Advances in Bipolar Disorder Treatment
Chapter 1

Effects of Cognitive Remediation in Patients with Bipolar Disorder

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Abstract

Neuropsychological studies have demonstrated that patients with bipolar disorder have persistent cognitive impairments even during euthymic phases of the illness. Cognitive remediation is accepted as an important therapeutic intervention in schizophrenia, but few studies provide data on whether the benefits extend to affective disorders.

Our aim in this study is to review quantitatively studies of cognitive remediation with samples that included cases of bipolar disorder. Six studies were found. The estimated ES reflect those reported in the literature on cognitive remediation for schizophrenia. As such conservative interpretations that cognitive remediation has at least equivalent benefits in bipolar disorder as demonstrated in schizophrenia.

Further studies are needed to examine the durability of any gains with cognitive remediation in patients with bipolar disorder and to determine if any changes in cognitive deficits lead to improvements in symptoms or functioning and/or whether post-intervention cognitive changes differ in character or magnitude from those reported in schizophrenia.

Introduction

Bipolar disorder (BD) is characterized by recurrent episodes of depression and/or mania, along with interepisodic mood symptoms that interfere with psychosocial functioning.
Despite periods of symptomatic recovery, two thirds of individuals with BD experience impairments in psychosocial functioning, particularly occupational functioning.

There are two determinants of psychosocial functioning in patients with BD even during euthymic phases of the illness: residual depressive symptoms and cognitive impairment [1].

In this context, the development of cognitive remediation, a new psychological intervention, is a major hope for improving cognitive impairment and functional outcome.

**Neurocognitive impairment in BD**

Neuropsychological studies have demonstrated that patients with BD have persistent cognitive impairments even during euthymic phases of the illness [2].

These impairments include difficulties in processing speed, sustained attention, verbal and visual memory and executive functioning, with the most severe impairments in executive functions and verbal memory, that seem to represent a trait more than a state in bipolar disorder.

The concept of “executive function” refers to the higher order control processes necessary to guide behavior in a constantly changing environment.

It includes abilities such as: planning, working memory, mental flexibility, response initiation, response inhibition, impulse control and monitoring of action.

These impairments are estimated to: 0.5-1.5 SD compared to general population [3].

Cognitive difficulties, often self-reported by individuals with bipolar disorder include sluggish thoughts, difficulties focusing, getting started on tasks, organizing complex tasks and managing multiple projects, difficulties remembering, and becoming easily overwhelmed. These difficulties lead to important cost of lost productivity in individuals with bipolar disorder due to occupational impairment.

The aetiology of these deficits remains poorly understood. However, the implication of factors related to the biological/genetic vulnerability to BD is likely well as «neurotoxic» effects of major mood episodes, in particular acute manic episodes that seem to play an important role in the worsening of these deficits over time.

Given the high rates of neurocognitive impairments in BD and their relevance to functional outcome, these deficits should be considered among the primary targets for treatment. And given their poor response to pharmacological treatment, major initiatives are under way to find new non-pharmacological interventions for cognitive impairment.

In this context, the development of specific cognitive remediation strategies is therefore a major hope for improving the quality of remission and functional outcome.
Cognitive Remediation

Cognitive remediation (CR) is a behavioural training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition or metacognition) with the goal of durability and generalization (Wykes, 2010).

This intervention is based on the concept of brain plasticity and neurogenesis, and supports the idea that the brain is capable of changes and development throughout the lifespan.

While all CR programs focus on cognition, there is considerable diversity in specific approaches.

CR programs vary, depending on whether they:

- Use a restorative or a compensatory approach
- Use computers or paper and pencil tasks
- Are for individuals or groups.

Restorative approach attempts to directly repair impaired cognitive skills by using drill and practice exercises. Whereas compensatory approach do not attempt to restore the impaired cognitive skill but rather to compensate for, or circumvent the deficit with reliance on intact cognitive skills.

Most CR programs use computers, although some programs exclusively use paper and pencil tasks and verbal discussions.

CR can be delivered even to individuals or groups. When a group approach is used, there are differences in whether the group does the same activity all together or whether participants work independently on an individualized program of exercises [4].

The sessions are usually held 2 or 3 times a week. Active treatment typically lasts 3 to 6 months but can range from several weeks to 2 years, depending on the treatment setting, goals, and/or severity of deficits.

Much of the focus of CR during the last decade has centered on:

- Brain injury
- Schizophrenia spectrum disorders
- Anorexia nervosa
- Obsessive compulsive disorder
- Attention deficit hyperactivity disorder
- Autism spectrum disorder

Several quantitative reviews have indicated cognitive remediation interventions to be effective in reducing cognitive deficits and improving the functional outcome of schizophrenia [5,6].

The Use of CR in BD

Despite the well-documented evidence for cognitive impairments that are robustly associated with functional disability, there is very little research reporting on CR strategies
with BD.

**Table 1:** Structured protocols of cognitive remediation interventions for schizophrenia.

<table>
<thead>
<tr>
<th>Cognitive training</th>
<th>Full name</th>
<th>Target</th>
<th>Computer assisted/Not computer assisted</th>
<th>Restorative/compensatory</th>
<th>Drill and practice</th>
<th>Individually tailored</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPT</td>
<td>Integrated Psychosocial Therapy</td>
<td>Cognitive functions, social skills and problem solving</td>
<td>Not computer assisted</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>INT</td>
<td>Integrated Neurocognitive Therapy</td>
<td>Cognitive functions and social cognition</td>
<td>Both</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CRT</td>
<td>Cognitive Remediation-Therapy</td>
<td>Cognitive functions</td>
<td>Not computer assisted session</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Cogpack</td>
<td>Cognitive Enhancement Therapy</td>
<td>Cognitive functions and social cognition</td>
<td>Computer assisted</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CET</td>
<td>Cognitive Enhancement Therapy</td>
<td>Cognitive functions and social cognition</td>
<td>Both</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>NEAR</td>
<td>Neuropsychological Educational Approach to Remediation</td>
<td>Cognitive functions and problem solving</td>
<td>Both</td>
<td>Restorative</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>NET</td>
<td>Neurocognitive Enhancement Therapy</td>
<td>Cognitive functions and social cognition</td>
<td>Both</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CAT</td>
<td>Cognitive Adaptation Training</td>
<td>Cognitive functions</td>
<td>Not computer assisted</td>
<td>Compensatory</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>TAR</td>
<td>Training of Affect Recognition</td>
<td>Social cognition</td>
<td>Both</td>
<td>Both</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SCIT</td>
<td>Social Cognition and Interaction Training</td>
<td>Social cognition</td>
<td>Both</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>SCST</td>
<td>Social Cognitive Skills Training</td>
<td>Social cognition</td>
<td>Both</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>SCET</td>
<td>Social Cognition Enhancement Training</td>
<td>Social cognition, ToM</td>
<td>Not computer assisted</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>MCT</td>
<td>Metacognitive Training</td>
<td>Metacognition</td>
<td>Not computer assisted</td>
<td>Restorative</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SSANIT</td>
<td>Social Skills and Neurocognitive Individualized Training</td>
<td>Cognitive functions, social cognition and social skills</td>
<td>Both</td>
<td>Restorative</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Seven studies of CR with samples including cases of BD were found. Five of them showed improvement in several areas of cognition.

In fact, Choi et al. in their study in 2005 included 48 patients, 26 of them received a diagnosis of a schizophrenia spectrum disorder, 10 a diagnosis of BD type I, 11 Major depressive disorder (MDD) and one Psychosis not otherwise specified. All participants completed 26 hours of computer-assisted cognitive exercises, delivered twice a week, over 13 weeks. Participants showed significant improvement in cognition and work-related behavior with an (effect-size (ES):0.55) [7].

McGurk et al. carried out a study including 44 patients in 2005, among whom 10 had BD. Participants were randomly assigned to receive either cognitive training and supported employment (CT+SE) or supported employment only (SE Only). They received 24 hours of computer-based cognitive exercises (Cogpack, version 6.0). Sessions require 45–60 minutes to complete, with patients usually completing two–three sessions per week for a total duration of about 12 weeks. Patients who participated in the program showed significantly greater improvements in several areas of cognitive functioning, as well as in depression, distress and self-esteem (ES = 0.33)[8].

A third study was undertaken Deckerbach et al. in 2010. It included 18 patients with BD and consisted of 50 minutes per week of non-computerized program, over 16 weeks. An improvement of residual depressive symptoms
and functioning was described. Patients with greater cognitive impairment tended to benefit less from the intervention (ES= 0.57) [1]. In their study, Martinez-Aran et al in 2011, involved a novel CR approach, which they have coined functional remediation, a treatment that integrates psychoeducation and CR strategies within an ecological framework. Treatment consisted of 21 weekly sessions of 90 minutes. Although this study is under way, authors suggested that functional remediation may be an important avenue for increasing the tranference of skills to daily functioning in people with BD [9].

Torrent et al, in 2013, carried out a multicenter randomized, rater-blind clinical trial including 239 patients with BD. Functional remediation (N=77) was compared with psychoeducation (N=82) and treatment as usual (N=80). The functional remediation program consisted of 21 weekly sessions each lasting 90 minutes. Patients were trained by paper-and-pencil exercises. Functional remediation differed significantly from treatment as usual, but not from psychoeducation (ES = 0.93) [10].

In their study, Meuselet al in 2009, investigated a special cognitive domain, which is working memory. They evaluated the efficacy of a Computer-assisted CR program, conducted over 10 weeks. Following completion of the treatment, participants improved on measures of delayed recall and working memory. It was observed that gains in cognitive functioning were positively correlated with psychosocial functioning.

Demant et al in 2013 are conducting a study to measure effects of cognitive remediation on cognitive dysfunction in partially or fully remitted patients with bipolar disorder. 40 patients with BD were included. Patients are randomized to receive weekly group-based CR treatment over 12 weeks in addition to standard treatment or standard treatment only. This study is under way [11].

According to literature, emerging evidence suggest that CR is an effective intervention for BD, and that these treatment effects translate into improvements in cognitive performance and possibly functioning.

Treatment outcome was influenced by:

- Treatment intensity
- Type of cognitive remediation program
- Therapist qualifications
- Patient levels of motivation
- Baseline sets of work habits
- Illness factors

Illness factors were the least likely to influence treatment outcome. The benefits of CR translate to practical gains for the participants.

The clinical skills developed can be readily applied to meaningful vocational goals, a point well taken by patients and staff and by itself a motivating factor for program participation.
Table 2: Studies of CR including cases of BD.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Participants number</th>
<th>Diagnosis</th>
<th>Methods</th>
<th>Duration</th>
<th>Outcome</th>
<th>ES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choi</td>
<td>2005</td>
<td>26 SKZ</td>
<td></td>
<td>26 hours of computer-assisted cognitive skills training and exercises</td>
<td>13 weeks</td>
<td>Improvement in cognition and work-related behavior</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 BD I</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>11 MDD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 PNOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McGurk</td>
<td>2005</td>
<td>32 SKZ</td>
<td></td>
<td>24 hours of computer-based cognitive exercises (called COGPACK)</td>
<td>12 weeks</td>
<td>Improvement in cognitive functioning with improvement in depression, distress and self-esteem</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 SAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 BD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meusel</td>
<td>2009</td>
<td>9 BD/MDD</td>
<td></td>
<td>Computer-assisted CR program</td>
<td>10 weeks</td>
<td>Gains in cognitive functioning correlated with psychosocial functioning</td>
<td>NS</td>
</tr>
<tr>
<td>Deckerbach</td>
<td>2010</td>
<td>15 BD I</td>
<td></td>
<td>50 mins per week of non-computerized programme</td>
<td>16 weeks</td>
<td>Improvements in executive functioning and increased overall psychosocial functioning</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 BD II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Torrent</td>
<td>2013</td>
<td>239 BD</td>
<td></td>
<td>90 minute weekly sessions of paper-and pencil exercises</td>
<td>21 weeks</td>
<td>Improvement in cognitive and in functional domains</td>
<td>0.93</td>
</tr>
<tr>
<td>Martínez-Aran</td>
<td>2011</td>
<td>BD</td>
<td></td>
<td>Functional remediation program .21 weekly sessions of 90 minutes</td>
<td>Still underway</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demant</td>
<td>2013</td>
<td>40 BD</td>
<td></td>
<td>Weekly group-based CR treatment over 12 weeks in addition to standard treatment, or standard treatment only</td>
<td>Still underway</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Psychoeducation in BD

It is defined as any intervention that educates patients and their families about their illness with a view to improving their long-term outcome. It involved illness awareness, detection of prodroms, adherence enhancement, substance use avoidance, regular habits and stress management. It has become considerably effective in increasing the functioning levels of patients with BD, with a long-term maintained efficacy [12].

Conclusion

Given that CR is only ‘one side of the coin’ it will also be relevant to look at the possible adjunctive use of CR with other psychological therapies such as psycho-education or cognitive behaviour therapy, especially for those with more difficult to treat problems.

References


