Clinical Psychology & Psychotherapy

WILEY

RESEARCH ARTICLE OPEN ACCESS

Exploring Temporal Relationships Between Anxiety, Mood and Mental Imagery in Patients With Bipolar Disorder: A Network Analysis

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Received: 3 May 2024 | **Revised:** 8 August 2024 | **Accepted:** 9 August 2024

Funding: This study was supported by a grant of Rino Zuid.

Keywords: anxiety | bipolar disorder | mental imagery | network analyses

ABSTRACT

Introduction: Bipolar disorder is a severe mental health problem with limited treatment success. There is a call for improving interventions, requiring an increased understanding of factors driving mood instability. One promising avenue is to study temporal associations between factors that appear relevant according to the emotional amplifier model of Holmes are changes in mood, anxiety and mental imagery.

Methods: The current study used data from a recent RCT for a secondary analysis which applied a network analysis approach to explore temporal associations between weekly measurements of mania, depression, anxiety and mental imagery measured during 32 weeks in two randomised groups ($N = 55$) receiving either imagery-focused cognitive therapy (ImCT) or group psychoeducation (PE).

Results: Both negative intrusive mental imagery and anxiety appeared central in the network analyses, driving changes in both mania and depression, but only in the PE group. In the ImCT group, only anxiety was driving changes in mania and depression.

Conclusion: Although exploratory, findings suggest that prior increases in anxiety and negative intrusive mental imagery might be associated with subsequent increases in depression and mania symptoms in patients with bipolar disorder. Anxiety might in turn increase negative intrusive imagery and associated negative emotions. Although more research is needed, results are in line with the emotional amplifier model and stress that future interventions with a focus on anxiety and imagery might help to improve psychosocial therapies for patients with bipolar disorder. In addition, this study suggests that a network approach is a helpful and feasible way to study mood instability, anxiety and mental imagery to increase our understanding of mechanisms underpinning mood instability.

Summary

- Network analyses are a feasible and helpful tool to explore mental imagery in bipolar disorder.
- Mood changes in bipolar disorder might be preceded by an increase in anxiety and mental imagery.
- The emotional amplifier model is helpful in increasing our understanding of mood changes in bipolar disorder.
- A better mechanistic understanding of the emotional amplified model is needed, possibly including its relationship with broader control/self-regulatory processes.

1 | Introduction

Bipolar disorder is a severe and chronic mental disorder characterised by episodes of depression and mania (APA 2013). Quality of life is markedly impaired in patients with bipolar disorder (Michalak, Yatham, and Lam 2005; Michalak et al. 2006), and it is estimated that this mental illness accounts for up to 10% of the burden of all mental and substance use disorders (Whiteford et al. 2013). The costs associated with this disorder are substantial and include both direct expenditure on treatment and the indirect costs of decreased productivity and excess mortality (Ketter 2010). Moreover, bipolar disorder has the highest rate of suicide attempts of all the psychiatric disorders, with recent estimates suggesting that a third to a half of individuals with bipolar disorder will attempt suicide (Miller and Black 2020). Bipolar disorder is also highly comorbid with a number of other mental disorders, notably anxiety and alcohol and substance misuse (Merikangas et al. 2007), which make both diagnosis and treatment more challenging.

There is a growing consensus for the need to understand the mechanisms of existing psychological treatments with an aim to increase effectiveness (Holmes et al. 2018). This is particularly relevant for bipolar disorder, where since the introduction of lithium in the 1970s, no further significant advances in pharmacotherapy have been made, with still limited understanding of how lithium affects symptoms (Geddes and Miklowitz 2013; Harrison et al. 2016). Despite evidence for effectiveness of pharmacological interventions for the various phases of bipolar disorder, patients may experience only partial recovery (NICE 2018), and after two manic episodes, the likelihood of relapse is as much as 80%. Cognitive-behavioural therapy (CBT) as an adjuvant to pharmacotherapy has a mild to moderate effect size in improving bipolar depressive symptoms severity and psychosocial functioning, with no effects on mania (Chiang et al. 2017). Studying the possible mechanisms driving the perpetuating and or precipitating factors that influence the course of bipolar disorder symptoms is therefore an important research focus. Among factors that can play an important role in the presentation of bipolar disorder are ongoing interepisode mood instability (Goodwin et al. 2016), mental imagery (Di Simplicio et al. 2016; Ivins et al. 2014; Moritz et al. 2014) and anxiety (Goodwin et al. 2016). Below, we discuss these one by one.

Bipolar disorder appears characterised not only by episodes of full-blown depression and mania but also by ongoing mood instability between episodes (Henry et al. 2008). Mood instability is seen as a common feature in mental health disorders and is associated with poor clinical outcomes (Patel et al. 2015). In bipolar disorders, mood instability is most often characterised as small changes in self-rated depression and mania and is increasingly acknowledged as an important factor in the experience of bipolar disorder (Bonsall et al. 2012; Goodwin et al. 2016). Using nonlinear time-series models with weekly measures, Bonsall et al. (2012) showed that most patients with bipolar disorder experienced day-to-day or week-to-week mood swings or changes in self-reported levels of mania and depression, below the criteria for full-blown episodes. This interepisode mood instability appears to predict relapse into an episode of mania or depression (Bonsall et al. 2015) and is a predictor of clinical and functional impairment (Gershon and Eidelman 2015; O'Donnell et al. 2018) after remission from manic or depressive episodes (Strejilevich et al. 2013).

Across mental disorders, mood instability is associated with mental imagery (Blackwell 2019), defined by the activation of perceptual information from memory to 'see with the mind's eye' or 'hear with the mind's ear' (Kosslyn, Ganis, and Thompson 2001). Mental imagery has been shown to be a significant transdiagnostic factor in all psychopathology (Ji et al. 2019) and highly relevant for patients with bipolar disorder (Gregory et al. 2010; Holmes et al. 2011). Specifically, mental imagery is thought to contribute to mood instability in bipolar disorder (Di Simplicio et al. 2016; Gregory et al. 2010; Hales et al. 2011). Holmes et al. (2008) propose a cognitive model, the emotional amplifier model, in which mental imagery is assumed to amplify anxiety, mania and depression in patients with bipolar disorder, increasing associated beliefs, goals and action likelihood. Within this cognitive model both mental imagery and anxiety may play a particularly important role.

Several studies support a link between anxiety and bipolar disorder presentation. Up to 90% of patients with bipolar disorder have been diagnosed with at least one anxiety disorder in their lifetime (Merikangas et al. 2007; Pavlova et al. 2015). In patients with bipolar disorder and comorbid anxiety disorder, mood instability appears more pronounced, which decreases treatment effectiveness and prognosis (Boylan et al. 2004). Anxiety is considered to be an independent marker of greater severity of bipolar illness (Otto et al. 2006) and patients with bipolar disorder who experience anxiety respond less well to pharmacotherapy (mood stabilisers) than patients suffering from bipolar disorder without anxiety (Henry et al. 2003). Hence, according to recently revised evidence-based guidelines for treatment of bipolar disorder, anxiety should be regularly monitored (Goodwin et al. 2016).

Although empirical evidence supports the emotional amplifier model (Holmes et al. 2011; O'Donnell et al. 2017), the specific relationships between mental imagery, anxiety and mood instability are still poorly understood and need further exploration. Specifically, information on which of these factors predicts the other at a future time point, as well as the strength of potential predictive relationships could help improve our understanding of the mechanisms underpinning mood instability in bipolar disorder. These improvements could lead to identifying new opportunities for interventions, such as fine-tuning imagery-focused cognitive-behavioural interventions. This is potentially

an important target because intervening on interepisode mood instability is a clinical unmet need and can complement the traditional classification approach focusing on relapse into episodes of mania or depression.

Exploring the specific relationships between mood instability, anxiety and mental imagery can be achieved by utilising a psychological network approach (Weintraub, Schneck, and Miklowitz 2020). The network approach views mental disorders as complex systems of causal elements and uses different statistical tools to help us gain insight into how this system might function or how one factor might influence another (Borsboom 2017; Bringmann 2021; Fried et al. 2020). The network approach focuses on quantifying the connections between relevant factors, such as key symptoms of a disorder, with a focus on the relationship between these factors over time. A network is defined as a set of nodes (the factors) and weighted connections (connections between the nodes), where the weight corresponds to the strength of the connection between nodes. This approach supports the exploration of the factor-to-factor relationships that give rise to mental illnesses, in contrast to traditional methods of analysing mental disorders that have examined the top-down latent structure of disorders via factor analysis and latent class analysis.

A few studies have used a network approach to study bipolar disorder (Curtiss et al. 2019; Koenders et al. 2015; Scott et al. 2021; Weintraub, Schneck, and Miklowitz 2020). However, to the best of our knowledge, no study has adopted a network approach to investigate the specific and time-lagged relationships between mental imagery, anxiety and mood instability.

This study aimed to quantify the time-lagged connections between mental imagery, anxiety and mood instability with network modelling techniques and to explore the nature of symptom-to-symptom relationships using data from a recent trial comparing imagery-focused cognitive therapy (ImCT) to psychoeducation (PE) in the treatment of bipolar disorder (van den Berg et al. 2022). This study aimed to improve our understanding of the working mechanisms of bipolar disorder and its relationship with mental imagery and anxiety. Informed by, among others, the emotional amplifier model by Holmes et al. (2008), we hypothesised that mania, depression, anxiety and mental imagery are positively associated and that mental imagery and anxiety act as precursors to the manifestation of mania and depression symptoms. Given that ImCT specifically targeted visual imagery as an intervention mechanism, the two groups were analysed separately. We did not intend to test for different hypotheses for ImCT and PE groups.

2 | Methods

2.1 | Participants

The current study *used data from a recent RCT for a secondary analysis* which applied a network analysis approach to explore temporal associations between weekly measurements of mania, depression, anxiety and mental imagery measured during 32 weeks in two randomised groups (N = 55) receiving either ImCT or PE group. The study recruited 62 participants from a specialised centre for bipolar disorders of a large psychiatric hospital in the Netherlands (from October 2018 to December 2020). Participants received either twelve 1-h sessions of manualised ImCT (Hales et al. 2018; Holmes et al. 2016, 2019) or six 2-h sessions of a manualised PE group (Zyto et al. 2020). All participants provided informed consent and agreed to monitor mood, anxiety and imagery. The trial was preregistered at Clinicaltrials.gov (identifier NCT03750305). Ethical approval was given by METC azM/UM (NL64193.068.18/METC183005).

Patients referred to the service received a diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; APA 2013) by a lead psychiatrist, clinical psychologist or specialised nurse after a semistructured intake procedure. Patients were included if they were aged between 18 and 68, had sufficient Dutch language ability and were willing to complete daily and weekly monitoring throughout the duration of the study (on average 32 weeks). They were excluded if they had learning difficulties, organic brain disease, severe neurological impairment or current severe substance or alcohol misuse (clinicians' assessment). Table 1 contains an overview of the demographic and patient characteristics and disorder-related information.

3 | Materials

3.1 | Procedure

Participants entered responses via a secure web-based system and were notified via email when a new survey was available. In a period of at least 20 weeks, participants provided daily self-report data (mood and anxiety), weekly (visual imagery, mood and anxiety), before (4 weeks), during (12 or 6 weeks, depending on group) and after the intervention (at least 16 weeks). The ImCT condition received 12 weeks of 1-h sessions, the PE condition received 6 weeks of 2-h sessions, all received a total of 12-h intervention. However, in the present study, we only considered the weekly measures as the daily data do not contain measures of visual imagery. Data from all phases including baseline, intervention and post intervention were included in the network analysis. Following best practices for estimating temporal networks with the mlVar package to avoid bias (Jordan, Winer, and Salem 2020), four participants who did not contribute at least 20 weekly responses were excluded from all analyses (one did not complete the intervention phase and three did not continue answering weekly questions after the intervention phase).

The remaining 55 participants (30 ImCT and 25 PE participants) completed a total of 1662 weekly measures (*median* = 32, range: 11 to 40). The median number of missing weeks per person was 0, with a maximum of 6 missing scores for one individual.

3.2 | Measures

3.2.1 | Altman Self-Rating Mania Scale (ASRM)

The ASRM is a five-item self-report measure of mania symptom severity, often used in research on bipolar disorders. The ASRM consists of five items, each scored on a 5-point Likert

TABLE 1 | Characteristics of the study cohort including demographics, bipolar diagnosis, comorbidity, illness variables and medication.

	N **= 61**
Demographic information	
Age, years, mean (SD)	45.02 ± 12
Gender, *n* (%)	
Female	35 (57.4%)
Ethnicity, *n* (%)	
White European	57 (93.4%)
Other	4 (6.6%)
Bipolar disorder characteristics	
Bipolar disorder, *n* (%)	
Type 1	31 (50.8%)
Type 2	30 (49.2%)
Comorbidity and clinical course, *n* (%)	
History of psychosis	18 (29.5%)
Comorbid anxiety disorder	5 (8.2%)
Personality disorder	5 (16.4%)
Years since diagnosis, number of	
Hospitalisations lifetime (SD)	9.1 (8.7)
Number of depressive episodes lifetime (SD)	1.3 (1.7)
0–4 episodes	41
5–9 episodes	10
> 10 episodes	8
Number of manic episodes lifetime	
0–4 episodes	51
5–9 episodes	6
> 10 episodes	3
Medication at screening, *n* (%)	
Mood stabiliser	43 (70.5%)
Antipsychotic	31 (50.8%)
Antidepressant	27 (44.3%)
Anxiolytic	28 (45.9%)

scale with answers ranging from 0 ('not more than usual') to 4 ('more than usual most of the time') each tailored to the item. Previous research showed good psychometric properties and good test–retest reliability for the ASRM (Altman, Hedekker, and Peterson 1997). Findings suggested that a cut-off score of < 4 is indicative for full symptomatic remission of (hypo)mania (Berk et al. 2008), a score of 5.5 and higher is indicative for (hypo)mania (Altman, Hedekker, and Peterson 1997).

3.2.2 | Quick Inventory of Depressive Symptomatology, Self-Report (QIDS-SR)

The QIDS-SR is a 16-item self-report measure of depression in which the nine DSM 5 symptoms of major depression are incorporated (Rush et al. 2003). Answers are scored on a four-point Likert scale, with answers ranging from 0 ('no change in my usual') to 3 ('great difficulty with') each tailored to the item. The QIDS-SR total score correlates highly ($r = 0.86$) with the Hamilton Rating Scale of Depression and has a high internal consistency (Cronbach alpha = 0.92). Scores of 5 or lower are indicative of no depression, scores from 6 to 10 indicating mild depression, 11 to 15 indicating moderate depression, 16 to 20 indicating severe depression and total scores greater than 21 indicating very severe depression.

3.2.3 | Beck Anxiety Inventory (BAI)

The BAI is a 21-item self-report questionnaire used for measuring the severity of anxiety (Osman et al. 1993). Answers are rated on a 4-point Likert scale with answers ranging from 0 (*not at all*) to 3 (*very much*) each tailored to the item. The BAI has a high reliability (Cronbach alpha = 0.95) and reasonable test–retest reliability ($r = 0.65$). A total score for all 21 symptoms ranges from minimal anxiety (0–7), mild anxiety (8–15), moderate anxiety (16–25), to severe anxiety (30–63).

3.2.4 | Visual Analogue Scale for Imagery (VAS-IM)

The VAS-IM consists of four imagery questions, together representing the negative impact of one's images during the past week, measuring negative intrusive imagery. The VAS-IM items were tailored to bipolar disorder populations and used in the pilot study (Holmes et al. 2016). Imagery questions were: 'How often did you experience intrusive imagery over the last week?', 'how much did these influence your daily life?', 'how much control did you experience over these images?' (reversed scoring) and 'how unpleasant were these images?', rated on a 11-point VAS-scale, ranging from 0 (*not at all*) to 11 (*all the time* or *very much*). The sum of the four scores served as a total score. Similar to the original studies using these VAS-imagery questions (Hales et al. 2018; Holmes et al. 2016), the VAS-IM was administered weekly throughout the present study.

Summary statistics for each of these measures across the 59 participants in the two conditions is shown in Table 2.

3.3 | Data Analyses

3.3.1 | Assumption Checks

We used the Lilliefors (Dallal and Wilkinson 1986) test of normality, based on the Kolmogorov–Smirnov test, to check whether each variable was normally distributed. The results for all four measures indicate violations of normality ($p < 0.0001$). The distribution of VAS-IM scores were near uniform; BAI, QUID-SR and ASRM showed a right-skewed distribution. To test if the measures were stationary over time, we used the

TABLE 2 | Summary statistics for the four research variables: Mania, depression, anxiety and mental imagery, separately for the imagery-focused cognitive therapy (ImCT) and the psychoeducation (PE) groups.

	BAI mean (SD)	QIDS-SR mean (SD)	ASRM mean (SD)	VAS-IM mean (SD)
ImCT	6.65 (7.18)	6.48 (6.01)	1.42 (2.46)	16.0 (8.57)
PE	8.11 (8.95)	6.90 (5.72)	1.41 (2.43)	12.9 (9.05)

Abbreviations: ASRM = Altman Self-Rating Mania Scale; BAI = Beck Anxiety Inventory; QIDS-SR = Quick Inventory of Depressive Symptomatology, self-report; VAS-IM = Visual Analogue Scale for Imagery.

TABLE 3 | Median in-degree and out-degree centrality measures for the four research variables: Mania, depression, anxiety and mental imagery.

	Weighted in-degree				Weighted out-degree			
	BAI	QIDS-SR	ASRM	VAS-IM	BAI ($t-1$)	QIDS-SR ($t-1$)	ASRM ($t-1$)	VAS-IM ($t-1$)
ImCT	0.14 (3)	0.19 (2)	0.21 (1)	0.12 (4)	0.37 (1)	0.10 (2*)	0.09 (4)	0.10 (2*)
PE	0.17 (2)	0.11 (4)	0.19 (1)	0.07 (3)	0.13 (2)	0.07 (4)	0.09 (3)	0.24 (1)
All	0.13 (3)	0.16 (2)	0.20 (1)	0.04 (4)	0.27 (1)	0.08 (3)	0.05 (4)	0.12 (2)

Note: Values are calculated separately for the imagery-focused cognitive therapy (ImCT, $n = 30$) group, the psychoeducation (PE, $n = 25$) group and all participants. In-degree and out-degree ranks are indicated in parentheses for each condition and overall. Asterisks denote rank tie.
Abbreviations: ASRM = Altman Self-Rating Mania Scale; BAI = Beck Anxiety Inventory; QIDS-SR = Quick Inventory of Depressive Symptomatology, self-report; VAS-IM = Visual Analogue Scale for Imagery.

Kwiatkowski–Phillips–Schmidt–Shin (KPSS) test of stationarity in a time series. The results show 24 violations of a level distribution (between 4 and 7 for each measure), indicating that for many variables, there is a trend in the data. However, only one violation of trend stationarity was found (QIDS-SR in one participant), indicating that with the inclusion of a slope parameter (this is referred to as Week), the assumption of stationarity may be appropriate.

3.3.2 | Network Estimation and Visualisation

Each participant was modelled independently, from the data preprocessing to the selection of optimal hyperparameters of the model. The scores from an individual were first preprocessed by subtracting the mean value and dividing them by the standard deviation. Afterwards, network connection weights were estimated using multiple multivariate ridge regression with the four measures in the current week as outcome measures and the time-lagged ($t-1$) values and the current week number as predictor values. The optimal regularisation strength parameter of the ridge regression (alpha) and coefficient values were selected via grid search (alpha values from 0.001 to 0.1 in steps of 0.001) by evaluating the out-of-sample data of a three-fold time-series split. All modelling was done in Python using the Scikit-learn package (Garreta and Moncecchi 2013).

To estimate the importance of each node in the network, the in-degree and out-degree centrality of each measure was computed (Table 3). The in-degree is the sum of the strength of all connections directed into a node, and the out-degree is the sum of the strength of all connections from that node to other nodes. These values were computed by adding the (unsigned) weighted in-degree and out-degree for each measure based on the median connection weight within each group. Because all connections in the network were from measures at ($t-1$) (from 1 week) to measures at time t (the next week), the in-degree was computed for measures at time (t), and the out-degree was computed for measures at time ($t-1$). The autoregressive connection from a measure at time ($t-1$) to (t) and the connection from the Week variable are excluded from the calculation of in-degree. The weighted centrality measures were computed based on the median connection strength between each measure.

4 | Results

4.1 | Descriptive Statistics

Table 4 indicates the mean, standard deviation and range of scores in each condition.

4.2 | Centrality of Measures

The centrality of each measure from the median network connection weights is shown in Table 3. Rather than focusing on the raw degree score, we instead evaluated the relative ranking of each measure as established by both in-degree and out-degree. The scores showed moderate agreement between the ImCT and PE groups. In both conditions mania (ASRM) had the highest in-degree ranking and nearly the lowest out-degree ranking (third and fourth). A similar but less strong pattern was also seen for depression (QIDS-SR). In contrast, in both conditions, anxiety (BAI) and/or negative intrusive imagery (VAS-IM) had a high out-degree ranking (both were first or second) and lower in-degree rank (mostly third or fourth). The most notable difference between the two groups is quantitative: Anxiety

had by far the highest out-degree ranking in the ImCT group, while imagery had the highest out-degree ranking in the PE group. However, both were at least as high as either depression or mania out-degree.

The network of connections between the depression, mania, anxiety and negative intrusive imagery measures over time are visualised in Figure 1 for each treatment group. The thickness of each connection (from source to target node) is proportional to the median partial correlation between score of the source measure at time ($t-1$) and score of the target measure at time (t). Connections from the Week node to a measure indicate how much that value changes from 1 week to the next on average, while the connections from a measure to itself visualise the strength of the auto (partial) correlation of that feature. The numeric median partial correlation between each measure is presented in Figure 2.

TABLE 4 | Descriptive statistics for mania, anxiety, depression and mental imagery scores.

Variable	Condition	Mean	SD	Min	Max
ASRM	ImCT	1.42	2.46	0	20
ASRM	PE	1.4	2.42	0	16
BAI	ImCT	6.65	7.18	0	42
BAI	PE	8.12	8.86	0	41
QIDS	ImCT	6.48	6.01	0	31
QIDS	PE	6.9	5.73	0	29
VAS-IM	ImCT	16.04	8.57	0	38
VAS-IM	PE	12.95	9.05	0	36
Week	ImCT	17.84	10.13	1	40
Week	PE	14.07	8.01	1	32

Note: There were 1627 total weeks with complete data and the median number of weeks per individual was 32 (range: 21–40).
Abbreviations: ASRM = Altman Self-Rating Mania Scale; BAI = Beck Anxiety Inventory; ImCT = imagery-focused cognitive therapy; PE = psychoeducation; QIDS-SR = Quick Inventory of Depressive Symptoms; VAS-IM = Visual Analogue Scale Imagery.

The most salient aspect of these networks are the connections from one measure to another. These coefficient values reflect approximations of the partial correlation between one measure at time ($t-1$) and another at time t. As such, they are directed from a measure in the previous week to a measure in the next week and might be predictive. For example, the strong positive correlation from anxiety (BAI) to mania (ASRM) indicates that if you have high anxiety scores 1 week, then you are more likely to have high mania scores the next week.

The strongest connections from one measure to another in the ImCT network are from anxiety to depression and to mania. Both are positive, suggesting that in this group, higher anxiety values were likely followed by higher levels of both depression and mania. Interestingly, the negative intrusive imagery measure does not have a strong relationship with any other measure. In the PE network, the imagery measure has strong connections where it has a positive partial correlation with future anxiety and depression scores. The anxiety measure has a strong positive correlation with mania also in the PE network but less so with depression.

Both the autocorrelations of measures over time, as well as the overall trend over time, showed consistent patterns across measures and groups. All measures showed a positive autocorrelation over time, suggesting that usually high values stay high and low values stay low. The magnitude of the autocorrelations was mostly higher in the ImCT group than the PE group. The change

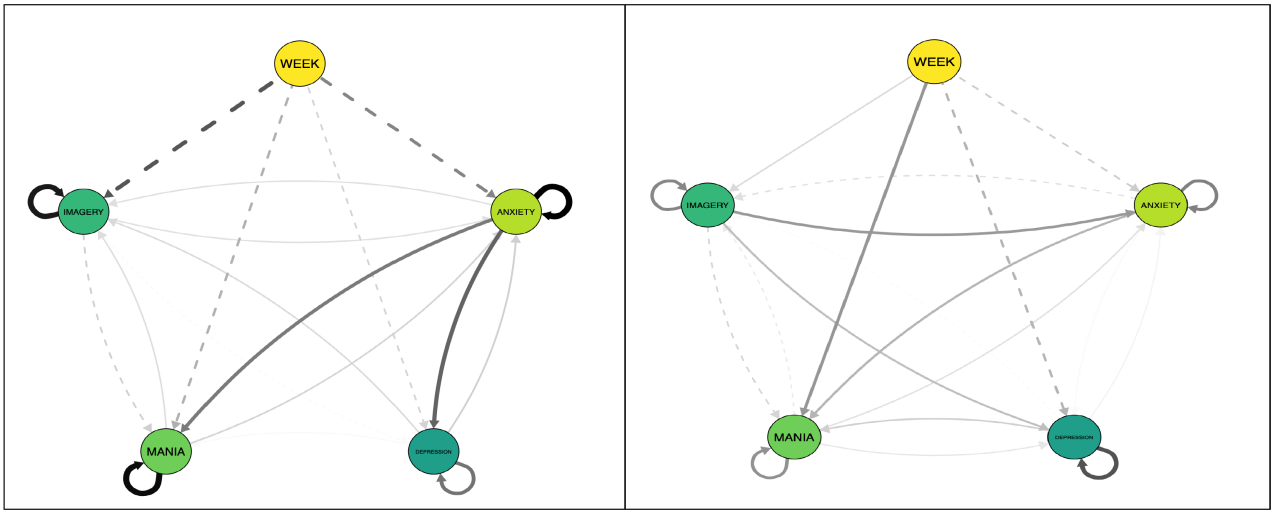

FIGURE 1 | Temporal effect network visualisation of median partial correlations between mania, depression, anxiety and mental imagery in the imagery-focused cognitive therapy and the psychoeducation groups. *Note:* The saturation and width of edges are proportional to the strength of the partial correlation. Dashed edges indicate a negative correlation. All arrows indicate a correlation from a previous time point ($t-1$) to the next point in time (t). Anxiety = weekly BAI (Beck Anxiety Inventory), mania = weekly ASRM (Altman Self-Rating Mania Scale), depression = weekly QIDS-SR (Quick Inventory of Depressive Symptomatology, self-report), imagery = weekly VAS-IM (Visual Analogue Scale for Imagery). Solid lines indicate positive correlations while dashed lines indicate a negative correlation between measures.

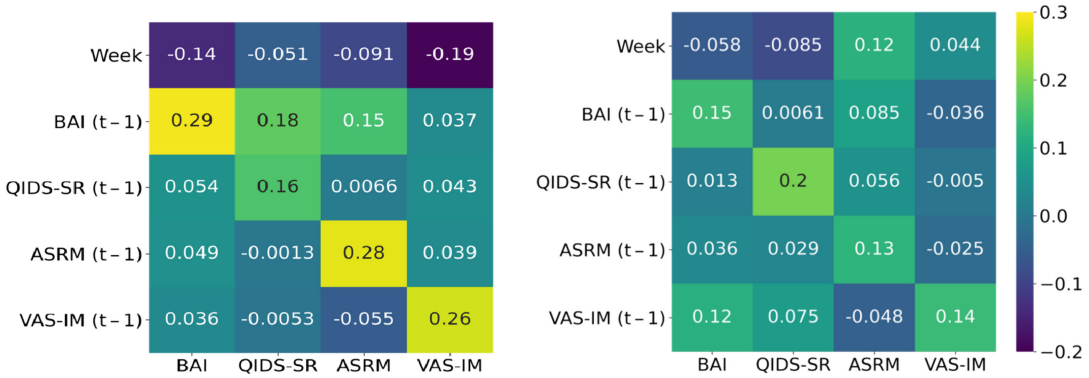

FIGURE 2 | Heat maps of median partial correlations between the four research variables: Mania, depression, anxiety and mental imagery, all measured at time (*t*), and the five predictor variables (the four research variables at time [*t* − 1] and the week number) for the imagery-focused cognitive therapy (ImCT) and psychoeducation (PE) groups. ASRM = Altman Self-Rating Mania Scale; BAI = Beck Anxiety Inventory; QIDS-SR = Quick Inventory of Depressive Symptomatology, self-report; VAS-IM = Visual Analogue Scale for Imagery; Week = the linear trend from week-to-week for each measure.

in measures over time, the linear trend indicated by the Week measure, showed a decrease over time in all measures in the ImCT group and a mixture of increases and decreases in the PE group.

5 | Discussion

The present study explored the relationship between mental imagery (specifically, negative intrusive mental imagery) and anxiety on changes in mania and depression during a period of average 32 weeks, using weekly self-report measures in patients with bipolar disorder. The aim was to contribute to an alternative way to conceptualising bipolar disorder, with the goal of informing future studies and update clinical practice.

First, as we hypothesised, and in line with the emotional amplifier model (Holmes et al. 2008), we found that in the PE group, negative intrusive mental imagery and anxiety had high out-degree centrality with strong positive connections from anxiety to mania and from imagery to depression, though negative intrusive imagery also had a positive connection to anxiety. Increases in negative intrusive mental imagery in 1 week were followed by increases in both anxiety and depression in the following week when controlling for the other predictors. Similarly, higher levels of anxiety were followed by higher levels of mania. These findings are in line with previous studies, where across mental disorders, a strong relationship was found between anxiety and negative intrusive mental imagery, including PTSD (Clark et al. 2016), GAD (Tallon et al. 2020) and transdiagnostically (Di Simplicio et al. 2016).

In contrast, though anxiety remained a strong predictor of other symptoms in the ImCT group, negative intrusive mental imagery had nearly the lowest out-degree of any measure, indicating that mental imagery did not predict other measures. It is possible that this difference might be attributed to the nature of the ImCT intervention. The focus of ImCT was on increasing control over problematic mental imagery (Holmes et al. 2019), which, if successful, might change the relationship between mental imagery and symptomatology. Future studies with adequate experimental manipulations could test to which extent control over any internal state/symptom (with reference to attentional, S-REF or perceptual control theories) versus specific control over imagery plays a role in maintaining symptomatology of bipolar disorder.

Changes in affect, as quantified by higher auto(partial) correlations, were higher in the ImCT group than the PE group for all measures except depression. These patterns align with more traditional statistical tests of stability of affect (van den Berg et al. 2022) and suggest that a network approach might be suitable to detect reliable changes in affect stability. One particular advantage of the network approach to measuring affect (in)stability might be that the autocorrelation is also a partial correlation, and thus, the influence of other measures can be incorporated. This perspective aligns with a growing body of literature which suggests that the network approach may be a suitable and informative for studying complex mental health problems such as bipolar disorder (Borsboom 2017; Fried et al. 2020).

Unlike previous studies on positive mood amplification in subclinical populations (O'Donnell et al. 2017), in both treatment groups, we failed to find a positive temporal relationship between negative intrusive mental imagery and mania. However, in hindsight, this finding is understandable: We selected an imagery measure that only addressed the unpleasant impact of emotional mental imagery on (hypo)manic affect. Our imagery measure asked about unpleasantness of imagery, while imagery associated with mania is often pleasant even if potentially detrimental (Ivins et al. 2014). Future studies using a broader inventory of intrusive mental imagery would be more likely to pick up on a potential relationship between mania and other forms of imagery.

The strong and predictive relationship between anxiety and mood supports previous findings stressing the important role of anxiety in mood instability (Boylan et al. 2004; Henry et al. 2003; Merikangas et al. 2007; Otto et al. 2006; Pavlova et al. 2015). Currently, most interventions for patients with bipolar disorder target symptoms of depression and mania but

not anxiety (Stratford et al. 2015). Future PE and CBT interventions could also aim to target anxiety, which in turn might increase effectiveness of these interventions. Moreover, these findings might also provide impetus to conduct a clinical trial that compares CBT with anxiety module versus CBT without anxiety module. This study found differences in predictive value between the ImCT and PE groups in anxiety and depression. This study was not designed to compare groups. These findings could be replicated and further explored in future studies designed to compare groups adding to our understanding of the relationships between anxiety, mood and mental imagery.

There are two limitations to a more general application of these results. First, recent work (van den Berg et al. 2022) suggests that changes in mood measured at a daily level might be more sensitive and informative for patients with bipolar disorder than weekly measures. Given the high survey compliance in this population for both daily and weekly measures, introducing daily measures of mental imagery is likely feasible without undue participant burden and may better capture the temporal relationship between imagery, anxiety and mood. Second, the data in this study were collected primarily to evaluate the impact of ImCT and PE interventions on patients with bipolar disorder. To obtain more precise estimates of the network structure for these measures in patients with bipolar disorder, these measures should be collected in a larger, more diverse patient population that is not actively undergoing treatment. It is entirely possible that differences in the duration or other aspects of the interventions could have had an effect on the network structure estimated or the set of participants who were included in this analysis (four participants withdrew from the PE group and none from the ImCT group). Unfortunately, neither the postintervention phase nor the baseline phase in the current study is sufficiently long to reliably estimate these network parameters without including data collected during the intervention phase. However, despite these limitations, we believe this work provides exciting new directions to understand the role of imagery and anxiety in more effectively treating bipolar disorder.

Despite these concerns, to our knowledge, the current study has been the first attempts to thoroughly explore the temporal network dynamics of mania, depression, anxiety and negative intrusive mental imagery in patients with bipolar disorder. Although exploratory, our findings confirmed the importance of addressing relationships between anxiety, negative intrusive mental imagery, mania and depression. However, a better understanding of the emotional amplifier model is needed, possibly including its relationship with broader control/self-regulatory processes. Further studies are needed using adequate experimental models in the emotional amplifier model, including control over imagery and whether this needs imagery-based techniques to be successful. As there was a high compliance with the measurements, and anecdotal feedback from participants was positive, future studies might use more frequent measurements to better capture the dynamic relationship between these measures. Further, a network approach could be a helpful tool to complement traditional investigations for treatment development. Clinically, our findings in combination with previous ones (van den Berg et al. 2022) indicate that current psychosocial interventions should be updated to target how both anxiety and mental imagery can play a role in the maintenance of manic and depressive symptoms. The recent trial on ImCT, in which these data were collected, appears to support these findings, showing a significant reduction in mood instability, levels of mania, depression and anxiety and problematic mental imagery (van den Berg et al. 2022).

Summarising the results from our exploratory analyses, both negative intrusive mental imagery and anxiety are key elements connected to mood changes in patients with bipolar disorder. Both show on average higher outgoing connections, while depression and mania have stronger incoming connections in the network. This is largely in agreement with the emotional amplifier model (Holmes et al. 2008). Mental imagery is associated with changes in levels of anxiety and depression in the PE group, but not in the ImCT group. Instead, in the ImCT group, changes in anxiety are associated with mania and depression, in the PE group with mania. These differences are consistent with the view that the ImCT may help patients prevent their mental imagery from cascading into anxiety, depression or mania. However, more detailed studies, measuring more frequently with additional mental imagery questions, are needed to further expand our understanding of the exact sequence and relationship between these symptoms. This might help to further conceptualise our understanding of the mechanisms driving mood instability and anxiety in bipolar disorder, which in turn can help improve psychosocial interventions.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restriction.

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