TECHNICAL COMMENTARY

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Occipital lobe

Introduction

The occipital lobe is located at the posterior section of the brain and primarily comprises the brain's visual cortices. There are two streams of visual information through the visual primary and association cortices, which deal separately with broad object details and motion, and fine detail and colours.

Schizophrenia has been associated with altered structure and function of the occipital cortex. Understanding of any brain alterations in people with schizophrenia may provide insight into changes in brain development associated with the illness onset or progression. Reviews contained in this technical summary reflect structural imaging (MRI, DTI), and functional imaging (fMRI, PET) investigations, as well as metabolic studies (MRS) of the occipital lobe in schizophrenia.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data are prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist, which describes a preferred way to present a meta-analysis[1]. Reviews rated as having less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large, there is a dose dependent response or if results are reasonably consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

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Results

We found 23 systematic reviews that met our inclusion criteria[3-25].

Structural changes

- Moderate to high quality evidence found reductions in occipital grey matter in people with schizophrenia compared to controls. Increased antipsychotic dose was associated with decreases in occipital grey matter over time, and decreases were associated with lower overall functioning.
- Moderate to low quality evidence also found a higher frequency of abnormal (reversed) asymmetry in the occipital lobe of people with schizophrenia.
- White matter tracts were reduced in the bilateral inferior fronto-occipital fasciculus and bilateral optic radiation in people with schizophrenia compared to controls.
- First-degree relatives of people with schizophrenia showed decreased left fusiform gyrus and increased right cuneus compared to controls.
- People at clinical high-risk for psychosis showed increased right fusiform gyrus compared to controls.

Functional changes

- Moderate quality evidence found reduced activation in the left middle occipital gyrus of people with schizophrenia compared to controls during executive functioning tasks. First-degree relatives of people with schizophrenia showed reduced activation during executive functioning in the right lingual gyrus compared to controls.
- Moderate quality evidence found reduced activation in the left middle occipital gyrus and the right inferior occipital gyrus during timing tasks, and increased activation in the occipital cortex during inhibition tasks.
- During memory tasks, there was reduced activation in the right lingual gyrus during episodic memory encoding, and reduced activation in the right cuneus and fusiform gyrus during episodic memory retrieval.
- During emotion tasks, there was reduced activation in bilateral fusiform gyrus during explicit emotion tasks and reduced activation in the right middle occipital gyri during implicit emotion tasks. During threat processing, there was reduced activation in the left fusiform gyrus during explicit threat processing and reduced activation in the fusiform gyrus extending into the cerebellum lobule IV/VI during implicit threat processing. During theory of mind tasks, there was decreased activation in the right lingual gyrus, the medial occipitoparietal, and the left lateral occipitotemporal regions.
- Compared to people with bipolar disorder, moderate quality evidence found people with schizophrenia showed increased activation in bilateral cuneus during facial affect processing.
- Compared to people with an autism spectrum disorder, moderate quality evidence found increased activation in schizophrenia in the right inferior occipital region during face emotion recognition.
- Moderate quality evidence found no difference in NAA or GABA levels between people with schizophrenia and controls.

Structural and functional changes

- Moderate quality evidence found decreased grey matter volume and decreased functional activity in the left fusiform gyrus of drug-free patients. There was also decreased grey matter volume and increased functional activity in the left fusiform gyrus and in the right lingual gyrus.

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Occipital lobe

Achim AM, Lepage M

Episodic memory-related activation in schizophrenia: meta-analysis

British Journal of Psychiatry 2005; 187: 500-509

View review abstract online

Comparison	**Functional activation during episodic memory tasks in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (medium-sized sample, direct, unable to assess precision and consistency) suggests decreased functional activation during memory retrieval tasks in the right fusiform gyrus.**
Occipital functional activity	
11 studies, N = 298 *Reduced activation in people with schizophrenia compared to controls in;* Right fusiform gyrus (medial temporo-occipital gyrus): Talairach coordinates 26, -74, -8, ALE: 0.0054, Voxel probability: 0.000004	
Consistency in results‡	No measure of heterogeneity is provided.
Precision in results§	No confidence intervals are reported.
Directness of results‖	Direct

Alustiza I, Radua J, Pla M, Martin R, Ortuno F

Meta-analysis of functional magnetic resonance imaging studies of timing and cognitive control in schizophrenia and bipolar disorder: Evidence of a primary time deficit

Schizophrenia Research 2017; 188: 21-32

View online review abstract

Comparison	**Functional activity during cognitive control and timing tasks in people with schizophrenia vs. controls.**

Occipital lobe

Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess consistency or precision) finds decreased activation in the left middle occipital gyrus and the right inferior occipital gyrus of people with schizophrenia during timing tasks.**
Occipital functional activity	
8 studies, N = 395 *Significant, decreased activation in people with schizophrenia during timing tasks was found in;* Left middle occipital gyrus (BA 18) Right inferior occipital gyrus (BA 18) There were no differences during cognitive control tasks.	
Consistency in results	Unable to assess; no measure of consistent is reported.
Precision in results	Unable to assess; no measure of precision is reported (CIs).
Directness of results	Direct

Brugger S, Davis JM, Leucht S, Stone JM

Proton magnetic resonance spectroscopy and illness stage in schizophrenia – a systematic review and meta-analysis

Biological Psychiatry 2011; 69: 495-503

View review abstract online

Comparison	**Metabolic N-acetyl aspartate (NAA) levels in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (medium-sized sample, consistent, unable to assess precision, direct) found no difference in NAA levels.**
NAA	
No difference between people with schizophrenia (all patients) and controls; 7 studies, N = 259, d = 0.06 95%CI not reported, p = 0.64, Q = 10.21, p = 0.42, I^2 = 2%	
Consistency in results	Consistent

Precision in results	Unable to assess; no CIs are reported.
Directness of results	Direct

Crossley NA, Mechelli A, Ginestet C, Rubinov M, Bullmore ET, McGuire P

Altered Hub Functioning and Compensatory Activations in the Connectome: A Meta-Analysis of Functional Neuroimaging Studies in Schizophrenia

Schizophrenia Bulletin 2016; 42: 434-42

View review abstract online

Comparison	**Comparison of functional activity in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess consistency or precision) suggests during inhibition tasks, there were over-activations in the occipital cortex.**
Occipital functional activity	
314 studies, N = 10,942 Inhibition tasks Over-activations in the occipital cortex.	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Delvecchio G, Sugranyes G, Frangou S

Evidence of diagnostic specificity in the neural correlates of facial affect processing in bipolar disorder and schizophrenia: a meta-analysis of functional imaging studies

Psychological Medicine 2013; 43(3): 553-69

Occipital lobe

View review abstract online	
Comparison	**Comparison of functional activation during facial affect processing in people with schizophrenia vs. people with bipolar disorder.**
Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess precision or consistency) suggests people with schizophrenia show increased activation in bilateral cuneus than people with bipolar disorder during facial affect processing.**
Occipital functional activity	
29 studies, 1,018 *People with schizophrenia were more likely to activate the cuneus bilaterally;* Left occipital cuneus (BA18): Talairach coordinates -6, -92, 18, cluster volume 1144mm^3 Right occipital cuneus (BA18): Talairach coordinates 10, -88, 20, cluster volume 416mm^3	
Consistency in results	No measure of consistency is reported.
Precision in results	No confidence intervals are reported.
Directness of results	Direct

Ding Y, Ou Y, Pan P, Shan X, Chen J, Liu F, Zhao J, Guo W

Brain structural abnormalities as potential markers for detecting individuals with ultra-high risk for psychosis: A systematic review and meta-analysis

Schizophrenia Research 2019; 209: 22-31

View review abstract online

Comparison	**Grey matter volume in people at clinical high risk of psychosis vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, consistent, direct, unable to assess precision) found increased grey matter volume in the right fusiform gyrus of high-risk individuals.**

Occipital lobe

Grey matter volume	
14 VBM studies, N = 1,331 *Increased grey matter volumes were found in people at high risk in;* Right fusiform gyrus (Z = 1.051)	
Consistency in results	Authors report consistent results.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Dong D, Wang Y, Jia X, Li Y, Chang X, Vandekerckhove M, Luo C, Yao D

Abnormal brain activation during threatening face processing in schizophrenia: A meta-analysis of functional neuroimaging studies

Schizophrenia Research 2018; 197: 200-208

View review abstract online

Comparison	**Functional activity during threatening face processing in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess consistency or precision) suggests during explicit threat processing, there was decreased activity in the left fusiform gyrus, and during implicit threat processing, there was decreased activity in the fusiform gyrus extending into the cerebellum lobule IV/VI.**
Occipital functional activity	
19 studies, N = 728 Explicit threat processing *Decreased activity in;* Left fusiform gyrus: 276 voxels, MNI coordinates -36, -52, -20, $p < 0.001$ Implicit threat processing *Decreased activity in;* Fusiform gyrus extending into cerebellum lobule IV/VI: 2,137 voxels, MNI coordinates 26, 4, 88, $p <$	

0.001	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Egerton A, Modinos G, Ferrera D, McGuire P

Neuroimaging studies of GABA in schizophrenia: a systematic review with meta-analysis

Translational Psychiatry 2017; 7: e1147

View review abstract online

Comparison	**GABA levels in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (medium to large sample, inconsistent, mostly imprecise, direct) finds no differences in GABA levels.**
GABA	
No significant differences between groups; 6 studies, N = 250, *g* = -0.30, 95%CI -0.90 to 0.03, *p* = 0.30, I^2 = 80% There were no moderating effects of diagnosis (first-episode psychosis vs. schizophrenia), age, illness duration, symptom severity, %grey matter or publication date.	
Consistency in results	Inconsistent
Precision in results	Imprecise
Directness of results	Direct

Gao X, Zhang W, Yao L, Xiao Y, Liu L, Liu J, Li S, Tao B, Shah C, Gong Q, Sweeney JA, Lui S

Association between structural and functional brain alterations in drug-

free patients with schizophrenia: A multimodal meta-analysis **Journal of Psychiatry and Neuroscience 2018; 43: 131-42** View review abstract online	
Comparison	**Overlap between regions of functional and structural alteration in drug-free people with first-episode schizophrenia vs. controls.** **Note; most patients were drug naïve.**
Summary of evidence	**Moderate quality evidence (large sample, mostly consistent, direct, unable to assess precision) suggests decreased grey matter volume and decreased functional activity in the left fusiform gyrus of drug-free patients. There was also decreased grey matter volume and increased functional activity in the left fusiform gyrus and the right lingual gyrus.**
Occipital grey matter volume and functional activity	
15 structural MRI studies, N = 971, 16 functional MRI studies, N = 831 *Significant decreased grey matter volume and decreased functional activity in;* Left fusiform gyrus: 1,075 voxels, MNI coordinates (-34, -54, -22), $p < 0.001$ *Significant decreased grey matter volume and increased functional activity in;* Left fusiform gyrus: 307 voxels, MNI coordinates (-36, -68, -12), $p < 0.001$ Right lingual gyrus: 123 voxels, MNI coordinates (18, -70, -12), $p < 0.001$	
Consistency in results	Authors report most findings were consistent.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Goghari MV

Executive functioning-related brain abnormalities associated with the genetic liability for schizophrenia: an activation likelihood estimate meta-analysis

Psychological Medicine 2001; 41: 1239-1252

Occipital lobe

View review abstract online	
Comparison	**Functional activation in relatives of people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess consistency or precision) suggests relatives show reduced activation during executive functioning in the right lingual gyrus.**
Occipital functional activity	
17 studies, N = 456 *Decreased activity in relatives of people with schizophrenia;* Right lingual gyrus: Talairach coordinates 10, -78, -2, cluster volume 216 mm^3	
Consistency in results	No measure of consistency is reported.
Precision in results	No confidence intervals are reported.
Directness of results	Direct

Haijma SV, Van Haren N, Cahn W, Koolschijn PCMP, Hulshoff Pol HE, Kahn RS

Brain volumes in schizophrenia: a meta-analysis in over 18000 subjects

Schizophrenia Bulletin 2012; 39(5): 1129-1138

View review abstract online

Comparison	**Grey matter volume in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, some inconsistency, precise, direct) found reductions in occipital grey matter volume in people with schizophrenia.**
Occipital grey matter volume	
Decreased grey matter volume in people with schizophrenia in; Occipital lobe: 9 studies, N = 700, *d* = -0.22, 95%CI -0.37 to -0.07, *p* = 4.1 × 10−3, Q = 7.6, *p* = 0.47, I^2 = 0% Fusiform gyrus: 10 studies, N = 690, *d* = -0.52, 95%CI -0.76 to -0.29, *p* = 1.2 × 10−5, Q = 19.0, *p* =	

0.0025, I^2 = 53%	
Consistency in results	Consistent for occipital lobe, inconsistent for fusiform gyrus.
Precision in results	Precise
Directness of results	Direct

Huhtaniska S, Jaaskelainen E, Hirvonen N, Remes J, Murray GK, Veijola J, Isohanni M, Miettunen J

Long-term antipsychotic use and brain changes in schizophrenia - a systematic review and meta-analysis

Human Psychopharmacology 2017; 32: doi: 10.1002/hup.2574

View review abstract online

Comparison	**Association between long-term antipsychotic dose and changes in brain volume over time (>2 years) in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (small to medium-sized sample, consistent, precise, direct) suggests increased antipsychotic dose was associated with decreased occipital lobe volume.**
Longitudinal changes in occipital volume	
Small, significant associations between long-term antipsychotic use and decreased occipital lobe; 3 studies, N = 168, *r* = -0.14, 95%CI -0.29 to 0.00, *p* = 0.052, I^2 = 0%	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Kronbichler L, Tschernegg M, Martin AI, Schurz M, Kronbichler M

Occipital lobe

Abnormal Brain Activation During Theory of Mind Tasks in Schizophrenia: A Meta-Analysis

Schizophrenia Bulletin 2017; 43: 1240-50

View review abstract online

Comparison	**Functional activity during theory of mind tasks in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess precision or consistency) suggests decreased activation in the right lingual gyrus, medial occipitoparietal, and left lateral occipitotemporal regions.**
Occipital functional activity	
21 studies, N = 623 *Decreased activation in;* Medial occipitoparietal: 128 voxels, MNI coordinates -4, -76, 14 Right lingual gyrus: 99 voxels, MNI coordinates 12, -58, 2 Left lateral occipitotemporal: 27 voxels, MNI coordinates -48, -72, 22	
Consistency in results	Unable to assess; no measure of heterogeneity is reported.
Precision in results	Unable to assess; no confidence intervals are reported.
Directness of results	Direct

Kyriakopoulos M, Bargiotas T, Barker GJ, Frangou S

Diffusion tensor imaging in schizophrenia

European Psychiatry: the Journal of the Association of European Psychiatrists 2008; 23(4): 255-273

View review abstract online

Comparison	**White matter integrity, assessed by voxel-based analysis, in people with schizophrenia vs. healthy controls**

Occipital lobe

Summary of evidence	**Moderate to low quality evidence (unclear sample size, direct, unable to assess precision and consistency) suggests reduced FA in the occipital lobe.**
Occipital functional activity	
15 studies, N = unclear Occipital lobe illustrated decreased FA in 5 studies between schizophrenia patients and controls.	
Consistency in results	No measure of heterogeneity is reported.
Precision in results	No confidence intervals are reported.
Directness of results	Direct comparison of white matter integrity between schizophrenia patients and controls

Li H, Chan R, McAlonan G, Gong Q-Y

Facial emotion processing in schizophrenia: A meta-analysis of functional neuroimaging data

Schizophrenia Bulletin 2010; 36(5): 1029-1039

View review abstract online

Comparison	**Functional activity during emotion processing tasks in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (medium-sized sample, direct, unable to assess consistency or precision) suggests people with schizophrenia showed decreased activation in bilateral fusiform gyrus during explicit emotion tasks, while implicit emotion tasks were associated with decreases in the right middle occipital gyri.**
Occipital functional activity	
18 studies, N = 228 *Overall decreased activation in people with schizophrenia;* Left fusiform gyrus: Talairach coordinates -38, -66, -13, 19 foci, 1768mm^3, 0.100 ALE	

Right fusiform gyrus: Talairach coordinates 38, -64, -10, 6 foci, 408mm^3, 0.097 ALE Right fusiform gyrus: Talairach coordinates 40, -50, -15, 5 foci, 408mm^3, 0.065 ALE *Decreased activation in people with schizophrenia during an explicit emotional task;* Left fusiform gyrus: Talairach coordinates -39, -65, -13, 18 foci, 1840mm^3, 0.082 ALE Right fusiform gyrus: Talairach coordinates 40, -52, -14, 5 foci, 472mm^3, 0.068 ALE Right fusiform gyrus: Talairach coordinates 38, -64, -10, 5 foci, 432mm^3, 0.097 ALE *Decreased activation in people with schizophrenia during an implicit emotional task;* Right middle occipital gyrus: Talairach coordinates 48, -72, 4, 2 foci, 216mm^3, 0.060 ALE	
Consistency in results	No measure of heterogeneity is reported.
Precision in results	No measure of precision reported
Directness of results	Direct

Minzenberg MJ, Laird AR, Thelen S, Carter CS, Glahn DC

Meta-analysis of 41 functional neuroimaging studies of executive function in schizophrenia

Archives of General Psychiatry 2009; 66(8): 811-822

View review abstract online

Comparison	**Functional activation in people with schizophrenia vs. controls**
Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess consistency or precision) suggests people with schizophrenia showed reduced activity in the left middle occipital gyrus during executive functioning tasks.**
Occipital functional activity	
41 studies, N = 1,217 *Decreased activity in people with schizophrenia in;* Left middle occipital gyrus: Talairach centre of mass -42, -70, 6, cluster volume 416mm^3	
Consistency in results	No measure of heterogeneity is reported.
Precision in results	No confidence intervals are reported.

Directness of results	Direct

Olabi B, Ellison-Wright I, McIntosh AM, Wood SJ, Bullmore E, Lawri, SM

Are There Progressive Brain Changes in Schizophrenia? A Meta-Analysis of Structural Magnetic Resonance Imaging Studies

Biological Psychiatry 2011; 70(1): 88-96

View review abstract online

Comparison	**Occipital grey matter volume changes over time (1-10 years) in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests no changes in grey or white matter over time in people with schizophrenia compared to controls.**
Occipital grey matter volume	
31 studies, N = 1,867 *No significant differences between groups;* Occipital GM: N = 282, 6 studies, *d* = -0.174, 95%CI -0.67 to 0.32, *p* = 0.491, I^2 = 69.9% Occipital WM: N = 227, 4 studies, *d* = -0.327, 95%CI -0.74 to 0.08, *p* = 0.117, I^2 = 45.9%	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Ragland JD, Laird AR, Ranganath C, Blumenfeld RS, Gonzales SM, Glahn DC

Prefrontal activation deficits during episodic memory in schizophrenia

American Journal of Psychiatry 2009; 166(8): 863-874

View review abstract online

Comparison	**Functional activation during episodic memory tasks in people**

	with schizophrenia vs. controls.
Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess precision or consistency) suggests activity during episodic encoding is reduced in the right lingual gyrus and during episodic retrieval it is reduced in the right cuneus of people with schizophrenia.**
Occipital functional activity during episodic encoding	
Significantly decreased activity in people with schizophrenia than controls; Right lingual gyrus: cluster volume 1192mm3, Talairach centre of mass 18, -86, 0	
Occipital functional activity during episodic retrieval	
Significantly decreased activity in people with schizophrenia than controls; Right cuneus: cluster volume 2568mm^3, Talairach centre of mass 16, -86, 10	
Consistency in results	No measure of heterogeneity is reported.
Precision in results	No confidence intervals are reported.
Directness of results	Direct

Sommer I, Aleman A, Ramsey N, Bouma A

Handedness, language lateralisation and anatomical asymmetry in schizophrenia: meta-analysis

British Journal of Psychiatry 2001; 178: 344-351

View review abstract online

Comparison	**Anatomical asymmetry in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to low quality evidence (large sample, inconsistent, imprecise, direct) suggest a higher frequency of abnormal (reversed) asymmetry in the occipital lobe in people with schizophrenia compared to controls.**

Anatomical asymmetry	
Higher frequency of absent or reversed occipital lobe asymmetry in people with schizophrenia; 5 studies, N = 579, weighted difference rate = 0.22, 95%CI 0.12 to 0.28, *p* = 0.01, Q = 87.55, *p* = 0.003	
Consistency in results	Inconsistent
Precision in results	Imprecise
Directness of results	Direct

Sugranyes G, Kyriakopoulos M, Corrigall R, Taylor E, Frangou S

Autism spectrum disorders and schizophrenia: meta-analysis of the neural correlates of social cognition

PLoS ONE 2011; 6(10): e25322

View review abstract online

Comparison	**Functional activation during face emotion recognition in people with schizophrenia vs. autism spectrum disorders.**
Summary of evidence	**Moderate quality evidence (large sample, direct, unable to assess precision or consistency) suggests increased activation in people with schizophrenia in the right inferior occipital region during face emotion recognition.**
Occipital functional activity	
17 studies, N = 511 *The following clusters showed increased activation in schizophrenia vs. autism spectrum disorders;* Right inferior occipital: Talairach coordinates 32, -84, -4, cluster volume 304mm^3	
Consistency in results	No measure of heterogeneity is provided.
Precision in results	No confidence intervals are provided.
Directness of results	Direct

Vitolo E, Tatu MK, Pignolo C, Cauda F, Costa T, Ando A, Zennaro A

White matter and schizophrenia: A meta-analysis of voxel-based morphometry and diffusion tensor imaging studies

Psychiatry Research: Neuroimaging 2017; 270: 8-21

View review abstract online

Comparison	**White matter integrity in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency or precision, direct) found white matter reductions in bilateral inferior fronto-occipital fasciculus and bilateral optic radiation.**
FA	
34 studies, N = 2,231 *There were white matter reductions in patients in;* Left inferior fronto-occipital fasciculus: 22,154 voxels, MNI coordinates (-31, -22, -7), p = 0.000725 Right inferior fronto-occipital fasciculus: 23,185 voxels, MNI coordinates (41, -31, -7), p = 0.001700 Left optic radiation: 7,923 voxels, MNI coordinates -34, -40, -1, p = 0.000797 Right optic radiation: 5,982 voxels, MNI coordinates 29, -19, 5, p = 0.002349 Longer duration of illness was associated with greater white matter reductions in the right inferior fronto-occipital fasciculus. Female patients showed greater reductions in the right inferior fronto-occipital fasciculus and the left optic radiation.	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Wojtalik JA, Smith MJ, Keshavan MS, Eack SM

A Systematic and Meta-analytic Review of Neural Correlates of Functional Outcome in Schizophrenia

Schizophrenia Bulletin 2017; 43: 1329-47

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View review abstract online	
Comparison	**Association between functional outcomes and grey matter volume in people with schizophrenia.** **Functional outcomes include global functioning, social functioning, resource needs, quality of life, socioeconomic status, independent living, employment, and role functioning.**
Summary of evidence	**Moderate quality evidence (unclear sample size, inconsistent, precise, direct) suggests better overall functioning is associated with larger occipital lobe volume.**
Occipital grey matter volume and functional outcome	
Better functioning was associated with larger volume in the occipital lobe; 6 studies, r = 0.30, 95%CI 0.10 to 0.50, p = 0.004, Q = 40.80, p < 0.001	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Xiao Y, Zhang W, Lui S, Yao L, Gong Q

Similar and different gray matter deficits in schizophrenia patients and their unaffected biological relatives

Frontiers in Psychiatry 2013; 4: 150

View review abstract online

Comparison	**Occipital grey matter volume in relatives and people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to low quality evidence (unclear sample size, direct, unable to assess consistency or precision) found decreased right fusiform gyrus and right cuneus in patients compared to controls and decreased left fusiform gyrus and increased right cuneus in relatives compared to controls.**
Occipital grey matter volume	

Occipital lobe

Regions of decreased grey matter volume in patients vs. controls; Right cuneus: Talairach coordinates 22, -98, -2, $p < 0.001$ Right fusiform gyrus: Talairach coordinates 44, -30, -20, $p < 0.0001$ *Regions of decreased grey matter volume in relatives vs. controls;* Left fusiform gyrus: Talairach coordinates -52, -42, -22, $p < 0.001$ *Regions of increased grey matter volume in relatives vs. controls;* Right cuneus: Talairach coordinates 10, -60, 32, $p < 0.001$	
Consistency in results	No measure of consistency is reported.
Precision in results	No measure of precision is reported.
Directness of results	Direct

Explanation of acronyms

ALE = activation likelihood estimate, CI = confidence interval, *d* = Cohen's *d* and *g* = Hedges' *g* = standardised mean differences, DTI = diffusion tensor imaging, FA = fractional anisotropy, fMRI = functional magnetic resonance imaging, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), MNI = Montreal Neurological Institute, N = number of participants, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), PET = positron emission tomography, Q = Q statistic (chi-square) for the test of heterogeneity, vs. = versus

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Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results, publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[26].

† Different effect measures are reported by different reviews.

ALE analysis (Anatomical Likelihood Estimate) refers to a voxel-based meta-analytic technique for structural imaging in which each point of statistically significant structural difference is spatially smoothed into Gaussian distribution space, and summed to create a statistical map estimating the likelihood of difference in each voxel, as determined by the entire set of included studies. Incorporated with the Genome Scan Meta-analysis (GSMA), the meta-analysis of coordinates from multiple studies can be weighted for sample size to create a random effect analysis. The ALE statistic (if reported) represents the probability of a group difference occurring at each voxel included in the analysis.

Fractional similarity network analysis refers to a network analysis technique in which secondary networks are identified within the larger framework of activity, creating a matrix for regional co-activity.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) which allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[26].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[27]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios

measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, *r*) indicate the strength of association or relationship between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An *r* of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent substantial heterogeneity and 75% to 100%: considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, this criteria should be relaxed[28].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C, which allows indirectcomparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available so is inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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