TECHNICAL COMMENTARY

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Family relationships

Introduction

Several familial traits have been associated with increased risk for schizophrenia. These include; familial high expressed emotion (hostility, emotional over-involvement, and critical comments); negative parental affective style (guilt induction, over-intrusiveness, and personal criticism); and communication deviance (lack of clarity in communication).

Method

We have included only systematic reviews with detailed literature search, methodology, and inclusion/exclusion criteria that were published in full text, in English, from the year 2000. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Reviews with pooled data are prioritized for inclusion. Reviews reporting fewer than 50% of items on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA[1]) checklist have been excluded from the library. The evidence was graded guided by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach[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 three reviews that met inclusion criteria[3-5].

- Moderate quality evidence suggests medium to large associations of poor relationships with parents in childhood, family instability, high communication deviance, and negative affective style for increased risk for schizophrenia.
- Moderate to high quality evidence suggests increased familial expressed emotion was related to more relapses in patients.

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Laurens KR, Luo L, Matheson SL, Carr VJ, Raudino A, Harris F, Green MJ

Common or distinct pathways to psychosis? A systematic review of evidence from prospective studies for developmental risk factors and antecedents of the schizophrenia spectrum disorders and affective psychoses

BMC Psychiatry 2015; 15: 205.DOI 10.1186/s12888-015-0562-2

View review abstract online

Comparison	**Childhood family relationship factors in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (small to medium-sized samples, appears consistent, imprecise, direct) suggests medium to large associations of poor relationships with parents in childhood, family instability, high communication deviance, and negative affective style for increased risk for schizophrenia.**

Family relationship factors

2 prospective studies (N = 193 and N = 85) reported significant, medium to large-sized effects of increased risk of schizophrenia with unsatisfactory or poor relationships with a parent during childhood, and a reduced risk of schizophrenia for good relationships with a parent.

Unsatisfactory relationship with mother: OR = 5.56, 95%CI 2.17 to 14.22, $p < 0.01$

Unsatisfactory relationship with father: OR = 5.88, 95%CI 2.29 to 15.07, $p < 0.01$

Poor parental relationship: OR = 4.31, 95%CI 1.51 to 12.32, $p < 0.05$

Good parental relationship: OR = 0.25, 95%CI 0.08 to 0.82, $p < 0.05$

1 prospective study (N = 678) reported a significant, medium-sized effect of increased risk of schizophrenia with atypical mother-child interactions during childhood (adjusted for sex and SES).

Atypical mother-child interactions: OR = 2.65, 95%CI 1.20 to 5.60, $p < 0.05$

1 prospective study (N = 103) reported a significant, medium-sized effect of increased risk of schizophrenia with more family instability or paternal conflict during childhood, but no significant association with maternal conflict.

Family instability: OR = 2.36, 95%CI 1.10 to 5.09, $p < 0.05$

Paternal conflict: OR = 2.41, 95%CI 1.12 to 5.20, $p < 0.05$

Maternal conflict: OR = 1.74, 95%CI 0.81 to 3.72, $p > 0.05$

1 prospective study (N = 51) reported a significant, medium-sized effect of increased risk of schizophrenia with parental high communication deviance during childhood, and no significant

differences with parental low communication deviance. High communication deviance: OR = 4.18, 95%CI 1.20 to 14.59, $p < 0.05$ Low communication deviance: OR = 0.15, 95%CI 0.02 to 1.25, $p > 0.05$ *1 prospective study (N = 52) reported a significant, large effect of increased risk of schizophrenia with negative parental affective style during childhood, and reduced risk of schizophrenia with benign parental affective style.* Negative affective style: OR = 14.02, 95%CI 3.18 to 61.82, $p < 0.01$ Benign (non-negative) affective style: OR = 0.05, 95%CI 0.01 to 0.38, $p < 0.01$

Consistency in results	Appears consistent.
Precision in results	Imprecise
Directness of results	Direct

O'Driscoll C, Sener SB, Angmark A, Shaikh M

Caregiving processes and expressed emotion in psychosis, a cross-cultural, meta-analytic review

Schizophrenia Research 2019; 208: 8-15

View review abstract online

Comparison	**Expressed emotion in families of people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large sample, consistent, imprecise, direct) suggests increased familial expressed emotion was related to more relapses in patients.**

Relapse

A small to medium-sized effect of more relapses in patients with high familial expressed emotion;

34 studies, N = 1,982, RR = 1.95, 95%CI 1.65 to 2.30, $p < 0.05$, $I^2 = 20\%$, $p = 0.1$

Relapse indicated by case record or assessed by a clinician showed fewer relapses than other methods of relapse assessment. There were no moderating effects of region, year of publication, study design, or study quality.

Consistency in results	Consistent
Precision in results	Imprecise

Directness of results	Direct

Roisko R, Wahlberg K, Miettunen J, Tienari P

Association of parental Communication Deviance with offspring's psychiatric and thought disorders. A systematic review and meta-analysis

European Psychiatry 2014; 29: 20-31

View review abstract online

Comparison	**Association of parental communication deviance with schizophrenia spectrum disorders in the offspring vs. controls.**
Summary of evidence	**Moderate quality evidence (large sample, inconsistent, imprecise, direct) suggests increased parental communication deviance in parents of people with schizophrenia spectrum disorders.**
Communication deviance scores	
A large, significant effect of more communication deviance scores in parents of people with schizophrenia; 7 studies, N ~ 1,139, *d* = 0.71, 95%CI 0.21 to 1.37, *p* = 0.007, I^2 = 89.5%, *p* < 0.001	
Consistency in results	Inconsistent
Precision in results	Imprecise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, *d* = Cohen's *d* and *g* = Hedges' *g* = standardised mean differences (see below for interpretation of effect size), I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, *p* = statistical probability of obtaining that result (*p* < 0.05 generally regarded as significant), RR = risk ratio, SES = socio-economic status, vs. = versus

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[6].

† Different effect measures are reported by different reviews.

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.

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).

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. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[6].

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[7]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios

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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 can provide an indirect 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.

‡ 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 represent 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[6];

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

§ 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[8].

‖ 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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