Schizophrenia Research 150 (2013) 58–63

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

The role of negative symptoms in the context of cognitive remediation for schizophrenia

Aida Farreny [a,*], Jaume Aguado [a,b], Susana Ochoa [a], Josep Maria Haro [a], Judith Usall [a]

[a] Parc Sanitari Sant Joan de Déu, Fundació Sant Joan de Déu, CIBERSAM [1], Spain
[b] University of Barcelona, Barcelona, Spain

ARTICLE INFO

Article history:
Received 5 April 2013
Received in revised form 24 July 2013
Accepted 10 August 2013
Available online 29 August 2013

Keywords:
Cognitive remediation
Schizophrenia
Neurocognition
Negative symptoms
Functional outcome
Mediated effects

ABSTRACT

Background: It has been suggested that the effect of cognitive remediation (CR) on functioning is mediated by the improvement in neurocognitive domains; especially executive function. However, the correlations are generally moderate and this has prompted the search for other mediators including negative symptoms (NS).
Aims: To investigate whether the effect of CR on functioning could be mediated by executive function and/or NS.
Method: In a previous study, 62 outpatients with schizophrenia were randomized to 32 group sessions of REPYFLEC CR or leisure activities. Functioning (Life Skills Profile; LSP), NS (PANSS) and executive function (Behavioral Assessment of the Dysexecutive Syndrome; BADS) were measured at baseline and post-therapy. To assess how the effect of REPYFLEC CR is expressed in functioning at post-treatment, an autoregressive mediation model was employed.
Results: There was a significant effect of the REPYFLEC CR compared with the control group in improving BADS total score and PANSS NS. There was also a significant association between NS and functioning while executive function was not significantly related to functioning. Finally, there was a significant intervention effect on functioning mediated by NS but not by executive function.
Conclusion: It is apparent that improving executive function does not lead directly to improved functional outcome and that NS might be closely linked to functioning in the context of our study.

1. Introduction

Cognitive remediation (CR) treatments in schizophrenia were designed to improve neurocognition on the assumption that progress in functioning might be mediated in this way. It has been suggested that the effect of CR on functioning is mediated by the improvement in specific neurocognitive domains (Vita et al., 2011), especially through executive function (Wykes et al., 2007; Penadés et al., 2010) and in particular, by planning improvement (Wykes et al., 2012). However, the correlations are generally moderate; accounting only for 20%–60% of the variance in functional outcome (Green et al., 2000), this has prompted a search for other variables that may account for the effect on real world performance such as negative symptoms (Greenwood et al., 2005; Bowie et al., 2008; Ventura et al., 2009; Bowie et al., 2010; Lin et al., 2013).

Some theoretical grounding has proposed that negative symptoms (NS) could be an important moderating (Greenwood et al., 2005) or mediating (Lipkovich et al., 2009; Ventura et al., 2009; Lin et al., 2013) mechanism in the relationship between neurocognition and functional outcomes in schizophrenia. However, to the best of our knowledge, the role of NS in the context of CR has not yet been explored. One possible explanation for this may be the small effect that is found in psychiatric symptoms after CR treatments (McGurk et al., 2007; Wykes et al., 2011) that no longer seem significant at follow-up (Wykes et al., 2011). Nevertheless, some authors have stated that even very small improvements may have an impact on learning skills or future functioning (Wykes and Spaulding, 2011). In addition, CR meta-analyses tend to study psychiatric symptoms without distinguishing between positive, negative and general psychopathology despite the likely heterogeneity within their expression and phenomenology that could complicate the understanding of symptoms in the context of CR.

There is evidence to suggest that patients with higher NS severity have poorer social competence and quality of life (i.e. Harvey et al., 2006; Kirkpatrick et al., 2006; Bowie et al., 2008; Klingberg et al., 2011), as well as neurocognitive deficits, and these have been a consistent determinant of psychosocial functioning in several studies (i.e. Green et al., 2000; Bowie et al., 2008; Penadés et al., 2010; Vita et al., 2011). As such, in the light of their collective impact on outcome, the link between NS and neurocognition in schizophrenia has also garnered considerable attention. Some authors have argued that NS

* Corresponding author at: Parc Sanitari Sant Joan de Déu, Research Unit, Dr. Antoni Pujadas, 42, Sant Boi de Llobregat, 08830 Barcelona, Spain. Tel.: +34 936406350; fax: +34 935569674.
E-mail address: afarreny@pssjd.org (A. Farreny).
[1] **C**entro de **i**nvestigación **b**iomédica **e**n **r**ed de **sa**lud **m**ental.

0920-9964/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.schres.2013.08.008

may be underpinned by neurocognitive deficits such as the impaired initiation of novel responses (Frith, 1992; Greenwood et al., 2008); and others have speculated that patients with higher levels of NS have particular impairments in reasoning and executive function (Villalta-Gil et al., 2006; Ventura et al., 2009). However, several studies have failed to establish a relationship between NS and neurocognition, leading to the conclusion that they represent semiautonomous disease processes (Bell and Mishara, 2006; Harvey et al., 2006; Kirkpatrick et al., 2006; McGurk et al., 2007; Lipkovich et al., 2009; Foussias and Remington, 2010).

A further critical issue concerns how best to measure NS within schizophrenia due to the features in the definition of NS and neurocognition that blur conceptual boundaries. Therefore, the correlation between neurocognition and NS may vary as a function of the definition of the NS construct (Harvey et al., 2006; Foussias and Remington, 2010). For instance, the *Positive and Negative Syndrome Scale* (PANSS) (Kay et al., 1987) is one of the most commonly used clinical rating scales for schizophrenia although some aspects of the illness appear to be cognitive in nature, such as deficits in abstract reasoning and stereotyped thinking, which are defined as NS and contribute to total scores on this dimension. Consequently, numerous authors have proposed differentiated factorial approaches to reduce confusion between NS and other domains such as neurocognition or functionality, suggesting that a five-factor model better characterizes PANSS data (Wallwork et al., 2012). It seems that this matter is still unresolved and there is no clear consensus on what factors proposed for the PANSS most appropriately group the psychiatric symptoms within schizophrenia.

Based on our preceding study which showed that patients in the CR group obtained significant improvements in executive function, NS and functional outcomes compared with patients in the control group (Farreny et al., 2012), our purpose was to explore possible underlying mechanisms in the context of CR, with a main focus on the role of NS. Previously, Wykes et al. (2012) explored whether there is evidence of neurocognition playing a mediating role in the relationship between CR and improved functioning. The mediator (planning improvement) was able to account for a proportion of the total effect on work quality and although there were other changes in cognition (memory and flexibility) these do not necessarily drive the key changes in outcome.

Thus, we hypothesized the mediating variables should be, at least, those showing significant improvement after CR and our first aim was to explore whether the putative effect of our treatment on functioning could be mediated by executive function and/or NS. In addition, we aimed to study cross-sectional and longitudinal associations between executive function, NS and functional outcomes to gain a better understanding of the mediation mechanism.

2. Method

2.1. Design

The study was a randomized controlled trial with 62 outpatients diagnosed with schizophrenia or schizoaffective disorder. The participants were randomized to 32 group sessions of REPYFLEC CR or to 32 group sessions of stimulating activities without specific objectives and focused on leisure.

2.2. Participants

Participants in the study were outpatients between 18 and 60 years, from the Barcelona metropolitan area, known to the Parc Sanitari Sant Joan de Déu Mental Health Services, who had been diagnosed at least two years previously with schizophrenia or schizoaffective disorder (American Psychiatric Association (APA) et al., 2002). Additional selection criteria included: finished primary studies or ability to successfully complete a reading comprehension task used for 13-year-old students; a Mini Mental State Examination score of 24 or more; and a Global Assessment of Functioning score between 40 and 70.

Patients were excluded if: 1) they were suffering acute illness exacerbation that required hospitalization; 2) they had intellectual disability or any identifiable neurological disorder; 3) they were participating in any type of psychological intervention (i.e., social skills training, cognitive remediation, cognitive behavioral therapy) differing from usual care; 3) they had a switch of antipsychotic drug the month before the trial or during the study period, and/or a diagnosis of alcohol or drug dependence within 6 months prior to inclusion.

2.3. Outcome measures

Neurocognition, functioning and psychiatric symptoms were measured at baseline and thereafter at 16 weeks (post-treatment).

2.3.1. Neurocognition

Behavioral Assessment of the Dysexecutive Syndrome (BADS) (Wilson et al., 1996). This battery consists of six tests and evaluates cognitive flexibility, inhibition of impulsive responses, planning and organization, working memory and time-estimation capacity. For each of the subtests a summary profile score is obtained (maximum of 4 and minimum of 0), and these are added together to produce an overall battery profile score (out of 24). All subtests (Rule shift cards, Action program, Key search, Temporal judgment, Zoo map and Six elements) were administered. We used the standardized score (mean: 100, standard deviation (SD): 15) for the total with a minimum of 12 and maximum of 129, with a higher score indicating better performance.

2.3.2. Functioning

The Spanish validation (Fernández de Larrinoa et al., 1992) of the *Life Skills Profile* (LSP) (Rosen et al., 1989) was used to assess functional outcome. This scale measures the overall level of functioning in people with chronic mental disorders in daily-living situations and tasks. The LSP consists of 39 items organized into five subscales: self-care; interpersonal behavior; social contact and communication; social relationships; and personal autonomy. Information is initially self-reported but subsequently contrasted with other observers (e.g. therapists, nurses, family members), providing an objective assessment of everyday abilities or achievements. The Spanish version has demonstrated high rates of internal consistency, inter-rater reliability and concurrent validity; and has been shown to be a good predictive scale in different clinical areas (Ballesteros-Rodríguez et al., 2002). Raw scoring was used for the total (min. 39–max. 156) with a higher score indicating a better result.

2.3.3. Psychiatric symptoms

The Spanish validation (Peralta and Cuesta, 1994) of the *Positive and Negative Syndrome Scale* (PANSS) (Kay et al., 1987) was used. Its items were originally grouped into scales for positive symptoms (7 items), negative symptoms (7 items) and general psychopathology (16 items). The interviewers administered the PANSS as part of a structured clinical interview and scored items on a scale from 1 (asymptomatic) to 7 (extremely symptomatic). Two distinct factorial proposals for negative symptoms are considered in this study:

Firstly, we considered the classical approach with the three-factor PANSS including positive and negative symptoms and general psychopathology (Kay et al., 1987). Regarding negative symptoms, this factor includes 7 items: blunted affect, emotional withdrawal, poor rapport, passive-apathetic social withdrawal, lack of spontaneity, difficulty in abstract thinking and stereotyped thinking. And secondly, we applied the recent model by Wallwork et al. (2012) that considered previous five-factor models and used a strong methodological approach to find the best consensus model for the PANSS. This resulted in a solution that distinguishes between positive, negative, disorganized, excited and depressed factors. The negative factor includes 6 items: blunted