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Metacognition and Cognitive Biases in the Treatment of Psychosis

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2018

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citation for published version (APA)

van Oosterhout, B. J. (2018). *Metacognition and Cognitive Biases in the Treatment of Psychosis*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

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Chapter 1

General introduction

Information processing in psychosis

Psychosis has for long been associated with negative symptoms and neurocognitive deficits. In recent years social cognition, metacognition and cognitive biases have been subjected to scientific research; these concepts are briefly explained below.

Neurocognition

Neurocognitive functioning is involved in patients with psychosis, with the most prominent dysfunctions in the areas of attention, memory and executive functioning (Rund & Borg, 1999). Deterioration usually occurs some time prior to the first psychotic episode, and at approximately 65 years of age (Harvey, 2014; Nuechterlein, Ventura, Subotnik, & Bartzokis, 2014), and is associated with poor functional outcome (Lin et al., 2011). More specifically, there is evidence that stable remission (no relapses) during the first year of psychosis predicts neurocognitive functioning, suggesting that the early clinical course is a good predictor for the long-term course (Rund et al., 2016). This evidence tends to diminish Kraepelinaean ideas that, in the presence of psychosis, neurocognitive functioning becomes a progressively deteriorating condition.

Social cognition

Social cognition is defined as *'the mental operations that underlie social interactions, including perceiving, interpreting, and generating responses to the intentions, dispositions, and behaviors of others'* (Green, Freeman, et al., 2008). This definition emphasises the direct link between social cognition and social behaviour; moreover, it is well established that social cognition contributes to functional outcome in patients with psychosis (Couture, Penn, & Roberts, 2006; Fett et al., 2011). For instance, Theory of Mind problems are common in patients with schizophrenia and are linked to functional outcome in general and, more specifically, to community functioning (Fett et al., 2011). In an expert survey, four core domains of social cognition were identified, i.e. emotional processing, social perception, theory of mind/mental state attribution, and attributional style/bias (Pinkham et al., 2014). Emotional processing is broadly defined as perceiving and using emotions (Green, Penn, et al., 2008) whereas social perception refers to decoding and interpreting social cues in others (Penn, Ritchie, Francis, Combs, & Martin, 2002; Sergi & Green, 2003; Toomey, Schulberg, Corrigan, & Green, 2002). Theory of mind/mental state attribution is defined as the ability to represent the mental states of others, including the inference of intentions, dispositions and/or beliefs. Theory of mind is also referred to as mentalizing, mental state attribution, or cognitive empathy (Frith, 1992; Penn, Addington, & A., 2006; Shamay-Tsoory, 2011). Attributional style/bias describes the way in which individuals explain the causes, or make sense of social events or interactions (Green, Freeman, et al., 2008; Penn et al., 2006)

Metacognition

In the field of psychosis, the concept of *metacognition* has become more prominent in both research and practice. Metacognition, including its subcomponents such as self-reflectivity and mastery, are profoundly linked with awareness of illness and social functioning in schizophrenia in general (Brune, Dimaggio, & Lysaker, 2011). Similarly, Moritz et al. (2013) use the term ‘metacognitive awareness’ which (hopefully) can intercept the progression from false appraisals of certain subclinical (‘as if’) experiences to fixed false (delusional) beliefs.

Cognitive biases

A bias is not a deficit in the cognitive apparatus but rather a ‘tuning’ problem. In general, there is evidence that specific cognitive biases are of importance in the cause and maintenance of paranoid symptoms and delusions (Garety & Freeman, 2013; Savulich, Freeman, Shergill, & Yiend, 2015) as well as hallucinations (Brookwell, Bentall, & Varese, 2013). The evidence suggests that paranoid psychosis is associated with generally reduced ‘data gathering’, selective avoidance of threat, and negative interpretations of hallucinations that elicit distress (Savulich, Shergill, & Yiend, 2012). A relationship between cognitive biases and neurocognitive functioning (such as working memory) has also been established (Baskak et al., 2015; Garety, Joyce, et al., 2013; Ochoa et al., 2014).

To summarise, problems in neurocognition, social cognition, metacognition and cognitive biases contribute to and/or are associated with psychotic symptomatology. Therefore, they might offer valuable insight/information to help decrease these symptoms.

This thesis investigates the extent to which a specific focus on cognitive biases and problems in metacognition has added value with respect to the latest treatment options for patients with psychotic symptoms. Since both neurocognition and social cognition have already been extensively researched, they are not addressed here.

First, presented below is a brief description of metacognition and cognitive biases.

Metacognition and cognitive biases

The term ‘metacognition’ is often referred to as the aspect of cognition that controls mental processes and thinking, or ‘thinking about thinking’ or ‘knowledge about knowledge’. Metacognition consists of metacognitive knowledge (what individuals know about themselves and others as cognitive processors), metacognitive regulation (regulation of cognition and learning experiences through a set of activities that help people control their learning) and metacognitive experiences (experiences that have something to do with the

current, ongoing cognitive endeavour) (Flavell, 1979). Consequently, adaptive metacognitive knowledge and beliefs enhance adaptive regulation and better functional outcome. Whereas, for instance, Fonagy et al. (1995) and Brüne et al. (2011) use a relatively broad definition of metacognition focusing on problems in understanding human interaction, in this thesis we use a narrower definition, as postulated by Wells et al. (1996; 2006), referring to metacognition as ‘cognitions about one’s own cognitions’. In their S-REF model, Wells et al. (Wells & Matthews, 1996) assume that transient mood disturbances associated with negative appraisals of life events are amplified into clinically depressive symptoms because the patient employs ruminative coping, threat monitoring, and other types of behaviour that lock him or her into an emotion-focused, self-perpetuating negative coping state.

Another mechanism associated with psychopathology is that of cognitive biases. Cognitive biases are shifts in the collection, appraisal and processing of information (for an overview see Peters et al., 2014). In general, there is attentional vigilance to cues associated with threat (selective attention), pessimistic interpretation of ambiguous items, and increased perception of the likelihood of occurrence of negative events (Mathews, Mackintosh, & Fulcher, 1997). Many of these biases are of transdiagnostic nature with selective attention and emotional reasoning being present in both anxiety and depression (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van, 2007; Berle & Moulds, 2013; Gotlib, Krasnoperova, Yue, & Joormann, 2004; McLaughlin & Nolen-Hoeksema, 2011). Here we focus on the most prominent biases in psychosis, i.e. data-gathering bias (jumping to conclusions), source-monitoring bias, confirmation bias, and belief inflexibility.

The jumping to conclusions (JTC) data-gathering bias is the most comprehensively studied of the cognitive biases associated with psychosis (Freeman, 2007; Garety & Freeman, 1999, 2013; So, Garety, Peters, & Kapur, 2010a). JTC is hypothesised to contribute to hasty decision-making, the accepting of false ideas, and the inability to consider alternative explanations and, hence, the formation and maintenance of delusional ideas (Colbert & Peters, 2002b; McKay, Langdon, & Coltheart, 2006, 2007; Moritz & Woodward, 2005). There is evidence that JTC is relatively stable over time and does not change with treatment (So et al., 2010a) and also that JTC is modifiable with treatment (Ross, Freeman, Dunn, & Garety, 2011; Waller, Freeman, Jolley, Dunn, & Garety, 2011). More recently, there is increasing evidence that JTC is associated with cognitive functioning and neurocognitive deficits, low IQ, and emotional biases (Garety et al., 2014; Jolley et al., 2014; Ochoa et al., 2014).

In patients who are schizophrenic or psychotic, source-monitoring errors consistently involve the attribution of self-generated items to outside sources (Vinogradov et al., 1997). Discrimination between sources of information is an attributional process of evaluating the context in which the information was remembered and the concept of source-monitoring

is thereby adopted to explain psychotic symptoms (Bentall, 1990; Brookwell et al., 2013; Waters, Allen, et al., 2012; Waters, Woodward, Allen, Aleman, & Sommer, 2012). This applies, in particular, to hallucinations in which an individual is, retrospectively, unable to distinguish between self-generated voices and other-person-generated voice sounds.

Similar to JTC is the confirmation bias; this is defined as a cognitive mechanism that ensures the immunity of a hypothesis to counter evidence for falsification, often subcategorised into three features, i) biased search of confirming evidence, ii) biased interpretation of confirming evidence, and iii) biased recall of confirming evidence, which are common in patients who are schizophrenic and delusion prone (Balzan, Delfabbro, Galletly, & Woodward, 2013). Subsequently, patients often display a lack of belief flexibility, often referred to as Belief Inflexibility (BI), which disallows persons to reduce plausible estimated yet false beliefs in the light of contradicting evidence (Garety, Hemsley, & Wessely, 1991; Moritz et al., 2013; Moritz & Woodward, 2006a). Belief inflexibility has been found in: i) patients with schizophrenia in general (Woodward, Moritz, Menon, & Klinge, 2008), ii) in a large proportion of deluded patients (So et al., 2012), iii) in patients with grandiose delusions (patients with persecutory delusions; Garety, Gittins, et al., 2013), and iv) in remitted patients (Colbert, Peters, & Garety, 2010). There is also evidence that belief inflexibility might function as a mediator between JTC and delusional conviction (Garety et al., 2005).

Models and treatment

In their models on psychosis, leading theorists included knowledge about *metacognition* and *cognitive biases* as determining factors in the acceptance and maintenance of the maladaptive beliefs about voices or salient stimuli (Freeman, 2007; Freeman, Garety, Kuipers, Fowler, & Bebbington, 2002b; Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001; van der Gaag, 2006). One of the few models explicitly taking reasoning (cognitive biases and processes) into account as a relevant factor in the emergence and maintenance of delusional beliefs, is the threat-anticipation model on delusions (Freeman, 2007; Freeman & Freeman, 2008; Freeman, Garety, Kuipers, Fowler, & Bebbington, 2002a) which identifies multiple causes of paranoid thinking (Figure 1.1).

In this model, of particular importance are emotion and affective processes, anomalous experiences (hallucinations/perceptual anomalies), reasoning (biases include JTC, BI) and social factors such as negative events and contexts. This model is based on a stress-vulnerability framework. Stress (caused by e.g. life events, daily stressors, or drug misuse) and vulnerability interact, and symptoms emerge. For individuals with psychosis, the arousal will cause confusion and initiates anomalous experiences, such as thoughts being experienced as voices or brief perceptual anomalies. These experiences or observed changes

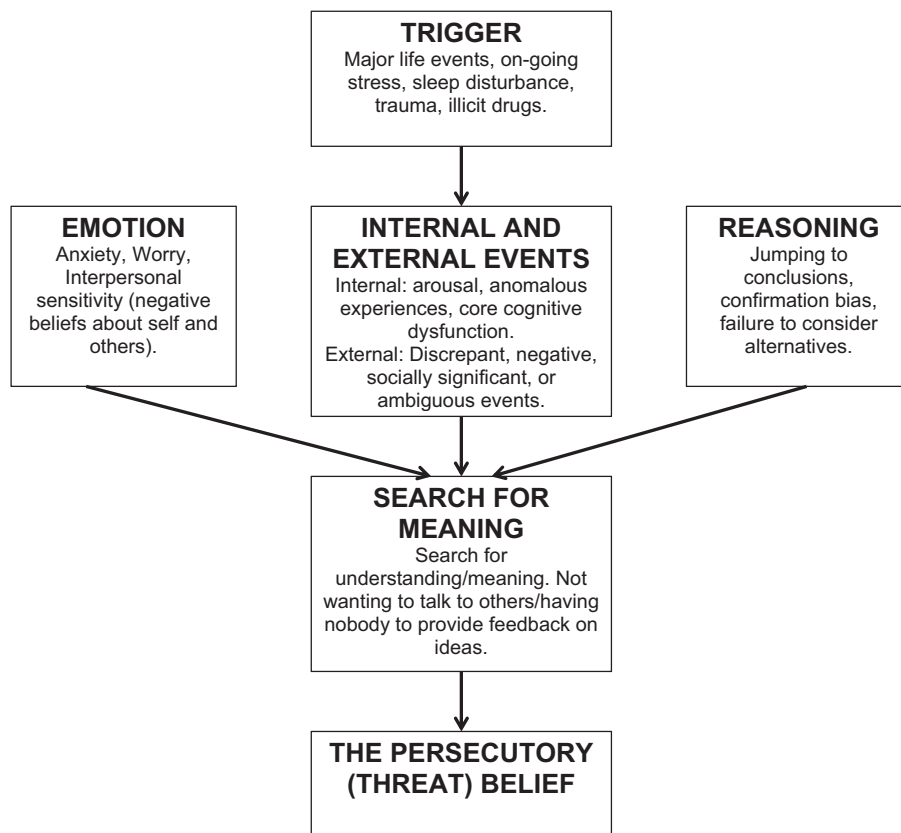


Figure 1.1 The threat anticipation model of paranoid thinking (Freeman et al., 2010).

require an explanation. A negative affective state makes it more likely for a person to adopt a threatening interpretation and reasoning biases. Engagement in worry, due to lack of functional metacognitive strategies, only strengthens the conviction of this newly adopted, negative belief of others persecuting. This often leads to odd, avoidant and even aggressive behaviour (Freeman, Pugh, Vorontsova, Antley, & Slater, 2010). This popular model is an example of how cognitive biases relate to the incidence and maintenance of delusions.

Wells was one of the first to introduce a metacognition-based therapy for patients with anxiety disorders (Wells, 2009; Wells & Matthews, 1996). This therapy, based on new insights on processes in anxiety disorders, has proven to be effective for generalised anxiety disorder (GAD) (van der Heiden, Muris, & van der Molen, 2012b; Wells et al., 2010) and is also promising in treating obsessive compulsive disorder and depressive disorder (Fisher & Wells, 2008; Wells et al., 2009). Metacognitive therapy, according to Wells, helps patients to identify patterns of worry, rumination, fixation of attention on threat, and coping behaviours. Dysfunctional

metacognitive beliefs (e.g. ‘worry helps me solve problems’ and ‘if I think a little longer I might find the solution’) enable this stressful state of mind and, in metacognitive therapy, patients are encouraged to adopt more functional metacognitive beliefs and strategies. Knowledge about cognitive biases has also been translated into treatment modules. For instance, Cognitive Bias Modification, is a treatment strategy which aims to alter these cognitive biases and is particularly effective in addressing and changing interpretation biases (Menne-Lothmann et al., 2014) and, to a lesser extent, in changing attentional bias in patients with anxiety and/or depressive symptoms (Hallion & Ruscio, 2011).

Regarding *treatment* of psychotic symptoms, over the years cognitive behavioural therapy (CBT) in psychotic symptoms (CBTp) has proven to be effective; moreover, meta-analyses have demonstrated modest but robust positive outcomes (Gould, Mueser, Bolton, Mays, & Goff, 2001; Jauhar et al., 2014; Turner, van der Gaag, Karyotaki, & Cuijpers, 2014b; Wykes, Steel, Everitt, & Tarrrier, 2008) leading to acceptance in treatment guidelines (NICE, 2009b; NWP, 2012). However, given the modest results of CBTp (small-to-medium effect sizes) and the similar results for pharmacological interventions (Leucht et al.) there is room for improvement by ameliorating existing therapies or developing new treatment methods.

Large-scale research on cognitive biases and metacognition has influenced the therapeutic landscape of psychosis with emerging therapies such as Metacognitive Training (Moritz & Woodward, 2007), Social Cognition and Interaction Training (Combs et al., 2007; Roberts & Penn, 2009), the Maudsley Review Training Programme (Waller et al., 2011) and Metacognitive Therapy (Hutton, Morrison, Wardle, & Wells, 2014). Table 1.1 presents the results of a systematic review on metacognitive training and treatment strategies addressing cognitive biases and/or metacognition. Since few of the studies are in a pilot or publishing stage, no firm conclusions can be drawn concerning their efficacy. Although RCTs on metacognitive training show mixed results, one RCT, the Maudsley Review Training Programme, has proven effective in improving state paranoia and reasoning.

This thesis focuses on the extent to which a specific focus on cognitive biases and metacognitive beliefs (metacognition) has added value with respect to the current treatment options for patients with psychotic symptoms.

The various issues and research questions are addressed below.

Metacognition in voice hearers and relationship with symptoms

In many cognitive models of psychopathology, appraisal of the experience, rather than the experience itself, determines distress. More specifically, classical CBT for auditory verbal hallucinations (AVHs) assumes that reactions to voices are mediated by beliefs about the

Table 1.1 Systematic review on metacognitive training and treatment strategies addressing cognitive biases and/or metacognition in psychosis

Name	References	Focus of treatment	Working principle	Efficacy
MCT (metacognitive training)	(Aghotor, Pfueller, Moritz, Weisbrod, & Roesch-Ely, 2010a; Briki et al., 2014a; Favrod et al., 2014b; Moritz, Andreou, et al., 2014a; Moritz et al., 2013a; Moritz, Vitzthum, Randjbar, Veckenstedt, & Woodward, 2010; van Oosterhout et al., 2014a)	Cognitive biases	-Psycho-education -Training	Mixed results on data-gathering, delusions and positive symptoms
MERIT	(Van Donkersgoed et al., 2014)	Metacognition and improving metacognitive capacity	Creating a narrative, stimulating metacognitive tasks	RCT not yet completed
MCTh (metacognitive therapy)	(Hutton, Morrison, Wardle, & Wells, 2014b)	Metacognitive beliefs	S-REF model, addressing metacognitive beliefs	Only pilot data available
Metacognitive Narrative psychotherapy	(Bargenquast & Schweitzer, 2014)	Enhancing recovery and self-experience	Enhancing metacognitive capacity	Only pilot data available
Dopaminergic modulation	(Andreou, Moritz, Veith, Veckenstedt, & Naber, 2014)	Cognitive biases: JTC and overconfidence in errors	Dopaminergic modulation	Small RCT: haloperidol reduces overconfidence in error responses
Maudsley Review Training Programme	(Waller et al., 2011) (Garety et al., 2015)	Changing reasoning processes	Computerised training	Improvements in state paranoia and reasoning
Social Cognition and Interaction Training	(Combs et al., 2007; Roberts et al., 2014; Wang et al., 2013)	Changing impairing socio-cognitive deficits	Training	Multiple RCTs, mostly positive on emotion perception, Theory of Mind, attribution, negative symptoms and social functioning
Reasoning Training (with elements of MCT)	(Ross et al., 2011)	Cognitive Biases	Training	Increased data-gathering but not for the severest cases
REFLEX	(Pijnenborg, Van der Gaag, Bockting, Van der Meer, & Aleman, 2011)	Impaired insight	Psychosocial intervention/training.	Not yet available

voices' identity, power, purpose, and the consequences of obedience and disobedience to the voices (Chadwick & Birchwood, 1994). More adequate beliefs about voices result in less distress and less avoidance (Birchwood & Chadwick, 1997). The relationship between beliefs about voices and distress is further strengthened by traumatic history (Andrew, Gray, & Snowden, 2008), low self-esteem (Fannon, Hayward, Thompson, Green, Surguladze, & Wykes, 2009; Paulik, 2012; Smith et al., 2006), and dysfunctional interpersonal schemata (Mawson, Cohen, & Berry, 2010). These confounders operate as metacognitive moderators and mediators.

Metacognitive beliefs about AVHs have been well investigated. There is evidence that distress is associated with metacognitive beliefs about self-consciousness, confidence in cognitive processes/beliefs about the uncontrollability of thoughts (Jones & Fernyhough, 2006a), the experienced control over the AVHs (Daalman et al., 2011) and unhelpful metacognitive beliefs in general (Morrison, French, & Wells, 2007a). Using a cross-sectional design, the study in **chapter two** explores the association between metacognitive beliefs and beliefs about voices in patients with severe AVHs; the study examines the hypothesis that metacognitive beliefs are better able to explain differences in levels of depression and anxiety than beliefs about voices.

Question 1: Are metacognitive beliefs better able to explain differences in levels of depression and anxiety than beliefs about voices?

Depressive symptoms in voice hearers and association with memory networks

With the emergence of the transdiagnostic approach in which similarities between different disorders are the subject of research rather than their differences, more general factors such as rumination (McLaughlin & Nolen-Hoeksema, 2011), sleep disturbances (Harvey, Murray, Chandler, & Soehner, 2011) and low self-esteem (Bentall et al., 2008) were found in the development of psychiatric problems. This knowledge enabled treatment approaches for AVHs, with less focus on changing beliefs about voices and more focus on changing metacognitive processes. Low self-esteem aggravates distress during AVHs. A therapeutic intervention aiming at both appraisal of the self and hallucinations might lower the levels of distress and comorbid depression. This assumption is also addressed by the study of Brewin (2006). He stated that all effective psychotherapies are based on competing memory networks in which successful treatment is able to change the hierarchy of accessibility of positive versus negative memory networks. Later, Korrelboom et al. developed competitive memory training (COMET) as a transdiagnostic training protocol that uses imagery, self-talk and posture to enhance positive self-esteem by making positive memories and emotions

more accessible by eliciting these positive memories over and over again (Korrelboom, de Jong, Huijbrechts, & Daansen, 2009). This transdiagnostic protocol was also tested in psychotic patients suffering from distress due to their AVHs. **Chapter three** describes an RCT which investigates whether depression can be ameliorated by weakening the associations between AVHs and easily-activated networks with negative self-evaluations, by strengthening the access to competing memories of self-esteem.

Question 2: What is the relevance of memory networks in depressive symptoms in patients with auditory verbal hallucinations?

Metacognitive training: efficacy (RCT)

Another therapeutic approach is Metacognitive Training (MCT). MCT is a group training of eight sessions based on two principles (Moritz & Woodward, 2007). The first is knowledge translation: cognitive biases are explained in a comprehensible way and are linked to delusion formation. The second principle is teaching awareness of the possible negative consequences of cognitive biases; it adopts a ‘back-door approach’ by first addressing cognitive biases instead of directly aiming at core delusional beliefs. Each module targets another cognitive bias; exercises demonstrating the fallibility of the human cognitive apparatus are discussed within the group. Participants are encouraged to express personal examples of these biases; then, discussion of ways to counter them serve to provide corrective experiences in a supportive atmosphere. Although this training module became increasingly popular, more evidence was required to establish its efficacy. **Chapter four** describes a large multi-centre RCT on the efficacy and cost-effectiveness of MCT. In this trial, 154 patients were randomly assigned to either MCT + Treatment as Usual (TAU), or to MCT alone. The main aim was to reveal whether MCT would prove efficacious in reducing delusions, subjective paranoid thinking, and ideas of social reference.

Question 3: Is metacognitive training able to reduce delusions and paranoia in patients with schizophrenia spectrum disorders?

Modifying biases with therapy

A similar development of treatment strategies as described for AVHs, also applies to delusions. Primarily, CBT focused on the appraisal of salient, ambiguous interpersonal cues leading to delusional distress. Later, it evolved into focusing more on cognitive processes and biases, rather than only on the content of the delusional beliefs (Freeman, 2007). Examples of such cognitive biases associated with delusions are data-gathering bias or jumping to

conclusions (JTC), belief inflexibility (BI), problems in theory of mind (Brüne, 2005), false-negative and false-positive errors in memory (Aleman, Hijman, de Haan, & Kahn, 1999; Moritz, Woodward, Cuttler, Whitman, & Watson, 2004), together with overconfidence in errors (Moritz & Woodward, 2006a) and biases in attributional style (Bentall, Kinderman, & Kaney, 1994). MCT aims to change these cognitive biases in order to lower delusional distress, intensity and plausibility. Regarding the nature of the association between cognitive biases and treatment response, published results on the ability of cognitive biases to mediate treatment response results are contradictory. The study in **chapter five** focuses on the question as to whether cognitive biases can be influenced by a single MCT session.

Question 4: Can Jumping to Conclusions and Belief Inflexibility be influenced by targeted training?

Metacognitive training: general efficacy (meta-analysis)

Metacognitive training (MCT) is available in 33 languages and implemented in routine care in many countries. However, because RCTs show mixed results on data-gathering, positive symptoms and delusions, it seemed necessary to evaluate its efficacy in terms of combining these mixed results. Therefore, **chapter six** describes a meta-analysis on MCT. Meta-analysis is a procedure used to pool effect sizes, increase statistical power and arrive at more robust estimates from studies with mixed results. Three meta-analyses were conducted on data-gathering, delusions, and positive symptoms. Hedge's g is reported as the effect size of interest. A 'trim and fill' procedure was used to correct for publication bias, and the statistical power was sufficient to detect small-to-moderate effects. In the final chapter of this thesis (**chapter seven**) the overall results are discussed.

Question 5: Is Metacognitive Training able to reduce delusions and paranoia, data-gathering and positive symptoms in patients with schizophrenia spectrum disorders?

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