Metacognition in severe mental disorders

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List of papers

Paper I   Østefjells, T., Melle, I., Hagen, R., Romm, K. L., Sönmez, N., Andreassen, O. A. and Røssberg, J. I. (2015). Unhelpful metacognitive beliefs in early psychosis are associated with affective symptoms and childhood social adjustment. *Schizophrenia Research,* **169**, p. 280-285.

Paper II   Østefjells, T., Melle, I., Aminoff, S. R., Hellvin, T., Hagen, R., Lagerberg, T. V., Lystad, J. U. and Røssberg, J. I. (2017). An exploration of metacognitive beliefs and thought control strategies in bipolar disorder. *Comprehensive Psychiatry,* **73**, 84-92.

Paper III   Østefjells, T., Lystad, J. U., Berg, A.O., Hagen, R., Loewy, R., Sandvik, L., Melle, I. and Røssberg, J. I. (2017). Metacognitive beliefs mediate the effect of emotional abuse on depressive and psychotic symptoms in severe mental disorders. *Accepted for publication in Psychological Medicine,* **doi:10.1017/S0033291717000848**.

Summary

Current diagnostic classification systems impose a core divide between affective and psychotic disorders, but empirical evidence does not necessarily support such a sharp distinction. Research shows that affective dysregulation and psychotic experiences or symptoms often co-occur in the general population as well as in bipolar and psychotic disorders, suggesting a complex interplay between affective dysregulation and psychosis. Early trauma is hypothesised to be important for the aetiology of both affective and psychotic symptoms and disorders, and individuals with early traumatic experiences often develop disorders characterised by an admixture of affective and psychotic symptoms. Still, relatively few studies have focused on common factors associated with affective dysregulation and psychosis in both bipolar and psychotic disorders.

One proposed common factor in psychological disorders is metacognition, which refers to *thinking about thinking*. The self-regulatory executive function (S-REF) model proposes that beliefs about thoughts can influence cognitive and behavioural responses to distress in a manner that prolongs emotional distress. Research shows that patients with both affective and psychotic disorders hold higher levels of metacognitive beliefs than healthy individuals, and indicates that such beliefs are linked to, and could influence, symptomatic affective dysfunction in these disorders. Metacognitive beliefs could thus be a common factor associated with affective dysregulation and psychosis in both bipolar and psychotic disorders. However, studies of bipolar disorders are scarce. Metacognitive beliefs further show an independent relationship to positive symptoms and their long-term course and a more chronic outcome ten years after a first psychotic episode, but it is not clear if this is true for early psychosis.

The main aim of this thesis was to investigate key metacognitive factors as outlined by the S-REF model—*metacognitive beliefs* and *thought control strategies*—in patients with bipolar or psychotic disorders. Specifically we sought to examine whether patients with bipolar or psychotic disorders report higher levels of metacognitive beliefs compared to controls. Further we sought to explore whether illness-related factors known to be relevant in bipolar or psychotic disorders were related to metacognitive beliefs. In regards to bipolar disorder we also aimed to

investigate whether patients with bipolar disorders report different use of thought control strategies compared to controls, whether illness-related factors relevant to bipolar disorders were related to use of specific strategies, and whether metacognitive beliefs would relate to use of thought control strategies above the illness-related factors. Finally, this thesis aimed to examine whether metacognitive beliefs could potentially mediate affective or psychotic symptom responses to early emotional trauma.

Papers I and II investigated the prevalence of metacognitive beliefs in early psychosis and bipolar disorders respectively, compared to controls. The papers further investigated relationships between such beliefs and specific illness-related factors. Paper II additionally explored the prevalence of thought control strategies in bipolar disorder compared to controls, and further investigated the relationships between metacognitive beliefs and use of thought control strategies above the influence of illness-related factors. The findings reported in Papers I and II show that patients with bipolar disorders or early psychosis report higher levels of the metacognitive beliefs implicated in the S-REF model when compared to controls. Paper II also show that patients with bipolar disorders report different use of thought control strategies to self-regulate distress when compared to controls. Findings from Paper I and II suggest that metacognitive beliefs are related to affective dysfunction in both patient groups, but with somewhat clearer findings for the early psychosis sample. Paper I additionally suggests that childhood social adjustment is related to metacognitive beliefs for patients with early psychosis, while Paper II suggests that an earlier age at onset of the affective illness is related to higher levels of some metacognitive beliefs in bipolar disorders. Further, Paper II shows that use of thought control strategies is mainly related to metacognitive beliefs, but use of punishment is related to age at onset of an affective illness.

Paper III examined whether metacognitive beliefs could potentially mediate affective or psychotic symptom responses to early emotional trauma. The findings suggest that moderate or more severe experiences of early emotional abuse are linked to higher levels of unhelpful metacognitive beliefs, and that these beliefs in turn mediate the stronger affective symptoms associated with the early emotional trauma. The results further indicate that this mediation pathway extends to positive symptoms, with more severe experiences of early emotional abuse being linked to higher levels of both

metacognitive beliefs and depression/anxiety, which together mediate the stronger positive symptoms associated with the emotional trauma.

In line with previous studies, our findings indicate that metacognitive beliefs are elevated in patients with bipolar and psychotic disorders, and could be a common factor. In line with theory, the results also suggest that metacognitive beliefs are closely related to use of thought control strategies. Our findings expand the literature by showing that *i)* metacognitive beliefs are relevant in early psychosis, *ii)* that metacognitive beliefs and linked to affective dysfunction in bipolar and psychotic disorders as well as to illness characteristics linked to a poorer long-term outcome, and *iii)* by implicating that metacognitive beliefs can mediate affective and psychotic responses to early emotional trauma.

The findings underline the clinical utility of metacognitive factors as a potential treatment target in ameliorating affective dysfunction in bipolar and psychotic disorders, particularly when there is a history of early emotional trauma. Future studies could benefit from clarifying whether metacognitive beliefs are stable or amenable to illness processes over time, and how they interact to other clinical variables and thought control strategies. This could further our understanding of the role such beliefs play in illness formation, maintenance, and long-term outcome, and shed light on the potential of their clinical application in severe mental disorders.

Abbreviations

BP-I	Bipolar disorder, type I (i.e. with mania or mixed mood)
BP-II	Bipolar disorder, type II (i.e. with hypomania only)
BP-NOS	Bipolar disorder not otherwise specified
CTQ	Childhood Trauma Questionnaire—Short Form
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
ICD	International Classification of Diseases and Related Health Problems
IDS-C	Inventory of Depressive Symptoms—Clinician Rated
MCQ-30	Metacognitions Questionnaire (short form, 30 items)
MCQ-UD	MCQ-30 subscale "Uncontrollability and danger"
NOS	Not otherwise specified
PAS	Premorbid Assessments Scale
PANSS	Structured Clinical Interview for the Positive and Negative Syndrome Scale
SCID-I	Structured Clinical Interview for DSM Axis I Disorders
SPSS	Statistical Package for the Social Science
TCQ	Thought Control Questionnaire
TOP	Thematically Organised Psychosis Study

1   Introduction

Current diagnostic classification systems impose a core divide between affective and psychotic[†] disorders, and hence encourage separate study and treatment. While this separation of 'affective illness from madness proper' prevails, empirical evidence does not necessarily support such a sharp distinction. Research shows that affective dysregulation and psychotic experiences or symptoms often co-occur, both in the general population (1-12), and in patients diagnosed with bipolar (13-18) or psychotic disorders (19-23), suggesting a complex interplay between affective dysregulation and psychosis. Common underlying risk factors for affective and psychotic disorders are increasingly highlighted in genetic studies (24). Research on early trauma also highlights its high prevalence in both bipolar (25-28) and psychotic disorders (29-32), and early trauma is hypothesised to be important for the aetiology of both affective and psychotic symptoms (33) – and disorders (34). Shared hereditary and environmental risk factors for both affective and psychotic outcomes has led to suggestions of an affective pathway to psychosis (7, 21, 35-37), and psychological models that recognise a specific role for affective dysfunction in positive symptoms (38, 39). Still, relatively few studies have focused on the mechanisms connecting bipolar and psychotic disorders and their shared environmental risk factors.

One proposed common factor in psychological disorders is metacognition (40-43). Metacognition refers to *thinking about thinking*, i.e. higher-order thinking, which enables analysis, understanding, and control of one's cognitive processes (42). The self-regulatory executive function (S-REF) model (42, 43) proposes that vulnerability to mental disorder is influenced by a cognitive style where metacognitive beliefs cause or prolong affective dysfunction by influencing what is perceived as threatening or distressing, and promoting ineffective strategies for self-regulation (42). In this model, unwanted cognitive or emotional experiences trigger meta-beliefs about thoughts, which in turn trigger threat-focused attention and ineffective coping strategies such as rumination, worry, and punishment. This cognitive style strains

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[†] While affective disorders with psychotic features are sometimes termed 'psychotic disorders' in the research literature, this thesis uses the terms 'affective' and 'psychotic' disorders in line with their classification in the major diagnostic manuals (i.e. an affective disorder with psychotic features is classified as 'affective').

limited cognitive resources, and may thus prolong emotional distress. Metacognitive beliefs are linked to both affective dysfunction (44-47) and trauma history (48) in bipolar and psychotic disorders, and seem to mediate affective responses to early emotional abuse in a non-clinical sample (49). The literature thus suggests a complex relationship between symptoms of bipolar and psychotic disorders, early trauma, and metacognitive beliefs.

Investigation of common factors associated with affective dysregulation and psychosis in both disorders could have important implications for further development of psychological models, and inform prevention efforts, early intervention, and treatment of symptoms. The main aim of this thesis was thus to further explore the role of metacognitive factors, using the S-REF model (42), in individuals with bipolar and psychotic disorders. A primary aim was to investigate how such factors interact with other illness aspects, and in particular affective symptoms. The thesis further sought to investigate whether metacognitive beliefs could potentially mediate affective or psychotic symptom responses to early emotional trauma.

1.1   Bipolar and psychotic disorders

Affective and psychotic disorders form one of the crucial dichotomies in modern psychiatric classification, and both the diagnostic and statistical Manual of Mental Disorders (DSM) (50) and the International Classification of Diseases (ICD) (51) impose a core divide between affective disorders – with or without psychotic features – and 'non-affective' psychotic disorders. Yet, evidence suggests genetic, aetiological, epidemiological, and clinical overlap between bipolar and psychotic disorders (22, 52, 53).

1.1.1 Key symptoms in bipolar and psychotic disorders

Bipolar disorders are characterised by severe alterations in mood, including hypomania or mania (the cardinal mood alteration for a diagnosis) and depression (18, 50, 51). Psychotic disorders encompass disorders where the primary symptoms are distorted conceptions of reality, or 'positive symptoms' (50, 51, 54). While the borders between the disorders are treated as dichotomous, schizoaffective disorder (which is characterised as a psychotic disorder) in many ways constitute an

'intermediate' category where both affective and psychotic symptoms are prominent and co-occur.

Outlined below are the key symptoms that contribute to a diagnosis of a bipolar or psychotic disorder. Notably, there are no individual symptoms that are entirely unique to only bipolar or psychotic disorders (55), and individual presentations with the same diagnosis can show great clinical heterogeneity. Specific requirements for each diagnosis are shown in Table 1 (p. 6).

Mania and hypomania

Manic states are typically characterised by an elevated and expansive mood, inflated or grandiose self-esteem, brisker mental activity (including quicker thought processes, increased and faster speech, and heightened perceptual acuity), brisker physical activity (including increased goal-directed activity and psycho-motoric agitation) with a corresponding decreased need for sleep, increased distractibility, heightened sexuality and impulsivity, and decreased risk-perceptions (18, 50). Manic states can also include irritability along with the above symptoms, or as the main mood state. To diagnose a manic episode, DSM 4th Edition (DSM-IV) requires the presence of elated mood and three additional symptoms, or irritable mood and four additional symptoms, lasting for at least one week, or causing hospitalisation, or with concurrent positive symptoms.

Hypomanic states are similar to manic ones, but the prefix 'hypo' denotes something that is under, or in this case, a milder form. Hypomanic states show the same symptomatic presentation, but DSM-IV requires a shorter duration to diagnose a hypomanic episode (at least four days), and that the mood state does not lead to hospitalisation (50). By definition, a hypomanic episode cannot include positive symptoms.

Depression

Depressive states are characterised by a pervasive depressed mood or loss of interest, marked fatigue, a sense of worthlessness or inappropriate guilt, suicidal thoughts, ideation or plans. Changes in mood are often accompanied by extreme indecisiveness or decreased ability to think/concentrate, changes in sleep (including insomnia, hyposomnia and hypersomnia), changes in weight or appetite, and psychomotoric retardation or agitation (18). DSM-IV requires the depressed mood or loss of interest

to be present persistently for a minimum of 14 consecutive days, along with a minimum of four other symptoms, to diagnose a depressive episode (50). Severe depressive episodes can be classified as being 'with' or 'without' positive symptoms.

Mixed mood states

Mood states in which features unique to both depression and mania occur either simultaneously or in very short succession are labelled as 'mixed' (18). DSM-IV allows a diagnosis of a mixed episode when symptoms of both mood modalities are present for at least one week, or shorter if hospitalisation is required (50).

Positive symptoms

Positive symptoms are denoted as such because they constitute an addition to normal experiences (56). Positive symptoms include delusions and hallucinations, the hallmark symptoms of psychotic disorders. Hence, they are often referred to as 'psychotic symptoms' in the non-psychosis literature.

Delusions are beliefs that are inconsistent with the person's culture, that persist despite evidence that the beliefs are not logical or true. Traditionally defined as fixed, false beliefs (50), research shows that delusions are not as absolute as originally believed, but complex and multidimensional phenomena (57). It has been suggested as more viable to consider a belief on several dimensions, but that no single characteristic should be neither necessary nor sufficient to render it as a delusion (58). Following this, a delusion can be characterised by the belief being unfounded; firmly held; resistant to change; preoccupying; distressing; interfering with social functioning; and involving personal reference (58, 59). In DSM-IV delusions can be denoted as 'bizarre' if they are perceived as completely impossible.

Hallucinations are sensory experiences in any modality (auditory, visual, olfactory or tactile) that are perceived without actual sensory input. In DSM-IV, hearing a voice that comments directly on the person's behaviour and thoughts (e.g. in a television commentator style) or multiple voices that converse amongst each other, is denoted as 'bizarre' hallucinations.

Negative symptoms

Negative symptoms are denoted as such because they constitute an absence of normal experiences or behaviours (60), and include *alogia* (reduced speech content or

meaning), *anhedonia* (loss of pleasure), and *avolition* (decreased motivation or ability to initiate and/or perform self-directed purposeful activities).

Other symptoms

Disorganised thinking includes formal thought disturbances where a person has trouble connecting their thoughts logically, is unable to communicate clearly due to rapid associations or use of meaningless words (neologisms), or stop communicating due to experiences of their thoughts being 'blocked'.

Disorganised behaviour includes inappropriate displays of affect (e.g. smiling or laughing while explaining how someone is trying to murder them and how serious this is), purposeless, repetitive, or extremely agitated behaviours, or catatonia (an unresponsive state characterised by lack of movement).

While these symptoms are often included under the heading of psychotic symptoms, factor analyses (e.g. 61) suggest they are separate from positive symptoms. The current thesis uses a five-factor structure in all analyses, and does not include disorganised thinking or behaviour when positive symptoms are discussed.

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Table 1: Diagnostic criteria for bipolar and psychotic diagnoses according to DSM-IV

Bipolar type I	At least one manic or one mixed episode.
Bipolar type II	At least one hypomanic episode and at least one depressive episode.
Bipolar NOS	Used when symptoms in the bipolar spectrum are present, but do not meet full criteria for any of the formal diagnoses mentioned above.
Schizophrenia	Requires the presence of ≥2 positive, negative or other symptoms (1 if hallucinations or delusions are 'bizarre') that co-occur for 1 month (1 week if adequate treatment) (criterion A), and co-occurring marked reduction in work or social function (criterion B). Continuous signs of the illness (i.e. criteria A and B + prodromal or residual periods) must last for ≥6 months.
Schizophreniform disorder	Criterion A and B for schizophrenia are met, but continuous signs of the illness (i.e. criteria A and B + prodromal or residual periods) last for <6 months.
Schizoaffective disorder	Requires that the A, B, and duration criteria for schizophrenia are met, including 2 weeks without a mood episode, and that criteria are met for any mood episode in a 'substantial* part' of the active and residual illness phases.
Delusional disorder	Delusions are present for ≥3 months, without meeting criterion A for schizophrenia. Function should not be markedly impaired as a result of delusional beliefs, but some specific impairment may occur. Bizarre behaviours should not be present. Tactile or olfactory hallucinations can occur in specific relationship to delusions.
Brief psychotic disorder	Delusions, hallucinations, disorganised speech or disorganised/catatonic behaviour is present for at least one day, but less than one month. When symptoms remit the person should recover fully to the functional level they had before the symptoms arose.
Psychotic disorder NOS	Used when psychotic symptoms are present, but do not meet full criteria for any of the formal diagnoses mentioned above, the information is not clear enough to make a more specific diagnosis, or information is contradictory.

Notes: All diagnoses require that the symptoms are not a direct consequence of a somatic condition, or use of medication or a substance.

* What constitutes a 'substantial' amount of time is not specified clearly in the DSM-IV manual. The UCLA SCID-I training programme suggests that affective episodes should overlap with positive symptoms for >20 percent of the active or residual illness phase to qualify for a diagnosis of schizoaffective disorder.

1.1.2 Overlap in symptoms across bipolar and psychotic disorders

Positive symptoms in bipolar disorders

Positive symptoms have been estimated to co-occur in 20—50 percent of patients with acute mania (17), with approximately 58 percent of patients with bipolar disorder experience at least one life-time positive symptom (62). Estimates for a life-time history of positive (psychotic) symptoms in bipolar disorder type I (BP-I) range as high as 62—76 percent for adults (13-16), while estimates for bipolar disorder type II (BP-II; where symptoms can, by definition, only be present during depressive episodes) range from 6 to 34 percent (15, 63-66). One study of individuals with a first psychotic episode as part of a bipolar or psychotic disorder even suggests that patients in these diagnostic groups can demonstrate similar levels of positive symptoms at first presentation (67).

Affective dysfunction in 'non-affective' psychotic disorders

Psychotic disorders are often specified as 'non-affective'. Still, all factor analyses of psychotic disorders (including studies that exclude affective disorders with psychosis) identify depression, or more broadly affective symptoms, as a distinct dimension of psychotic disorders (68). In line with this, the prevalence of depressive episodes in established psychotic disorders such as schizophrenia has been reported to be around 40 percent, but varies considerably with state (acute vs post-psychotic) and stage of illness (early vs chronic) (69). However, a longitudinal study finds that 80 percent of schizophrenia patients experience a clinically significant depressive episode at one or more times during the early phase of the illness (70), underscoring how cross-sectional rates can markedly underestimate the true prevalence of depressive symptoms in psychosis. Similarly, a 12-year follow-up study of patients with schizophrenia finds that depressive symptoms frequently mark the onset of schizophrenia, and is the most frequent co-occurring syndrome over a 12 year follow-up period (71).

Clinical relevance of overlapping symptoms

For BP-I, several studies report that concurrent positive symptoms are associated with a more severe outcome, specifically earlier (72), longer (73) and higher rates of hospitalisation (74), more severe, persistent and recurring mania (72, 74-76), and poorer response to lithium monotherapy (74). While positive symptoms are currently considered a marker of mood severity, not all studies find that patients with severe

mania rated as 'with' or 'without' psychotic features differ in mania severity, but rather that positive symptoms are related to an earlier age at onset, single relationship status, and having more comorbid anxiety and substance use (77). For BP-II, concurrent psychotic symptoms during depression are linked to a higher age, a higher number of hospitalisations, and more melancholic and catatonic features (66), suggesting that in BP-II psychotic symptoms are strongly associated with a specific and severe type of depression.

In psychotic disorders, evidence suggests that affective dysfunction such as depression is linked to poorer outcomes, including higher rates of suicidality (78) and completed suicides (79), less chance of psychotic symptoms remitting (80), higher relapse-rates, more co-morbid substance-related problems, poorer medication adherence, and poorer quality of life and family relationships (69). A 10-year follow-up study finds that first-episode psychosis patients who remained depressed during the first year of treatment have poorer symptomatic and functional prognosis (81). Similarly, further sequence analysis of the 12-year follow-up study mentioned above suggests that 27 percent of these patients show illness trajectories involving purely depressive or concomitant depressive, negative and positive symptoms, with a chronic illness course (82). However, the relationship between affective dysfunction and positive symptoms is not straightforward, and causality cannot be established. One study from the general population finds that most psychotic experiences occur in a context of affective dysregulation, with a bidirectional dose-response for greater levels of both affective dysregulation and psychotic experiences (7). In established psychotic disorders, one longitudinal study finds that depression in the early course significantly predict higher frequency of depressive and psychotic symptoms across five years (83), while another study finds that depression and positive symptoms co-occur—but do not necessarily predict each other—across 10 years (81).

In sum, evidence shows that individuals with bipolar disorder frequently experience positive symptoms (but lower levels than in psychotic disorders), while individuals with psychotic disorders have high rates of comorbid affective symptoms (albeit lower than in bipolar disorders) (84). Despite an increasing focus on the presence of positive symptoms in affective disorders and affective symptoms in psychotic disorders, there are currently no systematic reviews or meta-analyses summarising the prevalence or importance of the overlapping symptoms in either bipolar or

psychotic disorders. It is, however, clear that positive symptoms are highly prevalent in bipolar disorders and likely relevant to the clinical course and outcome, while depression is prevalent and clinically relevant in psychotic disorders.

1.1.3 Epidemiological and clinical perspectives

Bipolar and psychotic disorders share a range of characteristics, but also have distinct features (55, 85).

Prevalence

Bipolar disorders appear to form a spectrum of severity from the milder, sub-syndromal cyclothymia, to bipolar II disorder, to bipolar I disorder. Similarly, psychotic disorders seem to form a spectrum from briefer or unspecified psychotic illness, to delusional disorder, to schizophrenia. The most severe bipolar and psychotic spectrum disorders—bipolar disorder type I and schizophrenia—have a similar life-time prevalence of ~1 percent (55, 86-89). When the entire bipolar spectrum is included, life-time prevalence increases to 2.8-6.5 percent (90, 91). Estimates suggest a slightly lower life-time prevalence of 2.3 percent for all 'non-affective' psychotic disorders (89), which include the narrow schizophrenia spectrum (schizophrenia, schizophreniform and schizoaffective disorder), as well as the broader psychotic spectrum disorders (delusional disorder, brief psychosis, and psychotic disorder not otherwise specified).

Illness development and characteristics

Both bipolar and psychotic disorders typically develop in late adolescence or early adulthood, with an earlier age at onset for men (55). However, social and academic premorbid adjustment is clearly compromised in some patients with psychotic disorders, and is often seen as early as childhood (92). Studies of premorbid adjustment are scarcer in bipolar disorders, but similar deterioration in social adjustment possibly emerges for some patients in adolescence (93). This could also be an expression of the emerging illness; both disorders typically have a prodromal phase, with more subtle and unspecific signs of the illness. The prodromes overlaps considerably in characteristics, but with more marked affective changes in those who develop bipolar disorders and more attenuated positive symptoms in those who develop psychotic disorders (94). The diagnosis of bipolar disorder can be hard to ascertain as the index mood episodes in approximately half of the cases is depression

(95), while the diagnosis depends on the first (hypo)manic or mixed episode. A registry study suggests that approximately 44 percent of patients with a bipolar disorder will not be correctly diagnosed at initial contact with health services (96), resulting in the illness going untreated for months and years. Patients with psychotic disorders often experience diagnosable psychotic symptoms that can go untreated for similarly long periods of time (97). While the effects of untreated bipolar disorder on long-term outcomes is not fully known (98), the relationship between duration of untreated psychosis (DUP) and long-term outcome in psychotic disorders is well documented (99). Neurocognitive impairments also seem to represent a core feature of both disorders, but are more pronounced in psychotic disorders (100-102). However, levels of impairment could also depend more on life-time presence of positive symptom than diagnostic category (103).

Both disorders can be episodic, and are often recurrent. A high prevalence to incidence rate (~100 to 3 for bipolar and~100 to 4 for schizophrenia) indicate a high rate of chronicity or chronic across the life-span (55). While the life-time prevalence rates cited above might seem small, the World Health Organization (WHO) estimate that approximately 60 million people world-wide are affected by bipolar disorders and another 21 million by schizophrenia alone (104), suggesting that at least another 21 million people are affected by the remaining psychotic disorders. The illness characteristics make them among the most debilitating diseases known to humankind (54), and together the disorders are responsible for approximately four percent of the world total loss of disability-adjusted life years (105).

Causes of bipolar and psychotic disorders
Prevailing models of bipolar and psychotic disorders are not unified, but both focus on how biological, psychological and social factors integrate and give rise to the observable symptoms through a genetic or acquired vulnerability to stress, which interacts with environmental factors to trigger illness development (106-109). In line with this, both disorders have a high heritability rate, at ~60-80 percent (24, 110), co-aggregate in families (111), and show some overlap in specific genetic liabilities (112-117). One of the largest genetic epidemiology study of heritability patterns to date (24) finds that biological relatives of both bipolar disorder and schizophrenia have increased risk for both disorders, with shared genetic risk factors estimated to 30–40 percent, and shared environmental factors estimated to 3–6 percent. Both

disorders also show aberrant regulation in biological factors related to stress regulation (118).

Vulnerability to stress could also arise from, or be exacerbated by, environmental factors. Early trauma is a commonly proposed environmental factor in both disorders as it is robustly linked to a higher risk of both bipolar (25-28) and psychotic (29-32) disorders, and a more severe course and outcome. Individuals with bipolar or psychotic disorders and early trauma report more severe symptoms (27, 119-122), in particular more mood episodes (25, 123, 124) and positive symptoms (125-127) in bipolar disorder, and higher levels of depression in psychotic disorders (33, 119, 122). Early trauma is thought to be important in the aetiology of both affective and psychotic disorders (34), and patients with experiences of early trauma experiences seem to develop an illness characterized by combinations of multiple symptom domains, including depression, mania, anxiety and psychosis (33). A recent study indicates that early trauma and positive symptoms could be linked through affective symptoms (128), emphasizing that research needs to consider the interplay between these factors. Early trauma is thus proposed as an underlying risk factor for both affective dysfunction and positive symptoms.

The similarities outlined thus far do not necessarily challenge the categorical distinction between primarily affective and primarily psychotic disorders. However, from a clinical perspective, and as outlined in section 1.1.2, affective and psychotic disorders do not separate as neatly as the diagnostic criteria suggest. Based on close links between depressive and psychotic symptoms in the general population (1-12), it has been suggested that psychotic experiences represent the severe end of a common mental distress factor, which is also influenced by symptoms of depression and anxiety (129)—but that the co-occurrence of affective and psychotic symptoms only has distinct specificity and power in established mental disorders (1). This is in line with the suggestion of an affective pathway to severe mental illness, and to positive symptoms in particular (21, 37). Investigation of common factors associated with affective dysregulation and psychosis could thus have important implications for further development of psychological models, prevention efforts, early intervention, and treatment of symptoms.

A promising way to refine existing psychological knowledge about both bipolar and psychotic disorders is through the emerging theories concerning metacognitive processes as a generic factor in mental disorders.

1.2 Metacognition

Metacognition refers to *thinking about thinking*, i.e. higher-order thinking, which enables analysis, understanding and control of one's cognitive processes (42). In our everyday lives, we rely on metacognitive processes to monitor and control our thinking. For example, knowing how to memorise something and when it is sufficiently committed to memory requires several metacognitive processes. Understanding when the information is relevant and how to retrieve it also relies on metacognition. In brief, metacognition is involved in all cessation, perpetuation or modification of thoughts, making it crucial to efficient and functional information processing. Wells (43) proposes that what differentiates clinical groups from psychologically well-functioning individuals is not the content of their thoughts, but rather that their metacognitions—what is perceived as salient to the self, beliefs about thoughts, and coping strategies used to restore emotional balance—make them more vulnerable to mental disorder.

1.2.1 The Self-Regulatory Executive Function (S-REF) model

The self-regulatory executive function (S-REF) model (42, 43) is an information processing model that outlines factors involved in the aetiology and maintenance of psychological disorder. Specifically, it proposes that factors which modulate and control thinking itself (i.e. metacognitive processes) may contribute to prolong affective dysregulation, by influencing what we deem as distressing or dangerous, what our desired cognitive 'goal-state' is, and the strategies we employ to regulate distress. The S-REF model was developed in the context of anxiety and mood disorders, where emotional dysfunction is prominent, but is suggested as a generic model of how affective dysfunction is developed and maintained in any psychological disorder.

Two key constructs in the S-REF model are metacognitive knowledge, and metacognitive control strategies.

Metacognitive knowledge refers to theories and beliefs people hold about their cognitions. This knowledge can be consciously and verbally accessible, e.g. when a person believes that worrying is an advantageous strategy or that thoughts can be dangerous to their health. Metacognitive knowledge can also be implicit, comprising of rules or plans that guide our cognitive processing. Such plans control central cognitive processes, like allocation of attention, application of memory, and use of heuristics and biases when forming judgements. In research and this thesis, metacognitive knowledge is operationalised as *metacognitive beliefs*—i.e. assumptions that outline the perceived importance or consequences of specific thoughts.

Metacognitive control strategies are the responses people make in order to control the activities of their cognitive system. In everyday life such strategies are normally aimed at enhancing memory or recall. In psychological disorder such control strategies more typically attempt to control the stream of consciousness, e.g. worrying to solve problems, or trying to reappraise experiences to modify the emotional response. In research and this thesis, metacognitive control strategies are operationalised as *thought control strategies*.

Levels of cognition

Figure 1 (p. 14) outlines the S-REF model. Starting at the bottom of the figure, the model differentiates between three interacting levels of cognitive processing.

i. A lower-level network that processes internal and external stimuli automatically and reflexively. Lower-level processing is predominantly outside of conscious awareness, requiring a minimum of attentional resources.

ii. An on-line level of controlled processing, involved in regulation of thoughts and behaviour. On-line processing is amenable to varying degrees of consciousness as it consists of judgements, which depend on available attentional resources. Processing at this level also depends on

iii. A level of stored self-knowledge in long-term memory, which includes a metacognitive component, including declarative metacognitive beliefs about thinking that guide the appraisal of situations and events, and general, implicit plans for processing (e.g. control strategies), which direct on-line processing.

iii) Long-term memory

SELF-KNOWLEDGE

Including metacognitive beliefs and strategies

Belief elaboration

ii) Controlled processing

Accessing beliefs

Selection of generic plan

priming?

S-REF

Control of action

FINISH

Appraisal
(active worry/rumination)

Intensification/
supression of
activity

Intrusion

Monitoring

i) Automatic processing

Cognitive Info
Body state info
External info

LOWER-LEVEL PROCESSING UNITS

Figure 1: The Self-Regulatory Executive Function (S-REF) model
The model is adapted from Wells and Matthews (42) and Wells (43).

Any given state of affairs is assessed, and matched to a desired goal-state. In the case of a discrepancy, a general plan for processing is modified on-line to obtain the desired state. This is achieved through allocation of attentional resources and initiation of self-regulatory strategies perceived as appropriate to attain the desired goal-state. These three levels of cognition sustain the total range of processing operations available to any individual. However, processes can be executed within different 'modes' and 'configurations'.

Modes

The mode of processing refers to the perspective employed when considering thoughts and perceptions. The default is 'object mode' where thoughts and perceptions are accepted as accurate representations, without further evaluation (e.g. if something is perceived as a threat, this is taken at face value). In contrast, the metacognitive mode is a state where the individual is able to reflect on and evaluate thoughts and perceptions (e.g. the *perception* of threat is evaluated for its validity). In normal functioning we switch flexibly between the two modes. However, for individuals suffering from psychological disorder this flexibility is assumed to be reduced—as self-regulation is activated, cognitive resources are depleted and the individual becomes locked in object mode.

Configurations

Different configurations, or patterns of cognitive processes, may be activated within the three layers in the model. The S-REF model hypothesises that in all psychologically significant affective dysfunction, a self-regulatory (S-REF) configuration is central.

The S-REF configuration primarily focuses attention on the self, and appraises the personal significance of cognitions, body state, and external stimuli. In psychological disorders, processing occurs in object mode, which causes the individual to accept appraisals as accurate. S-REF processing is initiated by intrusions from lower-level processing to the controlled processing level. Such intrusions may be external in nature, but are as likely internal in origin (e.g. a thought or an unspecified physical sensation). When activated, the S-REF configuration utilises the stored self-

knowledge to generate an appraisal of the threat[‡] and select an appropriate coping strategy. S-REF activity is maintained by controlled processing and supported by long-term knowledge, but can directly impact on lower-level processing through implementation of specific strategies, e.g. attention allocation to monitor the perceived threat. Normally, on-line S-REF activity is brief: The individual selects a strategy to address the discrepancy between the current and desired state, by modifying beliefs or perceptions through task-focused coping. Once goals are achieved, S-REF processing is deactivated. However, in psychological disorder the self-regulatory goal is often unattainable, the self-regulation strategies are ineffective, or both—causing the S-REF configuration to become perseverative as the goal of self-regulation is not resolved. On completion, or in the case of persevered activity, S-REF activity can also modify the knowledge base in long-term memory in regards to the chosen regulatory strategy and results.

Maintenance of psychological disorder: A cognitive attentional syndrome

To most of us, appraisals are met with implementation of successful coping strategies, and periods of intense emotion and stress are brief, but this may not be the case in psychological disorder. When self-discrepancies remain, the S-REF configuration is apt to be prolonged or kept in a state of readiness for reactivation.

The model postulates that psychological dysfunction is associated with a non-specific cognitive attentional syndrome (CAS). CAS is characterised by use of worry and/or rumination, a focus on threat-detection, limited cognitive resources, and use of self-regulatory strategies that fail to modify negative beliefs. In other words: When an individual suffering from psychological disorder becomes distressed, the processing and coping activities—i.e. the CAS—are assumed to interfere with the needed cognitive adjustments, e.g. re-assessing the situation in a metacognitive mode and readjusting the self-regulatory goal or control strategies. This prevents the individual from returning to normal functioning, and rather extends the need for self-regulatory activity, thereby maintaining the distress.

[‡] The term 'threat' is used in a wide sense in this context, and includes everything that is perceived as distressing, including bodily, emotional, or cognitive experiences that are unwanted.

Several factors could contribute to prolong or keep self-regulatory processing in a state of readiness, including metacognitive beliefs or control strategies, a reliance on internal data to evaluate an external situation, and previous life-experiences and personality style.

In psychological disorder, difficulties with cognitive-emotional self-control often originate in the individual, such as a flawed experience of control; use of unhelpful coping strategies, preventing the person from gaining control; dysfunctional beliefs about self-regulation; or use of coping strategies that fail to modify maladaptive self-knowledge. Metacognitive beliefs, such as believing worry to be an effective and desirable coping strategy, also maintain S-REF activity.

The model assumes that much of the data individuals with psychological disorder use as reference guides in self-regulation are internal in origin: Memory, feelings, body states, and impressions of the self, influence appraisals of events and self-knowledge. Such internal data are part of the self-focused attention style associated with the CAS, and provide a benchmark for whether coping efforts should be terminated or continued. Interacting with individual factors mentioned above, as well as specific coping strategies directly involving attention (e.g. a sustained monitoring for threat) the 'felt' goal state where self-discrepancies are removed becomes a mirage—something that appears real or possible, but is in fact not so.

Metacognitive abilities mature gradually with normal development (130), and will interact with personality traits such as a disposition for self-focused attention, or a preference for emotion-focused coping strategies. Increased negative self- or other-knowledge, e.g. as a result of early traumatic experiences, is also assumed to influence the preservation of S-REF activity.

In summary, the S-REF model emphasises the role of metacognitive factors in taking control over information processing in a top-down manner. Specific beliefs about the importance or consequences of having some kinds of thoughts are assumed to activate a self-regulatory focus (S-REF configuration) which involves biased attention allocation focusing on threat-oriented and confirmatory information. In combination with ineffective strategies such as worry, rumination and punishment, this cognitive style prevents effective resolution of distress and prolongs affective dysfunction.

1.2.2 Metacognitive beliefs in bipolar disorders

Studies of metacognitive beliefs in bipolar disorder are scarce, but the S-REF model has received increasing empirical support in unipolar depression. Depressed individuals report significantly higher levels of metacognitive beliefs than both control participants (131, 132) and previously depressed individuals (131, 133), and such beliefs are linked to both state and trait depression (134, 135). Two studies have explored metacognitive beliefs in patients with a bipolar disorder when in a depressed episode, and compared them to individuals with unipolar depression in a depressed episode, and healthy controls (46, 47). Both studies found that metacognitive beliefs differentiated all patients (both unipolar and bipolar depressed) from healthy controls. Specifically, Batmaz *et al.* (47) found that all patients report higher levels of all unhelpful metacognitive beliefs than controls, except positive beliefs about worry, but found no differences between the unipolar and bipolar groups. Sarisoy *et al.* (46) found that all patients reported significantly higher beliefs on two subscales (beliefs about uncontrollability and danger, and need to control thoughts), compared to controls. In this study, the bipolar group also reported less confidence in cognition than unipolar depressed individuals. Looking at relationships with affective dysfunction for the bipolar group, Sarisoy *et al.* found that holding higher levels of all metacognitive beliefs were associated with more anxiety, while higher levels of positive beliefs about worry, beliefs about uncontrollability and danger, and believing that one needs to control thoughts was associated with more depression. In sum, these findings suggest that the S-REF model is applicable to depression in bipolar disorder, with converging findings of relationships between metacognitive beliefs and symptoms of depression.

1.2.3 Metacognitive beliefs in psychotic disorders

A recent meta-analysis shows that patients with psychotic disorders report higher levels of all metacognitive beliefs compared to healthy controls, and comparable levels to patients with affective disorders (136). Metacognitive beliefs have been independently associated with positive and affective symptoms in psychotic disorders (137), and with the severity and duration of positive symptoms at 10-year follow-up after a first psychotic episode (138). However, not all studies have supported a direct relationship between metacognitive beliefs and psychosis: One study found that differences in metacognitive beliefs between patients with a psychotic disorder,

individuals with psychotic-like experiences but no need for care, and healthy controls became non-significant when controlling for anxiety and depression (139). The authors suggest that metacognitive beliefs may be linked to more general psychopathology (e.g. anxiety and depression) rather than directly to positive symptoms.

In regards to affective dysfunction, the literature suggests that metacognitive beliefs about uncontrollability and danger significantly contribute to (44), or mediate (45), symptoms of anxiety and depression in people with schizophrenia. A recent study (137) found that metacognitive beliefs about uncontrollability and danger, the need to control thoughts, and positive beliefs about worry contributed to anxiety, while beliefs about uncontrollability and danger, and the need to control thoughts contribute to depression. Thus it seems that there is a clear relationship between metacognitive beliefs, psychosis, and affective dysfunction, but the nature of the relationship remains unclear.

The literature thus suggests similar relationships between metacognitive beliefs and symptoms of depression and anxiety in both bipolar and psychotic disorders. This is confirmed in the aforementioned meta-analysis (136), where the only difference between individuals with psychotic versus depressive or anxiety disorders were that psychotic individuals had higher positive beliefs about worry. The authors of the meta-analyses note that it is possible that their findings are inflated by comorbid factors. However, as outlined previously in this thesis, anxiety and depression commonly occur in both emotional and psychotic disorders, and may directly influence these (22).

In sum, the literature suggest that the five metacognitive beliefs implicated in the S-REF model are elevated in people with affective and psychotic disorders compared to people without a diagnosis, with apparent similarities between people with affective and psychotic disorders in regards to levels of metacognitive beliefs and relationship to affective symptoms. This could indicate that metacognitive beliefs are more closely linked to affective psychopathology. The findings also provide support for the proposal that vulnerability to dysfunctional affective regulation and prolonged distress across psychological disorders could be associated with metacognitive beliefs rather than specific diagnoses—or at least that metacognitive beliefs are a common factor across affective and psychotic disorders.

1.2.4 Thought control strategies in bipolar disorders

Thought control is often conceptualised as suppression, or 'not thinking about' unwanted thoughts (140). In depression, this specific strategy has been found to impact negatively on both the frequency of unwanted thoughts, and the emotional experience of having them (141). Miklowitz *et al.* (142) show similar findings for bipolar disorder, with patients reporting more frequent use of thought suppression than controls, while also being less successful in suppressing negative material. Wells and Davies (143) suggest that thought control strategies can be further differentiated into more specific ways of handling unwanted thoughts, and that some strategies might be helpful while others might not. They propose that reappraising a distressing thought or sharing it with others could be helpful strategies, while use of distraction, worry or punishment might prevent efficient self-regulation and prolong distress. Patients with depressive disorders have been found to report more use of thought control strategies than controls (133). The postulated unhelpful strategies of distraction, worry and punishment have also been found to correlate with symptoms of depression in depressed individuals (144). While thought control strategies are implicated in bipolar disorder, they remain understudied in general, and no studies have investigated such strategies beyond thought suppression.

1.2.5 Relationship between metacognitive beliefs and thought control strategies

Although both metacognitive beliefs and thought control strategies should contribute to a dysfunctional self-regulation style, only one study has so far explored the role of both. Halvorsen *et al.* (133) included patients with unipolar depression and controls, and found that groups of never depressed, previously depressed and currently depressed individuals could be correctly classified based on a continuum of increasing application of dysfunctional metacognitive beliefs and self-regulation strategies, with the currently depressed reporting the highest scores. There is thus some support for the claim that metacognitive beliefs interact with thought control strategies, and that this interaction may worsen with increasing depressive symptoms.

1.2.6 Metacognitive beliefs as a potential mediator of affective and psychotic symptoms

It has been proposed that mechanisms linking early trauma, depression and psychosis could involve maladaptive cognitive emotional regulation strategies, including rumination and worry (21). This is in line with the self-regulatory executive function (S-REF) model (42), which suggests that metacognitive beliefs should trigger an unhelpful cognitive style that at least moderates the strength of subsequent emotional distress, and possibly even mediates it.

Metacognitive abilities mature gradually within normal cognitive development (130), and metacognitive beliefs and control strategies are assumed to develop and be revised in relationship to previous experiences (43). It is thus reasonable to hypothesise that metacognitive beliefs and/or control strategies are influenced by early trauma experiences. While this relationship remains largely unexplored, four studies offer corroborating evidence for a relationship between metacognitive processes and early trauma: A study of patients with psychotic and bipolar disorders found that those with a history of any trauma reported more beliefs about thoughts being uncontrollable or dangerous, compared to patients without a trauma history (48). Rumination, which is part of the dysfunctional regulation in the S-REF model, mediated the relationship between early emotional abuse and symptoms of depression in children (145) and college freshmen (146). Only one study has specifically addressed the role of metacognitive beliefs in regards to early emotional abuse and affective response: Myers and Wells (49) found that beliefs about uncontrollability and danger mediated negative affective responses to early emotional abuse in a non-clinical sample. This raises the question of whether metacognitive beliefs could mediate affective responses to early emotional abuse in clinical populations.

1.2.7 Summary and topics that need further elaboration

In sum, the literature suggests that metacognitive processes, as defined by the S-REF model, may play a role in bipolar disorders and psychotic disorders, and in particular in relation to affective dysfunction. However, the prevalence and clinical correlates of metacognitive processes remain understudied in bipolar disorders, and in early stages of psychosis.

INTRODUCTION

Previous studies of metacognitive beliefs in psychotic disorders have included patients with unknown or mixed durations of illness, focused on patient subgroups with specific symptoms, or had relatively small samples. As unhelpful metacognitive beliefs may be linked to a worse outcome, the prevalence and correlates of such beliefs should be investigated in a representative population of patients close to first treatment. Further, despite knowledge that levels of affective symptoms influence metacognitive beliefs, severity of symptoms (positive, negative, or affective) have scarcely been investigated. Finally, key demographic and clinical factors known to influence psychotic disorders, such as premorbid adjustment or DUP, have rarely been explored in relation to psychotic disorders, and never in early stages of illness. There is thus a need for an integrated account of how metacognitive beliefs related to premorbid adjustment, DUP, positive and negative symptoms, and affective dysfunction in early stages of psychosis.

When the current study was initiated no studies investigating metacognitive processes in bipolar disorder had been published. The two studies that are now available have only included bipolar patients in a depressive episode, and only one of them has looked at interactions with affective symptoms. Relationships between metacognitive beliefs and key clinical aspects of bipolar disorder remain largely unexplored and thought controls strategies have yet to be investigated. There is thus a need for further studies of metacognitive factors in bipolar disorders, and an integrated account of how these relate to key clinical factors linked to premorbid function or outcome, such as age at onset, number of mood episodes, and mood symptoms.

Finally, the S-REF model proposes that metacognitive beliefs will mediate emotional responses and regulation. It is well established that early trauma experiences contribute to both bipolar and psychotic disorders, but the mechanisms underlying this relationship remain unclear. The literature supports a complex relationship between early emotional abuse, bipolar/psychotic disorders and symptomatology, as well as with metacognitive beliefs. There is thus an evidence-based rationale to expect metacognitive beliefs to mediate the relationship between early emotional abuse and affective symptoms, and it is further possible that affective symptoms link early trauma and positive symptoms.

2 Aims

The main aim of this thesis was to investigate key metacognitive factors, as outlined by the S-REF model, in patients with bipolar or psychotic disorders by exploring prevalence, clinical correlates, and the potential mediating role of metacognitive factors in both patient groups.

2.1 Paper I

The main aim of Paper I was to describe metacognitive beliefs as measured by the Metacognitions Questionnaire (MCQ-30) in a sample of patients with early psychosis, compared to healthy controls, and to examine whether clinical characteristics implicated in the severity or outcome of psychotic disorders were related to metacognitive beliefs. Specifically we investigated whether age, gender, duration of untreated psychosis, premorbid social function, or affective, negative or positive symptoms contributed to levels of specific metacognitive beliefs.

2.2 Paper II

The main aim of Paper II was to describe metacognitive beliefs as measured by the MCQ-30 and thought control strategies as measured by the Thought Control Questionnaire (TCQ) in a sample of patients with bipolar disorders, compared to healthy controls, and to examine whether clinical characteristics implicated in the severity or outcome of bipolar disorder were related to metacognitive beliefs or thought control strategies. Specifically we investigated whether age at onset of affective disorder, number and polarity of affective episodes, or symptom levels contributed to levels of metacognitive beliefs or thought control strategies. Finally we wanted to examine whether metacognitive beliefs influenced thought control strategies over and above other illness factors, as suggested by the S-REF model.

2.3 Paper III

The aim of Paper III was to expand on findings from Paper I and II, and examine whether metacognitive beliefs mediated symptom responses to early emotional abuse in patients with bipolar or psychotic disorders. Specifically we wanted to investigate whether metacognitive beliefs mediated the effect of early emotional abuse on

symptoms of depression/anxiety, and whether this metacognitive—affective pathway would extend to influence positive symptoms.

3   Methods

3.1   The Thematically Organised Psychosis (TOP) Study

This thesis is part of the TOP Study, an on-going multi-centre study focusing on bipolar and psychotic disorders. The TOP Study is based in the NORMENT KG Jebsen Centre for Psychosis Research, which is a collaboration between Oslo University Hospital, the University of Oslo, and the University of Bergen.

3.2   Design

The papers included in this thesis used cross-sectional data collected at inclusion to the TOP Study between February 2009 and January 2016.

3.3   Procedure

Patient participants were referred to the TOP Study from in- and outpatient clinics in the greater Oslo area. Healthy control participants were selected randomly from the same catchment area through statistical records. All participants provided written informed consent after receiving a complete description of the study.

Patients were interviewed by clinical psychologists, psychiatrists or medical doctors in psychiatric training who had completed general training and reliability checks for the TOP Study protocol, using the University of California Los Angeles (UCLA) programme (147). For DSM-IV diagnostics, mean overall kappa was 0.77 for both training videos and a randomly drawn subset of actual study patients (95%CI 0.60, 0.94). Patients completed a broad range of clinical assessments and self-reports.

Healthy control participants screened by trained research assistants over the phone to establish eligibility for study participation. Control participants were screened with the PRIME-MD interview (148) to capture possible symptoms of severe mental illness. If eligible, controls were later assessed in person by clinical interviewers.

Upon completion of the assessment battery, all participants received a monetary compensation of NOK 500 (approximately €55 or US$60).

3.4 Inclusion and exclusion criteria

General inclusion criteria for all participants were age 18-65, speaking and understanding a Scandinavian language well enough to complete the assessments, and being able and willing to give informed consent.

Patient participants had to have a primary diagnosis of a bipolar or psychotic disorder based on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (50). For study I eligible diagnoses were schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, or psychotic disorder NOS. Study I only included participants with the aforementioned diagnoses who had a maximum of two illness episodes, or no more than two years of adequate treatment[§] for psychosis (denoted as 'early psychosis'). For study II eligible diagnoses were bipolar type I, II, or NOS, regardless of illness or treatment duration. For study III all the aforementioned diagnoses were eligible for inclusion, regardless of illness or treatment duration.

Exclusion criteria for all participants were a history of severe head injury, IQ < 70, or neurological or developmental disorders. Control participants were further excluded if they had current symptoms of mental illness in need of treatment, a history of severe mental disorder, or a first-degree relative with a diagnosed severe mental disorder.

3.5 Participants

Paper I included 92 patient participants who met criteria for early psychosis as part of a primary psychotic disorder, and had completed clinical assessments and self-reports of metacognitive beliefs. Diagnoses included schizophrenia (52%), schizophreniform (8%), schizoaffective (12%) and delusional (11%) disorder, brief psychosis (2%), and psychotic disorder NOS (14%). Almost 36 percent of the sample had one clinically significant positive symptom (defined as a score of ≥4 on items P1 or P3 of the Positive and Negative Syndrome Scale Score; PANSS), and almost 19


[§] Adequate treatment was defined as antipsychotic medication used in appropriate dosage over ≥4 weeks, admission to hospital, or contact with specialised health care services because of a psychotic episode or diagnosis.

percent had both delusions and hallucinations. The sample also included 97 healthy controls, who completed self-reports on metacognitive beliefs.

Paper II included 80 patients who met criteria for a primary bipolar disorder with or without a history of psychosis, and had completed clinical assessments and self-reports of metacognitive beliefs and thought control strategies. Diagnoses included BP-I (64%), BP-II (31%) and BP-NOS (5%). The sample was largely depressed to some degree (62.5%) but also included euthymic patients (37.5%). Maniform symptoms were not prevalent: At least 85 percent scored below the 6.6 points related to a one-point change in general severity ratings (149) and the highest recorded score was 24. A little over half of the sample had a history of psychotic symptoms, but only two individuals had clinically significant delusions at time of inclusions, and none had clinically significant hallucinatory experiences. The sample also included 166 healthy controls who had completed self-reports on metacognitive beliefs and thought control strategies.

Paper III included 261 patients who met criteria for a primary bipolar (37.5% of total sample) or psychotic disorder, regardless of treatment duration. Diagnoses included BP-I (23%), BP-II (13%), BP-NOS (2%), schizophrenia (34.5%), schizophreniform (7%), schizoaffective (9%) and delusional (3%) disorder, brief psychosis (1.5%), and psychotic disorder NOS (7%). Clinically significant depression (as defined by PANSS G6 Depression ≥4) was present in 28 percent of the total sample (bipolar group 33%; psychosis group 25%). Maniform symptoms were rated for 79 percent of participants, and showed similar values as seen in Paper II. In the bipolar group, 51 percent of the sample (19.5% of total sample) had a history of psychotic symptoms, but again only two individual had clinically significant delusions at time of inclusions, and none had clinically significant hallucinatory experiences. Almost 28 percent of the psychosis group had one clinically significant positive symptom, and 20 percent had both delusions and hallucinations.

Figure 2 (p. 28) shows the overlap in patient samples between all three papers, specified for patients and controls. Further characteristics of each sample are specified in Table 1 of each paper.

2a)
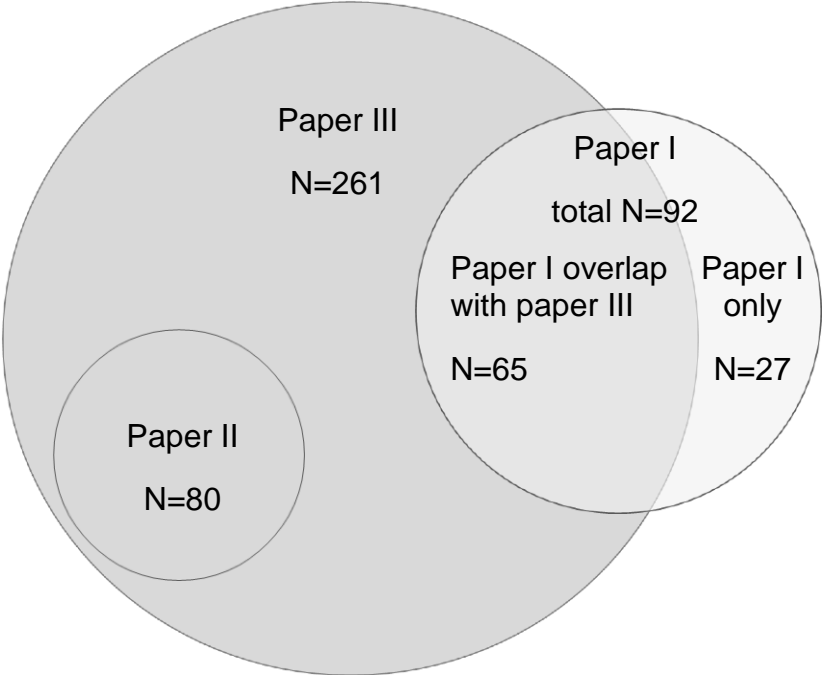
2b)
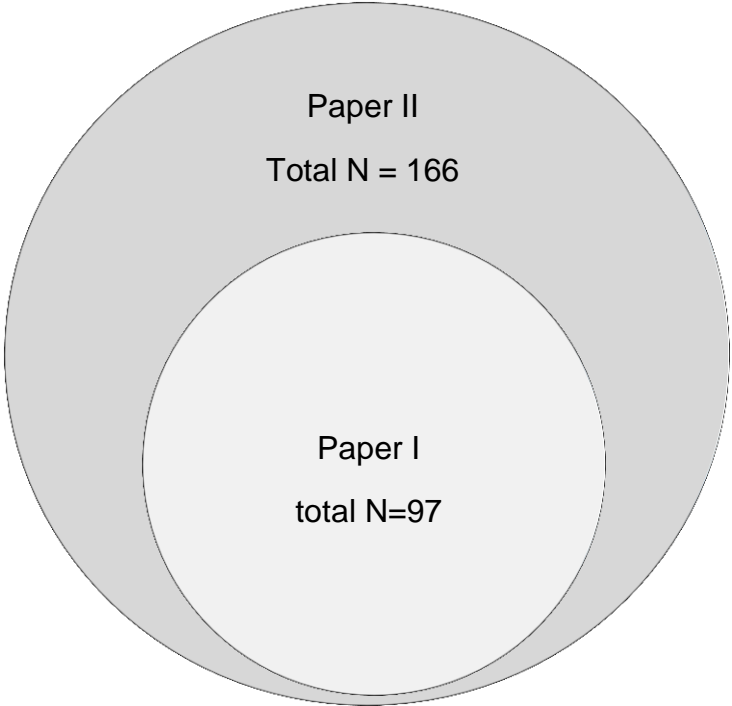
Figure 2: Venn diagrams outlining overlap and differences between samples
Diagram 2a) shows the overlap in patient samples included in Papers I, II and III.
Diagram 2b) shows the overlap in the control samples included in Papers I and II.

3.6 Assessments

Table 2 (p. 31) shows which measurements were included in each of the three papers.

3.6.1 Clinical interviews

Diagnosis

Diagnosis was assessed with the structured clinical interview for DSM-IV, axis I disorders (SCID-I) (50).

Age at onset

Age at onset of affective disorder (AAO) was determined as age at the time of the first mood episode as defined by DSM-IV criteria, regardless of polarity.

Number of affective episodes

Number of affective episodes was defined as total mood episodes reported by patients or identified in case notes that could be assumed to meet DSM-IV criteria for a depressive, hypomanic, manic or mixed episode. Episodes of hypomanic, manic and mixed quality were summarised to form number of (hypo)manic episodes.

Duration of untreated psychosis

Duration of untreated psychosis (DUP) was defined as weeks with symptoms qualifying for a score of 4 or more on PANSS items P1 Delusions, P3 Hallucinatory behaviour, P5 Grandiosity, P6 Suspiciousness, or G9 Unusual thought content before adequate treatment for psychosis.

Duration of treatment

Duration of treatment (DOT) was defined as time in months from first treatment adequate treatment for a psychotic or bipolar disorder to inclusion in the TOP Study.

Premorbid adjustment

Premorbid adjustment was assessed with the Premorbid Assessment Scale (PAS) (150). PAS is clinician-rated and assesses social and academic impairment on a 6-point scale ranging from 0 (*no impairment*) to 6 (*severe impairment*). The premorbid phase is defined as time from birth until 6 months before onset of mental disorder, and assessed for childhood (age 0-11), early adolescence (age 12-15), adolescence (16-18) and adulthood (age 19+). To avoid overlap with the prodromal period often seen in psychotic disorders, we only used the childhood subscales.

Global functioning

Global functioning and symptom level was measured by the Global Assessment of Functioning (GAF) scale (151), split version (152), which assesses symptoms and function separately.

Maniform symptoms

Maniform symptoms were assessed on the Young Mania Rating Scale (YMRS) (153). The YMRS is clinician-rated from 0 (*not present*) to 4 (*severe*); with four of the eleven items carrying double points for a rating of 1-4 (i.e. scores assigned are 2-8). Total scores range from 0 to 60.

Symptoms of depression/anxiety

In Papers I and III, symptoms of depression/anxiety were assessed on the Positive and Negative Syndrome Scale Score (PANSS) (56). Items are clinician-rated from 1 (*not present*) to 7 (*severe impairment*), assessing the past seven days. All analyses used the five factor consensus structure suggested by Wallwork *et al.* (61), which yields subscales (positive, negative, disorganised/concrete, excited and depression/anxiety). The depression/anxiety subscale includes items G2, G3, and G6. Because each five-factor subscale includes a different number of items, and to avoid confusion with the original three-factor structure, this thesis reports mean item scores for all PANSS subscales.

Symptoms of depression

In Paper II, symptoms of depression were clinician-rated on the Inventory of Depressive Symptoms—Clinician Rated (IDS-C) (154). The IDS-C assesses current symptoms of depression with 30 items that cover the nine diagnostic symptom domains used to characterize a major depressive episode in DSM-IV. It also rates symptoms commonly associated with depression (e.g. anxiety, irritability), and items relevant to melancholic, or atypical symptom features. Items are rated on a 4-point scale ranging from 0 (*not present*) to 3 (*severe*). Total score ranges from 0 to 84. Scores can be interpreted as degrees of depressive symptomatology, including no depression (0-11), mild (12-23), moderate (24-36), and severe depression (47-84).

Table 2: Overview of measurements by papers

Measurement	Paper I	Paper II	Paper III
Age at onset of affective illness		x	
CTQ Emotional abuse			x
Duration of treatment	x	x	x
Duration of untreated psychosis	x		
GAF Function	x	x	x
GAF Symptoms	x	x	x
IDS-C		x	
MCQ CC	x	x	
MCQ CSC	x	x	
MCQ NCT	x	x	
MCQ PW	x	x	
MCQ total		x	
MCQ UD	x	x	x
Number of affective episodes		x	
PANSS depression/anxiety symptoms	x		x
PANSS negative symptoms	x		
PANSS positive symptoms	x		x
PAS Childhood Academic function	x		
PAS Childhood Social function	x		
SCID-I	x	x	x
Thought Control Questionnaire		x	
YMRS maniform symptoms		x	

Notes: CTQ = Childhood Trauma Questionnaire (short form), GAF = Global Assessment of Function, IDS = Inventory of Depression Scale—Clinician rated, MCQ = Metacognitions Questionnaire (30 items), PANSS = Positive and Negative Syndrome Scale, SCID-I = Structured Clinical Interview for DSM Axis I Disorders, YMRS = Young Mania Rating Scale.

Positive symptoms

Positive symptoms were assessed on the PANSS (see 'Symptoms of depression and anxiety' on previous page for more details). The positive symptoms subscale includes items P1, P3, P5, and G9. This thesis reports mean item scores.

Negative symptoms

Negative symptoms were assessed on the PANSS (see 'Symptoms of depression and anxiety' above for more details). The negative symptoms subscale includes items N1, N2, N3, N4, N6, and G7. This thesis reports mean item scores.

3.6.2 Self-report measurements

Metacognitive beliefs

Metacognitive beliefs were self-rated on the Norwegian version of the Metacognitions Questionnaire-30 items (MCQ-30) (155). A total of 30 items are rated using a 4-point scale ranging from 1 (*do not agree*) to 4 (*agree very much*). It yields five factors representing distinct metacognitive beliefs: *Positive beliefs about worry (PW)* (e.g. "Worrying helps me cope"); *negative beliefs about the uncontrollability and danger of worry thoughts (UD)* (e.g. "My worrying could make me go mad"); *cognitive confidence (CC)* (e.g. "I do not trust my memory"); *beliefs about the need to control thoughts (NCT)* (e.g. "I should be in control of my thoughts all of the time"); and *cognitive self-consciousness (CSC)* (e.g. "I constantly examine my thoughts"). Each factor is based on six items, with subscale scores ranging from 6 to 24. The subscale scores can also be summarised to a total score (range 30-120). A higher score indicates more unhelpful beliefs.

Internal consistency reported by the authors was strong for each of the five beliefs, with Cronbach's alpha in the range of .72—.93. In the present study we found Cronbach's alpha in the range of .72—.89 for patients and .75—.84 for controls. In study I the MCQ subscales were moderately inter-correlated (mean Spearman's rho $[r_s]$ = 0.42), ranging from r_s = 0.20 (CC by CSC) to r_s = 0.68 (UD by NCT). In study II the MCQ subscales were also moderately inter-correlated (mean r_s = 0.36), ranging from r_s = 0.11 (PW by NCT) to r_s = 0.69 (UD by NCT).

Thought control strategies

Thought control strategies were self-rated on the Norwegian version of the Thought Control Questionnaire (TCQ) (143, 144), using a 4-point scale ranging from 1 (*never*)

to 4 (*almost always*). It yields four factors representing distinct thought control strategies: *Reappraisal* (e.g. "I try to reinterpret the thought), *Social Control/Reappraisal* (e.g. "I don't talk about the thought to anyone" or "I ask my friends if they have similar thoughts"), *Distraction* (e.g. "I think about something else), *Worry* (e.g. "I worry about more minor things instead"), and *Punishment* (e.g. "I punish myself for thinking the thought"). Each factor is based on six items, producing subscale scores ranging from 6 to 24. A higher score indicates more use of the specific thought control strategy. The social scale has three items that are reverse-scored, so that a lower score indicates more use of social control (keeping the thoughts to oneself), while a higher score indicates the use of social reappraisal (sharing the thought with others). The Thought Control Questionnaire was developed from open-ended semi-structured interviews with patients and controls, and has been tested in non-clinical (143) and clinical (144) samples.

Internal consistency for study II was strong for patients (Cronbach's alpha range of .70—.80), and acceptable-to-strong for controls (Cronbach's alpha range .69—.85). The TCQ subscales were weakly inter-correlated (mean r_s = 0.21), ranging from r_s = 0.06 (social by reappraisal) to r_s = 0.53 (worry by punishment).

Childhood trauma (early emotional abuse)

Early trauma experiences were self-rated with the Norwegian version of The Childhood Trauma Questionnaire-Short Form (CTQ-SF) (156). The CTQ-SF measures five distinct traumatic experiences: *Emotional, physical* and *sexual abuse*, and *emotional* and *physical neglect*. Instructions specify that only experiences before the age of 18 should be rated. Twenty-five items are scored on a 5-point scale ranging from 1 (*never true*) to 5 (*very often true*), yielding subscales ranging from 5 to 25. A higher score indicates more frequent trauma experiences.

This thesis used the *emotional abuse subscale* for detailed analysis. The authors have suggested cut-off scores to classify frequency of emotional abuse into categories of none, mild, moderate, severe or extreme. Presence of emotional abuse (EA+) was defined as a classification of moderate or higher levels of emotional abuse (i.e. scores of 13-25), while participants who reported no or mild levels (i.e. scores ≤ 12) were classified as not having experienced emotional abuse (EA-). Internal consistency for this subscale was strong in our patient sample (Cronbach's alpha = .87).

3.7   Missing data

Duration of untreated psychosis

In Paper I DUP was missing for three patients. Records showed that age at onset and first treatment for psychosis was within the same calendar year for all three. DUP was therefore estimated to 26 weeks as a 'best approximation'.

Duration of treatment

In Paper III duration of treatment was unknown for six patients, and no information was available to estimate this from. They were therefore excluded from mediation analyses when duration of treatment was included as a possible confounder.

Measures of affective symptoms

In Paper II, one participant had missing data on both IDS-C and YMRS, and was excluded from the regression analyses.

Metacognitive beliefs

Both patient participants and healthy controls had single missing items on MCQ-30 subscales. In Paper I this was true for five patients and five healthy controls.[**] In Paper II this was true for three patients and seven healthy controls. In Paper III, three patients had missing items on the MCQ-UD subscale. For all three samples combined, 13 individual patients and ten healthy controls had single missing items on the MCQ-30 subscales included in analyses. In all papers, missing MCQ items were replaced with the individual's relevant subscale mean.

Thought control strategies

In Paper II, two patients and four healthy controls had single missing items on TCQ subscales. These were replaced with the individual's relevant subscale mean.

Early emotional abuse

In Paper III, six patients had at least one missing items on the CTQ emotional abuse subscale. To prevent inflated rates of trauma experiences, missing items were treated conservatively and assumed to not have been present. Hence, replacement scores were set to the lowest value for missing items.

[**] The methods section in Paper I incorrectly states that 15 participants had single missing items on MCQ-30; the true number is 10 in total.

3.8 Statistical analyses

Analyses for all papers were conducted using The Statistical Package for the Social Sciences (IBM SPSS) versions 21 or 22 (157). For Paper III, the PROCESS tool for mediation/moderation analyses (158) was added to SPSS.

Data distribution shapes were inspected visually using histograms (all papers), Q-Q plots (Paper I and III) and plots for predicted versus observed residuals (Paper I and II). In Paper I DUP was significantly skewed to the right and a log transformed DUP was used in analyses to achieve residuals that were normally distributed. In Paper II and III residuals were normally distributed without any transformation of data, but in Paper II the MCQ subscale *positive beliefs about worry* required bootstrapping to achieve this normal distribution of residuals.

Level of significance was set to $p < .05$ for all analyses, and all tests were two-tailed (when applicable). Chi square tests were used to compare group differences in categorical data. Student's independent samples t-tests were applied when comparing groups on continuous data. Correlations were conducted with Spearman's rank correlations (Spearman's rho). Effect sizes were calculated with Cohen's *d* in Paper II. Multiple ordinary least-squares linear regression analyses were applied to examine factors related to metacognitive beliefs in Paper I and II, and factors related to thought control strategies in Paper II. Ordinary least-squares regression analyses were also applied to analyse the size and significance of mediating pathways in Paper III. The mediation models were contrasted with direct models estimated with simple ordinary least-squares linear regressions.

In Paper I t-tests were conducted to determine differences between patients with early psychosis and healthy controls on MCQ-30 subscale scores. Bivariate correlations between the MCQ-30 subscales and demographic and clinical variables were calculated. To estimate how much of the variance in MCQ-30 scores was associated with independent patient characteristics, we conducted five multiple regression analyses with each MCQ-30 subscale as a dependent variable. The independent model was theoretically driven and included age, gender, DUP, PAS childhood social adjustment, PAS childhood academic adjustment, DUP, PANSS positive subscale, PANSS negative subscale, and PANSS depression/anxiety subscale.

In Paper II we applied t-tests to determine differences between patients with bipolar disorder and healthy controls on MCQ-30 subscale scores, MCQ total score, and TCQ subscale scores. Bivariate correlations were calculated between MCQ-30 and other characteristics. To investigate how different scores on the MCQ-30 were related to independent clinical characteristics, we conducted multiple linear regression analyses with each MCQ-30 subscale as a dependent variable. The independent factors investigated were age at onset for the affective disorder, number of depressive episodes, number of (hypo)manic episodes, and current symptoms of depression (IDS-C) and (hypo)mania (YMRS). The same procedure was used to investigate the relationship between TCQ and independent clinical characteristics, with the addition of the MCQ-30 total score as an independent variable to account for the effect of metacognitive beliefs on thought control strategies. To further investigate the effect of depression state on the metacognitive beliefs where IDS-C was a significant predictor, a *post hoc* t-test was used to compare euthymic to depressed patients.

In Paper III differences between the two diagnostic groups (bipolar vs psychotic disorder) on MCQ-UD were assessed with a t-test. Correlations between CTQ emotional abuse, MCQ-UD and other characteristics were then calculated. Further, two mediation analyses were conducted with PROCESS, using ordinary least-squares regressions. The first analysis examined whether metacognitive beliefs mediated the relationship between early emotional abuse and symptoms of depression/anxiety in a simple mediation model, controlling for gender. The second analysis examined whether metacognitive beliefs and symptoms of depression/anxiety mediated the relationship between early emotional trauma and positive symptoms in a serial mediation model, controlling for gender and diagnostic group. Each mediation model was contrasted with a simple linear regression model where only emotional abuse predicted depression/anxiety, and positive symptoms, respectively.

A more comprehensive description of the statistical analyses used in this thesis is presented in the included papers.

3.9   Ethical Considerations

The TOP study is approved by the Regional Ethics Committee (2009/796) and the Norwegian Data Protection Authority, and completed in accordance with the Helsinki Declaration.

All participants provided written informed consent after a complete description of the study. Information explaining the purpose, procedures, data collection, data security and confidentiality was presented both in writing and in conversation. People who experience manic or psychotic episodes experience periods with impairments in, or even loss of, reality-testing. People with bipolar and psychotic disorders can also have cognitive deficits in attention and verbal memory, which can reduce their ability to make informed decisions. Consequently, information to patients was given face-to-face by trained clinicians that could evaluate their ability to give valid informed consent. Patients were encouraged to take the time they needed to decide before signing the consent form. Only patients with a clear understanding of the protocol and deemed able to give informed consent were included, and the ability to give informed consent was addressed and re-evaluated with the patient if new, relevant information arose.

A specific concern in regard to voluntary consent is feeling pressured to participate. The TOP Study sometimes had a greater assessment capacity and normally completed assessments more quickly than the referring clinics might be able to themselves. This could have motivated clinicians to suggest patients take part in the study to receive a quicker assessment. Or it could have pressured patients to participate for the same reason, even though they might not be fully comfortable with being part of a research study. Consequently, assessors specifically addressed and ensured that patients understood that participation was voluntary, and that declining to participate would not have any negative impact on their treatment opportunities.

The TOP study protocol is extensive, and the total time needed to complete it is an important concern. To ensure participants were not overwhelmed or had their daily activities severely disrupted by participation, assessors were flexible in regard to assessment duration and breaks, appointment times and frequency, and meeting location.

Some of the information collected in the studies was both sensitive and of a personal nature. To ensure confidentiality, data was labelled with continuously assigned ID numbers rather than personal identifiers. Clinical assessments were completed by trained clinicians who sought to create an empathic atmosphere and pace assessment speed to individual needs.

Some participants experienced severe social anxiety that made use of public transportation stress-inducing or even impossible. If needed, the TOP study provided patients with prepaid taxi fares to appointments, to avoid additional stress and discomfort, and to avoid additional strains on their economic situation.

All participants were informed about their right to withdraw from the study at any given time, without consequences for future treatment.

4   Summary of papers

4.1   Paper I

Unhelpful metacognitive beliefs in early psychosis are associated with affective symptoms and childhood social adjustment

Background Individuals with schizophrenia exhibit higher levels of unhelpful metacognitive beliefs compared to healthy controls, and such beliefs have been linked to higher levels of depression and anxiety, and a poorer long-term outcome. Still, the relationship between metacognitive beliefs and on-going severity of affective or psychotic symptoms has not been investigated, demographic or clinical factors that might contribute to unhelpful metacognitive beliefs in psychosis remain largely unknown, and no studies have specifically explored metacognitive beliefs in early psychosis.

Aims We examined *i)* differences in levels of unhelpful metacognitive beliefs between psychosis spectrum disorders, and healthy controls, and *ii)* to what extent demographic and clinical characteristics predicted levels of metacognitive beliefs in the early treated phases of psychotic disorders.

Method Patients (N=92) were included within two years of first treatment for a psychotic disorder. They were assessed on premorbid adjustment, positive and negative symptoms, depression/anxiety, and self-reported metacognitive beliefs (MCQ-30). Healthy controls (N=97) also completed MCQ-30. Factors impacting on metacognitive beliefs were explored with multiple linear regression analyses.

Results Patients in early treated stages of psychosis reported significantly higher scores on all metacognitive beliefs compared to controls.[††] Higher levels of depression/anxiety were related to higher levels of all metacognitive beliefs, except positive beliefs about worry. Poorer childhood social adjustment was significantly related to higher levels of all metacognitive beliefs, except cognitive confidence. Duration of untreated psychosis contributed significantly to more unhelpful beliefs

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[††] In Paper I, the results section correctly states that patients with early psychosis differ significantly from healthy controls on *all* metacognitive beliefs, while the discussion incorrectly states that they do not differ from controls on positive beliefs about worry. The *p*-value for the group difference on positive beliefs about worry is .015 (listed in Table 2 as '< 0.05'), and thus significant.

about cognitive confidence. Negative symptoms influenced lower scores on cognitive self-consciousness. Notably, positive symptoms showed no significant relationships with metacognitive beliefs in the regression models. The regression model explained 14—38 percent of the variance in specific metacognitive beliefs for patient participants, with the best fit for beliefs about needing to control thoughts and the poorest fit for cognitive confidence.

Conclusion Our results suggest that affective symptoms and childhood social adjustment could be important predictors of unhelpful metacognitive beliefs in the early treated phases of psychosis, in particular in relation to affective symptoms. This indicates potential psychopathological relationships that warrant further investigation for clinical relevance.

4.2 Paper II

An exploration of metacognitive beliefs and thought control strategies in bipolar disorder

Background Metacognitive beliefs are elevated in depressed states of bipolar disorder compared to healthy controls, and have been linked to symptoms of depression and anxiety, but studies are scarce. Demographic or clinical factors that might contribute to unhelpful metacognitive beliefs remain unexplored in bipolar disorders. Similarly, thought control strategies and their relevance to clinical factors and metacognitive beliefs have never been investigated in bipolar disorder.

Aims We examined i) differences in metacognitive beliefs and thought control strategies between individuals with bipolar disorder and controls, ii) to what extent clinical characteristics were related to levels of metacognitive beliefs, and iii) whether the same clinical characteristics and metacognitive beliefs were related to thought control strategies in bipolar disorder.

Method Patients with bipolar disorder (N=80) were assessed for age at onset of affective disorder, number of affective episodes, symptoms of mania and depression, metacognitive beliefs (MCQ-30) and thought control strategies (TCQ). Healthy controls (N=166) completed MCQ-30 and TCQ. Factors impacting on metacognitive beliefs and thought control strategies were explored with multiple linear regressions.

Results Patients with bipolar disorder reported higher levels of all unhelpful metacognitive beliefs compared to controls, except for positive beliefs about worry. Higher levels of affective symptoms were related to higher levels of cognitive self-consciousness and beliefs about uncontrollability and danger, and to lower cognitive confidence. Earlier age at onset of the affective illness was significantly related to higher levels of positive beliefs about worry, beliefs about uncontrollability and danger, and the need to control thoughts. Patients further reported more use of thought control strategies postulated to be unhelpful (social control, worry, and punishment) and less use of distraction, compared to controls. More use of thought control strategies were predominantly related to higher total levels of metacognitive beliefs, but an earlier age at onset of affective illness was related to more use of punishment as a specific strategy. The regression model explained 10—18 percent of the variance on each metacognitive subscale, fitting equally well for beliefs about uncontrollability and danger, and the need to control thoughts. The regression model explained 10—30 percent of the variance in use of specific thought control strategies, with the best fit for worry.

Conclusion Our results suggest that metacognitive beliefs and control strategies are relevant in bipolar disorder. Affective symptoms and age at onset of affective disorder could contribute to metacognitive beliefs in bipolar disorder, and influence the use of thought control strategies. This indicates potential relationships that warrant further investigation for clinical relevance.

4.3 Paper III

Metacognitive beliefs mediate the effect of emotional abuse on depressive and psychotic symptoms in severe mental disorders

Background Early trauma is linked to higher symptom levels in bipolar and psychotic disorders, and more severe illness courses in both disorders, including more psychotic symptoms in bipolar disorder and more affective symptoms in psychotic disorders. Still, the translating mechanisms are not well understood. Metacognitive beliefs could be a potential mechanism linking early trauma to symptom response in bipolar and psychotic disorders.

Aims This study examined whether the relationship between early emotional abuse and depression/anxiety symptoms was mediated by metacognitive beliefs about

thoughts being uncontrollable/dangerous, and whether this pathway extended to influence positive symptoms.

Method Patients (N=261) with bipolar or psychotic disorders were assessed for early trauma experiences, metacognitive beliefs, current depression/anxiety and positive symptoms. Mediation path analyses using ordinary least-squares regressions tested if the effect of early emotional abuse on depression/anxiety was mediated through metacognitive beliefs. We further investigated whether the effect of early emotional abuse on positive symptoms was mediated serially through a pathway of metacognitive beliefs and depression/anxiety.

Results Metacognitive beliefs about thoughts being uncontrollable and dangerous significantly mediated the relationship between early emotional abuse and depression/anxiety (ab = .26, CI_{BC} .15 to .40). The mediation model explained a moderate amount of the variance in symptoms (R^2 = .21), while a direct model where emotional abuse predicted depression/anxiety alone only explained a small amount of variance (R^2 = .04). The pathway from metacognitive beliefs to depression/anxiety extended to significantly mediate the relationship between early emotional abuse and positive symptoms (a_1db_2 = .05, CI_{BC} .02 to .10), indicating a serial mediation. The extended serial mediation model explained a moderate amount of the variance in symptoms (R^2 = .29), while a direct model where emotional abuse predicted depression/anxiety alone only explained a small amount of variance (R^2 = .03). Of note, paths between metacognitive beliefs and positive symptoms only, or depression/anxiety and positive symptoms only, were not significant. Gender influenced beliefs about uncontrollability and danger, with women reporting higher scores, but did not influence symptoms of depression/anxiety or positive symptoms.

Conclusion Our results indicate that early emotional abuse is relevant to depression/anxiety and positive symptoms in bipolar and psychotic disorders, and suggest that metacognitive beliefs could play a role in an affective pathway to psychosis. Metacognitive beliefs could be relevant treatment targets in regards to depression/anxiety and positive symptoms in bipolar and psychotic disorders.

5 Discussion

5.1 Summary of main findings

The main aim of this thesis was to investigate key metacognitive factors as outlined by the S-REF model—*metacognitive beliefs* and *thought control strategies*—in patients with bipolar or psychotic disorders. Specifically we sought to examine whether patients with bipolar or psychotic disorders report higher levels of metacognitive beliefs compared to controls. Further we sought to explore whether illness-related factors known to be relevant in bipolar or psychotic disorders were related to metacognitive beliefs. In regards to bipolar disorder we also aimed to investigate whether patients with bipolar disorders report different use of thought control strategies compared to controls, whether illness-related factors relevant to bipolar disorders were related to use of specific strategies, and whether metacognitive beliefs would relate to use of thought control strategies above the illness-related factors. Finally, this thesis aimed to examine whether metacognitive beliefs could potentially mediate affective or positive symptom responses to early emotional trauma. The main findings are:

Paper I

i.   Patients with early psychosis reported significantly higher scores on all metacognitive beliefs compared to controls.

ii.   Higher levels of metacognitive beliefs were related to higher levels of affective symptoms, and to poorer childhood social adjustment.

Paper II

iii.   Patients with bipolar disorder reported elevated scores on all metacognitive beliefs compared to controls, except for positive beliefs about worry.

iv.   Higher levels of specific metacognitive beliefs mainly related to higher levels of depression and an earlier age at onset of the affective illness.

v.   Patients with bipolar disorders reported more use of thought control strategies postulated to be unhelpful (social control, worry, and punishment) and less use of distraction, compared to controls. More use of thought control

strategies were predominantly related to higher total levels of metacognitive beliefs.

Paper III

vi. Metacognitive beliefs significantly mediated the relationship between early emotional abuse and depression/anxiety.

vii. Together, metacognitive beliefs and depression/anxiety significantly mediate the relationship between early emotional abuse and positive symptoms.

viii. Gender influenced beliefs about uncontrollability and danger, with women reporting higher scores.

5.2 Discussion of main findings

5.2.1 Group differences in metacognitive beliefs

In the first two studies we found that patients reported higher levels of all metacognitive beliefs compared to healthy controls, with the exception of positive beliefs about worry in the bipolar sample. This suggests that, compared to controls, clinical participants hold higher levels of most or all beliefs implicated in the S-REF model. The results are consistent with the two studies that have investigated metacognitive beliefs in depressed states of bipolar disorder (46, 47), and numerous findings for psychotic disorders (136, 159-161), and confirm that metacognitive beliefs can differentiate patients from healthy controls. Additional group comparisons between patients in our final sample revealed no significant differences in metacognitive beliefs between bipolar or psychotic diagnoses (results shown in Paper III, Table 1). This is in line with a recent meta-analysis, which found that individuals with affective and psychotic disorders report comparable levels of metacognitive beliefs (136).

5.2.2 Factors related to metacognitive beliefs in early psychosis

Symptoms of depression and anxiety

The findings reported in Paper I suggest that most metacognitive beliefs are related to current symptoms of depression and anxiety in the early psychosis sample. This replicates previous findings of an intrinsic relationship between unhelpful metacognitive beliefs and depressive symptoms in individuals from the normal population (155, 162), individuals with subclinical psychotic experiences (139, 163),

and an established psychotic disorder (44, 45, 137, 139, 163). The S-REF model proposes that unhelpful metacognitive beliefs are central to development and maintenance of affective dysfunction in psychological disorders (42, 43). Our findings support a co-occurrence of such beliefs and symptoms of depression and anxiety in early psychosis, but the cross-sectional design prevents conclusions about causality.

Positive symptoms

The meta-analysis by Varese and Bentall (163) concludes that metacognitive beliefs could play an independent role in psychosis beyond affective symptoms, but also raises the question of whether such beliefs are a result of positive symptoms rather than causing them. Notably, we found no significant relationships between positive symptoms and metacognitive beliefs in our early psychosis sample when controlling for depression/anxiety. Hence it could be questioned whether metacognitive beliefs have any direct relevance to positive symptoms in early psychosis, contrary to findings in more mixed or chronic psychosis samples (44, 137, 163), where such beliefs have also been linked to a more chronic illness trajectory (138). It should be noted that the levels of positive symptoms in our study sample was fairly low (PANSS Positive item mean = 2.4, range 1 to 5.5), which could affect our ability to detect a relationship.

Premorbid social adjustment

Further, poorer childhood social adjustment—i.e. showing less social initiative, having fewer stable friends, or spending more time alone—was independently associated with all types of unhelpful metacognitive beliefs, except for low cognitive confidence. This could suggest that metacognitive beliefs are related to psychological development occurring before mental illness is clearly present, as outlined by the S-REF model. In psychotic disorders, poor premorbid adjustment as measured by the Premorbid Adjustment Scale (PAS) is linked to a worse long-term symptom and quality of life outcome in chronic samples, and more negative symptomatology and poorer quality of life outcomes in first episode psychosis (164). These findings are stronger for the social adjustment subscale. It is thus also possible that the relationship with PAS social could indicate that metacognitive beliefs are generally related to a poorer long-term outcome in general, as PAS often signifies. This would be in line with findings from the OPUS trial (138), where metacognitive beliefs were related to a more chronic illness ten years after an initial psychotic episode. These

possible interpretations are also not mutually exclusive. Still, while PAS social comes temporally before our measures of metacognitive beliefs, the cross-sectional design prevents us from drawing conclusions about causality.

5.2.3 Factors related to metacognitive beliefs in bipolar disorder

Symptoms of depression

The findings reported in Paper II suggest that most metacognitive beliefs are related to current symptoms of depression in the bipolar sample. This replicates previous findings of an intrinsic relationship between unhelpful metacognitive beliefs and depressive symptoms in individuals from the normal population (155, 162), and patients who have previously or are currently experiencing unipolar depression (131, 133-135), or are currently in a bipolar depression (46, 47). The results overlap with our findings in regards to early psychosis, but are less clear in the bipolar sample.

State *vs* trait: Depressive symptoms versus episodes

It is of note that bipolar patients who were currently depressed scored significantly higher than euthymic patients on beliefs about uncontrollability and danger, and cognitive self-consciousness, which could indicate that these beliefs are more state-dependent. Cognitive confidence was not different between the two mood states, and thus seems more reliably related to bipolar disorder in our sample.

These findings are seemingly at odds with one previous study, which found no differences in previously and currently depressed patients (135), but in line with the general findings from another study, which finds that previously and currently depressed individuals differ on beliefs about uncontrollability and danger, and cognitive confidence—but with opposite findings from this thesis, as beliefs about uncontrollability and danger seemed independent of mood state (131). The final study comparing controls to individuals with previous or current depression offers a discriminant function analysis where increasing levels of metacognitive beliefs differentiated controls from previously and currently depressed individuals. It is therefore possible that elevated levels of metacognitive beliefs depend both on trait and state, i.e. that they differentiate controls from euthymic and currently depressed patients, but with current depression being associated with even higher levels of unhelpful metacognitive beliefs. Our findings are not able to shed further light on this, as this study lacks data on possible affective symptomatology for controls.

Finally it should be noted that our group of 'euthymic' participants included seven individuals who had in fact never been depressed, which could influence the metacognitive beliefs reported in this group.

Age at onset

Finally, our findings suggest that a younger age at onset of a diagnosable affective disorder (regardless of polarity) is related to more unhelpful metacognitive beliefs about uncontrollability and danger, and to belief about the need to control thoughts, in bipolar disorder. Because childhood premorbid adjustments is not as consistently impaired in bipolar disorder (and the adolescent period potentially overlaps with age at onset of the mood disorder, or a prodromal phase), age at onset was used as a proxy for vulnerability to mental disorder related to psychological development occurring before or at the time of onset of mental illness, as predicted by the S-REF model. It could, however, be argued that a younger age at onset is predominantly a marker of a more severe outcome in bipolar disorder, as it has been linked to more mood episodes and poorer symptom recovery (165). This does not preclude a developmental perspective on metacognitive beliefs, but could suggest that such beliefs may be linked to a more severe long-term outcome in bipolar disorder. Still, though age at onset comes temporally before our measures of metacognitive beliefs, the cross-sectional design prevents us from drawing conclusions about causality.

5.2.4 Thought control strategies: Group differences and related factors

Thought control strategies were assessed in participants with bipolar disorders, who reported different use of such strategies compared to healthy controls. The findings are in line with the only relevant previous study, which reported more use of negative thought suppression in patients with bipolar disorder (142).

Wells and Davies (143) proposed that two of the strategies (reappraisal and distraction) might be helpful, while three (social control, worry and punishment) could be potentially unhelpful strategies. For the proposed helpful strategies, patients used less distraction, but there were no differences in reappraisal. Our illness-focused model did not prove to be significant for either of these thought control strategies. Findings were clearer for the proposed unhelpful strategies, where patients reported more use of all strategies, and our illness-focused model explained significant variance in use of these. More use of unhelpful thought control strategies were

predominantly related to metacognitive beliefs.[‡‡] This indicates that metacognitive beliefs influence the use of thought control strategies and, specifically that, they relate to more use of strategies that could prevent the resolution of emotional distress. This is in line with the S-REF model (42, 43) and corroborates findings from the sparse previous research on both metacognitive beliefs and thought control strategies in unipolar depression (133).

In addition, a younger age at onset of the affective disorder was independently related to more use of worry and punishment as thought control strategies. This could suggest that psychological development at onset of illness could influence the specific thought control strategies an individual endorses, or – if an earlier age at onset is considered a marker of a poorer long-term outcome – suggest that use of worry and punishment might relate to this.

5.2.5 Metacognitive beliefs as a potential mediator of affective and psychotic symptoms

This study is the first to demonstrate that metacognitive beliefs can mediate the effect of early emotional abuse on depression/anxiety, and further on positive symptoms, in psychotic and bipolar disorders. This replicates the findings by Myers and Wells (49) in patients with bipolar and psychotic disorders, and expands on previous research (including the first two studies included in this thesis) showing an intrinsic relationship between metacognitive beliefs, affective symptoms, and severe mental disorders (29, 44, 46, 47, 166, 167). Our results suggest that specific metacognitive beliefs about thoughts being uncontrollable or dangerous function as a mechanism through which early emotional abuse could influence later symptomatic responses at a clinical level.

Depression/anxiety

Our findings are consistent with the S-REF model, which proposes that negative experiences can contribute to develop unhelpful metacognitive processes, which in turn prolong negative affect. It is, however, of note that the indirect effect of metacognitive beliefs accounts for substantially less of the variance in

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[‡‡] Due to a high correlation (r_s = .73) between the MCQ total score and the TCQ punishment subscale for patients, metacognitive beliefs were excluded from the final analysis of this thought control strategy.

depression/anxiety in our clinical sample, compared to the findings by Myers and Wells (49) in their non-clinical sample (21 versus 56 percent). It is possible that that the link between early emotional abuse and depression/anxiety may be more complex in established severe mental disorders. While Myers and Wells found that beliefs about uncontrollability and danger were only linked to emotional abuse, our correlational analyses show that all types of trauma were linked to metacognitive beliefs. Patients with severe mental disorders often report multiple traumas (168-170), and bipolar and psychotic episodes can constitute traumatic experiences in themselves (171). It is therefore possible that early emotional abuse only captures part of the traumatic experiences that can contribute to depression and anxiety in our sample.

Positive symptoms

The effect of early emotional abuse on positive symptoms was mediated serially through metacognitive beliefs and depression/anxiety. This is in line with a recent study suggesting that trauma is linked to positive symptoms through an affective pathway (128). In our sample this pathway depended on metacognitive beliefs about thoughts being uncontrollable or dangerous. This result holds when controlling for diagnostic group, despite higher positive symptoms in the psychosis group. It is also of note that this pathway was statistically significant despite low mean levels of positive symptoms in the total sample (average PANSS positive score = 1.9), which reduces the variability in the data. This could explain why the effect of this path from early emotional abuse to positive symptoms is relatively small (increased average PANSS positive score = 0.05 from early emotional trauma alone).

5.3 Discussion of methodology

5.3.1 Possible confounders

Gender

Both mediation analyses controlled for gender as a possible confounder. We found that females reported significantly higher levels of metacognitive beliefs about thoughts being uncontrollable or dangerous, which in turn affected depression/anxiety and positive symptoms. Studies of metacognitive beliefs in severe mental disorders have not focused on potential gender differences. In bipolar and psychotic disorders, some studies suggest gender differences in severity and outcome.

In bipolar disorders, greater associations have been reported between trauma and clinical characteristics in females (123), including more depressive episodes and more rapid cycling. In psychotic disorders the findings are inconsistent, but a recent review suggests that women may be more sensitive to stress and trauma, and hence more disposed to disorders closely linked to dysregulation of stress, including psychotic and affective disorders (32). It is possible that women could be more prone to affective and positive symptoms, and that elevated levels of metacognitive beliefs play a role in this.

Diagnostic group

Both mediation analyses also used core diagnostic group (bipolar *vs* psychotic disorder) as a covariate, as it was reasonable to assume that the bipolar sample might have more mood symptoms, and the psychosis sample might have more positive symptoms. There was no effect of diagnosis on depression/anxiety, but psychotic disorders had higher levels of positive symptoms. While our analysis did control for this, it is reasonable to question whether the pathway from emotional abuse to positive symptoms via metacognitive beliefs and depression/anxiety is equally relevant for all patients. This is particularly pertinent to the patients with a bipolar disorder who have never had diagnosable psychotic symptoms (N = 56, 26 percent of the total sample in Paper III). Due to power issues, separate analyses for the two diagnostic groups to clarify whether the pathway is significant in both samples are not feasible. It is possible that this pathway might only be relevant for the patients who have experienced positive symptoms.

Duration of treatment

Duration of treatment was included as a covariate because we noticed a different relationship between metacognitive beliefs and positive symptoms in Paper I, which could reflect a difference between early and more chronic psychosis patients. The sample in Paper III did not exclude psychotic patients with more than two illness episodes or treatment duration of more than two years. Total duration of treatment (for an affective disorder in the bipolar sample and a psychotic disorder in the psychosis sample) did not seem to influence any variables included in the mediation models, and was excluded from the final models.

Anxiety

While Papers I and III used the PANSS depressive subscale to measure depression, this scale comprises two items rating depression (G 6 Depression, and G3 Guilt), and one item measuring anxiety (G2 Anxiety). Hence the subscale and symptoms it measures has been referred to as depression and anxiety throughout this thesis and the papers. Paper II, however, used the IDS-C, which has 29 items measuring symptoms of depression and their associated behaviours, and one item measuring anxiety. Metacognitive beliefs are consistently related to anxiety disorders and symptoms (172), as is a diagnosis of bipolar disorder (173), and metacognitive beliefs did relate to anxiety in one of the two previous studies of depressed individuals with bipolar disorder (46). It is thus possible that anxiety constitutes a confounder in Paper II, as it has not been equally well accounted for in this study.

Depressive episodes vs depressive symptoms

Number of depressive episodes showed positive bivariate associations with beliefs about uncontrollability and danger, and cognitive confidence, but did not significantly contribute to the variance of any metacognitive beliefs in the regression analyses. While this might suggest that mood state is more important to metacognitive beliefs than previous experiences of depression, current symptoms of depression correlate significantly (r_s = .27, p < 0.05) with number of depressive episodes in our bipolar sample. A potential relationship between depressive episodes and metacognitive beliefs could thus be partially masked by this overlap between the variables.

5.3.2 Measurements

The present thesis has used standardised and widely accepted measures with good psychometric properties to study the phenomena at hand. To assure reliable assessments, all assessors were trained, calibrated and continuously supervised throughout the TOP study. Still, some aspects of assessment should be addressed.

Retrospective data

Collection and use of retrospective data warrant careful interpretation. Data collected on premorbid function, age at onset of illness, number of illness episodes and duration of treatment can be difficult to remember precisely. This is particularly so for individuals with low levels of insight or cognitive difficulties impacting on

memory. In order to balance this, objective data was gathered when possible, and routinely checked in regards to age at onset, duration of illness, and number of affective episodes.

Self-reports

The use of self-rated assessments is associated with some challenges, as the quantification of subjective data is done by the participants, and ratings could be influenced by patients' degree of positive symptoms or insight. However, an investigation of self-reports by individuals with schizophrenia indicates that patients' self-reports of affect and disposition are most often valid, despite lacking insight (174). Two of the key outcome measures for this thesis (the MCQ-30 and the TCQ) both rely on self-reports. Several studies have used the MCQ-30 in affective disorders and across the continuum of psychosis proneness to long-term schizophrenia (see 136, 163, and 175 for reviews), finding similar results to ours. Our clinical impression is thus that the MCQ is suitable to measure metacognitive beliefs in patients with bipolar and psychotic disorders. The TCQ has also previously been used with depressed and psychotic patients (133, 176). We also asked about trauma retrospectively, using a self-report measure. While studies of early trauma using retrospective self-reports are often questioned in regard to the potential influence of recall bias and possibly low reliability, studies investigating this have found that the CTQ-SF is a valid and reliable measure of early trauma for both bipolar (177) and psychotic (178) disorders.

Controls

The healthy control sample was screened for current or previous mental illness in need of treatment, and as such should not include depressed individuals. It is however unlikely that controls would not display normal variations in mood that could still yield low, but above minimal, scores on depression/anxiety. A shortcoming of the studies is therefore the lack of any affective measures in the control group, which prevents us from linking high scores on metacognitive beliefs to emotional variability in controls.

5.3.3 Representativity and generalizability

Our total sample included all participants recruited to the TOP Study between February 2009 and January 2016, who received a primary diagnosis of a bipolar or

psychotic disorder, and completed the MCQ-30 (all studies), and the TCQ (study II only). Participants were both in- and outpatients. The catchment area is the larger Oslo area, which covers about 15 percent of the total population of Norway and includes both urban and rural areas. This gives a relatively high degree of representativity. However, as study participation requires the ability to endure an extended research protocol, it is possible that participants in acute illness phases could have been indirectly excluded in some instances.

Trauma levels in the total sample show that 28 percent of the patient participants report moderate or more severe experiences of early emotional abuse. This is similar to early emotional abuse reports for both bipolar and psychotic disorders reported in other papers from the TOP Study sample (179, 180), as well as reports from other studies (170, 181).

The bipolar subsample represents all diagnostic subtypes, but includes a larger number of BP-I vs BP-II and bipolar disorder not otherwise specified (BP-NOS) (60 vs 35 vs 5 percent of the total bipolar sample used in Papers II and III). Considering that BP type I and II should have roughly the same prevalence rate in the general population in most countries, it is possible that our sample is skewed towards BP-I. The sample further represents a full range of depressive symptom levels seen in this patient group, from euthymic to varying degrees of depression severity, and as such analyses including depressive symptomatology should yield representative results. The same is true for depressive episodes. Unfortunately, maniform symptoms were poorly represented in the bipolar sample (YMRS mean 3.3, range 0 to 24), with 85 percent of the sample scoring below the 6.6 points related to a one-point change in general mania severity ratings (149). It is therefore likely that this sample does not have enough variability in scores to detect any relationship with maniform symptoms. Similarly, the mean number of (hypo)manic episodes was only two, suggesting that this variability could also be too poor to detect any relationships. About 57 percent of the sample had experienced positive symptoms, in line with the literature. However, at baseline inclusion the variation on PANSS positive symptoms was limited in the bipolar subsamples used in study III, with a mean item score of 1.3 in this group (range 1 to 3.3).

Our psychosis subsample included the full spectrum of primary psychotic disorders included in the DSM-IV. In the total psychosis sample, 55 percent received a

diagnosis of schizophrenia, which is in line with the relative prevalence rate among psychotic disorders in the general population. This subsample also has more men compared to women, but this is in line with epidemiological studies showing more men developing psychotic disorders. The sample had relatively low mean item scores on positive symptoms (PANSS positive mean item score just above 2 in both study I and III) but scores range from 1 to 5.5 in both samples (data not shown), suggesting that the samples represent most of the range covered by the PANSS positive subscale. Similarly, negative symptoms show a relatively low mean item score in study I (2.1) but ranges from 1 to 4.7 in both subsamples of psychosis patients (data not shown), suggesting that the samples represent most of the range covered by the PANSS negative subscale.

In sum, participants in the study were recruited from a well-defined area with no *a priori* control of significant personal or clinical factors. As a result, the findings in this thesis should be largely generalizable to the larger groups of individuals with bipolar and psychotic disorders.

5.4   Overarching discussion

The first study sought to expand existing knowledge about elevated metacognitive belief in psychosis to an early psychosis sample, and to explore whether clinical variables related to psychosis were associated with metacognitive beliefs. The second study sought to investigate if metacognitive beliefs were elevated in bipolar disorder, to explore whether clinical variables related to bipolar disorder were associated with metacognitive beliefs and thought control strategies, and whether metacognitive beliefs influenced thought control strategies. The third study sought to expand on the results of Papers I and II by investigating if metacognitive beliefs could mediate symptomatic responses to early emotional trauma at a symptomatic level.

Overall, metacognitive beliefs correlate with multiple clinically relevant factors, but are only associated with a few in regression analyses. Across the diagnostic groups, symptoms of depression (and anxiety) are strongly related to metacognitive beliefs. In the psychotic subsample, such beliefs also relate to premorbid social adjustment, with roughly comparable effect sizes as for the effects of depression/anxiety. For the bipolar group the findings are a little less clear, but age at onset is associated with some specific beliefs. The S-REF model assumes that metacognitive beliefs become

unhelpful before the onset of a psychological disorder, and contribute to maintain disorders. The model implicitly proposes that such beliefs are relatively stable during a psychological disorder, but will be amended with life experiences—for better or worse. There is, however, no research on the emergence of such beliefs before illness, or their stability over time. Longitudinal studies are thus needed before we can ascertain whether the links to premorbid social adjustment and age at onset of affective disorder indicate that elevated metacognitive beliefs are related to psychological development before or at the onset of illness. Similarly, studies are needed to clarify if metacognitive beliefs are independently linked to factors implicated in a poorer long-term outcome. This interpretation is in line with one previous study (138) linking such beliefs to a more chronic outcome ten years after the first psychotic episode, and is further corroborated by studies of more chronic samples than ours showing a direct relationship between metacognitive beliefs and positive symptoms (137), and even with negative symptoms (182). Unfortunately, the literature on metacognitive beliefs in bipolar or psychotic disorders does not yet include any studies with longitudinal or follow-up data.

In the psychosis literature, metacognitive beliefs have been proposed to potentially influence positive symptoms directly (39, 183). This has been criticised as research including affective symptoms suggest that these beliefs may be more strongly linked to general psychopathology rather than positive symptoms specifically (139, 161, 163). In this regard it is worth noting that the S-REF model proposes that how an individual processes information during distress will influence further information processing and regulation in a manner that *perpetuates distress*. The model thus outlines that metacognitive beliefs should constitute a key contributor to 'general psychopathology' such as depression and anxiety. Our exploration of metacognitive beliefs in bipolar disorders did not include positive symptoms due to low variance. Our findings in the early psychosis sample suggest that metacognitive beliefs are not directly related to positive symptoms in this patient group. However, the results from Paper III do show that individuals with early traumatic emotional experiences, which is known to increase distress and the risk of psychological disorder in general, report higher levels of metacognitive beliefs than non-traumatised patients. These beliefs further contribute to higher levels of depression, which in turn increase positive symptoms. This suggests a more complex interaction between life-experiences,

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metacognitive beliefs and symptomatic response than is typically addressed in the literature, but which is in line with the S-REF model.

Taken together, our results thus provide further support for an affective pathway to positive symptoms (21, 22, 37, 184), and indicate that specific metacognitive beliefs could play a key role in this pathway, particularly for women. It is possible that an affective pathway to psychosis could be stronger when there is a history of early emotional abuse, or other early experiences that influence emotion regulation. A recent review of the importance of depression in schizophrenia (21) finds that affective and positive symptoms seem to interact, not just in established psychotic disorders but also in sub-threshold individuals. Psychotic-like experiences are common in individuals with depressive and anxiety disorders (8, 185) and individuals at clinical high risk of developing psychosis (10, 186), and could be linked to an increased risk of transitioning to first-episode psychosis (187, 188). Similarly, metacognitive beliefs seem to be elevated in clinical high risk individuals (175), but at lower levels than seen in established psychotic disorders (160). This interplay between affective and positive symptoms suggests that affective symptoms could be relevant to positive symptoms of psychosis generally, and be exacerbated by early trauma and beliefs about thoughts being uncontrollable and dangerous.

A relevant question in this regard, is whether metacognitive beliefs *mediate* emotional responses, i.e. is a necessary mechanism through which emotional response is relayed, or *moderates* the strength of an emotional response when they get strong enough. The S-REF theory postulates metacognitive beliefs as a necessary mechanism in clinical levels of affective dysfunction, regardless of diagnosis—although it did originally only claim this for depression and anxiety disorders, and not specifically for (hypo)mania or psychosis. In line with this, the aforementioned study by Myers and Wells (49) showed that metacognitive beliefs about uncontrollability and danger mediated the effect of early emotional abuse on general negative affect in a non-clinical population. Another study (45) found that the effect of intrusive thoughts on depression and anxiety in schizophrenia was mediated by the same metacognitive beliefs. However, another study (189) suggests that beliefs about uncontrollability and danger, along with beliefs about the need to control thoughts, moderated the effect of stress on negative affect in a non-clinical sample, and that the effect of negative affect on subclinical paranoia was further moderated by cognitive

self-consciousness. It is thus not clear whether metacognitive beliefs are a prerequisite for emotional response and affective dysfunction, or if they contribute to exacerbate the strength of the effect. A further possibility is that metacognitive beliefs do mediate emotional responses, but only after they reach a 'critical' level or more strongly at higher levels (a *moderated mediation*).

5.5 Strengths and limitations

Several strengths and limitations have already been discussed in the individual papers included in this thesis but some issues warrant further discussion.

With the current studies, we have extended investigations of metacognitive beliefs to patients in early treated phases of psychosis. We have also added to the scarce literature on metacognitive beliefs in individuals with bipolar disorder, and provided the first study of thought control strategies in this population. Both patient groups have been compared to population representative healthy controls, which is rare in the literature. Paper I is the first study to examine a range of illness-relevant factors related to metacognitive beliefs in psychosis, and Paper II is the first study to examine a range of illness-relevant factors related to metacognitive beliefs and thought control strategies in bipolar disorders. Finally, Paper III is the first study to examine the relationships between early trauma, metacognitive beliefs, and symptoms of depression/anxiety in a large, well-characterised, representative clinical sample.

With regard to limitations, the conclusions from this thesis are limited by a cross-sectional design, which prevents investigation of the directions of the observed relationships. The mediation analyses assume a causal pathway, and early trauma reports suggest these experiences come temporally before metacognitive beliefs and symptoms, but the analyses cannot prove the direction. The underlying theory clearly supports a causal pathway in which specific metacognitive beliefs relay the effect of previous trauma on symptoms, and this was found by a longitudinal study of the role of metacognitive beliefs in depression and anxiety (190). However, our results should be replicated in a longitudinal design before conclusions about causality can be drawn.

It is possible that the relatively low levels of specific symptoms observed in our samples could prevent detection of associations with metacognitive beliefs or thought

control strategies. In Paper I we saw low levels of positive and negative symptoms. In Paper II we saw low levels of manic symptomatology and number of (hypo)manic episodes. Both papers could suffer from type II errors, i.e. a lack of significant associations when they do in fact exist. In Paper III low levels of positive symptoms could have influenced the effect of the extended mediation path in general, and particularly our ability to generalise these findings to bipolar patients with psychosis.

Finally, the data prevent us from comparing controls and patients on metacognitive measures while controlling for current fluctuations in mood. It is therefore possible that some of the observed group differences are driven by current levels of depression/anxiety. We are also not able to fully compare differences in state-trait in the bipolar sample (Paper II) due to this. How affective symptoms relate to metacognitive processes in healthy individuals should be addressed in future research to help clarify differences in state and trait effects of mood.

5.6 Clinical implications

With replication, our findings could have important clinical implications. Differences between patients and controls suggest that metacognitive beliefs and thought control strategies are relevant and could be clinically useful for individuals with a bipolar or psychotic disorder. Metacognitive beliefs are linked to current symptoms of depression (and anxiety) in these disorders, suggesting that such beliefs could be a viable treatment target to reduce affective symptoms. In bipolar disorder, targeting metacognitive beliefs could also help reduce the use of unhelpful thought control strategies. Assessing unhelpful metacognitive beliefs and thought control strategies when individuals with bipolar or psychotic disorders present for therapy could thus inform clinical formulation. Interventions targeting metacognitive beliefs are available, and have been proven effective in depression (191), and both feasible and acceptable in pilot studies for psychosis (192, 193). Such interventions may also be helpful in bipolar disorder and early psychosis, and could help tailor more personalized therapeutic interventions in relation to management and relapse-prevention, particularly in regard to depression.

6 Conclusion and questions for future research

Patients generally reported higher levels than controls on the five metacognitive beliefs proposed as relevant to mental disorder by the S-REF model, but there were no significant differences between patients with bipolar and psychotic disorders. For both patient groups higher levels of metacognitive beliefs were linked to more symptoms of affective dysregulation (depression/anxiety in early psychosis and depression in bipolar disorder). In the bipolar sample metacognitive beliefs also influenced the use of thought control strategies, as proposed by the S-REF model. This suggests that metacognitive beliefs are relevant across severe mental disorders, and potential treatment targets in both bipolar disorder and early psychosis, particularly in regard to affective symptoms. Future studies could benefit from investigating differential relationships between metacognitive beliefs and mood state versus trait.

Metacognitive beliefs were further linked to factors predating or related to the onset of illness in both groups, with somewhat clearer findings for early psychosis compared to the bipolar disorders. While this is in line with the developmental perspective of metacognitive beliefs predating mental illness proposed by the S-REF model, these relationships could also signify that metacognitive beliefs are linked to poorer symptomatic long-term outcomes in both bipolar and psychotic disorders. Follow-up studies could clarify whether metacognitive beliefs are a potential marker of a poorer long-term outcome, but ascertaining whether these beliefs develop before, and potentially cause, symptoms seen in bipolar and psychotic illnesses would require a longitudinal design.

In line with the suggestion that early experiences will shape metacognitive beliefs, such beliefs about thought being uncontrollable or dangerous were elevated in individuals with a history of early emotional trauma. These beliefs not only seem to increase depression and anxiety, but also to further increase positive symptoms. This provides further support to the proposed affective pathway to psychosis, and could indicate that metacognitive beliefs play a key role in it. Research including both bipolar and psychotic disorders might be better equipped to elucidate the interplay between affect and psychosis, as well as how such symptoms interact with metacognitive beliefs.

While this thesis included symptoms and episodes of both mood polarities in bipolar disorder, we must acknowledge that we have likely not been able to investigate this aspect of the disorder very well. Future studies could therefore benefit from investigating whether maniform symptoms and episodes show a similar relationship to metacognitive beliefs.

Metacognitive beliefs clearly influenced the use of most thought control strategies in bipolar disorder, supporting the S-REF model and adding to the clinical relevance of holding such beliefs. It would be beneficial to know whether similar relationships are observed in psychotic disorders, and whether the relationship is the same in early stages and more chronic representations of this patient group.

To summarise, the metacognitive factors explored in this thesis clearly differentiate patient participants from controls, and relate to clinical symptoms of affective dysfunction in both bipolar and psychotic disorders. For individuals who experience psychosis, such beliefs may also contribute to positive symptoms. Metacognitive beliefs are thus a viable treatment target in these patient groups, in regards to managing affective symptoms and possibly also reduce positive symptoms. Our findings suggest that future studies could benefit from clarifying whether metacognitive beliefs are stable or amenable to illness processes over time, and how they relate other clinical variables. This could further our understanding of the role such beliefs play in illness formation, maintenance, and long-term outcome, and shed light on the potential of their clinical application in severe mental disorders.

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