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A systematic review and meta-analysis of cognitive remediation in early schizophrenia

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ABSTRACT

Neurocognitive impairment predicts disability in schizophrenia, making intervention theoretically attractive as a means to minimise chronic disability. Many trials confirm that cognitive remediation (CR) produces meaningful, durable improvements in cognition and functioning but fewer focus on the early stages. We systematically reviewed CR trials in early schizophrenia to determine its efficacy on global cognition, functioning and symptoms.

Two reviewers independently searched electronic databases to identify randomised controlled trials investigating CR following a first episode of psychosis. Eleven trials with 615 participants were identified.

Random effect models revealed a non-significant effect of CR on global cognition (effect size = 0.13, 95% CI −0.04, 0.31; p0.14), $p < 0.05$ in sensitivity analysis (effect size 0.19; CI 0.00, 0.38). One of seven neurocognitive domains showed a significant positive effect (verbal learning and memory) and five others showed borderline significant benefits. There was a significant effect on functioning (0.18; CI 0.01, 0.36; $p < 0.05$) and symptoms (0.19; CI 0.02, 0.36; $p < 0.05$). CR's effect on functioning and symptoms was larger in trials with adjunctive psychiatric rehabilitation and small group interventions.

CR's effect sizes in early illness were smaller than those in chronic schizophrenia, perhaps because of participants' reduced scope for improvement, though trials' small number and size produces uncertain estimates of effect. However, significant benefits were seen in functioning and symptoms and moderator analyses indicate factors that may increase CR's effect. Findings here, theoretical considerations and trials in chronic schizophrenia suggest that targeting social cognition might also enhance its efficacy.

1. Introduction

The majority of the costs of schizophrenia ($63 billion in the USA in 2002, £12 billion in the UK in 2011) are not for treatment but are consequences of disability, e.g. indirect costs associated with care and loss of productivity (Andrews et al., 2012; Wu et al., 2005). The cognitive impairment evident in schizophrenia is a key driver of poor social functioning (Brekke et al., 2007, 2009). Deficits are seen in all areas of cognitive functioning (Heinrichs and Zakzanis, 1998) but social cognitive deficits arguably most directly drive dysfunction (Bora et al., 2006; Brekke et al., 2005; Couture et al., 2006).

Longer duration of untreated psychosis has been linked to worse cognitive function (Scully et al., 1997), suggesting that intervention close to the onset of psychosis is required to reduce the cognitive deficit and its subsequent impact on quality of life. Early intervention is known to reduce positive and negative symptoms (Petersen et al., 2005), significantly reduces the risk of relapse and the number of hospital admissions (Bark et al., 2003) and has positive effects on social and occupational functioning (Craig et al., 2004; Marshall and Rathbone, 2011). The level of functioning during the first years following the onset of psychosis can predict long term outcome (Birchwood et al., 1997; Harrison et al., 2001). Given the effectiveness of early intervention in other domains of schizophrenia, employing cognitive remediation (CR) treatment early in the course of schizophrenia would be expected to lead to improve long-term functional outcome.

Whatever the cognitive benefits of current antipsychotics, their effectiveness in specifically improving cognition sufficiently to benefit social function is undemonstrated, and specific cognition enhancing medications are not yet clinically available. This makes CR an attractive interventional strategy. CR is defined as a behavioural training-based intervention that aims to improve cognitive processes such as attention, memory, executive function, social cognition and metacognition with the goal of durability and generalisation (Cognitive Remediation Experts Workshop, Florence, April 2010). Meta-analysis shows that CR is effective across a wide range of cognitive domains (Wykes et al., 2011), particularly for social cognition, reasoning and problem solving.

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CR programmes that include an element of strategy training and are linked to rehabilitation programmes are most effective for improving functioning outcomes.

Successful CR trials have been conducted in a range of settings but few have studied the effectiveness of the intervention in early schizophrenia. If the time of first presentation is a "critical period" for cognitive decline, as with other symptoms (Birchwood et al., 1998), it is particularly important to determine the efficacy of CR at this point. There is some evidence that patients who receive CR at a younger age (Wykes et al., 2009) and at an earlier stage of schizophrenia (Bowie et al., 2014; Gupta et al., 2011; Lee et al., 2013) have greater functional, social and cognitive gains than older populations with the illness. Although a recent review of CR in early schizophrenia has been undertaken (Barlati et al., 2012), there is not yet a systematic review and meta-analysis of CR trials in this early phase, and several such trials have been conducted since the last major review of the area (Wykes et al., 2011). We therefore set out to conduct such a specific review and meta-analysis.

In this study, we hypothesised that CR would have a positive effect on cognition, symptoms and functioning of those experiencing a first episode of psychosis. We also hypothesised that this effect would be moderated by participant and treatment characteristics.

2. Method

2.1. Data sources

Databases were searched independently by two authors (ER and ZK) and included all abstracts published up to May 2015. The Cochrane Controlled Trials Register, PsycINFO, Embase, MEDLINE and Web of Science were searched using the terms:

(Cognit*) AND (remediation OR rehabilitation OR training) AND (early course OR early OR first episode OR adolescent) AND (schiz* OR psychosis OR psychotic).

Reference lists were hand-searched and first authors of included reports and those known to be conducting relevant research were contacted.

2.2. Study inclusion

The flow of study inclusion is displayed in Fig. 1. Where an abstract met inclusion criteria but no full report was available, authors were contacted for further information. Two reviewers (ER and ZK) screened all studies independently. ER assessed records for eligibility and contacted authors for further information. A random 50% of eligible studies were inspected by a second reviewer (ZK) and a kappa of over 0.7 reflected strong agreements between reviewers. Any disagreements were resolved in discussion with another researcher (RD).

2.3. Data extraction

Extracted information included: study design and duration; participant demographics and study setting; number of intervention groups and intervention/control details; measures used; outcomes and time points for collection and reporting; and sample size and summary data for each outcome. Where data were not available or were unclear, study authors were contacted for further information. The Cochrane Collaboration's 'risk of bias tool' was used to assess methodological

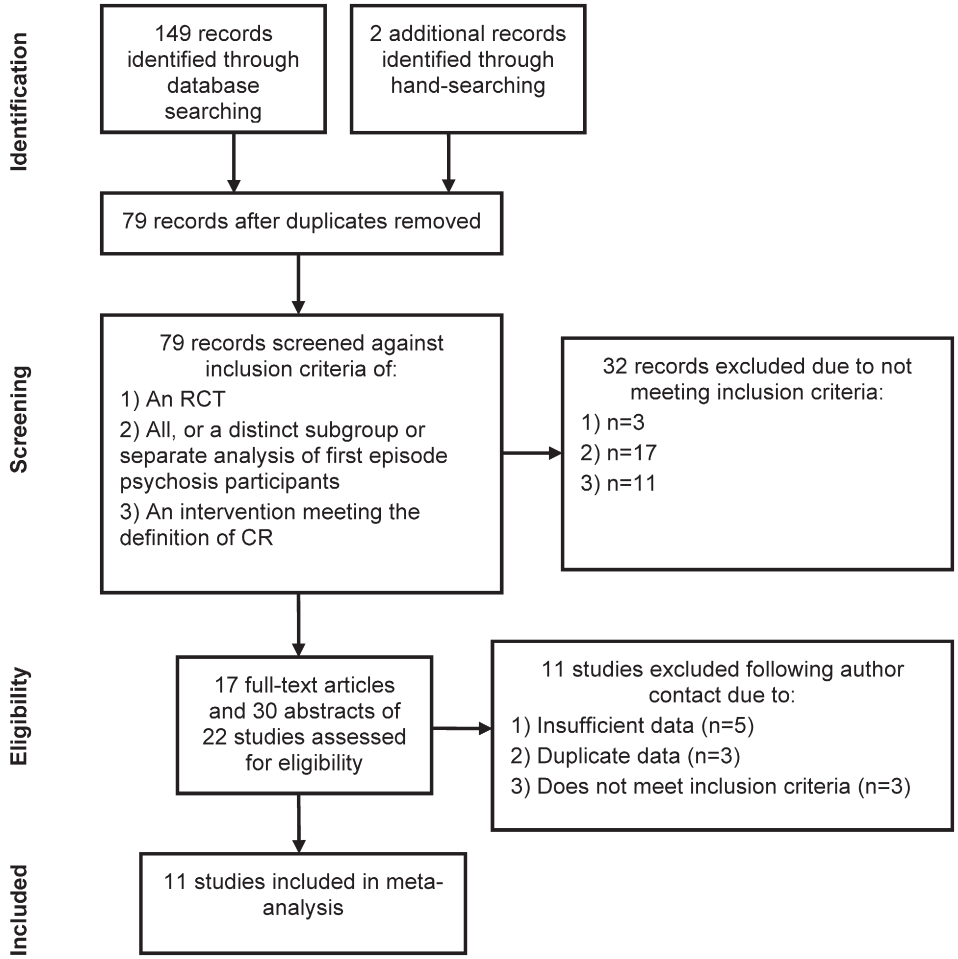

Fig. 1. Flow diagram of study identification and inclusion.

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