Does Mental Imagery Act as an Emotional Amplifier in Bipolar Disorders?

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Thesis abstract

Bipolar disorder is characterized by episodes of mania and depression and serious suicidal risks. Recent studies reported high mental imagery susceptibility (general use of imagery in daily life and emotional impact of prospective imagery) in euthymic bipolar patients. This thesis aims to: a) replicate these findings in patients at different phases of bipolar disorder and with varying degrees of bipolarity, and b) explore how mental imagery susceptibility, ruminative processing, and behavioural approach system (BAS) sensitivity interact to amplify mood symptoms.

Chapter 1 provides an overview of current theories of mood amplification and recurrence in bipolar disorders. Chapter 2 details the local validation of scales used in the thesis. Chapter 3 (Study 1) investigated whether mental imagery susceptibility, positive rumination and BAS sensitivity were elevated in remitted bipolar I disorder compared with major depressive disorder and non-psychiatric controls. Results suggested that these cognitive variables were elevated in remitted bipolar I disorder. Positive rumination also interacted with positive prospective images to predict bipolarity. Chapter 4 (Study 2) found that these cognitive variables were elevated in bipolar I disorder during manic and euthymic phases, compared to major depression. Further, the number of positive prospective images predicted recovery status and manic symptom severity. Chapters 5, 6 and 7 report that, compared with people without bipolar spectrum conditions, these cognitive characteristics were elevated in sub-threshold bipolar disorder (Study 3), individuals with high bipolar risks based on a

behavioural paradigm (Study 4), and individuals with high familial risk (Study 5). Studies 3-5 confirmed that positive and negative prospective images interacted with rumination to amplify hypomanic and depressive symptoms respectively. Chapter 8 (Study 6) showed that suicidal flash-forwards function as a psychological escape from perceived entrapment and defeat in suicidality. Based on these findings, Chapter 9 proposes novel imagery-based techniques for targeting problematic imagery in bipolar disorders.

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Thesis abstract (long version)

Bipolar disorder is a disabling, recurrent disorder characterized by episodes of mania and depression, affecting one to two percent of the general population. Apart from the psychosocial disabilities associated with these mood episodes, patients with bipolar disorders also have a higher prevalence of comorbid physical illnesses and suicide attempts than the general population. Effective treatments for bipolar disorder are needed to induce remission, extend the inter-episode well periods, and prevent the occurrence of new mood episodes. Current treatments of bipolar disorders are predominantly pharmacological, with limited application of adjunct psychological treatments. Furthermore, existing psychological treatments have limited efficacy in improving outcomes of bipolar disorders. Thus, novel psychological treatments based on empirical research are needed to improve the treatment outcomes and quality of life for people with bipolar disorders.

Recent studies show that euthymic patients with bipolar disorders are more likely to think in visual images than verbal cognitions (i.e. high general use of imagery in daily life). Furthermore, patients are also more emotionally affected by these reported visual images (i.e. emotional impact of future-oriented [prospective] images) than those without bipolar

disorders. Hence, people with bipolar disorders are considered as having higher mental imagery susceptibility than people without bipolar disorders. However, it is not at all clear how mental images experienced in the mind's eye are related to the pathological emotions, biased cognitions, and excessive approach or withdrawal behaviours characteristic of bipolar disorders. This thesis aimed to: a) replicate the findings of high mental imagery susceptibility in patients at different phases of bipolar disorder and with varying degrees of bipolarity; b) explore how mental imagery susceptibility, ruminative processing, and behavioural approach system (BAS) sensitivity interact to amplify mood symptoms in bipolar disorders, and c) investigate whether prospective images depicting suicidal acts or the aftermath of suicide (i.e. suicidal flash-forward imagery) might provide a form of psychological escape from the perceptions of entrapment and defeat that are thought to amplify the severity of suicidal ideation. Furthermore, a related hypothesis proposed that suicidal participants with high bipolar risks and high perceptions of entrapment were more likely to experience suicidal flash-forwards than those with low perceptions of entrapment.

Chapter 1 provides an overview of current theories of mood amplification and recurrences in bipolar disorders. It also highlights the unique properties of mental images as being emotionally more powerful and more likely to be acted upon than verbal cognitions of similar content. Recent research studies have provided preliminary evidence that patients with bipolar disorders have higher mental imagery susceptibility than people without bipolar disorders. Given this unique role played by mental images in amplifying emotions and promoting subsequent action as encapsulated within the image content, mental imagery is postulated to play a key role in the onset, progression, maintenance, and remission of mood episodes in bipolar disorders. Furthermore, since bipolar patients who reported ruminating about the content and meanings of their positive images had higher levels of euphoria and excitement compared to those who adopted a detached awareness of their images, this thesis further hypothesized that mental imagery might interact with positive prospective images in

amplifying hypomanic symptoms. Besides, if mental images are easily confused with real events, positive visual images might be construed as (simulated) positive life events. Previous research has reported that positive life events, especially BAS-relevant activation events, would trigger the hyper-sensitive BAS to respond with excessive BAS outputs in patients with bipolar disorders. Such BAS outputs have been found to correspond to the emotional, cognitive, and behavioural manifestations of mania. Therefore, the current thesis further hypothesized that repetitive rumination of positive prospective images might trigger the hypersensitive BAS to respond with excessive BAS outputs reminiscent of (hypo)mania.

Chapter 2 gives the rationale for the choice of scales used to measure mental imagery susceptibility and other cognitive processes in bipolar disorders (namely positive rumination, depressive rumination, BAS sensitivity, and positive over-generalization biases), as well as those for assessing clinical symptoms and diagnoses. As previous research on mental imagery and bipolar disorders was exclusively conducted in Western populations, these scales written in English were first validated in local non-clinical and clinical samples in Hong Kong. Results showed that all the scales used achieved satisfactory internal consistencies, inter-rater reliabilities and test-retest reliabilities before the commencement of the studies.

Previous research has found that patients with bipolar disorders had increased mental susceptibility levels (namely general use of imagery in daily life and emotional impact of prospective imagery), positive rumination (namely rumination of positive emotions and of positive self-qualities), positive over-generalizing biases (namely positive overgeneralization of current success experiences to other domains of life), and BAS hypersensitivity when compared to people without bipolar disorders. However, the participants recruited in these studies were mainly non-clinical student samples or clinical adult samples with possible residual anxiety symptoms. Given the high prevalence of intrusive images in patients with anxiety disorders and the high co-occurrence of anxiety in bipolar disorders, anxiety might be a significant confounder - and driver - of the hypothesized relationships between mental

imagery and bipolar disorders.

Chapter 3 describes Study 1, which addressed the above considerations by investigating whether mental imagery susceptibility, positive rumination and BAS sensitivity were elevated in patients with pure bipolar I disorder in remission (n = 62) compared with patients with major depression (n = 62) and non-psychiatric controls (n = 60). Results confirmed that these cognitive variables remained elevated in patients with bipolar I disorder even during full remission. Furthermore, positive rumination interacted with the number of positive prospective images to predict bipolarity through the moderating variable of BAS sensitivity. As such, the results suggest a cognitive model whereby repetitive savouring of meanings and emotions associated with positive images could lead to a heightened BAS, which in turn might be associated with the diagnostic category of bipolar I disorder.

If repetitive rumination of positive prospective images was a characteristic associated with bipolar I disorder in remission, what additional cognitive characteristics might be associated with the subsequent ascent of manic symptoms? Previous studies suggest that relapse of mania was associated with an intrusion of positive prospective images and past memories while depression was associated with past negative images. Building on the above preliminary evidence, Chapter 4 (Study 2) hypothesized that a decline in positive prospective images would be associated with a progressive resolution of manic symptoms in a group of hospitalized patients with acute bipolar mania (n = 50) over a twelve week period. Furthermore, a rise in negative prospective images would be associated with a progressive increase in depressive symptoms in the sub-group of bipolar I patients (n = 11) who experienced a mood switch from mania to depression at both four and twelve weeks. The results confirmed that, in the bipolar I group, a drop of positive prospective images from baseline to twelve weeks predicted recovery from mania while a drop of negative prospective images over the same time interval negatively predicted a switch from mania to depression. The study also found that levels of mental imagery susceptibility (namely use of imagery in

daily life and emotional impact of prospective imagery) and rumination of positive emotions were consistently elevated in the bipolar I group (n = 50) when compared to the major depressive group (n = 50) over a period of twelve weeks. What this study also added to the trait hypothesis of mental imagery susceptibility is that these imagery measures also varied with changes in mood symptoms in the bipolar I group, suggesting that these characteristics could be state-on-trait markers associated with bipolarity.

Although the above imagery characteristics and positive rumination were elevated in bipolar I disorder in symptomatic, euthymic, and remitted states when compared with non-psychiatric or major depressed controls, these heightened cognitive activities could be argued to be 'cognitive scars' inflicted by repeated mood episode insults rather than as trait markers associated with bipolarity. To further investigate the trait hypothesis of these cognitive variables, the studies in Chapters 5, 6 and 7 compared these variables in people with varying degrees of bipolarity (bipolar spectrum conditions) with those without such bipolar spectrum conditions. Specifically, Study 3 (Chapter 5) recruited a group of people with major depression who had a history of a number of lifetime hypomanic symptoms but falling short of the number and the severity required for a DSM-5 diagnosis of hypomania (known as 'sub-threshold bipolar disorder; n = 10), a second group of people with bipolar II disorder (n = 4), and a third group of people with pure major depression (n = 61). Study 4 (Chapter 6) recruited a group of non-clinical participants identified as meeting a threshold level of behavioural symptoms characteristic of hypomania as defined by scoring a total score above the criterion cut-off point of a well validated bipolar questionnaire (n = 18) from a random sample of non-clinical participants in the community (n = 80). These participants could thus be regarded as having a liability for developing full-blown bipolar disorders. Study 5 (Chapter 7) compared a sample of non-clinical individuals who were first-degree relatives (parents, siblings and offspring) of patients suffering from DSM-5 defined bipolar I disorder (n = 78) with a sample with a low familial risk (n = 76). The first-degree relatives of bipolar

I patients were thus defined as having a high familial risk of developing full-blown bipolar disorders. The samples in Studies 3-5 can be considered as having conditions that lie on the mild end of the bipolar spectrum, whereas those bipolar participants in Studies 1 and 2 can be considered as lying on the severe end of the bipolar spectrum. Chapters 5-7 concur in reporting that the levels of mental imagery susceptibility and positive rumination were higher among those with the bipolar spectrum conditions when compared to those without.

Study 3 (Chapter 5) found that repetitive rumination of positive prospective images was predictive of lifetime hypomanic symptoms while depressive rumination of negative images was predictive of current depressive symptoms among participants suffering from major depression with or without sub-threshold bipolarity. The above finding on positive images corroborates a similar finding reported in Chapter 3 (Study 1) that rumination of positive images was associated with the diagnosis of bipolar I disorder rather than major depression. As such, this provides preliminary evidence that rumination about the nature, meanings and consequences of experienced prospective images might be related to amplification of mood symptoms. Whether the mood symptoms being amplified are hypomanic or depressive in nature appears to be dependent on the emotional valence of the prospective images.

Furthermore, results from Study 4 (Chapter 6) suggest that these mental imagery susceptibility measures remained stable across a period of seven weeks among non-clinical participants with a high behavioural risk of developing bipolar disorders. As such, temporal stability of these measures over seven weeks might provide some additional support for the trait hypothesis of mental imagery.

While the results reported in Chapters 3-6 converge to support the trait hypotheses of heightened mental imagery susceptibility and positive rumination being associated with bipolarity, Study 5 (Chapter 7) further refined this hypothesis into an age-specific one. Specifically, at-risk individuals aged below 28 had higher levels of mental imagery

susceptibility than age-matched individuals without a high familial risk for bipolar I disorder. On the other hand, those at-risk individuals aged 28 or above had lower levels of these cognitive variables than the age-matched counter-parts. Such age-specific findings suggest that heightened imagery characteristics may be particularly associated with young at-risk individuals, a group being considered as having a particularly high risk of conversion into full-blown bipolar disorders.

Study 6 (Chapter 8) supported the hypothesis that suicidal flash-forwards might function as a psychological escape from perceived entrapment and defeat in suicidal individuals (n = 82). When compared to age-matched non-suicidal individuals (n = 80), the suicidal participants had higher levels of emotional impact of prospective imagery, perceived entrapment and defeat both at baseline and seven weeks' follow-up. Besides, suicidal flash-forwards were only present in suicidal participants at both time points. Finally, the presence of suicidal flash-forwards interacted with high levels of entrapment to predict high levels of suicidal ideation at both baseline and 7-week follow-up. Adding to the literature of increased suicidality in bipolar disorders, those suicidal individuals with high bipolar risks and high levels of entrapment were more likely to have suicidal flash-forwards than those suicidal individuals with high bipolar risks but low levels of entrapment.

Based on the above research findings, Chapter 9 proposes a new cognitive model that incorporates mental imagery susceptibility and ruminative processing as key factors in amplifying both (hypo) manic and depressive symptoms in bipolar disorders. The model also attempts to incorporate the contribution of high imagery susceptibility in promoting suicidal flash-forwards, especially among those suicidal individuals with a high behavioural risk for bipolar disorders. Using this novel cognitive model as groundwork, novel imagery-based strategies are proposed to be incorporated into classic cognitive-behavioural therapy for enhancing its efficacy in the treatment of bipolar disorders. This thesis proposes that an imagery-based case formulation based on the above cognitive model might be constructed and

shared between the cognitive-behavioural therapist and the patient. Given that patients with bipolar disorders have a high propensity to think in terms of visual images, an imagery-based case formulation is also more likely to be accepted than one that is based exclusively on verbal cognitions. Besides, such case formulation provides a clear rationale to the patient why certain imagery-based interventions might be helpful to reduce the severity of mood symptoms and inter-episode emotional instability.

The proposed imagery-based interventions can be divided into those that prevent the development of intrusive images (playing Tetris for at least thirty minutes after visual or narrated exposure to traumatic events), those that may alter the meanings of the reported prospective images (imagery re-scripting of positive and negative images; meta-cognitive re-appraisal of the theme of uncontrollability inherent in these recurrent and intrusive images), and those that promote compassionate images for self-soothing. Furthermore, given the close relationships between prospective images, ruminative processing and BAS sensitivity in amplifying mood symptoms, additional cognitive-behavioural interventions are also proposed to target these cognitive variables. If rumination of the nature, content and meanings of the prospective images is associated with mood amplification, disruption of these ruminative cycles by active distraction or mindfulness work might serve to break the vicious cycle. Furthermore, given that BAS sensitivity appears to be a final common pathway from imagery and rumination to full-blown (hypo)mania, BAS outputs associated with BAS hypersensitivity might be minimised by promoting adequate rest, moderating the amount and the pace of daytime behavioural activities, and seeking advice from trusted friends before turning impulsive decisions into action. Finally, based on some pertinent but unanswered questions arising from the current six studies, this thesis concludes by proposing some new research directions for future research into mental imagery in bipolar disorders.

Thesis Contents List

CHAPTER 1 – Introduction

1.1 Introduction

1.1.1 Conception of the evolution of bipolar disorders

1.1.1.1 Evolution of the concept of bipolar disorders

Bipolar disorder (BD) was first considered as a disease entity of its own in 1851, when Falret coined the term 'folie circulare' to describe the illness characterised by mania, depression and disease-free intervals (Falret, 1857 as quoted in Angst & Marneros [2001]). This interest in the relationship of mania and depression was revived almost 2000 years after Greek philosophers proposed melancholia as periods of extreme sadness ('*melas*' means black while '*chole*' means bile) and mania as periods of extreme elation (Greek word for 'relaxed' or 'loose' being '*manos*' while that for 'mental anguish' being '*ania*') (see Angst & Marneros [2001] for a more comprehensive review of the ancient views of mania and melancholia). In 1854, Baillinger presented the concept of '*folie a double forme'*, a disease in which mania and melancholia interchange with the interval being of no importance (Angst, 1997). Falret's concept was supported by Kahlbaum who introduced this concept into German psychiatry and coined the term '*circulares Irresein*' (circular insanity) to describe this disease (Angst, 1997).

Based on his phenomenological analysis of patients, Kraepelin considered mania and depression together as a unitary concept of 'manic-depressive illness' (Kraepelin, 1899; Angst, 1997). Kraepelin (1899) commented that if periodic mania (i.e. recurrent mania in the absence of depression) was indistinguishable from manic episodes of circular insanity, periodic melancholia (i.e. recurrent depression in the absence of mania) should be understood as a kind of circular insanity in which all the episodes took on a 'depressive hue', analogous

to periodic mania in which all episodes had a ‘manic hue’ (Kraepelin, 1899).

However, this unitary concept of manic-depressive illness was criticized for being too inclusive by Carl Wernicke and Karl Kreist. Wernicke (1900) proposed that manic-depressive illness should only be understood as described by Falret (‘*folie circulaire’*) or by Baillarger (‘*folie a double forme’*) (Wernicke [1900] as quoted by Angst & Marneros [2001]). Single episodes of mania or melancholia, recurrent depression or recurrent mania without changing into one another, Wernicke argued, should be regarded as different from manic-depressive illness (Wernicke [1900] as quoted by Angst & Marneros [2001]). Kleist, a colleague of Wernicke in Halle of Germany, differentiated between unipolar (i.e. disease with a single pole of either depression or mania) and bipolar affective disorders (i.e. disease with both poles of depression and mania) (Kleist [1953] as quoted by Angst & Marneros [2001]). The concepts of Wernicke and Kleist were unified by Karl Leonhard, who classified the phasic psychoses into ‘pure phasic psychoses’ (such as ‘pure melancholia’, ‘pure mania’, etc.) and ‘polymorphous phasic psychoses’, in which manic-depressive illness was included (Leonhard [1957] Angst & Marneros [2001]).

The nosological differentiation between unipolar and bipolar disorders was partially supported by subsequent studies conducted by Angst (1966) as quoted by Angst and Marneros (2001) and by Perris (1966) in Europe, and then further by Winokur and Clayton (1967) in the United States. Importantly, unipolar depression (UD) differed significantly from bipolar disorders (BD) in characteristics like genetics, gender, course and premorbid personality (Angst & Perris [1968] as quoted by Angst & Marneros [2001]). They also showed that ‘unipolar mania’ was genetically related to BD, leading them to argue that unipolar mania should have been subsumed under the category of BD (Angst & Perris [1968] as quoted by Angst & Marneros [2001]). This bipolar-unipolar distinction was formally adopted in the American Psychiatric Association’s (APA) diagnostic and statistical classification system for mental disorders in 1980 (Diagnostic & Statistical Manual of Mental Disorders 3rd ed.; DSM-

III; American Psychiatric Association, 1980).

1.1.1.2 Diagnostic classifications of bipolar disorders

An individual suffering from a manic episode experiences an unusual sense of elation, excitement, subjective racing of thoughts, and sense of over-optimism. This person will typically appear over-friendly, boastful of his or her own achievements and may behave recklessly, without considering the consequences. This period of abnormal mood must last at least one week and the symptoms must be severe enough to cause marked impairment in social or occupational functioning or to require hospitalization in both Diagnostic Statistical Manual of Mental Disorders Version IV- Trial Version (DSM-IV-TR; APA, 2000) and DSM-5 (APA, 2013).

A milder version of a manic episode with less marked functional impairment is known as ‘hypomania’, whereby the patient experiences an abnormal period of elevated, irritable or expansive mood with similar cognitive and behavioural symptoms of lesser severity. The diagnosis of ‘hypomania’ also requires the presence of at least three (if elated mood is present) or four symptoms (if only irritable mood is present instead of elated mood) and a duration of at least four consecutive days.

In contrast, a patient suffering from a major depressive episode feels depressed, and experiences hopeless and helpless feelings about themselves, the world and their future. The individual typically appears dejected, speaks and thinks slowly, and becomes listless and unmotivated to engage in previously enjoyable activities. In extreme cases, they can become hopeless and suicidal.

There are some patients who experience both manic and depressive symptoms concomitantly in the same episode of illness, or who rapidly alternate between mania and depression in the same episode, known as ‘mixed episodes’. In contrast to DSM-IV-TR (APA, 2000) which requires a patient to meet the full criteria for both mania and a major depressive

episode concurrently to be qualified as having a 'mixed episode', the DSM-5 has introduced a new specifier 'with mixed features'. The new specifier can now be applied to episodes of depression (in either major depressive disorder or bipolar disorders) when features of mania or hypomania are present, or to hypomania or mania when depressive features are present. This new addition is made with reference to the increasing evidence for substantial overlap in symptom presentation in both bipolar and major depressive disorders (also see section 1.1.1.5 on 'sub-threshold bipolarity and major depressive disorders').

In contrast to the DSM-IV-TR classification (APA, 2000) that emphasized the categorical system of classifying BD, DSM-5 has taken a dimensional approach to diagnosis (APA, 2013). BD are no longer considered as separate disorders but as related conditions on a continuum of behaviours, with some conditions reflecting mild symptoms (e.g. cyclothymia) and others much more severe (e.g. bipolar I disorder).

In contrast to DSM-IV-TR diagnostic classification (APA, 2000), DSM-5 mood disorders are now divided into two distinct chapters, one on bipolar and related disorders and the other on depressive and related disorders. The descriptions of BD are found in Chapter 3 of the DSM-5 manual and are classified into bipolar I disorder (BD-I), bipolar II disorder (BD-II), cyclothymic disorder, substance or medication-induced bipolar disorder, bipolar disorder due to another medical conditions, and other specified bipolar and related disorders. For the purpose of the current thesis, the following bipolar disorders are elaborated in a greater detail:

Bipolar I disorder (BD-I): this is characterized by the occurrence of one or more manic episodes or mixed episodes, with most individuals also experiencing one or more major depressive episodes. Patients experiencing recurrent episodes of mania (recurrent unipolar mania) are also classified as suffering from BD-I. Furthermore, patients who experience their first episode of mania will also be diagnosed as suffering from BD-I as such patients are believed to inevitably suffer from a recurrent course of illness characteristic of BD-I.

Diagnosis of mania has been enhanced with the inclusion of changes in activity and energy level, not just changes in mood, as key diagnostic criteria.

Bipolar II disorder (BD-II): this is characterized by the occurrence of one or more major depressive episode accompanied by at least one episode of hypomania. The symptoms should be clinically significant to cause impairment in daily functioning.

Other specified bipolar and related disorder: this diagnosis is applied when the symptoms of mood disturbance are characteristic of one of the above bipolar and related disorders but do not meet the full criteria. The clinician lists the specific reasons, with examples including hypomanic episodes of fewer than four days and major depressive disorder (i.e. sub-threshold bipolar disorder [sub-threshold BD] due to the duration not meeting the current criteria of hypomania; see section 1.1.1.5), or hypomanic episodes with insufficient symptoms and major depressive disorder (i.e. sub-threshold BD due to the number of symptoms not meeting the current criteria), or hypomanic episode without previous episodes of major depressive disorder (clinical hypomania only; see Studies 4 and 6), or short-duration cyclothymia lasting for fewer than 24 months. These could be included in the broad category of 'bipolar spectrum disorders (BSD)' (see section 1.1.1.5).

1.1.1.3 Classification of depressive disorders

Major depressive disorders (MDD) are also known commonly as 'unipolar depression (UD)'. This nomenclature aims to highlight that patients with MDD only experience depressive recurrences (i.e. single pole of depression). Once these patients experience depressive recurrences, they would be classified as MDD (recurrent episode) in DSM-5. In the current thesis, the term 'unipolar depression (UD)' is used interchangeably with 'major depressive disorder (MDD)'. Patients suffering from MDD were recruited as clinical controls of Studies 1, 2, and 3.

In DSM-5 diagnostic classification (APA, 2013), depressive disorders are classified into major depressive disorders (MDD), dysthymia, premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition, and other specified depressive disorder. For the purpose of this thesis, only major depressive disorder is further elaborated:

Major depressive disorders (MDD): An episode of major depression is defined as a period of at least 2 weeks during which there is either depressed mood, or loss of interest or pleasure in nearly all activities for most of the day nearly every day during this two-week period. A minimum of four additional symptoms are required, which include changes in weight, sleep, psychomotor activity; decreased energy; feelings of guilt or worthlessness; indecisiveness or poor concentration; or recurrent thoughts of death or suicidal ideas, plans or attempts. The symptoms must cause significant distress or impairment in daily functioning. The episode is not caused by the effects of a substance or another medical condition.

1.1.1.4 Relevance of the expansion of the diagnostic classifications of bipolar disorders to the current thesis

In summary, the DSM-5 has introduced certain changes in the diagnostic criteria for bipolar and depressive disorders and added new diagnostic categories, based on recent evidence for the validity and reliability of certain conditions such as sub-threshold BD and presence of hypomanic symptoms even in unipolar depression. DSM-5 has also taken a dimensional approach to diagnosis. As such, the current diagnostic criteria suggest that BD can be considered as a spectrum of bipolar conditions (i.e. bipolar spectrum disorders; BSD) ranging from other specified bipolar disorders like sub-threshold BD and recurrent hypomania, BD-II, to BD-I. The current thesis takes advantage of this bipolar spectrum concept to explore whether certain cognitive variables (e.g. daily use of imagery in daily life) are heightened in

people suffering from various forms of BSD when compared with people without such disorders. Identifying increased levels of these key cognitive variables across bipolar spectrum conditions of varying severity might provide some preliminary evidence for their role as trait factors underlying bipolarity.

As the DSM-5 classification was released in 2013, after the studies in the current thesis commenced, DSM-IV-TR classification (APA, 2000) was adopted. Furthermore, studies 1, 2 and 5 in the current thesis used the validated Chinese version of CB-SCID-I/P (So et al., 2003a) for confirming clinical diagnoses. Validated diagnostic criteria or clinical questionnaires were used for identification of relevant spectrum conditions that were newly incorporated into the DSM-5 classification (e.g. clinical hypomania and sub-threshold bipolar disorders).

1.1.1.5 Classification and expansion of bipolar spectrum disorders

Although the international diagnostic classification of psychiatric disorders has endorsed the binary concept of bipolar-unipolar dichotomy rather than the unitary concept of manic-depressive illness, the recognition of the category of 'other specified bipolar disorders' in DSM-5 might be considered as a compromised position in this debate. Historically, a concept of a continuum of manic conditions was first developed by Kretschmer and Bleuler (see Angst [1997] and Marneros [2001] for more comprehensive reviews). There is some clinical evidence supporting this hypothesis of a continuum of manic conditions encompassing illnesses with varying combinations and degrees of severity of mania and depression. For example, when examining hypomanic scores dimensionally across a group of patients with MDD, or with BD-II, or a combined sample of MDD and BD-II, hypomania scores were found to be normally distributed rather than bimodal (Akiskal & Benazzi, 2006). Furthermore, among those patients with MDD at the time of interview regardless of the mood

disorder diagnosis, there was a dose-response relationship between familial loading of bipolar illness and intra-episode hypomanic scores (Akiskal & Benazzi, 2006). The offspring of patients with full-blown BD were more likely to suffer from cyclothymia than the offspring of patients with non-affective psychiatric disorders (Klein, Depue & Slater, 1985). Patients with mild types of BSD were also more likely to have family members suffering from full-blown BD than those patients without such disorders (Akiskal et al., 2006).

If BSD include clinical disorders with various combinations of (hypo) mania and depression, 30-55% of unipolar depression (UD) might be considered as belonging to the BSD category (Benazzi, 1997; Angst et al., 2010). This expansion of the concept of BSD into the territory of UD is based further on recent literature that many patients suffering from UD reported having a past history of one or more hypomanic symptoms but falling short of the diagnostic criteria for hypomania (Angst et al., 2010; Merikanagas et al., 2011), as well as patients having 'atypical depression' (threshold depression mixed with sub-threshold hypomanic symptoms within the same mood episode) (Benazzi, 2006). This type of 'unipolar' depression with a past history of sub-threshold hypomania is coined as 'sub-threshold bipolar disorder' (sub-threshold BD; Westernmeyer, 2010). As the current diagnostic criteria of hypomania are stringent and sub-threshold hypomanic symptoms are difficult to detect by clinicians, sub-threshold BD is frequently under-detected and hence under-diagnosed (Akiskal et al., 2000).

1.1.1.6 Clinical implications of the expansion of the rubric of bipolar disorders

Clinical studies have indicated that up to 30%-55% of patients with MDD reported a past history of variable degrees of hypomanic symptoms (i.e. sub-threshold BD) upon careful diagnostic interviews (Benazzi, 1997; Benazzi & Akiskal, 2003; Cassano et al., 1992;

Hantouche et al., 1998; Manning et al., 1997). These patients with sub-threshold BD were also found to have a family history of BD similar to those patients with BD-I or BD-II (Merikangas et al., 2011). In the re-analysis of the data from the National Co-morbidity Survey replication study (NCS-R, Kessler & Merikangas, 2004) for identifying patients with MDD and a past history of sub-threshold hypomania, the lifetime and 12-month prevalence rates of BSD that included sub-threshold BD became similar to those of MDD alone (lifetime prevalence: 9.0% for BSD vs. 10.2% for MDD; 12-month prevalence: 3.3% for BSD vs. 5.4% for MDD) (Angst et al., 2010).

In reality, the expansion of BSD to include sub-threshold BD is of more than just theoretical and epidemiological interest. Patients suffering from MDD with a history of sub-threshold hypomanic symptoms have been found to report more severe depressive symptoms, more depressive recurrences, more frequent suicide attempts, greater comorbidity with anxiety, impulse control and substance use disorder as well as higher suicide rates than those with depression without such symptoms (Angst et al., 2003; Merikangas et al., 2008; Judd & Akiskal, 2003). Given that BSD can be diagnosed in up to 50% of patients with MDD and that BSD are associated with a poor clinical outcome, its identification among unipolar depression has important prognostic and treatment implications. If certain forms of highly recurrent depression are considered as a sub-threshold BD, BSD that span from highly recurrent depression, atypical depression, clinical hypomania, cyclothymia, BD-II, BD-I and recurrent mania are reminiscent of ‘manic-depressive illness’ as proposed by Kraepelin (1899).

Taking into consideration the bipolar spectrum concept, the current thesis (Study 3) examined whether the key cognitive variables of interest (e.g. emotional impact of future-oriented imagery) were elevated in people with sub-threshold BD compared to people with pure MDD. The relationships between these cognitive variables and the severity of clinical features of sub-threshold BD (e.g. depressive and anxiety symptoms) were also explored.

1.1.1.7 Bipolar symptoms in Asian population: are there any differences?

Three prevalence studies that used comparable diagnostic criteria and assessment concurred that the prevalence of BD in Asian countries was relatively low (Cho et al., 2007; Lee et al., 2007; Merikangas et al., 2007). The lifetime prevalence of BD-I and BD-II in Korea (Cho et al., 2007) and metropolitan China (Lee et al., 2007) was 0.2% and 0.1% respectively, whereas reported prevalence rates of BD-I and BD-II in the United States are as high as 2.1% (Merikangas et al., 2007). A regional survey in Hong Kong reported lifetime prevalence for BD as 0.15% (Chen et al., 1993). Apart from true difference in prevalence rates of BD, there might be other possible reasons.

In a local validation study of the Mood Disorder Questionnaire (MDQ; Hirschfield et al., 2000; a self-administered questionnaire for screening of BSD in general population; Hirschfield et al., 2003) in Hong Kong, Chung, Tso & Chung (2009) found that endorsement of MDQ items in the Hong Kong sample was roughly similar to that of the United States sample. However, only 17% of the Hong Kong sample reported having ever been so irritable that they shouted at people or started fights or arguments, compared to 36% of the US sample. The Chinese culture of containment of impulses and self-control, in contrast with the Western culture of self-expression of emotions, might explain this discrepancy (Aubert, Daigle & Daigle, 2004). Another local validation study of the MDQ (Hirschfield et al., 2000) and Hypomania Checklist-32 (HCL-32; Angst et al., 2005) in Hong Kong similarly found that lower cutoff scores of MDQ and HCL-32 would be needed for identifying people with clinical hypomania. Such phenomenon could be explained by the possible denial of hypomanic and manic symptoms among the Chinese population, probably related to fear of stigma and misconception about mental illness (Poon et al., 2012). Such cultural issues highlight possible under-reporting of bipolar symptoms in general Chinese population, particularly on self-administered questionnaires. Use of locally validated cut-off scores of the

mood scales is therefore needed to ensure accurate classification of participants into the appropriate diagnostic categories. Bearing this point in mind, the current thesis adopted locally validated cut-off scores of MDQ and HCL-32 for identifying people with clinical hypomania (Studies 4 and 6).

1.1.2 Current hypotheses of first onset and subsequent episode recurrences in bipolar disorders

1.1.2.1 Kindling theory

Post and colleagues proposed a kindling theory to explain the recurrent and fluctuating course of BD (Post & Weiss, 1989). Based on the observation that mood recurrence becomes more independent from preceding stressors and more autonomous with increasing number of episodes, Post's (1990; 1992) neuro-physiologically based 'kindling' hypothesis proposed that patients with BD become 'sensitized' after each mood episode, regardless of episode polarity. Through the process of neuro-chemical sensitization of the brain during a mood episode, the threshold level of the psychosocial stressor required for triggering a new episode may be progressively lowered with an increasing number of recurrences.

However, whilst some studies have supported that sensitivity to life events was restricted to earlier bipolar mood episodes (Glassner & Haldipur, 1983; Hammen & Gitlin, 1997), others reported higher sensitivity to life events occurring later in the course of illness (Ambelas, 1987; Dunner, Patrick & Fieve, 1979; Glassner, Haldipur & Dessauersmith, 1979). No relationship between number of episodes and kindling or sensitization has also been reported (Hlastala, Frank & Kowalski, 2000). A small longitudinal study observed a pattern of kindling in 50% of hospitalized patients with BD (Goldberg & Harrow, 1994). This sample was characterized by having at least three prior lifetime hospitalizations, and having less than

a one-year interval between two episodes. These individuals were found to have an increased risk of further and more frequent recurrences over a follow-up period of 4.5 years compared with patients who had a similar number of previous mood episodes but with a lower frequency (each episode separated by a well period of greater than one year). While more studies are needed to confirm this finding, this could imply that the kindling model might be applicable to only a selected subgroup of highly recurrent BD. Additional theories are needed to explain the phenomena of mood switch within the same mood episode and the polarities of the mood episodes.

1.1.2.2 Circadian rhythm disruption

Diagnostic criteria of both mania and depression have highlighted the importance of sleep and behavioural disturbances (First et al., 1996; see sections 1.1.2 and 1.1.3). Wehr and colleagues (1987) argued that sleep disturbance is the final common pathway for mania and provided evidence supporting the antidepressant effect of sleep deprivation in the treatment of the depressive phase of BD (Benedetti et al., 2001; Pflug, 1976; Wehr et al., 1979).

In connection with sleep-wake pattern disruption is the concept of circadian rhythm, defined as the pattern of biological activity which cycles over an approximately 24.5-hour period (Czeisler et al., 1999). Circadian rhythms are driven by oscillators (like body temperature and sleep-wake cycle), which are, in turn, entrained by external zeitgebers (clock-setting stimuli). Apart from external zeitgebers like light-dark cycle and seasonal variation, social zeitgebers from social interactions, daily tasks, and societal routines may also affect the operation of such a biological clock (Ehlers, Frank & Kupfer, 1988). It is generally accepted that there are weak (environmentally sensitive) and strong (environmentally insensitive) oscillators. Strong oscillators include body temperature, cortisol secretion, rapid eye movement sleep, and urinary potassium secretion while weak oscillators include the sleep-wake cycle and rest-activity cycle (Murray & Harvey, 2010).

Using a self-report 17-item measure of activity and social contact known as social rhythm metric (SRM) (Monk et al., 1990), significant disruptions of social rhythms have been reported in rapid cycling BD compared to controls, with a phase delay of a number of morning activities (Ashman et al., 1999). Lower SRM stability has also been found to predict future affective symptoms in BSD (Chang, Alloy & Abramson, 2003). Using wrist actigraphy (a wrist band with a small acceleration sensor that records movement over preset epochs), which measures fine-grained activity over a period of one week, Kupfer and colleagues reported that patients with bipolar depression had lower activity levels than patients with MDD, whereas patients with mania had the highest activity recordings (Kupfer et al., 1974). Jones, Hare & Evershed (2005a) also found that remitted bipolar individuals had weaker coupling of the sleep-wake rhythm to external zeitgebers and greater circadian instability when compared with healthy controls, providing further evidence of a disruption in the circadian rhythm that extends beyond acute mood episode.

1.1.2.3. Appraisal of circadian rhythm disruptions

Jones (2001; 2006) has elaborated on the circadian rhythm model further and proposed a model integrating the evidence of circadian instability and abnormal interpretations of circadian disruption in precipitating or maintaining BD, based partially on a model known as Schematic Propositonal Analogical and Associative Representation Systems (SPAARS; Power & Dalegleish, 1997). In the SPAARS account of emotion, external events are processed analogically in a rapid way. Such information processing at a sensory (analogical) level does not require linguistic interpretation to give rise to a specific meaning. However, further processing at a propositional level then utilizes abstract language-based capabilities. Schematic processes, the highest level of processing, integrate information from all other processing systems into knowledge at a level beyond the verbally expressible propositional level (Power & Dalegleish, 1997). Such schemas are an organised set of long-standing beliefs,

personal rules, and key cognitions that constitute an idiosyncratic concept about self, other people, and the world. Schemas formed are, however, still dynamic and flexible in response to changing inputs from different levels and guide different behaviours. With repeated presentation of the trigger, the associative level of processing allows the event to elicit immediate responses from propositional and schematic levels without going through the analogical level.

Jones (2001) argued that circadian disruption is integrated into the analogical stage of processing, so that events associated with significant circadian disruptions result in analogous effects of increased energy, alertness and hyperactivity. When such changes are internally attributed, these would give rise to positive propositional thoughts like 'being on top of the world'. At the schematic level, an individual with bipolar illness will then develop an overly positive self-view and an over-optimistic estimation about outcomes through integrating information from all other levels. This schematic appraisal is then associated with elevated mood and over-activity which will then exacerbate initial mood changes.

The crucial point is that, via the associative level of processing, once circadian-emotion links have been established, schematic appraisals may be less apparent, consistent with the findings that later bipolar episodes may be triggered by more minor or even no life events. This model also explains the occurrence of 'mixed emotional states' in bipolar disorder, when associative-emotion link might output elated mood, while the propositional knowledge of previous consequences of prodromal behaviours may output anxiety or dysphoria. Studies have found that individuals at risk of BD made more internal attributions for hypomanic experiences than those without the risk (Robbins & Kirkmayer, 1991; Jones, Mansell & Waller, 2006). However, this theory has not adequately addressed how this internal attribution bias of circadian rhythm instability could lead to mood switch from one polarity to the other in BD.

1.1.2.4. Behavioural approach system hyper-sensitivity theory

Behavioural approach system (BAS) is conceptualised as a brain system that regulates affect, cognition and action to support the pursuit of goals or reward incentives (Depue & Iacono, 1989; Gray, 1994). High BAS function is believed to relate to increases in confidence, energy, and approach activity in the pursuit of goals or reward incentives. Thus there are parallels between these BAS outputs and symptoms of mania. At a neurobiological level, Depue & Iacono (1989) hypothesized that the BAS involves dopaminergic (DA) projections from A10 nucleus in the ventral tegmental area (VTA) to frontal cortex, amygdala, nucleus accumbens, ventral pallidum, septum and hippocampus, with the DA activity in the nucleus accumbens playing a central role. They further implicated specific frontal cortical regions namely anterior cingulate cortex, orbitofrontal cortex and dorsolateral prefrontal cortex as the neurobiological substrates of BAS (Depue & Iacono, 1989). Left cortical frontal activity has also been identified as the potential neurological index of BAS activity (Davidson, 1999).

According to the BAS dysregulation model proposed by Depue and Iacono (1989), individuals with BD experience extreme fluctuations in activation and de-activation of the BAS. Early formulation of BAS dysregulation theory hypothesized that manic and depressive symptoms reflect an overly active or inactive BAS respectively (Depue & Iacono, 1989). Furthermore, individuals with BD or predisposed to BD experience greater variability in their state levels of BAS activation over time and across situations than those without these disorders or risks.

The BAS model of BD has recently been expanded, with vulnerability to BD being proposed as a reflection of a BAS that is hyper-sensitive to goal- and reward-relevant cues (Alloy & Abramson, 2010; Alloy, Abramson et al., 2009). This hypersensitivity can lead to excessive BAS activation in response to goal-striving or goal-attaining life events, and to excessive BAS deactivation in response to life events involving loss, failure or frustration of personal goals.

A series of studies have supported the presence of BAS hypersensitivity among patients with BD. People with BSD were found to have a greater BAS sensitivity than individuals without psychopathology (Urosevic et al., 2007). BAS sensitivity predicted relative amplification of manic symptoms over time in BD (Meyer, Johnson & Winters, 2001). High self-reported BAS sensitivity also predicts prospective increases in manic symptoms (Meyer et al., 2001), a greater likelihood and a faster onset of hypomanic and manic episodes (Alloy et al., 2008; Salavert et al., 2007) among patients with BSD. Higher BAS sensitivity individuals were also more likely to have a lifetime BSD and exhibited greater hypomanic personality and current hypomanic symptoms than moderate BAS sensitivity individuals (Alloy et al., 2006). Furthermore, high BAS sensitivity among students with BSD predicted a greater probability of conversion to BD-II over a follow-up period of 4.5 years (Alloy et al., 2012b). A recent prospective study reported that people with a high BAS sensitivity had a higher risk of subsequent onset of BSD than those with a low BAS sensitivity (Alloy et al., 2012a).

Furthermore, other studies have confirmed the role of BAS-relevant life events in triggering mood changes. Recent studies have found that the onset of hypomanic or manic episodes in at-risk individuals were more likely to be specifically preceded by goal-striving or goal-attaining life events (i.e. BAS-activating events) than general positive or negative life events, whilst depressive recurrence is more likely to be preceded by negative life events of loss and personal failure (i.e. BAS-deactivating events) (Johnson et al., 2008; Nusslock et al., 2007). Such goal-attaining life events might serve as reward incentive cues required to set off a cascade of BAS outputs leading to a full-blown hypomanic/manic episode. For example, after receiving positive feedback for their laboratory task performances (i.e. presenting with a goal-striving cue), people at an increased risk for BD reported a higher expectancy of success and an increased willingness to take up more challenging subsequent laboratory tasks reminiscent of BAS-driven cognitions and behaviours (Johnson, Ruggero & Carver, 2005).

1.1.2.5. Dysfunctional attitudes and cognitive schemas

The 'depression avoidance hypothesis' argued that mania arose from dysfunctional attempts to avoid depression (Neale, 1988). This hypothesis proposed that vulnerability to mania is associated with depressogenic psychological processes. At the level of cognitive biases, individuals with BD and MDD seem to share cognitive biases such as dichotomous thinking and internal attributional style (Alloy et al., 1999; Reilly-Harrington et al., 1999).

At the level of dysfunctional attitudes, patients with BD demonstrated higher levels of dysfunctional attitudes (particularly perfectionism and need for approval) and sociotropy than non-psychiatric control participants (Scott et al., 2000; Goldberg et al., 2008). Subsequent studies further identified more dysfunctional attitudes (greater need for achievement, greater dependency on others, and greater need for control of self) among those with BD and MDD when compared with non-psychiatric controls (Scott et al., 2000; Lam, Wright & Smith, 2004). However, factor analysis of the dysfunctional attitudes of the clinical groups revealed that the BD scored higher than MDD on the goal attainment sub-factor score of the Dysfunctional Attitude Scale (DAS; Power et al., 1994) (Lam et al., 2004).

At the level of cognitive schemas, negative self-esteem was found to be a robust predictor of manic and depressive relapse in patients with BD (Scott & Pope, 2003). Lower self-esteem was also found in patients with BD and MDD than healthy controls (Jones et al., 2005b). Furthermore, patients with BD also endorsed hyper-positive statements about themselves outwardly but embraced more negative core beliefs on implicit measures (Lyon, Startup & Bentall, 1999). Dysfunctional attitudes also correlated with negativistic core beliefs even during pure manic phases of MDD (Goldberg et al., 2008).

1.1.2.6. Rumination about positive and negative affect

The depression avoidance hypothesis (Neale, 1988) could be examined from another perspective by understanding the effort to avoid a negative emotional state in BD. The response style theory of depression (Nolen-Hoeksema, 1991) proposes that strategies used in response to depressed mood (i.e. distraction, risk taking, rumination, and problem-solving) might influence the duration and intensity of depression. Specifically, rumination refers to a repetitive focus on the content, causes and consequences of one's affective state without problem solving (Lyubomirsky & Nolen-Hoeksema, 1995) and involves adopting a first-person perspective in which the individual is immersed in the experience, focusing on recalling the details of the events that occurred and the emotions felt (Kross, Ayduk & Mischel, 2005). Ruminative processing of negative emotions has been associated with escalation of negative emotions (negative rumination; Nolen-Hoeksema, 2000), onset of the first episode of MDD (Nolen-Hoeksema et al., 2008) and of bipolar depression (Thomas et al., 2007). Patients with BD also adopted more risk-taking and active coping strategies in response to negative emotions than patients with MDD and non-psychiatric controls (Thomas et al., 2007). These strategies were also predictive of hypomanic personality traits in general population samples (Thomas & Bentall, 2002; Knowles et al., 2005) and could be conceptualised as active responses to avoid depression, therefore supporting the depression avoidance hypothesis (Thomas et al., 2007).

There is also some evidence of increased rumination to positive emotion in BD. Patients with BD had a tendency to dwell on positive feelings and thoughts following a positive life event and failed to return to the baseline (Feldman, Joorman & Johnson, 2008). This tendency is known as 'positive rumination', a process of immersing in the positive experience, focusing on recalling the details of the events that occurred and the positive emotions felt synonymous to the process of depressive rumination (Feldman, Joorman & Johnson, 2008). This positive rumination has been found to differentiate BD from non-

psychiatric controls (Gruber, Mauss & Tamir, 2011) and MDD (Johnson, McKenzie & McMurrich, 2008). Positive rumination also correlates with the levels of hypomanic symptoms in a college sample (Raes et al., 2009). The above results suggest that patients with BD exhibit difficulties in spontaneous recovery from emotional events. Gruber (2011) has labelled this phenomenon as 'positive emotional persistence' (PEP). Greater reports of reward-relevant emotions, such as joy, also predicted increases in manic symptoms at a 6-month follow-up in patients with BD (Gruber, Harvey & Johnson, 2009). A recent study has further confirmed that patients with BD reported greater rumination about both positive and negative emotions compared with non-psychiatric controls. Furthermore, rumination about positive and negative emotion was associated with greater lifetime mania frequency and greater lifetime depression frequency (Gruber et al., 2011).

In summary, there are five main theories to address the possible mechanisms of first onset and episode recurrences of BD:

- Kindling theory (Post, 1990) addresses the possible mechanism of episode recurrences through neuro-chemical sensitization of the brain after repeated insults by psycho-social life events. Evidence suggests that this model may only be applicable to a sub-type of highly recurrent bipolar illness.
- The appraisal theory proposed by Jones et al. (2001; 2006) attempted to synthesize the findings of circadian rhythm instability and internal attribution bias in BD, as well as the links between schematic, propositional and analogous processing (Power & Dalgleish, 1997) to explain mood episode recurrence and the presence of mixed affective state in BD. However, this hypothesis fails to address how and why patients with BD experience mood switch from one polarity to the other.
- The BAS hypersensitivity theory suggests that BD has a BAS that is over-sensitive to BAS relevant life events, leading to excessive BAS outputs in response to goal attaining events and reduced BAS outputs in response to loss and goal frustrating

events. High and low BAS outputs mimic symptoms reminiscent of mania and depression respectively. This theory does not address how mixed affective episodes and rapid cycling state may occur in BD.

- The cognitive theory highlights the similarities of BD and UD with respect to cognitive distortions and dysfunctional attitudes (Scott et al., 2000; Lam et al., 2004), providing a cognitive explanation of why the symptoms and cognitions of bipolar and unipolar depressions were similar. However, it fails to explain why mania might arise in BD but not in UD.
- The response style theory suggests that BD has higher trait levels of positive rumination than UD (Johnson, McKenzie & McMurrich, 2008). This failure of emotional recovery due to cognitive strategies of sustaining positive emotions might lead to persistent positive emotions and upward spiral of emotions culminating in mania. However, the theory does not explain cognitive mechanisms leading to mixed mood state and episode recurrence.

Therefore, more parsimonious theories which address the peculiarity of mood swings between the two polarities, the interaction of life events and first onset/recurrences of mood episodes, and the sub-syndromal instability during inter-episode periods are called for.

1.1.3 Current disease burdens of bipolar disorders

BD is a severe recurrent mental disorder with serious disabilities and heavy direct and indirect costs to the patients and to society. In 2009, the direct and indirect costs of BD were estimated to be US$151 billion (Dilsaver, 2009). A cross-sectional household survey in 11 countries has found that the lifetime prevalence rates were 0.6% for BD-I, 0.4% for BD-II, and 1.4% for subthreshold-BD (Merikangas et al., 2011). The severity of both manic and depressive symptoms as well as suicidal behavior increased incrementally from sub-threshold

BD to BD-I disorder. However, role impairment was similar across all bipolar sub-types.

Apart from psychiatric morbidity and mortality, BD is associated with comorbid medical conditions including hypertension, obesity and other metabolic disorders (Kupfer, 2005). Such medical conditions are also related to other common psychiatric comorbidities associated with BD, including substance and alcohol abuse (Merikangas et al., 2011). The lack of motivation and inactivity associated with the depressive phase of BD also accounted for the risk factors associated with obesity and related disorders (Kupfer, 2005). In summary, BD is a serious mental health problem that leads to serious psychosocial disabilities, increased physical and psychiatric co-morbidities, and shortened life spans due to physical illnesses and suicide. Reducing the illness severity and recurrence risks will have substantial impact on the direct and indirect costs to society.

1.1.4 Limitations in current treatment approaches of bipolar disorders

Pharmacotherapy remains the mainstay treatment for BD, despite being ineffective for up to a third of patients (Perlis et al., 2006). Many patients who do respond to pharmacological treatments still experience sub-threshold depressive symptoms which can be disabling (Judd et al., 2005). Furthermore, 37% of patients have a depressive or manic recurrence within one year, and 60% within two years (Perlis et al., 2006). Many patients suffer from drug-related side effects including metabolic syndrome and movement disorders (Geddes & Miklowitz, 2013). Another major challenge of pharmacotherapy is that the medications that minimize manic symptoms might worsen depressive symptoms while those that control depressive symptoms might risk causing a manic switch (Geddes & Miklowitz, 2013). There is a pressing need to improve the treatment of BD through a combination of pharmacological and psychological interventions (Geddes & Miklowitz, 2013).

Psychological approaches to treatment were developed based on the current evidence

that psychosocial factors might play a role in the onset, maintenance, and recurrence of BD (see section 1.1.2 for theories of onset and recurrence of bipolar disorders). Family therapy for bipolar disorders is delivered to patients and their caregivers to enhance their knowledge about BD and to improve communications and problem-solving skills. Family therapy has been found to reduce depressive relapses and improve social functioning over a 30-month follow-up period when compared with usual care (Miklowitz, Otto & Frank, 2007). However, treatment preferences, cultural taboo against public disclosure of family secrets, and availability of the caregivers would limit the acceptability of family therapy. Cognitive-behavioural therapy (CBT) aims to address the cognitive biases and dysfunctional assumptions associated with manic and depressive phases. CBT was found to reduce depressive relapses and enhance social functioning in patients with bipolar disorders over 24 months (Lam et al., 2005). However, a pragmatic study in UK community centres failed to replicate the results (Scott et al., 2006). A recent trial in Canada similarly failed to find an advantage of CBT over psychoeducation (Zaretsky et al., 2008). There is thus limited evidence suggesting that CBT might benefit patients with BD in preventing depressive relapses and it remains unclear which aspects of CBT are effective for BD. Interpersonal and social rhythm therapy (ISRT) is an adaptation of interpersonal therapy for depression and focuses on addressing interpersonal problems and regulating daily routines and sleep-wake rhythm. Patients who received ISRT had longer times to depressive recurrence and better social functioning in the 2-year maintenance phase than those who received conventional care (Weiss, Griffin & Kolodzjej, 2007).

In summary, despite some evidence that psychological treatments might be beneficial in reducing depressive relapses and enhancing social functioning of patients with BD, currently no psychological interventions have been found to minimize manic or depressive symptoms during acute relapse, to prevent subsequent manic recurrences, or to avert at-risk individuals for BD from developing full-blown clinical disorders. Novel psychological

interventions are urgently called for to augment pharmacotherapy and enhance recovery of patients with BD.

1.1.5. Mental imagery as a powerful amplifier of emotion, conviction and action

Mental images are characterized by their subjective resemblance to sensory impressions, as if ‘seeing with the mind’s eye or ‘hearing with the mind’s ear’ (Kosslyn, Ganis, & Thompson, 2001). They can involve multiple sensory modalities, including bodily sensations and feelings. Mental imagery has a powerful impact on emotions (Holmes & Mathews, 2010), and there are several explanations for why this might be. First, because of the paramount importance of rapid motor response to signals of danger, basic emotions linked with danger signals (like fear, anger, and surprise), can be elicited rapidly by sensory cues without the need to involve higher level processing. Therefore, some basic emotional systems in the brain may respond primarily to information contained in a sensory form and may be less directly responsive to information represented in more abstract symbolic form (Holmes & Mathews, 2010).

Second, it has been shown that there is a degree of competition between mental imagery and perceptual processes when they share the same sensory modality. For instance, holding a visual image selectively interfered with the detection of a faint visual signal, and auditory images ('hearing with the minds ear') likewise interfered with the detection of auditory stimuli (Segal & Fusella, 1970). In addition, mental imagery and perception in the same sensory modality activate the same brain areas. Visual mental imagery was found to activate the same areas in early visual cortex as visual perception (Kosslyn, Ganis & Thompson 2005). Similarly, perception and imagination of emotional scenes activate the same brain areas (Kim et al., 2007).

Third, the link between imagery and emotion is also related to autobiographical

memory. Images were frequently used when people were asked to recall recent personal events, and less frequently when asked to recall semantic information (Brewer, 1996). Neuroimaging studies have shown that remembering and imagining personal events can activate similar areas of the brain (Schacter, Addis & Buckner, 2007). Since the generation of images draws on information from autobiographical memory, the simulated mental image is likely to retain the emotions experienced during the actual event. The above findings might explain why mental imagery has such a powerful impact on emotion.

Experimental studies appear to support that mental imagery triggers a more powerful emotion than verbal representation of the same event. When a mental imagery group and a verbal-semantic group were asked to rehearse descriptions of negative scenarios in the assigned method, the imagery group showed a significant increase in state anxiety afterwards which was not observed in the verbal-semantic group (Holmes & Mathews, 2005). Holmes, Mathews, Dalgleish, and Mackintosh (2006) asked both mental imagery and verbal-semantic groups to listen to event descriptions that either began with potentially negative situations resolved in a benign or positive way or events that began with benign situations which ended positively. The imagery group showed a greater increase in positive affect and a greater decrease in state anxiety when compared to the verbal-semantic group. In another experimental paradigm, compared to verbal thought, using mental imagery again led to a more powerful impact on emotion and images were rated as being more 'real' (Mathews, Ridgeway, & Holmes, 2013). These results support the hypothesis that imagery has a more powerful impact on emotions than verbal processing, and this amplifying effect could be applied to both positive and negative affect depending on the emotional valence of mental images (Holmes & Mathews, 2010; Mathews, Ridgeway & Holmes, 2013).

Additionally, mental imagery can also enhance the subjective conviction about the possibility of the occurrence of an imagined event. For instance, imagining a certain candidate winning an election would increase the probability estimate of that candidate winning (Carroll,

1978), and imagining the symptoms of a disease increased the perceived likelihood of contracting the disease in the future (Sherman et al., 1985). This could be understood in terms of the availability heuristic, according to which the judgment of the likelihood of an uncertain outcome is based on its cognitive availability, that is, the ease with which the outcome can be pictured or imagined mentally. The more cognitively available, the more likely the outcome is perceived to happen in the future (Tversky & Kahneman, 1973).

Not only does imagery enhance the perceived probability of occurrence of events, imagining one's own future behaviour similarly increases the chance of enacting that behaviour subsequently (Gregory, Cialdini & Carpenter, 1982; Libby, Shaeffer, Eibach & Slemmer, 2007). Athletes are often instructed to repeatedly mentally simulate and rehearse their perfect sports performance sequence, so as to form a so-called 'mastery imagery' of their sports performance. Such mastery imagery during sports training has been found to enhance subsequent performance in actual field competitions (see Rumbold, Fletcher & Daniels [2012] for a systematic review). Imagery of specific sports skills also promotes athletes' acquisition and actual subsequent performance of individual motor skills (Martin, Moritz & Hall, 1999).

Furthermore, mental images are more likely than verbal descriptions to be confused with actual percepts, consistent with an overlap in the neurobiological processes involved in imagery and perception (Kim et al., 2007). People asked to imagine pictures of daily items in their minds were more likely to recall having actually viewed the pictures than when being asked to provide verbal descriptions of the items (Mathews, Ridgeway & Holmes, 2013).

In summary, mental imagery appears to elicit powerful emotion and can lead to a higher conviction of having experienced or going to experience an imagined event, and a greater likelihood of acting on the imagined event. People with heightened susceptibility to mental images would then be hypothesised to experience stronger positive and negative emotions, greater mood instability, endorse greater levels of conviction about what they have imagined, as well as become more geared towards imagined action than people who tend to

think predominantly in the form of verbal descriptions. As BD is characterized by rapid swings in mood, cognitions and behaviours, one might hypothesize that mental imagery might play a role given its unique impact on amplifying emotions, increasing conviction, and enhancing action.

1.1.6 Mental imagery and anxiety disorders

To understand the role of mental imagery in psychiatric disorders, two types of memory retrieval need to be clearly defined. A voluntary episodic memory includes deliberately recalling a particular event as a mental image (e.g. breakfast in the morning). An involuntary memory of the same event would be a spontaneous 'flashback' of that event (known as 'intrusive' memory with a sudden and unpredictable nature (Bourne, Mackay & Holmes, 2013)). Involuntary mental imagery can be divided into two main types: past-oriented imagery (memories in the form of images or 'flashbacks') and future-oriented imagery (also known as 'prospective' imagery or 'flash forwards'). Flashbacks can be described as vivid, sensory-perceptual emotional memories of distinct moments of a traumatic event that intrude involuntarily into the mind (Bourne, Mackay & Holmes, 2013). 'Flashbacks' are the hallmark symptom of post-traumatic stress disorder (PTSD) (Ehlers & Clark, 2000). Because of the powerful impact of imagery on emotion, patients experiencing these flashbacks feel as if they are re-experiencing the trauma (feelings of 'now-ness' and 'real-ness') and therefore become anxious (Ehlers & Clark, 2000). This type of mental imagery has also been found to occur in patients suffering from other anxiety and related disorders like agoraphobia (Day, Holmes & Hackmann, 2004), social phobia (Hackmann, Clark, & McManus, 2000; Stopa & Bryant, 2004), specific phobias (Pratt, Cooper, & Hackmann, 2004), obsessive-compulsive disorder (Speckens et al., 2007), health anxiety (Muse et al., 2010), and body dysmorphic disorders (Osman et al., 2004).

1.1.7 Mental imagery and major depressive disorders

Apart from the established relationship between mental imagery and anxiety disorders, depression has been shown to have high rates of distressing and intrusive memories in both verbal and imagery forms (Birrer, Michael, & Munsch, 2007; Patel et al., 2007). These intrusive images are usually related to past interpersonal difficulties and personal loss, reflecting main negative themes that trigger and maintain depression. Studies have shown that people with high levels of dysphoria have a reduced ability to voluntarily generate positive prospective imagery (Holmes et al., 2008). Another study has found that people with depression had greater levels of emotional impact of prospective imagery and higher levels of negative prospective imagery (Morina et al., 2010), as well as impoverished positive imagery vividness compared to non-depressed controls (Holmes et al., 2008). An excess of negative memories and images, coupled with a deficit of positive future-oriented images, potentially contributes to a lowered perceived likelihood of a positive future and a sense of hopelessness in depression (MacLeod & Moore, 2000), both of which are potential vulnerability factors for subsequent recurrence of depressive episodes (O'Connor, Connery & Cheyne, 2000).

1.1.8 Mental imagery and bipolar disorders

1.1.8.1 Mental imagery and pathological mood amplification

As discussed in section 1.1.5, mental imagery can amplify not only negative emotions but also positive emotional states (Holmes, Lang, & Shah, 2009; Holmes et al., 2006). If BD is characterised by extreme mood swings in both polarities, mental imagery may possibly have a role to play in the amplification of pathological positive and negative emotions in BD (Holmes et al., 2008). Holmes et al. (2008) proposed that patients with BD might be particularly susceptible to the occurrence and emotional impact of mental imagery. As

positive images may amplify positive emotion (Holmes, Lang & Shah, 2009) and represent a real positive goal to be attained (Conway, Meares, & Standart, 2004), people experiencing positive images might thereby become elated, physiologically aroused, and geared towards action in approaching the imagined positive goal (see Section 1.1.8.2 below about the role played by BAS in translating imagery-related emotions and behaviours into symptoms reminiscent of hypomania). These cognitive and behavioural manifestations are reminiscent of the symptoms characteristic of (hypo)mania. Heightened imagery susceptibility might also partially account for frequent episode recurrences and subsyndromal mood instability during inter-episode periods (Judd et al., 2003).

In support of this mental imagery hypothesis, Holmes et al. (2011) found that euthymic patients with BD (i.e. patients in an emotionally stable phase) had higher levels of general use of imagery in daily life (as measured by Spontaneous Use of Imagery Scale [SUIS]; Reisberg, Pearson & Kosslyn, 2003) and experienced greater impact of prospective imagery (as measured by IFES; Deeprose & Holmes, 2010) than healthy volunteers. Hales et al. (2011) showed further that patients with bipolar depression had higher levels of general use of imagery and experienced a greater emotional impact of prospective imagery than patients with MDD. However, it is not clear whether patients with remitted BD-I experience higher levels of mental imagery susceptibility than remitted MDD. Study 1 of the current thesis addressed this question by comparing mental imagery susceptibility levels between these two clinical groups. Furthermore, Study 1 also attempted to replicate the findings of Holmes et al. (2011) by comparing the mental imagery susceptibility levels in remitted BD-I and a second non-psychiatric control group.

Adopting a qualitative methodology, Gregory et al. (2010) reported that intrusive negative prospective images were found during the most recent depressive episode, while intrusive positive prospective images were found during the most recent hypomanic episode in patients with BD. Intrusive negative prospective images were significantly less frequent

during the euthymic phase than acute depressed phase, while intrusive positive prospective images were only present during the acute hypomanic episode. However, previous studies have found that people tend to remember major life events for only one year (Paykel, 1997) and forget minor life events very quickly (Brown & Harris, 1982). In other words, recall of the content and valence of images during previous mood episodes by Gregory et al. 's (2010) sample might be prone to under-reporting bias. Given this limitation in retrospective recall bias, Study 2 in the current thesis examined the changes in the number of prospective images of both positive and negative emotional valences in a group of in-patients with acute bipolar mania at baseline, four and twelve weeks, allowing a direct examination of the temporal relationships of the number of prospective images and the severity of elation and depression in BD. The use of a MDD control group also addressed the lack of control groups in Gregory et al.'s (2010) study. This study also investigated whether general use of imagery and emotional impact of prospective imagery were elevated in acute bipolar mania when compared with acute MDD, given the Hales et al.'s (2011) findings in bipolar depression. It is worth noting that the Impact of Future Events Scale (IFES; Deeprose & Holmes, 2010; see Section 2.3.2 for more details about the psychometric properties of IFES) is the only currently available scale for measuring emotional impact of prospective imagery. The IFES measures emotional impact of prospective imagery via statements measuring subjective feelings of intrusions, avoidance and hyper-arousal towards prospective images. The above three types of feelings were measured by the 'intrusion', 'avoidance' and 'hypervigilance' sub-scales of the IFES respectively (Deeprose & Holmes, 2010). Positive prospective images experienced might be appraised as less distressing and avoidant than negative images. If mania is associated with excessive positive images while depression with excessive negative images (Gregory et al., 2010; Holmes et al., 2008), the avoidance sub-scale of IFES would be expected to be higher in acute MDD than acute bipolar mania. Given that around 30% of BD-I patients with acute mania experience a switch to depression within the same episode (Gitlin

et al., 2003), resolution of manic symptoms may be accompanied by a gradual increase in depressive symptoms in a proportion of patients. If depressive symptoms are associated with negative prospective images (Gregory et al., 2010; Morina et al., 2010), it can be postulated that the IFES-A scores would increase in the BD-I group with an increase in negative prospective images with time. On the other hand, IFES-A scores would reduce with gradual reduction of negative prospective images in MDD.

1.1.8.2 How could mental imagery be linked to behavioural approach system dysregulation in mania?

Section 1.1.2.4 has provided some evidence about the role of behavioural approach system (BAS) hypersensitivity in BD. Given that mental imagery increases conviction about the real-ness of the imagined event, these prospective images might be perceived as real events that have happened or are about to happen (Mathews, Ridgeway & Holmes, 2013). An emotionally powerful prospective image of either valence might then function synonymously as a BAS-relevant activating or de-activating event (Alloy et al., 2012; also see section 1.1.2.3 for more details). In response to such prospective images, the hypersensitive BAS would be hypothesised to become excessively activated or de-activated. An overly active or inactive BAS would then give rise to either excessive approach behaviours reminiscent of mania or deficiency in approach behaviours reminiscent of depression respectively. Gregory et al.'s (2010) findings of positive prospective images during hypomania but negative images during bipolar depression appear to support this hypothesis. Until now, this hypothesis has not been examined. Study 1 of the current thesis examined the hypothesis that the BAS sensitivity meditates the relationship between mental imagery susceptibility and (hypo)manic symptoms in BD-I.

1.1.8.3 Mental imagery and rumination

In section 1.1.2.6, positive rumination was considered as a possible cognitive mechanism in explaining both failure of emotional recovery from a positive event the persistence of positive emotions across a variety of contexts of emotional valence. If mental imagery does contribute to amplifying pathological positive emotions in BD, could this act independently or interactively with positive rumination in emotional amplification? There is some preliminary evidence that there might be some interplay between positive mental images and positive rumination in amplifying positive emotions. Gruber, Harvey & Johnson's (2009) study specifically instructed participants with BD to recall past happy events and relive and see the scenes in the mind's eye (i.e. reliving the happy events in the form of visual images). The levels of positive emotion and physiological arousal were compared between those participants who ruminated and dwelled upon the meanings and emotions associated with the positive images and those who reflected upon these images in a detached and mindful manner. The results suggested that rumination about positive images might lead to an increase in self-reported and physiological indicators of positive emotions. However, this study only looked at the effects of positive rumination on voluntarily generated positive memories but not involuntary ones. Given the frequent occurrence of intrusive prospective images in patients with BD (Hales et al., 2011; Holmes et al., 2011), rumination about intrusive prospective images might be an important cognitive mechanism in amplifying emotions.

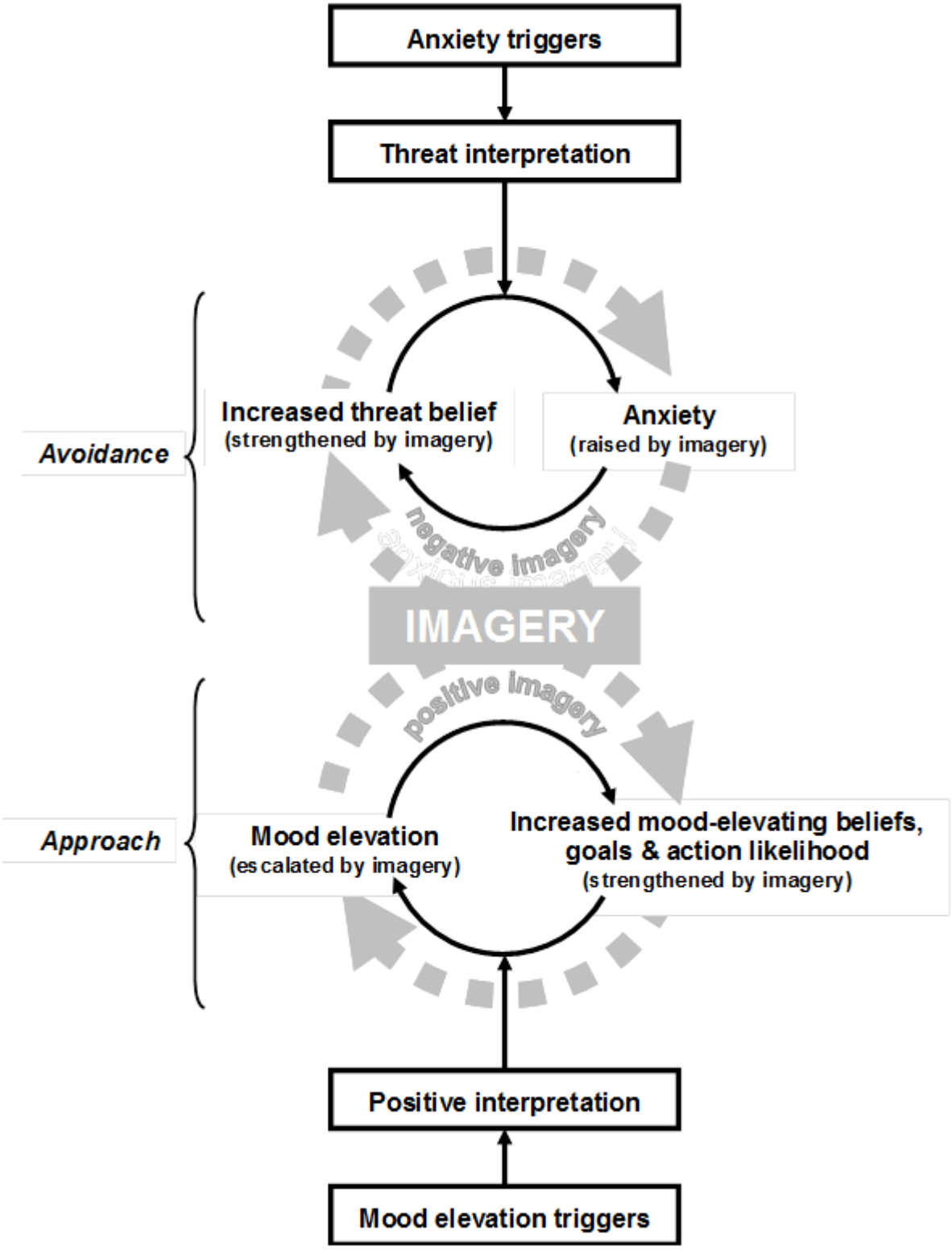
Furthermore, section 1.1.2.6 has pointed to the possible increase in rumination about negative emotions in BD (Feldman et al., 2008). Rumination about negative emotion was also associated with lifetime frequency of bipolar depression in BD (Gruber et al., 2011). If positive rumination might have some interplay with positive prospective images, a related hypothesis is that a parallel cognitive mechanism (i.e. rumination about negative prospective images) might amplify negative emotion in BD. Until now, both hypotheses have not been examined. Study 1 of the current thesis examined the hypothesis that rumination about

positive prospective images predicts (hypo)manic symptoms while Study 5 examined the additional hypothesis that rumination about negative prospective images predicts depressive symptoms.

1.1.8.4 Mental imagery susceptibility as a possible mechanism of explaining co-morbid anxiety disorders in bipolar disorders

Various Western studies have reported that anxiety disorders commonly co-occur in patients with BSD (Chen & Dilsaver, 1995; Merikangas et al., 2011; Angst et al., 2010). In recognition of the frequent occurrence of anxiety symptoms in BD, a new specifier of 'anxious distress' can now be added to the diagnosis of BD in DSM-V (APA, 2013). If both anxiety and BD are associated with heightened levels of mental imagery susceptibility (see Section 1.1.6 and Section 1.1.8), mental imagery might be a cognitive construct that could partially explain high co-morbidity of anxiety symptoms/disorders in BD. The hypothesised role played by mental imagery in explaining the co-occurrence of anxiety and BD is depicted in the following diagram 1 (Holmes et al., 2008).

Diagram 1: A hypothesised role of mental imagery in amplifying pathological positive and negative emotions in bipolar disorders (with special permission by E.A. Holmes)



However, until now the hypothesis of anxiety in BSD being predicted by mental imagery characteristics has not been tested. Study 3 investigates the relationships between mental imagery susceptibility and anxiety symptoms in MDD and sub-threshold BD. Furthermore, if the two loops shown in the diagram 1 are independent but interactive, it is important to control for anxiety symptoms in order to evaluate whether mental imagery susceptibility is indeed heightened in patients with BD per se (i.e. the lower loop of the diagram). A recent epidemiological study in Taiwan reported that only 30-40% of Chinese suffering from BD had comorbid DSM-IV anxiety disorders (Chang et al., 2012). Therefore, it is feasible to identify a sub-group of patients with BD without co-occurring threshold anxiety disorders to study the relationship between mental imagery susceptibility and BD. In the current thesis, studies 1 and 2 recruited participants with bipolar disorders without any co-occurring Axis 1 disorder (including anxiety disorder). Furthermore, the level of anxiety symptoms would be an important confounder to be controlled statistically when exploring the above relationships.

1.1.8.5 Mental imagery susceptibility as a possible trait marker of bipolarity

As discussed in the previous section 1.1.5 on manic-depressive illness and BSD, there is increasing evidence that highly recurrent depression and various types of BD may lie along a dimensional continuum to form a 'bipolar spectrum' (c.f. manic-depressive illness in Section 1.1.1.1, Angst, 2007; Angst et al., 2010; Goodwin & Jamison, 2007). If elevated mental imagery susceptibility could be observed in euthymic state in BD-I (Holmes et al., 2011; Study 1 of the current thesis), bipolar depression (Hales et al., 2012) and bipolar mania (Study 2 of the current thesis), sub-threshold BD (Study 3), mild hypomania (Study 4) and high bipolar risks based on familial inheritance (Study 5), there is a case to argue that

elevation in mental imagery susceptibility might be a trait marker associated with bipolarity. In support of the above hypothesis, Deeprose, Malik and Holmes (2011) recruited a convenience sample of non-clinical adults (mainly students) with an elevated risk for full blown BD or mild hypomania ('mild elated states' as defined by having scored a total cut-off score of 7 or above in Mood Disorder Questionnaire [MDQ; Hirschfeld et al., 2000] and found that the high-risk sample experienced greater emotional impact of prospective imagery (Deeprose, Malik & Holmes, 2011) and higher levels of general use of imagery in daily life (Malik et al., 2014) than healthy controls. Study 4 attempts to replicate and extend the above findings by investigating the changes in mental imagery characteristics in samples of high and low bipolar risks (using the same definition as in [Malik et al. 2014]) over a period of seven weeks. Study 5 investigated whether mental imagery susceptibility was also heightened in a group of first-degree relatives of patients with BD-I compared to a group of non-psychiatric controls without such familial risk.

1.1.8.6 Mental imagery, creativity and bipolarity

If mental imagery susceptibility is indeed elevated in BSD and people with high risks for BD and is associated with amplification of positive and negative emotions, a related question is why such traits would stand up to the selection pressure of human evolution. Holmes et al. (2008) proposed that creativity found in patients with BD (Santosa et al., 2007; Murray & Johnson, 2010) might be related to high susceptibility to mental imagery. Holmes et al. (2008) argued that the unique advantage of mental imagery in allowing novel and non-linear combinations of ideas into complex mental pictures might provide a fertile ground for creativity. Studies on eminent creative artists showed that a high percentage of them suffered from BD (Jamison, 1989). Santosa et al. (2007) also found that, compared to a non-psychiatric control group, patients with BD showed increased creativity as measured by the Barron-Welsh Art Scale assessing divergent thinking and creative insights about art forms

(BWAS; Barron, 1963). People with cyclothymia and relatives of patients with BD (i.e. people with high risks for full-blown BD) also had higher levels of creativity than normal controls, as measured by the quality and quantity of everyday creative involvement in both work and leisure activities (Richards et al., 1988). Enhanced creativity is associated with better problem-solving skills and thereby enhances survival and adaptation in the community (Richards, 1999). If mental imagery susceptibility did indeed enhance visual creativity in BSD, this would infer an evolutionary advantage to mental imagery susceptibility for survival in the gene pool despite its adverse impact on pathological emotions. This hypothesis offered by Holmes et al. (2008) has so far not been formally tested. Study 5 investigated the possible relationship between visual creativity and mental imagery susceptibility in first-degree relatives of patients with BD-I

1.1.8.7 Mental imagery and suicidality in bipolar disorders

1.1.8.7.1 Mental imagery in suicide: 'Flash-forward suicidal imagery'

In addition to its possible role as an emotional amplifier for both positive and negative emotions (Holmes, Lang & Shah, 2009), mental imagery has also been found to have a role to play in suicide (Holmes et al., 2007). Preliminary evidence reported that suicidal patients tended to have vivid prospective imagery about their future suicidal acts or the aftermath of death (known as 'flash-forward imagery' in order to distinguish from 'flash-back imagery' in PTSD) (Holmes et al., 2007). Recovered depressed patients also reported having suicidal imagery during their worst depressed points with suicidal ideation or behaviour (Crane et al., 2012). Furthermore, the content of flash-forward imagery among individuals with serious suicidal ideation was found to encapsulate details of violent deaths or rosy pictures about the aftermath of suicide (Hales et al., 2011; Holmes et al., 2007). Such flash-forwards might enhance the likelihood of actual suicidal attempts, especially when such imagery was

associated with a sense of comfort or triumph (Hales et al., 2011). In summary, suicidal flash-forward imagery might be a potentially valuable cognitive marker to be identified for people with serious suicidal ideation.

1.1.8.7.2 Mental imagery and arrested flight model in suicide

As mental imagery might represent a goal to be achieved (Conway, Meares & Standart, 2004), flash-forward imagery of suicide could encapsulate a specific goal for patients with serious suicidal ideas. One of the possible goals of such suicidal flash-forwards might be a desire to escape from an entrapped situation. The arrested flight model of suicide proposed by Williams (2001) has three components: (1) sensitivity to cues in the environment that signal defeat and entrapment leading to an urge to escape; (2) a sense of being unable to escape (cf. a sense of entrapment); and (3) a sense that this situation will remain static indefinitely (cf. sense of hopelessness about the future). The first component indicates a level of proneness to interpret even relatively neutral events as potentially humiliating and defeating, while the second component is related to deficits in interpersonal problem-solving skills. The third component of hopelessness is related to the projection of such a sense of entrapment into the future.

Crane et al. (2012) found that the severity of prior suicidal ideation was associated with lower levels of imagery-related distress but higher levels of imagery-related comfort, suggesting that the capability for suicide may be acquired via habituation to pain and fear of suicide through experience of suicidal imagery. Another possible explanation for the sense of comfort may be related to the perception of escape from the sense of entrapment resulting from such suicidal imagery. This hypothesis would then predict that the presence of suicidal flash-forward imagery would provide a relief from the sense of entrapment which in turn would worsen the severity of suicidal ideation in people with suicidal ideation. Study 6 tested this hypothesis by examining whether the interactions between suicidal flash-forward imagery

and sense of entrapment were predictive of severity of suicidal ideation.

1.1.8.7.3 Suicidal flash-forward imagery, sense of entrapment, and bipolarity

Studies have shown that people with BD have an increased risk of suicide when compared to people without any psychiatric illness (Merikangas et al., 2007; Angst et al., 2010; Hawton et al., 2005). Patients with bipolar depression and a past history of suicide have been found to report suicidal flash-forward images during the peak of their suicidal impulses (Hales et al., 2011). The BD group was also noted to be more preoccupied with the content of the suicidal flash-forward images than the MDD group, partly related to their correspondingly higher levels of emotional impact of prospective imagery (Hales et al., 2011).

As discussed in section 1.1.8.5 that mental imagery might be a possible trait factor associated with bipolarity, people with high bipolar risks might experience higher mental imagery susceptibility than those with low bipolar risks**.** One can postulate that suicidal participants with high bipolar risks would have higher levels of mental imagery susceptibility than those suicidal participants with low bipolar risks. Moreover, if suicidal flash-forwards indeed represent a specific goal of psychological escape from perceived entrapment, such suicidal images would be more likely to arise in those suicidal participants with high bipolar risks and strong entrapment sense than those suicidal participants with high bipolar risk but low entrapment sense. Study 6 of the current thesis prospectively studied this hypothesis by first splitting a group of individuals with suicidal ideation into high and low bipolar risk sub-groups. Then, in the high bipolar risk sub-group, the frequency of suicidal flash-forwards was compared between those with high and low perceived entrapment. .

1.2. Outlines and objectives of the studies

This thesis attempts to contribute to the understanding of the role of mental imagery susceptibility in various aspects of BD:

1) being a trait marker associated with bipolarity,
2) amplifying pathological positive and negative emotions (i.e. elation, depression and anxiety)
3) interacting with rumination and BAS sensitivity in the ascent of mania and depression,
4) being a predictor of visual creativity
5) acting as a goal of escape from perception of entrapment in people with suicidal ideation

The current thesis attempts to achieve the above aims by conducting six clinical studies that investigated mental imagery susceptibility in participants with different types of BSD and with high familial risks for BD.

The eight key hypotheses of the thesis and the studies conducted to examine these hypotheses are summarised as follows:

1. The general use of imagery in daily life would be higher in patients with remitted BD-I compared to patients with remitted MDD and people with no psychiatric disorders. This hypothesis was examined in Study 1. The increased level of tendency to use imagery in daily life would remain higher in patients with acute bipolar mania compared to patients with acute MDD. This was examined in Study 2.
2. Patients with BD-I in remission would have higher levels of emotional impact of prospective imagery than people with no psychiatric disorders. However, given that emotional impact of prospective imagery has been reported to be raised in both euthymic BD (Holmes et al., 2011) and remitted MDD (Morina et al., 2010), the levels

in patients with remitted BD-I and remitted MDD were hypothesized to be similar (Study 1). Furthermore, the levels of avoidance responses to prospective images as measured by the avoidance sub-scale of IFES would be higher in acute MDD than acute bipolar mania (Study 2). Mental imagery susceptibility (general use of imagery in daily life and emotional impact of prospective imagery) would also be persistently elevated over time among people with high risks for conversion to full blown BD, compared to people with low risks. This hypothesis was examined by measuring mental imagery susceptibility twice over a period of 7 weeks in a community sample with a bipolar phenotype (i.e. mild hypomania which is considered as having a high risk of conversion into full-blown BD; Rock et al., 2013) in Study 4. This hypothesis was examined again in people with high familial risks for BD in Study 5 by comparing the levels of mental imagery susceptibility in a group of first-degree relatives of patients with BD-I and a group of people with no such family history. Given that people with traumatic experiences experience strong emotional images (Ehlers & Clark, 2000), Study 5 also investigated whether childhood abuse was a predictor of emotional impact of prospective imagery.

3. It was hypothesized that the polarity and severity of mood swings in BD would be determined by the emotional valence and the number of the prospective images reported by the patients with BD. It was therefore postulated that the number of positive prospective images would decrease as the severity of manic symptoms declined in patients under treatment for bipolar mania, while the number of negative prospective images would increase as the severity of depression increased in patients with bipolar mania experiencing a mood switch to depression (Study 2).
4. Behavioural approach system (BAS) sensitivity would be a moderator of the relationship between mental imagery susceptibility and bipolarity. This hypothesis was examined in Study 1 by testing whether BAS sensitivity was a predictor of being

diagnosed as having BD-I rather than MDD in a group of patients with remitted BD-I and in another group with remitted MDD.

5. Rumination about positive prospective images would be predictive of manic symptoms in remitted BD-I (Study 1). Furthermore, rumination about negative prospective images would be predictive of depressive symptoms in MDD, sub-threshold BD, BD-II, and high bipolar risk groups. Specifically, the former hypothesis specifies that the interaction factor of positive rumination and the amount of positive prospective imagery would predict the diagnostic category of BD-I rather than MDD (Study 1). The latter hypothesis specifies that the interaction factor of depressive rumination and the amount of negative prospective imagery would be predictive of the severity of depressive symptoms in a group of patients with BD-II, sub-threshold BD, and MDD (Study 3) and people with high familial risks for BD (Study 5).
6. The severity of anxiety symptoms in BSD would be predicted by the levels of mental imagery susceptibility in a group of individuals with BD-II, sub-threshold BD, and MDD (Study 3).
7. First-degree relatives of patients with BD-I would be visually more creative than people without such a family history. Furthermore, the levels of visual creativity would be predicted by the levels of tendency to use imagery in daily life in both people with or without any family of first-degree relatives suffering from BD-I (Study 5).
8. Suicidal individuals would be more likely to report experiencing suicidal flash-forward images than non-suicidal individuals. Furthermore, suicidal individuals with high bipolar risks and high sense of entrapment would be more likely to experience suicidal flash-forward images than suicidal individuals with high bipolar risks but low sense of entrapment (Study 6).

In summary, the current thesis consists of six studies that recruited patients with BD-I in remission (Study 1), patients with acute bipolar mania (Study 2), patients with BD-II and

sub-threshold BD (Study 3), people considered as having high bipolar risk of conversion into full-blown BD due to their possession of a bipolar phenotype based on behavioural paradigm (Study 4) or their possession of high familial risks based on their first-degree relative being a patient with BD-I (Study 5), and people with suicidal ideation and high bipolar risks (Study 6). The comparison groups were: patients with MDD in remission (Study 1), patients with MDD (Study 2 and Study 3), people with low bipolar risk due to absence of the bipolar phenotype of mild clinical hypomania (Study 4), people with low bipolar risks due to absence of a family history of bipolar disorders (Study 5), and people with suicidal ideation but low bipolar risk (Study 6).

1.3. Value of understanding mental imagery susceptibility and related cognitive processes in bipolar disorders

As discussed in section 1.1.4, current pharmacological treatments for BD are not highly effective. There is a recent call for augmenting pharmacotherapy with psychological interventions to optimise the treatment outcome of patients with BD (Geddes & Miklowitz, 2013). It has been shown that CBT, interpersonal therapy, family and group therapies augment mood stabilisers in reducing rates of relapse over 1-2 years (see Section 1.4; Miklowitz & Scott, 2009). Specific mediating mechanisms of improving mood symptoms include enhancing medication adherence, improving self-monitoring skills of early signs and symptoms of relapse, teaching early intervention skills to forestall further deterioration of early symptoms of relapse, as well as strengthening interpersonal functioning (Miklowitz & Scott, 2009). However, further research is needed to understand more about the relative benefits of psychological interventions for different groups of patients, and the putative mechanisms of action.

As imagery has a more powerful impact on positive emotions than verbal processing,

cognitive behavioural therapy (CBT) to promote positive change has incorporated imagery interventions (Holmes, Arntz & Smucker, 2007). For example, promotion of positive images about the self was used to combat negative self-concepts in patients with borderline personality disorder (Giesen-Bloo et al., 2006). Image restructuring of pre-existing traumatic imagery to modify PTSD flashbacks into more benign images is now considered a standard component of CBT for PTSD (Ehlers & Clark, 2000). There is thus some evidence supporting the efficacy of imagery interventions in psychiatric disorders characterised by intrusive negative images.

If BD is shown to be a clinical disorder highly susceptible to mental imagery, imagery intervention may provide a strategy to enrich the current mainstream CBT for bipolar disorders. As there are many facets surrounding the use of mental imagery interventions, basic research is required to understand which aspects of mental imagery would be useful targets for intervention. The current thesis intends to provide some preliminary data on this unanswered question.

CHAPTER 2 - Choice of assessment instruments and the local validation of the Chinese versions of the scales

2.1 Introduction

As the current thesis aims to investigate a limited number of cognitive variables that might be associated with bipolar disorders (BD), only a selected number of questionnaires and clinical interviews were used. This chapter explains the rationale behind choosing a particular questionnaire, as well as the details of local validation of these questionnaires.

2.2 General procedures of scale validation

The English version of a scale was first translated into Chinese language and then back translated into English by a panel of experienced mental health professionals composed of two psychiatrists (the author of this thesis and another psychiatrist with six years of clinical experience), three mental health nurses and two occupational therapists. Any discrepancies between the original and back-translated versions were discussed and compromised between the panel members before a final translated version was adopted. Except for the Entrapment Scale (ES; Gilbert & Allan, 1998) and Defeat Scale (DS; Gilbert & Allan, 1998), all translated versions of the scales were given to a group of local hospital nursing staff twice within an interval of four weeks for completion (N = 10; 4 male and 6 female; mean age = 35.2 years, SD = 8.54). The Chinese translated versions of the ES and the DS were also prepared by the same expert panel. However, the sample was recruited from a group of community participants attending a mental health education talk (N = 60, mean age = 47.8 years, SD = 10.24). A sub-sample was then invited to complete the same scales again in two weeks' time (N = 25).

2.3 Scales for measuring the cognitive variables of interest: psychometric properties and local validation

2.3.1 Spontaneous Use of Imagery Scale (SUIS; Reisberg, Pearson & Kosslyn 2003; Appendix I)

This scale measures spontaneous use of imagery in everyday life. It consists of 12 items, each describing a certain day-to-day situation. Examples include "If I am looking for new furniture in a store, I always visualize what the furniture would look like in particular places in my home" and "When I think about visiting a relative, I almost always have a clear mental picture of him or her". Participants were asked to rate each item according to the degree to which each was appropriate for them, from 1 to 5, with *1* = never appropriate, *3* = appropriate half of the time, and *5* = always completely appropriate. It has been demonstrated high-vividness imagers (as measured by the Vividness of Visual Imagery Questionnaire, VVIQ [Marks, 1973]) scored higher on the SUIS than low-vividness imagers, showing that SUIS and VVIQ measured a related construct. The SUIS has a high internal consistency of 0.98 or higher (Reisberg, Pearson & Kosslyn, 2003). The SUIS had not previously been used with a Chinese population. The translated scale was found to have acceptable psychometric properties (internal consistency: Cronbach's alpha = 0.83; 4-week test-retest reliability, intra-class correlation = 0.89). This scale was chosen to allow comparisons of results obtained in this thesis with other imagery studies using the same scale (Hales et al., 2011; Holmes et al., 2011; Malik et al., 2014).

2.3.2 Impact of Future Events Scale (IFES; Deeprose & Holmes, 2010; Appendix II)

This scale was used to assess the emotional impact of prospective imagery. It was adapted from the Impact of Events Scales – Revised (IES-R; Weiss & Marmer, 1997), a self-report measure assessing symptoms of intrusion, avoidance and hyper-arousal characteristic of post-traumatic stress disorder. The IES-R requires participants to identify one previous stressful life event, and then rate the degree of impact or distress related to the stressful event.

In the original IFES, participants were first asked to identify three future events which they had been thinking about by imagining over the past 7 days and indicate whether each event was "positive" (positive prospective images) or "negative" (negative prospective images). Then they responded to 24 items which assessed intrusive pre-experiencing, avoidance and hyper-arousal. Examples include "Pictures about the future popped into my mind" (intrusive pre-experiencing), "I tried to remove thoughts of the future from my mind" (avoidance) and "Reminders of the future caused me to have physical reactions, such as sweating, faster breathing, or a racing heart" (hyper-arousal). In answering these items, participants were instructed to refer to their prospective imagery in general, or to focus on the prospective imagery that had affected them the most over the past week. The rating of each item ranges from *0* to *4*, with *0* = not at all, *1* = a little bit, 2 = moderately, *3* = quite a bit, and *4* = extremely. As a refinement to the original IFES and an attempt to increase the variability of the number of prospective images reported in this measure, participants in the current studies were asked to identify an unconstrained number of future events that they had been thinking about by imagining them over the past seven days (i.e. prospective images) and to indicate whether each event was positive or negative in emotional valence. An "IFES total" score, reflecting the emotional impact of prospective imagery, is calculated by summing the responses to all 24 items, giving a total score with possible range from 0 to 96. The IFES also yields three sub-scale scores; 'intrusion', 'hypervigilance' and 'avoidance'. The higher the

IFES total and sub-scale scores, the higher the level of emotional responses to the listed prospective images. Additionally, we created an "IFES total events" score (number of future events), an "IFES positive events" score (the number of IFES events labelled as positive in valence), and an "IFES negative events" score (the number of IFES events labelled as negative in valence) to test exploratory hypotheses relating to the number and valence of prospective images in the various studies in the current dissertation. The IFES has an acceptable 4-week test-retest reliability (intra-class correlation = 0.73) and a good internal consistency (Cronbach's alpha = 0.87) (Deeprose & Holmes, 2010). The IFES had also not been used in the Chinese population before it was used in the current studies. It was chosen as a measure of emotional impact of prospective imagery to facilitate cross-study comparisons as it has been used for this purpose in several imagery studies (Crane et al., 2012; Hales et al., 2011; Holmes et al., 2011; Malik et al., 2014). Furthermore, use of a self-administered scale rather than semi-structured imagery interview (Holmes et al., 2007) would minimise information biases related to the interviewers.

The English version was first translated into Chinese with reference to the Chinese version of Impact of Events Scale-Revised (Wu & Chan, 2003) and then back-translated into English. The validation procedures followed the same ones as stated in section 2.2. The translated version showed good internal consistency (Cronbach's alpha = 0.86) and good 4-week test re-test reliability (intra-class correlation = 0.84).

2.3.3 Response to Positive Affect Questionnaire (RPA; Feldman, Joorman & Johnson, 2008; Appendix III)

This is a self-report measure for assessing cognitive responses to positive affect. It consists of 17 items describing what people would think and do when they feel happy. Participants were asked to rate from 1 to 4 how frequently they would think and do as

described, with *1 = never* and *4 = always*. The items assess emotion-focus positive rumination (RPA-EF; rumination on positive mood and somatic experiences), self-focus positive rumination (RPA-SF; rumination on positive aspects of self and pursuit of personally relevant goals) and dampening (RPA-D; thoughts that would dampen positive moods). Examples include "Savour this moment" (emotion-focus), "Think about how proud you are of yourself" (self-focus) and "Remind yourself these feeling won't last" (dampening). The internal consistencies of the subscales were acceptable (Cronbach's alpha = 0.76 for emotion-focus, 0.73 for self-focus, and 0.72 for dampening) (Feldman, Joorman & Johnson, 2008). Similar to the SUIS and the IFES, RPA had not been applied to Chinese population before the conduct of the current studies. The RPA Questionnaire was used for measuring positive rumination as this was the only existing measure available for this purpose and would also allow comparisons with other Western studies (Gruber et al., 2009; Gilbert, Nolen-Hoeksema & Gruber, 2013).

The translated version also had acceptable psychometric properties (Cronbach's alpha: RPA-EF = 0.70; RPA-SF = 0.69; RPA-D = 0.72); 4-week test-retest reliability using intra-class correlation: RPA-EF = 0.82; RPA-SF = 0.81; RPA-D = 0.78). As the dampening subscale measures the cognitive effort in putting a brake on the persistence of positive mood, this is considered as a counteracting force for positive rumination (Feldman, Joorman & Johnson., 2008) and is therefore not included in the calculation of positive rumination scores.

2.3.4 Positive Overgeneralization Scale (POG; Eisner, Johnson & Carver, 2008; Johnson & Jones, 2009; Appendix IV)

This 18-item scale assesses the tendency to overgeneralize from a given successful experience to broader aspects of life. While positive rumination refers to repetitive focusing on positive emotions and positive self-attributes, positive over-generalisation refers to a

cognitive bias towards excessively optimistic conclusions drawn in response to a small initial success. Participants respond to items with responses ranging from 1 = *'I disagree with the statement a lot*' to 4 = *'I agree with the statement a lot'*. The scale is composed of three subscales: Lateral generalization (LG) from a good outcome in one domain to positive outcomes in other areas of life (e.g., 'When something good happens to me, it makes me expect good things in other parts of my life too'); Upward generalization (UG) from a good outcome in one domain to more lofty goals in the same domain (e.g., 'When one thing goes right, it makes me feel my possibilities are limitless'); and Social generalization (SG) (e.g., 'When someone compliments me about something I've said, it makes me think about impressing lots of other people'). Internal consistencies for the subscales ranged from Cronbach's alphas = 0.71 (SG) to 0.82(LG) (Eisner, Johnson & Carver, 2008). The POG was translated and validated in the same manner as the other scales. The translated POG was found to have good internal consistencies of Cronbach's alphas =0.69 (LG); 0.69 (UG), and 0.71 (SG). The 4-week test-retest reliabilities of the POG sub-scales were also good (intra-class correlations: 0.68 [LG], 0.72 [UG], and 0.73 [SG]). The RPA and POG have been found to be independent factors that predict the presence of manic symptoms (Johnson & Jones, 2009).

2.3.5 Ruminative Response Scale-Short Form (RRS-SF: Treynor, Gonzalez, Nolen-Hoeksema, 2003; Appendix V)

Rumination is often used to cope with negative mood that involves self-focused attention (Lyubomirsky & Nolen-Hoeksema, 1993). According to the response style theory, it is characterized by self-reflection (Morrow & Nolen-Hoeksema, 1990), as well as brooding (a repetitive and passive focus on one's negative emotions) (Nolen-Hoeksema, 1991; 2000). Rumination has been found to predict greater depressive symptoms and the onset of major

depressive disorder than distraction (Just & Alloy, 1997; Nolen-Hoeksema, 2000). The Ruminative Responses Scale Short Form (RRS-SF; Treynor, Gonzalez & Nolen-Hoeksema, 2003) was derived from the 22-item Ruminative Response Scale (RRS; Morrow & Nolen-Hoeksema, 1990) by removing the 12 items that were considered similar to the BDI-II items, so as to address the criticism of the observed relation between depression and rumination being due to item content similarity (Conway et al., 2000; Cox, Enns & Taylor, 2001; Roberts, Gilboa & Gitlin, 1998). The RSS-SF was found to positively correlate with the Beck Depression Inventory and the Trait Anxiety Scale, supporting its validity as a measurement of ruminative response style in non-clinical population (Natalio & Pablo, 2006). A validated Chinese version was used, which has had good internal consistency (Cronbach's alpha = 0.76) (Ng & Dinesh, 2008).

2.3.6 Behavioural Inhibition/Activation System Scales (BIS/BAS; Carver and White, 1994)

The BAS system underlies sensitivity to reward and guides approach behaviours and motivation for appetitive stimuli, with relations to positive emotions like joy, elation, and relief. The BIS System is activated when threat is detected so that the approach behaviour is inhibited, delaying approach and promoting withdrawal. BIS scores have been linked with anxiety and negative affect. The BIS/BAS Scales are 20-item self-report measures comprising a BIS scale and three BAS scales: Drive (4 items, such as 'I go out of my way to get what I want'), Reward Responsiveness (5 items, such as 'When good things happen to me, it affects me strongly'), and Fun Seeking (4 items, such as 'I am always willing to try something new if I think it will be fun'). Each item is answered using a four point Likert scale, ranging from '1 = *strongly disagree'* to '4 = *strongly agree'*. The scale yields BIS total score, BAS total score and three BAS sub-scale scores (summation of the three BAS sub-scale scores gives BAS total score). These scales have good convergent and divergent validity (Carver &

White, 1994). The translated Chinese scale was validated using the same method and the same sample as above. The BIS scale and three BAS scales were found to have good internal consistencies (Cronbach's alphas: BIS = 0.69; BAS-Drive = 0.74; BAS-Fun Seeking = 0.73; BAS-Reward responsiveness = 0.73). The 4-week test-retest reliabilities were also satisfactory (intra-class correlations: BIS = 0.68; BAS-Drive = 0.76, BAS-Reward responsiveness = 0.73, BAS-Fun seeking = 0.73). Numerous studies have supported the construct validity of the BIS/BAS Scales in relation to prefrontal cortical activity, affect, personality traits, and performance on response time to incentive cues (Carver, 2004; Heponiemi et al., 2003; Zinbarg & Mohlman, 1998). The current thesis used only the BAS total score and the BAS sub-scales scores from BIS/BAS Scale to measure BAS sensitivity.

2.3.7 Barron-Welsh Arts Scale (BWAS; Barron, 1963; 1972)

The BWAS is an empirically derived instrument that measures the subjects' ratings of 'like' and 'dislike' of 86 black and white images. Higher ratings reflect preference for more asymmetrical and complex figures over more symmetrical and simple figures. The scale is composed of a BWAS total score, and two sub-scores, BWAS-Like and BWAS-Dislike. BWAS-Like score measures the levels of preference for highly complex figures whereas BWAS-Dislike measures dislike for highly monotonous levels. As such, BWAS Like score measures one's positive discrimination for complex and novel figures while BWAS Dislike score measures one's negative discrimination for highly monotonous figures. Creative individuals in both visual arts, as well as in other disciplines, have higher BWAS scores (Barron, 1972). Furthermore, among the arts students, the BWAS scores correlated significantly with ratings of students' originality (Pearson's correlation = 0.40) (Rosen, 1955). The BWAS reflects a putative cognitive contribution to creativity, as it involves visual processing (observing the figures). BWAS scores have also been linked to emotionality, as it

also involves affective processing (determining and expressing personal likes or dislikes of the figures) (King & Curtis, 1991). BWAS has also been found to correlate positively with psychoticism (Eysenck & Furnham, 1993). As the scale only requires the participants to choose whether he or she likes or dislikes a picture to generate the total BWAS score and the 'Like' and 'Dislike' sub-scores upon a brief introduction by the author, the scale was not translated or validated into Chinese language.

2.3.8 Entrapment Scale (ES; Gilbert & Allan, 1998; Appendix VI)

Entrapment has been defined as a desire to escape from the current situation, tied with the perception that all escape routes are blocked (Gilbert & Allan, 1998). The entrapment scale (ES) consists of 16 items referring to the perception of being trapped and the desire to escape (e.g. "I am in a situation I feel trapped in'), and is rated on a five-point scale ranging from '1 = *Not at all like me'* to '5 = *Extremely like me'*. Higher scores indicate greater feelings of entrapment. The alpha coefficients for this scale ranged from 0.86 to 0.93 (Gilbert & Allan, 1998) and was 0.95 in another study (Taylor et al., 2009). The translated version had good internal consistencies (Cronbach's alpha= 0.92) and 2-week test-retest reliability was good (intra-class correlation = 0 .93).

2.3.9 Defeat Scale (DS; Gilbert & Allan, 1998; Appendix VII)

Defeat has been defined as a sense of failed social struggle, status loss and reduced social rank (Gilbert & Allan, 1998). Defeat concept suggests a lack of possible solutions or ways forward, similar to the idea of entrapment (Rooke & Birchwood, 1998). The two concepts also share an association with low social rank and loss of aspirations (Gilbert et al., 2002). Qualitative studies into entrapment have reported that individuals with depression

perceived themselves as being entrapped in a sub-ordinate social role, which is also seen as an aspect of defeat (Gilbert & Gilbert, 2003). The defeat scale includes 16 items referring to perceptions of failed struggle and low social rank (e.g. "I feel that I am one of life losers"). These are rated for their prevalence in the past one week, on a five-point scale ranging from '1 = *Never*' to '5 = *Always/all the time*'. Higher scores indicate greater feelings of defeat. Similar to the entrapment scale, the defeat scale has an alpha coefficient ranging from 0.93 to 0.94 (Gilbert & Allan, 1998). The translated version also had a good internal consistency (Cronbach's alpha = 0.94) and a good 4-week test-retest reliability (intra-class correlation =0.94).

2.3.10 Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003)

The 28-item Childhood Trauma Questionnaire assesses the levels of childhood maltreatment (CTQ; Bernstein et al., 2003). It is a self-administered scale that consists of five subscales: physical abuse (5 items), sexual abuse (5 items), emotional abuse (5 items), physical neglect (5 items), and emotional neglect (5 items), yielding a total score and five sub-scale scores. The Chinese version had high internal validity (Cronbach's alpha = 0.64) and 2-month test-retest reliability was 0.75 (Zhao et al., 2005). The Chinese version of CTQ has further been validated in a local study in Hong Kong (Cronbach's alpha = 0.79; Ng et al., 2011). This scale was used to measure the past experiences of abuse during childhood. Experiences of childhood traumas have been related to bipolar disorders (Etain et al., 2008) and to the reports of distressing and intrusive mental images (Hackmann, Clark & McManus, 2000). In the current thesis, only the CTQ total score was used to identify the severity of childhood maltreatment.

2.3.11 Life Events Checklist (LEC; Gray et al., 2004)

The LEC was developed to measure participants' experience of a wide range of traumatic experiences. LEC enquires about multiple types of exposure to potentially traumatic events (PTE). For each PTE, participants rate their experience of that event on a 5-point scale (1 = *happened to me;* 2 = *witnessed it;* 3 = *learned about it;* 4 = *not sure, and* 5 = *does not apply*). The LEC consists of 16 items inquiring about the experience of 16 different PTE known to result in post-traumatic stress disorders and other post-traumatic difficulties. It also includes an item inquiring about any other inordinately stressful experiences not captured by the above 16 items. LEC has been found to converge well with other established measures of PTE and to correlate with post-traumatic symptom severity in both a non-clinical student population and in war veterans attending a trauma clinic for treatment of trauma-related symptoms (Gray et al., 2004). The Chinese version of LEC was translated into Chinese and then back-translated into English by the research team of the Hong Kong Mental Morbidity Survey (HKMMS; Lam et al., 2014a; see Section 2.4 below for more details). The Chinese version was found to have a high inter-rater reliability (intra-class correlation = 0.92). The 2-week test-retest reliability was 0.65 (Lam et al., 2014a). The LEC was used to measure general lifetime experiences of traumas, so as to understand whether intrusive distressing images were associated specifically with childhood traumas or general lifetime traumas and to statistically control for traumatic experiences when exploring the relationships between imagery and mood symptoms.

2.4 Scales for measuring the clinical variables of interest: their psychometric properties and local validation

2.4.1 Chinese-bilingual Structured Clinical Interview for DSM-IV Disorders (Axis I, Patient version) (CB-SCID-I/P; So et al 2003a)

The Structured Clinical Interview for DSM-IV-TR (SCID) is a semi-structured interview for making DSM-IV-TR diagnoses (First et al., 1996). The SCID contains two separate interviews, namely the Axis I (SCID-I) and the Axis II (SCID-II) versions for DSM-IV-TR Axis I and Axis II Disorders respectively. For SCID-I, there are Patient (SCID-I/P) and Non-Patient versions (SCID-I/NP). The SCID-I/P has been translated into more than ten languages. The inter-rater reliability of the original SCID-I/P gave a kappa value of above 0.60 for most categories, which is comparable to the Diagnostic Interview Schedule (DIS; Robins et al., 1981) and Schedule for Affective Disorders and Schizophrenia (SADS; Endicott & Spitzer, 1978). SCID raters are either clinicians or mental health professionals trained to administer the assessments. The Chinese-bilingual version (CB-SCID-I/P; So et al, 2003a) was shown to be a reliable instrument for making DSM-IV-TR diagnoses in both patients and non-patients. In the current thesis, the author and each of the three independent psychiatrists with clinical experience of more than six years administered the CB-SCID-I/P to the study participants in the studies that involved making the DSM-IV-TR diagnoses for inclusion or exclusion purposes. Before commencement of the six studies of the current thesis, the author and the three co-investigators achieved good kappa agreements in administering the CB-SCID-I/P to outpatients with BD (n = 10), MDD (n = 10), anxiety disorders (n = 10), schizophrenia related disorders (n = 10) and non-clinical hospital staff (n = 10) (kappa agreements (k) for BD = 0.80-0.85; k for MDD = 0.82-0.84; k for schizophrenia and related disorders = 0.80-0.83; k for anxiety disorders = 0.77-0.79; k for no diagnosis = 0.85 – 0.88). These CB-SCID-I/P interviews also provided additional data on dates of first onset of

psychiatric symptoms, number of previous episodes of mood disorders, and the presence of co-morbid DSM-IV-TR Axis-I disorders.

2.4.2 Hypomania Checklist-32 (HCL-32; Angst et al., 2005)

This is a self-administered rating scale consisting of 32 items for the self-assessment of lifetime hypomanic symptoms in non-clinical participants (Meyer et al., 2007) and in clinical participants suffering from current or past history of MDD (Angst et al., 2005; Poon et al., 2012; Yang et al., 2011). The checklist adopts the dimensional perspective of a 'bipolar spectrum' ranging from normal 'highs' to hypomania and mania (Meyer & Keller, 2003). Participants are asked to remember 'a period when you were in high state and to indicate if specific behaviours, thoughts, or emotions were present in such a state'. Items include 'I need less sleep', 'I am less shy or inhibited', or 'I am more flirtatious and/or am sexually more active'. The questionnaire also asks about the duration of such highs and about their impact as 'positive and negative', 'positive', or 'no impact', or 'negative' on family life, social life and work. In addition, other people's reactions and comments on such episodes were questioned (positively, no comments or negatively). The HCL-32 has been found to be a valid and reliable scale for measuring hypomanic symptoms among both Western population (Angst et al., 2005) and Chinese population in Hong Kong (Poon et al., 2012), Taiwan (Wu et al., 2008), and Mainland China (Yang et al., 2011; Yang et al., 2012). In the first validation study (Angst et al., 2005), a two-factor solution was identified in the Italian and the Swedish samples analysed separately or combined as a single group, the two factors being 'active/elated' and 'risk-taking/irritable' hypomania. The first subscale had Cronbach's alphas ranging from 0.83 to 0.85, the second sub-scale from 0.72 to 0.75 and the total scale from 0.82 to 0.86. Data on the sensitivity and specificity of the total scale suggests that a score of 14 or more yields the best combination of sensitivity (80%) and specificity (51%) to

distinguish between BD and MDD (Angst et al., 2005). As a screening tool for BD among patients with MDD, a high sensitivity is desirable. The scale also had a positive predictive value of 73% and a negative predictive value of 63% (Angst et al., 2005). Apart from its use as a screening tool for hypomania among patients with MDD, the HCL-32 has also been used to screen for clinical hypomania in two non-clinical samples in Sweden and Germany (Meyer et al., 2007). The internal consistencies of the two subscales and the total scale in the two samples separately or lumped as one single sample were similar to the internal consistencies of those obtained from psychiatric samples (Meyer et al., 2007). Factor analysis in both non-clinical samples suggests that two factors similar to the ones extracted from psychiatric sample of Angst et al.'s (2005) study were obtained. When Meyer and his colleagues separated their sample into a hypomanic and a non-hypomanic group based on such highs being identified as leading to negative consequences and lasting for at least 4 days, the hypomanic groups had significantly higher mean HCL-32 total scores, more current depressive symptoms, were more likely to have received psychotherapeutic treatments and more often had a past history of MDD (Meyer et al., 2007). Such findings suggest that the HCL-32 is a valid and reliable instrument in detecting a history of clinical hypomania in both patients with MDD and in non-psychiatric community samples. The Hong Kong Chinese version (Poon et al., 2012) was validated and found to have a good internal consistency (Cronbach's alpha = 0.89) and a good 4-week test-retest reliability (intra-class correlation = 0.81) (Poon et al., 2012). From the receiver operation curve, the optimal cut-off score was only 11, yielding a sensitivity of 0.84 and a specificity of 0.70. This cut-off score was lower than the established cut-off score for the Caucasian population (see Section 1.1.7 on possible explanations for the lower HCL-32 total cut-off score in Chinese population).

2.4.3 Young Mania Rating Scale (YMRS; Young, Biggs, Ziegler, 1978)

This is a clinician-administered rating scale for assessing clinical symptoms of mania, consisting of 11 items that are rated according to the patient's subjective report of his or her clinical conditions over the past 48 hours and clinical observations made during the course of the clinical interview. The YMRS is a reliable and valid scale (Young, Biggs & Ziegler, 1978). A score of 20 or above identifies patients who are currently in mania, a score between 8 and 19 suggests current hypomania and a score of 7 or below represents euthymia (Chenggapa, Baker & Shao, 2003). An inter-rater reliability of kappa agreement was established between each co-investigator (three psychiatrists with over five years of clinical experience) and the author before commencement of the studies of this thesis. The kappa agreements between the author and the co-investigators ranged from 0.92 to 0.98. As YMRS is a rater-administered scale and all the raters use English in regular medical communication, the English version was used by the principal author and the co-investigators without translation into a Chinese version.

2.4.4 Mood Disorder Questionnaire (MDQ; Hirschfield et al., 2000)

MDQ consists of three categories of items: (1) 13 *yes/no* items assessing lifetime manic and hypomanic symptoms (*no* = 0, *yes* = 1); (2) one *yes/no* item assessing clustering of symptoms occurring at the same time (*no* = 0, *yes* = 1); and (3) one item regarding symptom severity on a scale from '*no problem* = 0' to '*serious problem* = 3'. A validated Chinese version with good validity and reliability was used (Chung, Tso & Chung, 2009). Scores on the 15 items were summed to give a total MDQ score (Hirschfield et al., 2000). Participants scoring seven or above were classified as being at high bipolar risk, and those scoring six and below were classified as being at low risk (Calabrese et al., 2006; Deeprose, Malik & Holmes, 2011). The MDQ showed good internal consistency (Cronbach's alpha = 0.83) and good test

re-test reliability in categorising people into high and low bipolar risk groups according to the above cut-off point across a 7-week period (see Study 3; *n* = 10; weighted kappa agreement = 0.88). Rock et al. (2013) reported that MDQ was a potentially useful tool to identify a common 'bipolar phenotype' in non-clinical population, which is characterised by subjective symptoms of mood elevation (increased energy, confidence, sociability, talkativeness, interest in sex, and decreased need for sleep). Such bipolar phenotype identified can be considered as lying at the mild end of the continuum of observable symptoms/behaviours that relates to the brain systems underlying BD (c.f. BSD in Section 1.1.1.5; Rock et al., 2013). Presence of this bipolar phenotype may be associated with an increased risk of subsequent development of full-blown BD (Tijssen et al., 2010a).

2.4.5 Beck Depression Inventory-II (BDI-II; Beck, Steer & Brown 1996)

The BDI-II measures the severity of self-reported depression but is also used for screening of the presence of clinical depression. The 21-item BDI-II is scored by summing the ratings for each of the 21 symptoms, and each symptom is rated on a 4-point rating scale ranging from 0 to 3. Participants rate each item on a scale of 0-3 according to how they have been feeling for the past 2 weeks, including the day of assessment, with 0 denoting 'no symptoms' and 3 denoting 'severe symptom'. For example, for the item of "sadness" in BDI, a score of '0' is given for choosing the answer of 'I do not feel sad', a score of '1' for the answer of 'I feel sad much of the time', a score of '2' for 'I am sad all the time', and a score of '3' for the answer of 'I am so sad or unhappy that I can't stand it'. Total scores range from 0 to 63. The BDI-II has a high internal consistency with a Cronbach's alpha of 0.93 among college students, and Cronbach's alphas of 0.91 to 0.92 among psychiatric outpatients, as well as a high one-week test-retest reliability (Pearson's correlation = 0.93) (Beck, Steer & Brown 1996). The concurrent validity of BDI with respect to clinical ratings was high (mean

correlation = 0.72 for psychiatric patients and 0.60 for non-psychiatric subjects) (Beck, Steer & Carbin, 1988). Comparisons between the BDI and the BDI-II suggest that the BDI-II is a stronger instrument in terms of its factor structure (Dozois, Ahnberg & Dobson, 1998). A validated Chinese version of BDI-II was used in the current study (Bryne, Stewart & Lee, 2004). The Chinese version has a good validity and reliability (6-month test-retest reliability: Pearson's correlation = 0.74; internal consistency: Cronbach's alpha = 0.91).

2.4.6 Beck Anxiety Inventory (BAI; Beck, 1988)

This is a self-administered rating scale consisting of 21 items assessing symptoms of anxiety. Participants rate how much they have been bothered by each symptom during the past week, including the day of assessment. Each item is rated from 0 to 3, with *0 = not at all*, *1 = mildly*, *2 = moderately*, and *3 = severely*. It has a high internal consistency with Cronbach's alphas ranging from 0.92 to 0.94 while the one-week test-retest reliability ranges from 0.73 to 0.75 (Fydrich, Dowdall & Chambless, 1992; Steer, Beck & Clark, 1993). It also has a good discriminant validity to discriminate participants with clinically significant anxiety symptoms and those without significant symptoms. A validated Chinese version with good internal consistency (Cronbach's alpha = 0.85) was used in this thesis (Che, 2006).

2.5 Scales used in the Hong Kong Mental Morbidity Survey (HKMMS; Lam et al., 2014a) which are relevant to the thesis

2.5.1 Hong Kong Mental Morbidity Survey (HKMMS; Lam et al., 2014b; Lam et al., 2014c)

This is a territory-wide cross-sectional study which aimed to study the prevalence of mental illness among a random sample of population of Chinese ethnic origin in Hong Kong.

Ten thousand households were selected on a stratified random sampling scheme (stratified according to geographical region and nature of private or public housing premises) from the population register of Census and Statistics Department of Hong Kong in 2011. Target participants (N = 5700) were an adult Chinese population in Hong Kong aged between 16 and 65 years. The survey involved administering the Clinical Interview Schedule-Revised (CIS-R; Lewis et al., 2002) to the selected participants. According to a set of pre-defined algorithm, a set of International Classification of Disease-10 (ICD-10) mental disorders were then derived from the CIS-R scores. The CIS-R Chinese version was validated locally as a reliable and valid instrument (Chan et al., 2013). The participants were also screened for the presence of psychotic and hypomanic symptoms by the Psychosis Screening Questionnaire (PSQ; Bebbington & Nayani, 1995) and asked to complete a set of questionnaires assessing a number of exposure factors related to the types of mental illnesses identified by the CIS-R. The variables of interest included socio-economic status, size of the household, drug and alcohol misuse, suicidal ideation etc.

HKMMS scales which were used in the current thesis are discussed as follows.

2.5.2 Beck Scale for Suicidal Ideation-Current (SSI-C; Beck, Kovacs & Weissman, 1979)

This is a well-validated 19-item scale that measures the level of suicidal ideation in the past seven days. SSI-C has been found to have a high internal consistency (alpha coefficient = 0.84), with the relationship between the SSI-C and past suicidal attempts being moderately correlated (r = 0.31; p < 0.001) (Beck, Brown & Steer, 1997). The validated Chinese version, which has a good internal consistency (Cronbach's alpha = 0.88) (Zhang & Brown, 2007), was used for identifying participants with current suicidal ideation in the HKMMS. A suicidal case was defined as a participant who scored 1 or above for both questions 4 and 5 while a

potential non-suicidal control is defined as a participant in the HKMMS with a score of zero for both questions 4 and 5.

2.5.3. Revised Clinical Interview Schedule (CIS-R; Lewis et al., 1992)

CIS-R is a fully structured psychiatric interview used by trained lay interviewers for measuring symptoms suggestive of neurotic disorders (Lewis et al., 1992). The CIS-R was designed to assess the presence and severity of common psychological symptoms (somatic symptoms, fatigue, concentration/memory problems, sleep problems, irritability, worry about physical health, depressive mood, depressive ideas, worry, free-floating anxiety, phobias, panic, compulsions and obsessions) in individuals aged 16 or above. Two screening questions in each section ask about the presence of the symptom during the past month and then there is a more detailed assessment of the presence, frequency, duration, and severity of symptom during the past seven days. For the HKMMS, all participants were administered the full interview. Each symptom section is scored on a scale ranging from 0 to 4 (except depressive ideas scored from 0 to 5). Additional questions enable the application of ICD-10 research diagnostic criteria using specially developed computerized algorithm (Singleton et al., 2001). The translated Chinese version was tested in a sample of psychiatric outpatients with common mental disorders (n = 140) and a non-clinical control group (n = 160). The kappa agreements of the computer-generated ICD-10 research diagnoses from CIS-R with the CB-SCID-I/P diagnoses were as follows: k = 0.68 for depressive disorders and k = 0.41 for anxiety disorders. For detection of depressive disorders, the sensitivity was 71% while the specificity was 95%. For detection of anxiety disorders, the sensitivity was 69% while the specificity was 79%. The CIS-R also had a high correlation with General Health Questionnaire (Goldberg & Hillier, 1979) (Spearman rho = 0.71) and a high correlation with Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) (Spearman rho = 0.76), suggesting that the CIS-R is a valid

scale in measuring severity of neurotic symptoms. The 2-week test-retest reliability of Chinese CIS-R total score in a selected sample of participants (n = 24) was also high (Pearson's correlation = 0.89) (Lam et al., 2014a). The results found are similar to the results from the UK (Lewis et al., 2002) and Greece (Skapinakis et al., 2013).

2.5.4 Psychosis Screening Questionnaire (PSQ; Bebbington & Nayani, 1995).

PSQ is a screening questionnaire for identification of psychotic symptoms in the past year. The PSQ has five probe questions (plus secondary questions) enquiring about mania, thought insertion, paranoia, strange experiences and hallucinations. In the HKMMS, respondents were asked all the items from the PSQ without the usual procedure of cutting off after a section was answered positively. Those participants who endorsed one or more psychotic symptoms (initial probe plus secondary questions) in the PSQ were then administered CB-SCID-I/P to verify the presence of DSM-IV-TR psychotic and related disorders. The PSQ questionnaire was first validated in a sample of 90 attendees of a general practice, followed by interviews with 50 psychiatric in-patients and 50 outpatients. The Chinese version of PSQ was also found to have a good internal consistency (Cronbach's alpha = 0.78). For detection of schizophrenia, the sensitivity was 81% while the specificity was 72%. For detection of bipolar disorders, the sensitivity was 78% while the specificity was 69% (Chang et al., manuscript submitted for peer review).

2.6 Conclusions

The current thesis, based on six studies, attempts to investigate the relationships of mental imagery susceptibility and various forms of bipolarity. The major variables of interest measured in these six studies were mental imagery susceptibility (as measured by SUIS and IFES). Other related cognitive variables of interest include RPA, POG, RSS-SF, and BAS. The clinical variables of interest include mood symptoms, suicidal ideation and DSM-IV-TR diagnoses as measured by YMRS, HCL-32, BAI, BDI-II, SSI-C, and CB-SCID-I/P. For those scales without a validated Chinese version (e.g., SUIS, IFES etc.), the scales were first validated in separate samples. All validated scales were found to have good internal consistencies and inter-rater reliabilities.

CHAPTER 3 - Study 1: Mental imagery susceptibility, positive rumination and behavioural approach system in remitted bipolar I disorder: a case-control study

3.1 Introduction

3.1.1 Mental imagery susceptibility in bipolar disorders: a need for replication?

Patients with bipolar disorders (BD) have a general tendency to think in mental images rather than verbal thoughts in daily life (Holmes et al., 2011; see section 1.1.8). They also rate their future-oriented (prospective) images as emotionally more powerful than non-psychiatric control participants (Holmes et al., 2011) and patients with major depressive disorders (MDD) (Hales et al., 2011). Furthermore, they experience more negative prospective images than non-psychiatric controls (Holmes et al., 2011) and patients with MDD (Hales et al., 2011). Indeed, excess negative prospective images were recalled during the most recent episode of bipolar depression by euthymic patients with BD (Gregory et al., 2010). The above findings suggest that these imagery characteristics might be specifically elevated in patients with BD when compared to patients with MDD or healthy controls. However, given the significant relationships between intrusive images and anxiety symptoms (Crane et al., 2012 & Sections 1.1.6 & 1.1.7), the elevation of mental imagery susceptibility (i.e. general use of imagery in daily life and emotional impact of prospective imagery) and the excessive number of negative prospective images reported in Hales et al.'s (2011) study might be explained by the presence of significant anxiety symptoms rather than a specific vulnerability of imagery use in BD.

To address more precisely the above question, it would be desirable to replicate these studies in a group of patients relatively free from significant mood symptoms in the inter-

episode well periods (i.e. patients with remitted BD). Remission from BD-I is defined conventionally as being euthymic with no marked manic symptoms. The absence of manic symptoms is defined by a Young Mania Rating Scale (YMRS) total score of 7 or less, with no core item of the YMRS having a score greater than 2 and all remaining 7 items scored 1 or less. In addition, the Hamilton Depression Rating Scale (HAM-D) score must be 7 or less. The Clinical Global Impression Bipolar Severity Score should also indicate that the patient is functionally recovered (i.e. score of 2 or lower) (Chenggapa, Baker & Shao, 2003). In the current study, remission of depressive symptoms in BD and MDD was defined by a score of 12 or less in Beck Depression Inventory-II (BDI-II) rather than HAM-D total score of 7 or less (Riedel et al., 2010). This set of criteria used to define remission from BD in the current study is likely to be more stringent than the criteria used in Holmes et al.'s (2011) study, especially when these criteria are complemented by the absence of any current diagnosis of BD-I (depressive or manic or mixed affective episode) or MDD as confirmed by CB-SCID-I/P (So et al., 2003a). The exclusion of comorbid DSM-IV-TR anxiety disorders in BD and MDD groups would also eliminate anxiety as a possible confounder of the relationships between imagery characteristics and bipolarity.

3.1.2 The role of positive cognitive styles in pathological positive mood amplification

In addition to the hypothesis of the role of mental imagery as an emotional amplifier in BD (Holmes et al., 2008), recent studies have shown that students with BD had higher levels of positive rumination than non-psychiatric and MDD controls (Johnson, McKenzie & McMurrich, 2008; see section 1.1.2.6). Rumination for positive affect predicted lifetime manic frequency in BD (Gruber et al., 2011). In addition, people at risk for mania were also found to have increased confidence and over-generalizing biases of prior successful

experiences to other areas of life (Eisner, Johnson & Carver, 2008). It is not known whether these positive cognitive styles were also observed in participants with BD in other ethnic populations. This study attempted to replicate these results in a larger Asian sample of patients with remitted BD-I.

3.1.3 Crossroad between mental imagery and positive cognitive processing style?

Studies have found that the onset of hypomanic or manic episodes in at-risk individuals was preceded more often by goal-striving or goal-attainment life events than non-specific positive or negative life events (Johnson *et al*., 2008; Nusslock et al., 2007). As postulated in section 1.1.8.2, positive future-oriented images might play a similar role as episode triggers in the form of BAS-relevant activating events. Patients with BD have reported more intense positive affect when visually imagining their positive memories in a ruminative mode than when visually imagining these memories in a detached observing mode similar to mindfulness approach (Gruber et al, 2009), suggesting that rumination about positive images might amplify pathological positive mood state. The current study explored whether savouring the positive emotions associated with positive prospective images might be a cognitive characteristic that differentiated patients with remitted BD-I from those with MDD.

3.1.4 Behavioural Approach System as a possible moderator of the relationship between positive rumination of visual images and (hypo) manic symptoms

Although the above hypothesis proposes a link between rumination of positive prospective images and an escalation of elated mood characteristic of mania, additional

cognitive mechanisms might be required to explain the complex array of cognitive and behavioural symptoms characteristic of (hypo) mania. One possible candidate for the link between these imagery characteristics and (hypo)manic symptoms might be the Behavioural Approach System (BAS) (Depue & Collins, 1999; Depue & Iacono, 1989; Whittle et al., 2006; see section 1.1.2.4). High BAS function was postulated to be related to increases in elation, confidence, energy, and activity in response to incentives and cues for rewards while low BAS function related to social withdrawal and depression (Depue & Collins, 1999; Depue & Iacono, 1989). BAS sensitivity of an individual refers to the responsiveness of the BAS in reaction to reward and goal pursuit/frustration (Alloy & Abramson, 2010). If BAS hypersensitivity could predict intensification of subsequent mood symptoms in BD (Johnson et al., 2001), it might similarly play a role in determining lifetime mood episode frequency. This study predicted that BAS sensitivity would be elevated in patients with remitted BD-I compared to two control groups. Additionally, the study investigated whether BAS sensitivity moderated the relationship between mental imagery susceptibility and the frequency of lifetime mood episodes. Lastly, positive rumination about prospective images might predict lifetime hypomanic symptoms through the moderation of a hyper-sensitive BAS. This study is the first to investigate the relationships between imagery characteristics, responses to positive affect, and BAS measures in a sample of clinical participants of ethnic Chinese origin.

3.2 Aims and objectives

The current study investigated the relationships between mental imagery susceptibility, responses to positive affect and initial success experiences, as well as behavioural approach system (BAS) in remitted BD-I by comparing (i) participants with remitted BD-I with (ii) a psychiatric control group of remitted MDD and (iii) a non-psychiatric control group.

The primary hypotheses were:

1. The remitted BD-I group will experience higher levels of emotional impact of prospective imagery and general use of imagery in daily life than the MDD and non-psychiatric control groups.
2. The remitted BD-I group will experience higher levels of positive rumination and responses to success experiences than the two control groups.

The secondary hypotheses are:

3. The remitted BD-I group will have higher levels of BAS Scales than the two control groups. The relationship between mental imagery susceptibility and the number of prior mood episodes will be moderated by BAS sensitivity.
4. The interaction between positive rumination scores and the number of positive prospective images will predict the diagnostic category of BD-I in remission. That is, a patient with remitted BD-I is more likely to be savouring their positive future-oriented images than a control patient with MDD. Furthermore, this relationship will be moderated by BAS Scales. That is, a patient with remitted BD-I is more likely to savour their positive prospective images which then triggers the hypersensitive BAS system for increased BAS outputs than a patient with remitted MDD.

3.3 Study methods

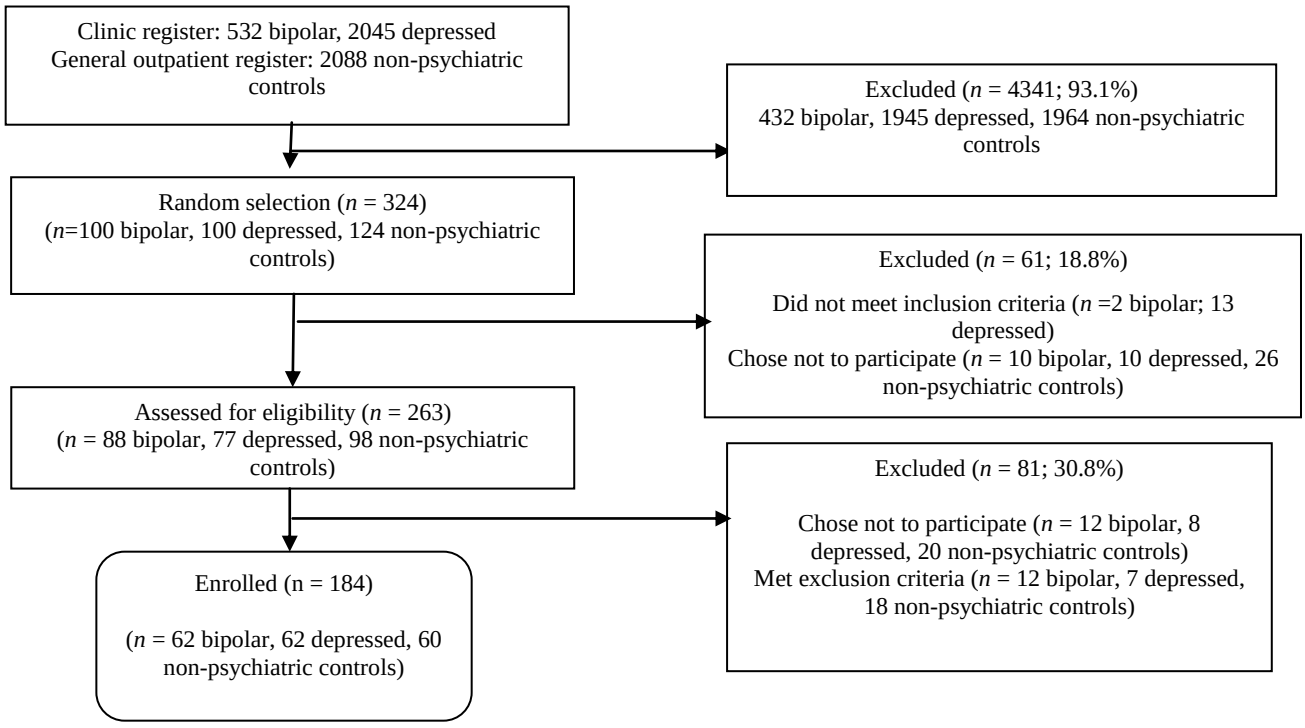
3.3.1 Participant recruitment

Participants were 62 patients with a DSM-IV-TR (APA, 2000) diagnosis of remitted BD-I; 62 patients with a DSM-IV-TR (APA, 2000) diagnosis of remitted MDD, single or recurrent episodes; and 60 non-psychiatric controls. Both psychiatric groups were recruited from a regional psychiatric outpatient clinic providing mental health services for all residents in a well-defined geographical region with a population of 600,000 people. The non-psychiatric control group was recruited from a public primary care clinic providing services for residents living in the same region as the clinical groups. The primary care clinic mainly provided general medical care for minor ailments (e.g. minor upper respiratory or gastro-intestinal symptoms etc.) or stable chronic medical conditions (e.g. type II diabetes, asthma etc.). The participants in the BD-I and the MDD groups were selected randomly using computer-generated random numbers from the full list of patients in the clinical register of the psychiatric clinic with a database of around 500 active cases of BD-I and 2156 active cases of MDD. The non-psychiatric control group was recruited randomly from the daily attendance lists of around 100 patients in the primary care clinic on the working days of the study period (see flow diagram 1). The study period spanned from January 2012-December 2013.

Inclusion criteria for all groups were: (1) being literate in Chinese, (2) aged 18-65 years, and (3) the BD-I group had to have a DSM-IV-TR lifetime or current diagnosis of BD-I in remission; the MDD group had to have a DSM-IV-TR lifetime or current diagnosis of MDD in remission, single or recurrent episodes; the non-psychiatric control group had to exhibit no lifetime or current DSM-IV-TR Axis-1 diagnosis and participants must not have been prescribed psychotropic medications. For defining remission of BD-I, the additional criteria have to be fulfilled: (1) being euthymic with no marked manic symptoms (as defined by

having a YMRS total score of 7 or less, with no core item of the YMRS having a score greater than 2 and the remaining 7 items scored 1 or less); (2) The BDI-II total score had to be 12 or less; and (3) The CGI Bipolar Severity Score should indicate that the patient was functionally recovered (i.e. score of 2 or lower). Exclusion criteria for all groups were: (1) the presence of additional current Axis-1 DSM-IV-TR diagnoses; (2) having a YMRS total score of 8 or above; (3) having a BDI-II total score of 13 or above; (4) being mentally incompetent to give an informed consent; (5) having received electroconvulsive therapy in the past 12 months; and (6) having been admitted as a psychiatric inpatient in the preceding three months. The study was approved by the local Research Ethics Committee (ethics committee reference number: KC/KE-09-0176/ER-3). Informed written consent was obtained from all participants.

Flow diagram 1: the recruitment of the research participants for Study 1



3.3.2 Assessment instruments

3.3.2.1 Demographic data

Age, gender, marital status, employment status, and years of education were recorded in a demographic questionnaire. The number and diagnoses of previous in-patient psychiatric admissions, types of psychotropic medications, and the time of first contact with the mental health care were retrieved from the Clinical Information System of the Hospital Authority, a comprehensive electronic clinical care record of all patients receiving health care in the Hospital Authority of Hong Kong.

3.3.2.2. Clinical measures

Chinese Bilingual Version of the Structured Clinical Interview for DSM-IV Axis I Diagnosis, Patient Version (CB-SCID-I/P; So et al., 2003a).

Young Mania Rating Scale (YMRS; Young et al., 1978).

Beck Depression Inventory-II (BDI-II; Beck et al., 1996): The validated Chinese version was used (Bryne et al., 2004). For the current study, the scale had a good internal consistency (Cronbach's α = 0.88).

Beck Anxiety Inventory (BAI; Beck, 1988; Fyrich et al., 1992): The validated Chinese version was used (Che, 2006). For the current study, the BAI had a good internal consistency (Cronbach's α = 0.85).

3.3.2.3 Imagery measures

The Spontaneous Use of Imagery Scale *(*SUIS; Reisberg, Pearson & Kosslyn, 2003): For the current study, the internal consistency of the translated version was high (Cronbach's α = 0.86).

The Impact of Future Events Scale (IFES; Deeprose & Holmes, 2010): For the current study, the internal consistency of the translated version was high (Cronbach's α = 0.94).

3.3.2.4 Positive cognitive processing style measures

The Response to Positive Affect Questionnaire (RPA; Feldman, Joorman & Johnson, 2008) measured positive rumination. In the current study, the internal consistencies of the relevant two sub-scales of translated version were high (Cronbach's α: RPA-EF=0.87; RPA-SF=0.85).

The Positive Overgeneralization Scale (POG; Eisner et al., 2008) measured response to success experiences. The translated POG was found to have good internal consistencies in the current study (Cronbach's alpha: POG-UG=0.97; POG-LG=0.92; POG-SG=0.93).

3.3.2.5 Lifetime trauma measures

Life Events Checklist (LEC; Gray et al., 2004): For the current study, the internal consistency of the translated version of LEC was found to be good (Cronbach's α = 0.89).

3.3.2.6 Behavioural Approach System (BAS) measures

BIS/BAS Scales (Carver & White, 1994): For the current study, the internal consistencies of the three BAS scales were good (Cronbach's alphas: BAS-Drive= 0.73; BAS-Reward Responsiveness= 0.87; BAS-Fun Seeking= 0.76).

3.4 Statistics

3.4.1 Sample size calculation

All analyses were conducted using STATA Version 12 (STATACorp, 2011). Based on the differences of SUIS and IFES between participants with BD and those with MDD (SUIS: BD = 47.0 [*SD* = 7.54] vs. MDD = 41.5 [*SD* = 7.13]; IFES: BD = 49.35 [*SD* = 13.74] vs. MDD = 33.90 [*SD* = 12.33]) (Hales et al., 2011), a minimum of 38 participants in each group was required to detect significant differences in SUIS total and IFES total with a power of 90% at an α level of 5%.

3.4.2 Statistical analyses

All continuous variables were first examined for Normality using visual plot examinations and Normality tests. Skewed continuous data were first normalised by square root transformation before conducting parametric analyses. Analysis of variance was used to compare demographic and clinical measures between the groups, so that any variables with significant differences between the groups would be included as co-variates in subsequent analysis of co-variance (ANCOVA). Differences in mental imagery susceptibility measures, positive rumination and response to initial success experience measures, and BAS scales between the three groups were assessed using ANCOVA followed by planned pair-wise tests, using gender, age, years of education, LEC total scores, and BAI total scores as covariates. BAI total and LEC total scores were included as they were potential theoretical confounders of the relationships between mental imagery susceptibility and BD (Holmes et al., 2008; Ehlers & Clark, 2000). Depressive symptoms and manic symptoms were not co-varied as they were hypothesised to be dependent variables determined by mental imagery susceptibility.

Pearson's chi-square or Fisher's exact tests were used for categorical data where appropriate. All t-tests were two-tailed, with a *p*-value of 0.05 or below being defined as statistically significant. Bonferroni's correction was performed to take account of the multiple comparisons ($p = 0.05/12 = 0.004$).

Stepwise hierarchical regression modelling was conducted for the two clinical groups as a whole sample to investigate the relationship between mental imagery measures and the number of prior mood episodes, after entering important baseline variables in Block 1. If the model was significant, another stepwise regression model was built up by entering BAS scales in Block 2 and mental imagery measures in Block 3.

The relationship between BD-I and MDD status and the interaction variable of positive rumination RPA-EF subscale X IFES Positive Events were first examined by logistic regression modelling for the two clinical groups as a sample using BD-I vs. MDD status as the dependent variable, and entering gender, age, years of education, and BAI total score in Block 1, followed by IFES positive events, positive rumination sub-scale RPA-EF and the interaction variable RPA-EF X IFES positive events in Block 2. A separate logistic regression modelling was repeated as above, but RPA-EF was replaced by RPA-SF and the interaction variable was replaced with RPA-SF X IFES positive events. To test for the moderation effect of BAS Scales in the relationship between BD-I and MDD status and interaction variables of RPA-EF X IFES positive events, regression modelling was repeated with BAS Scales entered in Block 2 and IFES- Positive events, RPA-EF, and RPA-EF X IFES positive events entered in Block 3. This model was repeated to test the moderation effect of BAS Scale on the relationship between RPA-SF X IFES positive events and the diagnostic status, by replacing the relevant variables with RPA-SF. Given the retrospective and cross-sectional nature of the data, the term predictor was used in a statistical sense for describing the relationships between dependent and independent variables in regression modelling.

3.5 Results

3.5.1 Demographic and clinical characteristics

Thirty-one percent of the MDD group and 58% of the BD-I group had recurrent or multiple prior mood episodes. Table 1 shows the demographic and clinical characteristics of the three groups. In summary, the mean age ($F[1, 3] = 8.03$, $p < 0.001$) and duration of illness ($F(1, 3) = 4.04$, $p < 0.001$) were significantly different across the three groups. Subsequent pairwise comparisons showed that the BD-I group had a lower mean age but significantly longer duration of illness than MDD group. The BD-I group also had a higher median number of prior mood episodes. As age and duration of illness were highly correlated, only age was selected as the covariate in subsequent multivariate analyses. On clinical measures, the BD-I group had higher YMRS total scores than the two control groups. However, the BD-I group had lower levels of BAI total scores and BDI-II total scores than the MDD controls but similar levels to the non-psychiatric control group. In summary, the BD-I group had higher levels of manic symptoms though the mean level was well below the threshold levels for hypomania or mania indicating that the BD-I group was euthymic. Furthermore, both BD-I and MDD groups were not suffering from sub-threshold depressive symptoms (sub-threshold depressive symptoms being defined as having a BDI-II total score of more than 20 and having a positive score of 1 in any of the core items of MDD in CB-SCID-I/P; Balazs et al., 2013) (see table 1 for further details).

Table 1: Demographic and clinical characteristics of the participants (*N*=162)

Characteristics	Bipolar I (*N* = 62)		Major depression (*N* = 62)		Non-psychiatric controls (*N* = 60)		Analysis (chi-squared test or analysis of variance)		Bipolar I vs.major depressive disorder groups (Bonferroni's test or chi-squared test); p-value		Bipolar I vs non-psychiatric groups (Bonferroni's test or chi-squared test); p-value	
	N	%	*N*	%	*N*	%	X^2	*p*	X^2	*p*	X^2	*p*
Male gender	24	38.7	19	30.6	27	45.0	2.32	0.31	0.60	0.45	0.60	0.43
Employed	32	51.2	39	62.9	43	72.9	5.0	0.07	1.60	0.20	5.80	0.07
Family history of mental illness	15	24.0	8	13.0	6	10.2	5.07	0.05	2.00	0.38	**4.10**	**0.03**
Having one or more LEC[d] events	11	17.7	16	25.8	16	26.7	1.76	0.42	1.20	0.28	1.50	0.22
Number on psychotropic medications												
Mood stabilizers	62	100	21	33.9	-	-			98	<0.0	-	-
Antidepressants	30	48.4	62	100	-	-			76	01 <0.0 01	-	-
	Mean	*SD*	Mean	*SD*	Mean	*SD*	*F*	*p*	*D*	*p*	*d*	*p*
Age (years)	42.5	11.2	47.5	11.4	50.5	11.0	**8.03**	**<.001**	**5.00**	**0.01**	**8.00**	**.001**
Years of education	12.2	4.8	9.7	5.0	10.8	4.8	1.71	0.18	2.60	0.20	1.40	0.93
Duration of illness (years)	11.0	6.4	5.6	6.4	-	-	**4.04**	**<.001**	**5.37**	**.001**	-	-
Number of prior mood episodes	4.0	2.5	1.5	0.5	-	-	-	-	**2.50**	**.001**	-	-
Number of prior depressive episodes	1.6	1.5	1.4	0.7	-	-	-	-	0.79	0.43	-	-
Number of in-patient psychiatric admissions	3.4	1.8	0.2	0.1	-	-	-	-	**3.20**	**.001**	-	-
BDI-II[a]	4.4	5.3	8.5	5.2	3.3	5.0	**15.01**	**<.001**	**-4.20**	**.001**	1.00	1.00
YMRS[b]	1.4	1.8	0.2	0.7	0.1	0.5	**25.20**	**<.001**	**1.20**	**.001**	**1.30**	**.001**
BAI[c]	6.5	5.8	13.4	6.8	5.8	5.6	**15.82**	**<.001**	**-6.90**	**.001**	0.61	0.55

a: Beck Depression Inventory-II; b: Young Mania Rating Scale; c: Beck Anxiety Inventory; SD=standard deviation; F=F-value ; d=mean difference; p=p-value

3.5.2 Mental imagery characteristics

Table 2 shows the mental imagery susceptibility measures of the three groups. Consistent with the first hypothesis, SUIS total scores differed significantly across the three groups (F[7, 184] = 28.01, $p < 0.001$, partial eta squared = 0.53). Planned pairwise analyses confirmed that the BD-I group had a higher mean SUIS total score than the MDD and non-psychiatric control groups (BD-I = 45.2 [*SD* = 9.26] vs. MDD = 24.8 [*SD* = 7.18]; planned

Bonferroni's test, $p<0.001$; BD-I = 45.2 [*SD* = 9.26] vs non-psychiatric control = 33.8 [*SD* = 8.52]; planned Bonferroni's test, $p < 0.001$).

The IFES total scores were also significantly different across the three groups ($F[7, 184] = 11.16$, $p < 0.001$, partial eta squared = 0.31). Also consistent with the first hypotheses, planned pairwise analyses revealed that the BD-I group had a higher mean IFES total score than the non-psychiatric control group (BD-I = 43.2 [*SD* = 19.77] vs. non-psychiatric control = 21.0 [*SD* = 17.34]; planned Bonferroni's test, $p < 0.001$). However, the BD-I group had a similar IFES total score to MDD control group (BD-I = 43.2 [*SD* = 19.77] vs. MDD = 41.5 [*SD* = 21.28]; planned Bonferroni's test, $p = 0.09$). There were marginally significant differences across the three groups in terms of IFES positive events ($F[7, 184] = 3.40$, $p=0.02$, partial eta squared = 0.12) and IFES negative events ($F[7, 184] = 2.72$, $p = 0.01$, partial eta squared = 0.10). Planned comparisons, however, revealed that the BD-I group was not significantly different from the MDD and non-psychiatric control groups in both IFES positive and IFES negative events (see Table 2).

In summary, the BD-I group had a higher level of general use of imagery in daily life than both control groups. Furthermore, the BD-I group had a higher level of emotional impact of prospective imagery than the non-psychiatric control group but a similar level as the MDD group. The total numbers of spontaneously reported positive and negative prospective images did not differ between the BD-I group and the two control groups.

Table 2: Mental imagery susceptibility measures of bipolar I, major depressive disorder, and non-psychiatric control groups (*N* = 184)

Characteristics	Bipolar I (*n* = 62)		Major depression (*n* = 62)		Non-psychiatric controls (*n* = 60)		Analysis of co-variance (ANCOVA*)		Bipolar I vs. major depression (Bonferroni's tests)		Bipolar I vs. non-psychiatric groups (Bonferroni's tests)	
	Mean	*SD*	Mean	*SD*	Mean	*SD*	*F*	*p*	*d*	*p*	*d*	*p*
IFES[e] total	43.2	19.77	41.5	21.28	21.0	17.3	**11.16**	**<0.001**	6.11	0.09	**19.94**	**<0.001**
SUIS[f] total	45.2	9.26	24.8	7.18	33.8	8.52	**28.01**	**<0.001**	**19.84**	**<0.001**	**11.88**	**<0.001**
IFES[e] positive events	1.1	0.81	0.7	0.83	1.2	0.92	3.40	0.02	0.24	0.14	-0.07	0.67
IFES[e] negative events	0.8	0.71	0.9	0.84	0.6	0.57	2.72	0.01	-0.10	0.33	0.04	0.83

e: Impact of Future Events Scale; f: Spontaneous Use of Imagery Scale; SD=standard deviation; F=F-value ; d=mean difference; p=p-value
*ANCOVA were conducted by using co-variates of gender, age, years of education, square root transformed BAI total scores, and square root transformed total number of traumatic events as measured by LEC.

3.5.3 Positive cognitive processing styles

As shown in Table 3, RPA-EF differed significantly across the three groups (F [7, 184] = 10.67, $p < 0.001$, partial eta squared = 0.30). Consistent with the second hypothesis, planned pairwise analyses showed that the BD-I group had higher mean levels of RPA-EF sub-scale score than the non-psychiatric control group (BD-I = 14.6 [*SD* = 3.98] vs. non-psychiatric control = 11.5 [*SD* = 3.17]; planned Bonferroni's test, $p < 0.001$) and the MDD control group (BD-I = 14.6 [*SD* = 3.98] vs. MDD = 9.8 [*SD* = 2.95]; planned Bonferroni's test, $p < 0.001$).

In addition, RPA-SF was also significantly different across the three groups (F[7, 184] = 11.67, $p < 0.001$, partial eta squared = 0.32), with planned pairwise comparisons showing that the BD-I group again had significantly higher levels of RPA-SF than the non-psychiatric group (BD-I = 10.9 [*SD* = 3.41] vs. non-psychiatric control = 8.0 [*SD* = 2.88]; planned Bonferroni's test, $p < 0.001$) and the MDD group (BD-I = 10.9 [*SD* = 3.41] vs. MDD = 6.4 [*SD* = 2.52]; planned Bonferroni's test, $p < 0.001$). In summary, the BD-I group had higher levels of positive rumination than the two control groups.

Also consistent with the second hypothesis, POG-LG were significantly different across the three groups (F[7, 184] = 10.77, $p < 0.001$, partial eta squared = 0.30), with the BD-I group having a higher mean POG-LG score than the two control groups (BD-I = 19.7 [*SD* = 6.30] vs. non-psychiatric control = 14.1 [*SD*=5.70]; planned Bonferroni's test, $p < 0.001$; BD-I = 19.7 [*SD* = 6.30] vs. MDD = 11.0 [*SD*=5.28]; planned Bonferroni's test: $p < 0.001$).

POG-SG also differed significantly across the three groups (POG-SG: F[7, 184] = 4.21, $p < 0.001$, partial eta squared = 0.15), with BD-I group having a higher mean POG-SG score than the MDD group (BD-I = 8.8 [*SD* = 3.88] vs. MDD = 5.7 [*SD* = 3.77], planned Bonferroni's test, $p < 0.001$) but marginally significantly higher mean scores than the non-psychiatric control group (BD-I = 8.8 [*SD* = 3.88] vs. non-psychiatric control = 7.7 [*SD* = 4.82]; planned Bonferroni's test, $p = 0.05$).

POG-UG had marginally significant differences across the three groups (POG-UG: F[7, 184] = 2.81, $p = 0.009$; partial eta squared = 0.10). Planned pairwise analyses, however, revealed that the BD-I group was not significantly different from the two control groups. In summary, the remitted BD-I group had a higher tendency to generalise success in one domain to success in other areas of life and to generalise a small success to a larger one in the social domain than the two control groups. However, the BD-I group had similar tendencies to generalise to more lofty goals in the same domain.

3.5.4 Behavioural Approach System (BAS) sensitivity

Consistent with the third hypothesis, the BAS Drive Scale was significantly different across the three groups (F[7, 184] = 28.00, $p < 0.001$, partial eta squared = 0.53). Planned pairwise comparisons revealed that the BD-I group had a higher mean BAS Drive scale score than the non-psychiatric control group (BD-I = 12.1 [*SD* = 1.68] vs. non-psychiatric control =

9.6 [*SD* = 2.11]; planned Bonferroni's test, $p < 0.001$) and the MDD control group (BD-I = 12.1 [*SD* = 1.68] vs. MDD = 8.0 [*SD* = 1.05]; planned Bonferroni's test, $p < 0.001$). The BAS Reward Responsiveness Scale also differed significantly across the three groups ($F[7, 184] = 10.53$, $p < 0.001$, partial eta squared = 0.29; see Table 3 for further details). Planned pairwise comparisons revealed that the BD-I group had a higher mean level than the non-psychiatric control group (BD-I = 16.0 [*SD* = 2.53] vs. non-psychiatric control = 14.4 [*SD* = 2.22]; planned Bonferroni's test, $p < 0.001$) and the MDD control group (BD-I = 16.0 [*SD* = 2.53] vs. MDD = 12.9 [*SD* = 1.34]; planned Bonferroni's test, $p < 0.001$). Finally, the BAS Fun Seeking Scale was also significantly different across the three groups ($F[7, 184] = 24.90$, $p < 0.001$, partial eta squared = 0.50). Again the BD-I group had a higher level than the non-psychiatric control group (BD-I = 11.4 [*SD* = 1.80) vs. non-psychiatric control = 9.4 [*SD* =1.49]; planned Bonferroni's test, $p < 0.001$) and the MDD group (BD-I = 11.4 [*SD* = 1.80) vs MDD = 7.90 [*SD* = 0.93); planned Bonferroni's test, $p < 0.001$). In summary, the BD-I group had a higher level of BAS sensitivity than the MDD and non-psychiatric control groups (see Table 3 for details).

Table 3: Positive ruminative style and behavioural activation system sensitivity measures of bipolar I, major depressive disorder, and non-psychiatric control groups (*N* = 184)

Characteristics	Bipolar I (*n*=62)		Major depression (*n*=62)		Non-psychiatric controls (*n*=60)		Analysis of co-variance (ANCOVA)*		Bipolar I vs. major depression groups (Bonferroni's test)		Bipolar I vs. non-psychiatric groups (Bonferroni's tests)	
	Mean	*SD*	Mean	*SD*	Mean	*SD*	*F*	*p*	*d*	*p*	*d*	*p*
RPA-EF[g]	14.6	3.98	9.8	2.95	11.5	3.17	10.67	**<0.001**	4.97	**<0.001**	3.49	**<0.001**
RPA-SF[h]	10.9	3.41	6.4	2.52	8.0	2.88	11.67	**<0.001**	4.51	**<0.001**	3.23	**<0.001**
POG-LG[j]	19.7	6.30	11.0	5.28	14.1	5.70	10.77	**<0.001**	8.48	**<0.001**	6.16	**<0.001**
POG-UG[k]	10.8	5.69	8.1	5.56	11.2	7.22	2.81	**0.009**	**2.49**	**0.05**	-0.39	1.00
POG-SG[l]	8.8	3.88	5.7	3.77	7.7	4.82	4.21	**<0.001**	2.90	**<0.001**	1.58	**0.05**
BAS[m]-drive	12.1	1.68	8.0	1.05	9.6	2.11	28.00	**<0.001**	4.18	**<0.001**	2.44	**<0.001**
BAS-reward responsiveness	16.0	2.53	12.9	1.34	14.4	2.22	10.53	**<0.001**	3.30	**<0.001**	1.68	**<0.001**
BAS-fun seeking	11.4	1.80	7.9	0.93	9.4	1.50	24.90	**<0.001**	3.39	**<0.001**	1.82	**<0.001**

g :Response to Positive Affect Emotion Focus subscale; h:Response to Positive Affect Self-Focus subscale; j: Positive Over-generalization Scale -Lateral Generalization subscale; k: Positive Over-generalization Scale -Upward Generalization subscale; l: Positive Over-generalization Scale-Social Generalization subscale; m: Behavioural Approach System Scale; SD=standard deviation; ; F=F-value ; d=mean difference; p=p-value *ANCOVA were conducted across the three groups by using covariates of gender, age, years of education, square root transformed BAI total scores, and square root transformed scores of total number of lifetime traumatic events as measured by LEC.

3.5.5. Prediction of prior lifetime mood episodes by mental imagery susceptibility and BAS scales

Also consistent with the third hypothesis, stepwise hierarchical modelling showed that SUIS total scores positively predicted the number of lifetime prior mood episodes in Block 2 after entering gender, age, duration of illness, the BAI total score, the YMRS total score, and the BDI-II total score in Block 1 (overall $R^2 = 0.38$, $p < 0.001$; $B = 0.02$, $SE = 0.04$, beta = 0.40, $p < 0.001$). When BAS total score was entered in Block 2 before entering mental imagery measures in Block 3, the BAS total score became the significant predictor (overall model $R^2 = 0.41$, $p < 0.001$; $B = 0.01$, $SE = 0.004$, beta = 0.27, $p = 0.002$) while SUIS total score was no longer significant (R^2 change = 0.02, $p = 0.43$). In summary, the general use of imagery predicted the number of prior lifetime mood episodes in BD-I and the relationship between these two variables was moderated by the BAS total score.

3.5.6 Relationships between mental imagery susceptibility, positive rumination, and BAS in predicting the diagnosis of bipolar I disorder

Consistent with the fourth hypothesis, the diagnosis of BD-I vs. MDD was predicted by the interaction variable of RPA-EF X IFES Positive Event (*B* = 12.37, *SE* = 3.54, wald = 12.19, *df* = 1, $p < 0.001$, Exp (B) =2.51). However, this was no longer the case when BAS Scales were entered (*B* = -12.02, *SE* = 8.60, wald = 1.96, *df* = 1, *p* = 0.16, Exp (B) = 0.001). The BAS Drive Scale became the only significant predictor of the diagnosis of BD-I (*B* = 1.87, *SE* = 0.62, wald = 9.03, *df* = 1, *p* = 0.003, Exp (B) = 6.46). The BAS Fun Seeking Scale was also marginally significant as a predictor of the diagnostic category (BAS Fun Seeking: *B* = 1.38, *SE* = 0.72, wald = 3.66, *df* = 1, *p* = 0.05, Exp (B) = 3.97).

Similar results emerged when the same logistic regression modelling was repeated with the RPA-SF, the IFES positive events, and the interaction variable of RPA-SF X IFES positive events as independent variables and bipolar/major depression diagnostic categories as the dependent variables. The diagnosis of BD-I vs. MDD was predicted by the interaction variable of RPA-SF X IFES Positive Event (*B* = 12.37, *SE* = 3.54, wald = 5.18, *df* = 1, *p* = 0.01, Exp (B) = 2.50). However, the diagnostic category of BD-I was no longer predicted by the interaction variable once the BAS Scales were entered (*B* = -8.22, *SE* = 7.75, wald = 1.12, *df* = 1, *p* = 0.29, Exp (B) = 0.001). The BAS Drive Scale again emerged as the significant predictor of bipolar status (*B* = 2.16, *SE* = 0.75, wald = 8.34, *df* = 1, *p* = 0.004, Exp (B) = 8.64). The BAS Fun Seeking Scale was only marginally significant (*B* = 1.32, *SE* = 0.71, wald = 3.50, *df* = 1, *p* = 0.05, Exp (B) = 3.76). In summary, consistent with the fourth hypotheses, rumination about positive prospective imagery predicts the diagnosis of remitted BD-I rather than MDD, with this relationship being moderated by the BAS and BAS Fun Seeking Scales.

3.6 Discussion

3.6.1 Mental imagery characteristics, positive cognitive processing styles and behavioural approach system sensitivity in remitted bipolar I disorder

This is the first study to investigate the relationships between mental imagery susceptibility, positive cognitive processing styles, and behavioural approach system (BAS) sensitivity in participants with remitted BD-I. The first key finding is that patients with remitted BD-I reported higher levels of general use of imagery in daily life, greater emotional impact of prospective imagery, heightened BAS sensitivity to incentives and reward cues, and heightened positive cognitive processing styles compared to the control groups. This is consistent with prior research reporting higher general use of imagery and emotional impact of prospective imagery (Holmes et al., 2011), heightened responses to positive affect (Feldman et al., 2008; Johnson, McKenzie & McMurrich, 2009), and increased confidence to initial successes (Eisner *et al*., 2008) in patients with BD compared to non-psychiatric control groups. The current study suggests that patients with BD-I, even in full remission with minimal mood symptoms, have similar cognitive characteristics as bipolar disorders with residual mood symptoms, providing some preliminary support that they might be cognitive characteristics specific to BD.

3.6.2 Prediction of lifetime prior mood episodes by mental imagery measures

The third key finding is that general use of imagery might predict the number of prior lifetime mood episodes, suggesting that frequent visualisation of thoughts might lead to emotional instability, an extreme form of which is the frequent recurrence of mood episodes

(Holmes et al., 2011; see Study 3 of Chapter 5). Furthermore, BAS sensitivity appeared to moderate this relationship by possibly amplifying emotional instability into a whole array of cognitive, behavioural and mood symptoms culminating into full-blown mania.

3.6.3 The links between mental imagery characteristics, positive cognitive processing styles, and behavioural approach system sensitivity in bipolar I disorder

How might positive rumination interact with positive images to contribute to the development of BD-I? The second key finding is that rumination about positive prospective images was a predictor of receiving a diagnosis of BD-I rather than MDD. Furthermore, this relationship was moderated by BAS sensitivity (particularly BAS Drive). Given that positive prospective images may represent desired goals to be attained (Conway et al., 2004) and enhance the perceived likelihood and conviction of occurrence of the imagined events (Carroll, 1978; Mathews et al., 2013), such positive prospective images may be perceived as 'positive life events' and provide a fuel for positive rumination. Rumination about such imagined positive events may then activate the BAS, resulting in a cascade of approach behaviours and cognitions characteristic of BD (Johnson, 2005; Mansell & Pedley, 2008).

3.6.4 Possible roles of prospective images in bipolar disorders

If positive rumination of positive images does indeed play a key role in the ascent of mania and positive ruminative style was already elevated in remitted BD, what additional factors might be responsible for activating BAS and kindling this bush of 'manic fire'? One possible candidate is the intrusion of increasing number of positive prospective images, which is partially supported by the study result of positive rumination of positive images being predictive of having the diagnosis of BD-I. Given that the levels of positive rumination were

already elevated in bipolar I disorder in remission, an ascent of mania might then depend on further increase in positive rumination, or an increase in the number of positive images, or both. A qualitative study of euthymic bipolar patients reporting a relative absence of prospective positive images during euthymia but an excess of such images during hypomania might support this hypothesis (Gregory *et al*., 2010). Study 2 of the current thesis investigated whether positive prospective images declined in number with resolution of manic symptoms in a group of in-patients with acute mania (see Chapter 4). The study confirmed that there was a drop in the number of positive prospective images with resolution of manic symptoms, supporting a key role played by positive prospective imagery in determining the severity of manic symptoms.

3.6.5 Putting research findings into a clinical example

The current study suggests that patients with remitted BD-I may have certain unique cognitive characteristics. Instead of thinking in words, they usually think about daily activities or events in the form of visual images. Furthermore, these images, especially those about future plans or events, are highly emotionally arousing. As these positive images might be perceived as signifying potential rewards or success, it is understandable why they might dwell upon them and savour the positive feelings associated with images depicting a positive future. Because of their heightened neurological sensitivity to these reward cues, their savouring and dwelling on these images would lead to increased positive mood, enhanced physiological activities and increased optimism. Upward spiralling of these emotional, cognitive, and behavioural characteristics may then culminate into a relapse into mania in these patients with BD-I.

3.7 Strengths and limitations

The study has several strengths. The clinical samples were recruited from a representative regional psychiatric clinic, thereby enhancing external validity to patients with BD-I and MDD residing in the same region in Hong Kong. The non-psychiatric controls were from a primary care clinic in the same geographic region, thereby controlling for various known and unknown confounders of the relationships between cognitive risk factors and mood symptoms. The use of non-psychiatric and MDD controls allows better understanding of whether the differences in mental imagery measures between BD-I group and non-psychiatric group were specific to remitted BD-I (Weβlau & Steil, 2014). Using structured clinical interviews and standardized cut-off points of mood scales to define remission enhanced the reliability in making the diagnoses of remitted BD-I. All the translated scales used were locally validated with good psychometric properties. An a priori sample size calculation ensured that the sample size was adequate to address primary hypotheses. Statistical modelling took account of theoretical and statistically significant covariates which allowed possible confounders of the relationships between mental imagery characteristics and mood symptoms to be controlled for, namely concurrent anxiety symptoms and lifetime traumatic experiences.

However, there are certain limitations. As this is a case-control study, the elevation of cognitive and imagery characteristics might be due to 'scar effects' of BD (Lewinsohn et al., 1981). Exclusive use of self-administered mental imagery measures might be prone to respondent and social desirability biases. Inclusion of objective measures like clinician administered imagery interview and laboratory measures of mental imagery susceptibility in future studies would enhance the convergent validity of the findings (Weβlau & Steil, 2014). As clinical participants were all receiving psychotropic medications, the alternative explanation of medications heightening mental imagery susceptibility measures cannot be

ruled out. However, previous studies on non-clinical participants without prior exposure to psychotropic medications reported similar findings of heightened mental imagery susceptibility among participants with high bipolar risks (Deeprose et al., 2012; Malik et al., 2014; see Studies 4 & 5). Although Bonferroni's correction has been made to address multiple comparisons, the possibility of type I errors cannot be fully eliminated. The current results require further replication in larger prospective studies in the near future.

CHAPTER 4 -Study 2: Mental imagery and bipolar mania: A prospective cohort study

4.1 Introduction

4.1.1 Cognitive approaches to mania and depression: a role for mental imagery?

Although there is a vast literature supporting the role of cognitive biases in the onset and development of depression and mood disorders (see Section 1.1.2.5 about dysfunctional attitudes and cognitive schemas in bipolar disorders), most investigations of cognitions have failed to specify the thinking modality or focused exclusively on verbal cognitions. Emerging evidence suggests that cognitions in the form of mental imagery may contribute to mood swings in bipolar disorders (BD) (Holmes et al., 2008). Gregory et al. (2010) found that euthymic patients with BD recalled having vivid positive intrusive prospective images during past hypomanic episodes but vivid negative ones during past depressive episodes. Furthermore, they also reported having more negative images during past depression than during euthymia. Furthermore, the bipolar depressed group reported having more negative prospective images than the major depressive disorder (MDD) group (Hales et al., 2011). However, Study 1 in this thesis found that a remitted BD-I group had a similar mean number of negative prospective images as a remitted MDD control group. Extrapolation of these findings may suggest that patients with BD-I might experience more negative prospective images when in a depressed state compared to euthymia. To date there has been no direct investigation of whether negative prospective images progressively increase from euthymia to acute bipolar depression. Furthermore, no study has explored the changes in positive prospective images from mania to euthymia in BD-I. The current study examined whether a

progressive decline in manic symptoms was associated with a concomitant decrease in the number of positive prospective images in a BD-I group.

Given that around 30-35% of patients with acute bipolar mania switch from mania to depression within the same mood episode (Gitlin et al., 2003), a prospective follow-up study of patients with BD-I from acute manic relapse to remission might provide an opportunity to identify a BD-I sub-group who had a mood switch to depression. As such, an analysis of this sub-group of patients might help to understand whether negative prospective imagery promotes switching from mania to depression, thus providing some indirect evidence that negative prospective images may be associated with depressive symptoms in BD. The current study therefore also examined the relative changes in the number of negative prospective images with increasing depressive symptoms in the BD-I sub-group that experienced a mood switch.

4.1.2 Emotional impact of prospective imagery and mood changes

A previous study found that a bipolar depressed group experienced higher emotional impact of prospective imagery than a unipolar depressed group (Hales et al., 2011), but Study 1 in this thesis found that the emotional impact of prospective imagery did not differ between remitted BD-I and MDD. A plausible extension of the above discrepant findings is that the emotional impact of prospective imagery might decline from acute bipolar depression to euthymia. So far, no study has examined the longitudinal changes in the emotional impact of prospective imagery from depression to euthymia in BD.

Similarly, no study has examined longitudinal changes in the emotional impact of prospective imagery from acute mania to euthymia. If mania were associated with powerful positive intrusive images (Holmes et al., 2008; Gregory et al., 2010) which might be considered as pleasant and enjoyable, such images may be repetitively dwelled on and

savoured rather than actively avoided. When emotional impact of prospective imagery was measured by IFES (Deeprose & Holmes, 2010), positive prospective images experienced during mania might be appraised as less distressing and avoidant than negative images (see Section 1.1.8.for more details). If mania is associated with positive images while depression with negative images (Gregory et al., 2010; Holmes et al., 2008), the avoidance sub-scale of IFES (IFES-A; i.e. the sub-scale measuring the avoidance feelings and behaviours in response to prospective images) would be expected to be higher in acute major depression than acute bipolar mania at baseline.

As around 60% of patients with BD experience sub-syndromal depressive symptoms between episodes (Judd et al., 2003), resolution of mania may be accompanied by a gradual increase in depressive symptoms in a substantial proportion of BD-I patients. If depressive symptoms are associated with increased emotional impact of prospective imagery and negative prospective images (Morina et al., 2010; Studies 3 & 5), IFES-A scores might then increase with gradual resolution of manic symptoms in the BD-I group as a whole. On the other hand, IFES-A scores might gradually reduce with gradual reduction of negative prospective images in MDD.

4.1.3 General use of imagery in daily life and mood changes

Besides the possible role of the number of prospective images in triggering episode recurrence, Study 1 also showed that the levels of general use of imagery in daily life of patients with remitted BD-I was higher than both remitted MDD and non-psychiatric control groups. Furthermore, individuals with bipolar depression reported higher general use of imagery than those with MDD (Hales et al., 2011). Study 4 and Study 5 in this thesis have similarly shown that this imagery characteristic was higher in people with high bipolar risks compared to people with low risks (see Chapters 6 & 7). A further indication of general use of

imagery in daily life being a trait marker of bipolarity would be its persistent elevation across different symptomatic states when compared to MDD. The current study examined whether general use of imagery remained elevated from acute manic to euthymic phases in BD-I when compared to MDD.

4.1.4 Positive rumination and manic symptoms

Previous studies have shown that patients with BD had higher levels of rumination about positive emotions and self-qualities than people without such disorders (Johnson, McKenzie & McMurrich, 2008; Study 1 in the current thesis). Furthermore, positive rumination was higher in people with high familial risks of BD compared to those without such risks (see Chapter 7). Positive rumination was also associated with the frequency of lifetime manic episodes (Gruber et al., 2011). Until now, no prospective study has examined whether positive rumination would remain elevated from acute relapse to subsequent remission in BD-I when compared to MDD. Previous studies have found that depressive rumination, as measured by the Response Styles Questionnaire (Nolen-Hoeksema, 1991), was elevated during remission but increased to higher levels during relapse of depression (see Nolen Hoeksema, 2000 for a review). As such, rumination of negative affect can be regarded as a state-on-trait marker of depression (Just & Alloy, 1997). Given that the Response to Positive Affect Questionnaire (RPA) was constructed and modelled heavily on Response Styles Questionnaire, positive rumination could be hypothesised to decrease from acute manic to remission states in BD-I. The current study examined whether positive rumination is higher in BD-I when compared with MDD. A related hypothesis is that the levels of positive rumination would decrease from acute mania to euthymic state in patients with BD-I.

4.1.5 Behavioural approach system sensitivity (BAS) in acute mania

Study 1 reported elevated BAS sensitivity in a remitted BD-I group compared to MDD and non-psychiatric control groups, consistent with previous findings that BAS sensitivity was elevated in BD (Uroservic et al., 2007). BAS sensitivity has been found to predict the intensification of manic symptoms but did not correlate with current manic symptoms in a state-dependent manner (Meyer, Johnson & Winters, 2001). However, the BAS scales correlated with current manic and depressive symptoms in an at-risk sample of college students (Meyer et al., 1999), suggestive of BAS being a possible state marker. Whether BAS sensitivity is a trait or state marker therefore remains to be elucidated. This study takes advantage of the longitudinal design to investigate whether BAS sensitivity might be elevated in BD-I across different symptomatic states when compared to MDD (i.e. a trait marker of bipolar I disorder). Finally, if BAS sensitivity predicted intensification of subsequent manic symptoms in BD-I (Meyer, Johnson & Winters, 2001), a related hypothesis is whether BAS sensitivity will be a predictor of recovery of mania with treatment.

4.1.6 Why a longitudinal follow-up study?

A prospective study will enable exploration of these hypotheses by observing serial changes of these cognitive characteristics from euthymic to acute symptomatic phases in patients with BD. Given that 25% of recovered patients with BD develop new depressive and manic episodes 21.4 weeks and 85 weeks after recovery respectively (Perlis et al., 2006), this method would require following up a large cohort of euthymic patients with BD for a long period of time. A cost-effective approach is to measure the changes of imagery characteristics from acute symptomatic to euthymic phases. The median time for symptomatic recovery from an acute manic episode is around six to twelve weeks (Angst & Preisig, 1995; Coryell, Endicott & Keller, 1990; Eaton et al., 1997), therefore enabling data collection within a

reasonable time frame. The current study adopted this method. A follow-up period of 12 weeks was selected in order to capture a reasonable number of patients with bipolar mania attaining euthymia by the end of the study.

4.2 Aims and objectives

The current study was a 12-week longitudinal study which aimed to measure the relative changes in the number of positive prospective images with a decline in manic symptoms in a group of BD-I patients admitted to an acute unit with mania. In order to understand the key roles played by the emotional valences of the prospective images in determining the severity of manic or depressive symptoms, a control group of in-patients with acute MDD admitted to the same psychiatric wards during the study period was also followed up longitudinally for 12 weeks.

The primary hypotheses were:

1. Compared with the MDD group, the BD-I group will have a progressive decrease in the number of positive prospective images from baseline to 12 weeks later. After 12 weeks, the two groups will have a similar number of positive prospective images as found in Study 1 (see Chapter 3).
2. Given the rewarding and exciting nature of the positive prospective images but unpleasant and threatening nature of negative prospective images, the BD-I group will have an increase in the level of the ‘avoidance’ sub-scale of IFES from baseline to 12 weeks' while the MDD group will have a progressive decrease with time.
3. Among patients with BD-I who experienced a mood switch from mania to depression, the emotional impact of prospective imagery will increase from

baseline to 12 weeks. The increase in IFES total score in this sub-group will be explained exclusively by the increase in IFES-A subscale score.

4. The BD-I group will have higher levels of general use of imagery in daily life than the MDD group at each time point.
5. The BD-I group will have higher levels of positive rumination than the MDD group at each time point. Levels of positive rumination will decrease with time in the BD-I group from baseline to 12 weeks.
6. BAS total scores will be higher in the BD-I group when compared with the MDD group at each time point.
7. Recovery from mania at 12 weeks will be predicted by baseline BAS sensitivity in BD-I group.

The secondary hypotheses were:

8. Recovery from mania in the BD-I group at 12 weeks will be predicted by the reduction in the number of positive prospective images from baseline to 12 weeks.
9. Switching from mania to depression at 12 weeks in a sub-group of participants with BD-I will be predicted by an increase in the number of negative prospective images from baseline to 12 weeks.

4.3. Methods

4.3.1 Study design

This was a prospective cohort study of two in-patient groups (a BD-I group with mania and an acute MDD group) admitted within one week to an acute psychiatric in-patient

unit of a regional hospital (Feb 2013-June 2015; the same unit of Study 1). Participants were then followed up at 4 weeks and 12 weeks after the index admission.

4.3.2 Participant recruitment

The inclusion criteria required that patients were:(1) capable of giving informed written consent; (2) aged at least 18 years; (3) ethnic Chinese who could speak, read and write Chinese; (4) fulfilling the DSM-IV-TR criteria for current diagnosis of MDD or BD-I (current episode manic) as verified by the Chinese Bilingual Version of the Structured Clinical Interview for DSM-IV-TR Axis I Disorder- Patient Version (CB-SCID-I/P; So et al., 2003a); and (5) having a YMRS total score of 20 or above (Young et al., 1978) for those participants with BD-I and a BDI-II total score of more than 21 (Beck, Steer & Brown, 1996) for participants with MDD.

The exclusion criteria of the study were: (1) suffering from DSM-IV-TR defined Axis I diagnosis of schizophrenia as the principal diagnosis; (2) having an additional DSM-IV-TR defined Axis 1 disorder; (3) at serious risks to self or others; (4) having electro-convulsive therapy in the preceding 12 months; and (5) suffering from serious life-threatening physical illnesses. The study was approved by the local research ethics committee (reference number: KC/KE-11-0085/FR-3).

4.3.3 Assessment instruments

4.3.3.1 Demographic data sheet

Baseline demographic data of gender, age, marital status, and current employment status were recorded. Furthermore, participants were asked about illness duration in years, number of past psychiatric hospitalizations, and current types of psychotropic medications

being prescribed. This information was verified by the Clinical Information System, an organization-wide computerised clinical information database containing demographic and clinical information for all patients who have had service contact with Hospital Authority of Hong Kong

4.3.3.2 Clinical measures: all clinical measures were administered at all three time points (except the CB-SCID-I/P)

Chinese- Bilingual Structured Clinical Interview of DSM-IV Axis-I Disorder-Patient Version (CB-SCID-I/P; So et al., 2003a; 2003b): CB-SCID-I/P was used to confirm the diagnoses in both groups (and exclude the current presence of other Axis-1 disorders) and illness duration.

The Beck Depression Inventory-II (BDI-II; Beck, Steer & Brown, 1996): Following the recommendations of Beck et al. (1996), a cut-off of 21 or above was used to define a patient as experiencing clinically significant depressive symptoms and a total score of between 13 and 21 is considered as having sub-clinical symptoms. Remission from the current depressive episode was defined in this study as having BDI-II total scores of 12 or fewer at both 4 weeks and 12 weeks. The validated Chinese version was used in the current study (Bryne, Stewart & Lee, 2004). Internal consistency for the current study was good (Cronbach's alpha = 0.92).

The Young Mania Rating Scale (YMRS; Young et al., 1978): In mania trials, a total score of 20 or above is commonly required for inclusion (Tohen et al., 2003). A total score of between 12 and 20 indicates hypomania (Chenggapa, Baker & Shao, 2003). Following treatment, participants scoring 7 or less are considered euthymic. Recovery from mania (i.e. remission from the manic episode) in this study was defined as having YMRS total scores of 7

or less at both 4 weeks and 12 weeks. Participants in the BD-I group who switched from mania to depression were defined by a YMRS total score of 7 or less and a BDI-II total score of 21 or more at both 4 weeks and 12 weeks. The two psychiatrists attained a good inter-rater reliability in YMRS rating before study commencement (weighted kappa = 0.90).

Beck Anxiety Inventory (BAI; Beck et al., 1988): The validated Chinese version was used (Che, 2006) in the current study, and it had a good internal consistency (Cronbach's alpha = 0.92).

4.3.3.3 Imagery characteristics, positive cognitive processing style measures, and behavioural approach system (BAS) measures: all cognitive measures were administered at all three time points

Spontaneous Use of Imagery Scale (Reisberg et al., 2003): The translated SUIS had a good internal consistency for the current study (Cronbach's alpha = 0.94).

Impact of Future Events Scale (IFES; Deeprose & Holmes, 2010): The IFES total score measures the overall levels of emotional impact of prospective images listed by the participants. The total score is the summation of three sub-scales scores (intrusion, avoidance, and hypervigilance sub-scales). As the emotional valence of the IFES events was rated as either positive or negative by the participant, this might be biased by the participant's prevailing mood state. To address this mood-dependent misclassifying bias, 10% of randomly selected IFES positive and IFES negative events from the whole sample at each of the three time points was re-classified as 'positive' or 'negative' by an independent blinded clinician. The weighted kappa agreements between the participants' ratings and the independent rater's rating were high (IFES positive events: $K = 0.95$, IFES negative events: $K = 0.96$), suggesting congruence between the participant's emotional valence ratings and those of an independent clinician not suffering from mood disorders. For the current study, the translated IFES had a

good internal consistency (Cronbach's alpha = 0.89).

Response to Positive Affect Scale (RPA; Feldman et al, 2008): For the current study, RPA-EF and RPA-SF sub-scales had good internal consistencies (Cronbach's alphas: RPA-EF = 0.86; RPA-SF = 0.84).

Behavioural Inhibition/Activation System Scale (BIS/BAS; Carver & White, 1994): For the current study, only the BAS scale and BAS total scores were used. The internal consistency of BAS total scale in the current study was good (Cronbach's alpha = 0.89).

4.4 Statistical analyses

As there were no data directly comparing mental imagery susceptibility measures of BD-I with mania and acute MDD, the sample size was calculated based on the standardized mean differences of SUIS and IFES between the BD-I with depression and MDD groups of Hales et al.'s (2011) study. A sample size of 38 participants in each arm would give a 90% power of identifying statistically significant differences in SUIS and IFES with an alpha level of 5%.

STATA 12.0 (STATACorp, 2011) was used for statistical analyses. Baseline demographic data and illness characteristics were compared using chi-squared tests and univariate analyses where appropriate. Clinical (YMRS total, BDI-II total, and BAI total) and key outcome variables (SUIS, IFES, BAS, and RPA) of the two cohorts (MDD and BD-I groups) were compared using repeated measure analysis of variance (rmANOVA), with Group factor (two levels: BD-I vs MDD groups) and Time factor (three levels: baseline, 4 weeks & 12 weeks). Baseline demographic and illness characteristics with statistically significant between-group differences were taken as covariates in the repeated measure

analysis of co-variance (ANCOVA) of the key variables of interest. BAI total scores at baseline were also included as one of the covariates as anxiety is theoretically associated with both imagery susceptibility and mood symptom variables. Planned univariate analyses were then performed if there were any significant main or interaction effects of the Group and Time factors.

Finally, logistic regression modelling was performed in the BD-I group with the categorical outcome of recovery from mania or not at the 12-week time point as the dependent variable, using changes in SUIS total scores, IFES total scores, IFES positive events, and IFES negative events from baseline to 12 weeks as the predictor variables and gender, age, years of education, baseline BAI scores, and illness duration as covariates. Participants with BD-I and with a BDI-II total score > 20 and YMRS total score < 8 at both 4 weeks and 12 weeks would be taken as those with a mood switch. Logistic regression modelling was then conducted for the BD-I group, with SUIS, IFES, IFES events, and RPA rumination sub-scale scores as independent variables and the status of having a mood switch or not as the dependent variable. Furthermore, gender, age, years of education, baseline BAI total score, and illness duration were also entered as co-variates in the logistic regression models. Due to the exploratory nature of the comparisons, all *p*-values of =/<0.05 were taken as statistically significant without Bonferroni's correction.

4.5 Results

4.5.1 Demographic and clinical characteristics

The study recruited 50 participants suffering from BD-I with mania and 50 participants suffering from MDD with clinical severity requiring in-patient care. All participants were first assessed at baseline after they had been hospitalised in the acute

psychiatric unit for a mean period of 6.5 days (*SD* = 2.31). The second assessment was performed at a mean period of 28.6 days (*SD* = 3.14) after baseline assessment. The third assessment was performed after a mean interval of 86 days (*SD* = 4.3) after baseline assessment. All participants were successfully traced at each time point. The demographic details and the clinical characteristics of the participants are shown in Table 1.

In brief, the BD-I group had a higher proportion of males, had received a longer period of education, and were less likely to be married or cohabiting than the MDD group. Furthermore, the BD-I group had been ill for a longer time and had more previous in-patient admissions. Bivariate correlational analysis of these potential covariates revealed that duration of illness was highly correlated with the number of previous hospital admissions (Spearman's rho = 0.67, $p < 0.001$). Gender was also highly correlated with the marital status (Chi-squared value = 8.69, $df = 1$, $p = 0.003$). To reduce collinearity, only gender and duration of illness were selected among these four variables as co-variates in subsequent parametric analyses. The other covariate included in subsequent multivariate analyses was years of education.

Repeated measure analysis of variance (rmANOVA) revealed that the Group X Time interaction effect was significant for YMRS total scores ($F[2, 97] = 90.0$, $p < 0.001$, partial eta squared = 0.91), with significant main effects of Group and Time (Group factor: $F[1, 98] = 366.63$, $p < 0.001$; Time factor: $F[2, 97] = 253.94$, $p < 0.001$). Planned pairwise analyses revealed that both groups had a significant decline in YMRS total scores with time. YMRS total scores were higher for the BD-I group than the MDD group at each time point. By 12 weeks, 64% ($n = 36$) of the BD-I group had recovered from the manic episode (see table 2 for further details).

A rmANOVA revealed that there was a significant Group X Time interaction for BDI-II total scores ($F[2, 97] = 61.92$, $p < 0.001$,partial eta squared = 0.56), with significant main effects of both Group and Time (Group factor: $F[2, 97] = 84.44$, $p < 0.001$; Time factor: $F[2, 97] = 12.69$, $p < 0.001$). Planned pairwise analyses showed that BDI-II total scores

progressively increased with time for the BD-I group but progressively decreased for the MDD group (see table 2 on page 110 for further details). Furthermore, the MDD group had a significantly higher level of BDI-II total scores than the BD-I group at baseline and at 4 weeks' follow-up, but not at 12 weeks' follow-up. Twenty-two percent (n = 11) of the BD-I group had switched from mania to depression by 12 weeks. Sixty-four percent (n = 32) of the MDD group were considered as having fully remitted by twelve weeks.

Table 1: Demographic and clinical characteristics of the bipolar I and major depressive disorder groups

	Bipolar I (n = 50)	Major depression (n = 50)	Statistics
Male gender (%)	21 (42)	10 (20)	Chi-value = 5.66, df = 1, $\mathbf{p = 0.02}$
Mean age (*SD*)	40.8 (13.04)	43.9 (10.06)	t= 1.31, df = 98, p = 0.20
Mean years of education (*SD*)	11.9 (2.96)	9.8 (2.89)	t= 3.55, df = 98, $\mathbf{p = 0.001}$
Marital status (married) (*%*)	22 (44)	44 (88)	Chi-squared value = 21.57, df = 1, $\mathbf{p = 0.001}$
Full time/part time employment (*%*)	25 (50)	17 (34)	Chi-squared value = 2.63, df = 1, p = 0.11
Mean duration of illness in years (*SD*)	14.1 (11.79)	5.5 (7.77)	t= 4.63, df = 98, $\mathbf{p < 0.001}$
Median number of past admissions (inter-quartile range)	3 (0-7)	0 (0-1)	Mann-Whitney's test: Z = -5.49, $\mathbf{p < 0.001}$

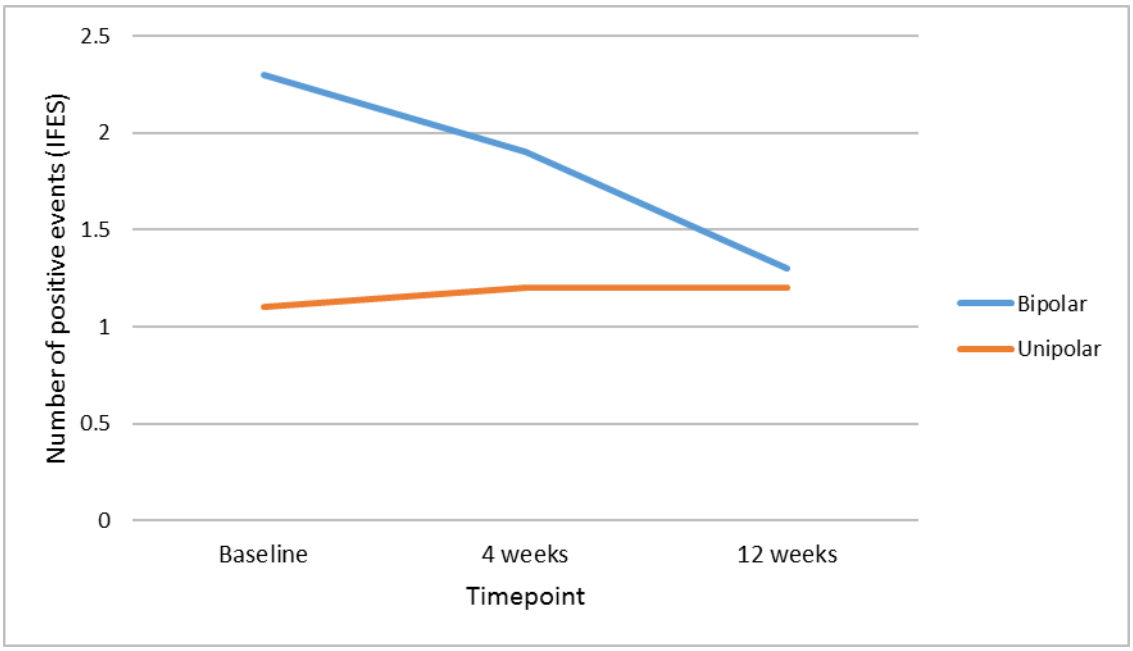
4.5.2 Change in mental imagery characteristics

4.5.2.1 Positive prospective imagery

There were strong positive bivariate correlations between the number of positive prospective images (IFES positive events) and manic symptoms as measured by YMRS total score at baseline (Spearman's rho [r] = 0.54, p <0.001), and at 4 weeks (r = 0.36, p = 0.001)

across the whole group. Consistent with the first hypothesis, there was a significant Group X Time interaction for IFES positive events (F[2, 93] = 15.22, p < 0.001, partial eta squared = 0.26), with significant main effects of both Group and Time (Time factor: F[2, 93]=7.31, p = 0.001; Group factor: F[1, 94] = 33.0, p < 0.001). No other main effects were significant. The interaction factors of Time X Years of education (F[2, 93] = 3.34, p = 0.04), and Time X Duration of illness (F[2, 93] = 3.79, p = 0.03) were marginally significant. Other interaction factors were not significant. Planned pairwise comparisons indicated that positive prospective imagery significantly declined from baseline to 12 weeks in the BD-I group (F[2, 44] =16.18, p < 0.001, partial eta squared = 0.42) but not the MDD group (F[2, 44] = 0.39, p = 0.68). In summary, consistent with the first hypothesis, the BD-I group had a progressive decrease in positive prospective images from baseline to 12 weeks while the MDD group did not have any significant change in the number of positive images. By 12 weeks, the number of positive prospective images experienced by the BD-I group approached that of the MDD group (see Graph 1 and Table 2 for details).

Graph 1: The changes in the number of positive prospective images (as measured by Impact of Impact Events Scale (IFES) positive events) with time in bipolar mania and major depressive disorder

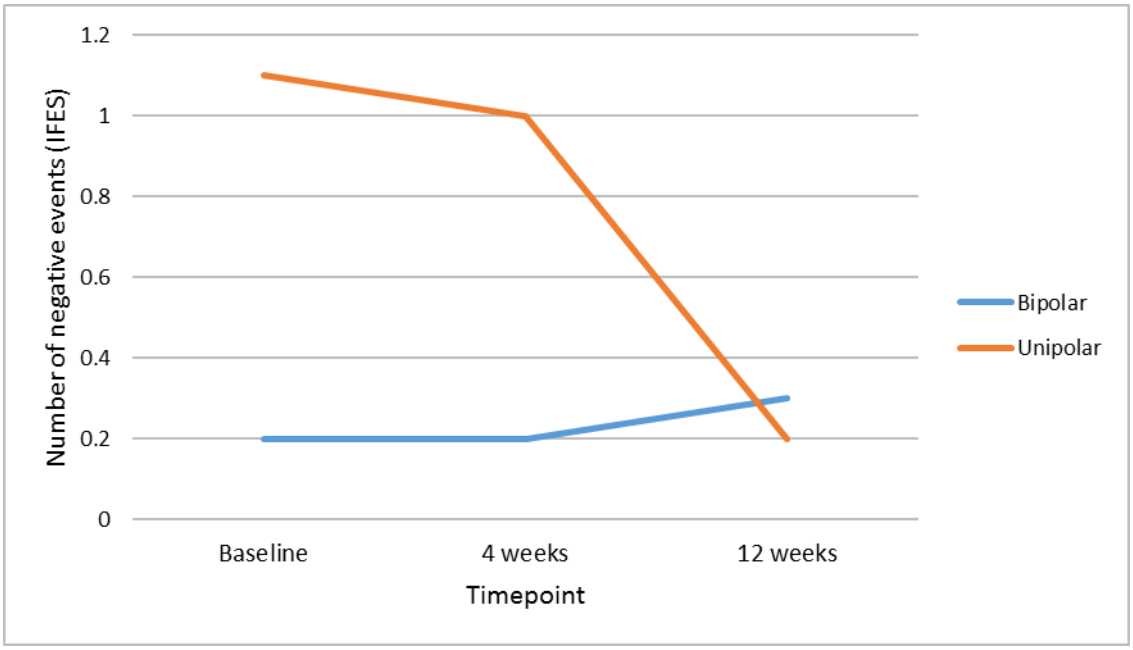


4.5.2.2 Negative prospective imagery

There was a significant bivariate correlation between the number of negative prospective images (IFES negative events) and depressive symptoms at each time point (Spearman correlations; [baseline] $r = 0.45$, $p < 0.001$; [4 weeks] $r = 0.44$, $p < 0.001$; [12 weeks] $r = 0.22$, $p = 0.03$) across the whole group. A repeated measure analysis of co-variance (rmANCOVA) revealed there was a significant Group X Time interaction for the IFES negative events ($F[2, 93] = 17.31$, $p < 0.001$, partial eta squared = 0.27), with significant main effects of Group ($F[1, 94] = 12.02$, $p < 0.001$). There was, however, no significant main effect of Time. No other interaction effects were significant. Planned pairwise comparisons revealed significant differences between the two groups at baseline and 4 weeks, with the BD-I group having lower IFES negative event levels than the MDD group. There was no difference between the two groups at 12 weeks. There was no significant differences in the number of negative prospective imagery in bipolar I group at

three time points (F[2, 44] = 0.32, p = 0.73). The major decline in negative prospective imagery across time was attributed exclusively to the MDD group (F[2, 44] = 30.45, p < 0.001)(see Table 2 and Graph 2 for details). However, further sub-group analysis of the BD-I participants with a mood switch revealed that there was an increase in negative prospective images with time (IFES negative events: F[2, 5] = 12.30, p = 0.01). Further sub-group analyses also revealed that there were no significant changes in negative prospective images with time in the sub-group of BD-I with recovery of mania at 12 weeks or in the sub-group of BD-I with residual mood symptoms. In summary, the resolution of depression in the MDD group was associated with a progressive decline in the number of negative prospective images. However, the resolution of mania in the overall BD-I group was not associated with any changes in the negative images. Further sub-group analysis revealed that there was a progressive increase in negative prospective images only in the BD-I subgroup with a mood switch.

Graph 2: Change in negative prospective imagery (as measured by Impact of Future Events Scale (IFES) negative events) with time in both groups



4.5.2.3 Emotional impact of prospective imagery (see Table 2 for details)

rmANCOVA were also performed to assess changes in IFES total and IFES sub-scores over time in both groups, using the above variables as covariates. There were no significant main and interaction effects for Group, Time and the co-variates in the comparison of IFES total scores between the BD-I and the MDD groups. However, consistent with the second hypothesis, there was a significant Group X Time interaction in IFES-Avoidance sub-scale score (IFES-A; F[2, 93] = 8.12, $p < 0.001$, partial eta squared = 0.15). There was no other significant interaction effect. The main effects of Time and Group were not significant. However, the main effects of education, illness duration, and BAI total scores were significant. Planned pairwise comparisons revealed that, compared to the MDD group, the mean IFES-A scores of BD-I group were lower at baseline, similar at 4 weeks, and higher at 12 weeks. Further sub-group analysis revealed that the increase in IFES-A sub-scale scores at 4 and 12 weeks were explained by the sub-group of BD-I patients with a mood switch (F[2, 5] = 16.10, $p = 0.007$). There was no significant change in the IFES-A subscale score in the MDD sub-group without a mood switch (F[2, 33] = 1.23, $p = 0.31$).

Another rmANCOVA revealed that there was no significant Time X Group interaction effect for the intrusion subscale (IFES-I) scores. The main effect of Group was also not significant. However, the main effect of Time was significant (F[2, 93] = 17.9, $p < 0.001$). No other main or interaction effects of the co-variates were significant. Planned analyses revealed that there were significant decline in the IFES-I sub-scale scores in both groups with time (BD-I: F[2, 44] = 6.65, $p = 0.003$; MDD: F[2, 44] = 14.82, $p < 0.001$). Further sub-group analysis revealed that the decline in IFES-I subscale score was explained exclusively by the BD-I subgroup without a mood switch (Mood switch: F[2, 9] = 3.27, p = 0.09; No mood switch: F[2, 29] = 7.46, p = 0.002). There was no significant Time X Group interaction effect for the hypervigilance subscale (IFES-H) scores. The only significant main effect was that of Age. The interaction or main effects of Group, Time, and co-variates were all non-

significant.

In summary, the two groups had similar levels of IFES total scores at each time point. However, IFES sub-scale score analyses revealed that there was a significant interaction effect of IFES-Avoidance subscale score between the two groups over 12 weeks, with a gradual increase in the scores with time in the BD-I group but a gradual decline in the MDD group. This increase in IFES-A subscale score in the BD-I group was explained by the increase in the sub-group with mood switch. However, the intrusion sub-scale scores dropped in both groups with time. Further sub-group analyses revealed that a decline in intrusion sub-scale score in the BD-I group was explained by the sub-group without a mood switch. There were no significant differences for the hypervigilance subscale scores between the two groups at each time point.

4.5.2.4 General use of imagery in daily life

A rmANCOVA revealed that there was no significant Group x Time interaction for SUIS total scores (F[2, 93]= 0.69, p = 0.51). There were significant main effects of Time (F[2, 93]= 3.87, p = 0.02) and Group (F[1, 94] = 11.94, p = 0.001). Consistent with the fourth hypothesis, planned pairwise analyses revealed that the BD-I group had a higher SUIS total score than the MDD group at each time point (baseline: t = 2.63, df = 98, p = 0.001; 4-week: t = 3.63, df = 98, p < 0.001, 12-week: t = 4.40, df = 98, p < 0.001). Furthermore, there was an unexpected finding of progressive increase in SUIS total scores with time in the BD-I group (F[2, 44] = 3.07], p = 0.05) but not in the MDD group (F[2, 44] = 1.33, p = 0.28). Consistent with the fourth hypothesis, the BD-I group had a higher level of general use of imagery in daily life than the MDD group at each time point. A new finding is that the general use of imagery in daily life appeared to increase with time in the BD-I group only.

4.5.3 Responses to positive affect in bipolar and major depressive disorder groups

A rmANOVA was conducted to assess changes in the Response to Positive Affect (RPA) sub-scales over time for the two groups. There was no significant Group x Time interaction for RPA-Emotion focus sub-scale (F[2, 93] = 0.25, p = 0.78). There were, however, main effects of Group (F[1, 94] = 6.17, p = 0.02) and Time (F[2, 93] = 6.48, p = 0.002). The main effects of covariates and the effects of other interaction factors were not significant (all p-values > 0.10). Consistent with the fifth hypothesis, planned comparisons revealed that the BD-I group had significantly higher levels of RPA-EF than the MDD group at all three time points. Also consistent with the fifth hypothesis, the BD-I group declined in RPA-EF significantly over time (BD-I: F[2, 44] = 3.44, p = 0.04). An unexpected finding is that the MDD group also had a decline in RPA-EF with time: (MDD = F[2, 44] = 3.85, p = 0.03).

For RPA-self-focus sub-scale, there was a significant Group x Time interaction (F[2, 93] = 5.31, p = 0.007). The main effect of Time was significant (F[2, 93] = 5.30, p = 0.007) but the main effect of Group was not significant (F[1, 94] = 0.28, p = 0.60). Also partially consistent with the fifth hypothesis, planned comparisons indicated that there was a progressive decline in RPA-SF levels with time in the BD-I group but not in the MDD group (bipolar: F[2, 44] = 10.11, p < 0.001; MDD: F[2, 44] = 0.27, p = 0.76). However, the RPA self-focus subscale scores were not significantly different between the two groups at each time point.

In summary, partially consistent with the fifth hypothesis, the BD-I group had a higher tendency to ruminate about positive emotions than the MDD group, with a progressive decline in this tendency with resolution of manic symptoms. The BD-I group also had a progressive decline in rumination over positive self-qualities with symptom resolution but this did not differ significantly from the MDD group.

4.5.4 Change in behavioural approach system (BAS) sensitivity

Among the bipolar group, bivariate correlations between the BAS total scores and the current manic symptoms at each time point were not significant (all *p*-values > 0.1). However, the baseline BAS total scores correlated significantly with the YMRS total scores at 4 weeks (Spearman's rho [*r*] = 0.44, *p* = 0.001) and at 12 weeks (*r* = 0.28, *p* = 0.05). However, there was no significant bivariate correlation between the BAS total scores and the current depressive symptoms at each time point (all *p*-values > 0.10). A rmANOVA revealed that there was a significant Group x Time interaction for the BAS total score (*F*[2, 93] = 12.35, *p* < 0.001, partial eta squared = 0.21). There was also a significant main effect of Group (*F*[1, 94] = 19.51, *p* < 0.001), with the BAS total scores being significantly higher in the BD-I group than the MDD group at all time points. The main effect of Time was not significant. No other main effects of co-variates or interaction effects were significant. In summary, consistent with the sixth hypothesis, the BD-I group had higher levels of BAS than the MDD group at each time point. Furthermore, the BAS sensitivity did not change significantly across time in either group.

Table 2: The clinical characteristics and cognitive measures in bipolar I and major depressive disorder groups at baseline, 4 weeks and 12 weeks (*N* = 100)

Time point	Baseline		4 weeks		12 weeks	
Group	Bipolar	Depression	Bipolar	Depression	Bipolar	Depression
YMRS (*SD*)	24.4 (3.44)	2.0 (1.65)	5.0 (4.94)	0.7 (1.33)	3.3 (4.75)	0.4 (1.13)
BDI (*SD*)	6.0 (5.24)	31.8 (8.04)	8.6 (5.41)	15.8 (8.94)	9.7 (7.14)	13.5 (10.01)
IFES positive events (*SD*)	2.3 (0.88)	1.1 (0.98)	1.9 (0.72)	1.2 (0.83)	1.3 (0.86)	1.2 (0.71)
IFES negative events (*SD*)	0.2 (0.44)	1.1 (1.07)	0.2 (0.56)	1.0 (0.80)	0.3 (0.53)	0.2 (0.69)
IFES intrusion score (*SD*)	13.0 (7.73)	13.8 (6.67)	12.0 (6.42)	12.9 (6.39)	9.9 (5.43)	10.6 (5.76)
IFES avoidance score (*SD)*	10.4 (5.74)	12.2 (6.01)	12.1 (3.32)	11.8 (4.61)	13.4 (5.06)	9.9 (5.01)
IFES hypervigilance score (*SD*)	9.6 (6.73)	9.7 (6.63)	8.6 (4.66)	9.5 (4.11)	8.8 (2.49)	9.2 (2.68)
SUIS total (*SD*)	38.3 (11.05)	32.7 (10.14)	41.5 (10.12)	34.1 (10.23)	43.1 (8.23)	35.7 (8.66)
RPA-EF (*SD*)	16.2 (3.21)	15.1 (2.92)	15.6 (2.28)	13.4 (4.22)	14.6 (3.16)	13.5 (4.55)
RPA-SF (*SD*)	12.0 (2.96)	11.2 (2.36)	11.8 (2.10)	11.5 (2.42)	9.8 (2.34)	11.4 (2.85)
BAS Scale total (*SD*)	39.2 (4.31)	37.4 (3.70)	39.6 (6.10)	32.5 (8.01)	41.2 (3.09)	35.1 (8.70)

YMRS: Young Mania Rating Scale; BDI-II: Beck Depression Inventory-II; IFES: Impact of Future Events Scale; RPA-EF: Response to Positive Affect Questionnaire- Emotion Focus Sub-scale; RPA-SF: Response to positive Affect Questionnaire: Self-Focus Subscale; BAS Scale: Behavioural Approach System Scale

4.5.5 The prediction of recovery from mania by BAS sensitivity and mental imagery susceptibility

Logistic regression modelling was first performed with recovery from mania or not as the dependent variable, with BAS total scores at baseline, 4 weeks, and 12 weeks as independent variables in the BD-I group. Covariates entered included gender, years of

education, illness duration, and BAI total score. The overall model was significant (Nagelkerke R^2= 0.17). Consistent with the seventh hypothesis, the status of recovery from mania in the BD-I group was predicted negatively by the baseline BAS sensitivity (BAS total score: *B* = -0.27, *SE* = 0.13, *wald* = 4.76, *df* = 1, *p* = 0.03, exp[*B*] = 0.46), but not by the BAS sensitivity at 4 weeks (*B* = -0.14, *SE* = 0.08, *wald* = 2.70, *df* = 1, *p* = 0.06, exp[*B*] = 0.87) or 12 weeks (*B* = -0.18, *SE* = 0.13, *wald* = 2.01, *df* = 1, *p* = 0.16, exp[*B*] = 0.83). In summary, baseline BAS sensitivity was a negative predictor of recovery from mania at twelve weeks.

Another set of logistic regression modelling was conducted using the same dependent variable of recovery from mania or not in the BD-I group. The independent variables included changes in IFES total scores, changes in SUIS total scores, changes in the IFES positive and negative events. Co-variates included were identical as in the above logistic regression modelling. The results revealed that the status of recovery from mania in BD-I group was predicted significantly by the mental imagery susceptibility measures (Nagelkerke's R^2= 0.53). Specifically, recovery from mania was predicted by the decline in the number of positive prospective images from baseline to 12 weeks (change in IFES positive events: *B* = 1.79, *SE* = 0.61, *wald* = 8.70, *df* = 1, *p* = 0.003, exp[*B*] = 5.99) and by the decline in the number of negative prospective images as measured by IFES negative events from baseline to 12 weeks (change in IFES negative event: *B* = 2.49, *SE* = 1.03, *wald* = 5.81, *df* = 1, *p* = 0.02, exp [*B*] = 12.03). Recovery status was also predicted by an increase in general use of imagery in daily life from baseline to 12 weeks (SUIS total score: *B* = -0.18, *SE* = 0.07, *wald* = 7.61, *df* = 1, *p* = 0.006, exp[*B*] = 0.83). In summary, consistent with the eighth hypothesis, the decline in positive prospective images was predictive of recovery from mania at 12 weeks. Additionally, and unexpectedly, both the decline in negative prospective imagery and the increase in the general use of imagery in daily life were also predictive of recovery of mania at 12 weeks.

4.5.6 Prediction of switching from bipolar mania to bipolar depression at 12 weeks

Logistic regression modelling showed that the status of a mood switch from mania to depression at 12 weeks in the BD-I group was predicted significantly by the mental imagery susceptibility measures (Nagelkerke's R^2= 0.53). Consistent with the last hypothesis, a mood switch to depression was predicted negatively by the decrease in the number of negative prospective images from baseline to 12 weeks (change in IFES negative events: B =-3.13, SE = 1.27, $wald$ = 6.06, df = 1, p = 0.01, exp(B) = 0.04). No other variables were found to be significant predictors.

4.6 Discussion

This is the first prospective study examining the relative changes in mental imagery susceptibility and response to positive affect measures with time in participants suffering from acute bipolar mania.

4.6.1 Positive prospective images from baseline to 12 weeks

The first key finding is that the number of positive prospective images decreased with the resolution of manic symptoms from baseline to 12 weeks in the BD-I only. A reduction in the number of positive prospective images from baseline to 12 weeks was a positive predictor of recovery from mania in the BD-I group. Conversely, one might extrapolate and argue that an increase in positive prospective images might lead to an ascent of manic symptoms in BD-I. Previous studies have suggested that mania might be triggered by goal-attaining positive life events while depression by goal-frustrating negative life events in BD (Johnson et al.,

2000; Johnson et al., 2008). Positive prospective imagery may depict 'goal-attaining life events' in the mind's eye (see Section 1.1.8.1 for details). In other words, a required fuel to kindle the bush of 'manic fire' as proposed in Chapter 1 might depend on the emergence of positive prospective images against a background of heightened trait imagery use and emotional impact of prospective imagery in remitted BD-I. However, it is also possible that positive prospective images might simply be the products of elated mood, therefore dropping as manic symptoms reduce. This possible explanation was first addressed in this study by examining whether the emotional valence of the listed IFES events reported by the participants would be congruent with professionals without known mood problems. To explore this hypothesis further, linear regression modelling was conducted again with the change in the number of positive prospective images from baseline to twelve weeks as the dependent variable and the dichotomous variable of recovery from mania or not as one of the independent variables. The results revealed that recovery from mania was not a significant predictor of the change in the number of positive prospective imagery ($B = 0.39$, $SE = 0.33$, $beta = 0.16$, $t = 1.17$, $p = 0.25$).

4.6.2 Negative prospective images from baseline to 12 weeks

The current study found that the number of negative prospective images did not change significantly with resolution of mania in the BD-I group as a whole. However, further sub-group analysis revealed that the BD-I subgroup with a mood switch to depression showed a progressive increase in the number of negative prospective images. Apart from playing a possible role in a mood switch to depression, negative future-oriented images might contribute to recovery of mania, as a drop in the number of negative prospective images from baseline to 12 weeks positively predicted recovery. Previous studies have found that mood lability, irritability and 'short depressive contaminations' (Bonsall et al., 2011; Winokur, 1979) were reported by over 70% of patients in acute mania (Goodwin & Jamison, 2007), all of

which are likely to be associated with negative intrusive images (Holmes et al., 2008; Holmes et al., 2011). A reduction in negative prospective images might therefore bring about a drop in these associated mood symptoms like irritability and anger. Presence of negative life events were also associated with delayed recovery from any mood episodes of BD (Johnson et al., 1997). As such, a drop in negative prospective images, as a possible proxy of negative life events, with time may be important in promoting recovery from mania (see Section 1.1.8.2). A possible alternative explanation is that many eligible participants initially confirmed to be suffering from BD-I with acute mania might subsequently develop depressive symptoms (i.e. both manic and depressive symptoms simultaneously or both types of symptoms rapidly alternating within a very short period of time). As such, a recovery from 'mania' would imply a simultaneous resolution of both manic and depressive symptoms, each of which might be associated with a drop in positive and negative prospective images with time respectively. A third possible explanation is the negative IFES events being the products of mood episode as cited in the last section. To examine this hypothesis, similar linear regression modelling was conducted using recovery from mania or not as one of the independent variables and the change in the number of negative prospective images from baseline to twelve weeks as the dependent variable. The results again revealed that recovery from mania was not a significant predictor of the change in the number of negative prospective imagery ($B = 0.29$, $SE = 0.18$, $beta = 0.22$, $t = 1.58$, $p = 0.12$). Further prospective studies on the relative changes of prospective images of both positive and negative emotional valences with time in a large sample of patients with bipolar I disorder.

Apart from playing a role in the possible descent of mania, prospective imagery may also play a role in the ascent of bipolar depression. The current study provided some indirect evidence for this hypothesis by examining the change in the number of prospective images in a sub-group of the BD-I patients with a switch from mania to depression by 12 weeks. The reduction in the number of negative prospective imagery from baseline to 12 weeks was a

negative predictor of a mood switch in this sub-group. In other words, switching from mania to depression among the BD-I group might be associated with a persistently elevated level of negative prospective images at least, or even an increase in the number of negative prospective images from baseline to 12 weeks. This finding provides additional support for the above hypothesis that emotionally distressing negative prospective images might act as 'proxy' negative life events in triggering the onset of bipolar depression. This echoes Gregory et al.'s (2010) finding that patients with BD reported having positive future-oriented images during hypomania and having negative intrusive memories and images during depressive phase.

However, these findings should be interpreted with caution as the mood switch in the current study was defined by having BDI-II total levels higher than 20 and YMRS total scores lower than 8 at both 4 weeks and 12 weeks. Although a key inclusion criterion of the BD-I group is the presence of the DSM-IV-TR diagnosis of bipolar I disorder, current manic episode at baseline, one could argue that the bipolar patients fulfilling the above BDI-II and YMRS criteria of a mood switch were simply having an unremitted mixed affective episode evolved throughout the study period. The YMRS total and BDI-II total scores at 4 and 12 weeks might have reflected the brief periods when the mood state has swung from brief mania to brief depression. In other words, a drop in negative prospective images could simply be considered a negative predictor of a switch from predominantly manic to depressive symptoms within an index mixed affective episode rather than a mood switch from mania to depression within an index manic episode. However, this finding would still provide some preliminary data on the role of negative prospective images in inducing depressive symptoms in BD-I. The above findings should thus be replicated in a larger sample of patients with BD-I being followed up longitudinally from euthymia to acute bipolar depression.

4.6.3 Emotional impact of prospective imagery

The current study found that BD-I group as a whole did not have significant differences in IFES total scores when compared to MDD at each time point. The lack of differences between the two groups at 12 weeks is congruent with the finding in Study 1 that the IFES total scores were similar in the remitted BD and MDD groups. The lack of significant differences at baseline and 4 weeks between the two groups suggests that BD-I group with acute mania did not experience higher emotional impact of prospective imagery than the acute MDD group. This finding has to be viewed with reference to previous findings that bipolar depression had higher levels of IFES total scores than unipolar depression (Hales et al., 2011). One possible explanation might be that anxiety was not controlled in Hales et al.'s (2011) study. Another possible explanation might be that bipolar mania might have a different emotional response to prospective images from bipolar depression.

As discussed in Section 4.1, IFES was originally designed to capture the negative impact of intrusive prospective images. However, if mania is associated with pleasant and exciting images of future success and personal fame, these are likely to be appraised as enjoyable and indulging. Therefore, the IFES-A subscale scores would be expected to be lower in mania than in depression. This hypothesis is supported by the finding that the IFES-A subscale scores were higher in acute MDD group than in the BD-I manic group at baseline. A further support also came from the additional finding that the IFES-A subscale scores increased with time only in the BD-I sub-group with a mood switch from mania to depression.

Unlike the IFES avoidance sub-scale, the intrusion and hypervigilance sub-scales capture the experiences associated with the intrusive occurrence and the physiological arousal associated with prospective images respectively. The current study revealed that the BD-I sub-group with a switch from mania to depression would experience increased avoidance towards the reported images. On the other hand, BD-I subgroup that eventually recovered or

at least did not have a mood switch to depression appraised their images as progressively less intrusive and sudden in occurrence. Interestingly, there were no significant differences in hypervigilance sub-scale scores between the two groups with time implying that this dimension of emotional impact might be less relevant to the change in mood state in BD-I.

The above findings suggest that emotional responses to prospective images might undergo subtle changes in various dimensions as BD-I progresses from one mood state to another. Future studies should prospectively follow two BD-I groups, one with mania and another with depression, and measure the changes in the IFES sub-scale scores to understand better about the differential appraisals of images during different mood states. In addition, new scales should be devised to measure the specific emotional responses to positive prospective imagery and to reflect positive aspects of intrusion and hypervigilance associated with pleasant and exciting images.

4.6.4 General use of imagery in daily life

The third key finding is that general use of imagery in daily life was elevated among patients with BD-I when compared with MDD regardless of symptom severity. Study 1 concurred that the level of general use of imagery in daily life among patients with remitted BD-I was higher than that of patients with remitted MDD or non-psychiatric controls. Combined with findings in Studies 3 to 5, the current finding suggests that general use of imagery in daily life might be a trait cognitive marker associated with bipolarity.

Another intriguing finding is that the levels of general use of imagery increased from acute symptomatic to euthymic states. In other words, the tendency to visualise thoughts as visual images was more pronounced when participants with BD-I were in a euthymic state than in an acute manic state. This finding corroborates with another key finding that an increase in general use of imagery in daily life could enhance recovery from mania in BD-I

group. This might be explained by a repetition effect, as the participants might not have noticed their use of visual images in daily life but repeated reminders in the form of SUIS questionnaires could increase awareness of these cognitive activities, resulting in greater endorsement of these items. One might then assume this repetition effect would also be detected in participants with MDD. However, this increase in general use of imagery in daily life with time was only observed in the BD-I group. In addition, one might not expect repetition effect to be a possible predictor of recovery from mania.

A second possible explanation is that certain cognitive or unknown factors (e.g. thought disorder) associated with acute mania might lead to an under-reporting bias of the tendency of general use of imagery in daily life. As mania resolves together with the improvement of these cognitive or other factors, patients might become capable of better understanding the SUIS questionnaire or become more aware of their tendency to think in visual images. Several neuro-cognitive variables including visual attention and ideational fluency have been reported to be impaired during acute mania in BD-I patients and were predictive of recovery from acute mood exacerbation (Jaeger et al., 2007). Future studies should incorporate these important neuro-cognitive variables as potential confounders in the investigation of the relationships between general use of imagery in daily life and recovery of bipolar mood episodes.

There is also a third possible explanation. Holmes et al. (2008) previously postulated that increased use of imagery might allow novel combinations of past and future scenarios and promote creativity, an important attribute of problem-solving skills (Murray & Johnson, 2010). Study 5 reported that the general use of imagery in daily life was a predictor of visual creativity (see Chapter 7). If high general use of imagery enhances creative problem-solving, this would facilitate effective resolution of life events (e.g. financial loss following reckless purchase of luxury items during mania) associated with delay in recovery from mania (Yan-Meier et al., 2011). If this were indeed the case, this would imply that the general use of

imagery in daily life might be a state and trait marker of bipolarity. Direct experimental studies that manipulate the general use of imagery in daily life are required to clarify whether increased visualising ability is indeed associated with enhanced problem-solving abilities and effective resolution of crises in BD-I.

4.6.5 Response to positive affect

The fourth key finding is that participants with BD-I tended to ruminate excessively about their positive emotions during mania. With the progressive decrease in the pathological positive emotions associated with mania, levels of rumination also declined progressively with time (i.e. a state factor). However, the levels in the BD-I group remained higher than those in MDD controls at 4 and 12 weeks, suggesting that positive rumination might be persistently elevated even in euthymic state in BD-I. This finding suggests that rumination about positive emotions might function as a trait and state factor synonymous with negative rumination for depression in BD-I (Just & Alloy, 1997; Nolen-Hoeksema, 2000). The finding is also consistent with the findings in the other studies of this thesis (Gruber et al., 2011; Studies 1, 3, and 5).

The finding of a progressive drop in rumination about positive emotions in MDD might sound counter-intuitive, as the MDD group would be expected to have a progressive decrease in negative emotions but an increase in positive emotions with recovery. While type I error associated with multiple comparisons might explain this intriguing finding, one should bear in mind that patients with depression do have a varying degree of bipolarity (see Section 1.1.1.1 and 1.1.1.5 and Chapter 5 for discussion on the dimensional views of bipolar spectrum disorders). Previous studies have found that mixed depression was associated with more suicidal ideation than pure MDD (Balazs et al., 2006), a critical clinical feature leading to acute psychiatric admission. This hypothesis of ‘mixed depression’ in this MDD group is

partially supported by the presence of sub-threshold though clinically non-significant hypomanic symptoms as measured by YMRS total scores. In other words, the positive emotions might provide a fuel for positive rumination, which dropped progressively with resolution of depression over time. The third possible explanation is that rumination over positive emotions might reflect an intense cognitive effort by the participants with MDD to combat the surge of negative feelings associated with depression. The use of this coping strategy would therefore reduce with gradual resolution of depression with in-patient treatment over time.

However, contrary to the fifth hypothesis of the current study, the rumination about positive self-qualities was found to be not significantly different between the two groups at each time point. This finding is not consistent with the finding of higher RPA-SF levels in remitted BD-I when compared to remitted MDD in Study 1. Furthermore, there was a progressive drop of RPA-SF with time in the BD-I group only. In other words, the results suggest that both BD-I and MDD groups had spent similar effort in dwelling upon the meanings associated with their positive self-qualities and attributes. With the resolution of manic symptoms in the BD-I group, it is conceivable that grandiose self-views for rumination would decline with time. What is more intriguing is that the MDD group had similar levels of positive rumination about personal attributes as the BD-I group. While the above hypotheses on rumination over positive emotions in MDD might account for the similar levels of RPA-SF in both groups, they cannot explain why the MDD group did not show a decline in RPA-SF with time. Again, type II error associated with the small sample of the current study might also explain the current non-significant findings. Further studies on the changes in responses to positive affect among patients with MDD are required to understand how these might contribute to the course and development of depression (Raes & Hermans, 2008; Raes et al., 2012).

4.6.6 Behavioural approach system changes

The BAS did not correlate with the current manic symptoms in a state dependent manner. However, baseline BAS correlated with manic symptoms at 4 weeks and 12 weeks, suggesting that baseline BAS predicted relative intensification of manic symptoms over time as previously suggested by Meyer et al. (2001). The additional finding that BAS level was higher in the BD-I group when compared with the MDD group at each time point is consistent with previous findings of BAS hyper-sensitivity in BD (Carver & White, 1994; Urosevic et al., 2007; Study 1 of the current thesis). The lack of significant changes over time also suggests that BAS was relatively stable irrespective of mood symptom changes across time (Alloy et al., 2008; Alloy et al., 2012; see Section 1.1.2.4). Moreover, the two findings corroborate with the last finding that baseline BAS was a negative predictor of recovery of mania at 12 weeks in the BD-I group. In other words, BAS hypersensitivity predicted intensification of manic symptoms over time and retarded recovery from a manic episode in BD-I. Overall, the above evidence appears to support the hypothesis that BAS sensitivity might be a vulnerability or trait marker of BD.

4.7 Strengths and limitations

The current study is the first prospective study to examine changes of mental imagery characteristics and responses to positive affect from manic to euthymic state in BD-I. The follow-up duration was long enough to allow recovery from mania for an appreciable proportion of the sample, thus enabling separate examination of changes in mental imagery characteristics in participants with recovery from mania and participants with a mood switch within the index manic episode. The study also statistically controlled for potential

confounders of the relationship between mental imagery susceptibility and mood symptoms like anxiety symptoms.

However, there are also a number of limitations. The sample size was small so the lack of significant decline in certain cognitive constructs between groups (e.g. the RPA-SF subscale and IFES-I/IFES-H sub-scales) and across time (e.g. BAS total score) might be due to type II errors rather than a true reflection of the stability of the cognitive constructs with time and mood changes. The small sample size also limited the chance to reliably test the predictive effects of interaction factors of positive imagery and positive rumination on recovery from mania.

Another major limitation is that the sample was exclusively recruited from an in-patient unit. This could lead to potential selection bias for participants with poor clinical outcome and prognosis, as well as an atypical sample of depressed patients with varying degrees of bipolarity (c.f. mixed depression as discussed in Section 4.6.5). The assumption that recovery from mania could be defined as having a YMRS total score<7 at both 4 weeks and 12 weeks might have resulted in the inclusion of some participants with a relapse of mania between four and twelve weeks but recovered by twelve weeks. As such, some of these participants could be regarded as having an unstable course of illness rather than a full recovery from mania. Furthermore, the diagnoses of complete recovery and mood switch were based on a priori defined YMRS and BDI-II scores rather than structured clinical interviews. Although the choice of cut-off thresholds were based on previous studies, some participants fulfilling the threshold values of YMRS and BDI-II might not be diagnosable clinically as having mania or depression. This might then lead to an over-estimate of the number of bipolar participants with complete manic recovery and with subsequent mood switch.

CHAPTER 5 - Study 3: Mental imagery in sub-threshold bipolar disorders and major depressive disorder: is there a difference between the two groups?

5.1 Introduction

5.1.1 Sub-threshold bipolar disorder as a bipolar spectrum disorder

Bipolar disorders (BD) are conventionally classified into bipolar I (BD-I) and bipolar II disorders (BD-II) (APA, 2000; Dunner, Fleiss & Fieve, 1976). This classification, however, is not without controversy. Recent experts have suggested that bipolar spectrum disorders (BSD) should be expanded to include other milder bipolar conditions than BD-I and BD-II (e.g. cyclothymia, recurrent hypomania, antidepressant-induced hypomania, and 'minor' elated states) (see Section 1.1.1.5). Angst, Gamma & Lewinsohn (2002) argued that the 'minor elated states' were characterized by either elation and hyperactivity of shorter duration (i.e. fewer than four days in duration) or milder severity (i.e. fewer than four symptoms characteristic of hypomania) than current DSM-5 criteria of hypomania (e.g. sub-threshold hypomania [sub-threshold BD], Angst et al., 2003; Angst et al., 2010; or minor clinical hypomania, Malik et al., 2014; Rock et al., 2013). When examining hypomanic scores dimensionally across a group of patients with MDD, or with BD-II, or a combined sample of MDD and BD-II, the distribution of the hypomania scores was found to be normally, rather than bimodally, distributed (Akiskal & Benazzi, 2006). Of particular clinical importance are the findings that, in comparison to patients with MDD, those with sub-threshold BD had more frequent suicide attempts, higher rates of familial bipolar disorders, greater comorbidity with anxiety, impulse control and substance use disorders, more irritability and agitation, as well as more severe and recurrent episodes of depression (Angst et al., 2010; Benazzi & Akiskal, 2003). Current evidence appears to support the assertion that BSD might encompass a range

of conditions from depression with varying degrees of bipolarity (hypomanic scores) to full-blown BD-I (see section 1.1.1 for the historical evolution of bipolar concepts and BSD).

5.1.2 Mental imagery susceptibility as a possible explanation of emotional instability and common co-occurrence of anxiety disorders in bipolarity

A puzzling question is *if* and in case *how* sub-threshold hypomanic symptoms in MDD might exacerbate the clinical severity of depression, worsen its course, and lead to the co-occurrence of anxiety disorders. There is evidence suggesting that sub-threshold bipolarity in MDD may be associated with increased mood instability resulting in frequent depressive recurrences (Angst et al., 2010). If poor clinical outcome of MDD with a past history of sub-threshold bipolarity are associated with its underlying emotional instability (Angst et al., 2010), a possible extension of this research is to understand whether factors associated with emotional instability in BD may also be found in individuals with sub-threshold BD. Furthermore, previous studies have found that patients with BD were more likely to suffer from anxiety disorders than MDD, possibly suggesting some shared genetic inheritance in BD and anxiety disorders (MacKinnon et al., 2002). One possible candidate for inducing emotional instability might be mental imagery susceptibility, which has been shown to be associated with BD. Patients with BD with an unstable course of illness were found to have higher levels of mental imagery susceptibility than those with a relatively stable course of illness (Holmes et al., 2011). Furthermore, Holmes et al. (2008) hypothesized that enhanced mental imagery susceptibility in BD might be a missing link that explains the high comorbidity of anxiety disorders in BD. In other words, mental imagery susceptibility might be a putative candidate of the shared inheritance between BD and anxiety disorders (see Sections 1.1.6, 1.1.7, & 1.1.8.1).

Study 1 and Study 2 provided preliminary evidence that both general use of imagery in

daily life and emotional impact of prospective imagery might be trait markers of BD-I. So far, there were no published data indicating that the levels of mental imagery susceptibility in sub-threshold BD were also higher than in MDD. If these imagery characteristics are trait markers of bipolarity, it could be hypothesised that they would also be elevated in people with milder variants of BSD (e.g. cyclothymia, recurrent hypomania or sub-threshold BD). Furthermore, Study 2 provides preliminary evidence that positive and negative prospective images might be associated with bipolar mania and depression respectively in BD-I. As such, high trait use of imagery and strong emotional responses to prospective images might lead to frequent occurrence of emotionally powerful images in BD-I. As a consequence, people with BD-I would experience frequent and extreme mood fluctuations, which is commonly regarded as emotional instability. Inter-episode sub-syndromal mood symptoms were associated with shorter time to subsequent relapses in BD (Judd et al., 2003). In other words, mental imagery susceptibility is associated with the number of past and future recurrences in BD-I. As aforementioned, sub-threshold BD is distinguished from MDD by having more frequent depressive recurrences (Angst et al., 2010). If sub-threshold BD is also associated with increased mental imagery susceptibility as BD-I, emotional instability induced by this heightened imagery susceptibility might be related to the frequent depressive recurrences in sub-threshold BD. The current study would investigate whether mental imagery susceptibility might predict the depressive recurrences.

5.1.3. Positive rumination, mental imagery susceptibility and sub-threshold bipolarity

Studies 1 and 2 provide preliminary evidence that positive rumination, especially rumination about positive emotions, might be a trait factor of bipolarity. If positive rumination was also shown to be elevated in sub-threshold BD, this would provide converging evidence that these constructs might be trait markers associated with bipolarity.

Furthermore, Study 1 provided some new evidence that patients with BD might excessively savour and ruminate about their visual future-oriented images, thereby leading to an activation of the behavioural approach system (BAS) and an array of symptoms characteristic of BD-I.

Although previous qualitative and quantitative studies have suggested that bipolar depression might be associated with intrusive negative prospective images (Gregory et al., 2010; Hales et al.,2011), the exact cognitive mechanism of negative prospective images leading to depressive symptoms remains to be elucidated. Previous studies have found that people with BD had a strong ruminative response to negative affect (Alloy et al., 2006; Johnson, McKenzie, McMurrich, 2008). Furthermore, excessive responses to negative affect strongly predicted lifetime frequency of depressive recurrences in BD-I (Gruber et al., 2011). If rumination about positive images might amplify positive emotions in BD-I (Gruber et al., 2009; Gruber, 2011; Study 1) and depressive rumination might lead to onset and recurrence of MDD (Nolen-Hoeksema, 2000), one related and testable hypothesis would be that rumination about negative prospective images might be a common cognitive mechanism that amplifies depressive symptoms in both BD and MDD. The current study sought to examine whether rumination about negative prospective images could predict depressive symptoms in a sample of depressed participants with varying degrees of bipolarity.

5.2 Aims and objectives

1. Compared with the MDD group, the sub-threshold BD group would have higher levels of general use of imagery and emotional impact of prospective imagery.
2. The levels of current anxiety symptoms and the presence of anxiety disorder will be predicted by mental imagery susceptibility measures in the whole sample group.
3. The presence of two or more episodes of prior episodes of depression will be predicted by the mental imagery susceptibility measures in the whole sample of participants with

depression with varying degrees of bipolarity.

4. Compared with the MDD group, the sub-threshold BD group would have higher levels of positive rumination.
5. The levels of lifetime hypomanic symptoms will be predicted by mental imagery susceptibility measures and positive rumination measures in the whole sample. The levels of current depressive symptoms will also be predicted by mental imagery susceptibility and negative rumination across the whole group. Furthermore, the relationship will be specifically predicted by the interaction variable of negative rumination and the number of negative prospective images across the whole group.

5.3 Study methods

5.3.1 Participant recruitment

Participants were recruited from a sub-sample of the Hong Kong Mental Morbidity Survey (HKMMS) using a random sample of Chinese adults aged 16 to 65 in Hong Kong (*N* = 5700) (see Section 2.5 for further details). Inclusion criteria for the current study were: (1) being a participant of the HKMMS study; (2) having a preliminary diagnosis of ICD-10 defined MDD verified by the Chinese version of Clinical Interview Schedule- Revised (CISR; Lewis et al., 1992; Lam et al., 2014a); (3) being screened to be free from current psychotic or manic symptoms by the Psychosis Screening Questionnaire (Bebbington & Nayani, 1995); (4) a diagnosis of the following disorders based on the Chinese Bilingual Structured Clinical Interview for DSM-IV-TR, Axis-1 Patient Version (CB-SCID-I/P; So et al., 2003a): MDD, single or recurrent episodes, or BD-I/-II. Exclusion criteria included being: (1) incapable of giving informed consent; (2) acutely suicidal or violent so as to demand immediate psychiatric attention; (3) diagnosed by CB-SCID-I/P (So et al., 2003b) to have a

primary Axis I diagnosis other than BD-I/-II or MDD. The study was approved by the local research ethics committee (reference number: KC/KE-13-0004/ER-2).

5.3.2 Assessment measures

5.3.2.1 Baseline demographic measures

Baseline demographic data of the recruited participants were retrieved from the database of the HKMMS. Data of interest included gender, age, years of education, and current employment status. Additional data were recorded in a demographic data questionnaire during the interview: family history of affective disorders, and having received treatment for MDD.

5.3.2.2 Clinical measures

The Chinese-bilingual Structured Clinical Interview for DSM-IV-TR Disorders (Axis I, Patient version) (CB-SCID-I/P; So et al., 2003a; 2003b): The author and another experienced psychiatrist administered the CB-SCID-I/P. They achieved good agreement in administering the CB-SCID-I/P (kappa agreement (*k*) for mood disorder module = 0.98; *k* for psychotic module =0 .99; *k* for anxiety disorder module = 0.98) before commencing the current study.

The criteria recommended by Zimmerman et al. (2009) were used to identify past history of sub-threshold hypomania among participants with MDD as defined by CB-SCID-I/P (So et al., 2003a). The presence of sub-threshold hypomanic symptoms was defined as having either: (1) elated or expansive mood which created troubles or was noticed by others as a change in functioning for a period of at least four days, but DSM-IV-TR hypomania criterion B (meeting the required minimum number of symptoms) is unmet; or (2) unusually irritable mood expressed by starting arguments, shouting or hitting people, and having at least three other manic symptoms, but criterion D (symptoms observable by others) is not met. For

the identification of sub-threshold hypomania using Zimmerman *et al*.'s (2009) criteria, the two investigators achieved an excellent agreement in the categorical diagnosis of the presence or absence of sub-threshold hypomania (weighted kappa agreement = 1.0) using videotaped interviews of ten cases of sub-threshold BD and ten cases of MDD.

The Hypomania Checklist-32 (HCL-32; Angst et al., 2005): For the current study, the scale containing the core 32 questions has a good internal consistency (Cronbach's alpha = 0.91).

The Young Mania Rating Scale (YMRS; Young et al., 1978): The two investigators again achieved excellent inter-rater reliabilities for identifying all conditions (all weighted kappa agreements => 0.90).

The Beck Depression Inventory-Second Edition (BDI-II; Beck et al., 1996): The validated Chinese version was used in the current study (Bryne, Stewart & Lee, 2004). The BDI-II also has a good internal consistency (Cronbach's alpha = 0.89) in the current study.

The Beck Anxiety Inventory (BAI; Beck, 1988): The validated Chinese version was used (Che, 2006). For the current study, the BAI also has a good internal consistency (Cronbach's alpha = 0.92).

5.3.2.3 Imagery and response to positive and negative affect measures

Spontaneous Use of Imagery Scale *(*SUIS; Reisberg et al., 2003): In the current study, the Chinese version of the scale was found to have good internal reliability (Cronbach's alpha = 0.78).

The Impact of Future Events Scale (IFES; Deeprose & Holmes, 2010): In the current study, the Chinese version of IFES had a good internal consistency (Cronbach's alpha = 0.82).

Response to Positive Affect Scale (RPA; Feldman et al., 2008): These two sub-scales of the Chinese version of RPA had good internal consistencies in the current study (Cronbach's alphas: RPA-EF = 0.84; RPA-SF = 0.74).

Ruminative Response Scale-Short Form (RRS-SF; Treynor, Gonzalez, Nolen-Hoeksema, 2003): For the current study, the validated Chinese version of the scale (Ng & Dinesh, 2008) had a good internal consistency (Cronbach's alpha = 0.75).

5.4 Statistical analysis

STATA Version 12 was used for statistical analyses (STATACorp, 2011). Sample size calculation was based on the mean standardized difference in IFES (mean standardized difference = 1.25) between participants with bipolar depression and those with pure MDD (Hales et al., 2011), as no previous study had compared the differences in IFES total scores between sub-threshold BD and pure MDD. Ten participants would be required in each group to achieve a power of 80% and a two-sided alpha significance level of 0.05.

Analysis of variance (ANOVA) was used to compare the groups if the data were normally distributed or could be transformed into normality. For data that were not normally distributed or could not be transformed into such, non-parametric analyses were used. If any of the demographic variables were found to be significantly different across the groups, they were first examined for collinearity. If certain variables were found to be high in collinearity with each other, the one with the highest correlations with all other correlated variables was selected as the covariate for subsequent analysis of co-variance (ANCOVA) with other un-correlated important covariates. Boot strapping method was employed in view of the small cell sizes in the BD-II and sub-threshold BD groups. Planned pairwise least significant difference (LSD) comparisons were conducted if the overall ANCOVA model was found to be significant. Categorical data were compared using chi-square tests.

Hierarchical stepwise regression was used to assess the predictive values of mental imagery susceptibility on current depressive and anxiety symptoms after entering the theoretical and statistically significant covariates for the whole sample. Similarly, hierarchical

stepwise regression was used to assess the predictive values of positive rumination (RPA-EF and RPA-SF) and mental imagery measures on lifetime hypomanic symptoms after entering the theoretical (gender) and statistically significant covariates (age and years of education) for the whole sample. Logistic regression modelling was used to assess whether the clinical and mental imagery and ruminative response measures would be predictive of having two or more episodes of prior lifetime depressive episodes (two episodes being the median of the number of prior lifetime depressive episodes for the whole sample) and the presence of co-morbid anxiety disorders for the whole sample. If any of the clinical measures were found to be significant, Sobel's test (Sobel, 1982) was used to test whether the clinical measures would mediate the relationships between mental imagery susceptibility measures and the above two dependent categorical variables for the whole sample.

As hypomanic scores were found to be normally distributed across a combined sample of patients with BD-II and MDD (Akiskal & Benazzi, 2006), it is possible that the cognitive mechanisms that underline emotional instability, comorbidity with anxiety symptoms, and amplify hypomanic/depressive symptoms might also be at play in depression with varying degrees of bipolarity. Therefore, all regression models of the current study were conducted using the whole sample.

5.5 Results

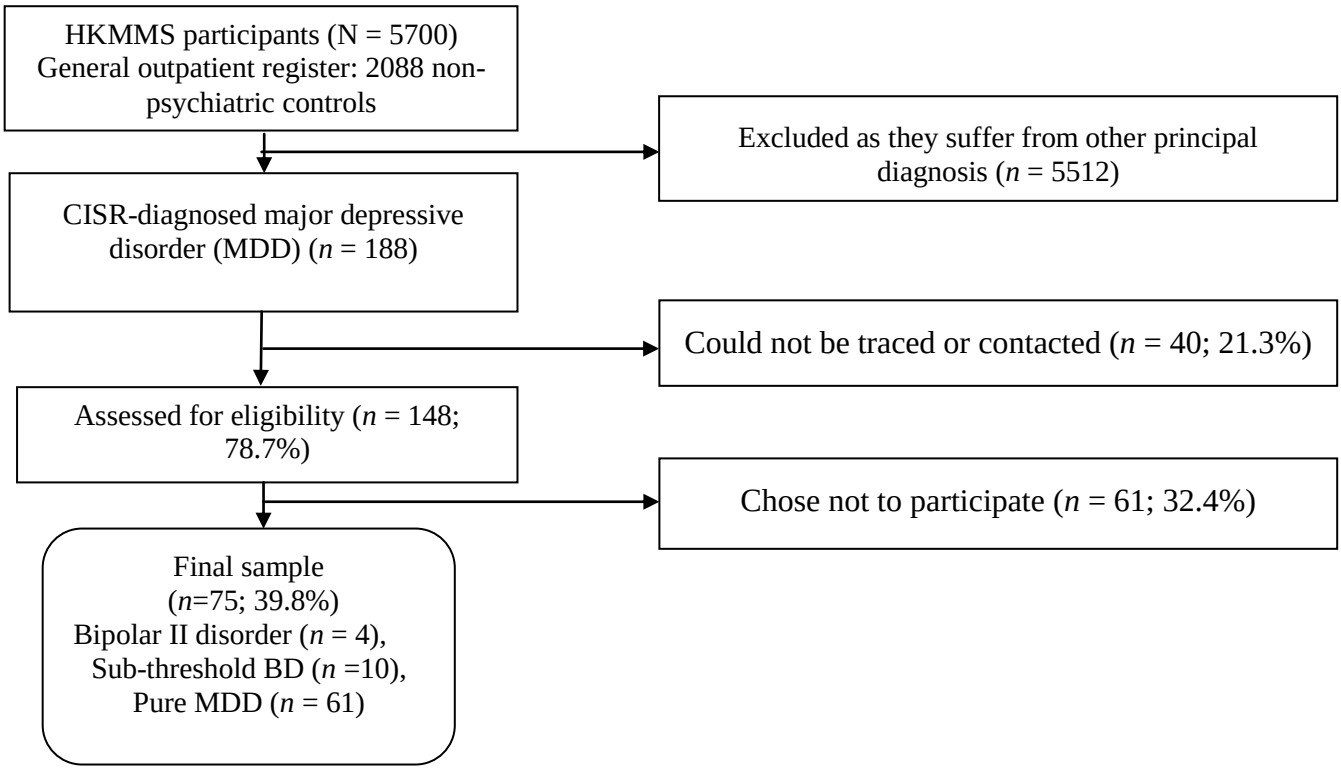
5.5.1 Participants' recruitment

188 participants out of 5700 participants of the HKMMS were identified as suffering from MDD using the CIS-R (Lam et al., 2014b). After a lapse of four to six months between the completion of the HKMMS interview and the commencement of the current study (mean lapse = 4.7 months), 78.7 % of participants (n = 148) were successfully re-contacted after

three repeated phone calls. After an initial phone explanation about the nature of the current study, 61 participants declined to participate. However, they provided verbal consent for utilising their existing data in HKMMS for preliminary analysis in the current study. Reasons for refusal to participate included lack of interest (n = 31) or time (n = 30). There were no differences in gender, age, years of education, geographical location, total scores of the Beck Hopelessness Scale (BHS; Beck, Weissman, Lester & Trexler, 1974) and the Beck Scale for Suicidal Ideation-Current Version (SSC-I; Beck, Kovacs & Weissman, 1979) as recorded in the HKMMS baseline data between those who participated (n = 87) and those who did not participate (n = 61).

Among the 87 participants screened to have MDD by CIS-R (Lewis et al., 1992), 12 (13.79%) were subsequently confirmed by the CB-SCID-I/P (So et al., 2003a) as not having any lifetime or current episode of MDD: four being free from any lifetime or current psychiatric diagnosis, six suffering from adjustment disorder, one suffering from obsessive-compulsive disorder, and one suffering from paranoid schizophrenia. Figure 1 depicts the sample recruitment process. The subsequent analyses were based on data obtained from 75 participants confirmed to be suffering from BD-II (n = 4), sub-threshold BD (n = 10) and pure MDD (n = 61).

Figure 1: Sample recruitment (N=75)



HKMMS: Hong Kong Mental Morbidity Survey; CIS-R: Clinical Interview Schedule- Revised

5.5.2 Demographic and clinical characteristics

Table 1 shows the demographic and clinical characteristics of the three groups. The three groups were not significantly different in gender distribution, employment status and family history of affective disorders. The sub-threshold BD group had a significantly lower mean age, a higher mean number of years of education, as well as a longer illness than the MDD group The three groups had similar proportions of participants currently on medications, which were approximately 50%. As age was highly correlated with years of education (Pearson's correlation = 0.45, $p < 0.001$) and illness duration (Pearson's correlation = 0.55, $p < 0.001$) and was more reliably measured than the other two demographic variables, age was selected as the demographic co-variate.

The BD-II and sub-threshold BD groups had significantly higher levels of BDI-II total

scores than the MDD group (BD-II =21.3 [*SD*=12.18] vs. sub-threshold BD = 23.8 [*SD* = 7.36] vs. MDD =15.0 [*SD* = 9.83]; *F*[3, 71] = 3.09, *p* = 0.03). In addition, the BD-II and sub-threshold BD groups also had significantly higher mean number of prior depressive episodes than the MDD group (BD-II = 5.5 [*SD* = 4.43] vs. sub-threshold BD = 4.2[*SD* = 3.21] vs. MDD = 1.3 [*SD* = 1.30]; *F*[3, 71] = 3.34, *p* = 0.03). Finally, the three groups were marginally significantly different in the levels of anxiety symptoms as measured by BAI total scores (*F*[4, 34] = 2.47, *p* = 0.06). In summary, both the BD-II and sub-threshold BD groups had more past depressive episodes and more severe depressive and anxiety symptoms in the current episode than the MDD group. These findings were reminiscent of the findings that bipolar depression has poorer clinical outcome and course than MDD (Angst et al., 2010; Merikangas et al., 2011).

Confirming the diagnostic categorization of groups, both the BD-II and sub-threshold BD groups also reported having higher levels of YMRS total scores than the MDD group (BD-II = 6.3 [*SD* = 4.32] vs. sub-threshold BD = 3.1 [*SD* = 2.40] vs. MDD = 1.5 [*SD*=1.21]; *F*[2, 75] = 3.88, *p* < 0.001). Both the BD-II and sub-threshold BD groups also had higher levels of HCL-32 total scores than the MDD group (BD-II = 16.8 [*SD* = 3.91] vs. sub-threshold BD = 10.0 [*SD* = 6.87] vs. MDD = 5.3 [*SD* = 5.26]; *F*[3, 71], *p* < 0.001). In summary, both the BD-II and sub-threshold BD groups had a greater number of lifetime hypomanic symptoms than the MDD group. However, both BSD groups were not currently manic as suggested by the YMRS total scores being well below the threshold levels for current mania (Chenggapa, Baker & Shao, 2003).

Table 1: Demographic and clinical characteristics of bipolar II, sub-threshold bipolar, and major depressed groups (N = 75)

Characteristics	Bipolar II (*n* = 4)	Sub-threshold bipolar (*n*=10)	Major depressive (*n*=61)	Analysis (chi-squared test or analysis of variance)		Bipolar II vs. sub-threshold bipolar (planned Bonferroni's test or Fisher's exact test)		Sub-threshold bipolar vs. major depressive (planned Bonferroni's test or Fisher's exact test)	
	n (%)	*n* (%)	*n* (%)	X^2	*p*	X^2	*p*	X^2	*p*
Male gender	1 (25.0)	2 (20.0)	18 (29.5)	0.40	0.82	-	0.67	-	0.42
Employed	1 (25.0)	5 (50.0)	22 (36.1)	0.99	0.61	-	0.39	-	0.40
Family history of affective disorders	2 (50.0)	4 (40.0)	10 (16.4)	4.92	0.09	-	0.73	-	0.08
Currently on treatment	2 (50.0)	5 (50.0)	33 (54.1)	0.08	0.97	-	1.00	-	1.00
On mood stabilizer		1 (10.0)	4 (6.60)	0.47	0.79	-	1.00	-	0.54
On antidepressants		4 (40.0)	24 (39.1)	0.33	0.85	-	1.00	-	1.00
Presence of comorbid anxiety disorders	2 (50.0)	6 (60.0)	18 (50.0)	3.96	0.14	-	-	-	-
	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*	*F*	*p*	*d*	*p*	*d*	*p*
Age (years)	56.6 (10.33)	46.2 (10.0)	55.7 (11.7)	2.99	**0.05**	10.30	0.15	9.52	**0.05**
Years of education	9.5 (4.51)	13.1 (4.7)	9.0 (5.0)	3.00	**0.05**	3.60	0.22	4.10	**0.05**
Duration of illness (years)	11.0 (6.42)	10.2 (6.6)	6.4 (5.4)	6.11	**0.03**	0.80	0.89	3.80	**0.04**
Number of prior depressive episodes	5.5 (4.43)	4.2 (3.21)	1.3 (1.30)	4.12	**0.02**	1.31	0.65	3.10	**0.05**
BDI-II[a]	21.3 (12.18)	23.8 (7.36)	15.0 (9.83)	4.10	**0.02**	8.30	**0.03**	8.83	**0.009**
YMRS[b]	6.3 (4.31)	3.1 (2.4)	1.5 (1.12)	8.88	**<0.001**	1.63	**0.05**	3.15	**0.04**
HCL-32[c]	16.8 (3.91)	10.0(6.87)	5.3 (5.26)	20.32	**<0.001**	11.26	**<0.001**	6.80	**0.03**
BAI[d]	21.0 (9.40)	21.2 (12.4)	15.1 (12.1)	5.49	**<0.001**	0.20	0.98	6.13	**0.001**
RSQ-SF[e]	28.8 (2.75)	26.7 (1.74)	25.8 (0.70)	0.61	0.55	-2.05	0.53	0.90	0.63
RPA-EF[f]	16.3 (0.96)	13.9 (3.41)	10.6 (4.51)	5.29	**0.007**	2.35	0.98	3.29	0.06
RPA-SF[g]	11.3 (1.26)	9.5 (3.10)	6.7 (2.86)	8.02	**0.001**	1.75	0.91	2.76	**0.02**

a: Beck Depression Inventory-II; b:Young Mania Rating Scale; c:Hypomania Checklist-32; d=Beck Anxiety Inventory; e: Response Style Questionnaire-Short Form; f: Response to Positive Affect-Emotion-Focus subscale; g: Response to Positive Affect-Self-Focus sub-scale

5.5.3 Mental imagery susceptibility

Table 2 summarises the differences in mental imagery susceptibility across the three groups. Consistent with the first hypothesis, a ANCOVA revealed a significant difference across the three groups in the IFES total scores ($F[3, 71] = 7.46$, $p < 0.001$). Planned pairwise

comparisons revealed that the sub-threshold BD group had a significantly higher mean IFES score than the MDD group (sub-threshold BD = 46.9 [*SD* = 8.17] vs. MDD = 31.2 [*SD* = 14.20]; $p = 0.002$). Furthermore, the BD-II group also had a greater mean IFES total score than the MDD group (BD-II = 55.5 [*SD* = 4.43] vs. MDD = 31.2 [*SD* = 14.20]; $p = 0.001$). There was no significant difference between the two bipolar groups in IFES total scores (BD-II = 55.5 [*SD* = 4.43] vs. sub-threshold BD = 46.9 [*SD* = 8.17]; $p = 0.26$).

Also consistent with the first hypothesis, multivariate analysis revealed that there was a significant difference across the three groups in the SUIS total scores ($F[3, 71] = 6.36$, $p < 0.001$). Planned pairwise comparisons showed that the sub-threshold BD group had a greater mean SUIS score than the MDD group (sub-threshold BD = 39.8 [*SD* = 8.55] vs. MDD = 31.5 [*SD* = 11.15]; $p = 0.05$). Furthermore, the BD-II group also had a greater mean SUIS total score than the MDD group (BD-II = 45.8 [*SD* = 4.35] vs. MDD = 31.5 [*SD* = 11.15]; $p = 0.008$). Again, there was no significant difference between the BD-II and sub-threshold BD groups in SUIS total scores (BD-II = 45.8 [*SD* = 4.35] vs. sub-threshold BD = 39.8 [*SD* = 8.55]; $p = 0.12$).

On the other hand, there were no significant differences in the total number of total number of prospective images of either emotional valence ($F[3, 71] = 2.50$, $p = 0.09$) the total number of negative prospective images ($F[3, 71] = 0.69$, $p = 0.56$) across the three groups.

In summary, the sub-threshold BD group had higher levels of general use of imagery in daily life and emotional impact of prospective imagery than the MDD group. There were no significant differences between the sub-threshold BD group and the MDD group in the total numbers of negative prospective images.

Table 2: Mental imagery susceptibility measures of bipolar II disorder, sub-threshold bipolar disorder, and major depressive disorder control groups (*N* = 75)

Characteristics	Bipolar II (*n* = 4)	Sub-threshold bipolar (*n* =10)	Major depressive (*n* = 61)	Analysis of variance (ANOVA)*		Bipolar II vs. sub-threshold bipolar groups (LSD test; *p*-value)		Bipolar II vs. major depressive disorder groups (LSD test; *p*-value)		Sub-threshold bipolar vs. major depressive disorder groups (LSD test; *p*-value)	
	Mean (*SD)*	Mean (*SD)*	Mean *(SD)*	*F*	*p*	*d*	*p*	*d*	*p*	*d*	*p*
IFES[e] total	55.5 (4.43)	46.9 (8.17)	31.2 (14.20)	7.46	**<0.001**	8.60	0.26	24.34	**0.001**	15.74	**0.002**
SUIS[f] total	45.8 (4.35)	39.8 (8.55)	31.5 (11.15)	6.36	**<0.001**	5.95	0.12	14.26	**0.008**	8.31	**0.05**
IFES[e] total events	2.1 (0.82)	2.5 (0.85)	2.0 (0.70)	2.50	0.09	0.50	0.43	0.05	0.87	0.55	0.11
IFES[e] negative events	0.8 (0.50)	1.4 (0.84)	1.2 (0.84)	0.69	0.56	0.65	0.23	0.41	0.34	0.24	0.51

e: Impact of Future Events Scale; f: Spontaneous Use of Imagery Scale

5.5.4 Prediction of anxiety symptoms and anxiety disorders by mental imagery susceptibility measures

Consistent with the third hypothesis, hierarchical stepwise regression analysis using gender, age, and years of education in the first step followed by SUIS total score, IFES total score, IFES total events, IFES negative events and RRS-SF in the second step confirmed that BAI total score was predicted positively by IFES total scores (*B* = 0.46, *SE* = 0.10, *beta* = 0.55, $p < 0.001$) but negatively by SUIS total scores (*B* = -0.31, *SE* = 0.12, *beta* = -0.28, *p* = 0.02). In addition, logistic regression modelling using the above demographic and imagery characteristic variables, as well as BAI total scores, BDI-II total scores, YMRS total scores and HCL-32 total scores showed that the presence of anxiety disorders was predicted positively by the BAI total score only (*B* = 0.14, *SE* = 0.05, *wald* = 9.96, Exp[B] = 1.16, *p* =

0.002). Given that the presence of anxiety disorders was predicted by BAI total score and BAI total score was predicted positively by IFES total score, another mediational analysis was performed. IFES total score predicted the presence of anxiety disorders through the mediating effect of BAI total score (Sobel's test: *test statistic* = 3.31; *SE* = 0.002; $p < 0.001$). Consistent with the third hypothesis, emotional impact of prospective imagery as measured by IFES total score predicted the presence of anxiety disorders through the mediating effect of the level of current anxiety symptoms for the whole sample.

5.5.5 Prediction of lifetime prior depressive episodes by mental imagery susceptibility measures

The three groups had similar levels of negative ruminative response to negative affect as measured by the RRS-SF total scores ($F[3, 71] = 0.61$, $p = 0.55$). Logistic regression was then conducted to assess the value of mental imagery characteristics in predicting having two or more prior lifetime depressive episodes, after controlling for gender, age, and years of education, YMRS total score, HCL-32 total scores, BDI-II total scores, and RRS-SF total scores. The HCL-32 total score was found to be the only significant predictor of having two or more prior depressive episodes ($B = 0.20$, $SE = 0.08$, wald = 6.25, Exp(B) = 1.22, $p = 0.01$). In brief, the presence of lifetime hypomanic symptoms in depression predicted the recurrence of depressive episodes for the whole sample.

5.5.6 Response to positive affect

Analysis of variance revealed that there was a significant difference across the three groups in the levels of rumination about positive emotions/responses to positive affect (RPA-EF: $F[3, 71] = 5.29$, $p = 0.007$). Planned pairwise comparisons revealed that the sub-threshold BD group had a significantly higher level of RPA-EF than the MDD group (sub-threshold BD

= 13.9 [*SD* = 3.41] vs. MDD = 10.6 [*SD* = 4.51], *p* = 0.03). The BD-II group also had a higher level of RPA-EF than the MDD group (BD-II = 16.3 [*SD* = 0.96] vs. MDD = 13.9 [*SD* = 3.41], *p* = 0.01). There were no significant differences between the BD-II and sub-threshold BD groups.

Analysis of variance also revealed a significant difference across the three groups in the levels of rumination about positive self-qualities (RPA-SF: *F* [2, 75] = 8.02, *p* = 0.001, partial eta squared = 0.18). Planned pairwise comparisons revealed that the sub-threshold BD group had a higher level of RPA-SF than the MDD group (sub-threshold BD = 9.5 [*SD* = 3.10] vs. MDD = 6.7 [*SD* = 2.86], *p* = 0.006), as did the BD-II group (BD-II = 11.3 [*SD* = 1.26] vs. MDD = 6.7 [*SD* = 2.86], *p* = 0.003). Again, there were no significant differences between the BD-II and the sub-threshold BD groups.

In summary, consistent with the fourth hypothesis, the sub-threshold BD group had higher levels of rumination about positive emotions and rumination about positive self-qualities than the MDD group.

5.5.7 Prediction of lifetime hypomanic symptoms by mental imagery susceptibility and response to positive affect

Stepwise hierarchical regression modelling was conducted with SUIS total scores, IFES total scores, total IFES negative event scores and total IFES event scores being entered into the equation as the second step in predicting severity of lifetime hypomanic symptoms as measured by HCL-32 total scores. Gender, age, and years of education were entered as the variables in the first step of the modelling equation. The overall fit of the model was significant (adjusted R^2 = 0.41, *F*[4, 75] = 14.28, *p* < 0.001). Also consistent with the fifth hypothesis, the model was explained solely by SUIS total score (*B* = 0.23, *SE* = 0.006, *beta* = 0.41, *p* < 0.001). Separate stepwise hierarchical regression modelling, with the same

demographic variables (gender, age, and years of education) being entered as the first step, was conducted where response to positive affect sub-scales (RPA-EF & RPA-SF total scores) and negative rumination (as measured by RRS-SF total score) were entered as the second step into the hierarchical model predicting HCL-32 total score. The overall fit of the model was again significant (adjusted $R^2 = 0.53$, $F[4, 75] = 6.78$, $p < 0.001$). The model was explained by RPA-SF total score ($B = 0.70$, $SE = 0.31$, $beta = 0.34$, $p = 0.03$) but RPA-EF was not a significant predictor ($B = 0.30$, $SE = 0.21$, $beta = 0.21$, $p = 0.16$).

As the status of having two or more prior lifetime episodes of depression was predicted by HCL-32 score but HCL-32 total score was predicted by general use of imagery in daily life (SUIS total score), a mediational analysis was conducted to examine whether SUIS might exert its effects on prior depressive recurrences through the mediating effect of HCL-32 total score. Consistent with the second hypothesis, SUIS total score predicted the presence of two or more episodes of past depression but this impact was through its effect on HCL-32 total score (Sobel's test: *test statistic* = 2.23; $SE = 0.002$; $p = 0.03$). Another mediational analysis was conducted to examine whether RPA-SF total score might also exert an effect on predicting the recurrence of depressive episodes via the mediating effect of HCL-32 total scores. The Sobel's test statistic was, however, not significant ($p = 0.43$)

In summary, both general use of imagery in daily life and rumination of positive self-qualities were predictive of the levels of lifetime hypomanic symptoms. Furthermore, general use of imagery in daily life predicted having two or more episodes of past depression through the mediating effect of lifetime hypomanic symptoms.

5.5.8 Prediction of depressive symptoms by mental imagery susceptibility measures and responses to negative affect

Stepwise hierarchical regression analysis was conducted to assess the predictive values of mental imagery susceptibility measures (SUIS total scores, IFES total scores, total IFES negative event scores and total IFES events scores) and the RSQ-SF total scores in predicting severity of current depressive symptoms as measured by BDI-II total scores, after entering gender, age, and years of education as the first step in the whole sample. Consistent with the fifth hypothesis, BDI-II total scores were predicted positively by IFES total scores (B = 0.94, SE = 0.28, $beta$ = 0.47, p = 0.002) and RRS-SF total score (B = 0.32, SE = 0.10, $beta$ = 0.42 p = 0.003).

Due to the limited sample size, the interaction variable of negative rumination (RRS-SF) and the number of negative prospective imagery as measured by IFES negative events was not entered into the hierarchical regression modelling for hypothesis testing. Instead, linear regression modelling was conducted to investigate the specific predictive value of this interaction variable on the levels of current depressive symptoms. The overall model was significant (F[3, 75] = 9.47, adjusted R^2 = 0.29, p < 0.001). The interaction variable (RRS-SF-SF X IFES negative events) was significant (B = 0.5, SE = 0.18, $beta$ = 1.19, p = 0.009) even when the RRS-SF total score and the number of IFES negative events were also entered simultaneously into the model (RSQ-SF: B = 1.4, SE = 0.29, $beta$ = 0.77, p < 0.001; IFES negative events: B = 13.3, SE = 4.87, $beta$ = 1.09, p = 0.008). Consistent with the fifth hypothesis, current levels of depressive symptoms were predicted positively by the emotional impact of prospective imagery and negative rumination. Furthermore, the rumination of negative emotional materials in the form of negative prospective images specifically predicted the current levels of depressive symptoms.

5.6 Discussion

5.6.1 Mental imagery susceptibility and sub-threshold bipolarity

This is the first study to investigate mental imagery susceptibility in people with sub-threshold BD. Consistent with the first hypothesis, the study showed that participants with sub-threshold BD experienced higher levels of emotional impact of prospective imagery and general use of imagery in daily life than participants with MDD. Previous studies have suggested that BSD might range from mild elated states to full-blown BD-I (Angst, 1997; Angst, 1998, Merikangas et al., 2011). As elevated general use of imagery and emotional impact of prospective imagery were found in BD-I in remission (Study 1), acute mania (Study 2), BD-II and sub-threshold BD (Study 3), the evidence collected so far provides some converging data that these imagery characteristics might be trait markers of bipolarity.

What is intriguing is that the emotional impact of prospective imagery was higher in the sub-threshold BD group than the MDD group, consistent with Hales et al.'s (2011) similar finding in bipolar depression. However, this is inconsistent with Study 1 of the current thesis, in which levels of emotional impact of prospective imagery were similar in both BD-I and MDD. One major difference between the BD and MDD groups in Study 1 and those in the current study is that depressive and anxiety symptoms were much higher in the current study than in Study 1. Similar high levels of depressive and anxiety symptoms were also observed in Hales et al.'s (2011) sample. As the current study has found that IFES total score was a significant predictor of BAI score, a post-hoc ANCOVA analysis with bootstrapping method was re-run by including BAI total score and BDI-II total score as co-variates on top of age, the results remained similar (ANCOVA model= $F[5, 69] = 9.07$, $p < 0.001$; sub-threshold BD vs. MDD, $p = 0.02$; BD-II vs. MDD, $p = 0.001$). Similar results were found for SUIS total score (ANCOVA model: $F[5, 69] = 4.89$, $p = 0.001$; sub-threshold BD vs. MDD, $p = 0.03$; BD-II vs. MDD, $p = 0.003$). The finding therefore supports that both general use of imagery

and emotional impact of prospective imagery persistently elevated in both BD-II and subthreshold BD when compared to MDD, implying that both were trait factors associated with bipolarity. However, the current finding might suggest that the difference in the IFES total scores between sub-threshold BD and MDD might only become apparent when mood is depressed up to a certain critical level that warrants a clinical diagnosis of threshold/sub-threshold bipolar depression. However, there is a second possible explanation that lies with the MDD control group in Study 1. Although the depressed control group was assessed to be in remission from clinical depression, the presence of lifetime sub-threshold hypomanic symptoms was not assessed by measuring the HCL-32 total scores or by applying the Zimmerman's sub-threshold hypomania criteria (Zimmerman et al., 2009). As such, there is a possibility that a proportion of this remitted depressed control group might be suffering from sub-threshold BD rather than pure MDD. If mental imagery susceptibility was associated with bipolarity, the presence of sub-threshold bipolarity in the depressed control group would then lead to an inflated mean IFES total scores resulting in a lack of significant differences between the remitted BD-I and MDD groups in Study 1 (c.f. the lack of significant differences between BD-II and subthreshold BD groups in current study). Further sub-scale analyses revealed that all three IFES sub-scales were significantly higher in sub-threshold BD than in MDD even after controlling BAI and BDI-II total scores. However, one would also expect SUIS levels to be similar in these two groups, which is not the case in Study 1. Further studies are needed to measure IFES total and sub-scale scores prospectively from bipolar depression to euthymia so as to address the hypothesis of IFES changes with a certain threshold level of depressive symptoms.

5.6.2 Mental imagery, current anxiety symptoms and the presence of comorbid anxiety disorders

The second key finding is that the levels of anxiety symptoms were predicted positively by the emotional impact of prospective imagery. Experiencing high emotional impact of prospective imagery may lead to an intensification of current anxiety symptoms, which might then culminate into the onset of full-blown anxiety disorders in patients with depression. Holmes *et al*. (2008) hypothesized that mental imagery susceptibility might be a key driver of both anxiety symptoms and pathological mood amplification in patients with BD. The current study provides some support for this hypothesis by finding that higher emotional impact of prospective imagery, a characteristic found in both sub-threshold and full-blown BD, might offer a possible link explanation for the frequent co-occurrence of anxiety disorders in people with BSD (Chantal et al., 2003; Simon et al., 2004). This imagery characteristic might then explain the differences in the rates of comorbidities of anxiety disorders in BD and MDD.

However, increased tendency to use imagery in daily life appeared to reduce current anxiety symptoms. This finding appeared to echo the finding in Study 2 that general use of imagery was predictive of recovery from mania. Thinking in terms of visual images allows novel combinations of ideas and 'time-travel' to the past and future (Holmes et al., 2008). As such, increased use of imagery might be associated with high creativity and divergent thinking (Holmes et al., 2008; Murray & Johnson, 2010; see chapter 8 for additional supportive findings). Such divergent thinking has been associated with better problem solving, an important factor in protecting against the onset and maintenance of anxiety disorders (Lara & Klein, 1999). Therefore, general use of imagery might confer some evolutionary advantage in promoting creativity but also contribute to emotional instability associated with bipolarity. Alternatively, general use of imagery might be a proxy marker of another neuropsychological variable that is associated with recovery from anxiety disorders.

5.6.3 Mental imagery, lifetime hypomanic symptoms and depressive recurrences

One of the clinical characteristics of BD is its highly recurrent nature (Goodwin & Jamison, 2007). Another key finding of the current study was that a high general tendency to use imagery in daily life exacerbated the intensity of lifetime hypomanic symptoms (emotional instability being one of the key symptoms of clinical hypomania), which then predicted an increased frequency of lifetime depressive recurrences in major depression with or without sub-threshold bipolarity. In other words, having a higher loading of lifetime hypomanic symptoms in depressive disorders predisposes a depressed patient to more frequent depressive recurrences. This finding is consistent with previous studies on bipolar depression having more prior episodes of depression than MDD (Forty et al., 2008; Mitchell et al., 2001). This finding echoes the finding in Study 1 that general use of imagery predicted lifetime frequency of both manic and depressive episodes in BD-I. If general use of imagery destabilizes mood by increasing the frequency of occurrence and the vividness of intrusive images, the polarities of mood swing would then depend on other imagery characteristics. Study 2 has provided some hints that the polarity of mood switch seems to be dependent on the emotional valence of prospective images. Future studies should directly manipulate the emotional valence of these images experimentally and measure the changes of physiological markers associated with positive and negative emotions (e.g. vagal tone increase in the emotion of joy; Gruber et al., 2009).

5.6.4 Mental imagery susceptibility, response to positive and negative affect, and depressive symptoms

Positive rumination was found to be elevated in people with sub-threshold BD when compared to MDD. This is also consistent with the findings in Study 1 and Study 2, as well as other recent studies (Feldman et al., 2008; Gruber et al., 2011). The evidence therefore also supports that positive rumination of emotional materials might be another trait marker associated with bipolarity.

Furthermore, this study found that BD-II and sub-threshold BD had similar levels of response to negative affect (i.e. negative rumination) as the MDD group, suggesting that negative rumination may be a common cognitive mechanism in triggering depression in both BD and MDD. The other key finding that both emotional impact of prospective imagery and responses to negative affect were predictive of current levels of depressive symptoms provides additional support that both powerful emotional responses to visual images and rumination about negative emotional materials may significantly exacerbate depressive symptoms in depression with varying degrees of bipolarity.

The current study has also provided some preliminary evidence that visual images of negative emotional valence could act as a fuel for depressive rumination. Study 1 provided new evidence that rumination about positive prospective images could amplify pathological positive emotions. The current study extrapolated this finding to the parallel effects of negative rumination about negative prospective images amplifying pathological negative emotions. In summary, this study and Study 1 have provided some preliminary data that people with BD had excessive tendency to ruminate both about their pathological positive and negative emotions, be they encapsulated in either positive or negative prospective images.

5.7 Strengths and limitations

The current study has several strengths. First, the participants with depression were recruited from a large representative community sample, with around 50% of participants being naïve to antidepressants or mood stabilizers, therefore avoiding selection bias towards people with more severe illness and minimizing the possible confounding effects of psychotropic medications on the relationships between mental imagery susceptibility and sub-threshold bipolarity. Second, participants were diagnosed as suffering from BD-II, sub-threshold BD or pure MDD using stringent validated operational criteria that allows comparability with other studies on sub-threshold bipolarity. Third, all the predictor variables were measured by locally validated instruments with good psychometric properties. The self-administered scales also minimized interviewers' biases, as the interviewers were not blind to participants' SCID-confirmed diagnoses.

However, the study also has a number of limitations. First, the small sample sizes of the bipolar II and sub-threshold bipolar groups would have led to a low statistical power in detecting certain significant differences in mental imagery susceptibility and ruminative response style measures between the three groups.

Second, there could have been a selection bias against those who were more depressed or ill than the study sample, as only 40% of those originally diagnosed as having a MDD by CIS-R in the HKMMS were recruited into the study. However, the responders and non-responders were found to have similar baseline demographic characteristics and mood symptoms captured in the first phase of the HKMMS. Third, the participants were recruited by a two-stage sampling method where only people diagnosed as suffering from MDD by the CIS-R were eligible for the administration of the CB-SCID-I/P in the second stage. Although the CIS-R has been found to have good sensitivity for diagnosing MDD, certain participants with depression might not have been detected by the CIS-R and therefore were not deemed

eligible for the current study. Fourth, the mental imagery susceptibility measures used in the current study were exclusively self-administered and might be subject to response and social desirability biases. Inclusion of objective measures like laboratory measures of imagery susceptibility in future studies would enhance the internal validity of the current findings. Finally, the measure of emotional instability was based on a proxy measure of lifetime hypomanic symptoms rather than real time sampling of mood fluctuations on a daily basis (Bonsall et al., 2011).

In conclusion, the current study provides additional evidence that increased imagery susceptibility, namely general use of imagery and emotional impact of prospective imagery, and positive rumination were elevated in sub-threshold BD, a type of BSD with hypomanic symptom severity intermediate between BD-II and pure MDD. As such, this would provide some support that these cognitive characteristics might be trait markers associated with bipolarity. The study also provides additional support that imagery characteristics might be key factors in amplifying negative emotions (both depressive and anxiety symptoms) in major depression with varying degrees of bipolarity.

CHAPTER 6 - Study 4: Bipolar risk and mental imagery susceptibility in a general population sample: a behavioural paradigm study

6.1 Introduction

6.1.1. Mental imagery susceptibility and bipolar risks

Minor elated states can be conceptualised as lying at the mild end of the bipolar risk continuum (Beesdo et al., 2009) and are reliably detected among the general population using questionnaire measures of hypomania such as the Mood Disorder Questionnaire (MDQ; Hirschfield et al., 2003; Deeprose et al., 2011; Malik et al., 2014; Rock et al., 2013). Previous studies have suggested that minor elated states confer an enhanced risk of full-blown bipolar disorders (BD) (Tjissen et al., 2010), are associated with increased comorbidity for depression and impulse control problems and can be considered as a common bipolar phenotype among the non-clinical general population (Rock et al., 2013). Increased general use of imagery in daily life and emotional impact of prospective imagery were found in remitted bipolar I disorder (BD-I) (Study 1), bipolar mania (Study 2), bipolar depression (Hales et al., 2011), bipolar II disorder (BD-II) and sub-threshold bipolar disorder (sub-threshold BD) (Study 3). These findings provide converging evidence that these two imagery characteristics might be trait markers associated with bipolarity. Another approach to investigate whether a certain characteristic may be considered a trait factor is to adopt a high risk behavioural paradigm (Riskind & Alloy, 2006). In such studies, participants are recruited who exhibit certain cognitive and behavioural vulnerabilities for bipolar disorder, without meeting the full criteria for the disorder (Just, Abramson & Alloy, 2001). Two recent studies divided non-clinical student samples into high (HR) and low bipolar risk (LR) groups based on a criterion cut-off

score on the MDQ. The two groups were then compared for their mental imagery susceptibility. Results showed that the HR group experienced greater emotional impact of prospective imagery, higher general use of imagery in daily life, and a greater number of negative prospective images than the LR group (Deeprose et al., 2011; Malik et al., 2014).

While these findings are potentially valuable, the studies suffer from a number of limitations. First, Deeprose et al.'s (2011) sample did not undergo any formal screening for the presence of psychiatric disorders. Second, in previous studies, the HR group showed higher levels of current depressive and/or anxiety symptoms than the LR group. Since distressing imagery has also been reported in patients with anxiety and depressive disorders (Morina et al., 2010; Patel et al., 2007), the presence of such symptoms might confound putative relationships between mental imagery susceptibility and bipolar risk. Third, previous studies did not rule out psychosis proneness, which has been associated with greater pre-living of imagined events (Winfield & Kamboi, 2010). Fourth, the samples comprised mostly UK students, and the extent to which findings will generalise across age groups and cultures is unknown (Poon et al., 2012; Schurhoff et al., 2000; Perlis et al., 2004). Fifth, previous studies administered imagery measures at a single time point. Whereas mental imagery susceptibility has been assumed to be stable in the absence of changes in mood or neurotic symptoms, this assumption has not been directly examined in a prospective study. The current study was conducted to address these limitations.

The current study aimed to replicate and extend the findings of Deeprose et al. (2011) and Malik et al. (2014) by recruiting a representative community sample of ethnic Chinese adults assessed to be free from psychotic or neurotic disorders. Participants categorised as being LR versus HR according to the MDQ completed imagery measures twice, seven weeks apart. This seven-week follow-up interval was selected as initial pilot data in healthy healthcare professionals (n = 20) indicated four-week test re-test stability of the IFES, suggesting the IFES might measure a trait-like imagery characteristic. We extended this

period to examine the stability of the IFES over a period of seven weeks, while minimising the risk of drop-out with longer follow-up periods. Mood symptoms in BD can fluctuate severely over this time period (Bonsall et al., 2011). Therefore, if imagery characteristics relate to bipolar risks but do not fluctuate with time, this would be of interest.

6.2 Aims and objectives

The study hypotheses were as follows:

1. Compared with the low bipolar risk (LR) group, the high bipolar risk (HR) group would show greater imagery susceptibility as assessed using the IFES total scores and the SUIS total scores.
2. This pattern of characteristics would remain stable over time – i.e. higher in the HR group at the seven weeks' follow-up.

6.3 Methods

6.3.1 Study design and participants

Participants (N = 80) were recruited from a random sample of adults aged 18 to 65 who participated in the Hong Kong Mental Morbidity Survey (HKMMS; see chapter 2 for further details on HKMMS). The 80 participants were randomly selected from 4902 participants in the HKMMS who were identified as being free from any CIS-R-defined neurotic disorders and PSQ-defined psychotic disorders. These participants also served as the control participants in Study 6 of the current thesis.

This sample size of N = 80 was selected to be manageable in terms of resources for this preliminary study, while sufficiently powered at 80% to detect a difference in IFES total

score between high and low bipolar risk groups at an alpha level of 0.05. The sample size calculation is based on Deeprose, Malik and Holmes's (2011) indication that a minimum of *n* = 18 participants in each group should be sufficient to detect a standardised mean difference of 0.95 on IFES total score. Given rates of sub-threshold bipolar symptoms of 20-25% in the general community (Lee, Ng & Tsang, 2009; Merikangas et al. 2007), a total sample size of 80 was selected to yield sufficient numbers in each group.

These 80 participants attended in person to complete a battery of questionnaires assessing mental imagery and bipolar risk, as well as other questionnaires unrelated to the current study. Participants were invited to complete the same procedure seven weeks later. None of the target participants declined to participate at baseline but only 57 participants were traced for follow-up, representing a dropout rate of 28.75%. The study was approved by the local research ethics committee (reference number: KC/KE-11-0204/ER-3).

6.3.2 Data collection

With the exception of the demographic characteristics, all measures were administered at baseline and at seven weeks' follow-up.

6.3.2.1 Baseline demographic characteristics

A demographic questionnaire administered at baseline yielded information on gender, age, years of education, marital status, the presence of past psychiatric illness, and use of psychiatric medications. The latter two were further verified by checking their electronic health records using the Clinical Information System of the Hospital Authority of Hong Kong.

6.3.2.2 Clinical measures

Mood Disorder Questionnaire (*MDQ*; *Hirschfield et al., 2000; Hirschfield et al., 2003; Chung et al., 2009)*: This was used to classify participants into HR versus LR groups (Calabrese et al., 2006; Deeprose et al., 2011; Malik et al., 2014). A validated Chinese version was used (Chung et al., 2009). In the current study, MDQ showed good internal consistency (Cronbach's alpha = 0.83) and good test re-test reliability in categorising people into HR versus LR groups according to the above cut-off point across a seven-week period (n = 10; weighted kappa agreement = 0.88).

Life Events Checklist (LEC; Gray et al., 2004; Liu et al., 2007): In the current study, internal consistency of the LEC was found to be good (Cronbach's alpha = 0.89).

Hypomanic checklist-32 (HCL-32; Angst et al., 2005; Poon et al., 2012): In the current study, the HCL-32 was included: 1) to exclude clinically hypomanic participants; 2) to validate HR versus LR grouping of participants based on a cut-off score on the MDQ. Previously, the HCL-32 has been used to identify sub-threshold bipolar symptoms among non-clinical population (Meyer et al., 2007). A total score of 18 and above plus a score of 2 and above on the 'risk-taking/irritable' hypomania scale was considered indicative of clinical hypomania in the general population (Meyer et al., 2007). In the current study, a previously-validated Chinese version of the HCL-32 with good sensitivity and specificity was used (Poon et al., 2012). The HCL-32 showed good internal consistency (Cronbach's alpha = 0.83) and good test-retest reliability (intra-class correlation = 0.88).

6.3.2.3 Imagery measures

Impact of Future Events Scale (IFES; Deeprose & Holmes, 2010): In the current study, internal consistency of the Chinese version of IFES was also good (Cronbach's alpha = 0.83).

Spontaneous Use of Imagery Scale (SUIS; Reisberg et al., 2003): In the current study, the translated version of SUIS showed good internal consistency (Cronbach's alpha = 0.83).

6.4 Statistical analysis

STATA-12 software was used for statistical analyses (STATACorp, 2011). First, continuous data were assessed for Normality by examining visual data plots, followed by tests for skewness and kurtosis. Skewed continuous data were Normalised using square root transformation prior to parametric analyses. Subsequently, participants were split into HR and LR groups based on a predefined cut-off score of seven at baseline on the MDQ. The categorical control variables gender and presence of past psychiatric illness were compared across high and low bipolar risk groups at baseline and at seven-week follow-up using Fisher's exact tests. The categorical control variable marital status (single/divorced vs. married/cohabiting) was compared across HR and LR groups at baseline and at seven-week follow-up using Chi-squared tests. Analysis of variance (ANOVA) was used to compare the continuous control variables of age, years of education, and mean LEC score across bipolar risk groups (between-subjects factor: bipolar risk Group; two levels: HR, LR) and time-points (within-subjects factor: Time; two levels: baseline, seven-week follow-up). If any of the control variables was found to be significantly different between the two groups at either time-point, the identified confounders would be entered as covariates in subsequent analyses comparing groups and time-points. A *p*-value of 0.05 was taken as the point of statistical significance. Due to multiple comparisons, the difference was considered as statistically significant when the *p* value was equal or less than $p = 0.006$ as calculated by using Bonferroni's correction.

Analysis of variance (ANOVA) was also conducted to compare HCL-32 total score across bipolar risk groups (between-subjects factor: bipolar risk Group; two levels: LR, HR)

and time-points (within-subjects factor: Time; two levels: baseline, seven-week follow-up). A main effect of the bipolar risk group in the predicted direction would provide evidence for the validity of bipolar risk groupings based on the MDQ cut-off score.

In order to evaluate the primary hypotheses regarding mental imagery susceptibility in participants at high risk of developing bipolar disorder, analyses of co-variance (ANCOVA) were conducted comparing IFES total score (i.e. impact of prospective imagery), IFES total events score, IFES positive and negative events scores, and SUIS total score across bipolar risk groups (between-subjects factor: bipolar risk Group; two levels: HR, LR) and time-points (within-subjects factor: Time; two levels: baseline, seven-week follow-up). Covariates used in the ANCOVA were age, years of education and LEC total scores. These covariates were included as they are theoretically important confounder variables of the relationship between mental imagery susceptibility and bipolarity (Angst et al., 2005; Holmes et al., 2008).

6.5 Results

6.5.1 Demographic and clinical variables

The baseline sample (N = 80) comprised 58 females and 22 males, with a mean age of 45.6 years (SD = 15.35). Seven participants at baseline volunteered having a past history of psychiatric treatment (three suffered from depression; one from mixed depressive and anxiety disorder; one from anxiety disorder; one from neurasthenia and one from insomnia) but none reported any current psychiatric treatment and none were identified as suffering from current anxiety, depression or psychosis based on the CIS-R and PSQ. None scored above 18 on HCL-32 total score and above 2 on the 'risk-taking/irritable' hypomania sub-scale, suggesting an absence of clinically significant hypomania (Meyer et al., 2007).

The sample was divided into HR and LR groups at each time-point according to the

MDQ cut-off criterion. At baseline, the HR group comprised 18 participants (22.5% of the total sample) and the LR group comprised 62 participants (see Table 1). At seven-week follow-up, the HR group consisted of 13 participants (22.8% of total sample) and the LR group consisted of 44 participants. There were no significant differences between the two groups at baseline or seven-week follow-up in gender, age, years of education, marital status, number of lifetime psychiatric illnesses or LEC traumatic events (see Table 1). Proportion of male gender, marital status, and having a past history of psychiatric illness, age, years of education, baseline HCL-32 total scores, and LEC total scores were also similar across patients who were successfully traced for follow-up and those who could not be traced for follow-up (all *p*-values>0.10). Missing data can thus be considered as missing at random.

6.5.2 Group differences in HCL-32 score

Providing convergent validity to the grouping of participants into HR and LR groups based on the MDQ, the ANOVA comparing mean HCL-32 total scores across risk group and time showed a main effect of Group and no interaction with Time (Group: $F[1,52] = 23.5$, $p < 0.001$; Group X Time; $F[1,52] = 0.12$, $p = 0.13$), with higher HCL-32 total scores in HR than LR at baseline (HR=18.3, *SD* = 3.44; LR = 12.9, *SD* = 4.53) and at seven weeks' follow-up (HR = 17.4, *SD* = 3.63; LR = 12.3, *SD* = 4.21; see Table 1).

Table 1: Demographic and baseline clinical measures in high and low bipolar risk groups (as defined by Mood Disorder Questionnaire; MDQ) at baseline (*N* = 80) and at 7-week follow-up (*n* = 57)

	High bipolar risk		Low bipolar risk		
Variables of interest	Baseline (*n* = 18)	Follow up (*n* = 13)	Baseline (*n* = 62)	Follow up (*n* = 44)	Statistic High vs low bipolar risk groups at baseline and 7-week follow-up
Demographic characteristics					
Male gender (%)	3 (16.7)	2 (15.4)	19 (30.6)	15 (34.1)	Baseline: Fisher's exact test: $p = 0.37$; Follow-up: Fisher's exact test, $p = 0.30$
Mean age (*SD*)	41.6 (13.61)	46.0 (15.46)	46.8 (15.73)	45.5 (16.07)	ANOVA Group X Time; $F(1, 56) = 0.59$, $p = 0.59$
Years of education (*SD*)	14.3 (5.27)	15.6 (4.49)	13.3 (4.81)	13.3 (5.29)	ANOVA Group X Time; $F(1, 56) = 0.02$, $p = 0.96$
Marital status:					
Single/divorced (%)	8 (44.4)	7 (53.8)	22 (35.5)	15 (34.1)	Baseline: $x^2 = 1.24$, $p = 0.27$; Follow-up: $x^2 = 3.14$, $p = 0.08$
Married/cohabiting (%)	10 (55.6)	6 (46.2)	40 (64.5)	29 (65.9)	
Clinical measures					
Presence of past psychiatric illness (%)	2 (11.1)	2 (15.4)	5 (8.1)	4 (9.1)	Baseline: Fisher's exact test, $p = 0.65$; Follow-up: Fisher's exact test, $p = 0.61$
Mean LEC[a]-total score (*SD*)	0.9 (1.28)	1.0 (1.41)	0.6 (0.91)	0.6 (0.87)	Group X Time $F(1, 56) = 1.04$, $p = 0.30$
Mean HCL-32[b] total score (*SD*)	18.3 (3.44)	17.4 (3.63)	12.9 (4.53)	12.3 (4.21)	Group X Time: $F(1, 56) = 0.12$, $p = 0.73$; Risk group: $F(1, 56) = 23.5$, $\mathbf{p < 0.001}$ Time: $F(1, 56) = 0.39$, $p = 0.54$

a: Life Events Checklist; b: Hypomanic Checklist-32

6.5.3 Mental imagery susceptibility across bipolar risk groups and time

ANCOVA comparing IFES total score across HR versus LR groups at baseline and follow-up showed no significant Group X Time interaction ($F[1, 52] = 1.76$, $p = 0.19$; see Table 2). Consistent with the first hypothesis, there was a main effect of Group ($F[1, 52] =$

13.08, $p = 0.001$, partial eta squared = 0.20), with higher IFES total scores in the HR than LR at baseline (HR = 32.8, *SD* = 12.50; LR = 23.3, *SD* = 10.69) and follow-up (HR = 36.3, *SD* = 14.60; LR = 22.6, *SD* = 9.21). Consistent with the second hypothesis, there was no main effect of time (F [1, 52] = 0.06, $p = 0.81$). In terms of the covariates, years of education had no effect on IFES total score (F [1, 52] = 0.11, $p = 0.74$), although there was a marginal effect of age (F [1, 52] = 10.8, $p = 0.002$) and number of past traumatic events (F [1, 52] = 6.70, $p = 0.01$). Interactions between covariates and the Time factor were all non-significant.

ANCOVA comparing SUIS scores across HR versus LR groups at baseline and follow-up showed no Group X Time interaction (F[1, 52] = 0.02, $p = 0.90$; see Table 2). Consistent with the first hypothesis, there was a main effect of Group (F[1, 52] = 12.9, $p = 0.001$, partial eta squared = 0.20), with higher SUIS scores in the HR than LR at baseline (HR = 40.4, *SD* = 6.90; LR = 32.2, *SD* = 9.15) and follow-up (HR = 44.1, *SD* = 9.34; LR = 35.6, *SD* = 9.07). There was no main effect of Time (F[1, 52] = 1.81, $p = 0.19$). None of the covariates was individually significant. Furthermore, the interactions between co-variates and Time factor were non-significant.

ANCOVA comparing IFES total events across HR versus LR groups at baseline and follow-up showed no significant Group X Time interaction (F [1, 52] = 3.44, $p = 0.07$) and no main effect of group (F [1, 52] = 0.04, $p = 0.84$) or time (F [1, 52] = 2.86, $p = 0.10$). None of the covariates were individually significant. Furthermore, the interactions between covariates and Time were non-significant (see Table 2).

ANCOVA comparing IFES positive event scores across high versus low bipolar risk groups at baseline and follow-up showed no significant Group X Time interaction effects (F [1, 52] = 0.17, $p = 0.68$) and no main effect of group (F [1, 52] = 2.39, $p = 0.13$) or time (F [1, 52] = 0.22, $p = 0.64$). The main effects of covariates were also not significant. Furthermore, the interactions between covariates and time factor were non-significant (see Table 2).

Table 2: Mental imagery characteristics between high bipolar and low bipolar risks (as defined by Mood Disorder Questionnaire; MDQ) at baseline (*N* = 80) and 7-week follow-up (*n* = 57)

	High Bipolar risk		Low bipolar risk		
Variables of interest	Baseline (*n* = 18)	Follow up (*n* = 13)	Baseline (*n* = 62)	Follow up (*n*=44)	Statistics: Repeated measures ANCOVA[&]
Mean (*SD*) IFES[c] total	32.8 (12.50)	36.4 (14.60)	23.3 (10.69)	22.6 (9.21)	Group X Time interaction: $F(1, 52) = 1.76$, $p = 0.19$; Main effect (Group): $F(1, 52) = 13.08$, ***p* = 0.001**; Main effect (Time): $F(1, 52) = 0.06$, $p = 0.81$
Mean (*SD*) SUIS[d] total	40.4 (6.90)	44.1 (9.34)	32.2 (9.15)	35.6 (9.07)	Group X Time interaction: $F (1, 52) = 0.02$, $p = 0.90$; Main effect (Group): $F(1, 52) = 12.90$, ***p* = 0.001**; Main effect (Time): $F (1, 52) = 1.81$, $p = 0.19$
Mean (*SD*) IFES number of events	2.5 (0.78)	2.5 (0.78)	2.7 (0.67)	2.4 (0.87)	Group X Time interaction: $F(1, 52) = 3.44$, $p = 0.07$; Main effect (Group): $F(1, 52) = 0.04$, $p = 0.84$; Main effect (Time): $F (1, 52) = 2.86$, $p = 0.10$
Mean (*SD*) IFES positive events	0.7 (0.32)	0.7 (0.35)	0.8 (0.25)	0.8 (0.31)	Group X Time interaction: $F (1, 52) = 0.17$, $p = 0.68$; Main effect (Group): $F (1, 52) = 2.39$, $p = 0.13$; Main effect (Time): $F (1, 52) = 0.22$, $p = 0.64$)

c: Impact of Future Events Scale; d: Spontaneous Use of Imagery Scale
[&]ANCOVA: repeated measures analysis of covariance was conducted using the following variables as covariates: age, years of education and square root transformed values of LEC total scores.

6.6 Discussion

The current study is the first to examine the relationship between mental imagery susceptibility and bipolar risk in a randomly selected general community sample of Chinese adults screened to be free from major psychiatric disorders. This is also the first study to

examine stability in mental imagery characteristics longitudinally over a period of seven weeks in participants identified as being at high risk of developing bipolar disorders. Findings may have relevance for understanding the possible role of mental imagery susceptibility in emotional instability and in BD.

6.6.1 General use of imagery in daily life, emotional impact of prospective imagery and bipolar risk

Participants with high risk of developing bipolar disorders reported higher levels of general use of imagery in daily life (SUIS) and experienced greater emotional impact of prospective imagery (IFES) than those with low bipolar risk. This is the first study confirming that such differences in imagery characteristics between HR and LR groups are present in a general community sample, and also in people from non-Western population. Such findings suggest that enhanced mental imagery susceptibility among people with high bipolar risk generalises cross-culturally (Malik et al., 2014).

Combined with recent evidence that general use of imagery was elevated in patients with remitted BD-I when compared with non-psychiatric control participants (Holmes et al., 2011; Study 1) and remained elevated in BD-I regardless of symptomatic state (Study 2), the results provide additional support that general use of imagery in daily life might be a trait factor associated with bipolarity.

Furthermore, consistent with previous studies (Deeprose et al., 2011; Malik et al., 2014), this study provides converging evidence that the emotional impact of prospective imagery is elevated in people with HR when compared with people with LR. Taking the findings of Study 1 into consideration, the emotional impact of prospective imagery might be another trait factor associated with bipolarity. However, given that this imagery characteristic is also enhanced in patients with MDD when compared with non-psychiatric control participants (Morina et al., 2010; Study 1), it might be a non-specific trait factor associated

with affective disorders (see Section 5.6.1 for an alternative explanation for the elevated IFES total scores in the remitted MDD group in Study 1). Although the lack of difference in the number of prospective images between the two risk groups at each time point may be related to type II error, another possible explanation may be that there was indeed no difference between the two groups. This latter explanation is consistent with the current thesis hypothesis that an increase in the number of prospective images might be a required fuel to trigger a full-blown mood episode (see Chapter 4 for further evidence on the role of positive prospective imagery in acute mania and Chapter 5 for further evidence on negative prospective imagery in major depression with varying degrees of bipolarity).

6.6.2 Stability over time

This study examined whether mental imagery characteristics and their relationship to bipolar risk status fluctuate spontaneously over time. Results indicate stability over time in mental imagery susceptibility, consistent with the hypothesis that mental imagery susceptibility may be a stable characteristic of individuals scoring highly on measures of hypomania such as the MDQ. In future research, prospective studies are needed to investigate, over a longer period of time, any causal relationship between mental imagery susceptibility and risk for developing bipolar disorders, for example in the event of a life stressor (cf. Malik et al, 2014).

6.7 Strengths and limitations

The current study has several strengths. First, it included Chinese adults selected at random from a larger representative community sample from a population-wide mental health survey. Second, the sample was screened to be free from important potential clinical

confounding variables, such as depressive/anxiety disorders and psychotic disorders. This addressed limitations of previous studies regarding the potential confounding effects of the relationship between mental imagery and bipolar risks by undiagnosed anxiety or depressive disorders, and the relationship between psychosis-proneness and mental imagery susceptibility. In addition, the use of the Life Events Checklist (Gray et al., 2004) for detecting the presence of traumatic life events allowed statistical controlling of this important confounder (Ehlers et al., 2004).

Third, the prospective design showing persistently elevated mental imagery among high versus low bipolar risk groups provides new evidence in support of the notion that mental imagery susceptibility may be a possible trait marker of bipolarity (Deeprose, Malik & Holmes, 2011). Study 5 will further explore this hypothesis by examining this cognitive construct in a sample of participants with high familial risks for developing bipolar disorders (i.e. first- degree relatives of patients with bipolar I disorder).

Fourth, higher HCL-32 total scores in the high relative to low bipolar risk group strengthens the validity of the MDQ criterion cut-off score of seven or above used for defining these groups. The patterns of responding on the HCL-32 suggest that the high bipolar risk group manifested a liability for BD, rather than suffering from full-blown DSM-IV-TR hypomania. This is exemplified by the high bipolar risk group having mean total HCL-32 total scores and mean 'risk-taking/irritable hypomania' factor scores which were both below the criterion cut-off scores for identifying current hypomania in a general community population (Meyer et al., 2007). The absence of clinically significant hypomania in the high risk group suggests that heightened imagery susceptibility contributes to emotional instability rather than being a consequence of clinical hypomania.

Finally, Chinese versions of established instruments used for measuring mental imagery susceptibility, current mood symptoms and bipolar risk status were developed and validated locally (Poon et al., 2012; Chung et al., 2009), bolstering validity of the findings.

The current study also has limitations. Although the choice of sample size was based on a priori sample size calculation, it is possible that type II errors occurred, missing clinically significant differences between the two bipolar risk groups on the total number of general and positive prospective images. Second, there was a dropout rate of 28.75% at 7 weeks' follow-up, which may have led to potential attrition bias. However, those who were successfully traced for follow-up and those who could not be traced were not significantly different in major demographic and clinical variables, suggesting that this limitation is not applicable. Third, the major outcome variable (bipolar risk) and predictor variables (mental imagery measures) were based on self-administered questionnaires, which might lead to recall and social desirability biases. Adding interviewer-based or laboratory measures to the battery of questionnaires might provide additional evidence for or against the validity of the questionnaire findings. Finally, the random adult age sample might have led to selection bias for people with risk of conversion to late-onset bipolar disorder, which may be clinically and genetically different from those with adolescent-onset bipolar disorder (Leboyer et al., 2005; see Chapter 7 for age-specific differences in mental imagery susceptibility between the high and low risk groups).

CHAPTER 7 - Study 5: Bipolar risk and mental imagery susceptibility: a familial high risk study

7.1 Introduction

7.1.1 Mental imagery susceptibility as a possible cognitive risk factor of bipolarity

Study 4 adopted a behavioural high risk paradigm to study the association between mental imagery susceptibility and bipolar risk. Another approach is to conduct high risk studies based on genetic vulnerability for developing bipolar disorders (BD). Studies show that late adolescents and young adult offspring of parents with BD have an increased risk of bipolar I (BD-I) and bipolar II (BD-II) disorders (Berterlson et al., 1977; Gershon et al., 1982). In addition, siblings and parents of patients with BD have higher rates of psychopathology (Akiskal et al., 1985). Furthermore, the prevalence and types of disorders exhibited by high-risk individuals varied in relation to their developmental level, with increased risk of BD in adolescents and young adults and increased risk of anxiety and depressive disorders in late adulthood (Henin et al., 2005; Radke-Yarrow et al., 1992). First-degree relatives of patients with BD therefore constitute a high genetic risk group that might provide important information on risk factors associated with the development of BD. Detecting the presence of heightened mental imagery susceptibility among people at high genetic risk of BD would support the hypothesis that mental imagery susceptibility might be a cognitive risk factor associated with bipolarity.

As 75% of people with BD have their illness onset by age of 26, (Kessler et al., 2005), those at-risk individuals who survive into adulthood or old age without developing BD might differ in bipolar vulnerability from adolescent or young adult at-risk individuals. If mental imagery susceptibility might be a trait marker associated with bipolarity, there might be

significant differences in mental imagery susceptibility between these two at-risk age groups. Therefore, adolescent or young adult participants with high familial risks for bipolar disorders might have higher mental imagery susceptibility than age-matched people without such familial risks, whilst older participants with high familial risks might or might not have higher mental imagery susceptibility than the age-matched people without such familial risks. This study will explore this age-specific hypothesis.

7.1.2 Responses to positive and negative affect as possible cognitive risk factors of bipolarity

Individuals with an elevated risk for BD as defined by a behavioural paradigm had a greater tendency to ruminate over positive emotional materials than non-clinical controls (Feldman, Joorman & Johnson, 2008). The current thesis found that a greater tendency of positive rumination (i.e. responses to positive affect) was found in patients with remitted BD-I (Study 1), acute mania (Study 2), and sub-threshold BD (Study 3) when compared to MDD or non-psychiatric controls. Further evidence of increased positive rumination in people with high familial risks for bipolarity would provide further support of positive rumination being a trait marker of bipolarity. Negative rumination (i.e. responses to negative affect) has also been proposed as a trait marker associated with depression (Nolen-Hoeksema, 2000). Ruminative processing of negative emotions has been associated with escalation of negative emotions in BD and was found to be higher in BD when compared to healthy controls (Johnson, McKenzie & McMurrich, 2008). Study 3 has further shown that sub-threshold BD had similar levels of negative rumination as MDD, suggesting that negative rumination is associated with bipolarity. We therefore predicted that people with high familial risks for BD would have higher levels of rumination to both positive and negative affect than those without such risks.

7.1.3 Mental imagery, responses to positive and negative affect, behavioural approach system (BAS) sensitivity, and bipolarity

Previous studies have reported elevated BAS sensitivity in people with high bipolar risks (HR) compared to those without such risks (LR) (Carver & White, 1994) and that students with high BAS sensitivity were more likely to develop bipolar spectrum disorders (BSD) than those with low BAS (Alloy et al., 2012). Study 2 has further shown that BAS sensitivity was persistently elevated in BD-I across symptomatic states, again pointing to its role as a trait marker of bipolarity. We therefore hypothesise that late adolescent or young adult at-risk individuals with high familial risks will have higher levels of BAS sensitivity than age-matched individuals without such familial risks.

Study 1 found that positive rumination about emotional materials in the form of positive prospective images predicted BAS Drive Scale, which in turn predicted higher likelihood of having BD-I rather than MDD. It is not known whether similar findings could be obtained in a sample of people with high bipolar risks. Evidence that similar cognitive mechanisms were at play in an at-risk population would provide some preliminary data that this process might be related onset of (hypo)mania in people at risk for BD. Thus, the current study hypothesized that an interaction between positive rumination and positive prospective images would predict lifetime hypomanic symptoms in a HR group. Furthermore, BAS sensitivity would moderate the relationships between positive rumination about positive prospective imagery and lifetime hypomanic symptoms.

Depressive rumination has been found to be elevated in people with BD (Gruber et al., 2011). Study 3 reported that depressive rumination about negative prospective imagery was predictive of current depressive symptoms in MDD with varying degrees of bipolarity. This study would hypothesise that this relationship will also be found in people with HR. If depression was related to excessive deactivation of BAS in relation to BAS de-activating

events, it would further be postulated that the relationships between negative rumination negative prospective imagery, and depressive symptoms would be moderated by the BAS sensitivity.

7.1.4 Mental imagery susceptibility, creativity, and bipolar risks

Holmes et al. (2008) suggested mental imagery may promote creativity by allowing novel and non-linear combinations of ideas into pictures. Given that patients with BD were more susceptible to mental imagery than those without the disorder, mental imagery susceptibility might be a possible candidate in enhancing creativity among people at high risk for BD (see Chapter 1 for more details). Visual creativity, one type of creativity, might be elevated among adolescents or young adults with high familiar risks for BD in comparison to an age-matched low bipolar risk group. The current study also attempted to explore this hypothesis.

7.1.5 Childhood trauma and strong emotional images

While genetic factors might play a role in determining individual susceptibility to mental imagery, previous research suggests that past traumatic experiences including childhood abuse might be associated with increased experiences of intrusive visual images in adulthood (Brewin et al., 2010; Hackmann et al.,2000). Childhood trauma has been found to be common and severe among people with BD and may worsen the clinical expression of the illness in terms of suicidal risks and inter-episode emotional instability (Etain et al., 2008). If mental imagery susceptibility is associated with emotional instability and suicidality (Holmes et al., 2008; Holmes et al., 2011; Studies 3 and 6), past traumatic experiences might then exert its adverse impact on emotional instability via the mediating effect of enhancing

mental imagery susceptibility. The current study hypothesised that emotional instability as reflected by lifetime hypomanic symptoms would be predicted by childhood abuse, and this relationship would be mediated by emotional impact of prospective imagery.

7.2 Study hypotheses

The primary hypothesis is:

1. Adolescent and young adult participants aged below the mean age of the group (i.e. aged 28) with high familial risk will have higher levels of mental imagery susceptibility, responses to positive and negative affect, and BAS total scores than control participants of the same age range.

The secondary hypotheses are:

2. The mean number of positive prospective images and positive rumination will predict BAS Drive Scale in the whole group. The BAS Drive Scale will moderate the relationships between the interaction factor of positive prospective imagery and positive rumination, and lifetime hypomanic symptoms. The interaction factor of depressive rumination and negative prospective images will negatively predict BAS Scales in the whole group. The BAS Scales will moderate the relationships between the interaction factor of negative prospective imagery and depressive rumination, and depressive symptoms.
3. Participants with high bipolar risks aged below 28 would have higher levels of visual creativity than participants with low risks of similar age range. The levels of visual creativity would be predicted by general use of imagery in daily life in the whole group.
4. The high risk group (HR) will have higher levels of childhood trauma than the low

risk group (LR). The relationship between childhood trauma experiences and emotional instability as measured by lifetime hypomanic symptoms will be moderated by the emotional impact of prospective imagery in the whole group.

7.3 Methods

7.3.1 Participant recruitment

First-degree relatives of patients with BD-I were approached to participate in the current study. The patients with BD-I were outpatients currently being followed up in a regional psychiatric clinic in Hong Kong. One hundred and fifty patients had their principal psychiatric diagnoses of BD-I verified by the Chinese Bilingual Version of Structured Clinical interview for DSM-IV-TR Diagnosis (CB-SCID-I/P; So et al., 2003a) for other unrelated studies conducted in the same clinic. The author first approached these patients to explain the study and then invited them to nominate a first- degree relative for potential participation. The author contacted the nominated first-degree relative by phone to explain the study, invited interested relatives for a face-to-face interview to assess eligibility and then obtained informed consent. In order to reduce high correlations among the participants due to genetic loadings, only one relative nominated by the patients with BD-I was invited to participate. If ineligible or unavailable for the current study, the relative was then requested to nominate another first- degree relative of the index patient for further screening. A total of 78 first-degree relatives of patients with BD-I was recruited. A group of non-psychiatric controls of similar age, gender distribution, years of education and region of residence (by individual matching) were recruited from the same pool sample of participants (N = 4902) in the Hong Kong Mental Morbidity Survey (HKMMS) used in Study 3. None of the control participants declined the invitation to participate. The study was approved by local research ethics

committee (reference number: KC/KE-12-0150/ER-2).

7.3.2 Inclusion and exclusion criteria

All high risk cases (HR) and low risk controls (LR) were: (1) able to read and write Chinese; (2) aged 18-65; (3) ethnic Chinese in origin; and (4) able to provide informed consent. For cases, they were: (1) a first-degree relative of a patient suffering from BD-I as verified in the Clinical Information System of Hospital Authority of Hong Kong and by CB-SCID-I/P (So et al. 2003a) and were being followed up in the regional psychiatric clinic concerned; (2) free from any current DSM-IV-TR diagnosis as verified by CB-SCID-I/P (So et al. 2003b); (3) scoring a total of 7 or fewer on the Young Mania Rating Scale (YMRS; Tohen et al., 2003) at the time of the interview; and (4) scoring a total of less than 12 on the Beck Depression Inventory (BDI-II; Beck, Steer & Brown, 1996) at the time of the interview. Non-psychiatric controls had: (1) a Clinical Interview Schedule-Revised (CIS-R; Lewis et al., 1992) total score of less than 7; (2) no past history of psychiatric treatment; (3) a total score of YMRS of 7 or fewer at the time of the interview; (4) a total BDI-II score of less than 12 at the time of the interview; and (5) no current DSM-IV-TR diagnosis as verified by CB-SCID-I/P (So et al. 2003b).

The exclusion criteria for both cases and controls were having: (1) any current DSM-IV-TR diagnosis as defined by CB-SCID-I/P (So et al., 2003b); (2) any neurological or organic disorders that have an adverse impact on intelligence or reasoning ability; (3) visual problems that might affect their ability to read the figures or pictures clearly; and (4) impaired capacity to give informed consent.

7.3.3 Assessment instruments

7.3.3.1 Baseline demographic data sheet

The datasheet recorded age, gender, years of education, and current employment status of each participant. The presence of any family history of psychiatric illness and the type of psychiatric illness if known to the participants, as well as their past history of psychiatric illness or treatment, were also recorded.

7.3.3.2 Clinical measures

Chinese-bilingual Structured Interview for DSM-IV (Axis I, Patient version) (CB-SCID-I/P) (So et al 2003a; 2003b): The author and another experienced psychiatrist achieved a criterion inter-rater reliability of weighted kappa agreement of at least 0.80 for all modules before commencement of the current study.

Beck Depression Inventory-Second edition (BDI-II; Beck, Steer & Brown 1996): A validated Chinese version was used (Zhang et al, 1989) which had a good internal consistency in the current study (Cronbach's alpha = 0.89).

Young Mania Rating Scale (YMRS; Young, Biggs & Ziegler 1978): The two raters previously established a good kappa agreement in another sample of patients with bipolar disorders (n = 10) and unipolar disorders (n = 10) of an unrelated study (weighted kappa = 0.94).

Hypomania Checklist-32 (HCL-32 Checklist; Angst et al., 2005; Poon et al., 2009): For the current study, the core 32 items of the HCL-32 Checklist had a good internal consistency (Cronbach's alpha = 0.90).

Beck Anxiety Inventory (BAI; Beck, 1988): The validated Chinese version was used (Che, 2006). In the current study, the internal consistency of the scale was good (Cronbach's alpha = 0.92).

7.3.3.3 Imagery characteristics, behavioural approach system (BAS) sensitivity measure, and positive and negative ruminative style measures

Spontaneous Use of Imagery Scale (SUIS) (Reisberg, Pearson & Kosslyn 2003): For the current study, the internal consistency of the translated version was good (Cronbach's alpha = 0.82).

Impact of Future Events Scale (IFES; Deeprose & Holmes, 2010): For the current study, the internal consistency of the translated scale was good (Cronbach's alpha = 0.93).

Behavioural Inhibition/Behavioural Approach System Scale (BIS/BAS Scale; Carver & White, 1994): For the present study, only the three scales assessing BAS functioning were used (BAS Drive, BAS Fun Seeking and BAS Reward Responsiveness). Cronbach's alphas for three BAS scales in the current sample were respectively 0.63, 0.61 and 0.62.

Response to Positive Affect Questionnaire (RPA Questionnaire) (Feldman, Joorman & Johnson, 2008): For the current study, the RPA-EF and RPA-SF sub-scales of the translated version had good internal consistencies (Cronbach's alphas; RPA-EF = 0.81; RPA-SF = 0.75).

Ruminative Style Scale-Short Form (RSQ-SF; Nolen-Hoeksema & Morrow, 1991): For the current study, the translated scale (Ng & Dinesh, 2008) had a good internal consistency (Cronbach's alpha = 0.88).

7.3.3.4 Creativity measure

Barron-Welch Arts Scale (BWAS; Barron, 1963): This measures visual creativity. This yields a BWAS total score, and two sub-scores, BWAS-Like and BWAS-Dislike.

7.3.3.5 Measures of lifetime traumatic experiences

Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2004; Zhao et al., 2005): The validated Chinese version was used (Zhao et al., 2005) which had a good internal consistency

in this study (Cronbach's alpha = 0.76).

Life Events Checklist (LEC; Gray et al., 2004; Lam et al., 2014a): For the current study, the translated scale had a good internal consistency (Cronbach's alpha = 0.77).

7.4 Sample size calculation and statistical analyses

Sample size calculation was based on the mean standardized difference in IFES total and SUIS total scores between people with HR and those with LR (Malik et al., 2014). The sample size was calculated to require at least 29 first-degree relatives of BD-I and 29 non-psychiatric controls, in order to achieve an alpha significance level of 5% and a power of 90%.

STATA 12 statistical software (STATACorp, 2011) was used for statistical analyses. The differences in baseline demographic and clinical data of continuous nature were compared between the two groups using independent t-tests if the data were normally distributed or were normalised after square root transformation. All categorical data were compared between the two groups by using cross tabulation tests. For comparison of mental imagery susceptibility (SUIS and IFES), the number of positive and negative prospective images, responses to positive and negative affect, BAS scales, as well as the levels of creativity and childhood traumas between the two risk groups, an analysis of co-variance was employed. Any baseline demographic variable found to be statistically significant between the two groups was entered as a covariate in the analysis of co-variance (ANCOVA). YMRS total score, HCL-32 total score, and BDI-II total scores were not included as covariates as they were considered as possible outcome variables of interest. As some theoretically important confounders including gender, age, and years of education were already controlled through individual matching, they were not entered as covariates in ANCOVA. However, in view of the discussion in Section 7.1, age X group interaction factor was added as a potential covariate to examine the specific hypothesis about age-specific differences in these imagery

characteristics, BAS sensitivity, visual creativity, and responses to positive and negative affect between the two risk groups. If age X group factor was significant in the ANCOVA models, the dependent variables were then examined for significant differences between the two risk groups by planned age-stratified univariate analysis, with the risk groups split based on the mean age of the whole sample. The demographic and clinical variables in the respective age-stratified groups would be examined for any significant differences. Those of significant differences would be included as co-variates in the age-stratified analyses. Bootstrapping method was applied in the multi-variate and univariate analyses. In view of the exploratory nature of these analyses, the significant *p*-value was set at 0.05.

Hierarchical stepwise regression was conducted with HCL-32 total score as the dependent variable, and IFES total score, SUIS total score, IFES negative events score, and IFES positive events score as independent variables for the whole sample. Demographic and clinical variables of theoretical and statistical significance were first entered into the hierarchical regression model as Block 1 (BAI total score, CTQ total score, and LEC total score), then bipolar risk status as Block 2, followed by IFES positive events, IFES negative events, IFES total and SUIS total scores as Block 3. Another set of hierarchical stepwise regression modelling was conducted with BDI-II total scores as dependent variable and identical independent variables as above. Another two sets of hierarchical regression modelling were then conducted as above to assess the predictive effects of response to positive and negative affect (as measured by RPA-FE and RPA-SF sub-scales and RSS-SF total respectively to replace the imagery characteristics of IFES total, SUIS total, IFES positive events, and IFES negative events) on HCL-32 total scores and BDI-II total scores respectively. If the independent variables of mental imagery susceptibility and responses to positive and negative affect were significant predictors of the outcome variables (HCL-32 total score and BDI-II total score), their interaction factors would then be examined . Due to the limited sample size precluding the incorporation of the interaction factors (i.e. IFES

negative events X RSS-SF total, IFES positive events X RPA-SF total and IFES positive events X RPA-EF total) into the above hierarchical stepwise regression modelling, linear regressions were performed to explore the predictive effects of the interaction factor of IFES negative events X RSS-SF total on BDI-II total scores, after controlling for the independent effects of IFES negative events and RSS-SF total scores. Similar linear regressions were conducted for the predictive effects of interaction factors of IFES positive events X RPA-EF, and IFES positive events X RPA-SF on HCL-32 total scores. Mediational analyses (Baron & Kenny, 1985) were performed to assess whether BAS levels could be a mediating factor between the above interaction factors and mood symptoms.

7.5 Results

7.5.1 Demographic and clinical characteristics

Ninety-two first-degree relatives of patients with BD-I were approached (see figure 1 for details). In summary, 15% of first degree relatives approached either refused to participate or were not eligible (*n* = 15), resulting in a sample of 78 participants with high bipolar risks. Their blood relationships with the patients were: 32.1% parents (*n* = 25), 39.7% siblings (*n* = 31), and 28.2% offspring of the patients (*n* = 22) (see flow diagram 1 below). Their proband ill relatives were suffering from BD-I with an early age of onset (mean age = 20.3; *SD* = 4.67) and had a large number of lifetime psychiatric admissions (median = 5; interquartile range= 3-8). None of the participants with low bipolar risk had any family history of bipolar disorder. All control participants (*n* = 76) were individually matched with the cases on a one-by-one basis, except that the last two cases were not matched with control participants due to funding issues.

Flow diagram 1: the recruitment of the research participants with high familial risks

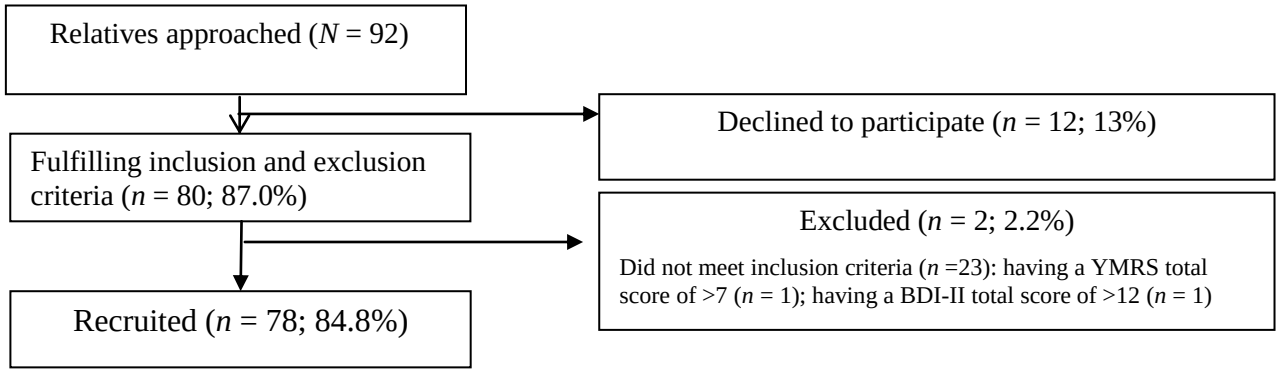


Table 1 shows the demographic and clinical characteristics of participants with high (HR) and low familial risks (LR) for bipolar disorders. As the two groups were individually matched in gender, age and years of education, these demographic variables were similar between the two groups. Furthermore, the two groups were found to have no significant current manic symptoms (YMRS total: HR = 0.3 [*SD* = 0.09] vs. LR = 0.1 [*SD* = 0.05]). Both groups had a similar proportion of participants with a history of psychiatric illness (HR = 3.8% vs. LR = 3.9%) or of affective illness (HR = 3.8% vs. LR = 1.4%; Fisher's exact test: *p* = 0.37). In brief, there were no significant differences in the baseline demographic variables between the two risk groups.

However, the two groups were significantly different in the levels of HCL-32 total score (HR = 11.5 [*SD* = 5.95] vs. LR = 8.5 [*SD* = 7.69]). None of the high risk participants with a HCL-32 total score of 11 or above fulfilled the additional required criterion of past hypomanic symptoms having negative impact on oneself or to others for the diagnosis of bipolar disorders (Poon et al., 2012). Although the participants with HR had no formal current psychiatric diagnosis, their current anxiety and depressive symptoms were still higher than those of the control participants (BDI-II total: HR = 5.6 [*SD* =6.36] vs. LR = 2.1 [*SD* = 2.74]; BAI total: HR= 6.2 [*SD* = 7.47] vs. LR= 1.6 [*SD* = 3.19]), but were still substantially below the threshold levels of clinical significance. In summary, the high risk group did not have clinically diagnosable mood disorders though reported having sub-threshold depressive and

anxiety symptoms and lifetime hypomanic symptoms.

Table 1: Demographic and clinical characteristics of the high and low bipolar risk groups (*N* = 154)

Demographic/clinical characteristics	High bipolar risk (*n* = 78)	Low bipolar risk (*n* = 76)	Statistics (chi-squared/*t*-value/z-value, degree of freedom, *p*-value)
Male (*%*)	35 (44.9)	36 (47.4)	X^2=0.10, *df* = 2, *p* = 0.76
Mean age (*SD*)	35.8 (15.25)	36.5 (14.91)	*t* = -0.30; *d.f.*= 152; *p* = 0.76;
Mean years of education (*SD*)	14.9 (3.22)	15.7 (3.96)	*t* = -1.44; *d.f.*= 152; *p* = 0.15
Past history of psychiatric illness (%)	3 (3.8)	3 (3.9)	X^2 = 0.01, *df* = 2, *p* = 0.97
Mean BDI-II[a] (*SD*)	5.6 (6.36)	2.1 (2.74)	*t* = 4.55; *d.f.*= 152; ***p* < 0.001**
Mean BAI[b] (*SD*)	6.2 (7.47)	1.6 (3.19)	*t*= 5.01; *d.f.*= 152; ***p* <0.001**
Mean YMRS[c] (*SD*)	0.3 (0.09)	0.1 (0.05)	*Z* = -1.04, *p* = .30
Mean HCL-32[d] (*SD*)	11.5 (5.95)	8.5 (7.69)	*Z* = -2.65, ***p* = 0.008**
Mean total CTQ[e] (*SD*)	41.5 (10.47)	35.2 (8.27)	*t* = 4.22, *d.f.* = 152, ***p* < 0.001**
Mean total LEC[f] *(SD)*	1.6 (1.65)	0.7 (1.09)	*t* = 4.28, *d.f.*= 152, ***p* < 0.001**

a: Beck Depression Inventory-II; b: Beck Anxiety Inventory; c: Young Mania Rating Scale; d: Hypomania Checklist-32; e: Childhood Trauma Questionnaire; f: Life Experiences Checklist; a=square root transformed value

7.5.2 Mental imagery susceptibility, response to positive and negative affect, and BAS sensitivity

Table 2 shows the key cognitive variables between the two risk groups.

Table 2: Mental imagery susceptibility and responses to positive and negative affect in the high and low bipolar risk groups (*N* = 154)

Cognitive measures	High bipolar risk (*n* = 78)	Low bipolar risk (*n* = 76)
Mental imagery susceptibility		
Mean total SUIS[g] (*SD*)	33.7 (11.03)	35.6 (9.49)
Mean total IFES[h] (*SD*)	23.0 (10.75)	20.2 (9.93)
Mean IFES positive events (*SD*)	1.3 (0.93)	1.7 (0.87)
Mean IFES negative events *(SD*)	0.6 (0.79)	0.3 (0.62)
Responses to positive/negative affect		
Mean RPA[i] sub-scales (*SD*)		
RPA-emotion focus (RPA-EF)(*SD*)	14.5 (2.99)	13.6 (3.19)
RPA-self-focus (RPA-SF) (*SD*)	10.1 (2.54)	8.6 (3.00)
Mean RSS-SF[j] (*SD*)	20.4 (5.59)	18.9 (5.17)
BAS sensitivity		
Mean BAS[k] Drive (*SD*)	10.9 (1.22)	10.2 (1.56)
Mean BAS Fun Seeking (*SD*)	11.4 (1.54)	10.5 (1.62)
Mean BAS Reward Responsiveness (*SD*)	15.7 (2.80)	16.2 (2.24)

g: Spontaneous Use of Imagery Scale; h: Impact of Future Events Scale; i: Response to Positive Affect Questionnaire; j: Response Style Scale – Short Form; k: Behavioural Activation Scale

Separate Analysis of co-variance (ANCOVA) with CTQ total score, LEC total score, BAI total score, and the interaction factor of Age X Group entered as the covariates was conducted for the key cognitive variables. Results showed that the overall multivariate model of SUIS total score was significant (corrected model: $F[5, 147] = 11.22$, $p < 0.001$; Age X Group interaction effect: $F[1,152] = 35.17$, $p < 0.001$; main effect of Group: $F[1, 152] = 14.63$, $p < 0.001$; main effect of LEC total: $F[1, 152] = 19.54$, $p < 0.001$).

The overall multivariate model of IFES total score was also significant (corrected model: $F[5, 144] = 11.99$, $p < 0.001$; Age X Group interaction effect: $F[1,149] = 3.51$, $p = 0.05$; main effect of BAI total: $F[1, 149] = 19.56$, $p < 0.001$; main effect of LEC total: $F[1, 149] = 15.44$, $p < 0.001$). For IFES positive events, the overall model was significant ($F[5, 144] = 2.26$, $p = 0.05$). However, no other main or interaction effects of Group or co-variates

were significant. Again for IFES negative events, the overall model was significant (F[5, 144] = 4.22, p = 0.001). The main effect of BAI total score was significant (F[1, 149] = 7.23, p = 0.008). However, other main effects of Group or co-variates and the interaction effect of Age x Group were not significant.

Furthermore, the overall multivariate model of RPA-EF was significant (F[5, 147] = 4.81, p < 0.001). The main effect of Group, BAI total score, and the interaction effect of Age X Group were significant (Age X Group: F[1, 152] = 10.74, p = 0.001; Group: F[1, 152] = 6.78, p = 0.01; BAI total: F[1, 152] = 7.33, p = 0.008). The multivariate model of RPA-SF was also significant (F[5, 147] = 6.16, p < 0.001). The main effects of Group, CTQ total score, and BAI total score were significant (F[1, 152] = 3.79, p = 0.005; CTQ total: F[1, 152] = 4.74, p = 0.03; BAI total: F[1, 152] = 4.25, p = 0.04) but the interaction effect of Age X Group was not (F[1, 152] = 2.63, p = 0.11).

The multivariate model of RSS-SF total score was also significant (F[5, 147] = 19.94, p < 0.001). Furthermore, the main effects of Group, CTQ total score, and BAI total score, as well as the interaction effect of Age X Group were all significant (Group: F [1, 152] = 7.75, p < 0.001; CTQ total: F[1, 152] = 4.10, p = 0.05; BAI total: F[1, 152] = 51.22, p < 0.001; Age X Group: F[1, 152] = 28.33, p < 0.001).

Finally, the overall multivariate model of BAS Drive was not significant (F[5, 147] = 1.91, p = 0.10). The overall model of BAS Fun Seeking Scale was also not significant (F[5, 146] = 1.99, p = 0.08). However, the overall multivariate model for BAS Reward Responsiveness was significant (F[5, 147] = 3.48, p = 0.005). The main effect of Group and the interaction effect of Age X Group were significant (Group: F[1, 152] = 5.63, p = 0.02; Age X Group: F[1, 152] = 3.90, p < 0.001).

In summary, significant interaction effects of Age X Group were found in the following key variables: SUIS total score, IFES total score, RPA-EF score, RSS-SF total score, and BAS Reward Responsiveness Scale score. The IFES positive and negative events scores,

BAS Fun Seeking Scale score were not significantly different between the two risk groups. For RPA-SF, HR group was higher than LR group but there was no age-specific effect observed.

The whole sample was age-stratified into two groups based on the mean age of the sample, one group aged below 28 years old (late adolescence/young adult group; $n = 66$), and the other aged 28 years old or above (adult group; $n = 88$). Univariate analysis revealed that the HR and LR groups aged below 28 were significantly different in years of education, CTQ total score, LEC total score, and BAI total score. Furthermore, the HR group had higher levels of HCL-32 total score and BDI total scores than the age-matched LR group. YMRS total scores were not significantly different between the two groups. For the risk groups aged 28 or above, CTQ total score, LEC total score, and BAI total score were significantly different between the two risk groups. Furthermore, the BDI-II total score was higher in the HR group. The HCL-32 total score and YMRS total score were not significantly different between the two groups. These demographic and clinical variables (except BDI-II, YMRS and HCL-32 total scores) of significant differences were used as co-variates in the respective age-stratified ANCOVA.

As shown in Table 3, the HR had a higher level of general use of imagery in daily life than the LR group aged below 28 (HR = 40.4 [*SD* = 9.00] vs. LR = 32.8 [*SD* = 9.66]; ANCOVA: corrected model: $F[5, 60] = 7.94$, $p < 0.001$; Group factor: $F[1, 65) = 7.93$, $p = 0.006$; LEC total: $F[1, 65] = 23.66$, $p < 0.001$). However, the direction of differences in the levels of general use of imagery were *reversed* between the two risk groups aged 28 or above, with the HR group having a lower level than the LR group (HR = 28.1 [*SD* = 9.53] vs. LR=37.6 [*SD* = 8.96]; ANCOVA; corrected model=$F[4, 82] = 6.99$, $p < 0.001$; Group factor: $F[1, 86] = 18.45$, $p < 0.001$).

As shown in Table 3 again, the HR had a higher level of emotional impact of prospective imagery than the LR group aged below 28 (HR = 25.7 [*SD* = 6.62] vs. LR = 20.7

[*SD* = 7.79]; ANCOVA: corrected model: $F[5, 60] = 11.77$, $p < 0.001$; Group factor: $F[1, 65] = 7.93$, $p = 0.006$; LEC total score: $F[1, 65] = 23.87$, $p < 0.001$; Years of education: $F[1, 65] = 16.33$, $p < 0.001$). However, the direction of difference in the levels of emotional impact of prospective imagery were *reversed* between the two risk groups aged 28 or above, with the high bipolar risk group having a lower level than the low risk group (HR = 19.8 [*SD* = 11.30] vs. LR=20.6 [*SD* = 12.92]; ANCOVA; corrected model=$F[4, 79] = 10.00$, $p < 0.001$; Group factor: $F[1, 86] = 7.37$, $p = 0.008$; BAI total score: $F[1, 86] = 21.39$, $p < 0.001$).

The RPA-EF was also significantly higher in the HR group aged below 28 ((HR = 15.9 [*SD* = 2.23] vs. LR = 15.1 [*SD* = 1.95]; ANCOVA: corrected model: $F[5, 60] = 3.27$, $p = 0.01$; Group factor: $F[1, 65] = 5.26$, $p = 0.03$). However, there was no significant difference in RPA-EF score between the risk groups aged 28 or above (HR = 13.4 [*SD* = 3.05] vs. LR = 13.2 [*SD* = 3.80]; ANCOVA: corrected model: $F[4, 82] = 2.35$, $p =0.06$; Group factor: $F[1, 86] = 1.94$, $p = 0.17$; BAI total score: $F[1, 86] = 4.63$, $p = 0.03$).

RSS-SF total scores were similar in the HR group aged below 28 (HR = 23.0 [*SD* = 5.31] vs. LR = 19.7 [*SD* = 4.43]; ANCOVA: corrected model: $F[5, 60] = 23.07$, $p < 0.001$; Group factor: $F[1, 65] = 2.68$, $p = 0.11$; BAI total score: $F[1, 65] = 30.46$, $p < 0.001$). On the other hand, the RRS-SF total score was significantly higher in the HR group aged 28 or above (HR = 18.4 [*SD* = 5.58] vs. LR = 18.2 [*SD* = 4.90]; ANCOVA: corrected model: $F[4, 82] = 9.30$, $p < 0.001$; Group factor: $F[1, 86] = 7.89$, $p = 0.006$; BAI total score: $F[1, 65] = 33.78$, $p < 0.001$).

The BAS reward responsiveness scale was also significantly higher in the HR group aged below 28 (HR = 16.7 [*SD* = 2.20] vs. LR = 15.8 [*SD* = 1.71]; ANCOVA: corrected model: $F[5, 60] = 4.00$, $p = 0.003$; Group factor: $F[1, 65] = 7.99$, $p = 0.006$; BAI total score: $F[1, 65] = 8.91$, $p = 0.004$). However, there was no significant difference in BAS reward responsiveness scale score between the risk groups aged 28 or above (HR = 14.9 [*SD* = 2.97] vs. LR = 15.8 [*SD* = 2.98]; ANCOVA: corrected model: $F[4, 82] = 1.01$, $p =0.41$).

In summary, consistent with the first hypothesis, there appears to be an age-specific effect that HR group aged below 28 had *higher* levels of general use of imagery in daily life and emotional impact of prospective imagery than LR group. However, general use of imagery and emotional impact of prospective imagery were *lower* in HR group than low risk group aged 28 or above. Furthermore, also consistent with the first hypothesis, the HR group had *higher* levels of responses to positive affect in the form of rumination about positive emotions than the LR risk group aged below 28. However, this was *similar* between the two risk groups aged 28 or above. On the other hand, the HR and LR groups aged below 28 had *similar* levels of response to negative affect, namely negative rumination. However, the HR group had *higher* level of negative rumination than the LR group aged 28 or above. Finally, BAS Reward Responsiveness Scale was higher in HR group aged below 28 when compared to the age-matched LR group. No significant differences in this scale were found between the risk groups aged 28 or above. RPA-SF was significantly higher in the HR group but there were no age-specific differences in the two risk groups. There were no significant differences between IFES positive and negative events scores, BAS Drive and Fun Seeking Scales between the two risk groups as a whole.

Table 3: Differences in clinical variables, mental imagery susceptibility, response to positive and negative affect between the high and low bipolar risks stratified by the mean cut-off age of 28 (*N*=154)

Cognitive characteristics	High vs. low bipolar risk (aged below 28)		High vs. low bipolar risk (aged 28 or above)	
	High risk (*n*=35)	Low risk (*n*=31)	High risk (*n*=43)	Low risk (*n*=45)
Clinical measures				
Mean HCL-32 (*SD)*	13.8 (4.63)	8.7 (6.88)	9.7 (6.32)	8.4 (8.28)
Mean BDI-II (*SD*)	4.9 (4.86)	2.1 (2.85)	6.2 (7.38)	2.1 (2.69)
Mean BAI (*SD*)	5.9 (6.77)	1.0 (1.77)	6.4 (8.06)	1.9 (3.86)
Mental imagery measures				
Mean SUIS total (*SD*)	40.4 (9.00)	32.8 (9.66)	28.2 (9.42)	37.6 (8.96)
Mean IFES total (*SD*)	25.7 (6.62)	20.7 (7.79)	19.8 (11.30)	20.6 (12.92)
Responses to positive and negative affect				
Mean RPA-EF (*SD*)	15.9 (2.23)	15.1 (1.95)	13.4 (3.05)	13.2 (3.80)
Mean RSS-SF (*SD*)	23.0 (5.31)	19.7 (4.43)	18.4 (5.58)	18.2 (4.90)

7.5.3 Rumination about emotional materials in the form of prospective imagery

Consistent with the second hypothesis, linear regression modelling revealed that the interaction factors of RPA-EF X IFES positive events and RPA-SF X IFES positive events were significant predictors of BAS-Drive Scale in high bipolar risk group after controlling for IFES positive events and positive rumination sub-scales (RPA-EF X IFES positive events: *B* = 1.44, *SE* = 0.08, *beta* = 1.44, *t* = 2.28, *p* = 0.03; RPA-SF X IFES positive events*: B* = 0.15, *SE* = 0.08, *beta* = 0.84, *t* = 1.98, *p* = 0.05). Mediational analyses revealed that BAS Drive mediated the relationships between the interaction factor of RPA-EF X IFES positive events and HCL-32 total score (overall model: *F*[2, 75] = 7.52, *p* = 0.001; BAS Drive: *B* = 1.01, *SE* = 0.36, *beta* = 0.32, *t* = 2.78, *p* = 0.007). BAS drive also mediated the relationships between the interaction factor of RPA-SF X IFES positive events and HCL-32 total score (overall

model: $F[2, 75] = 7.11$, $p = 0.002$; BAS Drive: $B = 1.03$, $SE = 0.36$, $beta = 0.33$, $t = 2.84$, $p = 0.006$). In summary, consistent with the second hypothesis, ruminations about the positive emotions and self-qualities associated with the positive prospective images would amplify hypomanic symptoms through the moderating effect of activating BAS Drive in people with high familial risk for bipolar disorders.

On the other hand, the interaction factor of depressive rumination (RSS-SF total) and the number of negative prospective imagery (IFES negative events score) was predictive of depressive symptoms (BDI-II total) (RSS-SF X IFES negative events: $B = 0.92$, $SE = 0.36$, $beta = 1.78$, $t = 2.57$, $p = 0.01$). In addition, the interaction factor of RSS-SF X IFES negative events was a negative predictor of BAS Reward Responsiveness ($B = -2.47$, $SE = 0.81$, $beta = -2.44$, $t = -3.03$, $p = 0.003$). Mediational analysis revealed that the interaction factor of RSS-SF total X IFES negative events was still predictive of current depressive symptoms even after controlling for BAS reward responsiveness (RSS-SF X IFES negative events: $B = 0.21$, $SE = 0.05$, $beta = 0.40$, $t = 3.87$, $p < 0.001$; BAS-Reward responsiveness: $B = -0.21$, $SE = 0.05$, $beta = -0.24$, $t = -2.33$, $p = 0.02$). In summary, partially consistent with the second hypothesis, depressive rumination about negative prospective images might lead to an increase in depressive symptoms through de-activating BAS reward responsiveness function. However, unlike rumination about positive prospective images, rumination about negative images appeared to increase depressive symptoms via both BAS reward responsiveness function and other unknown pathways.

7.5.4 Creativity and mental imagery susceptibility

Partial correlation controlling for years of education revealed that the BWAS Like Sub-scale was not significantly correlated with the BWAS Dislike Sub-scale (Pearson's correlation = -0.10, $df = 152$, $p = 0.25$). ANCOVA revealed that the HR group had a similar

level of visual creativity as measured by the BWAS total score as the LR risk group as a whole (HR = 23.0 [*SD* = 14.25] vs. LR = 26.8 [*SD* = 11.11]; corrected model: *F*[4, 146] = 3.25, *p* = 0.01, Group: *F*[1, 150] = 1.84, *p* = 0.18; LEC total score: *F*[1, 150] = 4.04, p = 0.03, BAI total score = 5.07, *p* = 0.03). However, the HR group had higher levels of the BWAS Like subscale score (HR = 9.4 [*SD* = 6.84] vs. LR = 6.2 [*SD* = 5.92]; ANCOVA; corrected model: *F*[4, 72] = 4.72, *p* < 0.001, Group: *F*[1, 150] = 9.30, *p* = 0.003; LEC total score: *F*[1, 150] = 5.40, p = 0.02, BAI total score = 5.20, *p* = 0.02). However the HR group had a lower level of the BWAS Dislike subscale score than the LR group (HR= 13.4 [*SD* = 10.55] vs LR = 20.6 [*SD* = 11.78]; ANCOVA; corrected model: *F*[4, 147] = 4.87, *p* = 0.001, Group: *F*[1, 150] = 10.98, *p* = 0.001).

Multivariate analyses of BWAS total score using BAI total score, LEC total score, CTQ total score, and the interaction factor of Age X Group as the covariates revealed that the overall model was significant (*F*[5, 150] = 9.57, *p* < 0.001). The interaction effect of Age X Group and main effects of Group and LEC total scores were also significant (Age X Group: *F*[1, 150] = 32.07, *p* < 0.001;Group: *F[*1, 150] = 13.11, *p* < 0.001; LEC total score: *F*[1, 150] = 5.34, *p* = 0.02). When the HR group was split into two groups based on the sample mean age, the HR group aged below 28 had similar levels of visual creativity as measured by the BWAS total score as the age-matched LR group (HR = 31.1 [*SD* = 14.06 vs. LR = 28.7 [*SD* = 10.82]; ANCOVA: corrected model: *F*[5, 60] = 3.06, *p* = 0.02; Group: *F*[1, 65] = 0.02, *p* = 0.88; LEC total score: *F*[1, 65] = 14.35, *p* < 0.001). However, the HR group aged 28 or above had lower levels of creativity than the age-matched LR group (HR = 16.2 [*SD* = 10.38] vs. LR = 25.5 [*SD* = 11.24]; ANCOVA: corrected model: *F*[4, 80] = 7.17, *p* < 0.001; Group: *F*[1, 84] = 10.94, *p* = 0.001; CTQ total score: *F*[1, 84] = 7.57, *p* = 0.007; BAI total score: *F*[1, 84] = 5.31, *p* =0.02).

Further subscale analysis revealed that, among the age band aged below 28, the BWAS Like Subscale was significantly higher in the HR group (HR = 12.7 [*SD* = 6.52] vs. LR = 5.4

[*SD* = 5.09]; ANCOVA: corrected model: $F[5, 605] = 10.41$, $p < 0.001$; Group: $F[1, 65] = 7.09$, $p = 0.01$; LEC total score: $F[1, 65] = 16.49$, $p < 0.001$; years of education: $F[1, 65] = 7.92$, $p < 0.001$)) but the BWAS Dislike Subscale was similar between the two groups (HR = 18.4 [*SD* = 10.85] vs. LR = 23.3 [*SD* = 8.78]; corrected model: $F[5, 60] = 2.08$, $p = 0.80$). For the age band aged 28 or above, the BWAS Like subscale scores were not significantly different between the two risk groups yet the BWAS Dislike subscale scores were significantly lower in the high bipolar risk group (BWAS Dislike: HR = 9.5 [*SD* = 8.44] vs. LR = 18.7 [*SD* = 13.28); ANCOVA: corrected model: $F[4, 81] = 5.09$, $p = 0.001$; Group factor: $F[1, 85] = 11.13$, $p < 0.001$). In summary, visual creativity was similar across the two risk groups as a whole. However, partially consistent with the third hypothesis, age-stratified analysis revealed that the high risk group aged below 28 had higher levels of the BWAS Like score but similar levels of the BWAS Dislike score than the low risk group of same age band. For the age band aged 28 or above, the high risk group had a lower level of the BWAS Dislike score but similar level of the BWAS Like score as in low risk group.

Stepwise hierarchical regression showed that general use of imagery in daily life predicted the levels of visual creativity after controlling for bipolar risk status, age, years of education, LEC total score, CTQ total score, HCL-32 total score, BAI total and BDI-II total scores ($B = 0.32$, $SE = 0.11$, $beta = 0.25$, $p = 0.003$) . Consistent with the third hypothesis, the general tendency to use imagery in daily life was a positive predictor of visual creativity.

7.5.5 Childhood trauma, lifetime traumatic life events, and emotional impact of prospective imagery

As shown in Tables 1 and 2, the HR group reported higher levels of childhood trauma (CTQ total: HR = 41.5 [*SD* = 10.47] vs. LR = 35.2 [*SD* = 8.27]; *t*-test: $t = 4.22$, $df = 152$, $p < 0.001$) and lifetime traumatic life events (LEC total: HR = 1.6 [*SD* = 1.65] vs. LR = 0.7 [*SD* = 1.89]; *t*-test: $t = 4.28$, $df = 152$, $p < 0.001$) than the LR group. Childhood trauma as measured

by CTQ total and traumatic life events as measured by LEC total were significantly but not highly correlated (Pearson's correlation = 0.35, $p < 0.001$). The number of childhood traumas remained as a significant positive predictor of the emotional impact of prospective imagery after controlling for age, years of education, HCL-32 total score, bipolar risk status, BAI and BDI-II total scores (CTQ total: $B = 0.22$, $SE = 0.12$, $beta = 0.13$, $p = 0.05$). Self-reported lifetime traumatic events as measured by the LEC were, however, not a significant predictor of the emotional impact of prospective imagery.

7.6 Discussion

7.6.1 Mental imagery susceptibility and bipolar risks

This is the first study to investigate the relationships between mental imagery susceptibility and bipolar risks using a matched controlled design comparing a group of participants with high familial risks of bipolar disorder and a group of control participants with a low bipolar risk. The key finding is that, when compared to people with low bipolar risks of a similar age range, increased levels of use of imagery in daily life and emotional impact of prospective imagery were restricted to at-risk individuals aged below 28. As the mean age of onset of bipolar disorder is around 22 to 25 years old (Kessler et al., 2005), this group would be considered as having a particularly high risk of developing BD.

On the other hand, at-risk individuals aged 28 or above had lower levels of general use of imagery in daily life and emotional impact of prospective imagery than the participants with low bipolar risk. This older at-risk group might be considered as having passed through the critical period without developing a full-blown bipolar disorder and might therefore have a lower bipolar liability than the average individuals. In other words, both imagery characteristics in HR individuals in comparison with LR individuals might be possible

cognitive risk factors associated with bipolarity, a finding consistent with the behavioural high risk study (Study 4).

One might argue that a decline in general use of imagery in daily life and emotional impact of prospective imagery with age might equally explain the opposite results obtained in the age-stratified analyses. However, both imagery characteristics appeared to be a stable construct over a period of time when mood was stable (see Chapter 6 for details), at least over a period of seven weeks. Further research is required to investigate whether a low level of mental imagery susceptibility among people might lead to some protection or resilience against developing BD, or even an increased liability for other late-onset bipolar related disorders (e.g. major depressive disorder; Henin et al., 2005).

Combining the findings that, when compared to non-clinical controls, increased levels of general use of imagery in daily life and emotional impact of prospective imagery were found in patients with remitted BD-I (Study 1) and people with high behavioural risks for BD (Study 4), the detection of high levels of general use of imagery and emotional impact of prospective imagery among young individuals with high familial risks provides converging evidence that they may warrant further exploration as a possible cognitive marker associated with BD. The finding of Study 3 that levels of lifetime history of hypomanic symptoms were positively predicted by the levels of general use of imagery in daily life may provide a possible explanation of the potential role in inducing emotional instability associated with bipolarity. However, given that the studies conducted were cross-sectional ones and that the predictive effect was modelled statistically, caution must be taken in interpreting the above results.

7.6.2 Responses to positive and negative affect in bipolarity

Another key finding is that people with high familial risks of bipolar disorder reported

a higher tendency to ruminate about their positive emotional materials than those with a low risk. Specifically, age-stratified analysis revealed that this was accounted for by the significant differences between the two groups aged below 28. What this finding adds to the literature is that the heightened trait rumination of positive affect was found in individuals with high bipolar risk as defined by familial predisposition, complementing a similar finding in people considered as having bipolar risks based on a behavioural paradigm (Feldman et al., 2008).

The finding that the HR group had higher levels of depressive rumination than LR group aged above 28 only further suggests that the adult HR individuals were more inclined to ruminate in response to negative affect than age-matched LR control participants. Previous studies found that people with BD endorsed more rumination in response to negative affect compared to those without BD (Johnson, McKenzie & McMurrich, 2008; Knowles et al., 2005; Thomas & Bentall, 2002). Further studies are called for to understand whether enhanced tendency of negative rumination is restricted to adult-onset BD or other adult-onset psychiatric disorders associated with high bipolar risks (like depressive and anxiety disorders). In brief, excessive responses to both positive and negative affect were observed in people with high familial risks for bipolar disorders.

7.6.3 Rumination about emotional materials in the form of prospective imagery

Excessive rumination of positive prospective images being predictive of more lifetime hypomanic symptoms suggested that an excess of positive prospective images might amplify lifetime hypomanic symptoms in people with high familial risks for bipolar disorders, a process which appeared to be moderated by BAS Drive functioning. The findings are consistent with Alloy et al. ‘s (2012) and Johnson’s (2005) hypotheses that at-risk participants for BD have a hypersensitive BAS that might become activated in face of BAS-activating

event (in the current study, repetitive rumination about positive materials in the form of positive prospective images), therefore leading to an ascent of cognitive, emotional and behavioural approach symptoms characteristic of hypomania (see Section 1.1.8.2). Supporting the hyper-sensitive BAS as trait marker associated with bipolarity, the current study also found that BAS Reward Responsiveness Scale was elevated in the HR group compared to the LR group aged below 28. However, this difference was not observed in the group above 28. As such, this provides further support of the possible role of BAS sensitivity as a vulnerability factor of BD in at-risk individuals aged below 28.

What this study also adds to the literature is that depressive rumination about negative prospective images might trigger depressive symptoms through both routes: (1) de-activation of BAS reward responsiveness, or (2) other unknown pathways. The hypothesised role played by depressive rumination of negative prospective images in deactivating the BAS reward responsiveness function is reminiscent of the theory of BAS deactivation being related to bipolar depression (Depue & Iacono, 1989). This study provides preliminary evidence that people with high bipolar risks and heightened responses to positive and negative affect would experience either pathological positive or negative emotions, depending on the emotional valence of the future-oriented images. A prospective study of changes in these imagery characteristics from prodromal phase to onset of full-blown illness among a large sample of young individuals with high familial risks of bipolar disorder are needed to verify these hypotheses.

7.6.4 Creativity, mental imagery susceptibility and bipolarity

Contrary to previous research findings (Furnham et al., 2008; Rawlings & Georgiou, 2004), the current study found that the HR group had similar levels of visual creativity as measured by the BWAS total scores than the LR group as a whole. However, age-stratified

analyses revealed that the HR group aged 28 or above had lower levels of visual creativity than the LR group, whereas the two risk groups aged below 28 had similar levels of visual creativity. The BWAS Like Sub-scale measures an individual's preference for complex figures while the BWAS Dislike Sub-scale measures an individual's distaste for simple figures. The lack of correlations between the two sub-scales in the current study suggests that the two preferences are not necessarily related. Srivasatva et al. (2010) found that the BWAS Like score was predicted by cognitive constructs of intuitive thinking measured by the Myers-Briggs Type Inventory (MBTI; Myers and McCaulley, 1985) and the Openness factor in the Neuroticism Extraversion Openness Personality Inventory (NEO; Costa and McCrae, 1985). On the other hand, the BWAS Dislike score was predicted by affective or related constructs of the Neuroticism factor in the NEO and the Cyclothymia (changeability of mood) factor measured by the Temperament Evaluation of the Memphis, Pisa, Paris and San Diego Auto questionnaire (TEMPS-A; Akiskal et al., 2005).

In the current study, sub-scale analyses revealed that the HR group aged below 28 had a higher level of the BWAS Like score than but similar level of the BWAS Dislike score as the LR group, suggesting that the young at-risk individuals had enhanced positive discrimination of complex figures that contributes to creativity. Individuals with an intuitive type preference on the MBTI tend to process new information using abstract concepts, ideas, and associations (Myers and McCaulley, 1985). Intuition is also highly correlated to openness to new experiences measured by the NEO (Myers and McCaulley, 1985). As such, the increase in the BWAS Like score in the at-risk adolescents and young adults suggests that their visual creativity was mainly contributed by cognitive attributes of openness to new experiences and intuitive thinking (Srivasatva et al., 2010). Although previous study has supported first-degree relatives of bipolar disorder being more creative than normal controls (Richards et al., 1988), there was no information about the prevailing temperaments or mood symptoms in these first-degree relative groups. Other studies that reported higher levels of

visual creativity in high bipolar risk group than healthy controls recruited samples of individuals with hypomanic traits and mania-proneness based on behavioural paradigms rather than a familiar risk sample (Furnham et al., 2008; Rawlings & Georgiou, 2004). It is possible that cyclothymic temperament or emotionality associated with hypomanic traits and mania proneness might contribute to increased visual creativity through an increase in the BWAS Dislike score, a component heavily influenced by affective components of neuroticism and cyclothymic personality, in these high behavioural and familial risk samples.

Interestingly, the HR group aged above 28 had a lower level of the BWAS Dislike scores but a similar level of the BWAS Like score as the LR group, suggesting that the older HR individuals had lower negative discrimination for monotonous figures that contributes to lower creativity. The lower levels of the BWAS Dislike scores in this at-risk older adult group might imply lower levels of neuroticism and changeability of mood characteristic of cyclothymic temperament as compared to the age-matched low bipolar risk group. The absence of such personality/temperamental attributes might be associated with higher levels of emotional stability (Akiskal et al., 2005). Emotional instability is a symptom commonly observed in initial prodromal syndrome of mania (Skjelstad, Malt & Holte, 2010) so that this low BWAS Dislike score might be a proxy marker of relative emotional stability in this resilient group of high risk individuals without developing full-blown BD during the critical risk period. However, the above hypothesis remains highly tentative and future studies on creativity in familial high risk studies should include these cognitive and affective constructs for better understanding of the relative contribution of these factors to visual creativity.

As the level of visual creativity measured by the BWAS total score was predicted positively by general use of imagery in daily life, the younger HR group aged below 28 would be expected to exhibit higher levels of visual creativity than the LR group. Post-hoc linear regression supported that general use of imagery in daily life was a predictor of the BWAS Like Subscale scores but not for the BWAS Dislike Score. This would point to the

contribution of active use of visual imagery in promoting intuitive and open thinking. However, there might be other explanations for the lack of differences in visual creativity between the two risk groups. First, this might be due to a small sample size with its associated type II error. Second, other areas of creativity not investigated in this study might be higher among the high bipolar risk group. Third, the current study recruited a sample of first-degree relatives of patients with early-onset and highly recurrent bipolar disorders. As such, they might have different cognitive and affective characteristics that contribute to lower visual creativity than the first-degree relatives of patients with less recurrent and severe bipolar disorders recruited in other studies. Further studies directly comparing the creativity levels in these two types of at-risk individuals are required to test this hypothesis.

7.6.5 Past traumatic experiences and mental imagery susceptibility

Another important finding is that HR participants reported higher levels of childhood maltreatment and lifetime traumatic experiences than LR participants, consistent with recent studies reporting that people with risks for BD had higher levels of childhood traumas than those without such risks (Tjissen et al., 2010). The presence of excessive lifetime traumatic experiences in the HR individuals suggests that people with HR are also more likely to experience lifetime traumas than those with LR. It is not clear whether people with HR were more likely to experience lifetime traumas due to adverse environments associated with their close social relationships with patients with BD or whether their bipolar risks might predispose them to experiencing more adverse traumatic events (e.g. through increased impulsivity; Askenazy et al., 2003). The finding that the number of childhood maltreatment experiences positively predicts the levels of emotional impact of prospective imagery is consistent with existing literature that distressing visual images occurred in people who experienced past significant traumatic events (Ehlers & Clark, 2000; Hackmann, Clark &

McManus, 2000). This provides some support for the notion that the increased levels of emotional impact of prospective imagery among HR individuals and patients with BD might be partially explained by distal environmental factors of past childhood traumatic experiences. Again, given the cross-sectional nature of this study, longitudinal studies assessing the changes in the levels of emotional impact of prospective imagery over time among children with history of childhood maltreatment are needed.

7.7 Strengths and limitations

The current study has several strengths. All first-degree index relatives of participants were confirmed as suffering from DSM-IV-TR defined BD-I, rather than relying solely on the participants' self-reports of their relatives' illness. This would ensure that the HR participants had high familial risks of BD-I rather than having diathesis to other psychiatric disorders. Second, all participants were confirmed to be not suffering from any lifetime or current bipolar spectrum disorders by both clinician administered structured clinical interview so that any differences found between the two groups are likely to be attributed to underlying differences in bipolar risks. Third, the participants were all confirmed to be free from any major psychiatric disorders that might confound the relationships between bipolar risks and mental imagery susceptibility. Fourth, control participants were well matched with HR participants on potential confounders of the relationship between cognitive characteristics, creativity and bipolarity including gender, age, and geographical location. Fifth, a priori calculated sample size had ensured that the current sample had enough power to address the primary hypotheses about significant differences in mental imagery susceptibility between the two risk groups. Potential confounders like anxiety, past and lifetime traumatic experiences were statistically controlled in the analyses. Finally, self-administered scales were all locally

validated and were used in other studies, thereby allowing valid cross-cultural comparisons of the current findings.

The study also has a number of limitations. First, the sample size was not large enough to address all the secondary hypotheses so the lack of significant differences in emotional impact of prospective imagery and visual creativity between the young at-risk individuals and age-matched controls might be due to type II error. On the other hand, multiple comparisons between different variables might also lead to type I error, thereby explaining some of the significant differences between the key outcome variables. Second, the cross-sectional nature of the study precludes any definitive conclusion about whether these cognitive characteristics were indeed responsible for certain emotional changes characteristic of bipolarity. For example, mild mood symptoms might arouse the interest and attention of the participants so that they would spend time ruminating about these positive and negative emotions, rather than the reverse proposition of mood amplification by such ruminations. A mild positive mood might also lead to a preferential recall of positive memories and imagination of a positive future outcome. Third, the cognitive measures employed were all questionnaires and therefore were subject to possible recall and social desirability biases. In future, laboratory measures like measurement of heart beat, vagal tone and facial expressions could also be used to corroborate the subjective measures of positive affect (Gruber et al., 2010). Fourth, the reports of childhood maltreatment and lifetime traumatic experiences were based on retrospective self-report which could be subject to recall bias. However, previous studies have suggested that such retrospective self-reports are accurate and may in fact be related to under-reporting rather than over-reporting (Widom & Shepard, 1996). Fifth, the raters were not blind to bipolar risk status, possibly leading to interviewers' bias in enhanced detection of key risk factors in the high bipolar risk group. However, key risk factors like mental imagery susceptibility, responses to positive and negative affect, BAS levels, and visual creativity were all measured by self-administered questionnaires without

active search of confirmatory information compatible with the hypotheses. Finally, creativity was measured by using only one single measure of visual creativity and this would fail to capture other aspects of creativity that might be important for enhancing problem solving and success in society.

CHAPTER 8 - Study 6: Mental imagery susceptibility, suicidality, and bipolarity in a general population sample

8.1 Introduction

8.1.1 Suicidal flash-forward imagery and cry of pain model

Previous research reported that individuals with strong suicidal ideation experience vivid imagery about suicidal acts or the aftermath of death ('flash-forward' suicidal imagery) (Crane et al., 2012; Holmes et al., 2007; Hales et al., 2011; see Section 1.1.8.7). Suicidal individuals also experience stronger emotional impact of general prospective images and more frequent negative prospective images than non-suicidal controls (Crane et al., 2012). However, the existing literature on suicidal flash-forward imagery has been limited to cross-sectional retrospective studies in small selected samples of mostly Caucasian populations. Moreover, the potential psychological function of suicidal flash-forward imagery remains unclear. A possible hypothesis is that suicidal images provide escape from distress (Crane et al., 2012; see section 1.1.8.7.1 in Chapter 1). Highly emotional prospective imagery, particularly suicidal flash-forwards, may encapsulate the desired goal of escape from a sense of entrapment and defeat. Comfort or triumph in association with escape from entrapment might intensify suicidal ideation.

8.1.2. Suicidal risks, suicidal flash-forward imagery and bipolarity

Patients with bipolar disorders (BD-I) have the highest risk of suicide when compared to major depressive disorder (MDD) and other Axis-I disorders like anxiety disorders and

schizophrenia (Chen & Dilsaver, 1996; Hawton et al., 2005). The most powerful predictors of suicidal acts among patients with bipolar disorders (BD) are a history of suicide attempts, subjective rating of severity of depression, pessimism, and impulsivity (Oquendo, Currier & Mann, 2006). If mental imagery amplifies pathological negative emotions (Holmes & Mathews, 2010; Studies 3 and 5) and is associated with emotional instability in BD (Holmes et al., 2011; Study 3), mental imagery susceptibility might play a role in exacerbating suicidal ideation amongst such patients. Therefore, the current study also hypothesises that suicidal individuals with a lifetime history of hypomanic symptoms (i.e. mild elated states, one of the milder forms of bipolar spectrum disorders (BSD) or a bipolar phenotype as suggested by Rock et al. [2013]; see Section 1.1.1.4 on the classification and expansion of BSD) will have higher levels of mental imagery susceptibility than those without such a history. In response to a high sense of entrapment, suicidal individuals with this bipolar phenotype might report having suicidal flash-forward images as a psychological relief from distress more often than those without the phenotype. As suicidal flash-forward imagery might serve as an escape from sense of entrapment, we hypothesise that suicidal individuals with this bipolar phenotype and a high sense of entrapment will report more suicidal flash-forward images than those suicidal participants with this phenotype but without a high sense of entrapment.

8.2. Aims and hypotheses

The primary hypotheses were:

1. Only suicidal individuals will report suicidal flash-forward imagery and those cases with suicidal flash-forwards will have higher suicidality levels than those without suicidal flash-forwards.
2. Suicidal individuals will report a greater emotional impact of prospective imagery, greater levels of entrapment and defeat perceptions than controls.

3. Resolution of suicidal ideation at follow up will be significantly associated with a reduction in suicidal flash-forward imagery, the emotional impact of prospective imagery and in perceptions of entrapment and defeat.

The secondary hypotheses were:

4. Suicidal flash-forward imagery and emotional impact of prospective imagery will interact with perceptions of defeat and entrapment in predicting suicidal ideation levels at baseline and at follow-up.
5. Suicidal cases with a lifetime history of hypomanic symptoms will have higher levels of emotional impact of prospective imagery than those suicidal cases without such a history.
6. Suicidal individuals with a lifetime history of hypomanic symptoms and high levels of entrapment will be more likely to report having suicidal flash-forwards than suicidal participants with a lifetime history of hypomanic symptoms but low levels of entrapment.

8.3 Material and Methods

8.3.1 Sample recruitment

Participants were recruited from a sub-sample of the Hong Kong Mental Morbidity Survey (HKMMS; see Chapter 2 for details). Inclusion criteria for the current study included: (1) being part of the HKMMS; (2) aged 18-65; (3) ethnic Chinese able to speak, read and write Chinese from residential homes in Hong Kong. Exclusion criteria included: (1) incapable of giving informed consent; (2) acutely suicidal or violent so as to demand immediate psychiatric attention. All participants who scored ≥ 1 in questions 4 and 5 on the

Beck Scale for Suicidal Ideation-Current (SSI-C; Beck et al., 1979) in the HKMMS were categorized as suicidal (n = 82). Eighty age and gender matched non-suicidal controls were randomly selected from the remaining pool (n = 5618) (score = 0 on both questions 4 and 5 of the SSI-C). The local research ethics committee approved the study (reference number: KC/KE-11-0204/ER-3). All participants who were found to be suicidal at either time point were advised to seek further psychiatric care as appropriate. At 7 weeks' follow-up, all baseline suicidal participants who were successfully contacted by phone at follow-up had been in contact with mental health services. A 7-week follow-up interval was selected as previous studies have shown that mood disturbance and suicidal ideation improved significantly when people were followed up six weeks after the week following a suicidal crisis (Pollock & Williams, 2004). This interval would therefore ensure that a reasonable proportion of participants with active suicidal ideation at baseline would have become less suicidal at the 7-week follow-up.

8.3.2 Assessment

Participants completed the following measures at baseline and at 7 weeks' follow-up.

8.3.2.1 Demographic and clinical characteristics

Gender, age, years of education, marital status, past and current psychiatric illnesses were recorded via a standardised questionnaire booklet administered before all other assessments. Current suicidal ideation was assessed with the Chinese version of the Beck Scale for Suicidal Ideation-Current (SSI-C) (Beck et al., 1979; Zhang & Brown, 2007). In the HKMMS, the Chinese version of SSI-C had a good internal consistency (Cronbach's alpha = 0.88; Lam et al., 2014a). For the current study, the SSI-C also had a good internal consistency (Cronbach's alpha = 0.87)

Hypomania Checklist-32 (Angst et al., 2005): The validated Hong Kong version was used (Poon et al., 2012). A total score of 18 and above plus a score of 2 and above on the 'risk-taking/irritable' hypomania sub- scale was considered indicative of having a history of lifetime significant hypomanic symptoms in the general population (Meyer et al., 2007). For the current study, the internal consistency for the core items is good (Cronbach's alpha = 0.87)

Clinical Interview Schedule-Revised (Lewis et al., 1992): The validated Chinese version was used. The CIS-R was used in the HKMMS for verifying the presence of DSM-IV-TR diagnoses. The schedule was administered by the research assistants of the HKMMS who has attained good inter-rater reliability (see Section 2.5).

8.3.2.2 Cognitions

Cognitions in the form of mental imagery and of entrapment and defeat perceptions were assessed using:

The Impact of Future Events Scale (IFES; Deeprose & Holmes, 2010) to identify: a) the presence of prospective imagery categorised as suicidal or not (from now referred to as "suicidal flash-forwards"), and b) the characteristics of all general prospective imagery, including frequency, valence and emotional impact (from now referred to "prospective imagery characteristics"). The translated Chinese version was used. For the current study, the translated version had a good internal consistency (Cronbach's alpha = 0.88).

Two main variables of interest were extracted from the IFES:

1) Mental imagery: suicidal flash-forwards. Participants were asked to write down emotionally significant future events, which they had imagined over the past 7 days (also known as total IFES events). They were not specifically instructed to report intrusive images about any future suicidal acts or aftermath of suicidal acts (i.e. suicidal flash-forwards). In this study, IFES events were coded as 'suicidal flash-forward imagery' or not based on whether

they fulfilled the themes defined by Hales et al (2011) as "imagining future suicidal acts or their aftermath" (e.g.'visualised harming myself with a knife' or 'visualised myself in a coffin being surrounded by my family members sobbing with regrets'). The principal investigator established an excellent inter-rater reliability (weighted kappa = 0.98) with an independent psychologist in categorisation of suicidal imagery and in distinguishing between 'the aftermath of imagined suicide' (e.g. 'thinking of getting close and living peacefully with my deceased parents in Heaven after my suicide') or 'details of imagined suicidal acts' (e.g. 'cutting my wrist with a razor in the bathroom to relieve my emotional pain') (weighted kappa agreement of 0.97).

2) Mental imagery: general prospective imagery characteristics. Emotional impact, frequency and valence of general (not limited to suicidal images) prospective imagery were assessed. Emotional impact of prospective imagery was indexed by the IFES total score. Frequency was indexed by the total number of IFES events recalled and listed. Valence was indexed by the number of prospective images rated as negative ('IFES negative events') or positive ('IFES positive events'). For the current study, the IFES core items assessing emotional impact of listed future events has a good consistency (Cronbach's alpha = 0.91).

3) Entrapment and defeat. In the current study, the translated Chinese version of Entrapment Scale (ES; Gilbert & Allan, 1998) had good internal consistencies (Cronbach's alpha = 0.92), as did the translated version of the Defeat Scale (DS; Gilbert & Allan, 1998) (Cronbach's alpha = 0.95).

8.4 Statistical analyses

STATA Version-12 was used (STATACorp, 2011). The power calculation for sample size was based on previous studies (Hales et al., 2011; Crane et al., 2012) (a minimum of 50 participants per group for 90% power at an alpha level of 0.05, and an attrition up to 30% = minimum of 80 participants per group at baseline). Baseline demographic and clinical data were compared between groups using Chi-square tests. For highly skewed continuous data, non-parametric analyses were conducted. Univariate analysis were used to compare continuous variables at baseline and at follow-up. Any baseline demographic variables that were found to be significantly different between the two groups would be controlled as covariates in the parametric analyses. Bootstrapping method was used as well. In order to determine whether a reduction in suicidal ideation is associated with any change in cognitions, separate repeated measure analyses of variance (rmANOVA) were conducted for suicidal cases (55/80 assessed at both baseline and follow-up), with cognition measures (suicidal flash-forward imagery, emotional impact of prospective imagery, valence of prospective imagery and entrapment and defeat scores) as dependent variables, group (suicidal vs. non-suicidal) as between-group factor and time (baseline vs. follow up) as within-group factor. Significant interactions were followed by post-hoc pairwise comparisons for analyses of suicidal and non-suicidal groups at baseline and at follow-up time points. Further, to determine the predictive value of the interaction between perceptions of entrapment/defeat and suicidal flash-forward imagery over suicidal ideation at baseline, a series of separate linear regression models were conducted with suicidality scores as the dependent variable. Predictive factors were the interaction between the presence of suicidal flash-forwards and entrapment and defeat perceptions, computed by multiplying the two variables. The dichotomous variable of suicidal flash-forward imagery presence (yes/no) was multiplied by binary variables of perceptions of defeat and entrapment created using median splits.

8.5 Results

8.5.1 Demographic and clinical characteristics of baseline and follow-up cohorts

Eighty-two out of 5700 participants in the Hong Kong Mental Morbidity Survey were identified as having current suicidal ideation in the preceding seven days ('suicidal cases'), giving a point prevalence of 14 per 1000 persons. The baseline cohort thus comprised of 162 participants (82 cases and 80 controls). The baseline demographic and clinical characteristics of the suicidal and control groups are shown in Table 1.

Seven weeks (M = 7.2 weeks; SD = 1.38) later, 70% of the baseline cohort (112 participants comprising of 35 suicidal and 77 non-suicidal control participants from the baseline cohort) was successfully followed up. For the 35 suicidal participants, 33 were derived from the baseline suicidal cohort (n = 82) but 2 in the baseline non-suicidal cohort (n = 80) became suicidal at 7 weeks' follow-up. Thirty-two per cent (n = 27) of suicidal participants and 28% (n = 23) of controls either refused or could not be traced for follow-up ('drop-outs'), with no significant differences in the proportions of dropouts in the suicidal and non-suicidal groups (χ^2 = 0.33; df = 1, p = 0.57). The proportion of participants with a history of psychiatric illness (26% dropouts vs. 30% non-dropouts; χ^2 = 0.32, df = 1, p = 0.57) or current psychiatric illness (20% dropouts vs. 28.6% non-dropouts; χ^2 = 1.32, df = 1, p = 0.25) were similar between the drop-out vs. non-dropouts. Furthermore, there were no significant differences in the mean age (dropouts = 46.1 (SD =15.42) vs. non-dropouts = 45.6 (SD = 15.27), t = -0.19, df = 160, p = 0.85), mean years of education (dropouts = 12.8 (SD = 4.25) vs. non-dropouts = 13.3 (SD = 5.46), t = 0.60, df = 160, p = 0.55), the proportion of male gender (26% dropouts vs. 30% non-dropouts; χ^2 = 0.20, df = 1, p = 0.65), and the proportion of participants being married (52% dropouts vs. 48% non-dropouts; χ^2 = 0.20, df = 1, p = 0.66).

The data were therefore noted to be missing at random.

There were no significant differences between the baseline and follow-up cohorts in gender, age, and level of baseline suicidal ideation (see Table 1). However, the proportion that was married was significantly lower among suicidal participants at baseline. At follow-up, 30% of participants still had acute suicidal ideation. No participants were lost due to completed suicide. The suicidal group also had a higher percentage of participants with a past history of or a current psychiatric illness under treatment. Therefore, marital status, presence of past psychiatric illness, and presence of current psychiatric illness were entered as co-variates in the subsequent ANCOVA analysis.

Table 1: Demographic and clinical characteristics for the suicidal cases and non-suicidal controls at baseline (*N* = 162) and at 7 weeks' follow-up (*N* = 112)

	Suicidal Cases		Non-suicidal controls		
Variables of interest	Baseline (*n* = 82)	7-week (*n*=35)	Baseline (*n*=80)	7-week (*n*= 77)	Statistic
Male gender (*%*)	24a (29.3)	9c (25.7)	22b (27.5)	24d (31.2)	χ2test: a=b (χ2 = 0.06, *df* = 1, *p* = 0.80), c=d (χ2 = 0.34, *df* = 1, *p* = 0.58)
Mean age (*SD*)	45.9a (15.27)	45.6c (14.91)	45.6b (15.35)	45.6d (15.73)	*t*-test: a=b (*t* = 0.12, *df* = 160, *p* = 0.90), c=d (*t* = 0.08, *df* = 110, *p* = 0.99)
Years of education (*SD*)	12.7a (5.28)	12.5c (5.70)	13.5b (4.90)	14.0d(5.12)	*t*-test: a=b (*t* = -0.99, *df* = 160, *p* = 0.32), c=d (*t* = -1.26, *df* = 110, *p* = 0.21)
Marital status					
Married/cohabited (*%*)	31 (34.8)	13 (37.1)	49 (61.3)	41.52 (53.2)	Baseline: x^2 = 8.91, *df* = 1, ***p* = 0.003**
Single/divorced/ Widowed (*%*)	51 (62.2)	22 (62.9)	31 (38.8)	36 (46.8)	Follow-up: x^2 = 2.50, *df* = 1, *p* = 0.11
Presence of past psychiatric illness (*%*)	40 (48.78)	28 (50.90)	7 (7.90)	6 (10.50)	Baseline cases vs. controls: χ2 = 31.51; *df* = 1; ***p* < 0.001**; Follow-up cases vs. controls: χ2 = 21.6; *df* = 1, ***p* < 0.001**
Presence of current psychiatric illness (*%*)	38 (46.34)	28 (50.90)	5 (5.00)	4 (7.00)	Baseline cases vs. controls: Fisher's exact test; ***p* < 0.001**; Follow-up cases vs. controls: Fisher's exact test: ***p* < 0.001**
Types of current psychiatric illness:					
Depressive disorder (*%*)	27 (32.90)	16 (29.10)	0 (0)	0 (0.00)	Baseline cases vs. controls: Fisher exact test; *p* < 0.001
Generalised Anxiety disorder (*%*)	29 (35.40)	19 (34.50)	1 (1.20)	1 (1.80)	Follow-up cases vs. controls: Fisher exact test; *p* < 0.001
Phobia (*%*)	6 (7.30)	4 (7.30)	0 (0.00)	0 (0.00)	

8.5.2 Cognitions

Table 2 shows mental imagery and entrapment and defeat measures at baseline and follow-up for both groups.

8.5.2.1 Mental imagery: suicidal flash-forwards

A total of 30 prospective images at baseline and 9 at follow-up were coded as suicidal flash-forwards. No participant at either time point reported more than one suicidal flash-forward image in the list of IFES events. Consistent with the first hypothesis, suicidal flash-forward imagery was exclusively present in suicidal participants (30/82 at baseline; 9/35 at follow up; Fisher's exact test at both time points: $p < 0.001$). Baseline suicidal participants with suicidal flash-forward imagery (30/82) had higher severity of suicidal ideation than those without such imagery (SSI-C total scores, independent t-test: $t = 9.86$, $df = 80$, $p < 0.001$). At 7 weeks' follow-up, there was no difference in severity of suicidal ideation (SSI-C total score, t-test with bootstrapping performed*:* $t = 0.73$, $df = 33$, $p = 0.47$; mean difference of SSI-C total scores = 2.07, 95% *CI*:-4.00, 8.56) between suicidal participants with suicidal flash-fowards (9/35) and those without (26/35). Furthermore, 53.3% of suicidal flash-forwards at baseline were about the aftermath following imagined suicide while 46.7% were about the details of their imagined suicidal acts. Overall, 50% of suicidal flash-forwards were rated as 'positive events'. All suicidal flash-forward imagery about actual acts of suicide at baseline were rated as 'negative events' and 81.3% of suicidal flash-forward imagery about the aftermath of suicide at baseline were rated as 'positive event' in IFES.

8.5.2.2 Mental imagery: general prospective imagery characteristics

As per the second hypothesis, the suicidal group had higher emotional impact of prospective imagery (IFES total) at baseline (corrected ANCOVA model: $F[4, 157] = 16.8$, $p < 0.001$; Group Factor: $F[1, 161] = 34.2$, $p < 0.001$; main and interaction effects of co-variates were non-significant with p-value > 0.10) and at follow-up (corrected ANCOVA model: $F[4, 107] = 13.11$, $p < 0.001$; Group: $F[1, 111] = 30.50$, $p < 0.001$; main or interaction effects of co-variates were all non-significant with p-values > 0.10)

The suicidal group reported a total of 211 positive and negative prospective images (41.7% were negative in valence and 58.3% positive) while the non-suicidal group reported a total of 206 (19.9% were negative in valence and 80.1% positive) at baseline. The proportion of positive and negative prospective images at baseline differed significantly between the two groups (chi-squared test: X^2= 23.21, df = 1, p < 0.001). Similarly, the suicidal group reported a total of 136 positive and negative prospective images (40.4% were negative in valence and 59.6% positive) while the non-suicidal group reported a total of 138 positive and negative prospective images (17.4% were negative in valence and 82.6% positive) at seven weeks' follow-up. Again, the proportion of positive and negative prospective images were significantly different between the two groups (X^2 = 17.75, df = 2, p < 0.001). The suicidal group reported having more negative prospective images in the last seven days than the control group at baseline ('IFES negative events'; corrected ANCOVA model: F[4, 157] = 5.16, p = 0.001; Group: F[1, 161] = 4.86, p = 0.03; other main or interaction factors of co-variates were non-significant with p-values > 0.10) and at follow-up (corrected ANCOVA model: F[4, 107] = 3.07, p = 0.02; Group: F[1, 111] = 6.65, p = 0.01; other main and interaction effects of co-variates were non-significant with p-values > 0.10) (see Table 2). The suicidal group also had significantly fewer positive prospective images than the non-suicidal controls at baseline ('IFES positive events'; corrected ANCOVA model: F[4, 107] = 7.35, p < 0.001; Group*:* F[1, 111] = 6.15, p = 0.01; other main and interaction effects of co-variates were non-significant) and at follow-up (corrected ANCOVA model: F[4, 107] = 3.07, p = 0.02; Group: F[1, 111] = 6.65, p = 0.01; other main and interaction effects of co-variates were non-significant).

Table 2: Mental imagery susceptibility, bipolarity, defeat and entrapment measures at baseline and at 7 weeks' follow-up

	Suicidal cases		Non-suicidal controls		
Variables of interest	Baseline (*n*=82)	7-week (*n*=35)	Baseline (*n*=80)	7-week (*n*=77)	Statistics
Suicidal Ideation					
Mean total SSI-C[a] score (SD)	12.80a (6.56)	12.6c (7.28)	0.25b (1.45)	0.3d (0.79)	Wilcoxon's rank sum-tests: a>b (z = 11.42, $\mathbf{p < 0.001}$), c>d (z = 9.34, $\mathbf{p < 0.001}$)
Lifetime Hypomanic symptoms					
HCL-32[b] total	14.4a (6.34)	13.5c(6.48)	14.1b(4.85)	14.d (4.84)	a=b (*t*-test; t = 0.88, df = 160, p = 0.38); c=d (*t*-test; t = 0.76, df = 110, p = 0.45)
Number of participants having significant hypomanic symptoms(%)	38a (46.3)	20c(57.1)	23b (28.8)	25d (32.5)	X^2 test: a>b: x^2 = 5.34, df = 1, $\mathbf{p = 0.02}$; c>d: x^2 = 6.10, df = 1, $\mathbf{p = 0.01}$
Mental Imagery Characteristics					
Presence of suicidal flash-forward images (%)	30a (36.58)	9 (25.71)	0b (0)	0d (0)	Fisher's exact test: a>b (p < 0.001); c>d ($\mathbf{p < 0.001}$)
Mean total IFES[c] (*SD*)	41.4a (15.74)	48.9c (16.74)	24.5b (11.28)	28.2d (14.42)	ANCOVA models: a>b(F(4, 157) = 16.8, $\mathbf{p < 0.001}$); c>d (F(4, 107) = 13.11, $\mathbf{p < 0.001}$)
Mean number of IFES negative events (*SD*)	1.1a (1.05)	1.1c (1.10)	0.5b(0.80)	0.5d (0.70)	ANCOVA models: a>b(F(4, 157) = 5.16, $\mathbf{p < 0.001}$); c>d (F(4, 107) = 3.07, $\mathbf{p = 0.02}$)
Mean number of IFES positive events (*SD*)	1.5a (1.07)	1.2c (1.19)	2.1b 0.88)	2.0d (1.05)	ANCOVA models: a<b(F(4, 157) = 7.35, $\mathbf{p = 0.001}$); c<d (F(4, 107) = 3.07, $\mathbf{p = 0.02}$)
Perceptions of entrapment and defeat					
Mean Entrapment total score (*SD*)	37.4a (13.18)	37.6c (19.44)	8.3b (8.88)	14.6d (14.29)	ANCOVA models: a>b(F(4, 156) = 74.08, $\mathbf{p < 0.001}$); c>d (F(4, 107) = 18.58, $\mathbf{p < 0.001}$)
Mean Defeat total score (*SD*)	54.0a (11.48)	48.5c (13.50)	29.9b(7.89)	34.6d (12.35)	ANCOVA models: a>b(F(4, 155) = 72.51, $\mathbf{p < 0.001}$); c>d (F(4, 107) = 18.65, $\mathbf{p < 0.001}$)

a: Scale for Suicidal Ideation-Current Version; b: Hypomania Checklist-32; c: Impact of Future Events Scale

8.5.2.3 Entrapment and defeat

Table 2 shows the measures of perception of entrapment and defeat for the suicidal and non-suicidal groups at both time points. Consistent with the second hypothesis, suicidal participants had a higher sense of entrapment than non-suicidal controls at baseline (overall ANCOVA model: $F[4, 156] = 74.08$, $p < 0.001$; Group: $F[1, 160] = 177.02$, $p < 0.001$; presence of past psychiatric illness factor: $F[1, 111] = 3.95$, $p = 0.05$; other main and interaction effects of co-variates were non-significant) and follow-up (corrected ANCOVA model: $F[4, 107] = 18.58$, $p < 0.001$; Group: $F[1, 111] = 29.51$, $p < 0.001$; Marital status : $F[1, 111] = 4.62$, $p = 0.03$; other main and interaction effects of covariates were non-significant). The suicidal participants also had a higher sense of defeat than non-suicidal controls at both baseline (Defeat total, overall ANCOVA model: $F[4, 155] = 72.50$, $p < 0.001$; Group: $F[1, 159] = 150.01$, $p < 0.001$; Marital status: $F[1, 159] = 9.21$, $p = 0.003$; other main and interaction effects of co-variates were non-significant) and follow-up (overall ANCOVA model: $F[4, 107] = 18.65$, $p < 0.001$; Group factor: $F[1, 111] = 15.83$, $p < 0.001$; Marital status factor: $F[1, 111] = 6.35$, $p = 0.01$; other main and interaction effects of co-variates were non-significant). When participants with suicidal flash-forward imagery were divided into those with positive ($n = 15$) and negative emotional valence ($n = 15$), the two groups were similar in proportion of male gender, proportion of being married, age and years of education. The two groups were similar in levels of suicidal ideation, sense of entrapment and defeat. However, the group with negative suicidal flash-forwards reported having a higher level of emotional impact of prospective imagery(IFES total: $t = 2.28$, $df = 28$, $p = 0.03$), fewer positive prospective images (IFES positive events: $t = -3.12$, $df = 28$, $p = 0.004$) and excessive negative prospective images (IFES negative events: $t = 2.53$, $df = 28$, $p = 0.02$).

8.5.2.4 Change of mental imagery, entrapment and defeat perceptions and suicidal ideation over time

For the 55 suicidal participants successfully traced at follow-up, 33 still reported suicidal ideation whilst 22 had their suicidal ideation resolved. Table 3 shows the changes in imagery characteristics among this suicidal cohort at baseline and 7 weeks' follow-up. Consistent with the third hypothesis, among those baseline suicidal participants who subsequently became non-suicidal at follow-up (n = 22), none of the nine participants who had suicidal flash-forward imagery at baseline reported such imagery at follow-up (McNemar test: $p < 0.001$). Additionally, there was no significant reduction in the proportion of participants reporting suicidal flash-forward imagery among those who were suicidal at baseline and remained suicidal at follow-up (n = 33) (McNemar test; $p = 0.24$).

Consistent with the third hypothesis, in the repeated measure ANCOVA for emotional impact of prospective imagery using marital status, presence of past and current psychiatric illness as the covariates, there was a significant Group (suicidal vs. non-suicidal) x Time (baseline vs. follow-up) interaction (F[1, 51] = 7.22, $p = 0.01$), with planned pairwise analyses showing a significant reduction in IFES total scores only in those baseline suicidal participants who became non-suicidal at follow up (F[1, 21] = 5.14, $p = 0.03$), but not in those who remained suicidal at follow-up (F[1, 32] = 3.02, $p = 0.09$). The other main and interaction effects of the co-variates were non-significant. Also consistent with the third hypothesis, there was a significant Group (suicidal vs. non-suicidal) x Time (baseline vs. follow-up) interaction for entrapment (F [1, 51] = 6.56, $p = 0.01$), with planned pairwise analysis showing a significant reduction in entrapment perception in the baseline suicidal group that became non-suicidal at follow up (F[1, 21] = 9.06, $p = 0.007$). Other main or interaction effects of the co-variates were non-significant. There was no significant group X time interaction either for valence of general prospective imagery (number of IFES positive events and IFES negative events) or for the perception of defeat in the same participants (see

Table 3 for further details).

Table 3: Changes in mental imagery susceptibility, entrapment and defeat measures for suicidal cases who remained suicidal (*n* = 33) and who became non-suicidal (*n* = 22) from baseline to 7 weeks' follow-up

	Suicidal cases remaining suicidal at 7 weeks (*n*=33)		Suicidal cases becoming non-suicidal controls at 7 weeks (*n*=22)		
Variables of interest	Baseline	7-weeks	Baseline	7-week	Statistics
Suicidal Ideation					
Mean total SSI-C[a] score (*SD*)	13.2a (7.26)	13.2c (6.99)	13.2b (5.98)	0.9d (1.25)	Repeated measure ANOVA: Group x time: $F(1,53) = 81.9,, p < 0.001$; post-hoc pairwise t-tests: a=c, b>d**, b=c, c>d**.
Mental Imagery Characteristics					
Presence of suicidal flash-forward images (*%*)	21a (63.3)	9c (27.3)	9b (40.9)	0d (0)	McNemar's test; a=c, b>d**
Mean total IFES[c] *(SD*)	42.4a (16.19)	48.7c (16.98)	42.1b (17.25)	36.8d (16.47)	Repeated measure ANOVA: Group X Time*: F* (1, 51) = 7.22, ***p* = 0.01**; post-hoc pairwise t-tests: c>d*; b>d*; a=c; a=b
Mean number of IFES negative events (*SD*)	1.2a (1.20)	1.1c (1.11)	1.1b (0.94)	0.8d (0.80)	Repeated measure ANOVA: Group X Time: *F* (1, 51) = 0.56, *p* = 0.46.
Mean number of IFES positive events (*SD*)	1.4a (1.12)	1.2c (1.23)	1.6b (1.26)	1.8d (1.10)	Repeated measure ANOVA: Group X time: *F*(1, 51) = 0.05, *p* = 0.83
Perceptions of entrapment and defeat					
Mean Entrapment total score (*SD*)	35.9a (12.98)	39.1c (18.95)	38.3b (14.33)	29.1d (13.79)	Repeated measure ANOVA: Group X Time *F* (1, 51) = 6.56, ***p* = 0.01**; post-hoc pairwise t-tests: a=c, b>d*, b=c, c>d*.
Mean Defeat total score (*SD*)	53.8a (11.18)	49.6c (13.04)	53.5b (13.15)	47.7d (13.47)	Repeated measure ANOVA: Group X Time *F* (1, 51) = 0.52, *p* = 0.47; post-hoc pairwise t-tests: a=c, b=d, a=b, c=d

a: Scale for Suicidal Ideation-Current Version; c: Impact of Future Events Scale

8.5.2.5 Predictive value of imagery characteristics and entrapment and defeat over suicidal ideation

Consistent with the fourth hypothesis, a linear regression model predicting baseline suicidal ideation using the presence of suicidal flash-forward imagery (FF; yes/no), presence

of entrapment (ES; high/low) and the interaction factor of FF X ES at baseline was significant (F = 14.80, df = 3, p < 0.001, adjusted R^2= 0.43). The main effect of suicidal flash-forward imagery was significant (B = 5.13, SE = 1.57, $Beta$ = 0.38, t = 3.26, p = 0.002) while the main effect of entrapment was not (B = 0.42, SE = 1.45, $Beta$ = 0.03, t = 0.29, p = 0.78). More importantly, the interaction of suicidal flash-forward and entrapment was significant (B = 6.29, SE = 1.70, $Beta$ = 0.42, t = 3.71, p = 0.001). Furthermore, another linear regression model predicting suicidal ideation at follow-up using the presence of suicidal flash-forward imagery (FF; yes/no), presence of entrapment (ES; high/low) and the interaction factor of FF X ES at baseline revealed an overall significant but weaker model (F = 3.18, df = 3, p = 0.03, adjusted R^2 = 0.11). However, main effects of suicidal flash-forward and entrapment, as well as the interaction of these two variables were all non-significant.

Also consistent with the fourth hypothesis, a linear regression model predicting baseline suicidal ideation using the presence of suicidal flash-forward imagery (FF; yes/no), presence of defeat (DS; high/low) and the interaction factor of FF X DS at baseline revealed an overall significant model (F = 11.99, df = 3, p < 0.001, adjusted R^2 = 0.38). The main effect of suicidal flash-forward imagery was significant (B = 5.89, SE = 1.87, $Beta$ = 0.44, t = 3.15, p = 0.003) while the main effect of defeat was not (B = -2.87, SE = 1.96, $Beta$ = -0.22, t = -1.47, p = 0.15). More importantly, there was a significant interaction between suicidal flash-forward and defeat (B = 6.04, SE = 2.38, $Beta$ = 0.41, t = 2.53, p = 0.01). Furthermore, another linear regression model predicting suicidal ideation at 7 weeks' follow-up using the presence of suicidal flash-forward imagery (FF; yes/no), presence of defeat (DS; high/low) and the interaction factor of FF X DS at baseline revealed an overall marginally significant but weaker model (F = 2.62, df = 3, p = 0.06, adjusted R^2 = 0.08). However, main effects of suicidal flash-forward and entrapment, as well as their interaction factor were all non-significant.

8.5.3 Mental imagery, bipolarity and suicidality

The proportion of participants with a lifetime history of significant hypomanic symptoms (i.e. having a bipolar phenotype or high bipolar risk for developing full-blown bipolar disorder; Rock et al., 2013) was significantly higher in the suicidal group than in the non-suicidal control group at baseline (46% cases vs. 29% controls, $X^2 = 5.34$, $df = 1$, $p = 0.02$) and follow-up (57% cases vs. 33% controls, $X^2 = 6.10$, $df = 1$, $p = 0.01$) (see Table 2 for details).

When the suicidal participants at baseline were divided into two groups based on their criterion threshold of this bipolar phenotype, 38 were defined as having significant lifetime hypomanic symptoms (HR) and 44 as not having such symptoms at baseline (LR). At 7 weeks' follow-up, 20 suicidal participants were defined as HR and 15 as LR. The two groups were similar in terms of proportions of male gender and of being married, mean age and years of education at baseline and at seven weeks' follow-up. Consistent with the fifth hypothesis, the suicidal sub-group with HR had higher levels of emotional impact of prospective imagery at baseline than LR at baseline (HR = 46.4 (*SD* = 16.14) vs. LR = 37.0 (*SD* = 14.19); $t = 2.79$, $df = 80$, $p = 0.007$). At 7 weeks' follow-up, there was no significant difference in IFES total between HR and LR.

For the proportions of suicidal flash-forward imagery, the two groups with suicidal ideation were not significantly different at baseline (HR = 14/38: 36.8% vs. LR = 16/44: 36.4%; chi-squared test: $x^2 = 0.002$, $df = 1$, $p = 0.96$) or at follow-up (HR= 8/20: 40% vs. LR = 5/15: 33.3%; chi-squared test: $x^2 = 0.16$, $df = 1$, $p = 0.69$). The suicidal participants with a history of significant hypomanic symptoms (HR; $n = 38$) were then divided into two groups based on the mean entrapment total cut-off score of 38; there were 22 suicidal cases with a high sense of entrapment versus 16 suicidal cases with a low sense of entrapment. Consistent with the final hypothesis, the proportion of HR individuals with suicidal flash-forward

imagery was higher in the high entrapment group than in the low entrapment group at baseline (11/22: 50.0% vs. 3/16: 18.8%; Fisher's exact test: $p = 0.05$). However, at 7 weeks' follow-up, there were no significant differences in the proportions of the individuals with suicidal flash-forward imagery between the two groups (6/20:30% vs. 3/15: 20%; Fisher's exact test: $p = 0.26$). Compared to LR participants, HR participants had higher mean number of general negative prospective imagery (HR = 1.5 [*SD* = 0.96] vs. LR = 0.4 [*SD* = 0.89], $t = 3.32$, $df = 36$, $p = 0.002$) and lower mean number of general positive prospective imagery (HR = 1.2 [*SD* = 0.92] vs. LR = 2.1 [*SD* = 0.96], $t = -2.92$, $df = 36$, $p = 0.002$). However, the severity of suicidal ideation was not significantly different between the two groups (HR = 13.3 [*SD* = 5.73] vs. LR = 11.4 [*SD* = 5.94], $t = 0.98$, $df = 36$, $p = 0.33$).

8.6 Discussion

This is the first prospective cohort study to investigate the relationships between mental imagery measures, perceptions of entrapment and defeat, suicidal ideation, and bipolarity. The study has shown that: 1) only suicidal participants reported experiencing suicidal flash-forwards compared to non-suicidal participants at baseline and follow-up, and at baseline participants with suicidal flash-forward imagery had higher suicidal ideation levels than those without. At both time points, the suicidal group reported: 2) a stronger emotional impact of general prospective imagery; 3) higher levels of entrapment and defeat perceptions than non-suicidal group; 4) suicidal flash-forward imagery, emotional impact of prospective imagery and sense of entrapment were significantly reduced among suicidal participants at baseline who became non-suicidal at follow-up; 5) suicidal ideation was significantly predicted by the interaction between the presence of suicidal flash-forward imagery and perceptions of defeat and entrapment; 6) emotional impact of prospective imagery was significantly higher among suicidal persons with a lifetime history of significant hypomanic

symptoms than those without; and 7) suicidal participants with a lifetime history of significant hypomanic symptoms and strong sense of entrapment were more likely to report suicidal flash-forward imagery than those with a lifetime history of significant hypomanic symptoms but weak sense of entrapment.

8.6.1 Suicidal flash-forward imagery and suicidal ideation

The current study extends previous evidence from small selected samples and retrospective interviews (Hales et al., 2011; Holmes et al., 2007), confirming the presence of suicidal flash-forward imagery in a representative group of currently active suicidal participants randomly recruited from the general population. Of note, suicidal participants with suicidal flash-forwards had more severe suicidal ideation than those without such imagery. As mental images represent goals to be achieved (Conway, Meares & Standart, 2004) and are more likely to be acted upon than verbal thoughts, this data suggests that suicidal flash-forward images may be a signal of impending suicidal acts (Holmes et al., 2007). Hence, exploring the presence of suicidal flash-forward imagery among people with suicidal ideation in primary or secondary care settings should not be neglected.

Moreover, the study extends previous data to a non-Caucasian population indicating that suicidal flash-forward imagery is likely to be a cross-cultural phenomenon. Possibly unique for the Asian population is the influence of a strong cultural belief about the actual existence of a life after death on the meanings of suicidal flash-forwards (Chan et al., 2005). The vast majority of suicidal participants appraised suicidal flash-forward imagery about the aftermath of suicide as positive. Images of a rosy desirable after-life would then serve as an effective escape from current entrapping predicament (especially in Asian populations). This exemplifies how understanding the idiosyncratic meanings of suicidal flash-forward imagery may aid suicidal risk assessment (Holmes et al., 2007). However, this does not

mean that suicidal flash-forwards with negative connotation can be ignored, given that levels of suicidal ideation were similar between participants with either positive or negative suicidal flash-forwards. Although the participants with suicidal flash-forwards who rated them as being negative in emotional valence had similar levels of entrapment and defeat as those with positive ones, those with negative suicidal flash-forwards reported having a stronger emotional impact of prospective imagery, fewer positive but excessive negative prospective images. Given that high emotional impact of prospective imagery predicts depressive and anxiety symptoms (Study 3 and Study 5) and excessive negative but fewer positive prospective images predicts hopelessness (Holmes et al., 2009), those participants with negative suicidal flash-forward might experience increased hopelessness associated with suicide.

This is the first prospective study reporting a significant reduction in suicidal flash-forward imagery in a group of actively suicidal participants that became non-suicidal over a follow-up period of seven weeks (but not in those remaining suicidal). The direction of this association cannot be established by the present data; however, the temporal link suggests that psychological interventions targeting suicidal flash-forward imagery might be a promising strategy to reduce suicidal ideation, consistent with imagery intervention being effective across a range of psychological disorders (Arntz, 2012). Future experimental studies could test whether manipulating suicidal imagery has a causal impact on the severity of suicidal ideation.

8.6.2 Emotional impact of prospective imagery and suicidal ideation

The findings that suicidal participants had stronger emotional impact of prospective imagery, more negative prospective images and fewer positive prospective images than non-suicidal controls is consistent with previous studies in depressed samples (Crane et al., 2012;

Patel et al., 2007). The concomitant reduction of both emotional impact of prospective imagery and suicidal ideation corroborates the potential key role played by the emotional impact of prospective imagery in the context of suicidal ideation.

8.6.3 Entrapment, defeat and suicidal ideation

Consistent with previous research on suicide and entrapment (Gilbert & Allan, 1998; Rasmussen et al., 2010), this study confirmed that sense of defeat and entrapment play an important role in active suicidal ideation. However, as sense of defeat did not reduce in suicidal participants that became non-suicidal at follow-up, it is possible that this cognition signals a major failure of hierarchical aims including the loss of a valued social role, position, or resource (Gilbert & Gilbert, 2003; Taylor et al., 2009), and represents a more stable construct than sense of entrapment.

8.6.4 Suicidal flash-forwards as a goal of escape from entrapment and defeat

Having a high sense of being entrapped in a difficult situation and a high sense of failed struggle against this situation might give rise to a strong urge to escape (Williams, 1997; Williams, 2001). This study provides evidence to support the model of psychological escape, suggesting that under such circumstances, suicidal flash-forward imagery in the form of suicidal acts or the aftermath of such acts might represent the goal of escape from, or even the goal of triumph against, such feelings of entrapment and defeat (Hales et al., 2011; Crane et al., 2012; Morina et al., 2010; Selby, Anestis & Joiner, 2007). The combination of emotionally charged, vivid, compelling suicidal flash-forward imagery with strong feelings of being entrapped and defeated in current life situations may then amplify suicidal ideation. If suicidal flash-forward images contain serene or even triumphant pictures about one’s after-life, it is

understandable why they would be appraised as pleasant and how the desire for escape and the compellingness of the imaginal form (Ivins et al., 2014) might increase the potential to act.

8.6.5 Mental imagery susceptibility, bipolarity and suicidality

The current study further confirms that suicidal participants were more likely to have lifetime hypomanic symptoms than the non-suicidal controls, echoing previous studies that patients with bipolar disorder were more suicidal than those with other disorders (Chen & Dilsaver, 1995; Hales et al., 2011). Furthermore, suicidal participants with a lifetime history of significant hypomanic symptoms experienced greater emotional impact of prospective imagery than those without such a history. They also reported more negative prospective images but fewer positive prospective images than those without a lifetime history of hypomanic symptoms. Lack of positive prospective images coupled with an excess of negative prospective images has been found to be associated with depression and hopelessness (Holmes et al., 2008). Furthermore, suicidal individuals with a lifetime history of hypomanic symptoms and a strong sense of perceived entrapment would have a stronger likelihood to encapsulate the idea of escape from entrapment in the form of suicidal flash-forward imagery than those with a similar lifetime history but a low sense of entrapment. Such suicidal flash-forward imagery might then enhance the probability of executing the imagined suicidal acts or acting towards the goal of the aftermath of suicide. Future studies should further examine the levels of mental imagery susceptibility in a larger sample of suicidal participants with and without a lifetime history of significant hypomanic symptoms. This finding highlights the clinical importance of assessing for the presence of bipolarity in suicidal participants and identifying the presence of suicidal imagery in suicidal individuals especially in face of strong sense of entrapment.

8.7 Strengths and limitations

The main strength of this study is that the sample was recruited from the community, thus avoiding selection bias for people with serious suicidal ideation presenting to casualty departments or secondary care services. The sample size was adequately powered to address the primary hypothesis. The use of a longitudinal design enabled direct assessment of prospective changes of mental imagery susceptibility in participants with a reduction in suicidality. The main limitation of the study is a 30% attrition rate, which introduces possible attrition bias and a small sample size at follow up, although missing data was confirmed to be missing at random. A further limitation is that suicidal ideation was measured only via a self-administered questionnaire. Future studies should also cross-validate subjective reports with clinical interviews and casualty room registers to provide a more accurate picture of actual suicidal behaviours. Similarly, self-reporting of suicidal flash-forward images on the IFES might have underestimated the presence of this imagery compared to previous studies, which elicited suicidal flash-forward imagery from all participants using face-to-face structured interviews (Hales et al., 2011; Holmes et al., 2007). However, the suicidal flash-forward images harvested from the list of spontaneous and intrusive suicidal images obtained in the IFES scale might be qualitatively different from those voluntary images elicited during structured imagery interview. The self-administered method would also avoid interviewer's bias in encouraging the suicidal participants to report suicidal flash-forward imagery. Lastly, the identification of participants with a lifetime history of hypomanic symptoms was based only on the self-administered questionnaire and might have over-estimated the presence of bipolarity among suicidal participants.

CHAPTER 9 - Overall discussion: Mental imagery in bipolar disorders: a novel cognitive model, clinical implications and future research directions

The six studies in the current thesis addressed the relationships between mental imagery susceptibility and pathological emotions in bipolar disorders (BD) using a range of study designs and recruiting study samples at different stages/types of BD. There are several key findings from the six studies.

9.1 General use of imagery in daily life as a specific cognitive trait marker of bipolar disorders

General use of imagery in daily life refers to the tendency to visualize thoughts in the form of mental images (Reisberg et al., 2003). Holmes et al. (2011) has found that euthymic patients with BD had higher levels of general use of imagery than non-psychiatric controls. Study 1 extends this finding by showing that this imagery characteristic remained elevated in remitted bipolar I disorder (BD-I) patients compared to major depressive disorder (MDD) or non-psychiatric controls. Study 2 extends this further by reporting that patients with BD-I had higher general use of imagery in daily life than those with MDD across symptomatic stages from acute bipolar mania to euthymia.

A possible explanation of elevated use of imagery in daily life in remitted BD is that it represents a 'cognitive scar' left behind by BD itself (Lewinsohn et al., 1981). However, previous studies (Deeprose et al, 2011, Malik et al., 2014, Meyer et al., 2011) and the current thesis (Study 4 and Study 5) converged in showing that general use of imagery was also elevated in people with high behavioural or familial risks for BD but without a full-blown BD. Study 4 further showed that this imagery characteristic remained stable over seven weeks in

non-clinical participants with high behavioural risks. Although Study 3 did not have a non-psychiatric comparison group, results showed that general use of imagery was also elevated among people with sub-threshold bipolar disorder (sub-threshold BD) (one type of bipolar spectrum disorders [BSD] with lower loadings of bipolarity than BD-I) when compared with MDD. Taken together, this evidence supports general use of imagery as a possible trait factor in BD.

However, an intriguing finding in Study 2 is that general use of imagery was not only elevated in BD, but this characteristic might increase to a higher level from acute to remission states. While this observation could be due to repetition effects or an epi-phenomenon associated with other factors associated with recovery from mania (e.g. neuro-cognitive markers) (see Chapter 4 for further details), the increase of this imagery characteristic might warrant further investigation and replication in future studies. If general use of imagery was associated with enhanced visual creativity (see Chapter 7 and section 9.2 below), increased visual creativity would enhance ability to solve current stressors and could promote recovery from mania (Yan-Meyer et al., 2011; Study 2). This finding might suggest that general use of imagery might also be a state marker on top of its role as a trait marker associated with BD.

However, elevated general use of imagery in BD might be a double-edged sword. The current thesis showed that general use of imagery was a predictor of lifetime prior mood episodes (Study 1) and of lifetime hypomanic symptoms (Studies 3 and 5). Study 3 also provided some preliminary data that general use of imagery also predicted prior depressive episodes through the moderating effect of lifetime hypomanic symptoms in depression with varying degrees of bipolarity. Lifetime hypomanic symptoms comprise elated or irritable mood, and approach behaviours characteristic of hypomania which may be considered indicators of emotional instability (Angst et al., 2005). As such, heightened general use of imagery upon remission might predispose a patient with BD to subsequent increase in emotional instability and sub-syndromal mood fluctuations during the inter-episode well

periods. Given that inter-episode sub-syndromal mood symptoms were predictive of shortened time to subsequent mood episode recurrence (Judd et al., 2003), increase in general use of imagery during remission might hasten subsequent mood episode recurrence. This disadvantage was counter-balanced by an advantage of increased creativity with enhanced trait imagery use (Study 5, Holmes et al., 2008). From a psychotherapeutic point of view, promoting general use of imagery in patients with acute bipolar mania might enhance recovery (Study 2) but paradoxically increase the risks of subsequent recurrence at times of remission (Studies 1 and 3). Although the above findings await further replication, this phenomenon highlights the importance of phase-specific interventions for different phases of BD (see Section 9.13 for further discussion).

9.2 Evolutionary advantage of general use of imagery in daily life: enhanced creativity

If this imagery characteristic was indeed a trait factor associated with amplification of pathological emotions, one would question why it would pass on from one generation to the next without extinction in the population gene pool. What evolutionary advantages might this trait offer to the population as a whole? According to Holmes et al. (2008), thinking in images might allow novel combinations of ideas into complex and creative concepts, and also facilitate people to travel backward or forward in time to search for possible solutions to problems. Such enhanced susceptibility to visual images might then be conducive to effective problem solving and to enhancing aesthetic and artistic achievements of the human race (Murray & Johnson, 2010).

Indeed previous studies have found that patients with BD were as creative as creative controls but more creative than non-creative control participants and people with MDD (Srivastava et al., 2007). High levels of creativity and BD were found in both eminent writers

and their first -degree relatives, as well as in those working in creative occupations (Kyaga et al., 2011). Study 5 supported the notion that young people aged below 28 with high familial risk for BD were more visually creative (at least in the BWAS Like subscale) than those without such risk. Furthermore, Study 5 showed that general use of imagery in daily life might be a positive predictor of visual creativity. If general use of imagery in daily life was associated with bipolarity, its value in enhancing creativity might confer the genes associated with bipolarity an evolutionary advantage to survive the selection pressure against bipolar illness.

9.3 Potential role of general use of imagery for monitoring risk of conversion to bipolar disorders

The presence of high general use of imagery in people with high behavioural (Study 4) or familial risks for bipolar disorders (Study 5) suggest that this imagery characteristic might warrant further investigations as a potential tool for screening those at risk for BD. Study 5 provided some preliminary evidence that non-clinical participants aged below 28 with high familial risks had higher levels of general use of imagery in daily life than non-clinical participants without such risks. On the other hand, counterparts aged 28 or over appeared to have lower levels of use of imagery than non-clinical participants without such risks. Given that the peak age of conversion to bipolar disorder is in the early 20s, individuals with high familial risks aged over 28 would have passed through this conversion period without developing BD. Such individuals might therefore be regarded as people with high familial risks who have survived the peak risk period uneventfully.

As Studies three and four showed that high levels of general use of imagery in daily life might be positive predictors of lifetime hypomanic symptoms, one might hypothesise that individuals with high familial risks but low general use of imagery might be at a lower risk of

developing BD. Conversely, young individuals with high familial risks and high general use of imagery might warrant extra clinical attention for monitoring of subsequent conversion to BD. This hypothesis remains highly tentative but may be examined prospectively by comparing the rate of conversion to BD among two groups of young asymptomatic individuals with high familial risks of bipolar disorders over a period of time: one group with a low general use of imagery and the other with high use. If at-risk individuals with high levels of general use of imagery in daily life were indeed confirmed to have a higher risk of onset of full-blown bipolar disorders, close monitoring of these individuals might theoretically lead to early identification of prodromal symptoms and timely intervention to minimize subsequent morbidity and disabilities associated with full-blown bipolar disorders.

Furthermore, if general use of imagery increases from acute manic to euthymic phases in BD (Study 2), this would imply that trait imagery might decline from euthymia to relapse of mania. As such, monitoring trait imagery use might provide a useful tool for relapse monitoring of BD. This hypothesis deserves further prospective studies.

9.4 Emotional impact of prospective imagery: a trait marker of bipolarity

The second key finding of the thesis is that people with high behavioural risks (Study 4) and familial risks (Study 5) experienced higher emotional impact of their intrusive mental images than non-clinical participants without such risks. Furthermore, this imagery characteristic appeared to remain relatively stable in the absence of major symptomatic changes over time (Study 4). These findings corroborate with those Western studies that the emotional impact of prospective imagery was elevated in at-risk individuals (Deeprose et al., 2010; Malik et al., 2014; Meyer, Finucaine & Jordan, 2011). Furthermore, the current thesis found that participants with sub-threshold BD had higher IFES total scores than those with

pure MDD (Study 3). It is therefore reasonable to propose that emotional impact of prospective imagery was increased in people with BSD (i.e. with a lower loading of bipolarity than BD-I and BD-II) when compared to non-clinical controls. Taking all the current evidence into consideration, emotional impact of prospective imagery might be elevated in people at high risks of developing bipolar disorders and could be considered as a possible trait marker associated with bipolarity. Future studies with a larger sample of at-risk individuals will help clarify whether this imagery characteristic is indeed elevated in an at-risk group when compared to a low risk group.

9.5 Emotional impact of prospective imagery: a state and trait marker of psychological distress?

While the emotional impact of prospective imagery appeared to be a trait marker associated with bipolarity, Study 1 found that the level of emotional impact of prospective imagery in patients with remitted BD-I was not significantly higher than in those with remitted MDD but both levels were significantly higher than in non-psychiatric controls. These findings suggest that elevated emotional impact of prospective imagery as a trait marker might not be specific to BD but might be present in MDD as well. An alternative explanation is that some participants with remitted MDD in Study 1 were in fact suffering from sub-threshold BD. Therefore, future studies comparing IFES scores between remitted BD-I and MDD groups should assess and take into account of the presence of subthreshold bipolarity in MDD groups (see also Chapter 5).

Study 6 further found that the emotional impact of prospective imagery was significantly higher in suicidal participants than non-suicidal controls. This holds true even when the analyses had taken into account of the presence of past and present psychiatric illness. This might suggest that high emotional impact of prospective imagery was still

experienced by suicidal participants without any psychiatric disorders. Furthermore, a decline in emotional impact of prospective imagery was associated with a concomitant reduction in suicidal ideation. Taking these results together, the current evidence suggests that the emotional impact of prospective imagery might also be a state marker associated with suicidal ideation, a psychiatric problem characterized by powerful suicidal flash-forward imagery (Holmes et al., 2007). Corroborative evidence further suggested that the emotional impact of prospective imagery might be a positive predictor of both current depressive and anxiety symptoms in people with high bipolar risks (Study 5), and in patients with sub-threshold BD (Study 3). Recent studies suggested that emotional impact of prospective imagery was also elevated among patients with anxiety disorders (Holmes & Mathews, 2010) and depressive disorders (Crane et al., 2012). Whether the emotional impact of prospective imagery might also function as a trait marker for MDD, anxiety disorders and other psychiatric disorders with distressing visual imagery await further research on at-risk groups.

Perhaps even more intriguing are the findings that depressed participants with threshold (Hales et al., 2011) or sub-threshold bipolarity (Study 3) had higher levels of emotional impact of prospective imagery than those with pure MDD. If patients with BD in remission had similar levels of emotional impact of prospective imagery as those with MDD in remission but higher than non-psychiatric controls (Study 1), the evidence obtained from these studies suggests that this imagery characteristic might be further elevated in BD from euthymia to bipolar depression (see Section 5.6.1). Study 2 found that the avoidance sub-scale of emotional impact of prospective imagery increased from bipolar mania to bipolar depression within the index mood episode across time. In other words, depression with varying degrees of bipolarity (sub-threshold BD, BD-II, or BD-I; see chapter 1 for further delineation of various types of BD) might confer an increased emotional sensitivity to intrusive images than depression without such bipolarity. This finding provides further support of the hypothesis that the emotional impact of prospective imagery might be a state-

on-trait factor associated with bipolarity, similar to the general use of imagery in daily life. If the emotional impact of prospective imagery predicted the severity of depressive/anxiety symptoms and suicidal ideation (Studies 3, 5 and 6), its association with bipolarity might explain why patients with bipolar depression would experience more severe depressive and anxiety symptoms, and more serious suicidal ideation than those suffering from pure MDD (Chen & Dilsaver, 1996; Hales et al., 2011; Hawton et al., 2005; Study 3). Further research is called for to clarify the relative changes of the emotional impact of prospective imagery in bipolar and unipolar depression with time and symptomatic changes.

From a clinical assessment perspective, if active bipolar depression is indeed associated with high levels of mental imagery susceptibility when compared to unipolar depression, measuring these imagery characteristics in patients presenting with depression might be an alternative method to direct enquiry of stigmatizing questions about bipolar symptoms in differentiating bipolar and unipolar depression. This is of great importance given that two thirds of patients with BD present with depression on their initial contact with psychiatric care (Judd et al., 2003). Misdiagnosis of bipolar depression as unipolar depression may lead to inappropriate prescription of antidepressants, which is associated with manic switch, intensifying suicidal ideation, and inducing rapid mood cycling (Goodwin & Miklowitz, 2013). From a treatment perspective, reducing the emotional impact of prospective imagery might also be an effective and realistic goal for imagery intervention in bipolar disorders (see section 9.13 for more details).

9.6 Emotional impact of prospective imagery and childhood maltreatment

Previous studies showed that recurrent intrusive images in a number of psychological disorders were related thematically to past memories of traumas (Brewin et al., 2010). What

this thesis adds to the literature is that intrusive images concerning the future (i.e. prospective images) might also be related to subjective reports of past childhood traumas. This association is unlikely to be confounded by negative mood state, as the relationship between past childhood traumas and emotional response to prospective imagery was found in individuals without any clinically significant psychiatric disorders and remained significant after controlling for current depressive and anxiety symptoms (Study 5). This finding highlights the importance of enquiring about childhood abuse in bipolar patients reporting vivid and emotionally strong images, even if such future-oriented images appear unrelated to any past childhood traumas. Previous studies have suggested that bipolar patients with a history of childhood abuse had an earlier onset of illness, a more recurrent course, and more severe suicidal ideation than those without such history (Garno et al., 2005; Carballo et al., 2008). Identifying such past history thus has some prognostic implications. Furthermore, recent literature has shown that imagery rescripting of early memories of socially traumatic events in patients with social phobia was effective in reducing negative self-image, memory distress, anxiety and fear of negative evaluation (Wild & Clark, 2011). From a treatment perspective, imagery rescripting of early traumatic memories might also be beneficial in reducing distressing and vivid future-oriented negative images in BD.

9.7 Prospective images of positive emotional valence acting as a fuel to manic fire

If general use of imagery and emotional impact of prospective imagery were already elevated in patients with BD in remission (Study 1) and in the at-risk state (Studies 4 and 5), an additional driving force would be required to trigger the cascade of events leading to ascent of manic symptoms. Previous studies have found that negative life events and positive life events, especially goal-striving and goal-attaining life events, might trigger manic and

depressive episode recurrences respectively (Johnson & Miller, 1997; Johnson et al., 2000). Gregory et al. (2010) reported that euthymic bipolar patients retrospectively recalled having positive future-oriented images during their most recent hypomanic episode. Echoing the above findings, Study 2 found that the number of positive prospective images dropped in tandem with the severity of manic symptoms in patients with bipolar mania. Finally, the reduction in the number of positive prospective images from baseline to 12 weeks was a significant positive predictor of recovery from mania. Indirect evidence also emerged from Study 1 that the number of positive prospective images did not differ between remitted BD-I, remitted MDD, and the non-psychiatric control group. The combined evidence appears to suggest that the drop in the number of positive prospective images might play a key role in the descent of manic symptoms in patients with BD.

Conversely, one might postulate that the ascent of manic symptoms in BD might be dependent on the increase in the number of positive prospective images during early stage of recurrence. Such positive prospective images, with their powerful impact on emotions and high subjective level of conviction (Holmes & Mathews, 2010), might act as 'proxy' positive life events to trigger onset of hypomania (Johnson, 2005). Longitudinal studies that prospectively follow up a large group of patients with BD from euthymia to acute mania would be required to investigate this hypothesis.

9.8 Prospective images of negative emotional valence acting as a fuel to depressive ice

Study 2 has also shown that the number of negative prospective images correlated significantly with the current levels of depressive symptoms at each time point in bipolar mania. Furthermore, the number of negative prospective images was associated with the status of mood switch from bipolar mania to bipolar depression. Indirect evidence also

emerged from Study 1 showing that the number of negative prospective images was similar in both BD-I and MDD groups in remission. Studies 4 and 5 converged in reporting that the number of negative prospective images was similar across individuals with and without high bipolar risks as defined by either a bipolar phenotype identified by MDQ or being first-degree relative of patients with BD.

9.9 Clinical utility of targeting intrusive images in bipolar disorders

The above findings provide some converging evidence that prospective imagery might act as a fuel in triggering the cascade of events leading to full-blown mood episodes in BD. As such, monitoring the number and the content of prospective images of both positive and negative emotional valences reported by bipolar patients might allow early identification of impending relapse. Although taking note of the emergence of excessively optimistic thoughts and beliefs has been advocated in relapse prevention of BD (Lam, et al., 2005), patients might encounter difficulty in describing these picturesque cognitions in verbal forms. Furthermore, given their high propensity to visualize cognitions in the form of intrusive images, patients with BD might find it easier to identify and report images. Given that therapists seldom enquire about the presence of intrusive images in patients with BD, open discussion and exploration of this topic could make the patient felt understood and enhance therapeutic alliance (Hackmann, Bennett-Levy & Holmes, 2011; Ng, Krans & Holmes, 2013; Ng, Di Simplicio & Holmes, 2015).

Apart from the potential value of monitoring clinical relapse, targeting future-oriented images might have additional therapeutic values. Given that positive or negative prospective images might be associated with bipolar mania or depression respectively, imagery-based intervention that attempts to transform these prospective images into more emotionally neutral

images might be valuable (Ng, Krans & Holmes, 2013). As such, imagery re-scripting may offer a therapeutic strategy to transform an emotionally charged future-oriented image into a safe, soothing and compassionate image (Gilbert, 2009; Ng, Krans & Holmes, 2013; Neff & Germer, 2012). Such soothing and compassionate imagery might induce a sense of safeness and tranquility (Gilbert & Procter, 2007), which may be an antidote to extreme mood swings characteristic of bipolar disorders (see 9.13 on new possible therapeutic strategies).

9.10 Responses to positive and negative affect and prospective imagery in bipolar disorders

Previous studies found that positive rumination was elevated in people with high bipolar risks (HR) (Feldman et al., 2008) and in patients with BD (Gruber et al., 2011). The current thesis also found that high levels of positive rumination (rumination about positive emotions and rumination about positive self-qualities) were found in people with high familial risks for BD (Study 5), patients with sub-threshold BD (Study 3), patients with remitted BD-I (Study 1), and patients with acute mania (Study 2). However, Study 2 suggests that the picture might be more complicated. The BD-I group had higher levels of rumination about positive emotions than the MDD control group, but a progressive decline in this cognitive processing style was associated with resolution of manic symptoms. On the other hand, levels of rumination about positive self-qualities were not significantly different between the BD-I and MDD groups. This finding is not compatible with the finding of the remitted BD-I group (Study 1) and sub-threshold BD (Study 3) having a higher level than MDD. While type II error due to small sample size might explain the lack of significant findings in Study 2, future studies should attempt to examine the different aspects of response to positive affect separately in larger studies.

How might positive cognitive processing style be related to the ascent of mania?

Previous studies have found that positive rumination predicted lifetime frequency of manic episodes (Gruber et al., 2011) and rumination of voluntarily conjured positive images about their personal life leads to increased self-rating of positive mood, and increased physiological arousal associated with positive emotions (Gruber et al., 2009). Savouring positive emotions and positive self-qualities encapsulated in the form of positive prospective images was a distinct characteristic of BD (Study 1), predicted lifetime hypomanic symptoms (Study 3), and amplified lifetime hypomanic symptoms through the mediating role of hypersensitive BAS among people with high familial risks for BD (Study 5).

A parallel process was also observed in depressive rumination. Previous studies found that patients with bipolar and unipolar depression might share similar maladaptive cognitive processing of emotions in the form of depressive rumination (Thomas & Bentall, 2002; Thomas et al., 2007). Dwelling upon negative emotions and meanings associated with negative prospective images might amplify pathological negative emotions in MDD with varying degrees of bipolarity (Study 3) and people at high familial risks for BD (Study 5).

9.11 Behavioural approach system (BAS) dysregulation and bipolar disorders

Study 1 concurred with Urosevic et al.'s (2007) study in reporting that patients with remitted BD-I had a higher BAS sensitivity than both non-clinical and MDD groups. Study 2 provided new evidence that a BD-I group had higher BAS sensitivity than a MDD group regardless of the severity of manic symptoms. Study 5 has similarly reported that BAS sensitivity was elevated in people with high familial risks for BD when compared with people without such risks. These findings provide additional support for BAS sensitivity being a trait factor associated with BD (Alloy et al., 2008).

9.12 Mental imagery susceptibility, responses to positive and negative affect, and BAS dysregulation in bipolar disorders

What are the links between prospective images, responses to positive and negative affect, and BAS dysregulation in BD? Positive rumination about positive prospective images was predictive of BAS sensitivity, which in turn predicted a study participant having a BD-I rather than MDD diagnosis (Study 1). Repetitive dwelling upon positive prospective images also predicted lifetime hypomanic symptoms in at-risk individuals for BD, the relationship of which was moderated by BAS sensitivity (Study 5). Furthermore, BAS sensitivity moderated the relationship between general use of imagery in daily life and the number of lifetime prior mood episodes (Study 1). These findings suggest that BAS sensitivity might play a role along the cascade of events from mental imagery susceptibility to the full ascent of manic symptoms in patients with BD.

How might mental imagery susceptibility influence BAS sensitivity? As mental images are more likely to elicit powerful emotions than verbal thoughts (Holmes et al., 2009), visualizing cognitions of emotional valence might mimic encountering real emotional events in the mind's eye. Some parallels can be drawn from the drug addiction field. According to the elaborated intrusion theory of craving (May et al., 2004; May, Kavanagh & Andrade, 2015), intrusive images associated with desired substances are initially pleasurable, as they share some cognitive properties of the actual desired activity or goal. This motivates the individual to ruminate on and savour the content and emotions of the images, by retrieving cognitive associations and creating further mental imagery of the target. These images sustain the motivation of rumination as they are emotionally charged. As such, this cognitive activity may take over individual's chain of thoughts and dominate experience (May et al., 2004). If BAS-activating events (or perhaps even positive images of goal-attaining or goal-striving events) are considered as 'objects of desire' in BD (synonymous to craved substances

in substance addiction), elaborated intrusion theory would predict that intrusive images of these desired objects would escalate in number, dominate the chain of thoughts, and hijack attention so that the individual's cognitive, emotional and behavioural responses would be geared towards any reward cues indicative of obtaining the desired objects (i.e. BAS becoming hyper-sensitive to reward cues). Indeed, studies showed that patients with drug and alcohol addiction (Franken, Muris & Georgieva, 2006) and non-clinical college students with drug or alcohol misuse (Franken & Muris, 2006) had higher BAS sensitivity levels (particularly BAS Drive and BAS Fun Seeking) than controls. The elaborated intrusion theory would also predict that failure to satiate the desire increases awareness of the discrepancy between the current state and the goal (May et al., 2004). When desire cannot be satiated, worsening of mood then triggers increasingly vivid and compelling 'contrasting' imagery of loss and failure with spikes of briefly pleasurable imagery, enhancing awareness of deficit and the worsening of mood. If the desire for fame and personal glory encapsulated in the positive images of patients with BD cannot be satiated, the elaborated intrusion theory would predict the occurrence of negative contrasting images interspersed with spikes of positive images, possibly associated with emotional instability which is characteristic of BD. Such occurrence of contrasting images in rapid succession would then depend on the high propensity to use imagery in daily life, an imagery characteristic that has been associated with BD (Holmes et al., 2011; current thesis). Given the high comorbidity between drug misuse and BD, this image intrusion theory might have special relevance to the current imagery hypothesis. An experience sampling study design that measures the moment-to-moment variations in the frequency, rate of change, and emotional valence of the prospective images might provide an opportunity to study this hypothesis (Bonsall et al., 2011).

9.13 Mental imagery susceptibility, suicidality and bipolarity

Study 6 replicated previous findings that suicidal mental images ('suicidal flash-forwards') were present in people with suicidal ideation (Hales et al., 2011; Holmes et al., 2007). Furthermore, Study 6 showed that suicidal participants were more likely to have a history of lifetime hypomanic symptoms than non-suicidal participants. Having a past history of lifetime hypomanic symptoms might be considered as a type of mild elated states, a condition along the BSD (Angst et al., 2005) and possibly one of the bipolar phenotypes with an increased liability for developing full-blown BD (Rock et al., 2013). Perhaps more intriguing is that Study 6 found that suicidal participants with a history of lifetime hypomanic symptoms were more likely to experience suicidal flash-forward imagery in the face of a high sense of entrapment than those suicidal participants with this bipolar phenotype but with a lower sense of entrapment. If suicidal flash-forward imagery was reported by people with strong suicidal ideation (Hales et al., 2011; Holmes et al., 2007; Study 6) and these visual images were associated with strong emotional impact and propensity of action (Holmes & Mathews, 2010), the occurrence of suicidal flash-forward imagery in suicidal participants with a past history of hypomanic symptoms, especially in the presence of high perception of entrapment, might understandably increase their likelihood of future suicidal acts. This finding highlights the importance of enquiring about the presence of suicidal flash-forwards in bipolar patients with suicidal ideation, especially in face of a strong sense of entrapment. Given that suicidal flash-forward imagery might provide a sense of relief or even triumph against perceptions of entrapment and defeat (Crane et al., 2012; Holmes et al., 2007; Hales et al., 2011; study 6), this might account for higher suicide rates in patients with BD (Raja & Azzoni, 2004). Furthermore, given the high propensity of visualizing cognitions in BD, imagery-based interventions of promoting a hopeful future, re-framing the meanings associated with suicidal images, and re-scripting the romantic connotation of suicidal acts or

the rosy aftermath of suicide into a more serene picture of eventual successful resolution of crisis without suicide might be viable interventions for suicidal ideation in BD (Holmes et al., 2007).

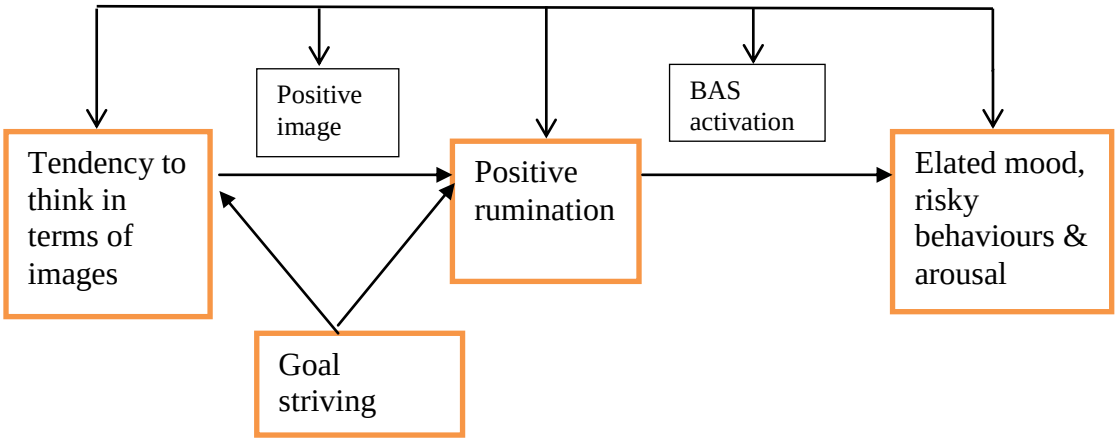
9.14 An integrated imagery-based micro-formulation within the cognitive-behavioural model of bipolar disorders

The current thesis proposes an imagery-based micro-formulation integrated within the broad cognitive-behavioural framework. The following case formulation might explain how mental imagery susceptibility in BD could play a role in amplifying pathological positive and negative emotions, increasing risks of recurrence, and enhancing suicidal risks. This imagery model attempts to provide a parsimonious framework that explains the occurrence of a diverse array of symptoms characteristic of BD – depression and hypomania/mania. Researchers have previously debated whether BD is better conceptualized as two independent comorbid illnesses (i.e. depression and mania/hypomania) or as one illness (Joffe, Young & MacQueen, 1999). According to the proposed imagery model, individuals with BD have heightened mental imagery susceptibility (i.e. general use of imagery in daily life and emotional impact of prospective imagery) as trait markers. The intrusions of prospective images of positive and negative emotional valence would then lead to a cascade of BAS outputs triggering hypomanic/manic and depressive episodes respectively. Such prospective images might be related to recent real positive or negative life events or due to novel combinations of past memories or anticipated future events. In other words, this imagery model views bipolar mania and bipolar depression on a continuum of one single illness. However, it must be stressed that the model is a highly speculative one requiring vigorous studies for examining its clinical utility and efficacy in improving the outcome of bipolar disorders.

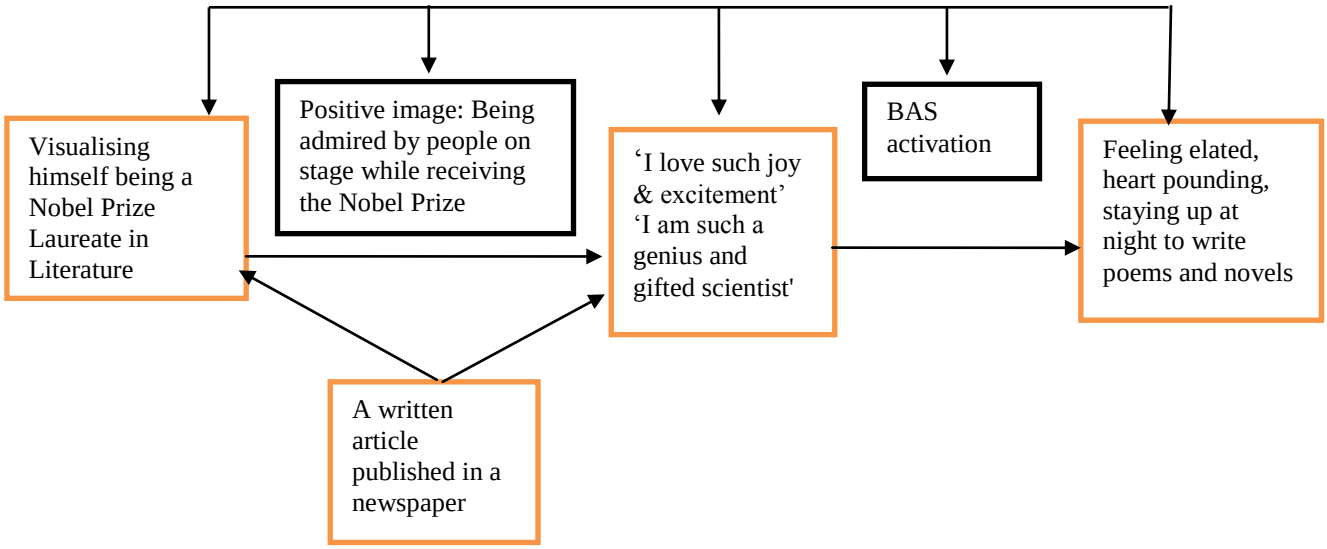
Mental images may represent real goals to be attained (Conway et al., 2004) and may

enhance the perceived likelihood and conviction of occurrence of the imagined events (Carroll, 1978, Mathews et al., 2013). As such, positive prospective images may serve as 'real' positive life events and provide a necessary 'fuel' for positive rumination (see Studies one, three and five). In response to such imagined success, patients with BD may then ruminate about the positive emotions and self-qualities associated with these positive images (Johnson, 2005; Gruber et al., 2010; Gruber et al., 2011; Studies 1, 2, 3 and 5). Excessive positive rumination of images might then lead to (hypo)manic symptoms through activating the BAS (Studies one and five). Elated mood might then lead to further occurrence of positive images through mood-dependent biased retrieval of past rosy memories (Eich & Lam, 1997) and thereby provides increased fuel for positive rumination. This model might potentially explain why mood episode recurrences were not necessarily preceded by 'real' life events, or may even become independent from them (Hlastala, Frank & Kowlaski, 2000). The following diagrams 1 and 2 depict this hypothetical model of the ascent of mania through the interactions between mental imagery susceptibility, positive cognitive processing styles, and BAS.

Flow diagram 1: A generic cognitive model of the hypothesized relationships between mental imagery, positive cognitive styles & behavioural approach system (BAS) in the ascent of manic symptoms



Flow diagram 2: A clinical example of how positive images interact with positive cognitive processing style in kindling the bush of manic fire



A parallel process might also occur for amplification of pathological negative emotions in bipolar depression. The occurrence of negative prospective images in the mind's eye might exert an equally powerful emotional impact as 'real' negative life events which have been found to predict depressive relapse in BD (Johnson et al., 2008). Given that people with high bipolar risks (Study 5) and patients with sub-threshold BD had elevated levels of depressive rumination (Study 5), bipolar depression might be triggered by negative prospective images. Study 2 has shown that mood switch from mania to depression in patients with bipolar mania was predicted negatively by a decrease in the number of negative prospective imagery from baseline to 12 weeks. Study 5 has further found that the interaction factor of negative prospective images (IFES negative events) and depressive rumination was predictive of current depressive symptoms. Depressive mood might also enhance retrieval of additional negative memories in the form of past-oriented intrusive images (Crane et al., 2012; Patel et al., 2007), thereby adding more snow to the heap of 'depressive ice'.

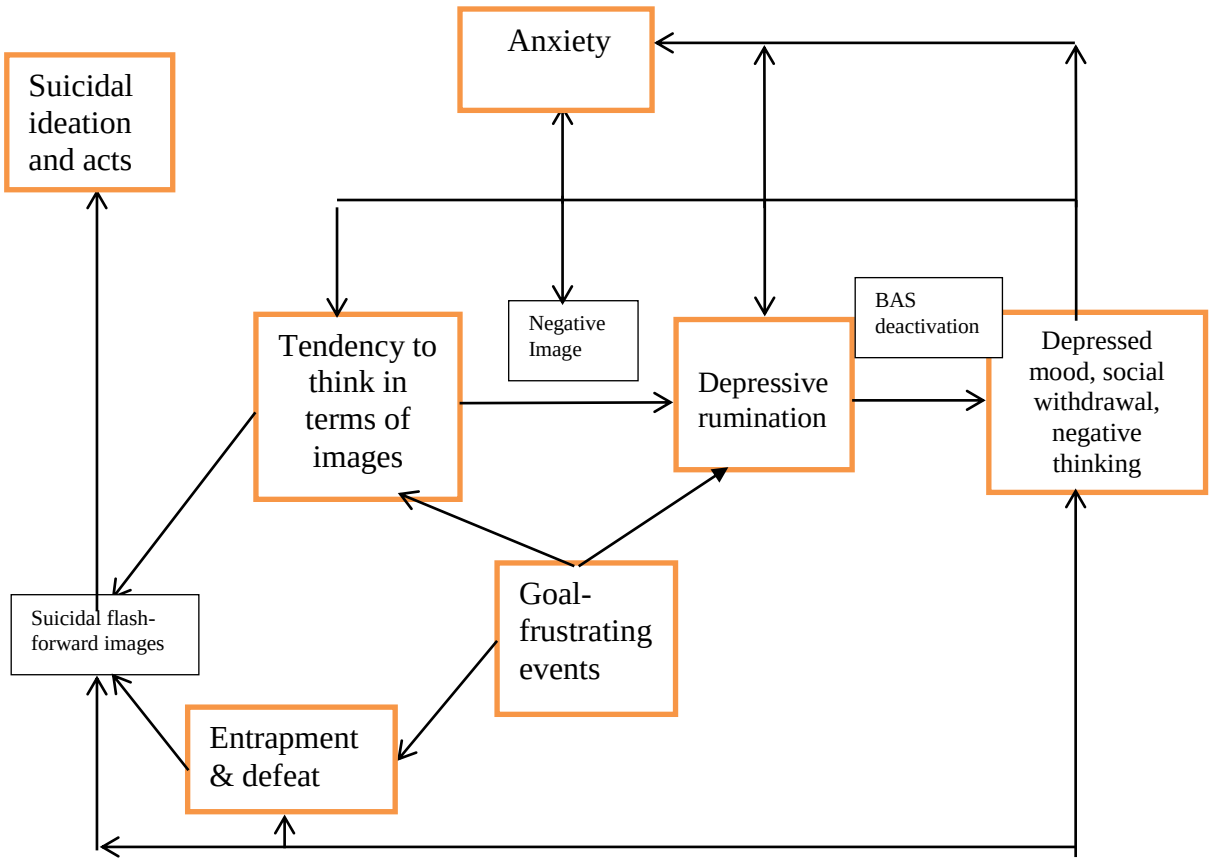
How might depressive rumination about negative prospective images lead to depressive symptoms in BD? The BAS hypersensitivity theory would predict that bipolar individuals would experience excessive de-activation of the BAS functioning in response to BAS-deactivating events (Urosevic et al., 2007), leading to social withdrawal, reduced energy, increased self-devaluation, and depressed mood, a vast array of symptoms reminiscent of MDD. Study 5 indeed found that repetitive rumination of negative prospective images would predict lower BAS sensitivity, which would in turn increase depressive symptoms. As such, this imagery hypothesis would also explain the presence of mood episodes of opposite polarities within an individual and the occurrence of mixed affective episode.

Around one third of patients with BD meet criteria for an anxiety disorder (Simon et al., 2004). Study 3 of the current thesis has found that intrusive negative prospective images might amplify anxiety symptoms in addition to depressive symptoms. As such, mental imagery might provide a link between the co-occurrence of anxiety and bipolar disorders (Holmes et al., 2008). Previous studies have suggested that anxiety comorbidity might intensify bipolar symptoms, increase the likelihood of having additional comorbid disorders, reduce treatment response, and increase rates of suicide and substance misuse (Keller, 2005), as well as a course of illness characterised by rapid cycling (Kupka et al., 2014). Future studies should examine this hypothesis by comparing mental imagery susceptibility in a group of people with pure BD with another group with BD comorbid with anxiety disorders.

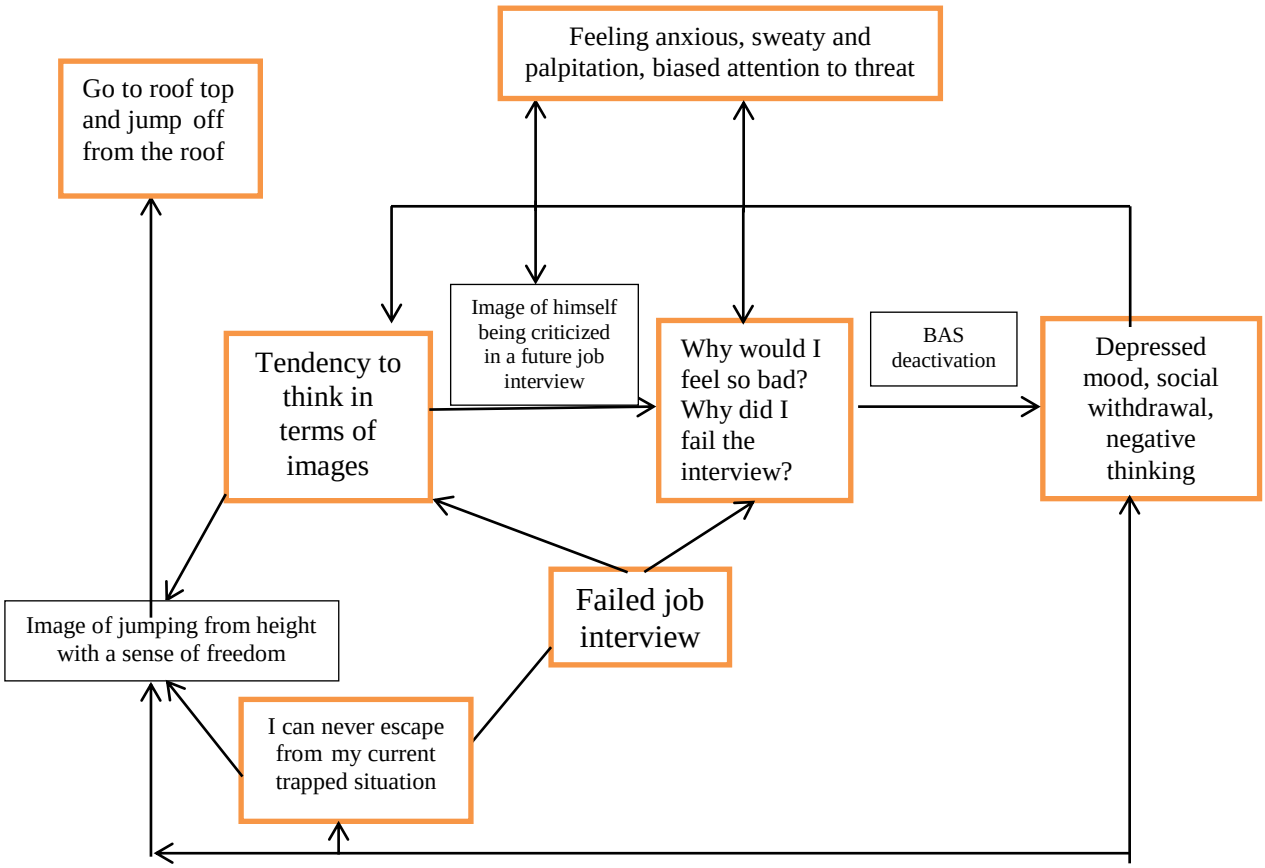
Perceptions of entrapment and defeat were also commonly found in patients with depression and anxiety (Taylor et al., 2011). Study 6 found that suicidal participants with a history of lifetime hypomanic symptoms and higher levels of entrapment were more likely to report suicidal flash-forward images than those suicidal participants with a similar history of hypomanic symptoms but lower levels of entrapment. If bipolarity is associated with heightened susceptibility to mental imagery, the goal of escape from entrapment might then be visualised as suicidal flash-forwards. If suicidal flash-forwards of actual suicidal acts or

aftermath of suicide were perceived as comforting they might enhance the probability of suicidal acts (Holmes et al., 2007; Hales et al., 2011). As such, the susceptibility to mental imagery might account for high suicide risks associated with BD (Hawton et al., 2005). Therefore, the proposed imagery hypothesis may also be able to explain two common psychiatric co-occurrences in BD – anxiety disorders and suicidality. The following flow diagrams 3 and 4 depict the ascent of depressive symptoms and associated pathological emotions through the inter-relationships of mental imagery susceptibility, depressive ruminative response style and BAS de-activation.

Flow diagram 3: A cognitive model of the hypothesized relationships between mental imagery, depressive rumination & behavioural approach system (BAS) in the ascent of depressive/anxiety symptoms and suicide



Flow diagram 4: A clinical example of how mental imagery susceptibility, response to negative affect, and BAS de-activation may interact to lead to depressive and anxiety symptoms, as well as suicidal ideation



9.15 Clinical implications

As BD is a severe and recurring disorder associated with serious disabilities, prompt resolution of acute mood episodes, prompt intervention of early signs of recurrence, and relapse prevention are important therapy aims. Studies have consistently shown that only 50-60% of patients with BD achieved full recovery with pharmacotherapy (Scott & Colom, 2008). Furthermore, the efficacy of psychological intervention as an adjunct treatment has been limited (Scott, Colom & Vieta, 2007). Novel treatments are needed to enhance the response and remission rates of patients suffering from BD.

If patients with BD have high propensity to think in mental images, predominant use

of verbal techniques in traditional cognitive-behavioural therapy (CBT) might not be able to fully grasp the vividness, compellingness and emotionality associated with their visual cognitions. As a result, attempts at verbal refutation might fail to 'hit the nail on the head' and even strain the therapeutic alliance (Ng, Di Simplicio, Holmes, 2015).

The current thesis has provided some preliminary evidence that mental imagery might be a possible key therapeutic target for timely intervention of early signs of relapse, hastening recovery of acute mood episode, and maintaining wellness during inter-episode periods. The following treatment strategies were proposed to enrich the imagery-based interventions suggested by Hackmann et al. (2011), based on the empirical findings of the current thesis and the personal clinical experience of the author as a cognitive therapist for twenty years.

9.15.1 Imagery-based micro-formulation

If BD is associated with mental imagery susceptibility, an imagery-based micro-formulation similar to diagram 2 and diagram 4 would be valuable (Ng, Krans & Holmes, 2013). This diagram could be further enriched with additional information of how a history of childhood traumas and genetic diathesis would predispose patients to enhanced emotional impact of their vivid images (see Study 5; Tjissen et al., 2002). Furthermore, patients could be educated about unique characteristics of mental images (being more 'real', foretelling future outcomes, and being more likely to be translated into action than verbal thoughts; Holmes & Mathews, 2010). Patients may then gain some cognitive distance from intrusive images and develop an adaptive meta-cognitive appraisal of them (Hackmann, Bennett-Levy & Holmes, 2012). Sharing such an imagery-based micro-formulation with patients who experience mental images might make them feel more understood, foster a sense of relief and hope, and thus help to strengthen the therapeutic alliance.

9.15.2 Normalising mental imagery susceptibility as an evolutionary advantage

Patients with BD usually feel distressed by their vivid and compelling negative intrusive images (Morina et al., 2010; Patel et al., 2007). As they tend to experience more intrusive images than people without BD, their experiences might not be understood by those around them and they might feel ashamed of sharing these inner experiences. As such, patients might try to suppress their images, a maladaptive strategy that would paradoxically lead to rebound intrusions with an associated sense of uncontrollability (Wells et al., 2010). While pointing out the futility of suppression as a strategy in controlling intrusive images, patients could also be informed of the existing literature on bipolar patients being more creative artistically than people without the disorders (Srivasta et al., 2007). Furthermore, patients could also be educated on how artistic creativity might be linked to their inherited trait of heightened use of imagery in daily life (Study 5). If creativity is associated with enhanced problem solving and divergent thinking in BD (Murray & Johnson, 2010), such increased propensity to think in terms of mental images may be normalised as a common but desirable trait among people in the general population. This normalising strategy could be enriched by behavioural experiments, for example, by encouraging the patient to conduct an online search for reports of creative people experiencing mental images or even opening a discussion forum online to discuss the advantages and disadvantages of having high trait use of imagery. This message could reduce self-stigma (Newman, Leahy, Beck & Reilly-Harrington, 2000) and encourage patients to adopt a creative, flexible and adaptive use of their gifted talent of visualising thoughts (see below for further strategies).

9.15.3 Use of imagery diaries to monitor and modify maladaptive thoughts and their associated meanings

Thought records are commonly used in CBT for a variety of psychological disorders. In view of their propensity to think in images, patients with BD could be taught to draw their cognitions in their thought diaries, together with a subjective rating of distress and excitement. Such 'imagery diaries' could be given as homework and then reviewed in the next session for further elaboration of their associated meanings. Such images could then be rehearsed or retrieved during the session so that their associated meanings could be explored and even re-scripted (see section 9.13.5 below for more details). Following an imagery re-scripting session (Ng, Krans & Holmes, 2013), such thought diaries could then be enriched by incorporating an 'alternative image' in juxtaposition with the reported maladaptive image. Regular practice of switching from a maladaptive to an adaptive mental image might be associated with a reduction in severity of the mood symptoms and an improvement in daily performance (Pictet et al., 2011; see below on what images might be considered as adaptive images). Routine monitoring of the frequency of patient's mental images with associated levels of emotionality and valence would facilitate early detection of an upsurge of maladaptive future-oriented images, a feature suggestive of impending change in the levels of hypomanic and depressive symptoms (see Study 2 in Chapter 5). Furthermore, such pictorial diaries could be fun for patients, and allow them to appreciate their artistic talent and creativity. Drawing the intrusive image would enhance patients' ability to 'distance' themselves from it and to appreciate images as images only.

9.15.4 Learning and practising behavioural strategies to reduce the vividness and compellingness of the intrusive images

Krans et al. (2011) have shown that people with a tendency to use visual images in

daily life (c.f. people with high levels of bipolarity) experienced more intrusive images even after listening to an actor-narrated 'journalist verbal report' of a traumatic traffic accident. Similar findings have also been shown in students with high levels of bipolarity (Malik et al., 2014). In other words, patients with BD might be particularly susceptible to developing intrusive and distressing images during their casual and regular encounter of people and events in daily life. Furthermore, patients with BD (Tjissen et al., 2010a) and people with high familial risks (Study 5) were found to have a greater likelihood of encountering traumatic events in their lives. In view of their increased risks of exposure to traumatic events and formation of traumatic images, behavioural strategies to prevent the formation of visual images upon encountering or even hearing about distressing events might reduce the number of prospective images, which have been shown in the current thesis to be related to the amplification of pathological emotions (Holmes et al., 2008).

Recent studies indicate that eye movement desensitisation reprocessing (EMDR) might help to reduce the vividness associated with mental images (van den Hout & Engelhard, 2012). Furthermore, playing Tetris for 30 minutes soon after witnessing a traumatic incident might reduce subsequent intensity and frequency of intrusive traumatic images (Holmes et al., 2009). The therapist could suggest that patients install Tetris on portable electronic devices. Behavioural experiments could then be designed to test whether playing Tetris games could reduce the vividness and emotionality of their intrusive images.

9.15.5 Learning cognitive strategies to modify the meanings associated with intrusive images

Therapists could discuss with patients on details of how images are processed, as well as the associated emotions and meanings. Maladaptive reasoning biases and faulty conclusions drawn from these images could be collaboratively examined, and these new meanings and conclusions could then be incorporated into the images during imagery re-

scripting work (Hackmann, Bennett-Levy & Holmes, 2011). At times, patients might be guided to think 'beyond the worst point' for negative images in order to fully establish the negative predictions (Butler, Fennell & Hackmann, 2010). However, patients might also be guided to think 'beyond the best point' (Ng, Krans & Holmes, 2013) and understand the interpersonal consequences and responsibilities associated with 'hyper-positive' images (e.g. the concern and worries of significant others about his or her financial liability as an aftermath of the positive future-oriented image of buying a red Ferrari car). Study 2 has shown that mood switching from mania to depression was associated with an increase in negative prospective images, suggesting that substituting 'a rosy image' with 'a threatening or distressing image' might promote mood switching from mania to depression or even induce mixed affective state.

If substituting hyper-positive images with negative images might pose risks of mood switch from mania to depression, what kind of images would be more adaptive? Gilbert (2009) recently proposed a three affect-regulation system in the brain which has evolved to achieve different functions. The threat and self-protection system detects and picks up on threats and then selects appropriate behavioural responses (e.g. fight, flight, or freeze) and gives rise to certain emotions (e.g. anxiety, anger, and disgust). The incentive, resource-seeking, drive-excitement system gives people positive feelings that guide and motivate people seeking out resources for survival and procreation. People with BD are postulated to have a dysregulation of this drive-excitement system (Gilbert, 2009; cf. BAS hypersensitivity theory; Alloy et al., 2008). The soothing, contentment, and safeness system enables people to bring a certain soothing, quiescence, and peacefulness to the self. Contentment is postulated to be a form of being happy with the way things are, feeling safe, and not striving or wanting (Gilbert, 2009). As such, patients with BD could be guided to replace their mental images of positive or negative emotional valence with a compassionate nurturer image or a safe image with interpersonal intimacy, affection and warmth or an image of contentment with what they are

(Lee, 2005). Such images can be human or non-human images (like a tree or a mountain). They can be explored in various sensory modalities, with compassionate attention to specific qualities of wisdom, strength, warmth, and non-judgement. At times, patients might also practise imagining themselves as deeply compassionate persons and then practise each day at becoming 'the compassionate self', with the appropriate facial expressions, body gestures, voice tones, and ways of thinking (Gilbert, 2009). The effectiveness of such imagery re-scripting could be gauged by routinely assessing patients' subjective levels of distress, excitement, and tranquillity/safeness throughout the re-scripting process. Repeated practice of such compassionate imagery could be assigned as homework. Given their greater use of imagery in daily life, patients with BD would probably report less difficulty in conjuring up these learnt images at home than people who are not good at visualising their cognitions as images. There is a surge of interest in the application of compassion-focused strategies for patients with BD (Lowens, 2010).

However, a word of caution is needed in using imagery-based interventions for people with BD. Signals of kindness and compassion from another person or oneself might activate the attachment systems (Mikulincer & Shaver, 2007). When that happens, some complex and unresolved memories, images or felt sense might become re-activated. The beginning of the experience of warmth and kindness might ignite sadness and grief. Indeed, some patients find compassion-focused imagery physiologically stressful (Rockliff et al., 2008). Given that physiological arousal may lead to an activation of the BAS functioning and possibly manic relapse (Mansell & Lam, 2003; Studies one, two and five), regular monitoring of the distress level and occurrence of negative intrusive images during such compassionate imagery work is required to facilitate identification of such complex emotions and work on resolving them accordingly.

Given that patients with suicidal ideation or acts, particularly those with bipolar depression, might conjure suicidal flash-forwards as a solution of escape from perceptions of

defeat and entrapment (Hales et al., 2011; Crane et al., 2012; Study 6), routine enquiry of the presence of such suicidal flash-forwards might be important for suicidal risk assessment. Given that people with suicidal flash-forwards were seriously suicidal (Holmes et al., 2007; Study 6), imagery-based interventions might also be employed to target and modify the meanings associated with such suicidal images.

9.15.6 Disrupting the chain of ruminative responses to positive and negative affect

The current thesis echoes previous findings that patients with BD and people with high bipolar risks had increased levels of positive rumination compared with those without such disorders or risks (Studies one, two, three and five). Recent studies have shown that people at risk for BD reported trait levels of joy (a positive emotion associated with reward) and pride (a positive emotion associated with achievement) but not compassion (a positive emotion associated with prosocial behaviours and connection with others) (Gruber & Johnson, 2009). On the other hand, depressive ruminative cognitive style was also found to be elevated among people with high bipolar risks (Study 5) and people with bipolar depression (Study 3). This finding is also consistent with other studies that bipolar depression is associated with elevated depressive rumination (Thomas & Bentall, 2002; Thomas et al., 2007).

Strategies used in the treatment of depressive rumination like passive distraction (e.g. listening to soothing music or watching scenes of peaceful scenery) or active distraction (e.g. moderate exercise) might also disrupt the chain of thoughts associated with positive emotions (Watkins et al., 2007). However, it is not clear whether positive affect associated with positive rumination might be a disincentive to the initiation of such distraction strategies. Furthermore, Thomas et al. (2007) suggested that rumination about initial dysphoria in bipolar patients might promote vigorous attempts to avoid negative emotion through focusing on neutral, pleasant or even high-risk activities, ultimately leading to BAS activation, excitement and

mania. Careful monitoring and education on adopting soothing strategies rather than risk-taking methods are therefore required when working with positive and depressive rumination. There is also a recent interest in adopting a detached mindful approach to the occurrence of negative intrusive images and the associated chains of thoughts. Mindfulness has been found to reduce cravings and subsequent drug use in drug users (Witkiewitz & Bowen, 2010) and reduce relapse in recurrent depression (Kuyken et al., 2010). Given that addiction shares some similarities with bipolar mania in terms of the presence of an object of desire, positive rumination, and approach behaviours towards reward goals (see Section 9.12), mindfulness-based interventions might hold similar promise for disrupting the vicious cycles of positive and depressive rumination in bipolar disorders. There is some recent encouraging initial evidence supporting its use in reducing between-episode anxiety (Perich et al., 2013) and depressive symptoms in BD (Williams et al., 2008).

9.15.7 Addressing the ascent of mania and depression through minimising hyper-responsiveness of behavioural approach system

Studies 1, 2 and 5 of the current thesis found that a common pathway from imagery characteristics and responses to positive and negative affect to onset of mania/depression might lie on BAS activation or deactivation. Modulating BAS functioning might be a sensible strategy to halt the ascent of manic or depressive symptoms in BD. Patients could be educated about the risks of approach behaviours towards goal pursuit in escalating manic symptoms (Johnson, 2005). As such, patients might need to adopt strategies to recognise any increase in elation and excess motor activities through daily mood and activity charting (or even use of actigraphy). Patients could also be coached in strategies to slow themselves and cool down their extreme emotions. For example, they could be taught to speak slowly, sit calmly, pause for a few minutes before committing any act, avoid sleep deprivation, moderate daytime

activities, and look for a buddy to give honest advice when being consulted for appropriateness of any possible impulsive acts (Newman et al., 2000).

In summary, the above section proposes a set of cognitive-behavioural and imagery-based interventions based on some findings obtained from the current thesis and other recent research literature. These strategies aim to enhance therapeutic alliance, patients' acceptance of their bipolar illness, adaptive reframing and use of their deficits as strengths (e.g. capitalising on their high tendency to use imagery in daily life for promoting creative solutions to problems and enhancing success in the use of imagery diaries), as well as re-constructing the content and meanings of their positive and negative intrusive images. These strategies are novel ones that demand further evaluation in efficacy trials involving patients with BD.

9.16 Future research directions

The six studies of the current thesis attempted to study the relationships between mental imagery susceptibility, responses to positive and negative affect, and mood symptoms in study samples with varying degrees of bipolarity. These studies provide some evidence supporting the notion that mental imagery characteristics and responses to positive and negative affect might be trait factors associated with bipolarity. However, there are many unanswered questions. First, what kind of positive prospective images might be particularly associated with mania? Future studies might need to carefully differentiate between types of positive images, given that manic relapse is associated with goal-striving or goal-attaining life events (Johnson et al., 2008). Second, which type of positive emotions might be particularly associated with mania? Gruber et al. (2008) has shown that mania was more associated with joy and pride than with compassion. Future studies could understand more about the exact nature of positive emotions and match these emotions with the content of the prospective

images to better understand the interactions between emotions and prospective images. Third, mania is also associated with other emotions like anger and irritability. How would such emotions arise in mania? Does mental imagery play a role in the amplification of such emotions? Fourth, although the current study provides some preliminary evidence for changes in negative prospective images predicting mood switch from mania to depression, future studies should recruit a sample of patients with rapid cycling bipolar disorder for more detailed investigation of the role of mental imagery in inducing sudden and unpredictable mood swings (Holmes et al., 2011). Fifth, what would be the predominant types of prospective images and emotions associated with dysphoric mania, mixed depression, and psychotic mania? How would these cognitive constructs differ from those of classic bipolar mania and depression? Sixth, little is known about the effects of age and illness duration on types of emotions associated with BD. A recent study has shown that middle-aged remitted patients with BD reported lower levels of reward-relevant emotions such as joy relative to a non-psychiatric control group (Gruber et al., 2009), raising the possibility of age-related or illness-related changes in how positive emotions might be affected by a diagnosis of BD. Chronic disruptions of social and occupational roles in society, stigma and discrimination, and prolonged deprivations of life opportunities might have reduced the opportunities for experiencing joy among these patients with long-standing BD. Whether imagery susceptibility has a role to play in such age-related decline in positive emotions awaits further investigations. It is also not clear whether long-term use of pharmacotherapy might lead to a dampening of reward-relevant emotions in aged people with BD. Seventh, if pharmacotherapy is effective in inducing remission in bipolar mania and depression, does it exert its mechanism via its effects on certain cognitive constructs? Study 2 has provided some indirect evidence here. As the bipolar participants in Study 2 were almost exclusively managed with pharmacotherapy during their in-patient stay, the progressive decrease in the number of positive prospective images could be mostly attributed to the effects of hospital environment and pharmacotherapy.

However, further studies should focus on the specific impact of pharmacotherapy on inducing changes in these cognitive constructs. Eighth, BD is associated with other psychiatric comorbidities like substance misuse, binge eating, and pathological gambling. According to the intrusion elaboration theory (May et al., 2004), images of craving might play a key role in the maintenance of such addictive behaviours. How might heightened mental imagery susceptibility associated with bipolarity play a role in increasing the co-occurrence of BD and these impulse control disorders? The current thesis has provided some intriguing findings in the field of mental imagery susceptibility in BD but has also generated a number of interesting testable hypotheses awaiting further verification in future studies.

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List of Appendices

APPENDIX I**: Spontaneous Use of Imagery Scale (SUIS)**

Please read each of the following descriptions and indicate the degree to which each is appropriate for you. Do not spend a lot of time thinking about each one, but respond based on your thoughts about how you do or do not perform each activity. If a description is always completely appropriate, please write "5"; if it is never appropriate, write "1"; if it is appropriate about half of the time, write "3"; and use the other numbers accordingly.

_____ a. When going to a new place, I prefer directions that include detailed descriptions of landmarks (such as the size, shape and color of a gas station) in addition to their names.

_____ b. If I catch a glance of a car that is partially hidden behind bushes, I automatically "complete it," seeing the entire car in my mind's eye.

_____ c. If I am looking for new furniture in a store, I always visualize what the furniture would look like in particular places in my home.

_____ d. I prefer to read novels that lead me easily to visualize where the characters are and what they are doing instead of novels that are difficult to visualize.

_____ e. When I think about visiting a relative, I almost always have a clear mental picture of him or her.

_____ f. When relatively easy technical material is described clearly in a text, I find illustrations distracting because they interfere with my ability to visualize the material.

_____ g. If someone were to tell me two-digit numbers to add (e.g., 24 and 31), I would visualize them in order to add them.

_____ h. Before I get dressed to go out, I first visualize what I will look like if I wear different combinations of clothes.

_____ i. When I think about a series of errands I must do, I visualize the stores I will visit.

_____ j. When I first hear a friend's voice, a visual image of him or her almost always springs to mind.

_____ k. When I hear a radio announcer or DJ I've never actually seen, I usually find myself picturing what they might look like.

_____ l. If I saw a car accident, I would visualize what had happened when later trying to recall the details.

APPENDIX II**: Impact of Future Events Scale (IFES)**

Please identify **as many future events as possible** which you have been thinking about by imagining over the past seven days (e.g. positive or stressful life events). For each event, please indicate whether your imagining of it was positive or negative by circling the appropriate response below.

1. _____ (Positive/Negative)

2. _____ (Positive/Negative)

3. _____ (Positive/Negative)

Below is a list of comments made by people about imagining events in the future. Please read each item, indicating how frequently each comment was true for you during the past 7 days due to imagining the future. If they did not occur during that time, please circle the "not at all" answer.

	Please circle the answer closest to the way you have felt about future life events **over the past 7 days**	Not at all	A little bit	Moderately	Quite a bit	Extremely
1.	**I believed my thoughts about the future would definitely happen and would become real……...**	0	1	2	3	4
2.	**I had trouble staying asleep ……...**	0	1	2	3	4
3.	**Other things prompted me to think about the future …….**	0	1	2	3	4
4.	**I felt irritable and angry…….**	0	1	2	3	4
5.	**I avoided letting myself get emotional when I thought about the future or was reminded about it ……...**	0	1	2	3	4
6.	**I thought about the future when I didn't mean to ...……**	0	1	2	3	4
7.	**Any reminders evoked feelings about the future …….**	0	1	2	3	4
8.	**I stayed away from reminders of the future.……....**	0	1	2	3	4
9.	**Pictures about the future popped into my mind ……...……..**	0	1	2	3	4
10.	**I was jumpy and easily startled …….**	0	1	2	3	4
11.	**I tried not to think about the future……..……**	0	1	2	3	4
12.	**I was aware that I had a lot of feelings about the future, but I didn't deal with them……...……..**	0	1	2	3	4
13.	**My feelings about the future were kind of numb ……..……..**	0	1	2	3	4
14.	**I found myself acting or feeling like it was really happening……**	0	1	2	3	4
15.	**I had trouble falling asleep…….**	0	1	2	3	4
16.	**I had waves of strong feelings about the future ……..**	0	1	2	3	4
17.	**I tried to remove thoughts of the future from my mind……..……**	0	1	2	3	4
18.	**I had trouble concentrating……**	0	1	2	3	4
19.	**Reminders of the future caused me to have physical reactions, such as sweating, faster breathing, or a racing heart……..**	0	1	2	3	4
20.	**I had dreams about the future……**	0	1	2	3	4
21.	**I felt watchful and alert……...**	0	1	2	3	4
22.	**I tried not to talk about the future…..……**	0	1	2	3	4
23.	**I felt energetic and excitable……...**	0	1	2	3	4
24.	**I felt elated and optimistic……..**	0	1	2	3	4

APPENDIX III: **Response to Positive Affect Scale (RPA)**

Study: _____Subject ID: _____ Session #: _____ Date: _____

RPA

People think and do many different things when they feel **happy**. Please read each of the following items and indicate on your scantron whether you never, sometimes, often, or always think or do each one when you feel happy, excited, or enthused. Please indicate what you generally *do*, **not** what you *think you should do*.

1	2	3	4
Almost never	Sometimes	Often	Almost always

When you are feeling happy, how often do you…

1) *...notice how you feel full of energy*
2) *...savour this moment*
3) *...think "I am getting everything done"*
4) *...think about how you feel up for doing everything*
5) *...think "I am living up to my potential"*
6) *...think "It is too good to be true"*
7) *...think about how happy you feel*
8) *...think about how strong you feel*
9) *...think about things that could go wrong*
10) *...remind yourself that these feelings won't last*
11) *...think "People will think I am bragging“*
12) *...think about how hard it is to concentrate*
13) *...think "I am achieving everything"*
14) *...think "I don't deserve this"*
15) *...think "My streak of luck is going to end soon"*
16) *...think about how proud you are of yourself*
17) *...think about the things that have not gone well for you.*

APPENDIX IV**: Positive Overgeneralisation Scale (POG)**

For each of the following statements, indicate how much you agree with it or how much you disagree with it. Do not leave any items blank. Be as accurate as you can be, and *try not to let your answer to any one item influence your answer to any other item*. Treat each one as though it is unrelated to the others. *There are no right or wrong answers*, you are simply to express your own personal feelings and opinions. Choose from these response options:

1 = I DISagree with the statement a lot
2 = I DISagree with the statement a little
3 = I agree with the statement a little
4 = I agree with the statement a lot

1. *Lateral Generalization*

___ If I succeed at something, it makes me feel I will succeed in other areas as well.
___When I succeed at something, it makes me think about the successes in other areas of my life.
___When something good happens to me, it makes me expect good things in other parts of my life too.
___Having one thing go right for me can change me from feeling just OK to seeing all the good in myself.
___When one thing goes right, it makes me feel my possibilities are limitless.
___If I do well on a project at work, I'm certain I'll be a great success in my career.
___When I do well at something I'm trying to do, it makes me feel that I'll be a success at everything in life.

2. *Upward Generalization*

___If someone praises the way I express something, it makes me think I can write a popular book.
___When people agree with me after I speak up in a group, it makes me think I could be elected to public office.
___When someone praises me for my participation in a support group, it makes me think of being the head of the support organization.
___When people laugh at my jokes, it makes me think I could be a good talk-show host.
___When I have a small financial success, it makes me believe I could become a millionaire.
___When someone admires me, I believe I could become famous.

3. *Social Generalization*

___When an attractive person smiles at me, I can tell it means s/he is hot for me.
___When I made my first friend here, I knew I'd be a big success socially.
___All it takes is one look from someone and I know that person is falling for me.
___After one good date, I know that person will be in love with me forever.

APPENDIX V**: Ruminative Response Scale-Short Form (RSS-SF)**

People think and do many different things when they feel sad, blue or depressed. I am going to read a list of possibilities. Please tell me if you never, sometimes, often, or always think or do each one when you feel down, sad or depressed. Please indicate what you generally do, not what you think you should do.

	Never	Sometimes	Often	Always
1. Think about how alone you are				
2. Think about your feelings of fatigue and achiness				
3. Think about how hard it is to concentrate				
4. Think about how passive and unmotivated you feel				
5. Think "Why can't I get going?"				
6. Think about a recent situation, wishing it had gone better				
7. Think about how sad you feel				
8. Think about all your shortcomings, failings, faults, mistakes				
9. Think about how you don't feel up to doing anything				
10. Think about 'why can't I handle things better?'				

APPENDIX VI**: The Entrapment Scale (ES)**

For each of the following attitude statements indicate the extent to which you think it represents your own view of yourself. Read each item carefully and circle the number to the right of the statement that best describes the degree to which each statement is Like You. Use the scale below. Please do not omit any item.

SCALE

0 = Not at all like me 1 = A little bit like me 2 = Moderately like me 3 = Quite a bit like me 4 = Extremely like me

1. I am in situation I feel trapped in.	0	1	2	3	4
2. I have a strong desire to escape from things in my life.	0	1	2	3	4
3. I am in a relationship I can't get out of.	0	1	2	3	4
4. I often have the feeling that I would just like to run away.	0	1	2	3	4
5. I feel powerless to change things.	0	1	2	3	4
6. I feel trapped by my obligations.	0	1	2	3	4
7. I can see no way out of my current situation.	0	1	2	3	4
8. I would like to get away from other more powerful people in my life.	0	1	2	3	4
9. I have a strong desire to get away and stay away from where I am now.	0	1	2	3	4
10. I feel trapped by other people.	0	1	2	3	4
11. I want to get away from myself.	0	1	2	3	4
12. I feel powerless to change myself.	0	1	2	3	4
13. I would like to escape from my thoughts and feeling.	0	1	2	3	4
14. I feel trapped inside myself.	0	1	2	3	4
15. I would like to get away from who I am and start again.	0	1	2	3	4
16. I feel I'm in a deep hole I can't get out of.	0	1	2	3	4

APPENDIX VII**: The Defeat Scale (DS)**

Below is a series of statements, which describe how people can feel about themselves. Read each item carefully and circle the number to the right of the statement that best describes how you have felt in the last 7 days. Use the scale below. Please do not omit any item.

SCALE

0 = NEVER 1 = RARELY 2 = SOMETIMES 3 = MOSTLY (a lot) 4 = ALWAYS

1.	I feel that I have not made it in life.	0	1	2	3	4
2.	I feel that I am a successful person.	0	1	2	3	4
3.	I feel defeated by life	0	1	2	3	4
4.	I feel that I am basically a winner.	0	1	2	3	4
5.	I feel that I have lost my standing in the world.	0	1	2	3	4
6.	I feel that life has treated me like a punch bag.	0	1	2	3	4
7.	I feel powerless.	0	1	2	3	4
8.	I feel that my confidence has been knocked out of me.	0	1	2	3	4
9.	I feel able to deal with whatever life throws at me.	0	1	2	3	4
10	I feel that I have sunk to the bottom of the ladder.	0	1	2	3	4
11	I feel completely knocked out of action.	0	1	2	3	4
12	I feel that I am one of life's losers.	0	1	2	3	4
13	I feel that I have given up.	0	1	2	3	4
14	I feel down and out.	0	1	2	3	4
15	I feel that I have lost important battles in life.	0	1	2	3	4
16	I feel that there is no fight left in me.	0	1	2	3	4

APPENDIX VIII: Research ethics approval confirmation email

From: Lyon CHAN, KCC SM(CR&E)
Sent: Friday, February 26, 2016 12:03 PM
To: Roger Man Kin NG Dr, KCC CSC(Mental Health) / KHPSY COS
Cc: Melissa CHOW, QEH PSII(CR&E); Emily TSE, QEH EA II(CR&E)
Subject: RE: Research Ethics Applications

Dear Dr NG,

We would like to confirm you that the following research projects have been reviewed and approved by the respective Panels of REC (KC/KE).

Project Title: Positive imagery as an emotional amplifier in bipolar disorder: A case-control study (Ref: KC/KE-09-0176/ER-3)
The above study was approved by our Committee on 4 December 2009.

Project Title: A cohort study of imagery, emotional reactivity and cognitive styles in bipolar disorder (Ref.: KC/KE-11-0085/FR-3)
The above study was approved by our Committee on 8 August 2011.

Project Title: A cohort study of relationship of bipolar trait, mental imagery and suicidal ideation (Ref: KC/KE-11-0204/ER-3)
The above study was approved by our Committee on 14 December 2011.

Project Title: Mental imagery, creativity and ruminative style in non-clinical relatives of bipolar I patients and non-psychiatric controls (Ref: KC/KE-12-0150/ER-2)
The above study was approved by our Committee on 11 December 2012.

Project Title: Prevalence of bipolar symptoms in major depressive disorder (Ref: KC/KE-13-0004/ER-2)
The above study was approved by our Committee on 8 March 2013.

Sincerely yours,

Lyon CHAN
Secreatary,
Research Ethics Committee (KC/KE)
Tel: 3506 7069 Fax: 2215 1101

APPENDIX IX**: List of publications related to the current thesis**

Ng, R. M. K., Krans, J., & Holmes, E. A. (2013). Mental imagery and psychopathology: Examples of post-traumatic stress disorder and bipolar disorder. In S. Lacey & R. Lawson (Eds.), *Multisensory imagery* (pp. 365–384). New York, NY: Springer Press.

Ng, R. M. K., Heyes, S.B., McManus, F., Kennerley, H. & Holmes, E.A. (2015). Bipolar risk and mental imagery susceptibility in a representative sample of Chinese adults residing in the community. *International Journal of Social Psychiatry, 62*, 94-102. DOI: 10.1177/0020764015597951.

Ng, R.M.K., Di Simplicio, M, & Holmes, E.A. (2015). Mental imagery and bipolar disorders: introducing scope for psychological treatment development? [Editorial]. *International Journal of Social Psychiatry, 62*, 110-113. DOI: 10.1177/00207640156159505.