

## REVIEW ARTICLE

# Cognitive dysfunction in schizophrenia and mood disorders and its treatment program: a comprehensive review

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## Abstract

Recently, cognitive dysfunction in psychiatric disorders has received much attention. Especially, remediation and training therapy for neurocognition and social cognition have been intensively studied. In this comprehensive review, we summarized previous findings on cognitive dysfunction in schizophrenia and mood disorders. We also introduced several major programs of Cognitive Remediation Therapy (CRT). CRT can be divided into restorative approaches that directly improve the cognitive functioning of the individual and compensatory approaches that modify the environment and human support. We suggested that these CRT programs has some characteristics and advantages compared to other conventional therapies including pharmacotherapy and psychological approaches.

## INTRODUCTION

Recently, cognitive dysfunction in psychiatric disorders has received much attention and the effects of therapeutic interventions have been reported. Cognitive functioning is the process of taking in information, collating, processing, judging, and expressing (Yamauchi, 2002). Cognitive function is related to various brain functions, which include a wide range of concepts. In this paper, we state that cognitive dysfunction can be divided into “neurocognition” and “social cognition” (Inadomi, 2018). Cognitive dysfunction prevents people from smoothly performing all the activities of daily living and social life. Therefore, it is widely accepted that the treatment of cognitive dysfunction is important. In this paper, we have introduced cognitive dysfunction, primarily in schizophrenia and mood disorders, and discussed the treatment, cognitive improvement therapy.

## NEUROCOGNITION

Neurocognition is a basic brain function used for various information processing, including memory, attentional functions, and executive functions (Ikebuchi, 2012). Memory is the function to retain an experience and to reproduce it in some form. Memory can be divided into short-term memory, working memory, episodic memory, semantic memory, and procedural memory, depending on the duration of retention and whether it is verbally expressed or not. Memory im-

pairment causes people to forget past events or tasks that others have asked them to do (Kaneda, 2013).

Attention can be classified into three categories: intensity (maintenance of attention, vigilance), selection (selection function, direction of attention), and control (control function, execution). Attention disorders can make it difficult for people to concentrate on watching TV programs or to pay attention to their surroundings and focus on the desired object.

Executive function is responsible for planning, execution, and monitoring. They are necessary for the effective accomplishment of a series of purposeful actions. For example, executive function impairment makes it difficult for people to plan, organize, and prepare a menu for cooking. As mentioned above, neurocognitive impairments have significant impacts on our lives.

## SOCIAL COGNITION

Social cognition is a more complex cognitive function related to emotions, interpersonal skills, and social life (Penn, 1997). Social cognition is defined as “consisting of the mental activities underlying social interaction, including the human capacity to perceive the intentions and nature of others” (Penn, 1997). It is considered an important cognitive function for smooth social life. There are two major streams of research on social cognition: one is the research that started in the UK to understand psychiatric symp-

toms such as delusions through the relationship between social cognition and thought disorder, and the other is the research that deals with the relationship between functional level and social cognition mainly in North America (Nemoto, 2009). The subordinate concepts of social cognition include emotional cognition, social perception, the theory of mind, and attribution style (Penn, 2008).

Emotional cognition and social perception refer to the perception of social signs such as reading facial expressions and gestures. These disorders can cause people to mistake other people's smiles for mockery, or to mistake friendly gestures for hostility.

The theory of mind is the ability of humans and apes to make assumptions about the beliefs and intentions of others. Due to disorders of the theory of mind, people assume that others must know what they know, and this can lead to interpersonal problems. The theory is sometimes described mixed with the ability to empathize. However, while the theory of mind is the ability to assume others' beliefs and intentions, empathizing is the ability to imagine others' emotions such as joy and sadness, and they are different abilities (Hynes, 2006).

The attribution style refers to how we explain the causes of various events, and are classified into two main categories: internal factors such as abilities and intention, and external factors such as circumstances and chance. For example, attribution bias causes people to blame others unilaterally when bad events occur, or to blame themselves for all bad events, resulting in low self-esteem (Penn, 2008). Thus, impairments in social cognition can affect social life and cause interpersonal problems.

## **THE RELATIONSHIP BETWEEN NEUROCOGNITION AND SOCIAL COGNITION**

It has been reported that neurocognition and social cognition are weakly related but different, and that social and nonsocial stimuli are processed by different neural systems (Green, 2005). It has been reported that social cognition directly affects social functioning, while neurocognition affects social functioning through social cognition (Fett, 2011). Also, in a meta-analysis, social cognition mediated neurocognition and social outcomes in patients with schizophrenia (Halverson, 2019).

One study showed that the association between neurocognition and social functioning was mediated by social cognition (Addington, 2010). And in a 12-month prospective study of patients with first-

isode psychosis, negative symptoms mediated cognition and social outcomes, and neurocognition and role outcomes (Griffiths, 2021). Further research will be conducted and discussed in the future.

## **COGNITIVE DYSFUNCTION IN SCHIZOPHRENIA**

In 1899, Kraepelin suggested that patients with schizophrenia have neurocognitive dysfunction, but it remained a hypothesis for a long time (Kraepelin, 1986). The cognitive dysfunction in patients with schizophrenia has been attracting attention since the late 1900s, and the studies have gradually been reported in the early 2000s. A meta-analysis of 47 studies found that patients with first-episode schizophrenia had moderate to major deficits in neurocognition in general, especially in the processing speed and verbal memory (Meshulam, 2009). In a comprehensive study of cognitive dysfunction, patients with schizophrenia and healthy controls were administered 41 different neuropsychological tests. The results showed that patients had impaired overall neurocognitive functioning, including verbal fluency, memory, attention, and executive function. In addition, the learning/memory deficits were the most discriminating between patients with schizophrenia and healthy controls. Moreover, the executive function/attention deficits in patients were most associated with the social outcome (Bilder, 2000). A systematic review investigating the relationship between neurocognition and job performance in patients with schizophrenia suggested that neurocognition influences employment, vocational rehabilitation, and job skills. It has been reported that neurocognition is also important for patients with schizophrenia to perform their jobs (Christensen, 2007).

Next, we discuss the social cognition of patients with schizophrenia. In a report reviewing 86 studies conducted between 1970 and 2007, patients with schizophrenia were asked to perform an emotion discrimination task in which they responded to the emotional state of a single facial expression stimulus and an emotion recognition task in which they were asked to rate the degree of category or emotion expression or dissimilarity for a pair of facial expressions. In both tasks, they were found to be poorer than healthy controls (Kohler, 2010). It has also been reported that patients with schizophrenia have a more diminished emotional recognition of unpleasant emotions such as fear, disgust, and sadness of others. In a videotape task, they had impaired social perception (Cor-

rigan, 1993). Using a task of rearranging the cartoon panels into a rational order by inferring mental states, patients with schizophrenia have impaired the theory of mind (Frith, 1996). Attribution studies have reported that patients with paranoia tend to blame the “other person” rather than the “situation” for negative events (Bentall, 2001). In a meta-analysis of 46 studies, social cognition of patients with schizophrenia was most strongly associated with the current and long-term occupational functioning, with a moderate effect size (Cowman, 2021). In another meta-analysis, poor insight in patients with schizophrenia was weakly associated with neurocognition but moderately correlated with the theory of mind, a form of social cognition (Subotnik, 2020). This suggests that treatment specifically targeting social cognition is important for improving occupational functioning and the insight in schizophrenia.

### **COGNITIVE DYSFUNCTION IN MOOD DISORDERS**

In mood disorders, the number of reports is lower than in schizophrenia, but research was rapidly accelerated after it was reported in 1975 that “both mild and severe depression has marked deficits in cognitive, motor, perceptual, and communicative tasks” (Miller, 1975). A recent meta-analysis reported that patients with major depression had deficits in verbal memory, visual memory, verbal fluency, and working memory, while patients with bipolar disorder had deficits in verbal memory, visual memory, and executive functioning, all of which were mild compared to patients with schizophrenia (Keefe, 2007). It has also been reported that executive functions are impaired during the depressive phase and remain impaired during remission, suggesting the importance of neurocognitive treatment in mood disorders (Nakano, 2008).

In social cognition, a paper reviewing 18 studies reported that patients with major depression showed a decline in the theory of mind compared to healthy controls, and that impairments in the theory of mind were significantly related to the severity of depressive symptoms (Bora, 2016). In an emotion recognition task, it has been reported that patients with major depression have a perceptual bias toward unpleasant emotions, such as sadness and anger, and are hypersensitive to them compared to healthy controls (Liu, 2012). In a meta-analysis, patients with schizophrenia were significantly lower in both the facial emotion recognition and the theory of mind compared to patients

with bipolar disorder (Bora, 2016). This suggests that although cognitive impairment is also reported in major depression and bipolar disorder, it is more severe in schizophrenia.

### **COGNITIVE REMEDIATION THERAPY**

Traditional classical cognitive training consists of repetitive training. As an example, it has been reported that the patient repeat a sustained execution test in response to a specific stimulus, which showed little improvement (Benedict, 1989). It has also been reported that patients with schizophrenia can improve their memory using encoding strategies (Koh, 1976). Furthermore, it has been reported that monetary rewards and verbal encouragement significantly improve the reaction time of patients with schizophrenia (Steffy, 1980). However, these studies were designed to test theories of cognitive dysfunction, not to develop treatments.

At the 2010 International Schizophrenia Research Conference, Cognitive Remediation Therapy (CRT) was defined as “a behavioral training-based intervention aimed at improving cognitive processes (attention, memory, executive functioning, social cognition or metacognition) with sustained and generalized improvement” (Matsui, 2018). In other words, CRT trains cognitive skills to function more effectively in school, work, and life. For example, in school or work, the goal of CRT is to help patients focus more and complete tasks more efficiently. CRT is an umbrella term, and various interventions have been reported for CRT, which are listed in Table 1.

CRT approaches can be divided into two main categories: restorative and compensatory approaches (Medalia, 2009). The restorative approach is based on the hypothesis of neuroplasticity of the brain, and patients improve their brain and cognitive functions by doing tasks that involve specific neurological activities. Various methods have been developed, such as implementing repetitive practice using drills and engaging in computer games. In contrast, the compensatory approach is to modify the environment and human support to compensate for cognitive dysfunction. Compensatory programs are assisted by structured calendars, medicine containers, and other aids that are designed to promote adaptive behavior in the home, institutional settings, and other settings, and to help them develop strategies for remembering tasks and objects (Maples, 2008; Velligan, 2000).

A meta-analysis comparing restorative and compensatory approaches in brain imaging found that

**Table 1.** Major cognitive improvement therapies reported (partially modified from the paper by Matsui)

Developer (Country)	Type
Delahunty A. (Australia)	Frontal/Executive Program; FEP
Brenner H. (Switzerland)	Integrated Psychological Therapy; IPT
Hogaty G.E. (USA)	Cognitive Enhancement Therapy; CET
Bell M. (USA)	Neurocognitive Enhancement Therapy; NET
Medalia A. (USA)	Neuropsychological Educational Approach to Rehabilitation; NEAR)
Sohlberg M.M. (USA)	Attention Process Training; APT
Silverstein S.M. (USA)	Shaping of Attention
Penn D.L. (USA)	Social Cognition and Interaction Training; SCIT
Twamley E.W. (USA)	Compensatory Cognitive Training; CCT
Moritz S. (Germany)	Metacognitive Training; MCT
Ikebuchi E. (Japan)	Vocational Cognition Ability Training by Jcores; VCAT-J

the former activates more targeted brain regions, while the latter promotes a more extensive activation of brain networks, and it is unclear which approach is more advantageous (Bon, 2018). A meta-analysis of 130 studies examining the effectiveness of CRT found that CRT was effective for cognition ( $d = 0.29$ ) and function ( $d = 0.22$ ). Important factors for effectiveness included “active and trained therapists,” “development of structured cognitive strategies” and “integration with psychosocial rehabilitation.” Additionally, candidates for the best target population included “fewer years of education,” “lower pre-morbid IQ” and “severity of baseline symptoms” (Vita, 2021).

### CRT PROGRAMS

The following are some of the major cognitive remediation programs as packages.

#### **Neuropsychological Educational Approach to Cognitive Remediation (NEAR)** (Medalia, 2002)

NEAR is one of the restorative approaches to CRT that focuses on neurocognition (Medalia, 2002). It consists of theoretical background in neuropsychology, behavioral and learning theories such as errorless learning and modeling, and educational psychology such as intrinsic motivation (Hodge, 2010). The aim of NEAR is not only to improve neurocognitive functioning, but also to promote the learning skills and attitudes, and to improve neurocognitive functioning in daily life and social situations (Medalia, 2009). The content and frequency of the program consist of two computer-based cognitive task sessions per week and one language session per week (Medalia,

2009). In the cognitive sessions, for example, game software such as “handing out menus to customers in a restaurant, taking their orders, delivering food on time, and placing the bills on the table” is used as tasks for attention allocation and executive functions. In the language session, bridging the content of the cognitive task session to real-life situations is conducted in a group work format (Medalia, 2002). Each session lasts about 60 minutes, and the recommended duration of the program is six months to one year. NEAR improves attention, problem-solving skills, working memory, processing speed and reaction times, and psychiatric symptoms in patients with schizophrenia (Medalia, 2002).

#### **Social Cognition and Interaction Training (SCIT)** (David, 2012)

SCIT is a program with a restorative approach focusing on social cognition (David, 2012). In SCIT, the process is emphasized, and the goal is to improve various functions that make up social cognition. It is based on the social cognition model of schizophrenia, including attributional style, the theory of mind, emotion recognition, and intolerance to uncertainty (Roberts, 2014). The content of the SCIT consists of 20 to 24 sessions and is divided into three parts. The first part is “Introduction and Emotional Training,” in which the patients learn the concepts of social cognition and the definition of emotions and is trained to identify emotions from facial expressions (David, 2012). The goal is to improve patients’ emotional perception using still and moving images and scenarios about social situations. The second part is “situational awareness,” which focuses on the attribution and

helping patients develop social cognitive strategies to avoid mistakes they tend to make in social situations (David, 2012). The third part is “Integration and confirmation,” in which patients are given a problem in their daily life and they work in groups to suggest a behavioral strategy based on the SCIT skills, aiming to strengthen and generalize the acquired skills (David, 2012). At the end of each session, homework is assigned, and at the beginning of the next session, a review of the homework is conducted. Five to eight people work in groups, each session lasts about 60 minutes, and takes about six months to complete. Mental health professionals who have been involved for treating patients with schizophrenia are considered to be the most appropriate therapists (David, 2012). As for the effects of SCIT, it improves hostility bias, which is the tendency to infer the hostility or malice of others in ambiguous situations, social function, and negative symptoms (Roberts, 2014). A comparison of SCIT and psychoeducation in patients with recent-onset schizophrenia also found a large effect size in the SCIT group for overall function, blame scores, hostility bias, affective cognition, and positive symptoms (Rocha, 2021).

#### **Metacognitive Training (MCT)** (Moritz, 2007)

MCT is a program of restorative approaches to cognitive bias in schizophrenia (Moritz, 2007). It uses cognitive-behavioral therapy techniques and aims to promote awareness of cognitive biases, to reflect them in the problem-solving repertoire, and to promote change (Moritz, 2010). There are eight modules and two cycles, each with the following content: “Attribution,” “Jumping to Conclusions,” “Changing Beliefs,” “To Empathize ...,” “Memory,” and “Mood.” MCT shares some content with SCIT but focuses on the mechanisms of hallucinations and delusions (Hayashi, 2020). The sessions on “Changing Beliefs” and “Mood” are included only in MCT. The sessions are 45 to 60 minutes in duration and include lectures and group work. After the session, participants are given a homework form to reflect on their experiences and are encouraged to generalize their experiences to their daily lives (Moritz, 2007). The target for MCT is mainly schizophrenia, but it can be applied to patients with other diagnoses as well. It is conducted in groups of three to 10 people, and the recommended trainer is a mental health worker with experience in treating patients with schizophrenia, but no license is required (Moritz, 2007). Regarding the effects of MCT, there are reports that MCT improved positive symptoms in patients with schizophrenia, as well

as self-reflectiveness and self-certainty in cognitive insights (Moritz, 2010; Hayashi, 2020). D-MCT for patients with depression has also been developed recently (Jelinek, 2017).

#### **Compensatory Cognitive Training (CCT)** (Twamley, 2012)

Compensatory cognitive training (CCT) is a manualized compensatory approach in which participants are taught how to compensate for their cognitive function using their residual functioning, with the goal of helping them cope with the demands of their environment in daily and social life by developing strategies that work for them (Twamley, 2012). It targets neurocognitive functions such as prospective memory, attention and vigilance, learning and memory, and executive functioning, respectively, and improves cognitive performance in life situations through the acquisition of internal strategies such as calendar use, self-talk, note-taking, and six-step problem-solving techniques (Mahmood, 2019). The CCT consists of 12 sessions, each of which includes the following: review of homework, troubleshooting of strategy use, rationale and psycho-education of target areas, demonstration and practice of each strategy, feedback on strategy use, and individual discussion of daily life (Mahmood, 2019). At the end of each session, homework on the strategies from that session is set up and reviewed for generalization in daily life in the next session (Twamley, 2012). The therapist will help each participant to identify the situations in which he or she will implement the strategies in life situations and ensure that the homework is conducted. The number of participants and frequency of the program are recommended to be two hours once a week in groups of four to six participants (Twamley, 2012). As for the effects of CCT, compared to the control group that received only medication, the group that received CCT showed improvements in verbal memory and negative symptoms, and at the 3-month follow-up, improvements in attention function, prospective memory, some social functions, and quality of life were also reported (Twamley, 2012). There are also reports of improvements in expressivity and social motivation with CCT, suggesting that CCT is effective in improving multiple aspects of negative symptoms (Mahmood, 2019).

#### **CONCLUSION**

We have outlined cognitive dysfunction in schizophrenia and mood disorders, and their treatment

programs. These have developed recently and are increasingly being reported. New programs are probably developed in the future. The important aspects of a CRT program are the objectives and outcomes. It is critical not only to improve cognitive function, but also to connect cognitive function to daily life and social function. And in our opinion, the effectiveness of the combination of these programs needs to be verified in the future.

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