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## Social cognition and treatment in psychosis

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# CHAPTER 8

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## *Summary and General Discussion*

## Summary

This thesis is concerned with social cognition and treatment of impaired metacognition and insight in psychosis. To shed more light on these topics, we performed a meta-analysis on social cognition in people who are at risk for psychosis. Secondly, we investigated empathy in schizophrenia; an element of social cognition that has been scarcely researched in this population. In addition, we synthesized the quantitative findings from published research, again using meta-analysis, to address the effectiveness of different treatment methods in improving insight in schizophrenia. Furthermore, we designed and carried out a multicenter randomized trial to investigate whether a new therapy, called the Metacognitive Reflection and Insight Therapy, can improve metacognition in schizophrenia and presented a case study of this therapy. In the current chapter, the main findings of these studies are summarized and integrated and clinical implications and directions for future research are discussed.

## Social cognition

Since social cognition is impaired in many people with schizophrenia (Mazza et al., 2012; Mehta et al., 2013), we wanted to investigate social cognition in people who are at risk for psychosis (the Ultra High Risk, UHR group) to see if social cognition is impaired before onset of psychosis. If so, social cognition might function as a marker for psychosis which can be used to detect people at risk at an early stage. It is important to detect the development of psychosis as early as possible, as research has shown that the onset of schizophrenia can be prevented by intervention in the early stages (Morrison et al., 2004; Amminger et al., 2010; Ising et al., 2014) and early intervention is critical to the development of the disease (Perkins, Boteva & Lieverman, 2005; Marshall et al., 2005; Chiliza et al., 2012).

Social cognition can be defined as the mental operations that underlie social interactions, which 'mediate responses to interpersonal settings of various types, including perception and interpretation of various types' (National Institute of Mental Health (NIMH), 2017). Four core research domains of social cognition are: emotional perception and processing, social perception and knowledge, theory of mind and attributional style (Pinkham et al., 2014). To examine social cognition in individuals at risk of psychosis, we performed a meta-analysis of the existing literature on the subject in Chapter 2. We found evidence for significant impairment of affect recognition and verbal Theory of Mind in the UHR group. Only a few studies were found on social knowledge and attributional style. Clearly, more studies are needed before an effect size can be calculated and conclusions can be drawn on the role of these elements of social cognition in the UHR group.

Effect sizes for the deficits in the UHR group were of moderate range, comparable with the severity of other cognitive deficits in people who are at high risk for psychosis. A recent meta-analysis on social cognition in people with schizophrenia found large effect sizes (Savla et al., 2013), which may suggest that people in the UHR group perform better than schizophrenia patients but worse than healthy controls. However, most studies in our meta-analysis did not find a correlation between transition to psychosis and problems in social cognition after controlling for IQ, education and baseline symptoms. This may indicate that social cognition in general is not a useful marker for the development of psychosis.

Not all people in the UHR group develop a psychosis; 19% according to a recent meta-analysis of Schultze-Lutter et al. (2015). The UHR group is heterogeneous, representing young people with several common mental disorders combined with mild psychotic symptoms. Some of them get better over time, some develop psychosis or other severe mental problems such as depression or bipolar disorder. Since social cognition is affected in this group, it seems to be a general problem for young people with mental disorders, transcending diagnosis. Social cognition functions as a direct predictor, mediator or moderator of social functioning (Wölwer et al., 2010); in particular emotion perception is linked to social functioning. People who are able to recognize emotions more accurately often have better social and occupational performance (Combs and Gouvier, 2004; Combs et al., 2011). Better social functioning affects mental health; adults who are more socially connected are healthier and live longer than others (Cohen, 2004; Umberson & Montez, 2010). It might therefore be important to focus on the improvement of social cognition in people in the UHR group, as it might improve social functioning and prevent worsening of illness.

Pinkham et al. (2014) highlight empathy as an important yet understudied aspect of social cognition and encourage more research on the subject. Empathy is usually measured with self-report measurements. However, empathy can be seen as a complex social-cognitive process, involving dynamic cues in the interaction between perceiver and the person whose affective state is being shared. Indeed, it is questionable whether self-report measurements can fully capture this process. To assess empathy in a more ecologically valid way, we used the Empathic Accuracy Task (EAT) in a large sample of schizophrenia patients and compared the results to healthy controls in Chapter 3. The EAT was developed by Zaki et al. (2008) and a Dutch version was designed by Aan het Rot & Hogenelst (2014). In this task the participant has to continuously estimate the emotional content of personal stories told in videos, using a turning device. His/her estimation is then compared to the emotional experience of the person who told the story in the video (the target).

Results show reduced overall empathic accuracy in patients. Both patients and controls scored low with less expressive targets, but controls performed better with more expressive targets. This is in line with research on emotion recognition in people with schizophrenia, which shows that patients with schizophrenia experience problems in reading facial expressions and recognizing emotional

prosody (Hoekert et al., 2007; Kohler et al., 2010; Petkova et al., 2014; Feingold et al., 2016). Whereas healthy people benefit from emotional cues in expressive persons, patients miss these cues and have less information to base their estimation of the other's emotional state on.

We assessed the correlation between the EAT and the IRI and QCAE, two well-known and often used empathy questionnaires. The EAT did not correlate with these questionnaires, which is in line with previous research. It seems that these questionnaires do not measure the same aspects of empathy as the EAT, as they measure one's own view of one's empathic abilities, which can be distorted. Insight is impaired in many people with schizophrenia (see for latest review: Elowe & Conus, 2016). It is possible that the view of schizophrenia patients (or people in general) of their own empathic performances is not accurate. Furthermore, self-report measurements are prone to different biases including intrusive symptoms biases, cognitive status biases and values and social comparison biases (McGurk et al., 2000; Hendryx et al., 2001; Bromley and Brekke, 2010; Patterson et al., 2001).

It may be best to see empathy as a multi-faceted construct encompassing multiple overlapping domains including the basic interpretation of emotional cues, the dynamic integration of these cues, affective and cognitive pathways and trait empathy as measured with self-report questionnaires. To understand empathic difficulties, it is important to account for these different aspects, especially the gap between one's belief and one's performance in empathy (Devlin et al., 2014; Zaki et al., 2008).

## Treatment in psychosis: insight

Many patients with schizophrenia have impaired insight into their condition (Dam, 2006) and poor insight is associated with many relevant factors (David, 2004) such as quality of life and social functioning (Drake et al., 2007). Therefore, it is important to study ways in which to improve insight in people with schizophrenia. To provide an overview of effective interventions, we conducted a meta-analysis of the effect of existing psychological and pharmacological treatments on insight in Chapter 4. The results show a moderate effect for specific interventions above treatment as usual. When we look at the different types of interventions, no clear answers on what interventions improves insight can be given as there was substantial variance in their nature and their methodology.

Regarding CBT, five studies were found, and the total mean effect size was small and not significant. Five studies on the effect of psycho-education on insight were found, with no overall effect, which may be due to a lack of power as total effect sizes were of moderate magnitude. No significant overall effect was found for the three studies on adherence therapy either, although results suggest it might improve insight in patients with affective psychosis over non-affective psychosis.

The other four categories (medication, skills training, video-observation and comprehensive interventions) were too small to calculate an effect size with.

However, the few studies on video-observation and the studies that examined comprehensive interventions that combined psycho-education, skills training and CBT are considered to be promising as large effect sizes were found.

Insight was not the primary outcome of almost half of the studies that were found. This suggests that insight is not frequently explicitly targeted for improvement. This may be due to the fact that insight is harder to operationalize than other symptoms such as hallucinations or depression, or due to the fact that clinicians often see insight as an artifact of symptoms.

Medication can be an important approach in raising insight, as shown in a recent study by Pijnenborg et al. (2015). In this study the effect of five antipsychotic drugs (haloperidol, amisulpride, olanzapine, quetiapine and ziprasidone) on insight in 455 patients with first-episode schizophrenia, schizoaffective disorder and schizophreniform disorder was examined in an open randomized controlled trial conducted in 14 European countries. The use of antipsychotics was correlated with improvements in insight over and above improvements in other symptoms. All drugs were effective in improving insight, with quetiapine being significantly less effective.

As our meta-analysis shows that insight can be improved with psychosocial interventions as well, insight might be best improved by a combination of treatment approaches. More specific approaches that especially target insight might be developed and more research is needed on which psychosocial interventions in combination with medication optimally improve insight in patients with psychosis.

## Treatment in psychosis: metacognition

Another concept that is associated with daily life functioning in schizophrenia is metacognition, which correlates among others with functional competence (Lysaker et al., 2011), stigma resistance (Lysaker & Dimaggio, 2014), social cognition and insight (Lysaker et al., 2011; Lysaker et al., 2010) symptoms (Nicolo et al., 2012; Macbeth et al., 2013) and therapeutic alliance (Davis et al., 2011). Given these correlations, improving metacognition might lead to improvements in daily life functioning. The Metacognition Reflection and Insight Therapy (MERIT) has been developed by Lysaker et al. (2011) to improve metacognition in people with schizophrenia. In this therapy patients are stimulated to think about the thoughts and feelings of themselves and others. In MERIT, metacognition is conceptualized as a hierarchical capacity and interventions that stimulate metacognition are based on the patients' current level of metacognitive functioning. Patients with lesser capacities need interventions that help them to master basic capacities, before attempting to more complex ones (Lysaker et al., 2011). Several case studies and two pilot studies show promising results of the MERIT therapy (Buck and Lysaker, 2009; Lysaker et al., 2007; Salvatore et al., 2009; Hillis et al., 2015; Kukla et al., 2015; De Jong et al., 2016).

A case study in which a patient with persistent negative symptoms is treated with MERIT is presented in Chapter 6. Negative symptoms are associated with major negative effects on quality of life and long-term outcome of patients (Milev et al., 2005; Kurtz et al., 2005; Möller, 2007; Barry & Hunter, 2012) and these symptoms often persist when positive symptoms subside. As they tend to be nonresponsive to pharmacotherapy (Buckley and Stahl, 2007; Barnes and Paton, 2011), other methods are needed to improve negative symptoms. Metacognition has been linked to negative symptoms (Lysaker et al., 2005; Nicolo et al., 2012; Macbeth et al., 2014; Luther et al., 2016). Without complex ideas of the self and others, there may be less reason to pursue goal-directed activities and less ability to construct meaning in daily activities, leading to the experience of negative symptoms. MERIT might therefore improve negative symptoms by improving metacognition.

In the presented case study, forty sessions of MERIT with Ann, a woman in her early 20s who had suffered a psychosis at the end of high school, are summarized. At the beginning of therapy, positive symptoms had mainly subsided but negative symptoms were still present. Before and after the therapy Ann was assessed with the Metacognitive Assessment Scale (MAS-A) and the Positive and Negative Symptoms Scale (PANSS) by an independent assessor. Results show an improvement in Self-reflection, Decentration and Metacognitive Mastery on the MAS-A. She did not improve on the Understanding the Other scale. After therapy, negative symptoms had decreased as is shown by PANSS outcome and reported by Ann. These improvements may be a result of the improvements in metacognition; she gained a better awareness of her own internal states and this seemed to lead to a richer internal experience. With a more complex representation of herself and a better understanding that there are multiple ways to interpret a social situation, Ann could make more sense of social interactions and her own thoughts and emotions in these situations.

As the above described case study and several other case studies and pilot studies show promising results of the MERIT therapy, we wanted to test the effectiveness of this therapy in a randomized controlled trial. In Chapter 5 we describe the research protocol of this trial. Thirteen therapists in six mental health institutions in the Netherlands participated in the study. Patients were randomly assigned to either MERIT or treatment of usual (TAU). Patients in the active group received forty sessions of MERIT. Before, after and six months after therapy the patients completed an assessment conducted by independent blind assessors, measuring metacognition and secondary outcomes symptoms, depression, stigma, quality of life, insight, empathy and social functioning.

In Chapter 7 the results of the trial are presented. Intention-to-treat analyses showed improvement in metacognition in both groups, with no significant differences between groups: MERIT was not more effective than TAU. However, patients in the active condition continued to improve on metacognitive Self-Reflectivity, leading to significant differences at follow-up. On average, scores on the MAS-A indicated that patients at baseline were able to recognize and distinguish between their different thoughts and emotions, but did not perceive

their thoughts are subjective and changeable. In other words: thoughts were accepted as facts. After MERIT, group average scores indicated having moved past being able to recognize that the ideas about oneself and the world are subjective and changeable. It must be noted that this was the average score of the group. There was considerable variance between participants, some people still didn't perceive their thoughts as subjective and changeable after therapy, where others scored far higher after therapy, being able to recognize and connect thoughts and feelings in the moment and over time.

Sensitivity analysis including only patients that completed the therapy showed improvements on Self-Reflectivity and Mastery at follow-up. At baseline patients' scores indicated that patients in both conditions on average responded to psychological challenges through gross avoidance and passive activities, such as following other's directions. At follow-up, in the MERIT condition, patients' scores indicated that they were able to respond to psychological challenges by actively choosing and engaging in specific activities and behaviors such as medication use, or seeking therapeutic interventions. Again, it must be noted that this represents the average group score. There was considerable variance between participants, some patients in the MERIT group still weren't able to actively choose solutions for their psychological problems after therapy, whereas others were not only able to change their thoughts to deal with problems but were also able to use knowledge about their own and others cognitions and emotions to come to solutions.

Difference between conditions only became evident at follow-up. One explanation for this effect is that metacognitive gains take some time to develop, even after therapy has been concluded. Such findings are not uncommon; a meta-analysis of cognitive therapy (Gould et al., 2001) has shown continued improvements after therapy was concluded.

Understanding the Other's Mind and Decentration appear less sensitive to change as no significant effects on these scales were found. It is possible that it is necessary to be able to think about your own thoughts and feelings before you can understand and think about what is occurring in the others mind (Dimaggio et al., 2008). One long-term case study has found the first improvements to Understanding the Other's Mind to occur after about 16 months (Lysaker et al., 2007).

Almost half of the patients that received MERIT did not complete the therapy, most of them dropped out before the tenth session, four before the start of the therapy. No significant differences on the four scales of metacognition were found between the drop-out group and the group that completed therapy. The large number of drop-outs might be the result of the long duration of the therapy. One of the patients stated "no connection with the therapist" as the reason for dropping out. Other reasons for drop-out were: too busy with work, too far to travel, alcohol/drugs problems and 'doing too well'. In post-treatment interviews conducted with the patients that completed the therapy, all respondents

indicated that they had found the therapy useful and would recommend it to others. The only negative effect that was mentioned was the intensive nature of the therapy.

Overall, MERIT is an intensive therapy (forty or more sessions) and might therefore not be the first treatment of choice for every patient, but it might be useful for specific groups of patients that do not respond to standard, short term therapies. For example, patients with severe problems in self-reflection that are not able to recognize their thoughts and feelings might not be able to reflect on their thought in Cognitive Behavioral Therapy and thus not benefit from it. MERIT can be used to improve self-reflection, after which other interventions can have more effect. However, as the improvement of self-reflection is only found in follow-up measures and not directly post treatment, more research is needed to shed more light on the role of MERIT in improving self-reflection.

## Clinical implications

Our research findings have several implications and suggestions for clinical practice.

It does not seem profitable to use social cognition as a marker for the development of psychosis in clinical practice, as general social cognition does not seem to predict transition, although more research is necessary on the subject. It does however seem important to focus on improving social cognition in people in the UHR group regardless if they develop psychosis or not, as social cognition is directly connected to social functioning and better social functioning improves mental health (Wölwer et al., 2010; Cohen, 2004; Umberson & Montez, 2010). As all people in the UHR group suffer from mental illness (such as depression/anxiety/substance abuse) in combination with mild psychotic symptoms, improvement of social cognition might lead to improvement of social functioning, hereby preventing the worsening of mental problems in the UHR group regardless of illness.

The selection of people who are 'at risk' for psychosis is part of clinical staging in schizophrenia. This was introduced to improve diagnosis and indication of fitting treatment, as people in early stages of the disease ask for other approaches than people who are chronically ill for many years (McGorry, 2007). However, the selection of people who are 'at risk' for psychosis may not always improve matters for patients in clinical practice. The UHR samples are highly heterogeneous. As stated, they represent people diagnosed with common mental disorders with a degree of psychotic experiences. Within the clinical staging model, it is assumed that these experiences are a precursor for the development of psychosis. However; it has been shown that psychotic symptoms can occur as a consequence of severity of multidimensional psychopathology, not necessarily indicating the development of psychosis (Cannon et al., 2008; Velthorst et al., 2009; Nelson et al., 2013).

It can be unnecessary stigmatizing to label all people with mild psychotic symptoms as 'pre-psychotic', as most of the people in the UHR group do not develop a psychosis in the future (19% according to a recent meta-analysis of Schultze-Lutter et al., 2015). Instead of focusing on predicting transition to psychosis, it might be more useful to take a more inclusive approach to all young people who seek help for mental problems transcending diagnosis, by focusing on the prevention of worsening of psychological illness in general. This might be done by focusing on improved access to a low-stigma, high-hope, small scale environment with acceptable language and interventions for all young people with psychological problems (Van Os & Guloksuz, 2017).

Our research on empathy shows that people with schizophrenia benefit less from emotional cues in expressive persons than healthy controls, contributing to reduced empathic accuracy. In clinical practice this knowledge can be used to educate patients that they might miss emotional cues of others which may lead to inaccurate conclusions of the emotional state of others. Health care workers and therapists might help people with empathic accuracy problems to compensate for these problems, for example by learning them to ask more about the emotions of others before drawing conclusions about their emotional state and intentions. It would be beneficial to develop interventions targeting the improvement of empathic accuracy.

Results also suggest that insight is a promising target for treatment in psychosis as it can be improved therapeutically. Insight might be best improved by a combination of medication and psychosocial treatment. More specific approaches targeting cognitive processes relevant for insight need to be developed with which people with schizophrenia can improve their insight. The Metacognition and Insight Therapy might be a novel way to improve metacognition in people with psychosis. However, given its intensive nature (forty or more sessions) it might not be the given treatment for every patient. As wide variations occur in the course of schizophrenia (Marengo, 1994), with large differences between symptoms, duration and course of illness, it seems logical that different treatment approaches are necessary to optimize treatment at an individual level. Whereas CBT might function as an effective treatment method for many patients with schizophrenia and might even be the first choice of intervention given its short duration and cost-effectiveness, MERIT might be a useful treatment method for those patients that do not benefit from short term interventions.

Furthermore, instead of implementing MERIT as a therapy by itself, it might be more functional as an addition to other therapies, in the sense that the therapist estimates the level of metacognition of the patient and adjust his/her interventions and communication to this level, whichever therapy he/she uses. For example; a therapist applying CBT or psycho-education uses the MAS-A and indicates that a patient is only able to recognize his thoughts but has no understanding of his feelings (self-reflection level 3). In this case, it is not useful to, for example,

elaborate on the thoughts and feelings of the patients and how they are interconnected (self-reflection level 7). The therapist can use this information in CBT and psycho-education by taking more time on introducing feelings, knowing this may take more time for the patient to comprehend. In this way, MERIT might be a useful way to level with the patient and adjust interventions in such a way that they connect to the experience and perception of the patient.

## Future research

Our findings provide a framework for future research in social cognition and treatment in psychosis. Recent studies suggest that verbal TOM and the recognition of emotions in faces can possibly function as markers for the development of psychosis. In general, more research is needed on the subject of emotion discrimination, prosodic emotion recognition, attributional bias and social perception/knowledge in the UHR group, as only a few studies on the subject were found.

Pinkham et al. (2014) highlighted empathy as an area of importance within the field of social cognition and psychosis but did not define this construct as a separate domain of social cognition, due to its possible overlap with Theory of Mind. Since many authors present empathy as a separate construct (Shamay-Tsoory, 2011), additional research is needed at a fundamental level to identify the possible overlap and unique elements of empathy and TOM within the domain of social cognition. Additionally, more research is needed to identify the distinctions and overlap between the elements within the empathy construct. Notably, more research is needed on the effects of specific interventions such as CBT, psycho-education and adherence therapy on insight. More importantly, research should focus on the development of specific, comprehensive interventions to improve insight in schizophrenia, as insight is correlated with several factors of daily life functioning.

Furthermore, research is needed to investigate if the Metacognitive Reflection and Insight Therapy is especially useful for specific patient groups. Given its intensive nature, it does not seem logical to offer MERIT to every patient with schizophrenia, as more cost-effective methods are already available. However, considering the wide variety in course, symptoms and duration of illness in schizophrenia, it might be useful for specific groups of patients that do not respond to standard, short term therapies. During the course of the randomized controlled trial we conducted, we found that it was not easy to investigate a long-term therapy in this population with vulnerable patients that tend to drop-out for all kinds of reasons. However, as many patients with schizophrenia still suffer from their illness on a daily basis for long periods of time, sometimes their whole life, present treatment options seem far from optimal for all patient groups. Methodological difficulties should therefore not prevent researchers from investigation long term treatment methods for patients with schizophrenia. Innovative, well-designed studies are the only way forward to enhance our knowledge of underlying factors and hence create opportunities for the development of effective treatments.