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Integrated cognitive remediation and standard rehabilitation therapy in patients of schizophrenia: persistence after 5 years

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ABSTRACT

Cognitive remediation, often used in combination with standard rehabilitation programs, represents the best available tool to treat cognitive impairments in patients with schizophrenia. However, there are still open questions about durability of effects and generalization of cognitive improvements to functional outcome. This study aims to investigate the persistence of both cognitive and functional effects of combined cognitive remediation plus standard rehabilitation interventions, 5 years after completion of the intervention, also comparing different durations of the standard rehabilitation. Sixty patients diagnosed with schizophrenia and previously treated with a 6 months intervention, consisting of standard rehabilitation plus 3-months of cognitive remediation, either followed by another year of standard rehabilitation or routine psychiatric treatment, were reassessed with neuropsychological and functional measures 5 years after the intervention. Results show that cognitive abilities remained stable after 5 years in both groups, while functional performance significantly decreased in patients treated with the 6 months intervention only. Data thus suggest that cognitive effects persist even after 5 years, while a longer standard rehabilitation following the cognitive remediation program may be needed to achieve a stable functional gain.

1. Introduction

Cognitive impairments are considered a core feature of schizophrenia (Bryce et al., 2016) and are recognized as the most important predictors of functional outcome and quality of life (Rispaud et al., 2016). In the past years, different cognitive remediation therapy (CRT) programs have been developed and their effectiveness on cognition has been widely demonstrated (Bryce et al., 2016; Deste et al., 2015), while there is still variability regarding their results on psychosocial and daily functioning. In this respect, literature supports the efficacy of CRT as a part of a broader rehabilitation treatment, with potentiating effects on functional outcome (Mcgurk et al., 2007; Reeder et al., 2006; Vauth et al., 2005). Wykes and van der Gaag suggested that "CRT should not be a stand-alone therapy in clinical practice, but rather it should be part of comprehensive programs for rehabilitation and recovery so that any improvement following CRT can be exploited in further training or recovery therapy" (Wykes and van der Gaag, 2001). Different studies provided additional support, showing that CRT, delivered as a bridging intervention added to or immediately followed by a standard rehabilitation, leads to significantly greater functional improvements (Bosia et al., 2014, 2007; Cavallaro et al., 2009; Mcgurk et al., 2007; Poletti et al., 2010) that either intervention alone.

The generalizability of CRT effects on functional outcome is a crucial issue in rehabilitating patients with schizophrenia (Cavallaro et al., 2009). Indeed, daily functioning is the main target and the final goal of any therapeutic enhancement strategy (Wykes and van der Gaag, 2001). In a disorder characterized by severe and persistent impairments in everyday functioning, it is necessary to achieve meaningful improvements in patients' ability to acquire community living skills (Bowie et al., 2012). The differential rates of improvement, the enhanced core deficit domains and the functional effect all support the hypothesis that the interaction between CRT and standard rehabilitation potentiates outcome (Bell et al., 2001). More precisely, CRT may reduce the so-called "cognitive limiting factors" by improving cognitive abilities, whereas standard rehabilitation provides an ecological environment in order to use and reinforce mental activity (Cavallaro et al., 2009). In addition, combining CRT with a standard rehabilitation program may also contribute to maintenance over time of CRT effects (Mueller et al., 2015). In fact, to our knowledge, the few studies investigating the

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durability of CRT effects used a combined treatment. Deste et al. found that the advantages of CRT in addition to usual rehabilitation remained significant for both cognitive and functional measures one year after the end of the treatment (Deste et al., 2015). Moreover, McGurk and colleagues found that patients who underwent a cognitive training plus supported employment had significantly better work outcomes over a 2–3 years follow-up period than those who only received supported employment (McGurk et al., 2007). In line with these results, previous research from our group showed not only that the effects of CRT combined with standard rehabilitation treatment on cognitive performance persisted after one year of follow-up, but that the improvement in daily functioning progressively increased at the 6-months and one-year follow-up as well (Poletti et al., 2010). Furthermore, Eack et al. showed that an early application of a combined neurocognitive and social-cognitive rehabilitation program, the Cognitive Enhancement Therapy (CET), could confer substantial benefits on both cognitive domains and functional outcome over a 2-year follow-up (Eack et al., 2009). Similarly, Hogarty and colleagues found that the effects of CET versus the Enriched Supportive Therapy (EST), both delivered over a two-year period, were broadly persistent one year after treatment (Hogarty et al., 2006).

Taken together, all these evidences suggest that an integrated rehabilitative approach including CRT plus a standard rehabilitation seems to be more effective, in terms of both generalizability of results to daily functioning and apparently also durability (Mueller et al., 2015).

Despite the acknowledgment that combined interventions are needed to potentiate outcome, research focused mainly on CRT, while features of the associated standard rehabilitation interventions have been less explored.

Moreover, previous research was conducted over follow-up periods ranging from 6 months (Wykes et al., 2003) up to a maximum of three years (Eack et al., 2009; McGurk et al., 2007), but data concerning the durability of combined rehabilitative treatment effects after longer periods are lacking.

Given these evidences, in this study we focused on a 5-year follow-up in order to better investigate the long-term durability of cognitive gains and their generalization to functional areas. We evaluated, through a cognitive and functional assessment 5 years after the completion of interventions, the effects of two integrated treatments consisting of a Computer-assisted CRT added to standard rehabilitation therapy of different duration. Indeed, we hypothesized that extending one year of standard rehabilitation program after a combined training could contribute to better maintain cognitive and functional results over time. If confirmed, our hypothesis could reflect on daily clinical practice contributing to structure rehabilitative interventions in order to achieve better and more durable cognitive and functional improvements.

2. Materials and methods

2.1. Participants

This is a monocentric retrospective study. Sixty patients (35 males and 29 females) diagnosed with schizophrenia according to DSM-IV-TR (American Psychiatric Association, 2000) criteria, that participated to a previous study evaluating the effects of CRT combined with standard rehabilitation, were enrolled at the Disease Unit for Psychotic Disorders of IRCCS San Raffaele Hospital, Milan, Italy. All patients that participated to the previous study were contacted either through their psychiatrist (for patients still followed at the Disease Unit for Psychotic Disorders of IRCCS San Raffaele Hospital) or by telephone, to ask their availability to participate to the present study. After a complete description of the study, informed consent to participation was obtained. The protocol followed the principles of the Declaration of Helsinki and was approved by the local Ethical Committee.

To be included, patients had to satisfy DSM-IV-TR diagnostic criteria for schizophrenia and the following conditions:

- No significant changes in psychopathologic status (requiring hospitalization or major change in pharmacologic treatment) in the last 3 months; and
- No evidence of substance dependence or abuse, comorbid diagnoses on Axis I or II, epilepsy, or any other major neurological illness or perinatal trauma, or mental retardation.

2.2. Design

All enrolled patients were assessed for neurocognitive performance and daily functioning within the fifth year after the end of an integrated treatment, which included CRT and a standard rehabilitation therapy (SRT), described in Cavallaro et al., 2009.

In details, all patients were treated with the following integrated treatment:

- 3 months of three 1-h sessions a week of Computer-assisted CRT, performed with the Cogpack Software® (Marker, 2007) consisting of domain-specific neurocognitive exercises, aimed at training the cognitive functions impaired in the patient. Sets of exercises were individually created for each patient on the basis of the quality of baseline performances at neuropsychological assessment: for each poor performance, a domain-specific exercise was included, while for each good performance a non-domain-specific exercise was added. Exercises were then adaptively graded for difficulty by the software, based on patients' performance during the course of the session. The program records the performance of each patient for every session, allowing patients to receive feedback and therapists to have a course profile of each patient. CRT was administered by trained psychologists, blind to the assessments, whose role was to motivate patients and assist them in completing exercises and trying different strategies, without giving them the solutions to the exercises.
- 6 months of standard rehabilitation therapy (SRT), focusing on the main community goals of social abilities, work and autonomy. The SRT included non-cognitive subprogrammes of the integrated psychological therapy (Brenner et al., 1992), social skills training programs for residential, vocational, recreational functioning (Roder et al., 2002) and psychoeducation. Each patient participated in the program for a total of 3 times a week and took part in groups of five-nine participants lasting approximately 1.5 h each. Therapists were trained clinical psychologists and rehabilitation therapists, blind to the assessments.

After this integrated treatment, which was performed according to a previous research protocol (Cavallaro et al., 2009), patients were followed naturalistically in different settings. During the program 5 patients dropped out: 3 subjects due to hospitalization, 2 subjects due to change of residence. Of the 60 enrolled patients, 33 underwent an additional year of SRT in the rehabilitative out service, while the remaining 27 were followed up at the clinic as outpatients. Main reasons to discontinue the rehabilitation program were distance from the site and/or poor autonomy in transfers. Finally, we compared patients who underwent only the 3 months CRT + 6 months SRT protocol (CRT/SRT) with patients who continued another year of SRT (CRT/SRT+).

2.3. Measures

According to the original protocol (Cavallaro et al., 2009), all patients were evaluated for psychopathology by means of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), administered by trained psychiatrists, and for intellectual functioning through the Wechsler Adult Intelligence Scale–Revised (Wechsler, 1997), administered by trained psychologists, before starting the CRT/SRT program.

Patients were also assessed for neurocognitive performance and daily functioning at baseline (before starting treatment) and at 6 months (after treatment) with the following scales:

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