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Targeting anxiety to improve quality of life in patients with schizophrenia

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ABSTRACT

Background: Several studies suggested that anxiety can significantly affect the outcome of schizophrenia. Despite this evidence, non-pharmacological interventions targeting anxiety are still heterogenous. This study aims to test the efficacy of a novel training specifically designed to target anxiety in patients with schizophrenia. Innovatively, this training, beyond psychoeducation and problem solving, also targets Theory of Mind, as it provides coping strategies.

Method: Twenty-seven outpatients with schizophrenia received a novel rehabilitative training targeting anxiety (Anxiety Management Group [AMG]) combined with a Computer-Assisted Cognitive Remediation (CACR), and twenty received CACR plus a control intervention (Control Newspaper discussion Group [CNG]). All patients were assessed at baseline and after treatment for quality of life, neurocognition and anxiety.

Results: After training, patients treated with AMG + CACR showed significantly greater improvements on anxiety. A significant increase in quality of life was observed only for AMG + CACR group. Moreover, the participants' appraisal showed a significant difference between treatment groups with higher ratings among patients who received the AMG + CACR.

Conclusions: This study thus suggests feasibility and efficacy of the proposed intervention, that could be implemented in rehabilitative programs for patients with schizophrenia with potential benefits also on disease course and outcome.

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1. Introduction

Anxiety is commonly observed in schizophrenia [1,2] and high levels of stress can affect outcome, although the mechanisms have not been clarified yet [3–8]. Specifically, anxiety seems to trigger a decline in daily functioning, quality of life, self-esteem and self-efficacy [4,5,9–11]; symptoms exacerbation or relapse [7–9,12]; greater distress [12], as well as higher rates of suicide [13]. The relationship between anxiety and clinical consequences might be associated to coping strategies used by patients [12]. In schizophrenia, coping strategies seem to be maladaptive due to the symptoms, such as delusions and hallucinations [12,14,15], as well as to cognitive impairment [16]. Neurocognitive deficits could interfere with appraisal processes and response to stressors,

leading patients to choose ineffective strategies, such as avoiding the problem or isolating themselves [12]. Indeed, impairments in sustained attention, executive functions and memory are related to poorer problem solving and maladaptive coping [16–18]. Despite these premises, only few non-pharmacological treatments targeting anxiety in patients with schizophrenia have been reported, mainly through case report and open trials [3] and not addressing cognitive deficits. Most studies used progressive muscle relaxation techniques, not specifically designed for patients with schizophrenia, to reduce state anxiety, with inconclusive results [19]. One of the first stress management group therapies was introduced by Starkey, adapting a previous intervention, consisting of relaxation training, social skills development and emphasis on personal control [20]. To our knowledge, only one study included a structured stress management program to a rehabilitation intervention already combining pharmacological and psychosocial treatment, suggesting that it may provide patients with skills for coping with acute stressors and reduce the likelihood of

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subsequent acute exacerbation of symptoms with need for hospitalization [21].

To sum up available data, although still sparse and heterogeneous, but the data highlight the potential clinical relevance of rehabilitation intervention targeting the way patients manage anxiety in response to daily, familial and symptom-related stressors. Clearly, further research is required [1]. Evidence also suggests a key role of neurocognitive deficits in determining increased levels of anxiety, leading to the hypothesis that conjointly treating anxiety and cognitive deficits might be even more effective in improving patients' quality of life and course of the illness.

In line with these observations, the current study evaluates the feasibility and effectiveness of a newly developed intervention targeting anxiety symptoms (Anxiety Management Group [AMG]) combined with a specific training for neuropsychological dysfunctions (Computer-Assisted Cognitive Remediation [CACR]), in a sample of clinically stabilized outpatients diagnosed with schizophrenia.

Our primary aim is to investigate the effects of the combined intervention on both anxiety and quality of life while evaluating the degree of patients' satisfaction relative to the treatment. Our secondary goal is to examine the possible relationship between anxiety, neurocognition, psychopathology and functioning.

2. Materials and methods

2.1. Study design

This study evaluated the effectiveness of a combined intervention including computer-assisted cognitive remediation (CACR) and a novel rehabilitative training targeting anxiety (Anxiety Management Group [AMG]), compared to CACR plus a control intervention (Control Newspaper discussion Group [CNG]), balanced for treatment frequency and intensity.

We compared data from two different protocols performed at different time points. The control group was indeed selected from a previous randomized single blind trial performed to evaluate effectiveness of socio-cognitive training [22], while no randomization was performed for the CACR + AMG. All patients meeting inclusion criteria were naturalistically assigned to the intervention.

Both groups lasted 16 weeks and provided the same number of hours of rehabilitation treatment to all patients, (i.e. 3 hours of CACR plus 1 hour of AMG or CNG every week).

All patients were re-assessed within one week after the end of training.

All interventions were conducted by trained psychologists.

Raters were blind to the treatment condition.

The sample was composed of fifty-five outpatients with DSM-IV-R schizophrenia, recruited from the Department of Clinical Neurosciences, IRCCS San Raffaele Hospital of Milan. The diagnosis was ascertained by trained psychiatrists by using medical records and DSM-IV-R Structured Clinical Interview American Psychiatric Association [23]. Patients were all clinically stabilized since at least three months and responders to psychopharmacological treatments, as defined by a reduction $\geq 30\%$ of PANSS Total score. Exclusion criteria were: substance dependence or abuse, comorbid diagnosis on Axis I or II, major neurological illness, perinatal trauma and mental retardation. Patients had been treated with a stable dose of the same antipsychotic therapy for at least 3 months and remained on the same medication throughout the study. All subjects provided informed consent to a protocol approved by the local Ethical Committee, following the principles of the Declaration of Helsinki.

2.2. Assessments

2.2.1. Anxiety assessment

Anxiety was measured with the State Trait Anxiety Inventory form Y (STAI-Y; [24]), a 20-item questionnaire that asks participants to rate the extent to which they experience various manifestations of anxiety. Items produce a score about *trait anxiety*. Higher scores indicate higher levels of anxiety. Previous researches showed the reliability of this inventory used with patients affected by schizophrenia [12,25–27].

2.2.2. Quality of life

Quality of life was assessed with the Quality of Life Scale (QLS; [28]), a 21-item instrument that uses a seven-point rating scale. Specific anchors are provided for each item, with a score of 0 representing severely impaired quality of life and a score of 6 indicating high level of quality of life in regard to the specific item. The QLS assesses emotion and motivation, interpersonal relations, occupational role, and possession of common objects.

2.2.3. Appraisal of stress management treatment

After AMG was completed, patients were asked to complete a questionnaire created on the basis of an available measure [29,30], to evaluate the degree of patients' satisfaction relative to the treatment. The questionnaire focuses on areas such as usefulness to daily life, fun and recommendation of the training to other people. The patient has to express whether he agrees or not with 11 sentences, providing an open and critical feedback regarding their experience within the group treatment. Each sentence is rated on a five-point Likert scale (where 1 = fully disagree, 2 = disagree, 3 = not sure, 4 = agree, 5 = fully agree).

2.2.4. Psychopathological assessment

Global psychopathology was assessed by means of the Positive and Negative Syndrome Scale (PANSS; [31]) administered by trained psychiatrists.

2.2.5. Neuropsychological assessment

Cognition was evaluated with the Italian version of the Brief Assessment of Cognition in Schizophrenia (BACS; [32]), a neuropsychological battery designed in two versions (A and B) to evaluate patients before and after treatments, without the results being influenced by recall. The entire battery lasts approximately 30 minutes, and consists of the following tests: words recall (verbal memory); digit sequencing (working memory); token motor task (psychomotor speed and coordination); symbol coding (processing speed); semantic and letter fluency (verbal fluency); tower of London (executive functions) [33]. The test was administered by trained psychologists.

The scales were administered by trained rehabilitation therapists.

2.3. Interventions

Each group was formed by a minimum of 4 to a maximum of 8 patients. For each group session there was only one psychologist who guided the patients through the focus of the session. All interventions were conducted by trained psychologists with at least 5 years of experience in cognitive behavioral therapy with patients affected by schizophrenia.

2.3.1. Computer-assisted Cognitive Remediation Therapy (CACR)

CACR consisted of two 1-hour sessions/week of domain specific computer-aided exercises lasting 12 weeks (24 completed sessions). This program includes different neurocognitive exercises aimed at training specific cognitive areas among the ones known to

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