Targeting anxiety to improve quality of life in patients with schizophrenia

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

To sum up available data, although still sparse and heteroge-
nous, 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 dysfunc-
tions (Computer-Assisted Cognitive Remediation [CACR]), in a
sample of clinically stabilized outpatients diagnosed with schizo-
phrenia.

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 interven-
tion 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]), bal-
anced for treatment frequency and intensity.

We compared data from two different protocols performed
during 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 naturally 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 using by 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 treat-
ments, as defined by a reduction > 30% of PANSS Total score.
Exclusion criteria were: substance dependence or abuse, co-
morbid diagnosis on Axis I or II, major neurological illness,
perinatal trauma and mental retardation. Patients had been
brought 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
of 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 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 ses-
sions). This program includes different neurocognitive exercises
aimed at training specific cognitive areas among the ones known to

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