Reviewer's report

Title: Cognitive deficits in schizophrenia: an updated meta-analysis of the scientific evidence

Version: 1 Date: 9 April 2011

Reviewer: Jenny McCleery

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The following constitute major compulsory revisions.

Unfortunately, the review as a whole does not meet accepted quality standards for systematic reviews and meta-analyses.

Methods

The objective of the review is not clearly stated. Does it aim to be a comprehensive review of all areas of cognitive functioning in all patients with schizophrenia?

The methods are not described in full separately from the results.

Inclusion and exclusion criteria for studies are not clearly described. Details are needed covering participants, study designs and outcome measures.

The search strategy is inadequate. The search terms are too narrow, e.g. 'cognitive deficit*' would not pick up many studies concentrating on specific cognitive domains. Cognition as a core term should be expanded. The same is true for the other search terms. Each bit of the search string should be expanded to cover many more possible terms. Why is 'schizophrenia patients' used rather than 'schizo*'? The sources searched are limited. No mention is made of language restrictions. This strategy is likely to have missed many studies.

There is no description of how studies were selected (Process of selection? How many authors involved? How were disagreements resolved?)

There is no description of how data was extracted and how the quality of data extraction was assured. (How many authors extracted data independently? How was it checked?)

No attempt is made to distinguish high quality and poor quality studies and study quality is not discussed as a source of heterogeneity.

There is no discussion of other potential sources of bias, e.g. publication bias.

The rationale and methods used to divide the studies by different areas of cognitive functioning is inadequately described. The reader needs to see which outcome measures were assigned to which areas. It is insufficient to refer to a
descriptive table in the previous version of the review which will not be accessible to most readers (not open access). For example, semantic memory is well-recognised to be one of the cognitive domains most affected in schizophrenia, but is not distinguished as an area of memory functioning in this review. What is done with studies reporting semantic memory measures? What about retrieved studies reporting on other cognitive domains, e.g. visuospatial function, or executive function measures which were not primarily concerned with cognitive flexibility?

No explanation is given of the decision to perform subgroup analyses of in- and out-patients. These are presumably intended as proxies for severity. According to the authors' own account in the Introduction, other characteristics are of particular interest when considering cognitive impairment in schizophrenia, e.g. age of onset, duration of illness. There is no attempt made to consider how the data could be used to address these questions.

The methodological limitations of the review are not discussed in any systematic way.

Results

The description of the included studies is extremely general. It is usual (and useful) in such reviews to tabulate the key elements of the included studies, even when numbers of studies are large.

The review contains no information about the outcome measures identified in the included studies. I picked one unfamiliar study from the reference list (Corrigan 1992 – a study whose title suggests it focuses on social cognition) to see where it fitted into the cognitive areas analysed. I was unable to retrieve the full text easily, but the abstract indicates that, as well as measures of social information processing, it included measures of ‘recall memory and vigilance’. Yet, it is included only in the executive function list of Table 1. This reinforced my wish to see the outcome measures reported in order to understand this classification decision. Incidentally, this study which is Corrigan (1992) in the reference list appears as Corrigan (1991) in Table 1.

The first subtitle in the text is 'Memory functioning.' However, it appears that what is actually included here is the 47 studies classified under what the authors earlier termed 'memory efficiency' – a term whose meaning remains unclear, but which seemed to be some kind of residual group. 'Memory functioning' was used earlier as a term covering all 129 memory studies. The 47 'memory efficiency' studies now seem to be used to draw global conclusions about memory. This inconsistent use of terminology makes it hard to understand what is included in each analysis.

If in- versus out-patient status is a proxy for severity, then the fact that out-patients perform worse than in-patients on memory functioning is worthy of comment. It seems surprising that so few studies (e.g. 33/129 studies assessing memory) gave any indication of the setting of the study. If this information was
missing, was there any attempt to get it from the study authors?

It is highly questionable whether a single summary effect estimate is useful given the high degree of clinical heterogeneity. Random effects meta-analysis can be useful when there is heterogeneity of unknown origin, but that is not the case here. There are multiple reasons why these studies can be expected to differ in outcome, i.e. multiple reasons why they cannot be assumed to be measuring any single underlying effect size.

The authors suggest that the lower heterogeneity among studies all using digit span as the outcome measure than among studies using a range of different memory measures illustrates the impact of methodological heterogeneity. Surely it arises because the digit span studies are all measuring the same construct (working memory) while the mixed studies are not. This is not methodological heterogeneity; it is simply mixing apples with pears.

It would be helpful if the authors would explain why they are so concerned by a numerical excess of patients over controls. When total numbers in both groups are large for each analysis, as they are here, this need not be a problem. Imbalances in baseline characteristics between patient and control groups are a separate issue of concern.

The use and reporting of the meta-regression requires specialist statistical review.

Age is notoriously difficult to use as an explanatory variable in this context, being so strongly confounded with duration of illness, course and severity of illness, duration of treatment, etc. The authors should comment on these problems.

Conclusions

“A heterogeneity so high as that found in our results, shows that there are diffuse and structural problems in considering all the studies performed in this area of research as belonging to the same class of studies.”

This is true - and it follows that the subsequent conclusions are not entirely justified. It is certainly the case that more methodological consistency in this field would have benefits. However, not all the studies reviewed here are attempting to answer the question the authors are asking. Methodological heterogeneity, in the sense that the authors have used it, is not “illegal” (illegitimate?) when studies are not seeking to answer the same question. As the authors correctly point out, it is already well-established that patients with schizophrenia have widespread cognitive deficits. The field has moved on to ask more nuanced questions. When studies ask different questions, then different methods may be entirely appropriate. It is not reasonable to lump all such studies together, without distinction, and then blame the primary research for the heterogeneity.

This review is itself devoid of theoretical background and in combining data from studies including disparate patient groups and using different outcome measures, it does little to advance either theory or practice.
Minor essential revisions

The software package used for the analysis is not reported.

The standard of the English is, on the whole, adequate, but there are places where the meaning is obscure. Examples include (but are not limited to) the following:

Abstract: 'contribute to reducing the high degree of not-overlapping information offered by the single studies'

Introduction, para 3: 'It is unclear if these cognitive problems are specific for schizophrenia or may be linked to typical or generic intervening and concomitant factors which may be associated with the chronic development of the disease'

There are also many instances where it is reasonably easy for a native English speaker to determine the meaning by some educated guesses; this may be harder for other non-native speakers. Overall, the manuscript would benefit enormously from detailed copy-editing by a native English speaker.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.