



Persistence of effectiveness of cognitive remediation interventions in schizophrenia: A 1-year follow-up study



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ABSTRACT

Objectives: Cognitive remediation interventions are effective in patients with schizophrenia, but the durability of their effects is still under debate. This study aimed to investigate the 1-year persistence of the effectiveness of cognitive remediation.

Methods: Patients with schizophrenia treated with cognitive remediation or usual rehabilitation were reassessed with clinical, neuropsychological and functional measures 1 year after cognitive remediation.

Results: At the 1-year follow-up, the advantages of cognitive remediation remained significant for clinical variables and specific cognitive domains. Functional measures showed increasing improvement at follow-up.

Conclusions: The study suggests that the effectiveness of cognitive remediation in schizophrenia persists after 1 year.

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1. Introduction

Cognitive impairment is broadly recognized as a core feature of schizophrenia (Green et al., 2004; Keefe et al., 2006), and is widely considered to be among the most important predictors of psychosocial outcome (Bowie et al., 2006, 2008) and quality of life (Alptekin et al., 2004).

In recent years, different cognitive remediation (CR) interventions have been developed (for review see Vita et al., 2014), and their effectiveness in ameliorating patients' cognitive performance and psychosocial functioning has been extensively demonstrated (McGurk et al., 2007; Wykes et al., 2011; Medalia and Saperstein, 2013). Despite the increasing amount of data supporting the benefits of CR interventions, a number of questions are still to be answered. Among them is the persistence of their effects over time.

Only a few studies include long-term follow-up data of patients previously treated with CR. In a meta-analysis by Roder et al. (2011), Integrated Psychological Therapy (IPT) showed efficacy in improving neurocognition, social cognition, psychosocial functioning and negative symptoms, and its positive effects were maintained over an average follow-up period of 8.1 months. Eack et al. (2010) found that with Cognitive Enhancement Therapy, applied for a period of 2 years in the early course of schizophrenia, improvement in functional outcome was

maintained at 1-year follow-up. The effects of Cognitive Remediation Therapy (CRT) were still apparent after 6 months of follow-up in a study by Wykes et al. (2003) in which CRT was applied for 3 months. In the meta-analysis by Wykes et al. (2011), the effects of CR on global cognition seemed durable, but the effects on symptoms were no longer significant at follow-up.

The aim of this study was to further analyse whether the cognitive and functional effects of CR in patients with schizophrenia persist beyond the time of application of the remediation method in a naturalistic setting of care.

2. Materials and methods

2.1. Patients

The patients recruited had participated in a previous study (Vita et al., 2011) that included 84 patients aged 18–50 years fulfilling the DSM-IV-TR (American Psychiatric Association, 2000) diagnostic criteria for schizophrenia, and followed in the rehabilitative centres of the Departments of Mental Health of Brescia and Cremona Hospitals (Italy). Exclusion criteria were as follows: (a) a concomitant diagnosis of mental retardation or of substance use disorder; (b) severe positive symptoms or impulsive behaviour requiring a higher security setting; (c) significant changes in psychopathologic status (requiring hospitalization or major change in pharmacologic treatment) in the last 3 months. Fifty-six patients had received a CR intervention

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(cognitive training of IPT ($n = 26$) or computer-assisted cognitive remediation (CACR) ($n = 30$)) in addition to usual rehabilitation. Another group of patients ($n = 28$) received non-cognitive-oriented rehabilitation interventions, with the same intensity and duration of CR (treatment as usual (TAU)). CR sessions took place twice a week over a 6-month period. Further details about the study design and CR and TAU interventions are reported in Vita et al. (2011). All patients received antipsychotic treatment and were followed naturalistically in different rehabilitation settings, representative of the Italian psychiatric services.

All patients were assessed at baseline (t0) and after 6 months of treatment (t1) with clinical (Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987)), neurocognitive and psychosocial functioning (Health of the Nation Outcome Scale (HoNOS) (Wing et al., 1998; Lora et al., 2001)) measures. Patients received a comprehensive battery of neuropsychological measures, chosen to assess the main cognitive domains found to be impaired in schizophrenia (Nuechterlein et al., 2004). Four cognitive constructs were used to represent specific domains of cognitive functioning (processing speed, working memory, verbal memory and executive functions) and expressed as z scores relative to normative data for the Italian population (Vita et al., 2011). A global cognitive composite score was calculated by averaging the other cognitive indexes.

In the present study, patients treated with CR or TAU for 6 months were reassessed with the same neuropsychological, clinical, and functional measures 1 year after completion of the randomized CR or TAU intervention (t2). During the follow-up, they were treated naturalistically in the outpatient facilities of the centres involved in the study and received pharmacological treatment and non-structured psychosocial interventions.

2.2. Statistical analysis

To investigate differences in outcome measures between the groups (CR vs TAU), repeated measures analysis of variance was performed. In this study, measures at t0, t1, and t2 were used as dependent variables, time (with the 3 levels t0, t1 and t2) as the within-factor variable and group (CR vs TAU) as the between-factor variable.

Analysis of variance comparing the mean outcome variables of the 2 groups at each end point, after covarying them for patient's age (see below) and the rating of the same variable at baseline, was performed to test whether differences between groups were detectable and those demonstrated at t1 were still detectable after 1 year. Two-tailed P values <0.05 were considered statistically significant. Data were analysed using SPSS 14.0.

3. Results

Fifty-four patients were reassessed 1 year after the completion of CR (t2). Fifteen patients had been treated with IPT, 22 with CACR, and 17 with TAU. No between-group differences in dropout rates at t2 emerged either when comparing the three groups, or the group of patients receiving cognitive remediation versus the TAU group (chi-squared tests). The demographic characteristics of the patients assessed at t2 are presented in Table 1. No significant baseline differences in any variables were detected between patients assessed at follow-up and the whole group of patients assessed at baseline ($n = 84$). Demographic comparison between patients who underwent CR ($n = 37$) and TAU ($n = 17$) assessed at t2 showed a lower age at baseline ($P = 0.030$) in patients treated with CR. For this reason, and for its possible impact on treatment outcome (Wykes et al., 2009), age was included as a covariate in the subsequent analyses. Given the purpose of the study to investigate the persistence over time of the effects of cognitive remediation, we decided to work with data actually assessed at long term (t2) in individual patients, and did

Table 1

Demographic characteristics of the sample completing the follow-up.

Variables	N, mean \pm SD
N	54
Sex (M/F)	34/20
Age (years)	39.77 \pm 9.35
Age at onset (years)	24.70 \pm 7.76
Duration of illness (years)	15.63 \pm 8.62
School (years)	10.17 \pm 2.89
FSIQ (WAIS-R)	85.23 \pm 10.99
Chlorpromazine equivalents at baseline (mg)	670 \pm 430

SD, standard deviation; FSIQ, Full Scale Intelligence Quotient; WAIS-R, Wechsler Adult Intelligence Scale-Revised.

not use statistical methods that could treat missing data, so modifying or enhancing our results.

Repeated measures analyses of variance, covaried by age (ANCOVA) and measures at t0, t1, and t2 in the CR and TAU groups are presented in Table 2. Analyses of group differences in clinical, cognitive and functional variables at t1 and t2 are reported in Table 3.

3.1. Clinical variables

Repeated measures ANCOVA revealed significant time and time \times group interaction (better outcome for CR) effects in PANSS positive, negative and total scores. A group effect was found only for the PANSS positive subscale. Univariate ANCOVA, covaried for baseline values and age, confirmed also at t2, the better outcome observed for CR than for TAU detected at t1 for all clinical measures.

3.2. Neuropsychological variables

Repeated measures ANCOVA revealed a time and time \times group effect (better outcome for CR) in the processing speed domain. A time effect was also found for verbal memory and a time \times group interaction (better outcome for CR) was significant in the working memory domain. Univariate ANCOVA revealed a better outcome with CR compared with TAU at t1 in processing speed and working memory. At t2, the superiority of CR vs TAU was confirmed only for processing speed.

3.3. Functional variables

A time and time \times group effect (better outcome for CR) was observed for HoNOS total score. ANCOVA at different end points revealed a significantly better global outcome in the CR group compared with the TAU group at t2 that was not detected at t1.

4. Discussion

In this study, we aimed to investigate the persistence of the effectiveness of CR treatment 1 year after completion of the intervention. A clear change in clinical severity over time was found in both treatment groups, with a significantly better outcome in the CR group. The superiority of CR over TAU, already significant after completion of CR, was still present 1 year after the completion of treatment. This suggests that the clinical effects of CR persist in the medium term.

Change in processing speed over time was different between the groups. The better outcome in the CR group compared with TAU both at t1 and t2 underlines that the positive effect of CR on processing speed is sustained in the medium term. On the other hand, the superiority of CRT on working memory did not persist over time. This suggests that this cognitive function may need to be constantly retrained to maintain the differential beneficial effect of CR compared with TAU. HoNOS scores, on the contrary, did not show any significant difference between the groups at t1, whereas a significant advantage of the CR intervention emerged at t2. This latter result may suggest that the

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