REVIEW

Schizophrenia and cognitive dysfunction

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Abstract : Schizophrenia is a psychiatric disorder with cognitive dysfunction as a core symptom along with positive and negative symptoms. Cognitive dysfunction in schizophrenia can be broadly classified into neurocognitive and social cognitive deficits, with these deficits significantly influencing social functioning. Therapeutic interventions aiming to enhance neurocognition and social cognition have been developed. In this review, we describe the characteristics of cognitive dysfunction in patients with schizophrenia, its relationship to social function, and intervention strategies. J. Med. Invest. 71 : 205-209, August, 2024

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SCHIZOPHRENIA AND COGNITIVE FUNCTION

Schizophrenia is a psychiatric disorder with positive symptoms, such as delusions and hallucinations, and negative symptoms, such as decreased emotional expression and motivation, as well as cognitive dysfunction (1). A study that followed first-episode schizophrenic patients for 5 years reported that about half of them maintained symptom recovery for more than 2 years, and a quarter of the subjects maintained adequate recovery of social function (2). The inadequate rate of recovery of social function has led to studies exploring clinical factors associated with recovery of social function and the association between cognitive function and recovery of social function in the initial or chronic phase (3-5).

This review discusses the characteristics of cognitive dysfunction in schizophrenia, its relationship to social functioning, and treatment strategies.

COGNITIVE DYSFUNCTION

Cognition encompasses various abilities and refers to the ability to perceive, process, manipulate, and respond to information (6). Cognitive function is the foundation that supports cognition and is categorized into neurocognition and social cognition. Neurocognition and social cognition are somewhat related but, to some extent, independent cognitive functions (7).

1. Neurocognition

Neurocognition underlies information processing and includes processing speed, attention, working memory, verbal learning, and executive functioning. Saykin *et al.* (8) were the first to use a battery of standardized neuropsychological tests to compare neurocognition in untreated schizophrenic patients and healthy subjects. They reported extensive neurocognitive deficits in the patient group. This study led to research on neurocognition using standardized neuropsychological tests.

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1. 1 Assessment of Neurocognition

Neurocognitive domains that are impaired in patients with schizophrenia include working memory, attention/vigilance, verbal learning and memory, visual learning and memory, reasoning, problem solving, and speed of processing (9). Standardized neuropsychological tests that measure these neurocognitive functions include the Cogstate Schizophrenia Battery (10, 11), Brief Assessment of Cognition in Schizophrenia (12, 13), and Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery (MATRICS) (14, 15). Furthermore, the Schizophrenia Cognition Rating Scale (16, 17) was developed as an interview-based test rather than a task-based one.

1.2 Neurocognition and Social function

Quality of life (QOL) is an indicator of social function. It can be categorized as subjective or objective QOL. Subjective QOL pertains to an individual's self-assessment and encompasses overall well-being and life satisfaction, whereas objective QOL refers to evaluations made by others regarding the individual and encompasses daily functioning aspects such as home life, work, and leisure activities (18, 19). The correlation coefficients between subjective and objective QOL have been reported to be weak to moderate (20, 21), making each an independent treatment target.

Studies examining the association between subjective and objective QOL and neurocognition have reported that neurocognition is associated with objective QOL rather than subjective QOL (22, 23). Furthermore, studies examining the relationship among objective QOL and positive symptoms, negative symptoms, depressive symptoms, adverse effects, and neurocognition have found that attention and processing speed significantly predicted objective QOL along with negative and depressive symptoms (24, 25).

2. Social cognition

Social cognition refers to the ability to understand the intentions and feelings of others (26). The following four types of social cognition are reduced in schizophrenia (27, 28) :

1. Theory of Mind Ability to infer the intentions and beliefs of others
2. Social perception Ability to recognize social roles, rules, and situational context
3. Attributional bias Biases, such as inferring the causes of

positive and negative events
4. Emotion processing Ability to identify, understand, and control emotions

2.1. Assessment of social cognition

Unlike neurocognition, there are no standardized social cognition tests that measure all four social cognitions simultaneously. Therefore, it is recommended that a combination of tests measuring each ability be administered. However, due to the psychometric properties of each test, the use of Hinting task, Penn Emotion Recognition Test (ER-40), and Bell Lysaker Emotion Recognition Task (BLERT) is most desirable ; Reading the Mind in the Eyes Test (Eyes), The Awareness of Social Inferences Test (TASIT), and Intentional Bias Task (IBT) are acceptable for use ; and Mini Profile of Nonverbal Sensitivity (MiniPONS) and The Social Attribution Task-Multiple Choice version (SAT-MC) are not recommended for use in clinical trials (27).
1. Theory of Mind Hinting task (29), Eyes (30), and TASIT (31)
2. Social perception MiniPONS (32), and SAT-MC (33)
3. Attributional bias IBT (34)
4. Emotion processing BLERT (35), ER-40 (36)

2.2. Social cognition and social function

Maat *et al*. (37) examined the association among theory of mind, emotion processing, working memory, processing speed, reasoning, problem solving, and verbal comprehension ; positive and negative symptoms ; and subjective QOL. Their findings suggest that theory of mind was more related to subjective QOL than neurocognition or psychotic symptoms. They also reported that the theory of mind interacts with psychotic symptoms, and significantly predicts subjective QOL in patients with high psychotic symptoms. In addition, Kurtz *et al*. (38) reported that emotion processing, measured before the start of cognitive rehabilitation, was associated with improvements in objective QOL. These results indicate that social cognition is associated with a broader range of QOL factors than neurocognition, making social cognition an intervention target for improving social function. However, both neurocognition and social cognition have small explanatory rates of 6% and 16% for social function (39) ; thus, other factors need to be considered when aiming to restore social functioning.

3. Cognitive function and social function

Both neurocognition and social cognition are significantly associated with QOL (23, 37, 38). On the other hand, depressive, negative, positive, and extrapyramidal symptoms have a significant negative impact on QOL (20, 21, 24, 25). Interventions targeting psychotic symptoms, mood symptoms, and cognitive function are needed to improve QOL. In addition, the side effects of pharmacotherapy should be minimized. A summary of the relationship between clinical factors and QOL is presented in Figure 1.

COGNITIVE-ENHANCING APPROACHES

Because cognitive dysfunction is associated with QOL in patients with schizophrenia, cross-sectional studies have been conducted to examine clinical factors associated with the exacerbation of cognitive dysfunction as well as intervention studies aimed at improving cognitive dysfunction. We describe a treatment approach targeting neurocognition and social cognition.

1. Neurocognition
1.1. Pharmacological approaches

Sinkeviciute *et al*. (40) used a meta-analysis to examine whether glutamatergic, cholinergic, serotonergic, dopaminergic, GABA-ergic, noradrenergic, and miscellaneous medications improve neurocognition. They reported that combining all the different neurotransmitter systems acting in different mechanisms had a small positive effect size on overall neurocognition. When each neurotransmitter system was analyzed separately, the glutamatergic system had a small but significant effect on overall neurocognition and working memory. Cholinesterase inhibitors also had a marginally significant effect on working memory. A meta-analysis by Sinkeviciute *et al*. (40) suggested that the ameliorative effect of pharmacotherapy on neurocognitive dysfunction is small.

1.2. Cognitive remediation therapy for Neurocognition

Cognitive remediation therapy (CRT), which works on cognitive function itself, has been shown to improve cognitive function. CRT targeting neurocognition includes the frontal/

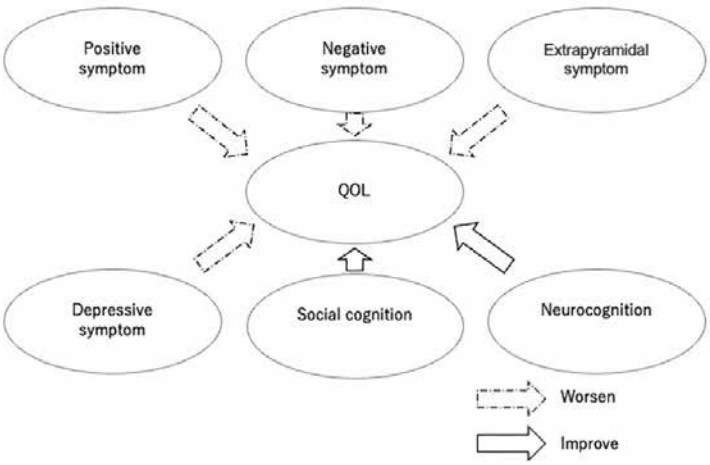

Figure 1. Relationship between clinical variables and QOL. Positive, negative, extrapyramidal, and depressive symptoms decrease QOL. Social cognition and neurocognition improve QOL.

executive program (41) and the Neurological and Educational Approach to Cognitive Remediation (NEAR ; 42).

NEAR consists of a PC session aimed at improving cognitive function and a bridging session aimed at generalizing the coping strategies acquired in the PC session to everyday life (42, 43). Hodge *et al*. (44) conducted a randomized controlled trial using NEAR in patients with schizophrenia. The results showed that verbal and visual memory, attention, and executive function improved immediately after the intervention, and these improvements were maintained for 4 months after treatment was discontinued. Furthermore, they reported that neurocognition and social function improved, and these improvements were maintained up to 4 months after the intervention.

1.3. Other therapy

Physical activity has a positive impact on neurocognitive function (45). Xu *et al*. (46) performed a meta-analysis to examine the effects of aerobic exercise on neurocognition in patients with schizophrenia and found that aerobic exercise improved verbal learning and memory, reasoning, and problem solving, but not processing speed, attention/vigilance, working memory, and visual learning and memory.

2. Social cognition

2.1. Pharmacological approaches

Two studies examined whether pharmacotherapy improves social cognition (47, 48). Both studies examined the effects of antipsychotic medications on social cognition ; however, neither study showed robust results for improving social cognition. It is possible that the study design, drug use, and dosage were inconsistent, and that the improvement effect could not be detected because the patients were already on medication when the study was conducted.

2.2. CRT for social cognition

CRT for social cognition includes social cognition and interaction training (SCIT) and metacognitive training (MCT). SCIT targets emotion processing, attribute bias, and theory of mind, whereas MCT targets attribute bias and theory of mind.

A study of recent-onset schizophrenia reported that emotional processing and attribute bias improved before and after SCIT (49). On the other hand, a study of schizophrenic patients with an average of more than 20 years after onset reported no significant improvement in social cognition before and after SCIT (50). These results suggest that the effect of SCIT on social cognition may be influenced by the duration of illness.

2.3. Other therapy

Xu *et al*. (46) reported that aerobic exercise was not effective in improving social cognition in patients with schizophrenia. Govindaraj (51) conducted 20 sessions of yoga therapy for 15 schizophrenia patients whose symptoms were stabilized by antipsychotic medication. The study revealed an improvement in the integration score of social cognition, specifically in the theory of mind and social perception. Few studies have examined the effects of physical activities, such as exercise and yoga, on social cognition ; therefore, the accumulation of research results is desirable.

3. Summary of Cognitive-Enhancing approach

CRT and physical activity have demonstrated improvements in both neurocognition and social cognition (44, 46, 49, 51). However, the effects of CRT on social cognition may vary depending on the duration of illness. Regarding pharmacotherapy, studies have shown limited or negligible improvement in cognitive function (40, 47, 48), partly due to methodological limitations. Figure 2 shows the effect of each treatment on the improvement of cognitive function.

CONCLUSION

In this review, we described the characteristics of cognitive dysfunction in individuals with schizophrenia, exploring its relationship to social function and intervention strategies. Although robust evidence suggests an association between cognitive function and the recovery of social function, no intervention method has shown significantly superior efficacy in enhancing cognitive function. Moreover, different intervention strategies affect different cognitive domains. Thus, interventions aimed at improving cognitive function in patients with schizophrenia may benefit from a combination of different treatment modalities, including pharmacotherapy, CRT, and exercise therapy.

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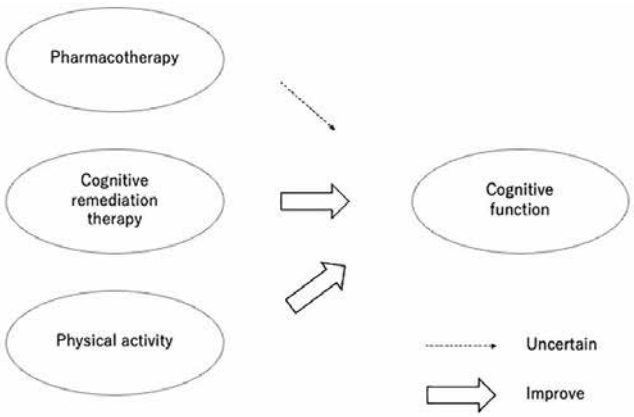

Figure 2. Effect of Cognitive-enhancing Approaches. Cognitive remediation therapy and physical activity improve cognitive function. The effect of pharmacotherapy on cognitive function is not established.

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