



## Cognitive remediation in schizophrenia—The view from India



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### ABSTRACT

The prevalence and disability due to Schizophrenia (SZ) in India is similar to other parts of the world. Cognitive impairments are also present in a large group of Indian persons with SZ. Interventions to address these impairments – termed cognitive remediation or cognitive retraining – are being tested all over the world. Indian research on remediation in schizophrenia has been eclectic and is reviewed here. Some investigators have focused mainly on symptom control and quality of life, as yoga could be a cost effective and culturally acceptable intervention for remediation and rehabilitation. Although participants were not exhaustively tested for improvement in cognitive function in the majority of such trials, published results are encouraging.

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### 1. Introduction

Cognition denotes information processing and requires a broad range of mental processes (Thara, 2007). Cognitive impairment is an important predictor of functional outcomes including occupational

functioning and life satisfaction (Thorsen et al., 2014; Velligan et al., 2000; Bowie et al., 2010). Schizophrenia is associated with deficits in various cognitive processes that result in disorders of complex thinking and ideation, resulting in difficulty in dealing with 'psychological and social challenges in daily life' (Lysaker et al., 2015). Drug free or un-medicated patients with schizophrenia show severe cognitive deficits (O'Carroll, 2000), suggesting that the cognitive impairment cannot be attributed solely to medication effects. Memory dysfunction, disturbance of executive functions, and general cognitive functioning are affected (Tandon et al., 2009; Keefe

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and Harvey, 2012). Cognitive strategies were developed to address these deficits (Eack et al., 2010; Eack, 2012; Eack, 2012).

## 2. Cognitive remediation (CR) in schizophrenia

Cognitive rehabilitation is a confluence of therapeutic activities based on brain-behaviour relationships (Hegde, 2014). Functional improvement is achieved by re-establishing or reinforcing previously learned adaptive patterns of behaviour, facilitating improvement in cognitive functions through compensatory mechanisms and sometimes facilitating new patterns of activity through external compensatory mechanisms.

Cognitive remediation aims to improve cognitive functions impaired due to schizophrenia using different techniques. Most CR approaches focus on higher-level cognitive domains, such as attention, memory, and executive function or on increasing and utilizing neuroplasticity through basic tasks, such as early perceptual processing and working memory. The ultimate goal is to improve day to day social functions as well as occupational rehabilitation (Zaytseva et al., 2013). Typically, the remediation relies on reinforcement and learning through repeated sessions. Training sessions can last for 1–2 h and the duration of training varies; some programs last up to six months. Programs combining CR combined with other rehabilitation techniques yielded better results and generalizability to improve functioning (Zaytseva et al., 2013). Therapists used pen and pencil or computerized approaches (Thorsen et al., 2014). Clinically stable patients gained more benefit (Zaytseva et al., 2013).

It is not clear how long the benefits of CR last, and whether 'booster sessions' are needed (Shriharsh et al., 2003). The results of CR studies may be affected by randomization and blinding procedures, different numbers of subjects among intervention groups and control groups, effect of concurrent medications especially different types of antipsychotics, generalizability and cost benefit ratio with intensive therapist involvement. All these factors need to be considered before this treatment is recommended for regular use (Thorsen et al., 2014).

## 3. How does cognitive remediation work?

CR is said to influence brain structure as well as function. Brain imaging studies have shown that improvement in neurocognitive performance and neural changes may go together (Thorsen et al., 2014). In support, CR-induced changes including hyper or hypo activity of brain regions and circuits, particularly in prefrontal, middle frontal, parietal, temporal, para hippocampal and limbic areas have been reported (Thorsen et al., 2014). Some areas such as prefrontal cortex (PFC), cortical midline regions, parietal and temporal cortex, insula, and amygdala may show areas of increased activity (Thorsen et al., 2014). CR has also been associated with neuroprotective effects against grey matter loss in temporal brain regions associated with cognition (e.g. hippocampus, parahippocampal gyrus) and with increase of serum brain derived neurotrophic factor (BDNF) levels (Michalopoulou et al., 2015). CR may strengthen existing or compensatory structures and activity and also promote neuroplasticity. Improvement in brain functioning detected after CR therapy among patients with SZ might be attributable to increase of the interhemispheric information transfer between the bilateral prefrontal cortices via the corpus callosum (Penades et al., 2013). CR affects insular activation to a lesser extent, thus indicating that CR influences cognition more than affective functions.

## 4. Schizophrenia in India

Schizophrenia (SZ) is as chronic and disabling an illness in India (Math et al., 2007), as it is in other parts of the world (Shankar et al.,

1995; Srinivasan and Thara, 1997). In view of its reported beneficial effects in other parts of the world, Indian investigators have also begun to evaluate CR among patients with SZ. These efforts have been constrained by limited resources. Hence investigators have evaluated a number of different approaches. The present review summarizes and evaluates peer reviewed publications published by investigators in Indian settings.

## 5. Indian studies of cognitive deficits in schizophrenia

Publications from India on cognitive deficits in schizophrenia date back to 1987 (Chandiramani and Varma, 1987) but sampling issues make it difficult to generalize their results. In general, Indian studies reported cognitive deficits similar to those from Western patient populations (Dalal and Sivakumar, 2010). Cognitive deficits were not correlated with current employment status or to level of performance at work in a schizophrenia sample of 100 subjects from Chennai, but negative symptom scores were correlated with social functioning, and employment status was correlated with poor work performance (Srinivasan and Tirupati, 2005). These authors opined that social pressures better accounted for the working status of their subjects than cognitive dysfunction. In a sample from Mumbai (N 50, cases and controls), cognitive deficits were present during remission but did not have a statistically significant relationship to disability (Krishnadas et al., 2007). At Delhi, no statistically significant differences in performance were reported between cases and parents using the Trail Making Test (TMT). Among patients, TMT performance, which assesses attention and working memory, was correlated with severity of auditory hallucinations (Bhatia et al., 2009). Factor analytic studies reported distinct dimensions of neuro cognition and social cognition from Bengaluru (Mehta et al., 2014). Although social cognition is recognized as being distinct from neurocognition, several investigators have focused on social cognition in conjunction with cognitive functions, using a tailored assessment schedule called SOCRATIS (Mehta et al., 2011a,b).

## 6. Cognitive remediation research in India

The first study to evaluate a combination of pharmacotherapy and cognitive retraining was an international four arm clinical trial conducted at Bengaluru, India and sites in the USA (D'Souza et al., 2013). The four groups were: (1) D-serine (30 mg/kg)+ cognitive retraining (CRT) (2) D-serine + control CRT (neutral TV shows), (3) CRT+ placebo, and (4) placebo+ control CRT. The computerized CRT modules targeted attention, memory, verbal- visuospatial working memory, and executive function. Sessions lasted for 5 h per week, for 2-3 days/week and were supervised by a clinical psychologist. Among the participants, Indian subjects completed assessment at 3 months (n=69) and at six months (N=43). CRT resulted in significant improvement in Verbal Working Memory, and a trend toward improvement in Attention/Vigilance (Table 1).

## 7. Vocational rehabilitation as cognitive enhancement

Vocational training can improve cognitive functions. The vocational training services available to a study involving Indian subjects were simple ones such as notebook manufacturing, bookbinding, offset printing, carton making, medicine cover making, horticulture (for men) and bookbinding, spinning, and medicine cover making (for women) (N=34) (Suresh Kumar, 2008). Cognitive functions were evaluated using the Mini Mental State Examination (MMSE) only. Subjects who attended the rehabilitation services performed better on orientation, attention, language and total MMSE scores. Better scores on MMSE were positively correlated with occupational functioning and cognitive

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