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Introduction

Computed tomography (CT) imaging is a method for visualising the structural organisation of the brain using the attenuation of X-rays to generate image contrast [1, 2]. Tissues in regions of interest are highlighted based on their X-ray absorption properties, as dense tissues attenuate X-rays more than soft tissues, and air attenuates the least. Three-dimensional images are generated from a series of two-dimension X-ray images taken around a single axis of rotation.

Schizophrenia has been associated with structural alterations in many brain regions. Understanding of any neurological structural alterations in patients with schizophrenia using CT may provide insight into brain changes associated with the development or progression of illness. Studies have focused on individual regions but also whole brain investigations to identify differences between patients with schizophrenia and healthy controls.

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. As part of a wider search for all topics included in the library, reviews on CT for schizophrenia 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. The decision to include or exclude reviews was conducted in duplicate by two independent reviewers with any disagreements settled by discussion. All quality assessments and data extraction have been completed in duplicate by two reviewers who were not masked to review authors.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (formerly the QUOROM statement) which describes a preferred way to present a meta-analysis [3]. Reviews were assigned a low, medium or high possibility of reporting bias* depending on how many items were checked. For instance, a low possibility of bias would be assigned to reviews checking over 66% of items, a medium possibility between 33 and 66% and a high possibility would be given to reviews checking less than 33%. Reviews rated as having a high possibility of reporting bias 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 randomized controlled trials (RCT) may be downgraded to moderate, low or very 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
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low associated risks (see end of table for an explanation of these terms)[4]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of the Schizophrenia Research Institute.

Results

See table below for a detailed summary of the available evidence pertaining to CT. We found two systematic reviews that met our inclusion criteria [1, 2]. One review was excluded for having a high probability of reporting bias [5].

See PRISMA checklist for review quality assessments.

Conclusions

• Moderate quality evidence suggests reduced temporal lobe volume in patients with schizophrenia

• Low to moderate quality evidence is unclear as to the utility of structural imaging as a means of identifying individual structural abnormalities in patients following a first episode of psychosis
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*Goulet K, Deschamps B, Evoy F, Trudel JF.*

**Use of brain imaging (computed tomography and magnetic resonance imaging) in first-episode psychosis: review and retrospective study.**

*Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie 2009; 54(7):493-501*

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| Comparison                                                                 | Classification of structural imaging scans in patients following a first episode of psychosis, into four groups based on the degree of structural abnormality observed: normal; abnormal with no clinical impact; abnormal with impact on management but unlikely to cause psychosis; abnormal with possible causal link to psychotic symptoms  
| Note – not all studies were controlled |
| Summary of evidence                                         | Low to moderate quality evidence (large sample size, indirect, unable to fully assess precision or consistency) is unclear as to the usefulness of structural imaging as a means of identifying individual structural abnormalities in patients following a first episode of psychosis |
| Individual structural abnormalities                                  | 384 CT scans from five studies were collated in total  
| No meta-analysis                                                  | 78 (20.8%) of these were rated as benign abnormalities with no clinical impact  
| 4 (1%) of these were rated as unlikely to have causal links to psychosis  
| 5 (1.3%) of these were rated as abnormal with possible causal links to psychotic symptoms including possible infarcts of caudate nucleus and parietal cortex; ischemic changes; and colloid and arachnoid cysts. |
| Consistency in results                                      | No measure of consistency reported, although results appear inconsistent |
| Precision in results                                          | No measure of precision reported |
| Directness of results                                          | Indirect assessment of structural abnormality in psychosis |
**Zakzanis, K.K., Poulin, P., Hansen K.T., Jolic D.**

**Searching the schizophrenic brain for temporal lobe deficits: a systematic review and meta-analysis**

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<table>
<thead>
<tr>
<th>Comparison</th>
<th>Temporal lobe volume in patients with schizophrenia vs. healthy controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Summary of evidence</strong></td>
<td>Moderate quality evidence (moderate sample size, direct, unable to assess precision and consistency) suggests a temporal lobe volume deficit in schizophrenia, however the average magnitude of this deficit is not sufficient to attribute any causative role in schizophrenia aetiology</td>
</tr>
</tbody>
</table>

**Bilateral whole temporal lobe volume**

**Meta-analysis results reported at baseline**  
Small effect size suggesting decreased temporal lobe volume in patients with schizophrenia  
2 observational studies, N unclear  
\[d = 0.49, \text{SD} = 0.55\]

**Laterality of temporal lobe volume**

**Left temporal lobe**  
Small effect size suggesting decreased left temporal lobe volume in patients with schizophrenia  
3 observational studies, N = 80  
\[d = 0.30, \text{SD} = 0.21\]

**Right temporal lobe**  
Small effect size suggesting decreased right temporal lobe volume in patients with schizophrenia  
3 observational studies, N = 80  
\[d = 0.26, \text{SD} = 0.14\]
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<table>
<thead>
<tr>
<th>Risks</th>
<th>Not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consistency in results</td>
<td>No measure of heterogeneity provided</td>
</tr>
<tr>
<td>Precision in results</td>
<td>No confidence intervals provided</td>
</tr>
<tr>
<td>Directness of results</td>
<td>Direct</td>
</tr>
</tbody>
</table>

Explanation of acronyms

CI = Confidence Interval, CT = computed tomography, $d = \text{Cohen's } d$ and $g = \text{Hedges' } g = \text{standardized mean differences}$ (see below for interpretation of effect sizes), $F = \text{ratio of between sample variance and within sample variance}$, $N = \text{number of participants}$, $p = \text{statistical probability of obtaining that result } (p < 0.05 \text{ generally regarded as significant})$, $SD = \text{standard deviation}$
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 which 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[6].

† Different effect measures are reported by different reviews.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomized trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardized 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. 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 and over represents a large effect[6].

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives which are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives which are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

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 large effect is considered if RR > 2 or < 0.5 and a very large effect if RR > 5 or < 0.2[7]. 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 unforeseen 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. Unstandardized (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. Standardized regression coefficients represent the change
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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 which are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives which are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively, some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) which is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I² 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. I² 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[7].

¶ 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 indirect comparisons 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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Many thanks to Dr Melissa Green for reviewing this summary of evidence.

School of Psychiatry, University of New South Wales; Black Dog Institute, Prince of Wales Hospital, Sydney
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References