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Social cognition and treatment in psychosis

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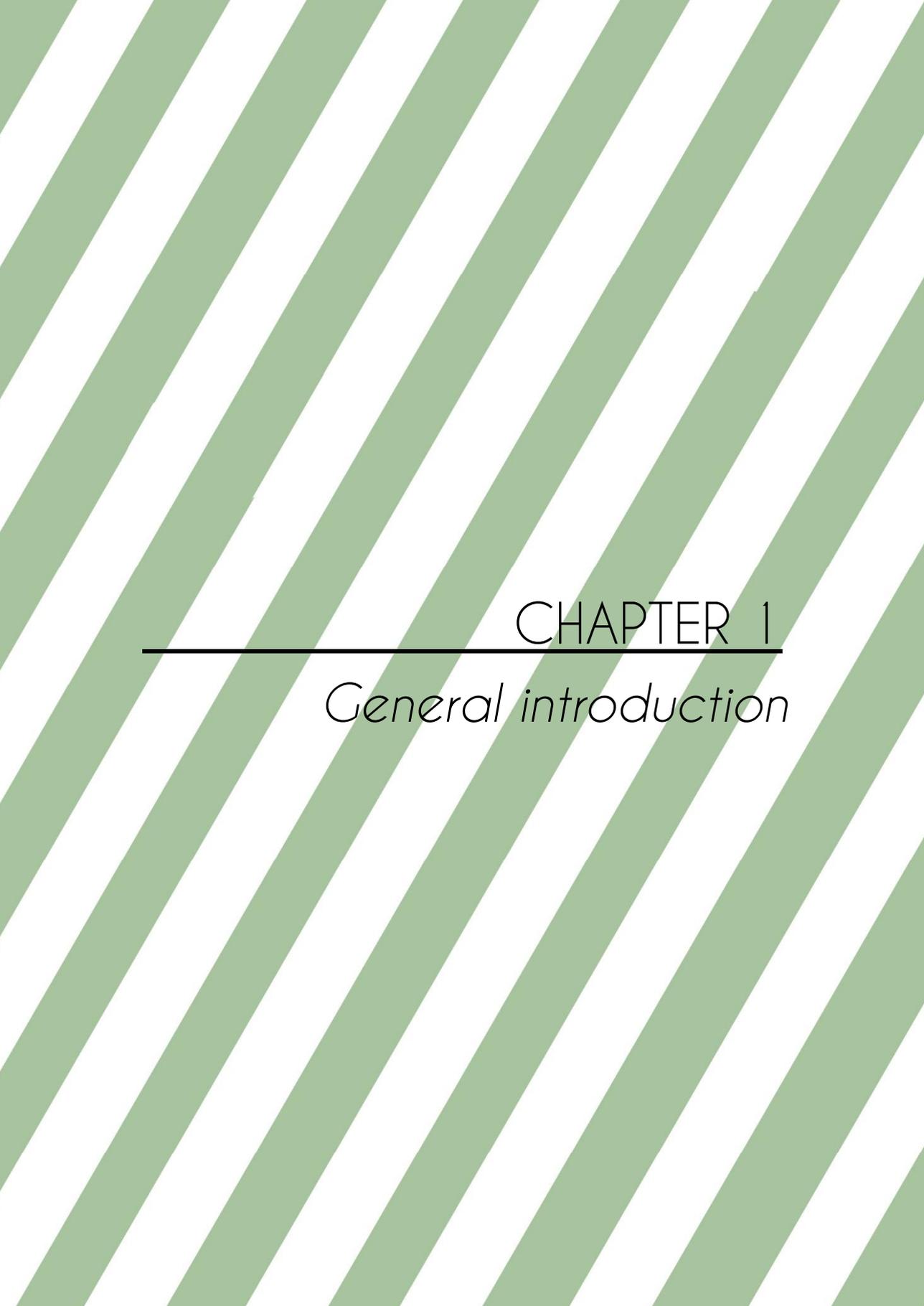
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CHAPTER 1

General introduction

Schizophrenia

Definition

Schizophrenia is an illness with a range of symptoms that can be divided into positive and negative symptoms. Positive symptoms are experiences that are largely absent in healthy individuals, while negative symptoms are present in healthy individuals and lacking in patients. Some people with schizophrenia also suffer from disorganized thoughts and speech (DSM IV-TR, APA). In addition to positive and negative symptoms, schizophrenia is characterized by cognitive symptoms, i.e. impairments of memory, attention and executive functioning (Owen et al. 2016).

The prevalence of schizophrenia is estimated at about 1% and the incidence is averaged at 15.2 /100.000 persons per year, with variations between studies (McGrath, Saha, Chant & Welham, 2008). It usually develops in adolescence (Van Os & Kapur, 2009) and is more common in men than in women (Aleman, Kahn & Selten, 2003).

Wide variations occur in the course of schizophrenia (Marengo, 1994; An der Heiden & Hafner, 2000). Some people have episodes of illness with full remission of symptoms between episodes, while others may have little variation in their symptoms over the course of years. Some people fully recover while others stay very ill for the rest of their life.

Impact on daily life

Schizophrenia can have a severe impact on the daily life of patients. The symptoms can interfere with social functioning (Kundu et al., 2013; Robertson et al., 2014), causing problems in education, employment and relationships. Negative symptoms seem to have a greater influence on long term functioning than positive symptoms (Wunderink et al., 2013). Stigmatizing beliefs regarding schizophrenia from society and the patients themselves can further reduce functioning and quality of life (Staring et al., 2009; Holubova et al., 2016; Picco et al., 2016). Schizophrenia is also associated with other invalidating factors such as cognitive problems (Green & Harvey, 2014) and impaired insight (Amador & David, 2004). Mortality rates are three times higher in comparison to the healthy population, caused partly by the larger suicide rate (Auquier, Lancon, Rouillon & Lader, 2007).

Clinical staging in psychosis

People in the early stages of schizophrenia ask for other treatment approaches than people who are chronically ill for many years. To improve diagnosis and the indication of fitting treatment for people with psychosis, McGorry (2007) proposed

a clinical staging model based on work of Fava and Kellner (1993), who first introduced clinical staging in psychiatry. This model defines the extent of the progression of the disease at a particular point in time and where a person lies along this continuum (Wood et al., 2011). It differentiates between early stages and later stages and strengthens the clinicians' capacity to select treatments relevant to earlier stages. A summary of the stages identified by McGorry et al. (2007) is presented below.

- 0: Increased genetic risk of psychotic disorders without any current symptoms.**
- 1a: Mild or non-specific symptoms, mild functional change or decline.**
- 1b: Ultra high risk: moderate but subthreshold symptoms, with functional decline.**
- 2: First episode of psychotic disorder, with moderate-severe symptoms and functional decline.**
- 3a: Incomplete remission from first episode.**
- 3b: Recurrence or relapse of psychotic episode.**
- 3c: Multiple relapses of psychotic episodes.**
- 4: Severe, persistent or unremitting illness.**

Figure 1.1: *Clinical staging in psychosis.*

Many people show certain vulnerabilities years before the onset of schizophrenia (phase 1a and 1b). For example they may experience subclinical positive symptoms, social withdrawal, depressive symptoms and disturbances in thought and speech (Schultze-Lutter et al., 2010). To study the early development of psychotic disorders, a risk group has been defined, called the Ultra High Risk (UHR) group (phase 1b). The people in this group meet the following criteria: presence of attenuated psychotic symptoms (APS) and/or a family history of schizophrenia combined with problems in functioning and/or presence of one or more brief limited intermittent psychotic symptoms (BLIPS) such as delusions and hallucinations (McGlashan, Miller & Woods, 2001; Yung & McGorry, 2007; Bora et al., 2014). Up to 36% of the people in this group develop schizophrenia within three years (Fusar-Poli, Bonoldi et al., 2012).

There is accumulating evidence 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 & Lieberman, 2005; Marshall et al., 2005; Chiliza et al., 2012).

Therefore, it is important to identify markers that may predict the development of psychotic disorders and other mental illnesses, enabling early detection and intervention. One possible vulnerability marker for the development of schizophrenia is reduced social cognition. A meta-analysis on this topic is presented in **Chapter Two**.

Social cognition

Definition and elements

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). Extensive research has been done on social cognition in schizophrenia in the last twenty years. Four core research domains have been identified, using expert surveys (Pinkham et al., 2014): emotional perception and processing, social perception and knowledge, theory of mind and attributional style.

Emotional perception and processing represent lower order basic processes such as the recognition of emotional content in faces and voices of others (Edwards et al., 2001; Hoekert et al., 2007). Social perception and knowledge encompass higher order processes such as the decoding of non-verbal communication and the recognition of social cues (Ihnen et al., 1998). Another domain that received extensive research is Theory of Mind (TOM); the mental capacity to infer the mental states of others (Brüne, 2005; Sprong et al., 2007). The fourth domain of social cognition is attributional style: the tendency to attribute the cause of events to the self, others or the environment (Lee et al., 2004; Langdon et al., 2010). Impairments in these four domains have been found in patients with chronic schizophrenia as well as patients with first-onset psychosis (Mazza et al., 2012; Bora & Pantalis, 2013), in the acute phase as well as the remission phase of the disease (Mehta et al., 2013). First degree relatives of people with schizophrenia show moderate difficulties in social cognition as well (Lavoie et al., 2013).

In addition to these four domains, Pinkham et al. (2014) highlight empathy as an important area within the field of social cognition. Empathy is generally defined as the ability to share and understand the emotional states of others (Eisenberg & Miller, 1987; Elliot et al., 2011). A differentiation can be made between affective and cognitive empathy. Affective empathy is the ability to empathize with others in an intuitive, unconscious manner via shared circuits in the brain. When seeing other people feel something, the same areas in the brain are activated as when feeling something yourself (Keyser & Gazzola, 2006). Cognitive empathy on the other hand, is the ability to interpret the thoughts and feelings of others in a more conscious way (Blair 2005; Frith & Frith, 2008). This form of empathy has considerable overlap with Theory of Mind (Pinkham et al., 2014). Both cognitive (Brüne, 2005; Biedermann et al., 2012; Savla et al., 2013) and affective (Bonfils et al., 2016) empathy are impaired in people with schizophrenia.

Measuring social cognition

Tests that measure social cognition can be divided into the same domains as described above. Emotion perception and processing is usually measured using

static, video or prosody tasks. Examples of static tests are the Facial Expression of Emotion: Stimuli and Tests (FEEST; Young et al., 2002), the Face Emotion Discrimination Test and the Face Emotion Identification Test (Kerr & Neale, 1993). These tasks make use of pictures of faces representing basic emotions (Ekman & Friesen, 1976). The participant has to identify the correct emotions in the pictures. As static cues of faces are far removed from real world social interaction, video tasks are developed to measure emotion perception and processing in a more ecologically valid way, for example the TASIT (McDonald et al., 2003). This test comprises videotaped vignettes of everyday social interactions, in which the participant has to identify the correct emotion portrayed by the actor in the scene.

Social perception and knowledge is measured with a wide range of instruments measuring different aspects of the domain. For example, the Abbreviated Trustworthiness Task (Adolphs et al., 1998; Bellugi et al., 1999) measures how someone infers the trustworthiness of strangers. In this task the participant is shown 42 faces and is asked to judge how much he/she trusts the person on a seven-point scale ranging from -3 (very untrustworthy) to +3 (very trustworthy). Scores are compared to the scores of a reference group, resulting in an average rating on trustworthy faces and an average rating on untrustworthy faces. The Relationships Across Domains test (RAD; Sergi et al., 2009) examines the understanding of social relationships, based on relational models theory. It assumes that people use four different relational models to interpret social interaction and consist of short stories describing the relationship between a male and a female. After reading the story, the participant has to determine if statements about the relationship of the characters are correct or incorrect. The RAD assesses if the participant recognizes the relational model presented in the story. The Situational Feature Recognition Test (Corrigan et al., 1996) was developed to test the recognition of features of social situations that vary in level of abstraction, from concrete features (actions and roles) to more abstract features (rules and goals). Social situations are presented to the participant, who has to identify which features would fit this particular situation.

A wide variety of measures is available to assess Theory of Mind. A distinction can be made between verbal TOM tasks, using stories in which the participant has to take the perspective of one of the characters and visual TOM tasks, in which the participant is shown pictures in which he/she has to infer the mental state of others. Examples of verbal TOM tasks are the Strange Story Task and the Faux Pas Task. The Strange Story Task (Happé et al., 1994) consists of eight neutral stories and eight TOM stories containing a mistake, persuasion or white lie. The participant has to detect these features in the TOM stories. The Faux Pas Task (Baron-Cohen et al., 1999) consists of ten stories of social situations. In five of these stories, someone says something without taking the feelings of another person into consideration. Again, the participant has to detect these mistakes in the story by taking the perspective of one of the characters. An example of a visual TOM task is the Reading the Mind in the Eyes Task (RMET; Baron-Cohen et al., 2001) in which the participant has to look at pictures of faces of strangers and decide which one of two words best describes what the person in the picture is feeling or thinking.

Attribution bias is usually measured with a questionnaire, for example the Internal, Personal and Situational Attributions Questionnaire (IPSAQ; Kinderman & Bentall, 1996). In this test the participant has to rate positive and negative events as being caused by themselves (internal), other people (external-personal) or the situation (external-situational).

Empathy is also commonly measured with self-rated questionnaires. An example of a widely used instrument is the Interpersonal Reactivity Index (IRI; Davis, 1983), with two subscales measuring cognitive empathy (the Perspective Taking subscale and Fantasy subscale) and two subscales measuring affective empathy (Empathic Concern and Personal Distress subscales). It consists of 28 statements. The participant has to indicate whether the statement applies to him/her on a six point scale. The IRI was not originally developed to distinguish between cognitive and affective empathy and concerns have been raised about its psychometric properties (Michaels et al., 2014; Horan et al., 2015). An example of a more recently developed instrument is the Questionnaire of Cognitive and Affective Empathy (QCAE, Reniers et al., 2011). This instrument was especially designed to address limitations of existing empathy instruments. It was developed from items of several existing self-report measures and tested with extensive analysis in a large healthy sample. It consists of 31 items, divided into a Cognitive Empathy Scale and an Affective Empathy Scale. The participant has to indicate if the statements applies to him/her on a four point scale.

It has been debated whether questionnaires can fully capture complex real-life empathy. To test empathy in a more ecologically valid way, the Empathic Accuracy Task (EAT; Zaki et al., 2008) was designed. It consists of video clips in which a person describes an emotional autobiographic story. The participant has to judge the emotional content of these stories continuously on a nine point scale (1=negative to 9=positive) with a turning device. Empathic accuracy is assessed by the extent to which the perceiver rating of the targets emotion matches the targets own judgement of the story. In **Chapter Three** a study is presented that investigates empathic accuracy in a sample of schizophrenia patients in comparison to healthy people. The correlation between the EAT and the IRI, QCAE and Faux Pas is also presented.

Metacognition

Definition and elements

The term metacognition was first used by Flavell in 1979, who defined metacognition as thinking about thinking. Ever since it has been widely studied, for example by Wells (2009) and Moritz et al. (2011). Metacognition includes mental activities ranging from discrete acts such as recognizing thoughts and feelings to more synthetic acts, in which thoughts and feelings are integrated into a larger, complex representation of the self, others and the world (Lysaker et al., 2013). It can be divided into four core, interdependent elements (Semerari et al., 2003; Lysaker et al., 2005): self-reflection, understanding the other, deceneration and

metacognitive mastery.

Self-reflection is the ability to reflect on your own thoughts and emotions. A simple (discrete) form of this element is the ability to recognize a thought in your mind and the ability to recognize this thought as your own. A more complex form of self-reflection is the ability to distinguish between different forms of thoughts, for example to be able to name one thought as a wish and another as a decision and see the difference between those two. An even more complex form is the ability to connect thoughts and feelings in a moment and to understand how they influence each other. The most complex form of self-reflection is the ability to synthesize cognitions and emotions over time and in different moments into a coherent and complex representation of your own mind.

Understanding the other is the ability to reflect on the thought and feelings of others. An example of this element is the ability to recognize a thought in the others mind. In more complex ways of understanding the other, one is able to detect and name thoughts and feelings of the other person, and is able to see how they influence each other. In the most complex (synthetic) form of this element, someone is able to form an integrated idea of the mental states of another person across time, forming a coherent representation of the mind of the other. This element is especially interconnected with self-reflection, as fMRI studies found overlap in regions of the brain that are activated when reflecting on oneself and when reasoning about the mind of others (van Veluw & Chance, 2014).

Decentration is the ability to understand that everybody has their own separate life and that the world does not evolve around you solely. When someone has zero decentration, he/she assumes to be the center of other people's mental activities. In more complex forms of decentration, a person can recognize that others can perceive and interpret events in a validly different way than his/her own interpretation and is able to see the world as involving unique individuals, each with their own thoughts, feelings and representations.

Metacognitive mastery is the ability to use reflections of self/others and decentration to deal with psychological problems. At the base of this element lies the ability to detect psychological problems in the first place. When someone is able to do so, simple ways of responding to these problems are avoidance or seeking support from others. A more complex way of responding to a psychological problem is changing how you think about the problem or yourself. The most complex form of metacognitive mastery is the ability to respond to psychological challenges by utilizing unique metacognitive knowledge about yourself and others. For example: someone understands that he has the tendency to have paranoid thoughts that usually lead to negative outcomes when he acts on them. He also sees that his girlfriend has a less paranoid mindset which leads to less problems. In a given situation he can recognize the paranoia in his own mind and can decide not to go along with it but instead he is able to adapt the view of his girlfriend to change his own view and deal with the situation in a different way.

When conceptualized this way, metacognitive dysfunction is more than just a missing skill. It is the inability to make complex sense of experience and integrate interpersonal information into a larger whole (Lysaker, Bob et al., 2013).

Metacognitive capacities allow persons to form a detailed picture of their own

mental states, of the wishes and intentions of others, and of the inner and social cues that trigger psychological pain, and thereby to cope with challenges and solve complex social problems [...] in the larger frame they make it possible for persons to make sense of their dilemmas, to find meaning in life and to ultimately adapt to a changing environment (Lysaker, Erickson et al., 2011).

Correlation with other constructs

Metacognition has some considerable overlap with other constructs. Theory of Mind and empathy both refer to the understanding of the mind of others, an element of metacognition. Furthermore, the term mentalization that is often used in other fields, especially the field of personality disorder treatment and research, also focuses on how people think about mental states (Semerari et al., 2007) and involves many similar processes as metacognition. It does, however, not include the mastery dimension and is discussed primarily in the context of a attachment theory (Bateman & Fonagy, 2011; Dimaggio & Lysaker, 2015). Social cognition and metacognition show considerable overlap as well. Both are concerned with reflection on cognitive processes of one's own and others thoughts and both moderate the relationship between neurocognition and functioning in schizophrenia (Vauth et al., 2004; Lysaker, Shea et al., 2010; Schmidt et al., 2011). Metacognition however focuses on synthesizing psychological experiences into mental representation of varying complexity, whereas social cognition is more concerned with the accuracy of perceptions and representations (Minor et al., 2015; Buck et al., 2015).

Measuring metacognition

Several instruments have been developed to assess (elements of) metacognition. Most of these instruments are designed to measure more discrete aspects of the concept, for example the ability to recognize specific thoughts and feelings, and the ability to identify and correct mistakes in one's own thought process. An example is the Cognitive Biases Scale (DACOBS; van der Gaag et al., 2013), intended to measure cognitive biases. This questionnaire consists of seven subscales: jumping to conclusions, belief in flexibility bias, attention to threat bias, external attribution bias, social cognition problems, subjective cognitive problems and safety behaviors.

These subscales can be grouped into three higher order scales: cognitive biases, cognitive limitations and safety behaviors. Another example of an instrument measuring discrete metacognition is the Meta-cognitions Questionnaire (MCQ; Cartwright-Hatton & Wells, 1997), intended to measure the beliefs someone has about his/her own thought process. This questionnaire consists of 65 items that can be rated on a 4-point scale, from 1 (I do not agree) to 4 (I agree very much). It has five subscales: positive beliefs about worry, negative beliefs about uncontrollability of thoughts and corresponding danger, cognitive confidence, negative beliefs about thoughts in general and cognitive self-consciousness.

To measure more synthetic forms of metacognition, in which thoughts and feelings are integrated into a larger, complex representation of the self, others and the world, Semerari et al. (2003) developed the Metacognition Assessment Scale (MAS). It was originally developed to measure metacognition in people with personality disorders and was adapted and shortened by Lysaker et al. (2005) for the use with people with psychotic disorders (Metacognitive Assessment Scale Adapted, MAS-A). It consists of four scales related to the subdomains as described above: self-reflectivity, understanding the others mind, decentration and mastery. In contrary to previously described measurement instruments, the MAS-A is not a questionnaire but a hierarchical rating scale with which transcripts of a conversation with a participant is scored on metacognitive activity. Each scale ranges hierarchically from discrete metacognitive activities to more complex, synthetic metacognitive activities. To obtain a transcript of a conversation, the Indiana Psychiatric Illness Interview (IPII; Lysaker et al., 2002) can be used. It consist of five open questions, designed to elicit the life story and illness story of the patient. The MAS-A can be scored by trained raters on the resulting transcript. The ecological validity of this scale is considered to be high, as metacognition is rated on what the participant demonstrates in the moment when discussing his/her own life.

Metacognition and daily life functioning

Daily life functioning of patients with schizophrenia is linked to metacognition in several ways. Lower levels of metacognition correlate with lower levels of functional competence (Lysaker, McCormick et al., 2011), lower stigma resistance (Lysaker & Dimaggio, 2014), and less favorable reports of the subjective experience of recovery (Kukla et al., 2013). Better metacognitive mastery is linked to better social cognition and more insight (Lysaker, Erickson et al., 2011; Lysaker et al., 2010) and metacognition has been found to mediate the impact of neurocognitive deficits on social function, after controlling for symptoms (Lysaker et al., 2010). In addition to these daily life aspects, impaired metacognition has also been associated with more severe negative symptoms (Lysaker et al., 2005; Nicolo et al., 2012; Macbeth et al., 2013) and low quality of therapeutic alliance (Davis et al., 2011). Additionally, lower levels of metacognition predict future severity of negative symptoms, even after controlling for concurrent levels of negative symptoms (Hamm et al., 2012).

As metacognition is linked to these important aspects of daily life functioning, improvement of metacognition with treatment might be a feasible way to improve daily life functioning of patients with schizophrenia.

Treatment in Schizophrenia

Evidence based treatment

In the Netherlands, patients with schizophrenia are treated with a combination of antipsychotic medication, case management, psycho-education, family interventions, reintegration programs and cognitive behavioral therapy (Trimbos Instituut, 2012). To expand and improve treatment options for people with schizophrenia, new forms of treatment are regularly introduced in international literature. Randomized controlled trials, reviews and meta-analyses investigate the effectiveness of these new treatment methods in their ability to reduce invalidating factors such as symptoms and stigma or their ability to improve other factors such as insight, metacognition, quality of life and daily life functioning of patients with schizophrenia. In **Chapter Four** a meta-analysis is presented, reviewing which treatment forms improve insight in schizophrenia patients.

Changing metacognition in psychosis

Some interventions are especially designed to improve specific deficits in schizophrenia. One such intervention is the Metacognitive Reflection and Insight Therapy (MERIT; Lysaker et al., 2011). This manual-based individual psychotherapy aims to improve the four elements of metacognition, as described by Semerari et al. (2003) and Lysaker et al. (2005): self-reflection, understanding the other, decentration and metacognitive mastery.

Metacognitive Reflection and Insight Therapy

The MERIT treatment protocol is not a step-by-step program but is target driven. In the conversation with the patient, the therapist looks for targets: signs of metacognition. He investigates if the patient is aware of his/her own thoughts and the thoughts of others and categorize the degree of metacognitive complexity. To do this, the therapist uses the levels of the metacognition assessment scale (MAS). He/she adjusts the intervention according to the level of metacognition of the patient and aims to stimulate the patient to perform ever more complex metacognitive tasks. A randomized controlled trial to investigate the effectiveness of the MERIT therapy is presented in **Chapter Five**. The results of this trial are presented in **Chapter Seven** and a case study in which a patient with severe negative symptoms is treated with MERIT is described in **Chapter Six**.

Outline

This thesis is concerned with treatment, social cognition and metacognition in schizophrenia. The thesis consists of five parts. In the **first part**, a general introduction is given in which key concepts and theories are discussed.

The **second part** encompasses two chapters on the topic of social cognition. First, a meta-analysis is presented on social cognition in individuals at ultra-high risk (UHR) for psychosis. Impaired elements of social cognition in UHR are discussed, as well as possible markers for transition and suggestions for future research. The second chapter concerns another important element of social cognition: empathy. Different measurement instruments of empathy are reviewed and compared, and the difference between schizophrenia patients and healthy controls in cognitive and affective empathy as measured with these instruments are discussed.

The **third part** of this thesis focuses on treatment of insight in psychosis. A meta-analysis is presented in which changes in insight during different forms of treatment for psychosis are reviewed. The effect of common treatment interventions such as Cognitive Behavioral Therapy and Psycho-education on insight are presented, association of elevated insight with depression is discussed and suggestions are made for targeting insight in future intervention programs.

The **fourth part** is concerned with the treatment of metacognition in psychosis. This part consists of three chapters. Firstly, a protocol of a multi-center randomized controlled trial of a manual-based individual therapy is presented. This therapy, the Metacognition Reflection and Insight Therapy (MERIT), aims to improve metacognition in patients with schizophrenia. Secondly, a case study is described of a first episode patient with severe negative symptoms receiving MERIT. The elements of the therapy are discussed in more detail and differences before and after therapy in metacognition and symptoms are addressed. In the final chapter of this part the result of the randomized controlled trial are discussed including improvement of patients on metacognition directly after therapy and after a follow-up period of six months.

In the **last part** of this thesis the results of the preceding chapters are integrated in a general discussion of the main findings and a final conclusion.