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Investigating the cognitive skills of patients with schizophrenia in acute and clinically stable phase

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Introduction

Theoretical background of the study

Cognition, as a psychological concept basically means the process of getting and assimilating all kind of information. Within cognition, social cognition and neurocognition in schizophrenia are widely investigated with different methods and in various study designs. The impairment of these fields and their relationship with social functioning is well known in schizophrenia. Neurocognition is any form of the basic cognitions, which are linked to the functioning of specific areas of the brain. Social cognition defines how people think about themselves and others in the social world. It includes all the social and emotional skills that are needed for successful interpersonal interactions. Theory of mind (ToM) or mentalization, emotion recognition ability, attributional style, social knowledge and social perception are the five primary domains of social cognition. Theory of mind (ToM) is the ability to attribute mental states to the self and others. This ability helps to represent the different mental states of others in order to deduce others' intentions, desires and thoughts. It includes understanding false beliefs, intentions, deception, hints, irony, faux pas and metaphor.

Schizophrenia is often considered as a disease of the brain, and impaired cognitive functioning is a core symptom of the illness and a dominant part of the symptomatology. Several studies have described that patients with schizophrenia are characterized by marked cognitive deficits, mainly in the areas of attention, visual memory, working memory and executive functions. Their cognitive performance is consistently worse compared to healthy individuals in certain tests measuring neurocognitive functions. Many studies about ToM also described that patients with schizophrenia have shown deficits in this ability compared to healthy and other psychiatric controls. The present dissertation is engaged in social- and neurocognitive skills of patients with schizophrenia within the cognitive skills of these patients.

Longitudinally, schizophrenia is usually characterized by different episodes, i.e. periodic relapses and remission phases. During relapse, patients with schizophrenia show specific psychotic symptoms, while the remission state is mainly characterized by milder and predominantly negative symptoms. Unfortunately, remissions are usually time-limited periods in the course of schizophrenia. Nevertheless, being in symptomatic remission does not mean that patients are doing completely well, since the remaining milder symptoms may negatively affect their functioning.

Controversy exists in the literature regarding cognitive functioning in schizophrenia. In several studies patients in remission have shown improved executive functioning compared to those in relapse. Another research found only weak correlation between improved symptoms and changes in cognitive dysfunctions. These studies were characterized by a cross-sectional design. In several longitudinal studies, it has been concluded that the neurocognitive performance of patients with schizophrenia is notably stable regardless of clinical state, mentioning the trait-like characteristics of the disorder. Furthermore, previously no significant differences in neurocognitive performance of patients with schizoaffective disorder between relapse and remission were reported, which also suggests its trait-like nature.

Some earlier investigations did not find ToM deficits in remitted patients. The majority of recent investigations found that ToM deficits are present also in remission. The trait-like components of ToM deficits are further supported by studies that found that healthy siblings and first-degree relatives of patients with schizophrenia performed worse on ToM tests than non-relative healthy controls, but better than patients.

However, only a few studies examined ToM in a longitudinal setting. A recent study found that deficits in ToM are

relatively stable in time, but not fully independent of symptom state: ToM impairments were present during acute and also in relatively remitted phases, but more salient during symptomatic periods. The trait features of the illness were also confirmed. These longitudinal studies not only examined ToM during a longer period of time (6–12 months), but also emphasized that subjects were in a relatively stable state at all visits.

Several studies found that the impairment of emotion perception among patients with schizophrenia is also a significant feature of the illness. Individuals with schizophrenia show deficits in emotion recognition compared with healthy controls. Previous studies suggest that patients in remission may perform better in emotion recognition than patients in relapse, while others found that emotion recognition is stable over time in schizophrenia. In another study healthy siblings performed better than patients but worse than controls on emotion identification and discrimination tests, which promotes the hypothesis of the trait-like nature of emotion recognition deficits.

Aims of the study

The wide literature of cognition considers the social-, and neurocognition as different fields but their detachment

regarding their functioning is in question. Linked to this and to the controversy results of studies in the literature regarding the state-, or trait characteristics of cognitive skills a question has been expressed that the deficits mentioned above are trait-like (always present during the patient's life) or state-like (appear due to relapse, and their existence and severity depend on the patient's actual state) and if there is difference between the two fields in this aspect.

Based on literature date it may be hypothesized that fluctuation of symptom severity has different impact on the examined fields, thus it influences the neurocognitive functioning less, but has more effect on social cognition. Our hypothesis is that the changing of social cognition as a highly organized complex cognitive function more tightly linked to the changing of clinical symptoms (typically state-like) than the more basic neurocognitive functions (typically trait-like). The sensitivity of ToM or emotion recognition within social cognition to the changes in symptom state is uncertain. ToM as a more complex function expectedly fluctuates with the state more significantly. In addition, we suppose the existence of trait-like components in all of the tested functions, which can be concluded the chronic nature of the disease.

Based on the mentioned above our aims were the follows:

Evaluation of ToM and emotion recognition skills in patients

with schizophrenia with RMET and FEEST in acute then in clinically stable state. Investigating correlations between the tests and changing of clinical state.

Evaluation of neurocognitive skills in patients with schizophrenia with CANTAB test in acute then in clinically stable state. Investigating relations between neurocognitive functions and changing of clinical symptoms.

Associations between social cognition, neurocognitive skills and the effect of changing of psychotic symptom severity on these functions.

Determining the state-, and trait nature in social-, and neurocognitive functions with the applied tests.

Materials and methods

Patients with schizophrenia meeting the DSM-IV criteria took part in our study. Patients were recruited from the inpatient units of the University of Debrecen Medical and Health Science Center, Department of Psychiatry, Debrecen, Hungary. Exclusion criteria were the following: any severe somatic illness, drug or alcohol addiction or abuse, major depressive disorder and schizoaffective disorder in the lifespan. Research diagnosis was based on diagnostic interviews guided by clinicians independent of this study. These interviews included the Structured Clinical Interview

for DSM Disorders — Clinician Version (SCID-CV) and Research Version (SCID-RV). Age-matched control persons were healthy individuals who had no history of any psychiatric disorder or family history of psychosis. None of the control subjects had a history of substance abuse (alcohol, THC, hallucinogens, cocaine, opiates, inhalants, methamphetamines or other stimulants), which could potentially influence their performance. Furthermore, none of the control subjects took antipsychotics or other psychotropic medications like benzodiazepines (BZDs), antidepressants or mood stabilizers. All participants signed a written consent form. The study was performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans, and it was approved by the Regional and Institutional Ethics Committee.

Patients and healthy subjects were tested with the RMET (Reading the Mind in the Eyes Test) assessing mentalization ability, the 'Ekman 60 Faces Test' (Facial Expressions of Emotion: - Stimuli and Test (FEEST)) measuring emotion recognition skill, and CANTAB (Cambridge Neuropsychological Test Automated Battery) measuring neurocognitive skills.

In order to assess symptom severity among patients the PANSS (Positive and Negative Syndrome Scale) was used by

a trained psychologist, who assessed all patients.

Patients were examined twice – first in an acute phase (as soon as they were able to cooperate, on average within 4 days after admission), and for the second time in a clinically stable state. The clinically stable state was defined as being discharged by the patient's physician from the inpatient ward and being treated as an outpatient therein after. Controls were tested only once, since we assumed that their performance would be stable over time due to the disposition of the tests — there was no feedback about the correctness of the given answers at all.

Furthermore, the subgroups of patients in negative and positive symptomatic remission (PSR and NSR) were also defined in our investigation according to the criteria published by the Remission in Schizophrenia Working Group (RSWG). Patients were categorized into these subgroups according to their PANSS scores: (1) Positive symptomatic remission (PSR) was defined as ≤ 3 on the following items: P1, P2, P3, G5 and G9. (2) Negative symptomatic remission (NSR) was defined as ≤ 3 on items N1, N4, and N6. Emotion recognition and ToM in the subgroup of patients in NSR were also compared to healthy controls at the second visit.

Results

Social cognition (RMET, FEEST):

There was a significant improvement in psychotic symptom severity between study visits. At the second visit 22 subjects reached the criteria for PSR, and 15 patients reached the criteria for NSR. Healthy controls outperformed patients at baseline. Patients showed a marked improvement in ToM at the second assessment. Subjects with schizophrenia still performed worse in the clinically stable state than controls. The subgroup of patients at the second visit who fulfilled the criteria for NSR did not differ significantly from healthy controls at the second visit. Based on our results mentalization has also trait-and state-like components.

There was a strong and constant negative correlation between negative symptom severity and RMET total score at both assessments. Only at the second assessment did the PANSS total and general symptom score correlate significantly with the RMET total score. No correlation was found between positive symptom score, antipsychotic medication dose, benzodiazepine dose or RMET at any visit.

Patients showed a marked improvement also in emotion recognition at the second assessment. Subjects with schizophrenia still performed worse in the clinically stable state than controls. Healthy controls also outperformed the

subgroup of patients who fulfilled the criteria for NSR at the second visit.

There was a significant relationship between negative symptom severity and emotion recognition total score at both assessments. Emotion recognition did not correlate with antipsychotic medication dose, benzodiazepine dose, PANSS total or general symptom scores. Our results suggest that emotion recognition also has state-and trait-like characteristics in schizophrenia.

Emotion recognition as indexed by the FEEST and ToM as indexed by the RMET showed a very strong positive correlation at both study visits in the patient group, which supports the notion that emotion recognition and mentalization are all part of social cognition and influence each other through different processes.

Neurocognition (CANTAB):

Patients showed significantly worse performance in all of the administered CANTAB tests (SRM, PAL, SWM, SOC, RVP) compared to healthy controls in both states (relapse and clinically stable state).

The overall sum of the positive symptoms of PANSS were correlated with the performance of patients in the SWM subtest in acute phase. Negative symptoms were significantly

correlated with PAL and SRM. General symptoms of PANSS also correlated with the PAL (paired associated learning) during relapse and in clinically stable state. There was no correlation between the positive symptoms of PANSS and any of the subtests in clinically stable state.

Our results suggest that the neurocognitive dysfunctions are persistent in all phases of the disorder and may represent the core symptom of the disease.

Associations between the specific domains of neurocognition and social cognition

In line with previous findings in literature social cognition and neurocognition are related domains, we also found correlation between PAL and the tests measuring ToM and emotion recognition in acute phase, while SRM was correlated with emotion recognition in clinically stable state. PAL and emotion recognition was still correlated in clinically stable state.

Conclusions

The relevance of the dissertation is assessing social cognition and neurocognition among patients with schizophrenia in acute and clinically stable state. The deficit of social cognition and neurocognition in schizophrenia is clear in our study according to previous literature data. We also found that measuring the two components of social cognition with the applied tests these functions are mostly state-like, while the more basic neurocognitive skills are trait-like. The results support our hypothesis that changes of social cognition as a complex cognitive function more tightly linked to the changes of clinical symptoms (more state-like) than the primary neurocognitive functions (more trait-like). Furthermore, ToM as a more complex function fluctuated more with the state of illness, which difference between ToM and emotion recognition supports that ToM has a higher level of functioning. Our results also showed that social cognition has trait-like component, because ToM and emotion recognition were still found to be impaired even in clinically stable state compared to healthy controls. Neurocognitive impairment exists during both states suggesting that these deficits might be permanent, although there can be a mild improvement in some cognitive fields. We also found relationship between neurocognition and

social cognition, which proved that these domains are related in line with previous studies.

According to our results, PAL test showed significant correlations with PANSS negative symptoms and with all tests measuring social cognition, thus it can be concluded that PAL is the most sensitive test of global functioning. It could be used as an early screening method due to its utility of detecting early dysfunctions. Finally, the social cognition can be improved in schizophrenia, therefore it may be the target of some rehabilitation programs.

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List of publications related to the dissertation

1. **Balogh, N.**, Ágerházi, A., Berecz, R.: Neurocognitive changes in patients with schizophrenia during relapse and early remission.
   Eur. J. Psychiat. 29 (3), 199-209, 2015.
   IF: 0.711
2. **Balogh, N.**, Ágerházi, A., Berecz, R., Csukly, G.: Investigating the state-like and trait-like characters of social cognition in schizophrenia: A short term follow-up study.
   Schizophr. Res. 159, 499-505, 2014.
   IF: 3.923

List of other publications

3. Inczédy-Farkas, G., Benkovits, J., **Balogh, N.**, Álmos, P., Scholtz, B., Zahuczky, G., Török, Z., Nagy, K., Réthelyi, J., Makkos, Z., Kassai-Farkas, Á., Ágerházi, A., Tűzkő, J., Janka, Z., Bitter, I., Németh, G., Nagy, L., Molnár, M. J.: Magyar szkizofrénia-biobank a szkizofréniakutatás és a személyre szabott orvoslás szolgálatában.
   Orv. Hetil. 151 (35), 1403-1408, 2010.
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