Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplementary Methods

Study selection and data extraction

We searched PubMed, EMBASE and PsychINFO databases from inception to 1 October 2016. The following keywords were used: "(magnetic resonance imaging OR MRI) AND volume AND (schizophrenia OR psychosis)." In addition, we searched reference lists of included studies and previous meta-analyses to identify additional studies.

The inclusion criteria were: (1) original studies reporting measures of regional brain volumes in patients and healthy controls; (2) All patients experiencing a first episode of psychosis or, if this is not explicitly stated, group mean illness duration of not greater than three years; (3) studies of patients with a diagnosis of schizophrenia, schizoaffective disorder or schizophreniform disorder; (4) Sufficient data presented to calculate mean and standard deviation of measures for both groups; (5) Diagnosis in accordance with Diagnostic and Statistical Manual of Mental Disorders (version III-R, IV or V) or International Classification of Diseases (version 9 or 10) criteria; (6) Study written in English.

We considered discrete brain structures analysed in the study of Haijma and colleagues:[1] regions were included in our analysis if at least ten studies met inclusion criteria. Abstracts were first screened to select potentially eligible papers. The full text of such papers was then reviewed in full to determine inclusion. Where there were indications that samples overlapped between studies, we included only the study with the largest sample size. The screening, selection and data extraction process were repeated to double-check the results.

Measures reported by subgroup (e.g. male vs. female) were included as separate results where patient subgroup sample sizes were greater than 10; otherwise, results were combined into a single measure. To avoid double-counting, where results from a single control group were

included alongside results from multiple patient subgroups, we adjusted its size by dividing by the number of times it appeared in our analysis.[2] Data presented by subregion (e.g. left vs. right, grey vs. white matter) were combined to give a single measure, assuming a correlation of 0.5 between subregions, although this is likely conservative.[3] Data presented in graphical form were extracted using the Web Plot Digitizer tool where possible (http://arohatgi.info/WebPlotDigitizer).

We did not attempt to assess the risk of bias at the level of the individual study.

Outcome measures for variability

Measures of variability, such as standard deviation or variance, exhibit asymmetrical non-normal sampling distributions (Chi and Chi-squared respectively).[13] However, these approximate the normal distribution as sample size increases, and the rate of convergence is increased dramatically by log-transformation,[14] allowing us to derive effect-size estimators of between-group differences in population variability, which may be combined using standard meta-analytic techniques.[15]

In meta-analysis, the summary effect size is a weighted average of the individual study effect size estimates. In fixed-effect analysis, the weighting factor is the sampling precision (inverse variance) of each estimate, while in random effects analysis this is modified to take account of inconsistency between studies. For log variability ratio, sampling variance $S^2_{\ln VR}$ is given by:

$$S^2_{\ln VR} = \frac{1}{2\left(n_p - 1\right)} + \frac{1}{2(n_c - 1)}$$

Where n_p and n_c are the sample sizes for patient and control groups respectively in each case. For log coefficient of variation ratio, sampling variance $S^2_{\ln CVR}$ is given by:

$$S^2_{\ln CVR} = \frac{s_p^2}{n_p \bar{x}_p^2} + \frac{1}{2(n_p - 1)} + \frac{s_c^2}{n_c \bar{x}_c^2} + \frac{1}{2(n_c - 1)} - 2\rho_p \sqrt{\frac{1}{2(n_p - 1)} \frac{s_p^2}{n_p \bar{x}_p^2}} - 2\rho_c \sqrt{\frac{1}{2(n_c - 1)} \frac{s_c^2}{n_c \bar{x}_c^2}}$$

Where $\bar{x}_p$ and $\bar{x}_c$ are the reported means, s_p and s_c are the reported sample standard deviations and ρ_p and ρ_c are the correlations between reported (log-transformed) means and standard deviations, for patient and control groups respectively in each case.

Outcome measures for mean differences

We selected Hedges' g,[4] with bias-correction via large-sample approximation,[5] as our outcome measure for mean volume differences between patient and control groups. Hedges' g is given by:

$$g = \frac{\bar{x}_p - \bar{x}_c}{s^*}$$

Where $\bar{x}_p$ and $\bar{x}_c$ are the reported patent and control sample means, and s^* is the pooled standard deviation, calculated as:

$$s^* = \sqrt{\frac{(n_p - 1)s_p^2 + (n_c - 1)s_c^2}{n_p + n_c - 2}}$$

Where s_p and s_c are the reported sample standard deviations and n_p and n_c are the sample sizes for patient and control groups respectively in each case. The sampling variance S_g^2 is given by:

$$S_d^2 = \frac{n_p + n_c}{n_p n_c} + \frac{g^2}{2(n_p + n_c)}$$

Data for all outcome measures are provided in the supplementary data file.

Statistical analysis

We constructed separate multivariate random effects models for lnVR, lnCVR and Hedges' g measures using the 'rma.mv' function in the metafor package to conduct meta-analysis of all regions simultaneously. Random effects were added to the model for each region reported within each study. Region was entered into the model as a categorical moderator to obtain separate summary effect-size estimates for each region. We fitted multivariate random effects models to data across all regions of interest using restricted maximum likelihood estimation for Hedges' *g*, *lnVR* and *lnCVR*. We used an omnibus Wald-type chi-square test of the null hypothesis that the model coefficients were equal to zero.

We assessed the goodness of fit of multivariate models employing differing covariance structures. In increasing order of complexity, these were compound symmetric (CS; 12 independent parameters) heteroscedastic compound symmetric (HCS; 21 independent parameters) and unstructured (UN; 61 independent parameters). We used ANOVA to establish whether the more complex models offered a significantly better description relative to the simpler models.

Meta-regression

We tested the effect on our outcome measures of mean and (for variability measures) standard deviation of duration of psychosis and duration of treatment, as well as the proportions of patients in each study group with diagnoses of schizophreniform and schizoaffective disorder

(we did not conduct a separate analysis for other psychosis-spectrum diagnoses as very few studies included such patients).

Publication Bias and Inconsistency for meta-analysis of mean differences

Publication bias was assessed across all regions simultaneously by visual inspection of funnel plots of standard errors against regional residuals, as well as via the excess significance test,[6] the p-curve method,[7,8] and a multivariate analogue of Egger's regression test.[9] Inconsistency was assessed using the I^2 statistic.

eResults. Supplementary Results

Table S1 below gives details of included studies. The vast majority of studies matched patients and controls for sex and age and presented results unadjusted for age and sex, with only two exceptions.[10,11] Details of effects sizes for individual studies (including subgroups) may be found in tables S5-14.

Statistical Analysis

For both VR and CVR, multivariate meta-analytic models assuming heteroscedastic compound symmetric (HCS) covariance structures provided a better (complexity-adjusted) fit to the data than either the simpler models compound symmetric (CS) covariance structures or the more complex models assuming unstructured (UN) covariance structures (see table S2).

Meta-regression

We found a significant effect of mean duration of psychosis on mean volume differences, as measured by Hedges' *g*, ($\chi2=33.31$, $p<.001$). Significant effects at the individual region level were found for amygdala ($z=3.80$, $p<.001$) and putamen ($z=2.54$, $p=.01$), with greater duration of psychosis associated with lower volume in these regions, and, in the opposite direction for the thalamus ($z=2.39$, $p=.02$). We also found a significant effect of mean duration of treatment on mean volume differences as measured with Hedge's g ($\chi2=108.39$, $p<.001$). Greater duration of treatment was associated with lower amygdala volume ($z=9.68$, $p<.001$), as well as higher thalamus ($z=2.39$, $p=.02$)

and lateral ventricle volumes (z=2.18, p=.03). Finally, we found a significant effect of regional segmentation method on mean volume differences ($\chi 2$=26.21, p=.02), with automatic segmentation associated with lower mean volumes (larger differences between patients and controls) for caudate (z=2.07, p=.04) and thalamus (z=3.27, p=.001) in patients than manual segmentation (see table S4 for further details of meta-regression analyses).

eDiscussion. Supplementary Discussion

Meta-regression analyses found a significant effect of segmentation method on mean volume difference, with significant effects at the individual region level seen for caudate and thalamus, with reduced volume of these structures relative to healthy controls associated with automatic, rather than manual, segmentation. This volume reduction may reflect an effect of increased motion artefact in patients, similar to that reported for (automated) morphometric approaches.[118]

eTable 1. Details of Included Studies

Study	Number of patients[2]	Number of controls[2]	Regions included	Schizophrenia[2]	Schizoaffective Disorder[2]	Schizophreniform Disorder[2]	Other[2]	Duration of illness (years)[2]		Duration of treatment (years)[2]		Segmentation
								Mean	SD	Mean	SD	
Aas et al. (2012)[12]	83	63	Amygdala	N/A	N/A	N/A	N/A	1.14	0.15	NA	NA	Manual
Ballmaier et al. (2008)[13]	21	21	Caudate, putamen	21	0	0	0			0.07	0.10	Manual
Barr et al. (1997)[10]	32	42	Lateral ventricle, hippocampus	26	6	0	0	2.90	3.20	NA	NA	Ventricle: automated; hippocampus: manual
Bartzokis et al. (2011)[14]	11, 13	14	Frontal lobe	9, 11	2, 2	0	0	0.50	0.49	0.67, 0.55	0.18	Manual
Bilder et al. (1994)[15]	31, 39	22, 29	Frontal lobe, temporal lobe	58	12	0	0	2.90	NA	0.12	NA	Manual
Bodnar et al. (2010)[16]	40, 17	57	Hippocampus	31, 13	9, 3	1	0	NA	NA	NA	NA	Manual
Bogerts et al. (1990)[17]	12, 22	10, 15	Temporal lobe	12, 22	0	0	0	1.40	6.00	0.18	0.16	Manual
Bois et al. (2015)[18]	34	36	Hippocampus, amygdala	34	0	0	0	0.50	NA	NA	NA	Automated
Boonstra et al. (2011)[19]	16	21	Third ventricle, lateral ventricle, caudate, putamen	8	6	2	0	3.31	NA	NA	NA	Automated
Boonstra et al. (2011)[20]	57	56	Lateral ventricle, third ventricle	57	0	0	0	NA	NA	NA	NA	Automated

Cahn et al. (2002)[21]	20	20	Third ventricle, lateral ventricle, caudate, thalamus, hippocampus, frontal lobe	20	0	0	0	1.46	2.27	0.00	0.00	Automated
Chakos et al. (1994)[22]	29	10		21	8	0	0	0.80	NA	0.03	NA	Manual
Chakos et al. (2005)[23]	34	14	Hippocampus	N/A	N/A	N/A	N/A	1.03	0.98	1.03	0.98	Manual
Choi et al. (2005)[24]	22	22	Caudate, thalamus, anterior cingulate cortex	22	0	0	0	2.52	3.13	NA	NA	Manual
Chua et al. (2003)[25]	19	29	Lateral ventricle	19	0	0	0	2.33	2.31	NA	NA	Automated
Chua et al. (2007)[26]	26	38	Caudate, lateral ventricle	23	0	0	3	0.33	NA	NA	NA	Automated
Collinson et al. (2009)[27]	27, 12	19, 8	Caudate, lateral ventricle	27, 12	0	0	0	1.10, 0.92	1.11, 0.89	NA	NA	Manual
Coscia et al. (2009)[28]	25, 10	23, 10	Thalamus	29	3	3	0	1.20	NA	0.00	0.01	Manual
Crespo-Facorro et al. (2000)[29]	26	34	Anterior cingulate cortex	26	0	0	0	0.95	1.46	0.00	0.00	Manual
Crespo-Facorro et al. (2007)[30]	53, 30	23, 15	Caudate	31, 13	2, 1	15, 6	5, 3	0.93	1.51	0.09	NA	Automated
Crespo-Facorro et al. (2009)[31]	81, 36	83	Putamen, thalamus, lateral ventricle, frontal lobe, temporal lobe	82, 0	0	0.36	0	1.47	2.95	0.09	NA	Automated
Dasari et al. (1999)[32]	20	16	Thalamus	15	4	1	0	2.37	2.14	NA	NA	Manual

Degreef et al. (1992)[33]	40	25	Lateral ventricle, third ventricle	40	0	0	0	1.70	NA	0.03	0.05	Manual
del Re et al. (2015)[34]	19	19	Lateral ventricle	16	3	0	0	0.70	0.70	NA	NA	Manual
DeLisi et al. (1991)[35]	30	20	Lateral ventricle, third ventricle, caudate, frontal lobe, temporal lobe	16	9	4	1	0.75	NA	NA	NA	Manual
DeLisi et al. (1992)[36]	12, 15	15, 18	Lateral ventricle, temporal lobe	8, 10	2, 2	0	2, 3	NA	NA	0.04	NA	Manual
Ebdrup et al. (2010)[37]	38	43	Lateral ventricle, third ventricle, caudate, putamen, hippocampus	39	0	0	0	3.36	4.41	NA	NA	Automated
Emsley et al. (2015)[38]	22	23	Caudate, putamen	13	0	9	0	0.78	0.78	0.00	0.00	Automated
Emsley et al. (2015)[39]	22	23	Thalamus	13	0	9	0	0.78	0.78	0.00	0.00	Automated
Ettinger et al. (2001)[40]	38	29	Thalamus	N/A	N/A	N/A	N/A	0.59	0.48	0.06	0.06	Manual
Ettinger et al (2004)[41]	20	18	Frontal lobe	N/A	N/A	N/A	N/A	0.14	0.13	NA	NA	Manual
Fannon et al. (2000)[42]	37	27	Lateral ventricle, third ventricle, temporal lobe	15	4	18	0	0.60	0.48	0.06	0.06	Manual
Fornito et al. (2008)[43]	40	40	Anterior cingulate cortex	40	0	0	0	0.10	NA	NA	NA	Automated

Gilbert et al. (2001)[44]	16	25	Thalamus	15	1	0	0	NA	NA	NA	NA	Manual
Glenthoj et al. (2007)[45]	19	19	Caudate, putamen	19	0	0	0	1.56	1.54	0.01	NA	Manual
Gunduz et al. (2002)[46]	51	28	Caudate, putamen	34	4	13	0	1.82	3.02	0.01	0.02	Manual
Gur et al. (1998)[47]	20	17	Frontal lobe, temporal lobe	20	0	0	0	2.80	3.80	0.00	0.00	Manual
Gur et al. (2004)[48]	15, 16	34, 46	Amygdala	15, 16	0	0	0	NA	NA	2.23, 1.47	3.98, 1.97	Automated
Gutiérrez-Galve et al. (2015)[49]	27	25	Frontal lobe, temporal lobe	20	7	0	0	1.15	1.90	0.28	0.15	Automated
Hadjulis et al. (2004)[50]	20, 20	20, 20	Frontal lobe, temporal lobe	40	0	0	0	1.33	1.20	NA	NA	Manual
Hasan et al. (2014)[51]	41	53	Hippocampus	41	0	0	0	NA	NA	NA	NA	Manual
Hirayasu et al. (2001)[52]	17	17	Frontal lobe	17	0	0	0	0.11	0.11	NA	NA	Manual
Ho et al. (2007)[53]	46	46	Lateral ventricle, frontal lobe, temporal lobe	46	0	0	0	2.40	3.10	0.25	NA	Automated
Ho et al. (2010)[54]	46	46	Hippocampus	46	0	0	0	2.40	3.10	0.25	NA	Automated
Huang et al. (2015)[55]	18, 18	18	Thalamus	18, 18	0	0	0	0.50, 1.04	0.49, 1.01	NA	NA	Automated
James et al. (1999)[56]	29	20	Lateral ventricle, third ventricle, hippocampus, amygdala	29	0	0	0	NA	NA	NA	NA	Manual
James et al. (2004)[57]	16	16	Thalamus, frontal lobe	16	0	0	0	NA	NA	NA	NA	Manual

Joyal et al. (2003)[58]	18	22	Amygdala	16	2	0	0	0.83	0.75	NA	NA	Manual
Juuhl-Langseth et al. (2012)[59]	18	33	Lateral ventricle, third ventricle, caudate, putamen, thalamus, hippocampus, amygdala	15	3	0	0	1.40	0.80	0.31	0.27	Automated
Kalmady et al. (2014)[60]	28	37	Hippocampus	28	0	0	0	NA	NA	NA	NA	Manual
Kalus et al. (2005)[61]	14	14	Amygdala	14	0	0	0	2.22	2.23	NA	NA	Manual
Kawano et al. (2016)[62]	19	15	Hippocampus	19	0	0	0	0.04	NA	NA	NA	Automated
Keshavan et al. (1998)[63]	16	17	Caudate, putamen	13	3	0	0	5.80[1]	5.18	NA	NA	Manual
Koenders et al. (2015)[64]	80, 33	84	Caudate, putamen, thalamus, anterior cingulate cortex, hippocampus, amygdala	57, 24	13, 4	7, 5	2, 0	1.78, 1.91	NA	0.33, 0.42	NA	Automated
Koo et al. (2008)[65]	39	40	Anterior cingulate cortex	39	0	0	0	0.22	0.31	0.06	NA	Manual
Kumra et al. (2011)[66]	52	48	Anterior cingulate cortex	34	16	2	0	2.40	2.00	NA	NA	Manual
Laakso et al. (2001)[67]	18	22	Hippocampus	16	2	0	0	0.83	0.75	NA	NA	Manual
Lang et al. (2001)[68]	30	23	Caudate, putamen	29	1	0	0	NA	NA	0.07	0.05	Manual
Lang et al.	29	22	Thalamus	26	2	0	1	NA	NA	0.10	0.07	Manual

(2006)[69]												
Lappin et al. (2014)[70]	20	32	Hippocampus	20	0	0	0	NA	NA	NA	NA	Automated
Lawrie et al. (2001)[71]	34	36	Lateral ventricle, third ventricle, caudate, thalamus, frontal lobe, temporal lobe	34	0	0	0	NA	NA	NA	NA	Manual
Lim et al. (1996)[72]	22	51	Lateral ventricle, third ventricle	22	0	0	0	0.25	NA	NA	NA	Manual
Malchow et al. (2013)[73]	20, 29	30	Caudate, putamen, thalamus, hippocampus, amygdala	20, 29	0	0	0	0.83, 0.78	1.24, 0.94	0.06, 0.05	0.04, 0.04	Manual
Matsumoto et al. (2001)[74]	40	40	Hippocampus	40	0	0	0	1.33	1.20	0.56	0.74	Manual
McCarley et al. (2002)[75]	15	18	Hippocampus, amygdala	15	0	0	0	NA	NA	0.26	NA	Manual
Meisenzahl et al. (2010)[76]	45	138	Hippocampus	45	0	0	0	1.40	2.70	NA	NA	Manual
Molina et al. (2004)[77]	22	44	Frontal lobe	22	0	0	0	0.60	0.20	0.00	0.00	Manual
Molina et al. (2005)[78]	17	12	Frontal lobe, temporal lobe	17	0	0	0	2.30	1.40	0.00	0.00	Manual
Nakamura et al. (2007)[79]	29	36	Lateral ventricle, frontal lobe, temporal lobe	29	0	0	0	NA	NA	0.06	NA	Manual
Narr et al. (2004)[80]	45, 17	30, 30	Hippocampus	45, 17	0	0	0	NA	NA	0.02	NA	Manual
Narr et al.	51, 21	37, 41	Lateral ventricle	51, 21	0	0	0	NA	NA	0.02	NA	Manual

(2006)[81]												
Niemann et al. (2000)[82]	20	20	Hippocampus, temporal lobe, amygdala	20	0	0	0	NA	NA	NA	NA	Manual
Nopoulis et al. (1995)[83]	24	24	Lateral ventricle, frontal lobe, temporal lobe	22	2	0	0	0.27	NA	0.17	NA	Manual
Ohnuma et al. (1997)[84]	10	10	Lateral ventricle, third ventricle, temporal lobe, frontal lobe	10	0	0	0	0.50	NA	NA	NA	Manual
Premkumar et al. (2006)[85]	34	18	Lateral ventricle, putamen, thalamus,	34	0	0	0	0.47	0.20	NA	NA	Manual
Premkumar et al. (2008)[86]	35	20	Hippocampus, frontal lobe, temporal lobe	14	4	17	0	0.65	0.64	NA	NA	Manual
Preuss et al. (2005)[87]	25	50	Thalamus	25	0	0	0	1.14	0.88	NA	NA	Manual
Puri et al. (2001)[88]	24	12	Lateral ventricle	24	0	0	0	1.15	1.81	0.05	0.06	Automated
Qiu et al. (2009)[89]	32	49	Thalamus	32	0	0	0	2.80	2.10	NA	NA	Automated
Qiu et al. (2013)[90]	28	28	Hippocampus, amygdala	28	0	0	0	0.24	0.24	NA	NA	Automated
Rais et al. (2012)[91]	20	26	Lateral ventricle, third ventricle	19	1	0	0	NA	NA	NA	NA	Automated
Rao et al. (2010)[92]	18	19	Thalamus	18	0	0	0	1.81	0.14	NA	NA	Manual
Razi et al. (1999)[93]	13	31	Hippocampus, amygdala	N/A	N/A	N/A	N/A	0.62	0.78	NA	NA	Manual

Reig et al. (2011)[94]	31	94	Frontal lobe, temporal lobe	31	0	0	0	0.18	0.14	0.09	0.18	Automated
Rich et al. (2016)[95]	28	96	Caudate, putamen, thalamus, hippocampus, amygdala	N/A	N/A	N/A	N/A	0.36	0.27	NA	NA	Automated
Rizos et al. (2011)[96]	20	21	Hippocampus	20	0	0	0	NA	NA	NA	NA	Manual
Rosa et al (2010)[97]	62	94	Lateral ventricle	47	0	15	0	0.84	1.10	0.20	0.18	Manual
Röthlisberger et al. (2012)[98]	23	22	Anterior cingulate cortex	N/A	N/A	N/A	N/A	NA	NA	NA	NA	Manual
Salgado-Pineda et al. (2003)[99]	13	13	Thalamus	13	0	0	0	NA	NA	NA	NA	Manual
Salokangas et al. (2002)[100]	11	19	Lateral ventricle, frontal lobe, temporal lobe	11	0	0	0	NA	NA	NA	NA	Manual
Segal et al. (2010)[101]	6	38	Anterior cingulate cortex	6	0	0	0	2.00	NA	NA	NA	Manual
Smith et al. (2003)[102]	33	19	Hippocampus	32	1	0	0	NA	NA	0.19	0.25	Manual
Sumich et al. (2002)[103]	25	16	Hippocampus, amygdala	12	3	10	0	0.67	0.63	0.06	0.06	Manual
Szeszko et al. (1999)[11]	19	26	Anterior cingulate cortex	17	2	0	0	2.22	NA	0.12	NA	Manual
Szeszko et al. (2003)[104]	46	34	Hippocampus, amygdala	31	5	10	0	3.00	NA	0.06	NA	Manual
Szeszko et al. (2007)[105]	31, 20	56	Anterior cingulate cortex	36	8	7	0	3.31[1], 1.77	NA	0.06, 0.1	NA	Manual

Takayanagi et al. (2011)[106]	23, 29	18, 22	Anterior cingulate cortex, hippocampus, amygdala	23, 29	0	0	0	1.12, 0.89	1.19, 0.96	NA	NA	Automated
Tauscher-Wisniewski et al. (2005)[107]	37	37	Caudate	27	2	5	3	2.03	2.63	NA	NA	Manual
van Erp et al. (2016)[108]	206, 46, 148	170, 55, 81	Lateral ventricle, caudate, putamen, thalamus, hippocampus, amygdala	N/A	N/A	N/A	N/A	NA	NA	NA	NA	Automated
Velakoulis et al. (2006)[109]	31, 15	87	Hippocampus	31, 0	0, 15	0	0	NA	NA	NA	NA	Manual
Verma et al. (2009)[110]	24, 15	14, 15	Hippocampus, amygdala	N/A	N/A	N/A	N/A	NA	NA	1.24, 0.95	NA	Manual
Vita et al. (1995)[111]	19	15	Lateral ventricle, frontal lobe, temporal lobe	19	0	0	0	1.60	1.20	NA	NA	Manual
Watson et al. (2012)[112]	25	25	Hippocampus, amygdala	25	0	0	0	NA	NA	1.20	0.77	Manual
Whitworth et al. (1998)[113]	32	41	Lateral ventricle, hippocampus, amygdala	41	0	0	0	0.69	1.48	0.01	NA	Manual
Williams et al. (2009)[114]	23	26	Frontal lobe, temporal lobe	35	0	0	0	NA	NA	0.48	NA	Automated
Witthaus et al. (2010)[115]	23	29	Hippocampus, amygdala	23	0	0	0	NA	NA	0.00	0.00	Manual

Wood et al. (2001)[116]	17	26	Hippocampus, temporal lobe, amygdala	17	0	0	0	0.08	NA	NA	NA	Manual
Zipursky et al. (1998)[117]	46	61	Lateral ventricle	46	0	0	0	3.30[1]	2.90	NA	NA	Manual

N/A: Details not available.

1Defined as a first episode sample (duration of illness may include from first prodromal and/or psychotic symptoms rather than from diagnosis);

2Where the study reports and analyses data separately for sub-groups (such as males and females) these are shown for each sub-group here. In some studies where the patients are analysed in sub-groups the controls are not sub-divided. In these cases the number of controls is adjusted by the number of sub-groups in the meta-analysis to avoid double-counting (see methods for further details).

eTable 2. Results of Meta-analytic Model Comparison

	Model	df	AIC	BIC	Log likelihood	Log-ratio test vs simpler model	P-value
VR	UN	61	62.42	279.15	29.79	14.09	>.99
	HCS	21	-3.49	71.12	22.75	31.57	<.001
	CS	12	10.07	52.71	6.96	-	-
CVR	UN	61	19.08	235.81	51.46	15.42	>.99
	HCS	21	-45.50	29.12	43.75	32.37	<.001
	CS	12	-31.13	11.51	27.56	-	-
Hedges' g	UN	61	524.18	740.91	-201.09	30.38	.86
	HCS	21	474.56	549.17	-216.28	31.39	<.001
	CS	12	487.95	530.59	-231.98	-	-

(UN; HCS; CS: unstructured; heteroscedastic compound symmetric; compound symmetric covariance structures. AIC: Akaike information criterion. BIC: Bayesian information criterion)

eTable 3. Comparison of Regional Differences in Variability

	Amygdala		Caudate		ACC		Frontal Lobe		Hippocampus		Lateral ventricle		Putamen		Temporal Lobe		Thalamus		Third ventricle	
	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value	ΔIn(C)VR	P-value
Amygdala			0.05	.38	0.12	.11	0.02	.75	0.03	.59	0.22	.002	0.11	.10	0.11	.36	0.10	.12	0.31	.01
Caudate	0.08	.20			0.17	.01	0.07	.25	0.03	.50	0.18	.01	0.07	.26	0.06	.27	0.10	.09	0.31	.005
ACC	0.22	.001	0.13	.03			0.10	.18	0.14	.03	0.35	<.001	0.24	.002	0.23	.001	0.27	<.001	0.48	<.001
Frontal lobe	0.12	.09	0.04	.62	0.10	.15			0.04	.50	0.25	<.001	0.14	.04	0.13	.04	0.17	.01	0.38	<.001
Hippocampus	0.03	.64	0.05	.39	0.18	.001	0.09	.15			0.21	.001	0.11	.09	0.09	.08	0.13	.02	0.34	.001
Lateral ventricle	0.09	.15	0.01	.92	0.13	.04	0.03	.64	0.06	.29			0.11	.12	0.12	.09	0.08	.23	0.13	.20
Putamen	0.01	.90	0.09	.20	0.23	.002	0.13	.09	0.05	.60	0.10	.15			0.01	.87	0.03	.66	0.24	.03
Temporal lobe	0.00	.98	0.08	.16	0.22	<.001	0.12	.05	0.03	.64	0.09	.15	0.01	.90			0.04	.53	0.25	.03
Thalamus	0.03	.64	0.12	.09	0.25	<.001	0.15	.03	0.07	.29	0.12	.05	0.02	.85	0.04	.64			0.21	.05
Third ventricle	0.02	.90	0.10	.35	0.23	.03	0.14	.20	0.05	.64	0.11	.28	0.00	.98	0.02	.90	0.02	.90		

All p-values are adjusted so $p<0.05$ is significant after false discovery rate correction for multiple comparisons. Upper right section (blue): comparisons of log variability ratio (ΔlnVR). Lower left (red): comparisons of log coefficient of variation ratio (ΔlnCVR) comparisons. ACC = anterior cingulate cortex.

eTable 4. Results of the Meta-regression Analyses

Moderator	Effect-size measure	Omnibus test		Significant regional effects			
		χ^2	pval	Region	Estimate	z	pval
Duration of psychosis (mean)	lnVR	11.63	.31	-			
	lnCVR	14.02	.17	-			
	Hedges' g	33.31	<.001	Amygdala	-0.38	3.80	<.001
				Putamen	-0.19	2.54	.01
				Thalamus	0.23	2.39	.02
Duration of psychosis (standard deviation)	lnVR	6.36	.78	-			
	lnCVR	7.41	.69	-			
Duration of treatment (mean)	lnVR	6.81	.74	-			
	lnCVR	10.17	.43	-			
	Hedges' g	108.39	<.001	Amygdala	-7.20	9.68	<.001
				Lateral ventricle	1.79	2.18	.03
				Thalamus	2.03	2.39	.02
Duration of treatment (standard deviation)	lnVR	3.27	.92	-			
	lnCVR	4.41	.82	-			
Proportion schizophreniform psychosis	lnVR	4.55	.92	-			
	lnCVR	3.93	.95	-			
	Hedges' g	8.47	.58	-			
Proportion schizoaffective disorder	lnVR	21.01	.02	Hippocampus	-0.43	2.13	.03
	lnCVR	25.92	.004	Hippocampus	-0.46	2.33	.02
				ACC	-0.83	2.28	.02
	Hedges' g	4.73	.91	-			
Segmentation method	lnVR	8.30	.60	-			
	lnCVR	6.94	.73	-			
	Hedges' g	25.63	.004	Caudate	-0.38	2.07	.04
				Thalamus	-0.58	3.27	.001

lnVR = log variability ratio. lnCVR = log coefficient of variation ratio. ACC = anterior cingulate cortex.

eTable 5. Individual Study and Subgroup Effect Sizes

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Aas et al. (2012)	-0.15	0.01	-0.08	0.01	-0.46	0.03
Bois et al. (2015)	0.16	0.03	0.25	0.02	-0.54	0.06
Gur et al. (2004)	0.34	0.05	0.61	0.04	-3.57	0.23
Gur et al. (2004)	0.54	0.04	0.39	0.04	2.49	0.13
James et al. (1999)	-0.01	0.04	0.02	0.03	-0.2	0.08
Joyal et al. (2003)	0.38	0.05	0.51	0.03	-0.61	0.11
Juuhl-Langseth et al. (2012)	0.01	0.05	0.02	0.03	-0.09	0.09
Kalus et al. (2005)	0.04	0.08	0.13	0.06	-0.75	0.15
Koenders et al. (2015)	0.05	0.02	0.21	0.01	-1.23	0.04
Koenders et al. (2015)	-0.16	0.03	0.04	0.02	-1.76	0.07
Malchow et al. (2013)	-0.3	0.06	-0.17	0.04	-0.75	0.12
Malchow et al. (2013)	-0.48	0.05	-0.36	0.04	-0.81	0.11
McCarley et al. (2002)	0.31	0.07	0.29	0.04	0.15	0.12
Niemann et al. (2000)	0.47	0.05	0.46	0.04	0.14	0.1
Ohnuma et al. (1997)	0.29	0.11	0.47	0.08	-1.25	0.24
Qiu et al. (2013)	0.17	0.04	0.35	0.02	-1.15	0.08
Razi et al. (1999)	0.08	0.06	-0.05	0.03	0.5	0.11
Rich et al. (2016)	0.07	0.02	0.14	0.02	-0.81	0.05
Sumich et al. (2002)	0.08	0.05	0.16	0.04	-0.51	0.11
Szeszko et al. (2003)	0.02	0.03	0.06	0.02	-0.22	0.05
Takayanagi et al. (2011)	-0.28	0.05	-0.24	0.04	-0.33	0.1
Takayanagi et al. (2011)	-0.28	0.04	-0.24	0.03	-0.33	0.08
van Erp et al. (2016)	-0.2	0.01	-0.12	0	-0.63	0.01
van Erp et al. (2016)	0.13	0.02	0.09	0.01	0.35	0.04
van Erp et al. (2016)	0.06	0.01	0.06	0.01	-0.02	0.02
Velakoulis et al. (2006)	0.28	0.03	0.27	0.02	0.05	0.06
Velakoulis et al. (2006)	0.33	0.05	0.29	0.03	0.26	0.09
Watson et al. (2012)	-0.08	0.04	-0.01	0.03	-0.52	0.08
Whitworth et al. (1998)	-0.05	0.03	-0.03	0.02	-0.13	0.06
Witthaus et al. (2010)	0.21	0.04	0.27	0.03	-0.57	0.08

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 6. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Anterior Cingulate Cortex

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Choi et al. (2005)	-0.07	0.05	0	0.03	-0.46	0.09
Crespo-Facorro et al. (2000)	-0.08	0.04	-0.04	0.02	-0.18	0.07
Fornito et al. (2008)	-0.03	0.03	-0.07	0.01	0.17	0.05
Koenders et al. (2015)	-0.21	0.02	-0.18	0.01	-0.21	0.04
Koenders et al. (2015)	-0.22	0.03	-0.2	0.02	-0.14	0.05
Koo et al. (2008)	-0.06	0.03	0.09	0.02	-0.93	0.06
Kumra et al. (2011)	-0.33	0.02	-0.25	0.01	-0.39	0.04
Röthlisberger et al. (2012)	-0.16	0.05	-0.1	0.02	-0.2	0.09
Segal et al. (2010)	0.24	0.11	0.24	0.08	0	0.19
Szeszko et al. (1999)	-0.33	0.05	-0.27	0.02	-0.2	0.09
Szeszko et al. (2007)	-0.03	0.04	-0.04	0.02	0.06	0.07
Szeszko et al. (2007)	-0.02	0.04	0.08	0.03	-0.58	0.09
Takayanagi et al. (2011)	0.3	0.05	0.37	0.03	-0.5	0.1
Takayanagi et al. (2011)	-0.12	0.04	-0.1	0.02	-0.1	0.08

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 7. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Caudate

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Ballmaier et al. (2008)	-0.01	0.05	-0.01	0.05	-0.28	0.1
Boonstra et al. (2011)	-0.15	0.06	-0.11	0.05	-0.3	0.11
Cahn et al. (2002)	-0.14	0.05	-0.14	0.04	0.03	0.1
Chakos et al. (1994)	-0.13	0.07	-0.12	0.06	-0.01	0.13
Choi et al. (2005)	0.38	0.05	0.36	0.04	0.17	0.09
Chua et al. (2007)	0.05	0.03	0.17	0.03	-0.94	0.07
Crespo-Facorro et al. (2007)	-0.05	0.03	-0.08	0.02	0.17	0.05
Crespo-Facorro et al. (2007)	0.25	0.06	0.26	0.05	-0.01	0.11
DeLisi et al. (1991)	-0.28	0.04	-0.23	0.03	-0.26	0.08
Ebdrup et al. (2010)	0.15	0.03	0.22	0.03	-0.59	0.06
Emsley et al. (2015)	0.28	0.05	0.15	0.04	0.88	0.1
Ettinger et al. (2004)	0.1	0.06	0.18	0.04	-0.45	0.11
Glenthoj et al. (2007)	-0.14	0.06	-0.1	0.05	-0.4	0.11
Gunduz et al. (2002)	0.07	0.03	0.05	0.02	0.14	0.06
Juuhl-Langseth et al. (2012)	0.02	0.05	-0.07	0.04	1.04	0.1
Keshavan et al. (1998)	-0.04	0.06	0.09	0.05	-0.87	0.13
Koenders et al. (2015)	0.14	0.02	0.16	0.02	-0.24	0.04
Koenders et al. (2015)	0.21	0.03	0.25	0.02	-0.35	0.05
Lang et al. (2001)	0.29	0.04	0.33	0.03	-0.33	0.08
Lawrie et al. (2001)	0.13	0.03	0.09	0.02	0.3	0.06
Malchow et al. (2013)	0.14	0.06	0.18	0.05	-0.42	0.12
Malchow et al. (2013)	0.21	0.05	0.27	0.05	-0.62	0.11
Rich et al. (2016)	-0.13	0.02	-0.17	0.02	0.34	0.05
Tauscher-Wisniewski et al. (2005)	-0.18	0.03	-0.16	0.02	-0.18	0.05
van Erp et al. (2016)	0.11	0.01	0.11	0	-0.02	0.01
van Erp et al. (2016)	-0.16	0.02	-0.2	0.02	0.35	0.04
van Erp et al. (2016)	-0.03	0.01	-0.03	0.01	0.02	0.02

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 8. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Frontal Lobe

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Bartzokis et al. (2011)	0.1	0.13	0.18	0.11	-0.91	0.26
Bartzokis et al. (2011)	-0.36	0.12	-0.36	0.1	0.12	0.22
Bilder et al. (1994)	0.29	0.03	0.32	0.02	-0.21	0.06
Bilder et al. (1994)	-0.17	0.04	-0.14	0.03	-0.24	0.08
Cahn et al. (2002)	-0.05	0.05	0.01	0.04	-0.58	0.1
Crespo-Facorro et al. (2009)	0.06	0.02	0.08	0.01	-0.19	0.04
Crespo-Facorro et al. (2009)	0.09	0.03	0.08	0.02	0.1	0.05
DeLisi et al. (1991)	0.04	0.04	0.07	0.03	-0.2	0.08
Gur et al. (1998)	0	0.06	0.07	0.04	-0.45	0.11
Gutierrez-Galve et al. (2010)	0.32	0.03	0.33	0.02	-0.11	0.05
Hadjulis et al. (2004)	-0.16	0.05	-0.1	0.04	-0.48	0.1
Hadjulis et al. (2004)	0.11	0.05	0.18	0.04	-0.47	0.1
Hirayasu et al. (2001)	-0.21	0.06	-0.14	0.04	-0.55	0.12
Ho et al. (2007)	0.13	0.02	0.17	0.02	-0.6	0.05
James et al. (2004)	-0.44	0.07	-0.32	0.05	-1.04	0.14
Lawrie et al. (2001)	0	0.03	0.02	0.02	-0.13	0.06
Molina et al. (2004)	-0.15	0.04	-0.18	0.02	0.2	0.07
Molina et al. (2005)	-0.29	0.08	-0.31	0.06	0.15	0.14
Nakamura et al. (2007)	-0.24	0.03	-0.18	0.03	-0.71	0.07
Nopoulos et al. (1995)	-0.1	0.04	-0.05	0.03	-0.41	0.09
Ohnuma et al. (1997)	0.07	0.11	0.17	0.09	-1.02	0.23
Premkumar et al. (2008)	-0.23	0.04	-0.17	0.03	-0.5	0.08
Reig et al. (2011)	-0.09	0.02	-0.05	0.02	-0.29	0.04
Salokangas et al. (2002)	-0.34	0.08	-0.29	0.06	-0.38	0.15
Vita et al. (1995)	0.33	0.06	0.3	0.03	0.09	0.12
Williams et al. (2009)	0.02	0.04	0.04	0.03	-0.16	0.08

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 9. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Hippocampus

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Barr et al. (1997)	-0.04	0.03	0.15	0.02	-1.17	0.06
Bodnar et al. (2010)	-0.29	0.03	-0.24	0.03	-0.56	0.06
Bodnar et al. (2010)	-0.08	0.05	-0.06	0.04	-0.21	0.09
Bois et al. (2015)	0.05	0.03	0.12	0.02	-0.63	0.06
Cahn et al. (2002)	-0.04	0.05	0	0.04	-0.44	0.1
Chakos et al. (2005)	0.07	0.05	0.16	0.04	-0.75	0.11
Ebdrup et al. (2010)	0.06	0.03	0.08	0.02	-0.27	0.06
Hasan et al. (2014)	0.34	0.02	0.36	0.01	-0.13	0.04
Ho et al. (2009)	-0.1	0.02	0.02	0.02	-1.2	0.05
James et al. (1999)	-0.03	0.04	0.01	0.03	-0.26	0.09
Juuhl-Langseth et al. (2012)	-0.05	0.05	-0.02	0.04	-0.33	0.09
Kalmady et al. (2014)	0.41	0.03	0.53	0.02	-0.92	0.07
Kawano et al. (2016)	-0.08	0.06	-0.08	0.05	-0.02	0.12
Koenders et al. (2015)	0.1	0.02	0.12	0.01	-0.14	0.04
Koenders et al. (2015)	0.12	0.03	0.12	0.02	0.01	0.05
Laakso et al. (2001)	0.23	0.05	0.26	0.04	-0.18	0.1
Lappin et al. (2014)	0.06	0.04	0.1	0.04	-0.54	0.08
Malchow et al. (2013)	0.06	0.06	0.19	0.04	-0.76	0.12
Malchow et al. (2013)	0.31	0.05	0.41	0.04	-0.5	0.1
Matsumoto et al. (2001)	-0.1	0.03	-0.04	0.02	-0.4	0.05
McCarley et al. (2002)	0.2	0.07	0.3	0.05	-1.07	0.14
Meisenzahl et al. (2010)	0.16	0.02	0.21	0.01	-0.63	0.06
Narr et al. (2004)	0.11	0.03	0.17	0.02	-0.56	0.1
Narr et al. (2004)	-0.08	0.05	-0.03	0.04	-0.23	0.1
Niemann et al. (2000)	0	0.05	0.03	0.04	-1.45	0.1
Premkumar et al. (2008)	0.14	0.04	0.29	0.03	-0.61	0.07
Qiu et al. (2013)	-0.07	0.04	-0.01	0.03	0.26	0.11
Razi et al. (1999)	0.01	0.06	-0.05	0.04	-0.33	0.05
Rich et al. (2016)	0.03	0.02	0.05	0.02	-0.72	0.1
Rizos et al. (2011)	-0.68	0.05	-0.63	0.04	-4.55	0.28
Smith et al. (2003)	0.18	0.04	0.61	0.04	-0.61	0.05
Szeszko et al. (2003)	0	0.03	0.06	0.02	-1.06	0.11
Takayanagi et al. (2011)	-0.33	0.05	-0.24	0.04	-1.07	0.09
Takayanagi et al. (2011)	-0.33	0.04	-0.23	0.03	-0.06	0.01
van Erp et al. (2016)	0.1	0.01	0.1	0	0.01	0.04
van Erp et al. (2016)	0.07	0.02	0.07	0.02	-0.17	0.02
van Erp et al. (2016)	0.03	0.01	0.05	0.01	-0.56	0.06
Velakoulis et al. (2006)	0.06	0.03	0.12	0.02	-0.78	0.09
Velakoulis et al. (2006)	-0.45	0.05	-0.37	0.04	-0.52	0.12
Verma et al. (2009)	-0.27	0.06	-0.19	0.04	-0.71	0.14
Verma et al. (2009)	0.05	0.07	0.14	0.05	-1.02	0.09

Watson et al. (2012)	0.07	0.04	0.19	0.03	-0.86	0.06
Whitworth et al. (1998)	-0.42	0.03	-0.27	0.02	-0.45	0.08
Witthaus et al. (2010)	-0.35	0.04	-0.3	0.03	-1.6	0.13
Wood et al. (2001)	0.35	0.05	0.47	0.04	-0.53	0.03

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 10. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Lateral Ventricle

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Barr et al. (1997)	0.29	0.03	0.03	0.02	0.6	0.06
Boonstra et al. (2011)	-0.42	0.06	-0.57	0.05	0.22	0.11
Boonstra et al. (2011a)	-0.06	0.02	-0.05	0.01	-0.02	0.04
Cahn et al. (2002)	-0.57	0.05	-0.45	0.05	-0.16	0.1
Chua et al. (2003)	-0.14	0.05	-0.3	0.03	0.47	0.09
Chua et al. (2007)	0.19	0.03	-0.01	0.03	0.71	0.07
Collinson et al. (2009)	0.16	0.05	0.1	0.03	0.14	0.09
Collinson et al. (2009)	1.39	0.12	0.62	0.09	0.96	0.23
Crespo-Facorro et al. (2009)	0.21	0.02	0.04	0.01	0.41	0.04
Crespo-Facorro et al. (2009)	0.31	0.03	0.1	0.02	0.49	0.05
Degreef et al. (1992)	0.5	0.03	0.26	0.03	0.67	0.07
del Re et al. (2015)	0.67	0.06	0.21	0.04	0.84	0.11
DeLisi et al. (1992)	-0.23	0.08	-0.19	0.06	-0.15	0.15
DeLisi et al. (1992)	0.28	0.07	0.09	0.05	0.53	0.13
DeLisi et al. (1991)	0.35	0.04	0.15	0.03	0.62	0.09
Ebdrup et al. (2010)	-0.14	0.03	-0.12	0.02	-0.03	0.06
Fannon et al. (2000)	0.56	0.03	0.3	0.02	0.55	0.07
Ho et al. (2007)	0.59	0.02	0.23	0.02	0.78	0.05
James et al. (1999)	0.46	0.04	0.07	0.04	0.51	0.09
Juuhl-Langseth et al. (2012)	0.01	0.05	-0.36	0.03	0.99	0.1
Lawrie et al. (2001)	0.53	0.03	0.3	0.03	0.33	0.06
Lim et al. (1996)	0.08	0.03	-0.12	0.03	0.64	0.07
Nakamura et al. (2007)	0	0.03	-0.22	0.02	0.51	0.06
Narr et al. (2006)	-0.18	0.02	-0.06	0.02	-0.31	0.05
Narr et al. (2006)	0.06	0.04	-0.01	0.03	0.19	0.07
Nopoulos et al. (1995)	0.41	0.04	0.21	0.03	0.39	0.08
Ohnuma et al. (1997)	1.09	0.11	0.85	0.09	0.86	0.22
Puri et al. (2001)	0.31	0.07	0.18	0.05	0.41	0.13
Rais et al. (2012)	0.69	0.05	0.35	0.04	0.47	0.09
Rosa et al. (2010)	0.13	0.01	-0.09	0.01	0.44	0.03
Salokangas et al. (2002)	0.2	0.08	-0.02	0.06	0.54	0.15
van Erp et al. (2016)	0.06	0.01	0.03	0	0.05	0.01
van Erp et al. (2016)	0.29	0.02	0.2	0.02	0.15	0.04
van Erp et al. (2016)	-0.08	0.01	-0.18	0.01	0.17	0.02
Vita et al. (1995)	0.16	0.06	-0.04	0.05	0.7	0.13
Whitworth et al. (1998)	0.45	0.03	0.08	0.02	0.7	0.06
Zipursky et al. (1998)	0.34	0.02	0.16	0.01	0.5	0.04

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 11. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Putamen

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Ballmaier et al. (2008)	-0.22	0.05	-0.1	0.05	-3.25	0.22
Boonstra et al. (2011)	0.79	0.06	0.74	0.05	0.41	0.11
Crespo-Facorro et al. (2009)	-0.04	0.02	-0.01	0.02	-0.16	0.04
Crespo-Facorro et al. (2009)	0.21	0.03	0.23	0.02	-0.11	0.05
Ebdrup et al. (2010)	0.25	0.03	0.26	0.03	-0.1	0.06
Emsley et al. (2015)	0.28	0.05	0.3	0.04	-0.09	0.09
Glenthoj et al. (2007)	-0.55	0.06	-0.5	0.05	-0.33	0.11
Gunduz et al. (2002)	0.31	0.03	0.33	0.03	-0.18	0.06
Juuhl-Langseth et al. (2012)	0.02	0.05	0.01	0.04	0.2	0.09
Keshavan et al. (1998)	-0.21	0.06	-0.12	0.06	-0.29	0.12
Koenders et al. (2015)	0.16	0.02	0.24	0.02	-0.67	0.04
Koenders et al. (2015)	0.06	0.03	0.2	0.03	-1.3	0.07
Lang et al. (2001)	0.15	0.04	0.17	0.04	-0.13	0.08
Malchow et al. (2013)	0.14	0.06	0.18	0.06	-0.34	0.12
Malchow et al. (2013)	0.33	0.05	0.37	0.05	-0.34	0.1
Premkumar et al. (2006)	0.27	0.04	0.12	0.04	0.82	0.09
Rich et al. (2016)	0.17	0.02	0.15	0.02	0.18	0.05
van Erp et al. (2016)	-0.08	0.01	-0.03	0	-0.48	0.01
van Erp et al. (2016)	-0.15	0.02	-0.22	0.02	0.57	0.04
van Erp et al. (2016)	-0.06	0.01	-0.05	0.01	-0.13	0.02

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 12. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Temporal Lobe

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Bilder et al. (1994)	0.03	0.03	0.08	0.02	-0.48	0.06
Bilder et al. (1994)	0.02	0.04	0.06	0.03	-0.33	0.08
Bogerts et al. (1990)	-0.61	0.1	-0.63	0.08	0.2	0.18
Bogerts et al. (1990)	0.09	0.06	0.2	0.05	-1.12	0.13
Collinson et al. (2009)	0.13	0.05	0.15	0.04	-0.23	0.09
Collinson et al. (2009)	-0.37	0.12	-0.28	0.08	-0.74	0.22
Crespo-Facorro et al. (2009)	0.17	0.02	0.18	0.01	-0.15	0.04
Crespo-Facorro et al. (2009)	0.19	0.03	0.18	0.02	0.14	0.05
DeLisi et al. (1992)	0.37	0.08	0.34	0.06	0.34	0.15
DeLisi et al. (1992)	0.15	0.07	0.21	0.05	-0.61	0.13
DeLisi et al. (1991)	0.23	0.04	0.25	0.03	-0.15	0.08
Fannon et al. (2000)	-0.03	0.03	0.04	0.02	-0.42	0.07
Gur et al. (1998)	0.08	0.06	0.21	0.04	-0.89	0.12
Gutierrez-Galve et al. (2010)	0.06	0.03	0.1	0.02	-0.37	0.05
Hadjulis et al. (2004)	-0.06	0.05	-0.01	0.04	-0.57	0.1
Hadjulis et al. (2004)	0.32	0.05	0.36	0.04	-0.29	0.1
Ho et al. (2007)	0.15	0.02	0.17	0.02	-0.35	0.04
Lawrie et al. (2001)	0.31	0.03	0.29	0.02	0.15	0.06
Molina et al. (2005)	0.23	0.08	0.18	0.06	0.56	0.15
Nakamura et al. (2007)	0.06	0.03	0.1	0.02	-0.37	0.06
Niemann et al. (2000)	0.32	0.05	0.31	0.04	0.09	0.1
Nopoulos et al. (1995)	0.08	0.04	0.1	0.03	-0.2	0.08
Ohnuma et al. (1997)	0.21	0.11	0.26	0.09	-0.58	0.21
Reig et al. (2011)	0.22	0.02	0.19	0.02	0.32	0.04
Salokangas et al. (2002)	-0.18	0.08	-0.22	0.06	0.35	0.15
Vita et al. (1995)	0.22	0.06	0.21	0.05	0.08	0.12
Williams et al. (2009)	-0.05	0.04	-0.02	0.03	-0.39	0.08
Wood et al. (2001)	0.21	0.05	0.27	0.04	-0.59	0.1

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 13. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Thalamus

Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Cahn et al. (2002)	-0.47	0.05	-0.43	0.04	-0.34	0.1
Choi et al. (2005)	0.03	0.05	0.01	0.04	0.17	0.09
Coscia et al. (2009)	0.19	0.04	0.29	0.04	-1.05	0.09
Coscia et al. (2009)	0.28	0.11	0.43	0.09	-1.62	0.27
Crespo-Facorro et al. (2009)	0.12	0.02	0.17	0.01	-0.41	0.04
Crespo-Facorro et al. (2009)	0.24	0.03	0.27	0.02	-0.21	0.05
Dasari et al. (1999)	0.39	0.06	0.47	0.05	-0.93	0.12
Emsley et al. (2015a)	0.23	0.05	0.2	0.04	0.28	0.09
Ettinger et al. (2001)	0.24	0.03	0.29	0.02	-0.49	0.06
Gilbert et al. (2001)	0.36	0.05	0.57	0.03	-0.89	0.11
Huang et al. (2015)	0.31	0.09	0.36	0.06	-0.18	0.17
Huang et al. (2015)	0.58	0.09	0.6	0.05	-0.08	0.17
James et al. (2004)	0.19	0.07	0.27	0.05	-0.75	0.13
Juuhl-Langseth et al. (2012)	0.02	0.05	0.01	0.04	0.16	0.09
Koenders et al. (2015)	0.19	0.02	0.17	0.01	0.24	0.04
Koenders et al. (2015)	0.22	0.03	0.17	0.02	0.51	0.06
Lang et al. (2006)	0.22	0.04	0.27	0.04	-0.68	0.08
Lawrie et al. (2001)	0.51	0.03	0.52	0.02	-0.07	0.06
Malchow et al. (2013)	-0.1	0.06	-0.05	0.05	-0.52	0.12
Malchow et al. (2013)	-0.35	0.05	-0.34	0.04	-0.19	0.1
Preuss et al. (2005)	0.14	0.03	0.18	0.02	-0.29	0.06
Qiu et al. (2009)	-0.12	0.03	-0.08	0.02	-0.39	0.05
Rao et al. (2010)	-0.23	0.06	-0.12	0.04	-0.68	0.11
Rich et al. (2016)	0.05	0.02	0.05	0.02	-0.1	0.05
Salgado-Pineda et al. (2003)	0.04	0.08	0.3	0.07	-2.3	0.26
van Erp et al. (2016)	0.06	0.01	0.03	0	0.3	0.01
van Erp et al. (2016)	-0.03	0.02	-0.09	0.02	0.6	0.04
van Erp et al. (2016)	0.17	0.01	0.21	0.01	-0.44	0.02

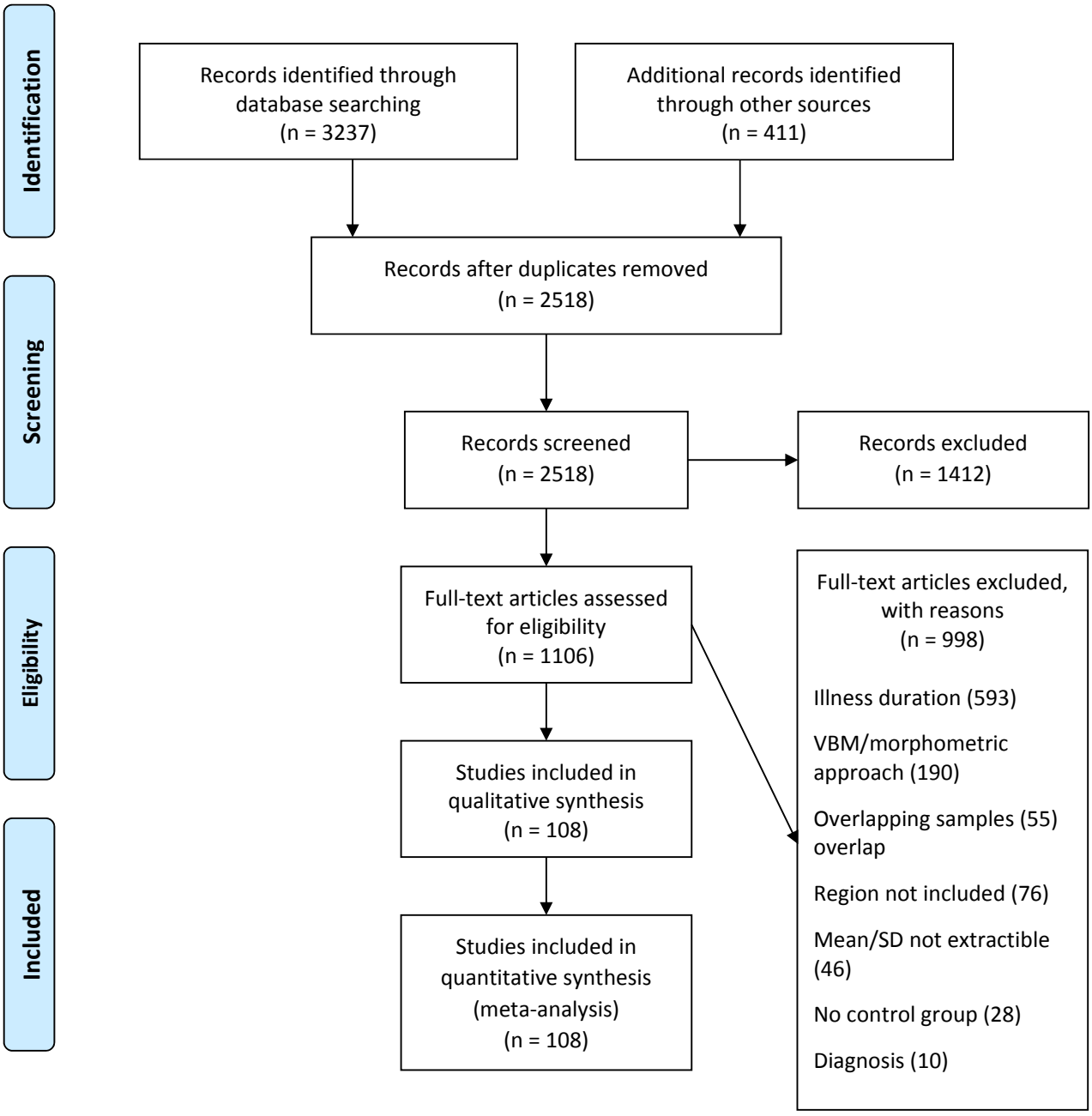
lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

eTable 14. Individual Study and Subgroup Effect Sizes for All Outcome Measures for Third Ventricle

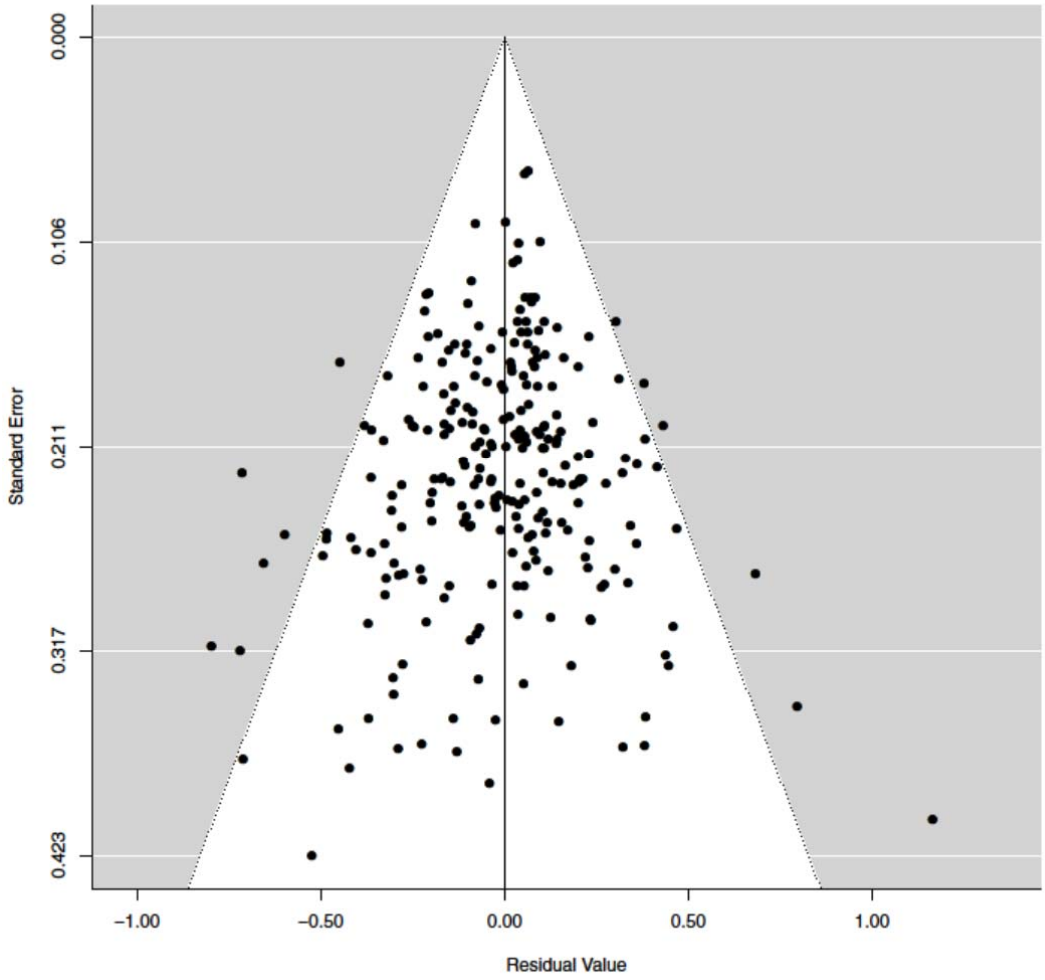
Study	lnVR	lnVR var	lnCVR	lnCVR var	Hedges g	Hedges g var
Boonstra et al. (2011)	0.65	0.06	0.23	0.02	0.82	0.12
Boonstra et al. (2011a)	0.25	0.02	0.09	0.01	0.36	0.04
Cahn et al. (2002)	-0.12	0.05	-0.43	0.02	0.66	0.11
Degreef et al. (1992)	0.16	0.03	-0.01	0.02	0.58	0.07
DeLisi et al. (1991)	0.68	0.04	0.6	0.02	0.23	0.08
Ebdrup et al. (2010)	-0.06	0.03	0.01	0.01	-0.2	0.06
Fannon et al. (2000)	0.69	0.03	0.44	0.01	0.6	0.07
James et al. (1999)	0.63	0.04	0.36	0.02	0.85	0.09
Juuhl-Langseth et al. (2012)	0.01	0.05	-0.08	0.03	0.52	0.09
Lawrie et al. (2001)	1.1	0.03	0.69	0.02	0.45	0.06
Lim et al. (1996)	-0.07	0.03	-0.3	0.01	0.54	0.07
Ohnuma et al. (1997)	0.75	0.11	0.61	0.06	0.39	0.2
Rais et al. (2012)	0.17	0.05	0.07	0.02	0.25	0.09

lnVR: log variability ratio; lnCVR: log coefficient of variation ratio; var: sampling variance.

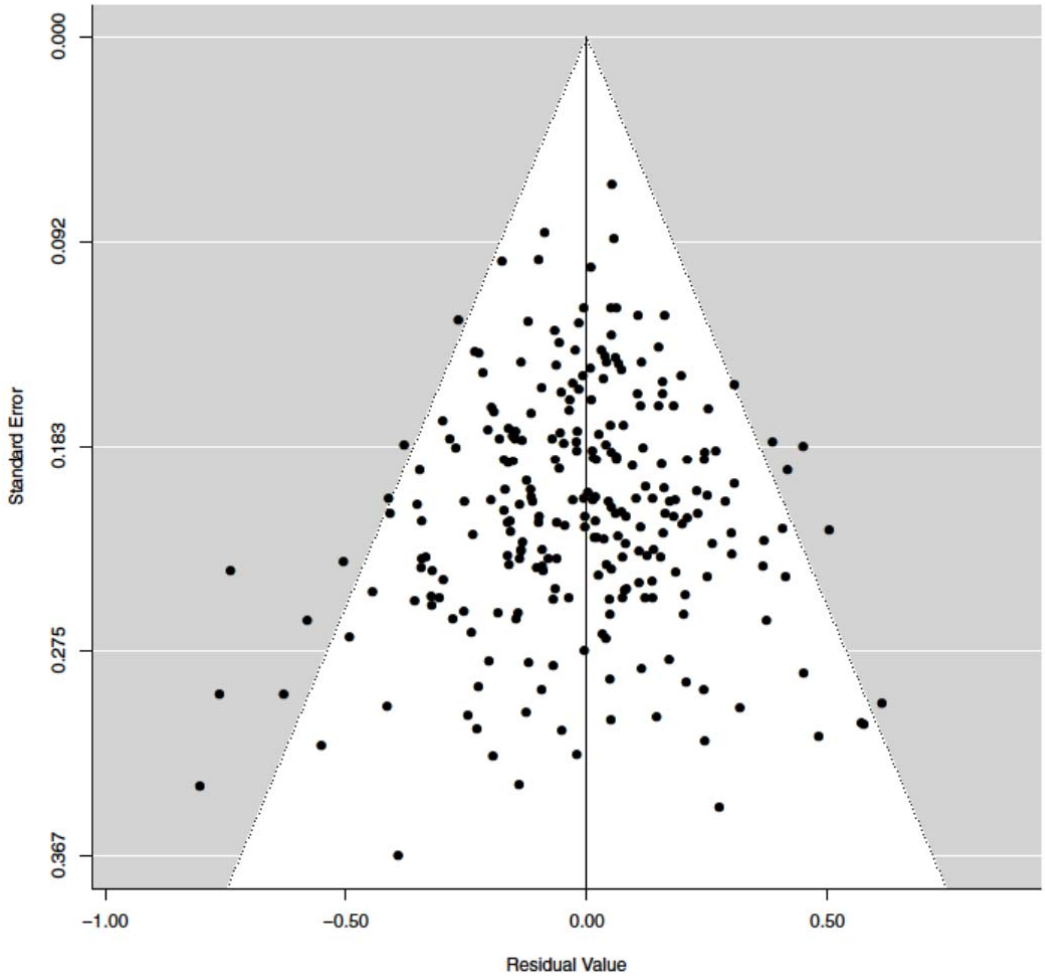
eFigure 1. PRISMA 2009 Flow Diagram



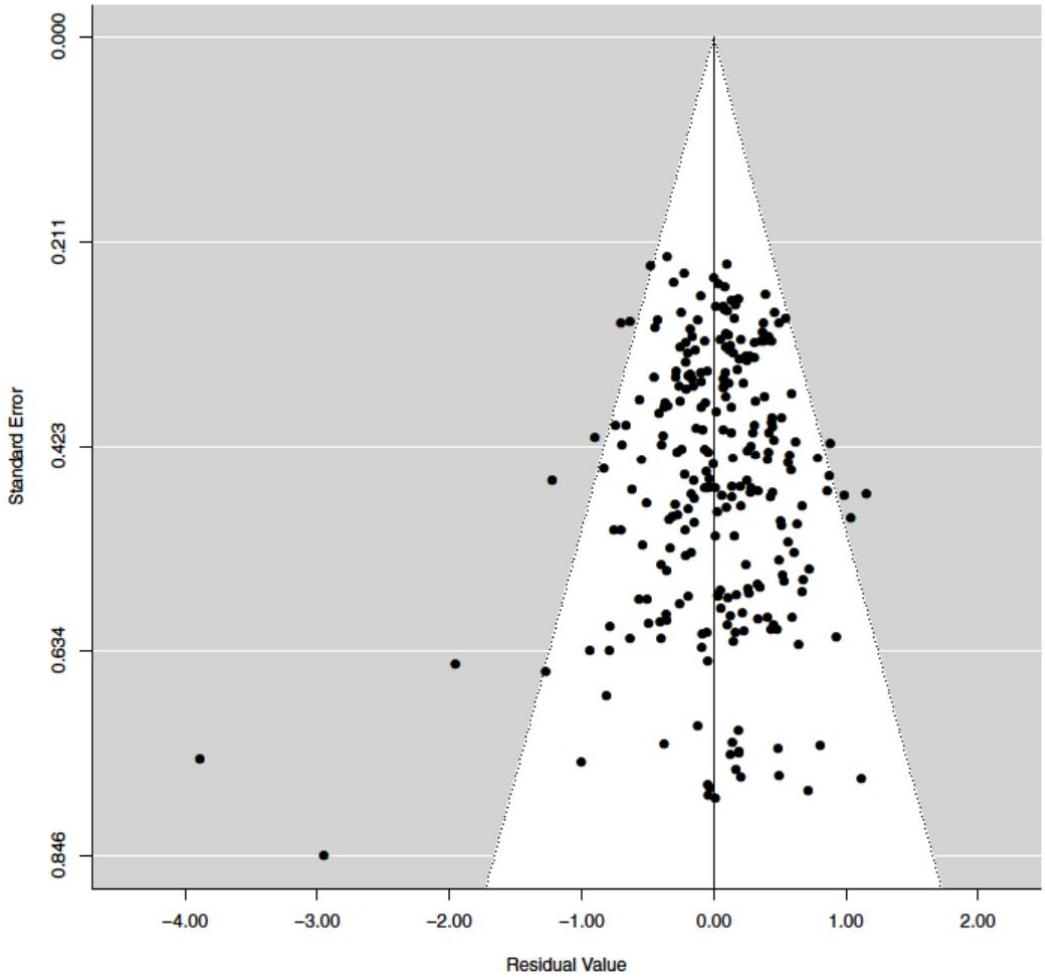
Publication Bias and Inconsistency



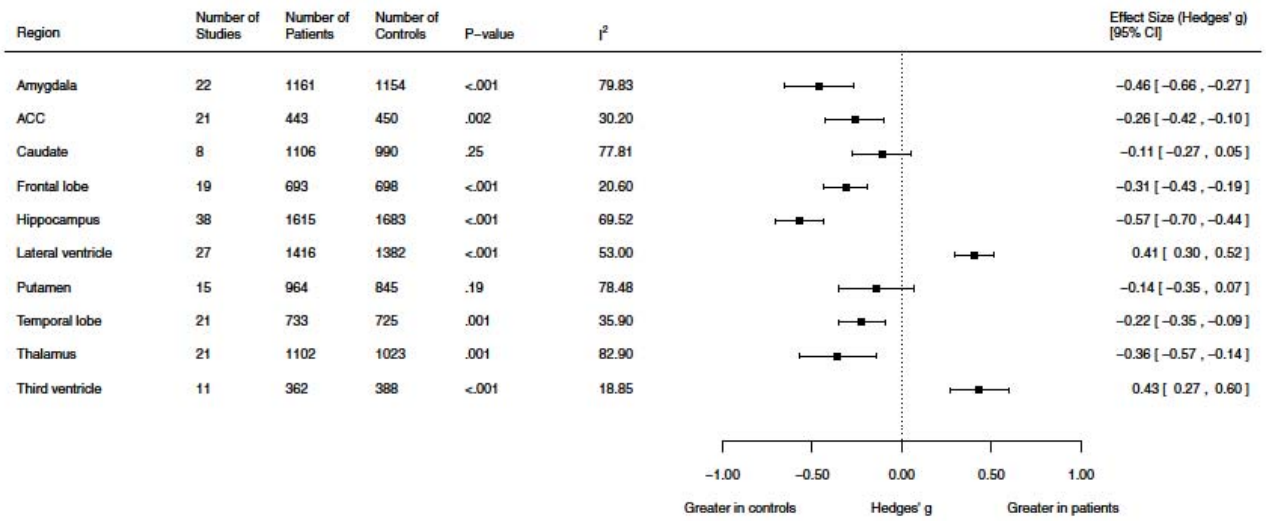
eFigure 2. Funnel Plot of SE and Residual Value (Individual Estimate Minus Pooled Regional Estimate) for Log Variability Ratio Across All Regions of Interest



eFigure 3. Funnel Plot of SE and Residual Value (Individual Estimate Minus Pooled Regional Estimate) for Log Coefficient of Variation Ratio Across All Regions of Interest

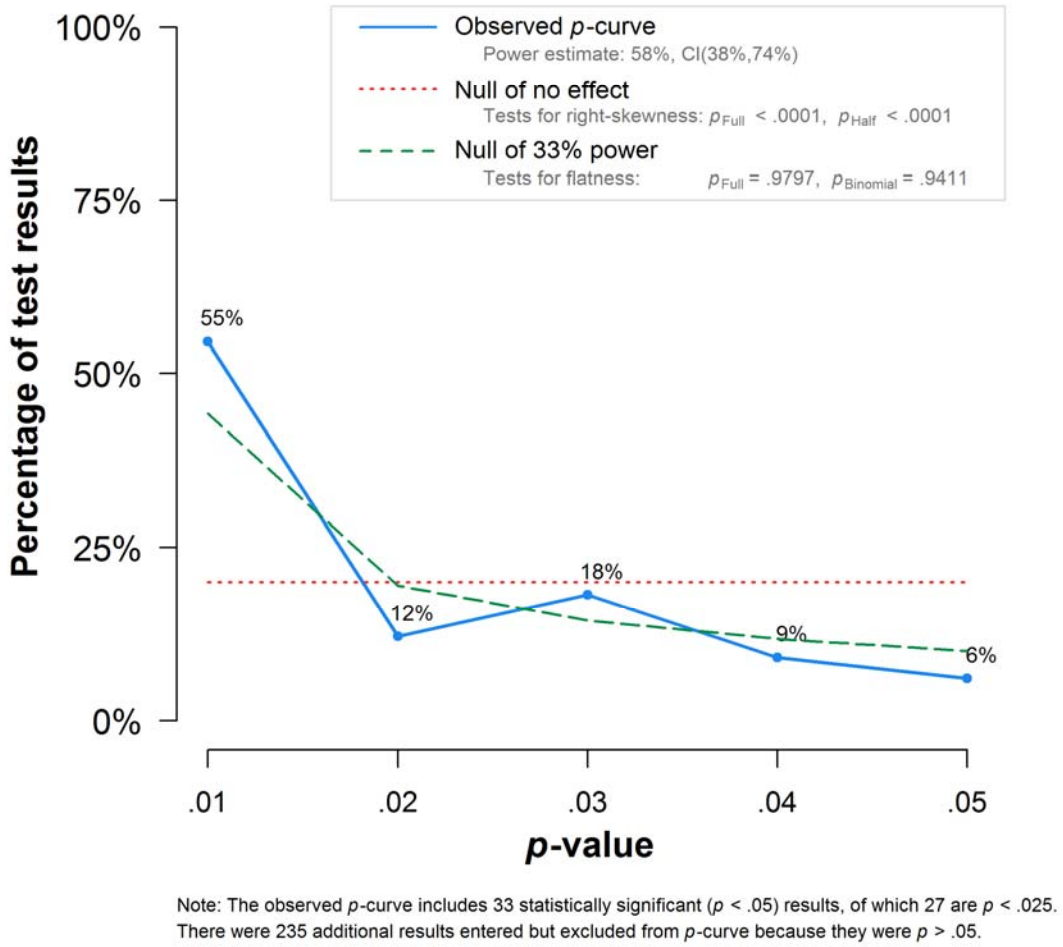


eFigure 4. Funnel Plot of SE and Residual Value (Individual Estimate Minus Pooled Regional Estimate) for Hedges *g* Across All Regions of Interest



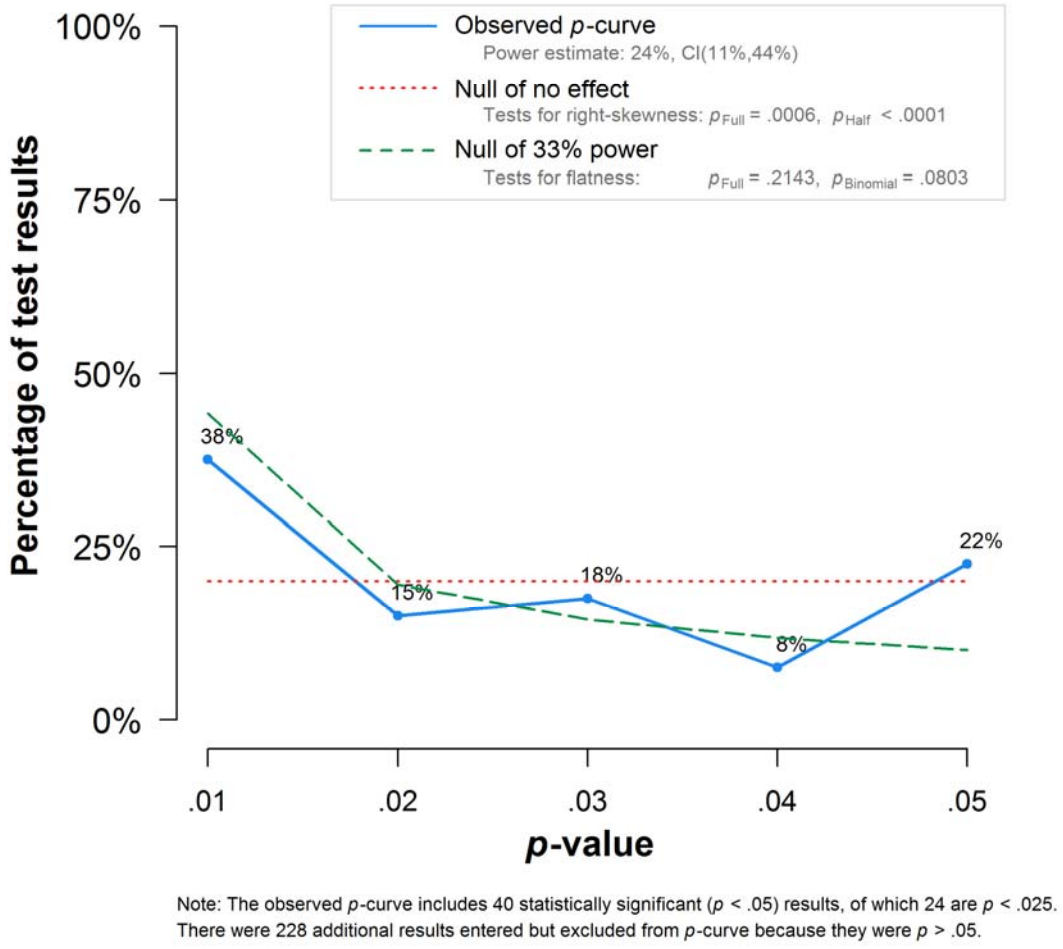
eFigure 5. Forest Plot Showing Effect Sizes for Mean Differences in Regional Brain Volumes kin Schizophrenia Following Removal of Outlying Estimates

No significant differences in results relative to the primary analysis were found. Mean volumes of the third and lateral ventricles were significantly increased, whilst mean volumes of thalamus, temporal lobe, hippocampus, frontal lobe, anterior cingulate cortex, and amygdala were significantly reduced in schizophrenia. ACC = anterior cingulate cortex; CI = Confidence Interval; I2 = Cochrane's I2 statistic.

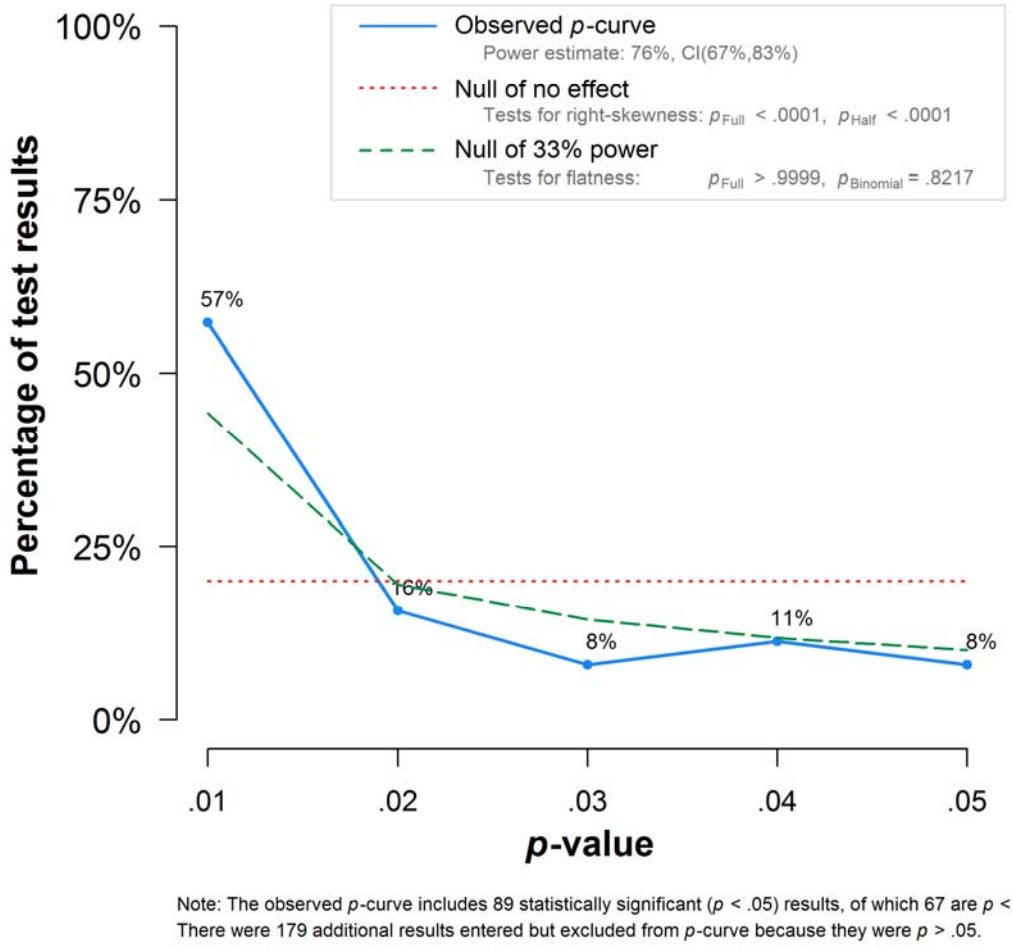


Note: The observed *p*-curve includes 33 statistically significant ($p < .05$) results, of which 27 are $p < .025$. There were 235 additional results entered but excluded from *p*-curve because they were $p > .05$.

eFigure 6. *P* Curve for Log Variability Ratio (lnVR)



eFigure 7. *P* Curve for Log Coefficient of Variation Ratio



Note: The observed *p*-curve includes 89 statistically significant ($p < .05$) results, of which 67 are $p < .025$.
There were 179 additional results entered but excluded from *p*-curve because they were $p > .05$.

eFigure 8. *P* Curve for Hedges *g* (Mean Differences Analysis)

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