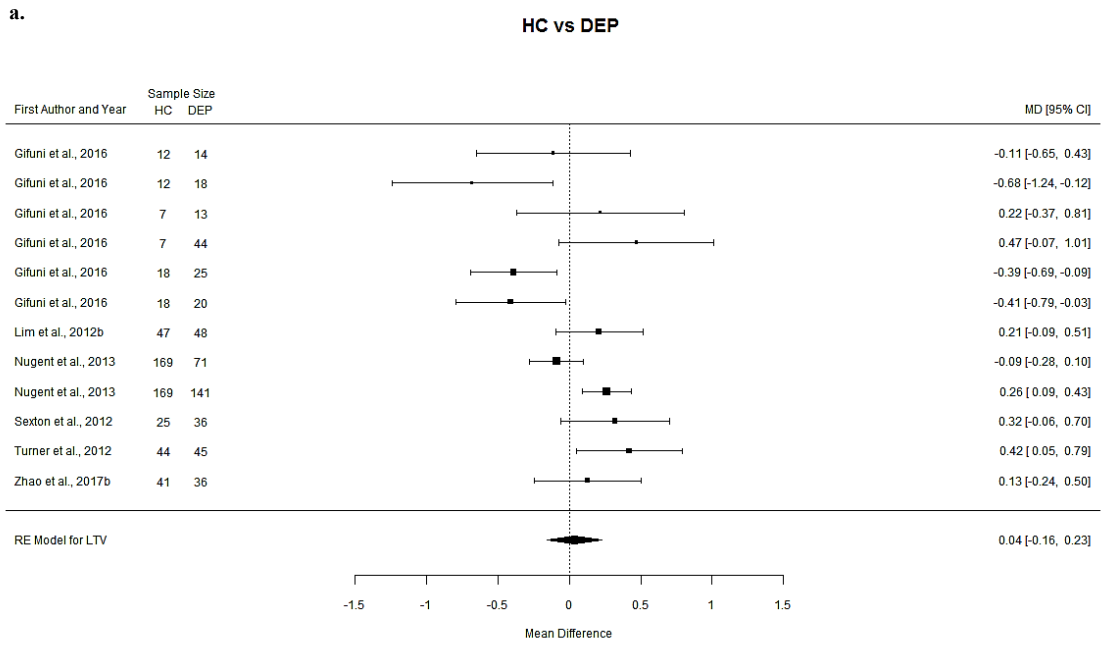

Supplemental Figure S39. LTV forest plot
Forest plot of main analysis (**a**).

LTV: left thalamus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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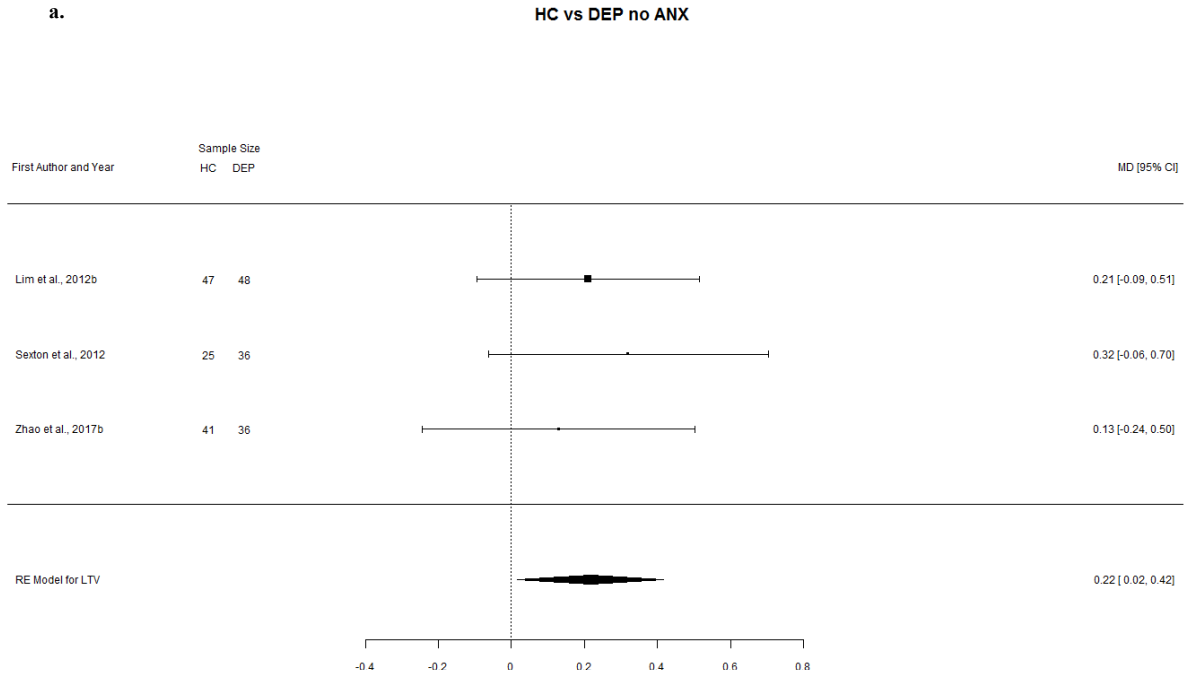

Supplemental Figure S40. LTV assessment of anxiety comorbidity forest plot
Forest plot of main analysis (**a**) excluding anxiety disorders (no ANX).

LTV: left thalamus volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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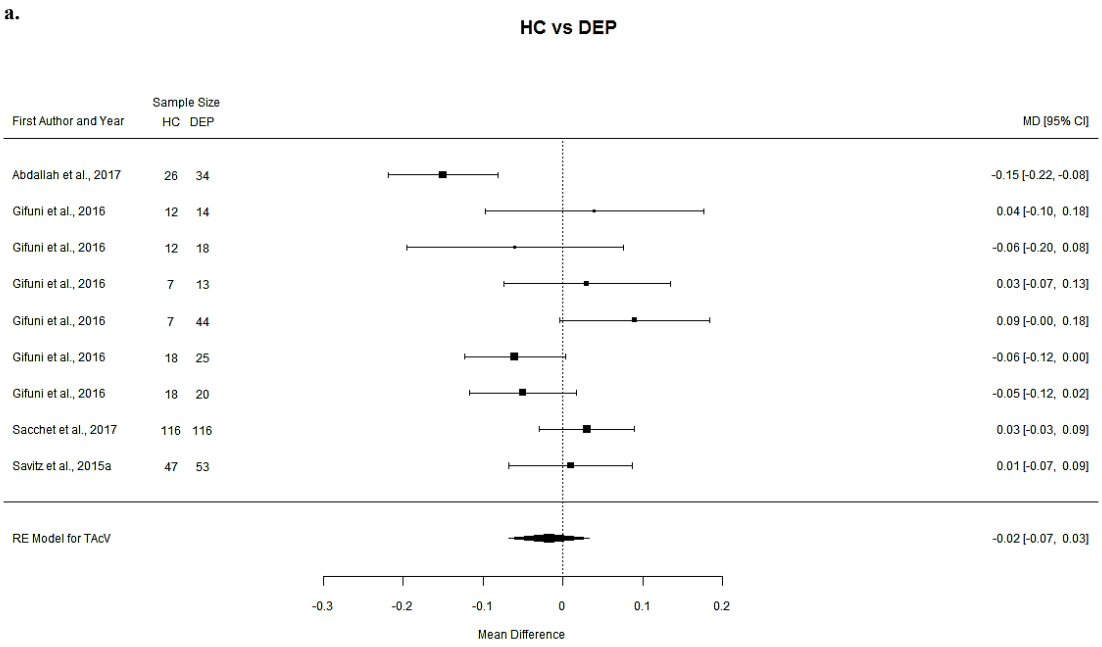

Supplemental Figure S41. TAcV forest plot
Forest plot of main analysis (**a**).

TAcV: total accumbens volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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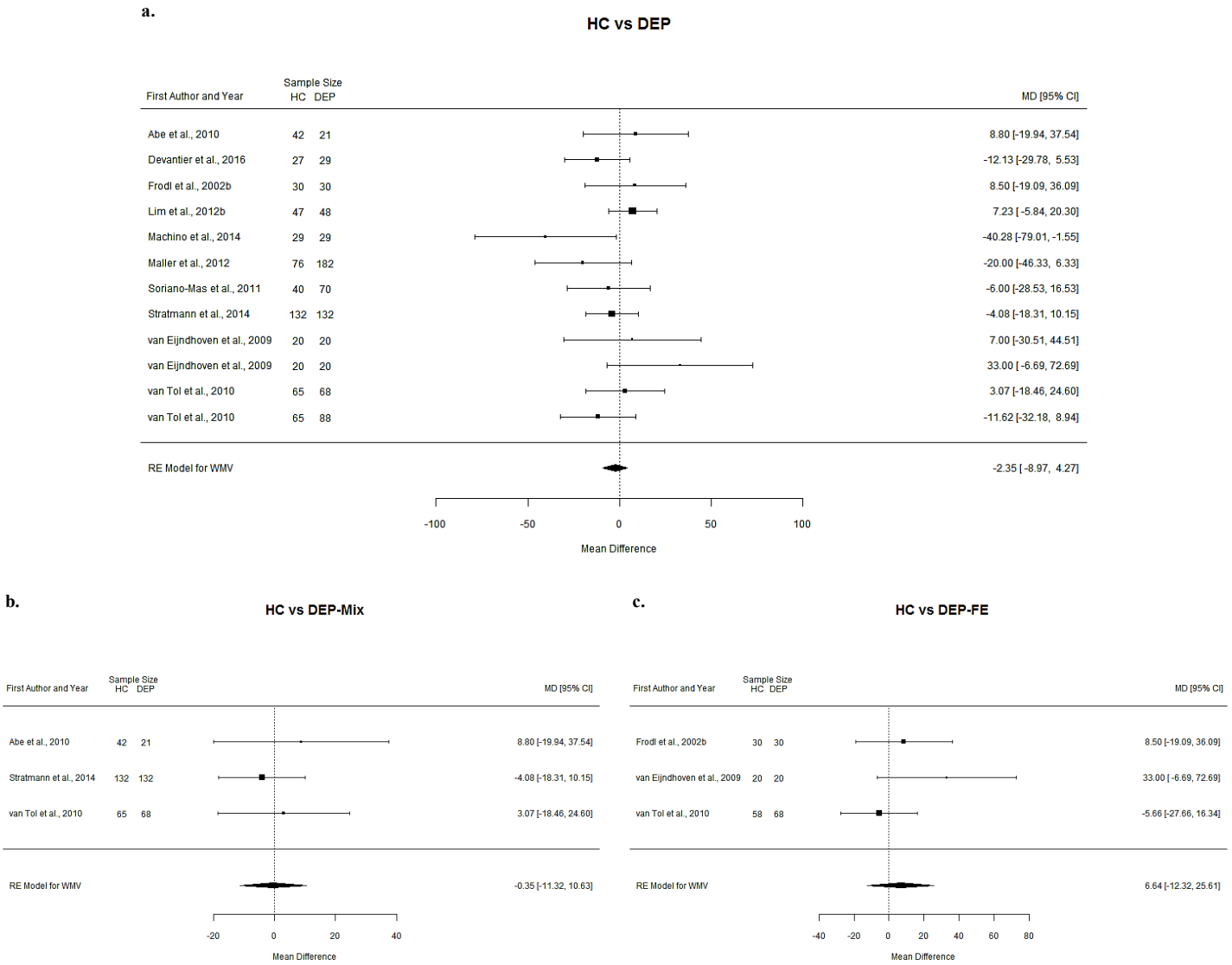

Supplemental Figure S42. WMV forest plots
Forest plots of main analysis (**a**), and subgroup analyses for heterogeneous depression (Mix) (**b**) and first-episode depression (FE) (**c**).

WMV: white matter volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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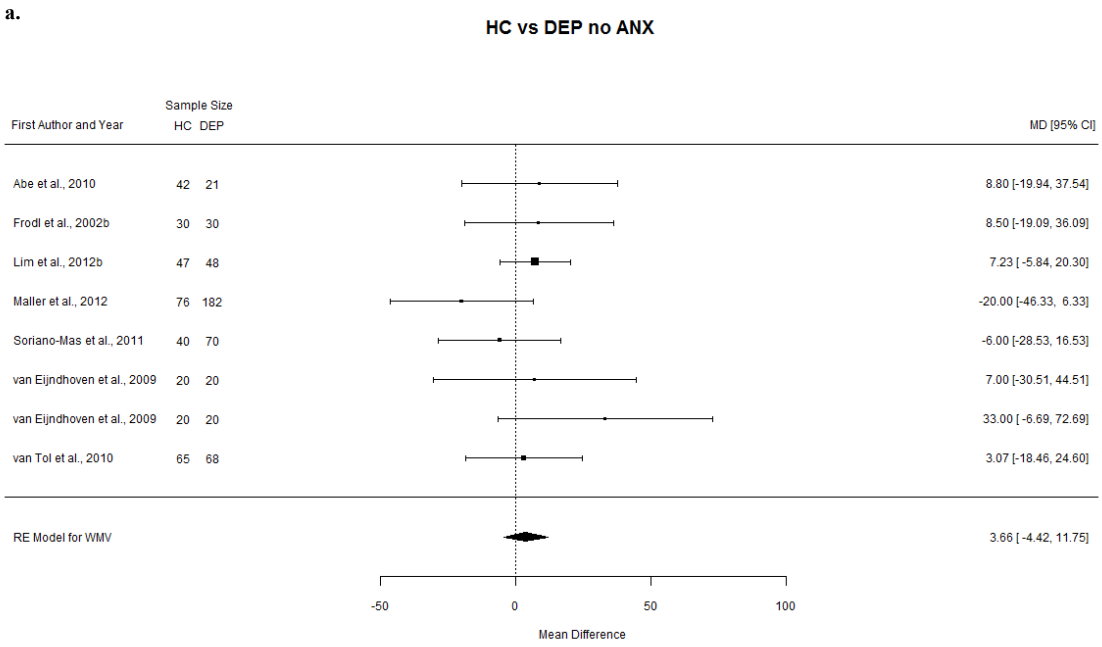

Supplemental Figure S43. WMV assessment of anxiety comorbidity forest plot
Forest plot of main analysis (**a**) excluding anxiety disorders (no ANX).

WMV: white matter volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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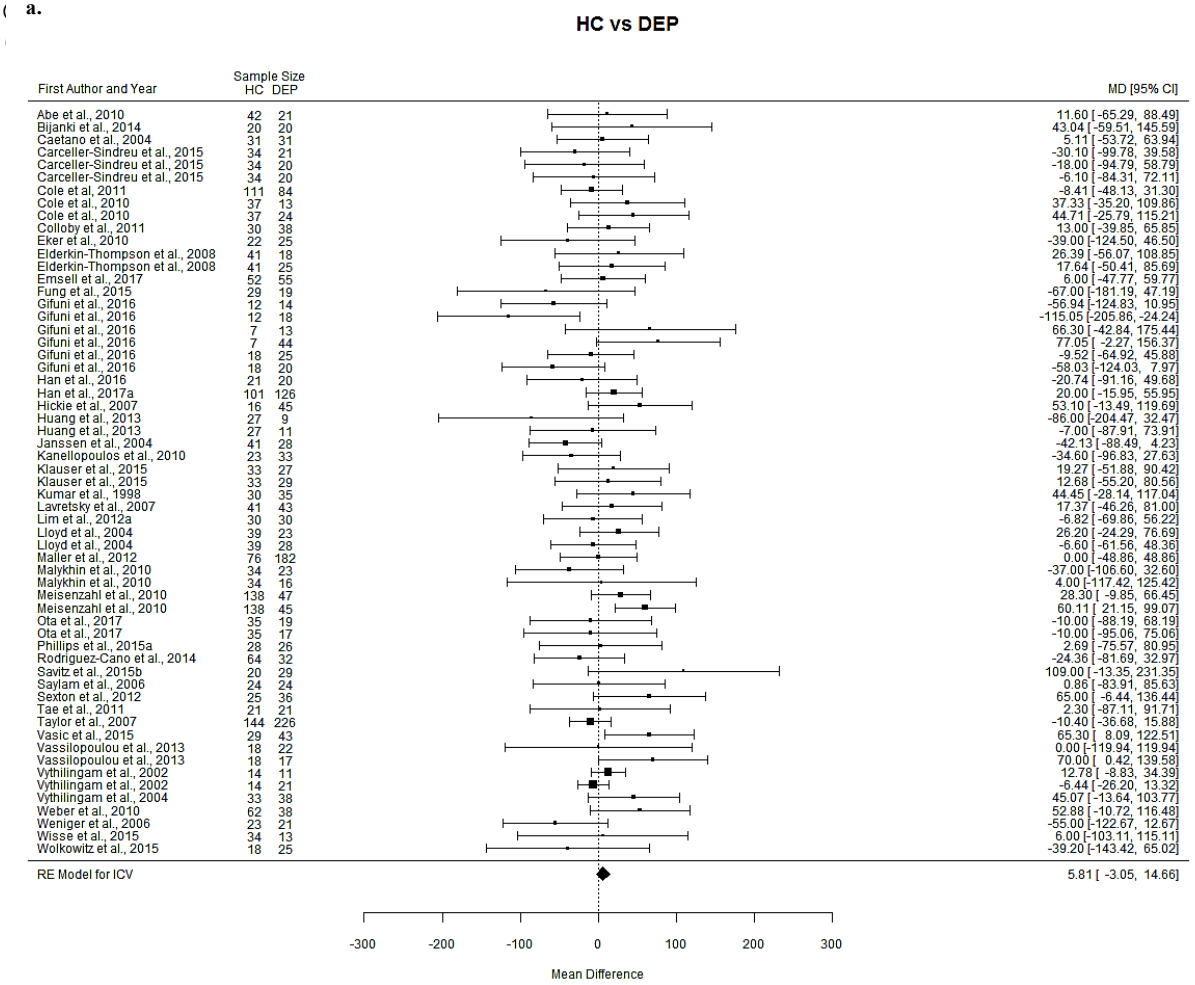

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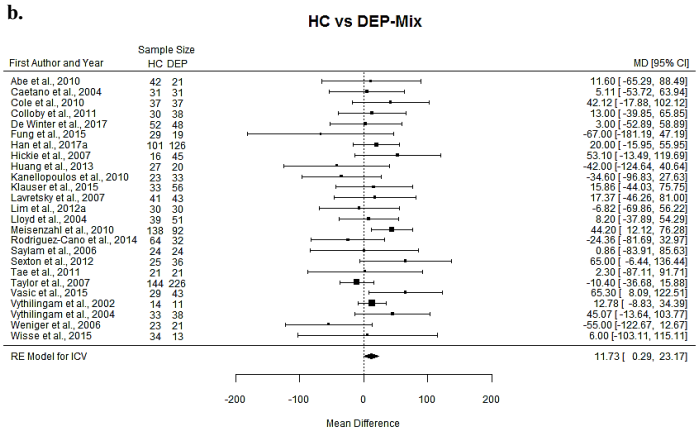

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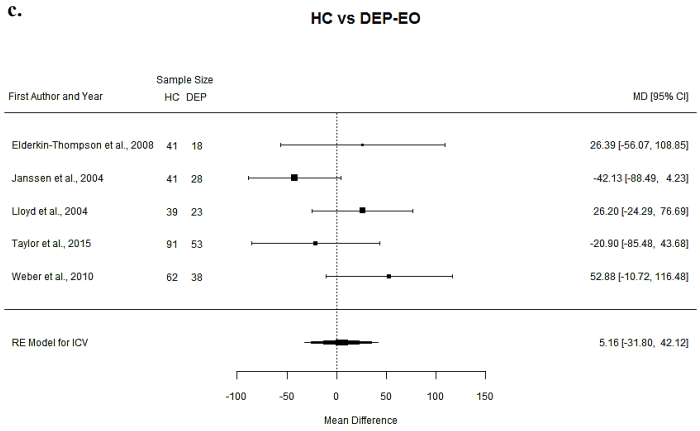

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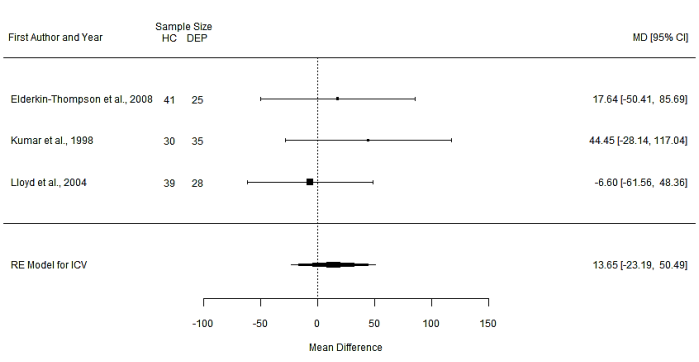

Supplemental Figure S44. ICV forest plots

Forest plots of main analysis (**a**), and subgroup analyses for heterogeneous depression (Mix) (**b**), early-onset depression (EO) (**c**), and late-onset depression (LO) (**d**).

ICV: intracranial volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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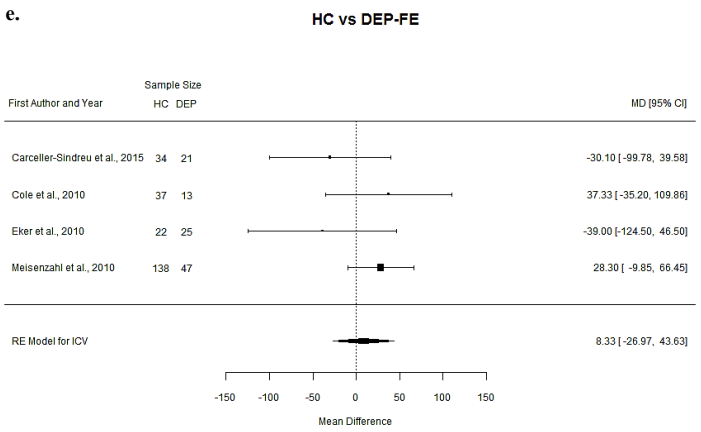
e.



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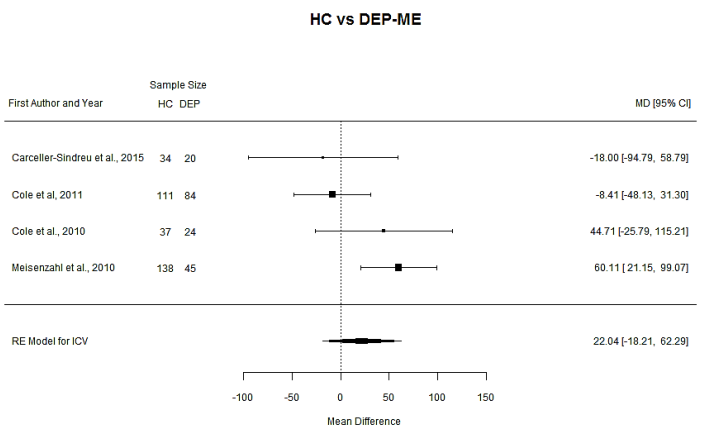

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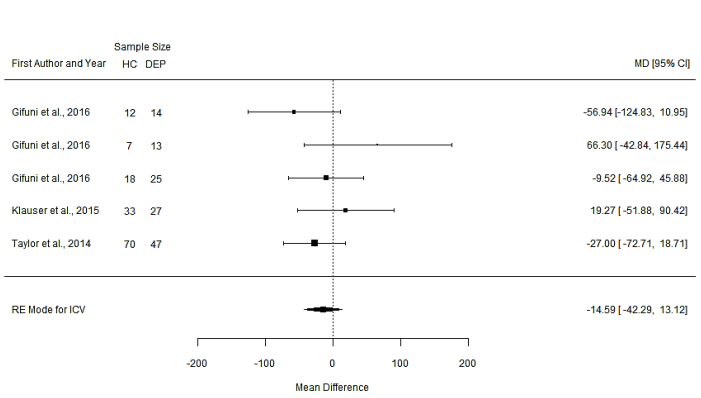

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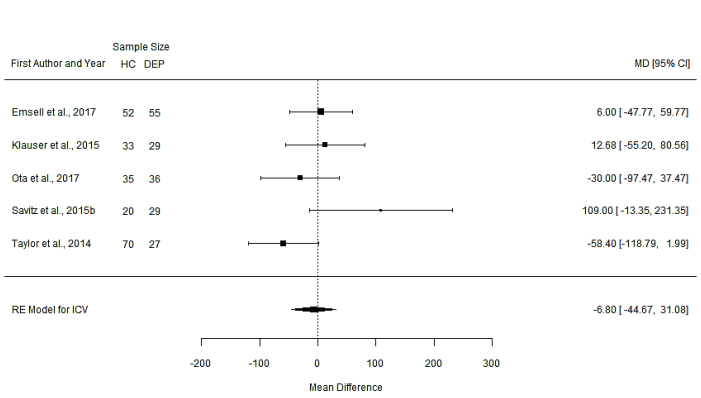

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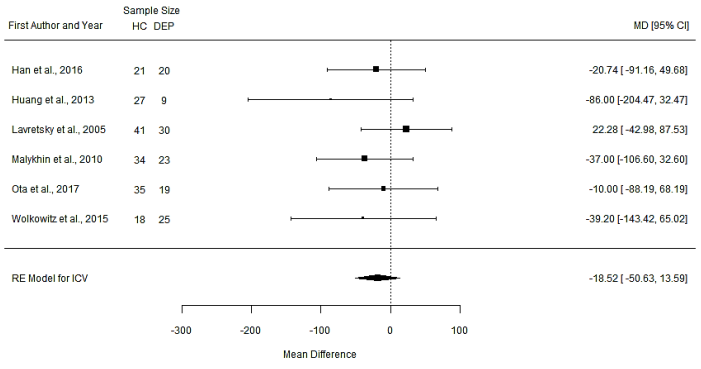

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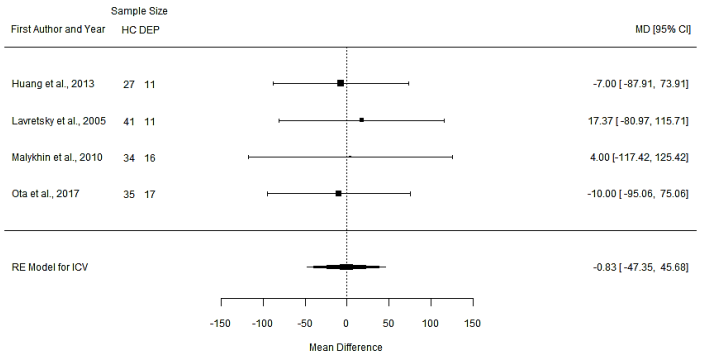

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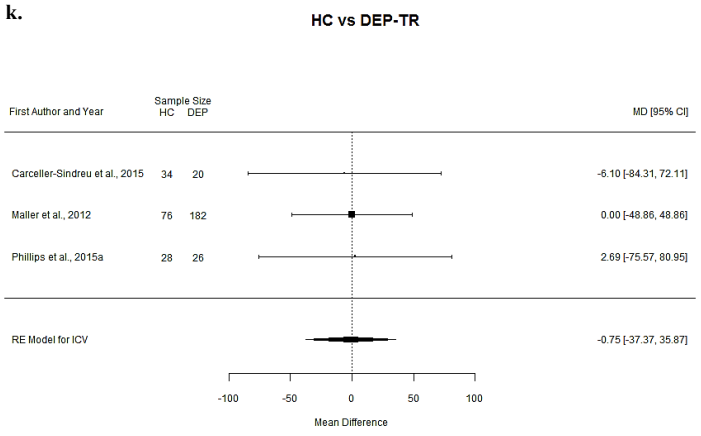

Supplemental Figure S44. ICV forest plots (continued)
Forest plots of subgroup analyses for first-episode depression (FE) (**e**), multiple-episodes of depression (ME) (**f**), depression in remission (Rem) (**g**), current depression (Cur) (**h**), non-medicated depression (noMed) (**i**), medicated depression (Med) (**j**), and treatment-resistant depression (TR) (**k**).

ICV: intracranial volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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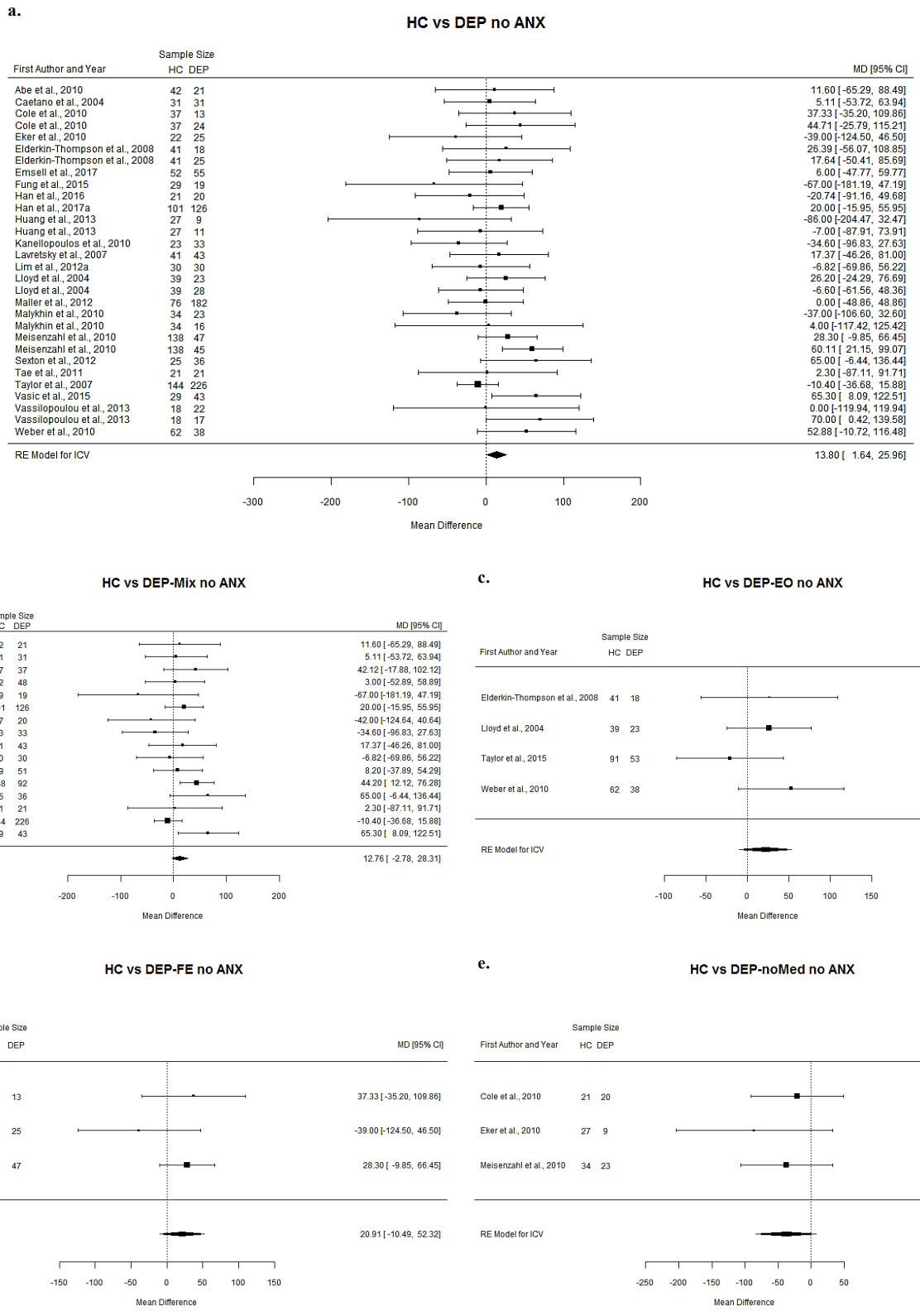

Supplemental Figure S45. ICV assessment of anxiety comorbidity forest plots
Forest plots of main analysis (**a**) and subgroup analyses for heterogeneous depression (Mix) (**b**),early-onset depression (EO) (**c**), first-episode of depression (FE) (**d**), and non-medicated depression (noMed) (**e**) excluding anxiety disorders (no ANX).

ICV: intracranial volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.

Appendix 1 to Espinoza Oyarce DA, Shaw ME, Alateeq K, et al. Volumetric brain differences in clinical depression in association with anxiety: a systematic review with meta-analysis. *J Psychiatry Neurosci* 2020.
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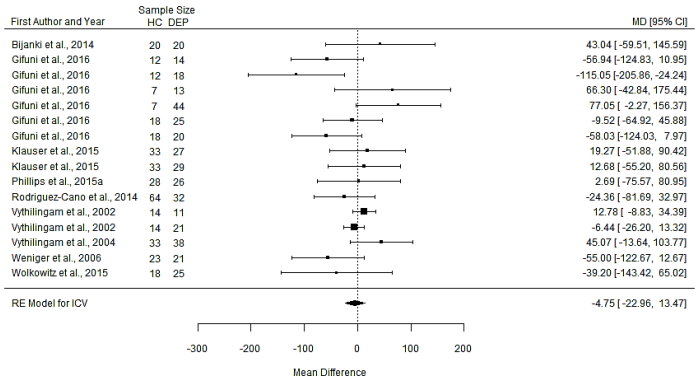
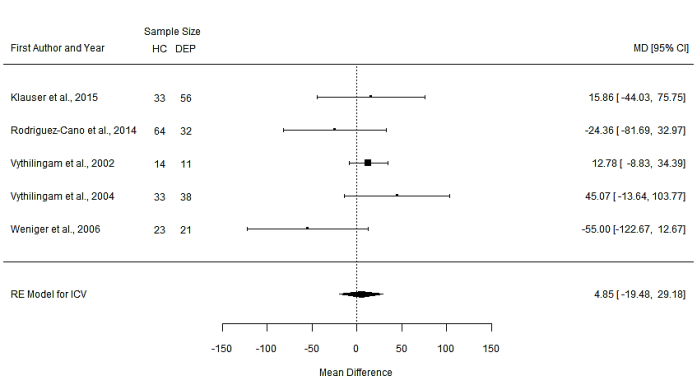
f.



g.



Supplemental Figure S45. ICV assessment of anxiety comorbidity forest plots (continued)
Forest plots for main analysis (**f**), and subgroup analysis for heterogeneous depression (Mix) (**g**) comorbid with anxiety disorders (no ANX).

ICV: intracranial volume, HC: healthy controls, DEP: depressed individuals, RE: random-effects model, MD: mean difference, CI: confidence interval.