

Arcuate fasciculus

Introduction

The arcuate fasciculus is a bundle of axons that connects the temporal cortex and inferior parietal cortex to locations in the frontal lobe. One of the key roles of the arcuate fasciculus is connecting Broca's and Wernicke's areas, which are involved in producing and understanding language. Therefore, there may be anomalies in the arcuate fasciculus of people with schizophrenia who experience auditory-verbal hallucinations.

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-analysis¹. 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).

Results

We found two systematic reviews that met our inclusion criteria^{3, 4}.

- Moderate quality evidence found reduced white matter integrity in the bilateral arcuate fasciculus, including bilateral anterior and posterior segments, and the left long segment.
- Moderate quality evidence found reduced white matter integrity in the left, but not the right arcuate fasciculus in people with schizophrenia who experience auditory-verbal hallucinations.

Geoffroy PA, Houenou J, Duhamel A, Amad A, De Weijer AD, Curcic-Blake B, Linden DEJ, Thomas P, Jardri R.

The arcuate fasciculus in auditory-verbal hallucinations: A meta-analysis of diffusion-tensor-imaging studies

Schizophrenia Research 2014; 159(1): 234-7

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Comparison	The relationship between white-matter integrity and auditory-verbal hallucinations in people with schizophrenia vs. controls.
Summary of evidence	Moderate quality evidence (medium-sized sample, direct, precise, inconsistent) suggests decreased white matter integrity in the left, but not the right arcuate fasciculus in people with schizophrenia who are experiencing auditory hallucinations.
White matter integrity	
<i>There was reduced fractional anisotropy in the left arcuate fasciculus of people with hallucinations;</i> 5 studies, N = 256, $g = -0.42$, 95%CI -0.69 to -0.16, $p < 0.10^{-3}$, $I^2 = 58\%$ <i>There was no difference in the right arcuate fasciculus;</i> 5 studies, N = 256, $g = -0.19$, 95%CI -0.47 to 0.09, $p = 0.18$, $I^2 = 75\%$	
Consistency in results	Inconsistent
Precision in results	Precise
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.
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Arcuate fasciculus

Summary of evidence	Moderate quality evidence (large sample, unable to assess consistency or precision, direct) found white matter reductions in bilateral arcuate fasciculus, including bilateral anterior and posterior segments, and the left long segment.
White matter integrity	
34 studies, N = 2,231 <i>There were white matter reductions in;</i> Left arcuate fasciculus: 24,480 voxels, MNI coordinates (-34, -40, -1), $p = 0.000112$ Right arcuate fasciculus: 23,307 voxels, MNI coordinates (44, -38, -1), $p = 0.000258$ Left anterior segment of arcuate fasciculus: 5,391 voxels, MNI coordinates (-51, -7, 15), $p = 0.000036$ Right anterior segment of arcuate fasciculus: 8,780 voxels, MNI coordinates (50, -10, 29), $p = 0.000378$ Left posterior segment of arcuate fasciculus: 11,088 voxels, MNI coordinates (-34, -40, -1), $p = 0.000313$ Right posterior segment of arcuate fasciculus: 12,107 voxels, MNI coordinates (41, -34, -4), $p = 0.001262$ Left long segment of arcuate fasciculus: 7,639 voxels, MNI coordinates (-34, -40, -1), $p = 0.000218$ A higher percentage of male patients showed reduced white matter traits in the right posterior segment of arcuate fasciculus, while female patients showed reduced white matter traits in the left long segment of the arcuate fasciculus.	
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

Explanation of acronyms

CI = confidence interval, g = Hedges' g = standardised mean differences, 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, vs. = versus)

Arcuate fasciculus

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 small⁵.

† 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 effect⁵.

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 ⁶. InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios

Arcuate fasciculus

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. 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 relaxed⁷.

|| 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.



Arcuate fasciculus

References

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