

Appendix 1 to Gao X, Zhang W, Yao L, et al. Association between structural and functional brain alterations in drug-free patients with schizophrenia: a multimodal meta-analysis. *J Psychiatry Neurosci* 2017.

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Table S1

Imaging Methodology Quality Assessment Checklist

Category 1: Subjects

1. Patients were evaluated prospectively, specific diagnostic criteria were applied, and demographic data was reported
2. Healthy comparison subjects were evaluated prospectively, psychiatric and medical illnesses were excluded, and demographic data was reported
3. Important variables (e.g. illness duration, severity of illness, drug status, non-drug therapy status) were checked either by stratification or statistically
4. Sample size per group > 10, and no significant difference in age and sex existed

Category 2: Methods for image acquisition and analysis

5. Magnet strength at least 1.5T
 6. Whole brain analysis was automated with no a-priori regional selection
-

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7. Coordinates reported in a standard space

8. The imaging technique used was clearly described so as it could be reproduced

9. Measurements were clearly described so that they could be reproduced

10. Results have been corrected for multiple comparison

Category 3: Results and conclusions

11. Statistical parameters for significant and important non-significant differences were provided

12. Conclusions were consistent with the results obtained and the limitations were discussed

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Table S2

Meta-analysis results of structural MRI

	MNI	SDM-Z	P	Voxels	Cluster breakdown (number of voxels)
Cluster of decreased gray matter volume (patients<controls)					
Left fusiform gyrus	-26,-54,-16	-2.584	0.000154853	771	Left fusiform gyrus (382) Left cerebellum, hemispheric lobule VI (182) Left parahippocampal gyrus (21) Left hippocampus (15)
Left inferior frontal gyrus	-46,16,0	-2.497	0.00023222	649	Left inferior frontal gyrus (314) Left insula (166)

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					Left temporal pole, superior temporal gyrus (106)
Right superior temporal gyrus	52,-6,-6	-2.098	0.002043664	330	Right superior temporal gyrus (124)
					Right insula (97)
					Right rolandic operculum (12)
					Right middle temporal gyrus (11)
					Right temporal pole, superior temporal gyrus (10)
Left supramarginal gyrus	-56,-40,36	-2.387	0.000490248	293	Left supramarginal gyrus (117)
					Left inferior parietal gyrus (104)
					Left superior temporal gyrus (64)

Cluster of increased gray matter volume (patients>controls)

Right lingual gyrus	6,-34,-6	1.895	0.000005186	466	Right lingual gyrus (62)
					Cerebellum, vermic lobule III (36)

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					Left cerebellum, hemispheric lobule IV/V (31)
					Left lingual gyrus (18)
Right superior frontal gyrus, orbital part	6,60,-22	1.617	0.000805080	155	Right gyrus rectus (79)
					Right superior frontal gyrus (38)

(a) Voxel probability threshold: $P=0.005$

(b) Peak height threshold: $z=1$

(c) Cluster extent threshold: 100 voxels. Regions with less than 10 voxels are not reported in the cluster breakdown.

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Table S3

Analyses of subgroups and sensitivity analyses of structural studies

Subgroup analysis	Increased gray matter volume		Decreased gray matter volume			
	Right lingual	Right superior frontal	Left fusiform	Left inferior	Right superior	Left supramarginal
	gyrus	gyrus	gyrus	frontal gyrus	temporal gyrus	gyrus
Studies with slice thickness \leq 1.5 mm at acquisition (n=13)	YES	YES	NO	NO	YES	YES
Studies using \leq 8 mm smoothing kernel (n=10)	YES	YES	YES	NO	NO	YES
Studies using 1.5T MRI (n=10)	NO	NO	YES	YES	YES	NO
Studies with an additional correction step (n=9)	YES	YES	YES	YES	YES	YES
Studies of drug-naive patients (n=14)	YES	YES	YES	YES	YES	YES

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Jackknife sensitivity analysis, discarded study

2003Salgado-Pineda	YES	YES	YES	YES	YES	YES
2005Jayakumar	YES	YES	YES	YES	YES	YES
2007Prasad	YES	YES	YES	YES	YES	YES
2007Chua	YES	YES	YES	YES	YES	YES
2008Meda	YES	YES	YES	YES	YES	YES
2008Witthaus	YES	YES	YES	YES	YES	YES
2010Venkatasubramanian	YES	YES	YES	YES	YES	YES
2011Berge	YES	YES	YES	YES	YES	YES
2013Suazo	YES	YES	YES	YES	YES	YES
2013WentingRen	YES	YES	YES	YES	YES	YES

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2013XiaofengGuo(S)	YES	YES	YES	YES	YES	YES
2013XiaofengGuo(L)	YES	YES	YES	YES	YES	YES
2014WenbinGuo	YES	YES	YES	YES	YES	YES
2014JunLi	YES	YES	YES	YES	YES	YES
2014Nenadic	YES	YES	YES	YES	YES	YES
2016Yue	YES	YES	YES	YES	YES	YES

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Table S4

Meta-analysis results of functional MRI

	MNI	SDM-Z	P	Voxels	Cluster breakdown (number of voxels)
Cluster of hypoactivation (patients<controls)					
Right inferior frontal gyrus, opercular part	46,10,30	-3.221	0.000006437	893	Right inferior frontal gyrus, opercular part (432) Right inferior frontal gyrus, triangular part (152) Right precentral gyrus (98) Right middle frontal gyrus (17)
Right angular gyrus	40,-60,52	-2.719	0.000062704	331	Right angular gyrus (166) Right inferior parietal (excluding supramarginal and angular) gyrus (140)

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Right superior parietal gyrus (25)

Right insula	38,14,-14	-2.439	0.000266016	339	Right insula (197)
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Right inferior frontal gyrus, orbital part (44)

Right temporal pole, superior temporal gyrus (30)

Cluster of hyperactivation (patients>controls)

Left striatum	-28,-2,4	3.273	~0	2761	Left superior temporal gyrus (685)
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Left insula (564)

Left rolandic operculum (335)

Left lenticular nucleus, putamen (296)

Left striatum (189)

Left heschl gyrus (164)

Left postcentral gyrus (69)

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					Left supramarginal gyrus (44)
					Left pons (17)
Right striatum	26,-2,8	1.919	0.000929713	212	Right insula (71)
					Right striatum (48)
					Right lenticular nucleus, putamen (34)
Left inferior occipital gyrus	-34,-76,-12	2.178	0.000299335	168	Left fusiform gyrus (83)
					Left inferior occipital gyrus (42)

(a) Voxel probability threshold: $P=0.005$

(b) Peak height threshold: $z=1$

(c) Cluster extent threshold: 100 voxels. Regions with less than 10 voxels are not reported in the cluster breakdown.

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Table S5

Analyses of subgroups and sensitivity analyses of functional studies

Subgroup analysis	Hyperactivation			Hypoactivation		
	Left striatum	Right striatum	Left inferior occipital gyrus	Right inferior frontal gyrus, opercular part	Right angular gyrus	Right insula
Studies with slice thickness <5 mm at acquisition (n=13)	YES	NO	NO	YES	NO	YES
Studies using ≥ 8 mm smoothing kernel (n=15)	YES	YES	YES	YES	YES	YES
Studies using 1.5T MRI (n=8)	YES	NO	NO	YES	NO	NO
Studies with an additional correction step (n=16)	YES	YES	YES	YES	YES	YES
Studies performing task (n=11)	YES	NO	NO	YES	NO	YES

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Studies of drug-naive patients (n=8)	YES	YES	YES	YES	YES	NO
Jackknife sensitivity analysis, discarded study						
1997Andreason	YES	YES	YES	YES	YES	YES
2010Scheef	YES	YES	YES	YES	YES	YES
2013Ren	YES	NO	NO	YES	NO	YES
2015Guo	YES	YES	YES	YES	YES	YES
2014 Hadley	YES	YES	YES	YES	YES	YES
2003Hofer	YES	YES	YES	YES	YES	YES
2004Jones	YES	YES	YES	YES	YES	YES
2005Weiss	YES	YES	YES	YES	YES	YES
2005Boksman	YES	YES	YES	YES	YES	YES

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2008Scheuerecker	YES	YES	YES	YES	YES	YES
2010Comilo	YES	YES	YES	YES	YES	YES
2011Nejad	YES	YES	YES	YES	YES	YES
2013Bin	YES	YES	YES	YES	YES	YES
2014Schlagenhauf	YES	YES	YES	YES	YES	YES
2015Lesh	YES	YES	YES	YES	YES	YES
2016Zheng	YES	YES	YES	YES	YES	YES
2016Cui (1) ¹	YES	YES	YES	YES	YES	YES
2016Cui (2)	YES	YES	YES	YES	YES	YES

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Table S6

Regions with altered gray matter volume showing significant statistical heterogeneity between studies (voxelwise $p < 0.005$)

Description	MNI coordinate	SDM-Z	P	Voxels
Right insula	38,-16,-2	4.039	~0	1372
Left fusiform gyrus	-36,-60,-16	2.414	0.00026	264

Table S7

Regions with altered regional metabolism showing significant statistical heterogeneity between studies (voxelwise $p < 0.005$)

Description	MNI coordinate	SDM-Z	P	Voxels
Left insula	-36,-6,10	2.209	0.00155	184

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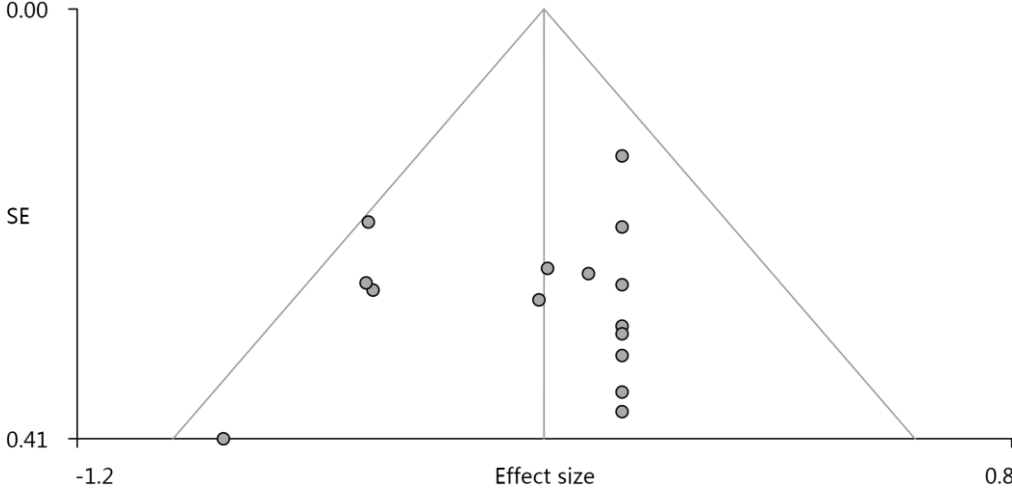
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Table S8

Results of the funnel plots and Eager test

Brain areas	Funnel plots	Eager test
Left fusiform gyrus		T= -0.74, P= 0.473

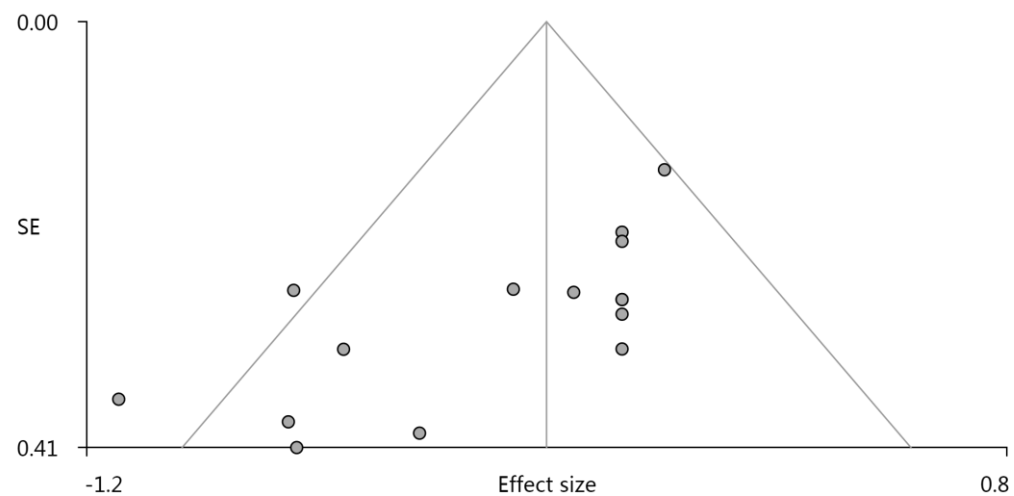
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Left inferior frontal gyrus



T= -3.65, P 0.003

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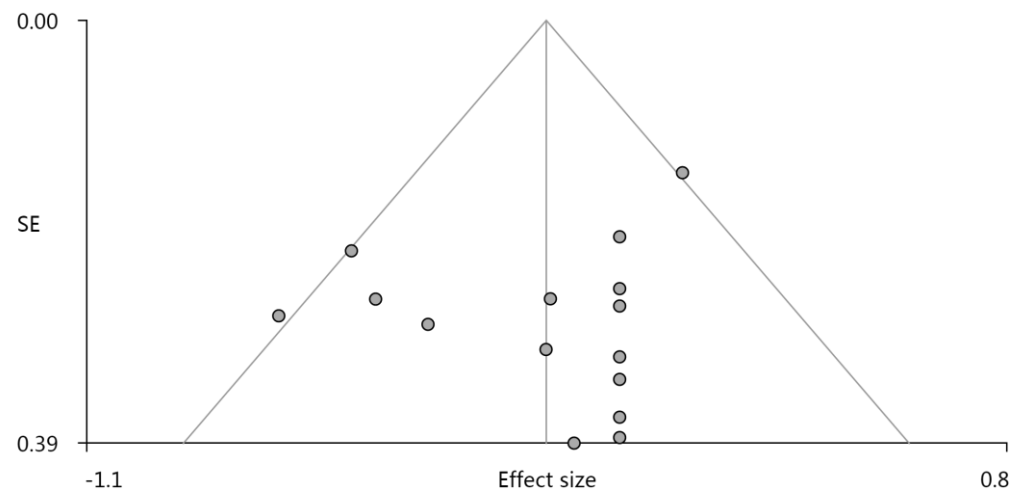
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Right superior temporal

gyrus



T=-0.96, P= 0.355

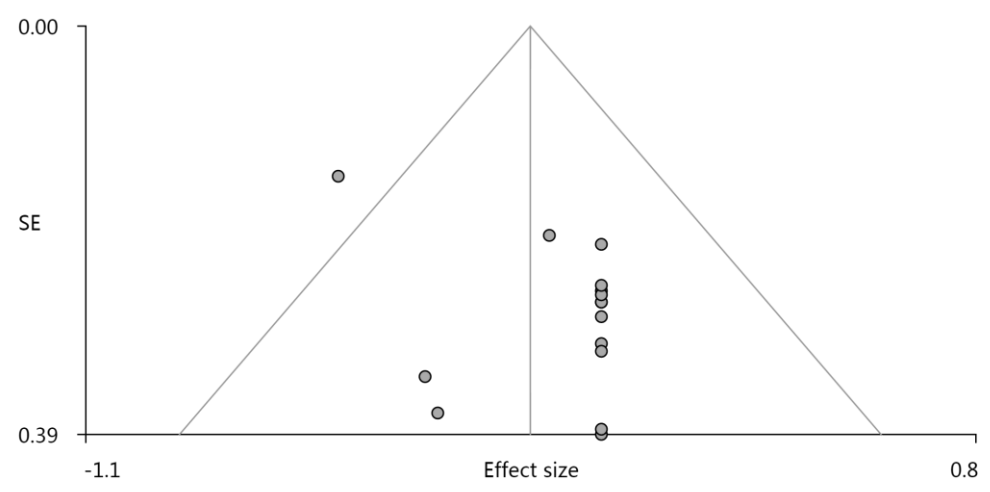
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Left supramarginal gyrus



T= 2.56, P= 0.024

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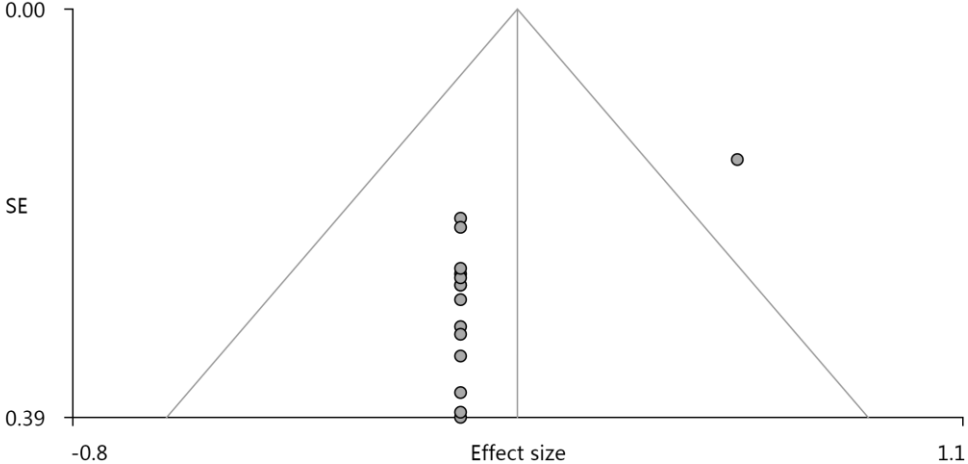
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Right lingual gyrus

T= -3.75, P= 0.002



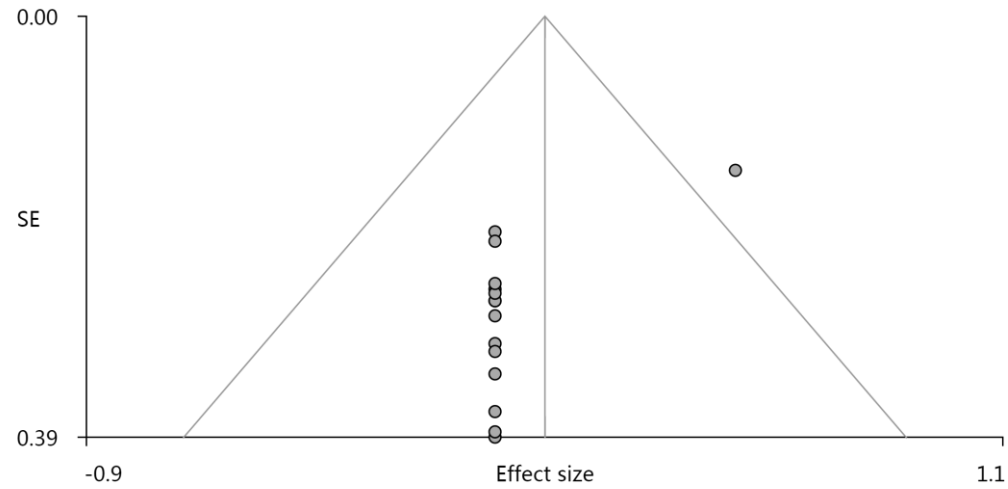
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Right superior frontal
gyrus, orbital part



T= -3.80, P= 0.002

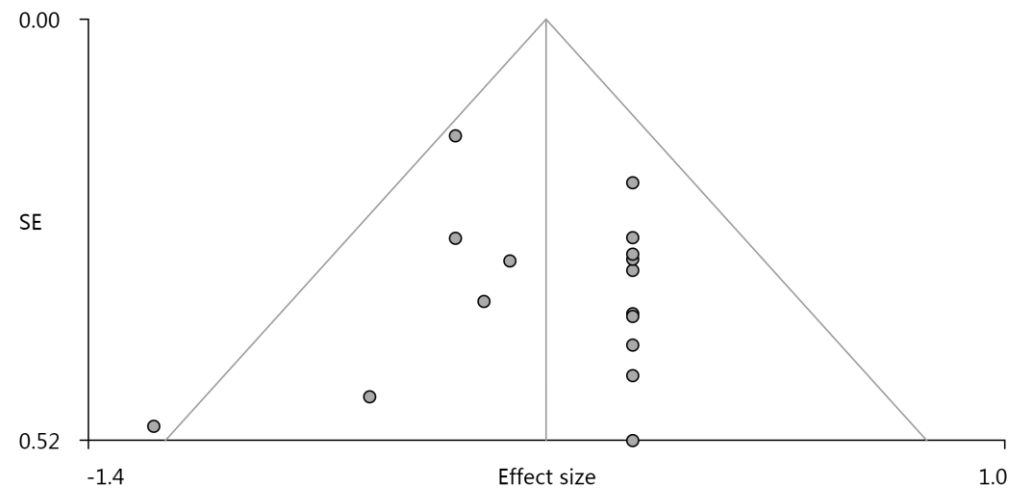
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Right inferior frontal gyrus



T=0.49, P= 0.629

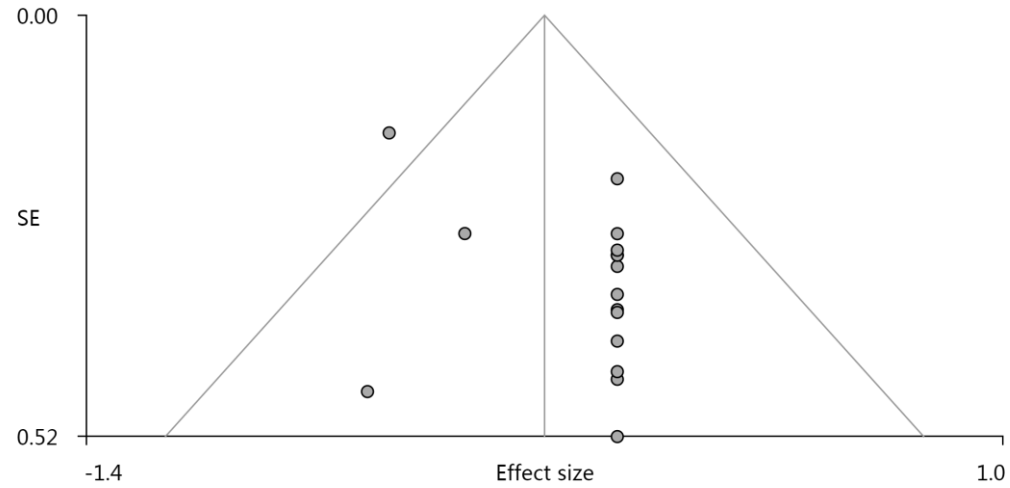
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Right angular gyrus



T= 2.63, P= 0.020

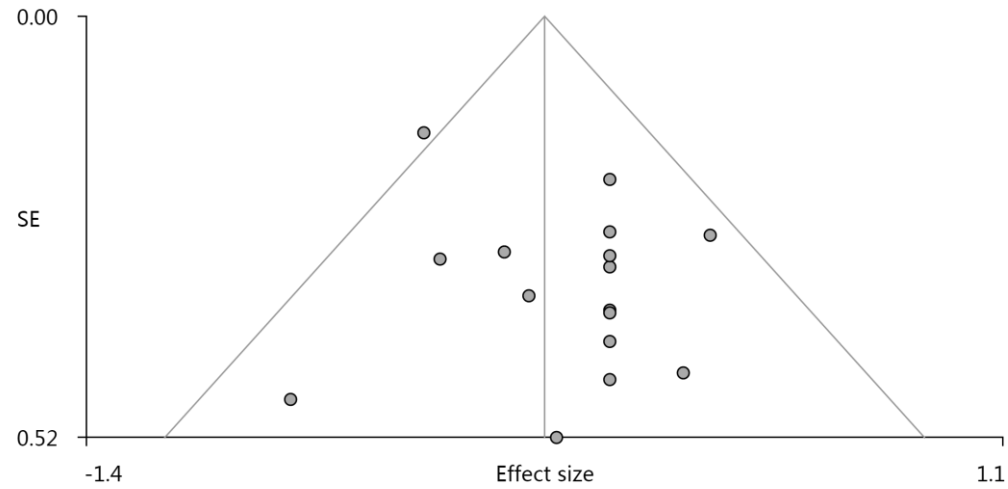
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Right insula



T=1.48, P= 0.161

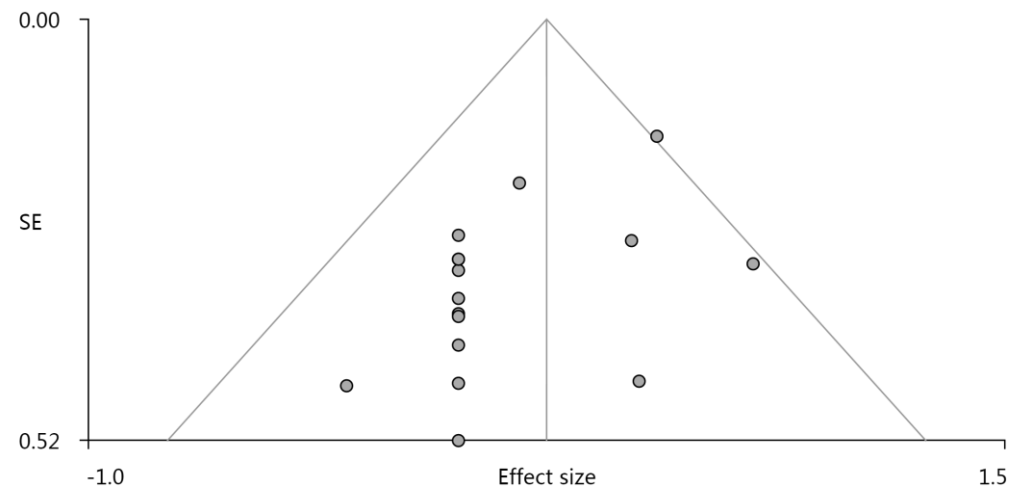
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Left striatum



T=-2.61, P= 0.021

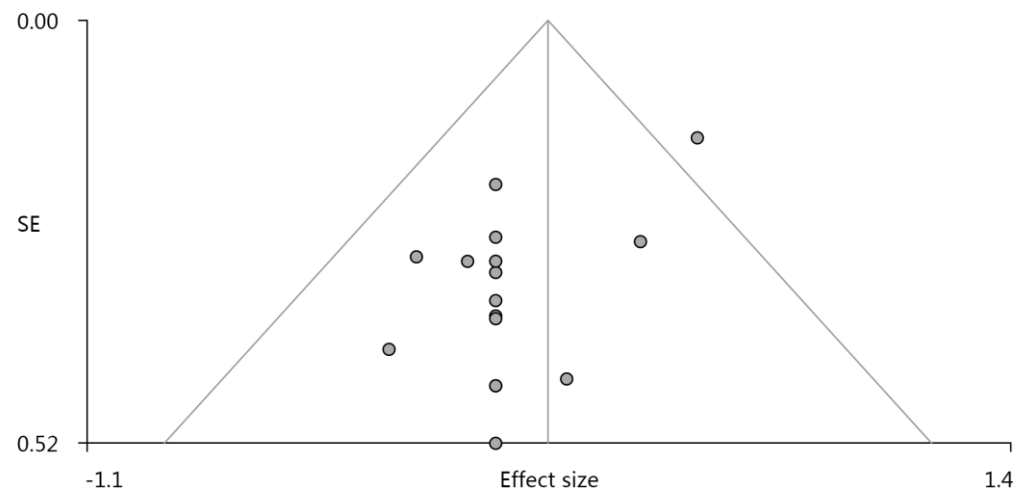
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Right striatum



T= -3.35, P= 0.005

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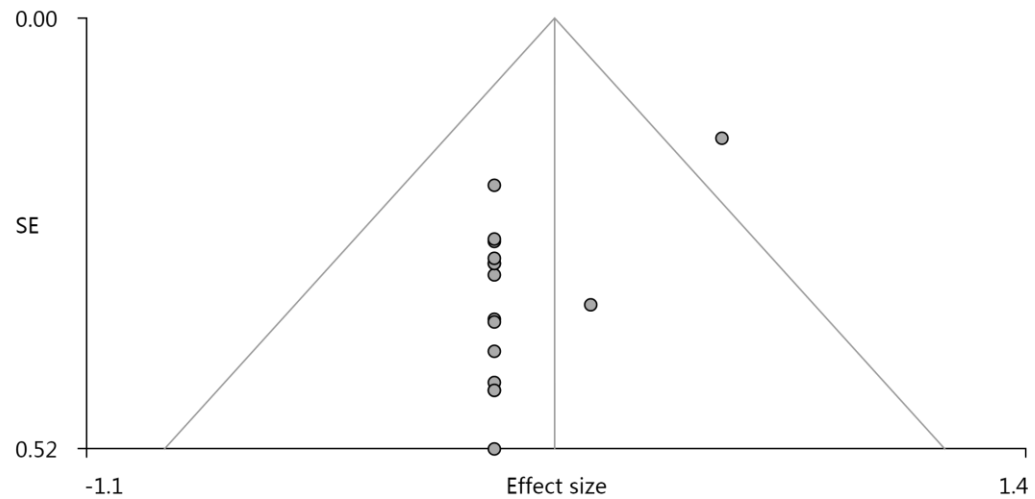
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Left inferior occipital

gyrus



T=-3.61, P= 0.003

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