TECHNICAL COMMENTARY

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Disorganised symptoms

Introduction

Key features of the symptoms of disorganisation include disorganised speech and behaviour, as well as inappropriate affect. Severely disorganised speech is difficult to follow, being incoherent, irrelevant and/or illogical. These symptoms are sometimes called positive formal thought disorder. Disorganised speech may also be deprived of content, which is sometimes called negative formal thought disorder. Disorganised behaviour includes bizarre or inappropriate behaviour, actions or gestures. Inappropriate (incongruous) affect involves exhibiting incorrect emotional responses for a given context.

Symptoms of disorganisation have been identified as risk factors for poor illness outcome, and have a significant negative effect on a person's day-to-day functioning and quality of life. There is evidence to suggest that disorganisation symptoms may be associated with impaired cognitive performance.

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 given priority for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews with 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 to 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 four systematic reviews that met our inclusion criteria[3-6].

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- Moderate to high quality evidence suggests small to medium-sized associations between positive and negative formal thought disorder and poor cognition in the areas of memory, attention, processing speed, planning, semantic processing and social cognition. Positive formal thought disorder was particularly associated with poor inhibition and syntactic comprehension, while negative formal thought disorder was particularly associated with poor fluency.
- Moderate to high quality evidence suggests a small to medium-sized effect of more formal thought disorder symptoms in people with schizophrenia than in people with bipolar disorder. This effect is significant only in non-acute, stable patients.
- High quality evidence shows significant concordance of disorganisation symptoms in siblings with schizophrenia. Low quality evidence suggests unclear concordance in twins.

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Bora E, Yalincetin B, Akdede BB, Alptekin K

Neurocognitive and linguistic correlates of positive and negative formal thought disorder: A meta-analysis

Schizophrenia Research 2019; 209: 2-11

View review abstract online

Comparison	**The association between formal thought disorder and neurocognitive function in people with schizophrenia.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) suggests small to medium-sized associations between positive and negative formal thought disorder and poor cognition in the areas of memory, attention, processing speed, planning, and semantic processing. Positive formal thought disorder was particularly associated with poor inhibition and syntactic comprehension, while negative formal thought disorder was particularly associated with poor fluency.**

Cognition

Positive and negative formal thought disorder was associated with poorer overall cognition;

Positive: 36 studies, N = 1,813, r = -0.21, 95%CI -0.14 to -0.27, I^2 = 43%

Negative: 22 studies, N = 1,573, r = -0.24, 95%CI -0.18 to -0.30, I^2 = 17%

Both positive and negative formal thought disorder were significantly associated with verbal memory, visual memory, working memory, attention, processing speed, planning, and semantic processing.

Positive formal thought disorder was specifically associated with inhibition and syntactic comprehension.

Negative formal thought disorder was specifically associated with fluency.

Consistency in results‡	Consistent
Precision in results§	Precise
Directness of results‖	Direct

de Sousa P, Sellwood W, Griffiths M, Bentall RP

Disorganisation, thought disorder and socio-cognitive functioning in schizophrenia spectrum disorders

British Journal of Psychiatry 2019; 214: 103-12

View review abstract online

Comparison	**The association between formal thought disorder and social cognition in people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests a medium-sized association between formal thought disorder and poor social cognition. More recent studies and studies of inpatients showed the largest effect sizes.**

Social cognition

Formal thought disorder was associated with poorer social cognition;

123 studies, N = 9,107, r = −0.313, 95%CI -0.346 to -0.279, $p < 0.001$, I^2 = 60%

Subgroup analyses found medium-sized associations with theory of mind and emotion recognition, and smaller associations with social perception, emotion regulation, and attributional biases.

Studies of inpatients reported larger associations than studies of outpatients.

More recent studies reported larger associations than older studies.

There was no effect of patient age or specific thought disorder symptoms.

Consistency in results‡	Inconsistent
Precision in results§	Precise
Directness of results‖	Direct

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Rietkerk T, Boks MPM, Sommer IE, Liddle PF, Ophoff RA, Kahn RS

The genetics and symptom dimensions of schizophrenia: review and meta-analysis

Schizophrenia Research 2008; 102: 197-205

View review abstract online

Comparison	**The heritability of disorganisation symptoms assessed through the concordance of symptoms in twins and siblings with schizophrenia.** **Note: disorganisation symptoms included formal thought disorder, inappropriate affect and bizarre behaviour.**
Summary of evidence	**High quality evidence (large sample, consistent, precise, direct) suggests a small effect of concordance of disorganised symptoms in siblings with schizophrenia. Low quality evidence (1 small study) is uncertain of the concordance in twins.**
Symptom heritability, measured by OPCRIT	
A small, significant effect suggests concordance of disorganised symptoms in siblings with schizophrenia; 4 studies, N = 753, r = 0.28, 95%CI 0.21 to 0.34, $p < 0.0001$, I^2 Q < 0.001, p = 0.48 1 study of twins concordant for schizophrenia (N = 57 pairs) suggested heritability is significantly associated with disorganisation symptoms in monozygotic twins (r = 0.63, $p < 0.005$) compared to dizygotic twins (r = 0.24).	
Consistency in results‡	Consistent for siblings
Precision in results§	Precise for siblings
Directness of results‖	Direct

Yalincetin B, Bora E, Binbay T, Ulas H, Akdede BB, Alptekin K

Formal thought disorder in schizophrenia and bipolar disorder: A systematic review and meta-analysis

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Schizophrenia Research 2017 185: 2-8 View review abstract online	
Comparison	**Formal thought disorder in people with schizophrenia vs. people with bipolar disorder.**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests a small to medium-sized effect of more formal thought disorder symptoms in people with schizophrenia compared to people with bipolar disorder. This effect was significant only in non-acute patients.**
Formal thought disorder **Thought, Language, and Communication Disorders scale and the Thought Disorder Index**	
Small to medium-sized effect of more formal thought disorder symptoms in people with schizophrenia; 19 studies, N = 1,189, *d* = 0.30, 95%CI 0.07 to 0.53, *p* < 0.001, I^2 = 70.7% Subgroup analysis showed larger effects for both positive and negative disorganisation symptoms when the analysis contained only stable, non-acute patients. There were no significant differences in thought disorder symptoms in acute inpatients.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, *d* = Cohen's d, standardised mean difference, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, OPCRIT = Operational Criteria checklist for psychotic disorders, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), *r* = correlation coefficient, 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; 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[7].

† Different effect measures are reported by different reviews.

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.

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) that 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 medium effect, and 0.8 and over represents a large effect[7].

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[8]. 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.

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

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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.

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 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 be considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[7];

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

§ 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, these criteria should be relaxed[9].

‖ 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 that 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 and is therefore 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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