TECHNICAL COMMENTARY

Speech and hearing deficits

Introduction

Subtle deviations in various developmental trajectories during childhood and adolescence may foreshadow the later development of schizophrenia. Studies exploring these deviations (antecedents) are ideally based on representative, population-based samples that follow the cohort from birth through childhood and adolescence to adulthood. These studies can provide unique insights into the changes in developmental trajectories that may be associated with later development of 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 and related disorders. 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 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 four systematic reviews that met our inclusion criteria[3-6].

- Moderate to high quality evidence suggests medium to large effects of early language dysfunction in children who later developed schizophrenia. These include abnormal speech, delays in talking, poor quality of expressive and receptive language, and poor oral and reading ability in school. A small effect was found for poor word association ability.

- Moderate to low quality evidence suggests a medium to large increased risk of childhood speech and hearing impairment in people with schizophrenia.

SCHIZOPHRENIA LIBRARY

Harper S, Towers-Evans H, MacCabe J

The aetiology of schizophrenia: what have the Swedish Medical Registers taught us?

Social Psychiatry and Psychiatric Epidemiology 2015; 50: 1471-1479

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Comparison	Childhood speech and hearing problems in Swedish people with schizophrenia vs. Swedish people without schizophrenia.
Summary of evidence	Moderate to low quality evidence (small to medium-sized sample, imprecise, direct) suggests childhood speech and hearing problems in people with schizophrenia.

Childhood hearing problems
A large, significant effect of increased hearing impairment in childhood in adults with schizophrenia; 1 study, N = 233, OR = 6.0, 95%CI 1.6 to 23.2, *p* < 0.05

Childhood speech problems
A medium, significant effect of increased speech impairment in childhood in adults with schizophrenia; 1 study, N = 233, OR = 2.6, 95%CI 1.4 to 4.9, *p* < 0.05

Consistency in results‡	Not applicable (one study per outcome)
Precision in results§	Imprecise
Directness of results‖	Direct

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

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BMC Psychiatry 2015; 15: 205. DOI 10.1186/s12888-015-0562-2 View review abstract online	
Comparison	**Childhood speech and language problems in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, appears consistent, imprecise, direct) suggests a medium to large effect of early language dysfunctions in children who later developed schizophrenia. These include abnormal speech, and poor expressive and receptive language ability. A small effect was reported for poor word association ability.**
**Childhood speech and language problems**

1 prospective study (N = 12,204) reported a medium sized effect of more speech problems in childhood in adults with schizophrenia;

OR = 3.89, 95%CI 1.34 to 11.32, *p* < 0.05

1 prospective study (N = 2,068) reported a large effect of increased rates of abnormal speech, and a small effect of poor expressive language and word association ability in childhood (adjusted for the effects of race, sex, parental education level, parental socioeconomic status, and age at time of examination);

Abnormal speech; OR = 12.70, 95%CI 2.46 to 65.66, *p* < 0.05

Expressive language and word association: OR = 0.71, 95%CI 0.57 to 0.89, *p* < 0.05

1 prospective study (N = 2,808) reported a medium sized effect of increased rates of a developmental language disorder in childhood;

OR = 3.55, 95%CI 1.93 to 6.54, *p* < 0.01

1 prospective study (N = 678) reported a large effect of poor receptive language and a medium sized effect of poor expressive language in childhood;

Receptive language: OR = 14.01, 95%CI 7.50 to 26.17, *p* < 0.01

Expressive language: OR = 2.08, 95%CI 1.13 to 3.83, *p* < 0.05

1 prospective study (N = 4,746) reported no differences in non-structural speech;

OR = 2.2, 95%CI 0.7 to 7.3, *p* > 0.05

1 prospective study (N = 207) reported no differences in verbal associative ability;

OR = 0.73, 95%CI 0.30 to 1.80, *p* > 0.05

Consistency in results	Appears consistent
Precision in results	Imprecise, apart from expressive language and word association test.

Directness of results	Direct

Linszen MMJ, Brouwer RM, Heringa SM, Sommer IE

Increased risk of psychosis in patients with hearing impairment: Review and meta-analyses

Neuroscience and Biobehavioral Reviews 2016; 62: 1-20

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Comparison	Childhood hearing impairment in schizophrenia vs. controls.
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, imprecise, direct) suggests a small to medium-sized increased odds of childhood hearing impairment in adults with schizophrenia, however this effect was not significant after adjusting for publication bias.**

Childhood hearing impairment
A medium-sized, significant effect of increased hearing impairment in childhood in adults with schizophrenia; Schizophrenia: N = 50,490, OR = 3.15, 95%CI 1.25 to 7.95, $p < 0.05$, I^2 = 54% Not significant after adjusting for publication bias: OR = 1.81, 95%CI 0.78 to 4.18, $p > 0.05$

Consistency in results	Inconsistent
Precision in results	Imprecise
Directness of results	Direct

Welham J, Isohanni M, Jones P, McGrath J

The Antecedents of Schizophrenia: A Review of Birth Cohort Studies

Schizophrenia Bulletin 2009; 35(3): 603-623

View review abstract online

Speech and hearing deficits

Comparison	Childhood speech and language in schizophrenia vs. controls.
Summary of evidence	Moderate to high quality evidence (large samples, appears consistent, imprecise, direct) suggests a medium to large effect of early speech and language dysfunctions in children who later developed schizophrenia. These include delay in talking, poor quality of expressive and receptive language and poor oral and reading ability in school.

Childhood speech and language problems
1 British cohort (N = 4,746) reported speech delay at age 2 and from age 6 to age 15 children who later developed schizophrenia had more speech problems than controls (measured by physician);
OR = 2.8, 95%CI 0.9 to 7.8, p = 0.04
1 British cohort (N = 12,537) reported teacher rated speech and reading as poor at age 7, however parent rated speech acquisition and quality was rated as normal at age 7;
No statistics reported.
1 U.S. cohort (N = 8,013) reported abnormal speech at age 7 (measured by speech pathologist);
OR = 12.7, 95%CI 2.46 to 65.66
The same cohort reported decreased language performance at age 7 (measured by Auditory-Vocal Association Test);
OR = 0.71, 95%CI 0.57 to 0.89
1 New Zealand cohort (N = 972) reported that at ages 3, 5, 7 and 9 receptive (not expressive) language was poorer than controls (measured on Reynell Developmental Language Scales);
SDs between 0.2 and 0.6 – no OR, CIs or p-values reported

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

Explanation of acronyms

CI = Confidence Interval, N = number of participants, OR = odds ratio, p = probability of obtaining that result (p < 0.05 generally regarded as significant), SD = standard deviation, vs. = versus

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Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au   Page 5
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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[7].

† Different effect measures are reported by different reviews.

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, an 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. An 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.

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 moderate effect, and 0.8 and over represents a large treatment effect[7].

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).

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 dependent 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.

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‡ 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. 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[7];

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

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§ 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[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 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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