TECHNICAL COMMENTARY

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IQ and academic performance

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 developmental trajectories that may be associated with later development of schizophrenia[1].

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[2]. 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)[3]. 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 five systematic reviews that met our inclusion criteria[1, 4-7].

- High quality evidence suggests children who develop schizophrenia in adulthood have lower IQ scores when compared to children who do not develop the disorder.
- Moderate to high quality evidence suggests impairment in childhood on a range of cognitive functioning measures.
- Moderate quality evidence suggests children who develop schizophrenia in adulthood may achieve lower academic performance, but not in mathematics.

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- Moderate to high quality evidence suggests a small effect of lower education level in people with ultra high-risk mental states.

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Dickson H, Laurens KR, Cullen AE, Hodgins S

Meta-analyses of cognitive and motor function in youth aged 16 years and younger who subsequently develop schizophrenia

Psychological Medicine 2012; 42(4): 743-755

View review abstract online

Comparison	**Prospective or record linkage assessment of IQ and academic performance in childhood and adolescence, and the schizophrenia in adulthood.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests children (≤ 16 years) who later develop schizophrenia have lower intelligence quotient (IQ) scores than children who do not develop the disorder.** **Moderate quality evidence (imprecise) also suggests lower general academic performance, but not mathematical ability in children who later develop schizophrenia.**

IQ

Children who developed a schizophrenia spectrum disorder in adulthood obtained significantly lower IQ scores than children who did not develop the disorder;

Aged ≤ 16 years: 13 studies, N = 27,960, d = 0.51, 95%CI = 0.38 to 0.65, $p < 0.001$, Q = 26.55, $p < 0.05$, I^2 = 54.8%

Aged ≤ 13 years: 11 studies, N = 24,678, d = 0.51, 95%CI = 0.38 to 0.64, $p < 0.001$, Q = 19.11, $p < 0.05$, I^2 = 47.7%

Authors state that comparison group, IQ measure, or diagnostic outcome did not explain the heterogeneity.

General academic performance

Children who developed a schizophrenia spectrum disorder in adulthood obtained a trend effect towards lower general academic achievement scores than children who did not develop the disorder;

Aged ≤ 16 years: 5 studies, N = 725,820, d = 0.25, 95%CI = -0.03 to 0.53, p = 0.08, Q = 40.72, $p < 0.001$, I^2 = 90.2%

Mathematics

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No significant differences in mathematical performance; Aged ≤ 16 years: 4 studies, N = 6,459, *d* = 0.21, 95%CI = -0.09 to 0.51, *p* = 0.16, Q = 7.96, *p* < 0.05, I^2 = 62.3%	
Consistency in results‡	Inconsistent
Precision in results§	Precise for IQ, imprecise for academic achievement and mathematics
Directness of results‖	Direct

Fusar-Poli P, Tantardini M, De Simone S, Ramella-Cravaro V, Oliver D, Kingdon J, Kotlicka-Antczak M, Valmaggia L, Lee J, Millan MJ, Galderisi S, Balottin U, Ricca V, McGuire P

Deconstructing vulnerability for psychosis: Meta-analysis of environmental risk factors for psychosis in subjects at ultra high-risk

European Psychiatry 2017; 40: 65-75

View review abstract online

Comparison	**Premorbid educational level in people with ultra high-risk (UHR) mental states, which are determined as; attenuated psychotic symptoms, brief and limited intermittent psychotic symptoms, and genetic risk and functional deterioration.**
Summary of evidence	**Moderate to high quality evidence (large sample, consistent, imprecise, direct) suggests a small effect of lower education level in people with ultra high-risk mental states.**
Education level	
A significant, small effect of lower education level in people with UHR states than controls; 7 studies, N = 1,831, OR = 1.466, 95%CI 1.047 to 2.053, *p* = 0.026, I^2 0%, *p* = 0.616 There was no evidence of publication bias.	
Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct

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MacCabe JH

Population-based cohort studies on premorbid cognitive function in schizophrenia

Epidemiologic Reviews 2008; 30: 77-83

View review abstract online

Comparison	**Prospective assessment of cognitive functioning and academic performance in childhood and adolescence and the later development of schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large samples, consistent, imprecise, direct) suggests children who develop schizophrenia in adulthood achieved lower functioning across a range of cognitive measures compared with their peers.** **Moderate quality evidence (inconsistent) suggests they may also achieve lower school performance.**

Cognitive functioning

1 British population-based cohort (N = 4,746) given a broad range of cognitive tests at the ages of 8, 11, and 15 years reported that children who were to develop schizophrenia as adults scored consistently lower on all measures, particularly nonverbal tests, controlling for socioeconomic status and sex.

1 British nested case-control study (N = 12,537) reported the children who were to develop schizophrenia showed a stable pattern of deficits of approximately 0.6 to 0.7 SDs at 7 and 11 years across a wide range of neuropsychological assessments and teachers' ratings of school work. The subjects were 28 years of age at the end of follow-up, so the study was biased in favor of early onset schizophrenia cases.

1 New Zealand population-based cohort (N = 1,036) reported a significant difference between adults with schizophreniform disorder and adults without for lower IQ and receptive (not expressive) language at the ages of 3, 5, 7, 9, and 11 years, after adjusting for obstetric complications.

1 Swedish male army conscripts cohort (N = 50,087) assessed at age 18 years in four domains: mechanical and general knowledge and verbal and visuospatial ability. Overall IQ was highly predictive of schizophrenia, with controlling for socioeconomic status, behavioural adjustment in childhood, drug misuse, urban upbringing, family history of psychiatric disorder, and psychiatric disturbance at the time of testing. Mechanical knowledge showed the strongest association.

1 Swedish male army conscripts cohort (N = 109,643) given a range of cognitive tests, poor scores strongly predicted schizophrenia, controlling for pregnancy and birth difficulties. The technical and logic scores were the strongest predictors. Subjects were followed for a mean of only 5 years from

18 years, so there was a strong bias toward early onset cases. 1 Israeli army conscripts matched nested case-control study (total N = 10,806), aged 16 to 17 reported significantly worse performance than controls on all cognitive measures. There was also an excess of patients in the highest two performance bands (not statistically tested) 1 Finish male army conscripts cohort (N = 195,019) at mean age of 20 reported poor performance on a test of visuospatial reasoning, but arithmetic reasoning and verbal reasoning showed no difference.
Academic performance
2 population-based cohorts and 1 nested case-control study (N = 727,226); 1 North Finnish population-based cohort (N = 11,017) reported being in a lower class than expected at age 14 years was a significant risk factor for schizophrenia in adulthood; OR = 2.5, 95%CI 1.2 to 5.1, $p < 0.05$. Children who were in their normal class at age 16 years who would later develop schizophrenia did not differ in their grade-point average from their peers. Boys with excellent school performance at the age 16 years had a fourfold increased risk of schizophrenia compared with controls – this finding was absent in girls. 1 Finish nested case-control study (N = 808) assessed school grades and teachers' ratings at 7 to 11 years with three factors: academic, nonacademic, and behavioural. Small difference between cases and controls were found only on the behavioural measure. There was no difference in class rank, although cases were less likely to proceed to high school. 1 Swedish population-based cohort (N = 715,401) assessed school performance at age 15 to 16 years, and reported a grade-point average of at least 2 SDs below the population mean across all school subjects for children who developed schizophrenia in adulthood; hazard ratio = 3.87, 95%CI 2.80 to 5.34, $p < 0.05$. Receiving the lowest grade of ''E'' was independently associated with schizophrenia in adulthood ($p < 0.001$ in every compulsory school subject), and a higher grade-point average had a protective effect. There was no evidence of confounding by migrant status, low birth weight, hypoxia, parental educational level, or socioeconomic group.

Consistency in results	Appears consistent for cognitive functioning and inconsistent for academic performance.
Precision in results	Imprecise where CIs are reported.
Directness of results	Direct

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IQ and academic performance

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

Comparison	**Prospective assessment of IQ and academic performance in childhood and adolescence and the later development of schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large samples, consistent, imprecise, direct) suggests children who develop schizophrenia in adulthood achieved lower scores on IQ tests covering a range of impairments (verbal, nonverbal and mathematical) compared with their peers.** **Moderate quality evidence (inconsistent) suggests children who develop adult schizophrenia also achieved lower academic performance.**

IQ

1 British cohort (N = 4,746) reported consistently lower mean scores on verbal, nonverbal and mathematical tests in children who later developed schizophrenia (measured at age 8, 11 and 15), adjusting for sex and socio-economic status. Vocabulary and reading were less affected.

1 British cohort (N = 12,537) reported a range of intellectual impairments (measured at age 7, 11 and 16) including poor English, reading, spelling and mispronouncing words ($p < 0.001$ – measured on Southgate word recognition test and Reading Comprehension test).

1 U.S. cohort (N = 693) reported IQ declines between ages 4 and 7 years (measured on Stanford-Binet and WISC) in those who develop schizophrenia in adulthood; OR = 6.62, 95%CI 2.52 to 17.42, $p < 0.05$.

1 U.S. cohort (N = 8,013) reported lower performance on verbal and nonverbal tests at ages 4 and 7 years (measured on Stanford-Binet and WISC). At age 7 years, deficits were observed involving spatial reasoning, verbal knowledge, perceptual-motor speed and speeded processes of working memory.

1 New Zealand cohort (N = 972) reported lower performance on standard IQ tests at ages 3, 5, 7, 9, 11 and 13 years (measured by Peabody Picture Vocabulary Test, Stanford-Binet, WISC, and a battery of standard neuropsychological tests). At age 13 years, impairments were found on attention, executive functioning and motor tasks, but not memory and learning tasks.

1 Danish cohort (N = 6,923) reported lower cognitive function at age 12 and 18 years and cognitive

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decline between these ages (measured by Harnquist test, Børge Priens cognitive test).
Academic performance
1 British cohort (N = 12,537) reported reading, English, number work and book use as being poor at age 7 years (measured by teacher assessment) in children who developed schizophrenia in adulthood. 1 Finish cohort (N = 10,569) reported increased odds of attaining only a basic educational level at ages 14 and 16 years. More children at age 14 years who later developed schizophrenia were in a class below normal level or in a special school or class (measured by school data). At age years 16 there was no association with lower school marks, yet 'excellent' school marks were observed in boys who later developed schizophrenia OR = 3.8, 95%CI 1.6 to 9.3, $p < 0.05$. For adolescents at age 16 years who later developed schizophrenia, having good school performance (top 20%) was associated with a higher risk of suicide (measured from national registers); hazard ratio = 3.56, 95%CI = 0.97 to 13.05, $p < 0.05$.

Consistency in results	Appears consistent for cognitive functioning and inconsistent for academic performance.
Precision in results	Imprecise
Directness of results	Direct

Woodberry KA, Giuliano AJ, Seidman LJ

Premorbid IQ in schizophrenia: a meta-analytic review

American Journal of Psychiatry 2008; 165(5): 579-587

View review abstract online

Comparison	**Prospective assessment of premorbid IQ in childhood or adolescence and the later development of schizophrenia.**
Summary of evidence	**High quality evidence (large samples, consistent, direct, precise) suggests children who develop schizophrenia in adulthood achieved lower IQ scores compared with their peers.**
Premorbid IQ	

IQ and academic performance

Significant, medium effect of lower IQ in children who developed schizophrenia in adulthood: 10 cohort and 8 case-control studies (N = 628,381), age ranged from 3 to 26 years, *d* = -0.54, (no CI, reported as significant), Q = 29.60, $p < 0.05$, $I^2 = 42.5\%$ To investigate significant heterogeneity, one study was removed from the analysis that had an "atypical comparison sample ascertainment method"; this reduced heterogeneity; Q = 8.73, $p > 0.05$. Authors report that all studies with pre- and post-onset testing within the same sample suggested that a significant decline in the IQ of individuals with schizophrenia was associated with the onset of psychosis.	
Consistency in results	Consistent
Precision in results	CIs not reported, although graph indicates data are precise.
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), DSM-III = Diagnostic and Statistical Manual of Mental Disorders 3, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), IQ = intelligence quota, N = number of participants, OR = odds ratio, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), Q = Q statistic (chi-square) for the test of heterogeneity, RDC = Research Diagnostic criteria, vs = versus WISC = Wechsler Intelligence Scale for Children

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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[8].

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† 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[9]. 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[8].

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).

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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.

‡ 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[8];

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

§ 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[10].

‖ 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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