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REVIEW ARTICLE

Rumination in bipolar disorder: a systematic review

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Objective: To conduct a systematic review of the literature about the symptom of rumination in bipolar disorder (BD).
Methods: We searched the MEDLINE (PubMed), ISI Web of Knowledge, PsycINFO, and SciELO databases using the descriptors ''rumination'' and ''bipolar disorder'' and no time limits. This strategy yielded 105 references, of which 74 were selected. Inclusion criteria were studies involving patients with BD and the use of at least one validated scale for the assessment of rumination. Review articles were excluded. Seventeen articles were ultimately analyzed and included in the review.
Results: Rumination is present in all BD phases, is a stable interepisodic symptom, is associated with symptoms of depression, anxiety, and hypomania, and may occur in response to both positive and negative affect. There is no research on rumination and neurobiological findings in patients with BD.
Conclusions: Rumination seems to be independent of mood state, but shows close relationship with it. It is possible that rumination has a negative impact on cognitive and executive functions, particularly inhibitory control. Finally, rumination is an important symptom in both phases of BD, and, therefore, may be a useful target for further exploration as a dimensional domain and a transdiagnostic phenomenon in Research Domain Criteria (RDoC) projects.

Keywords: Bipolar disorder; rumination; executive function; cognitive emotion regulation; Research Domain Criteria; transdiagnostic approach

Introduction

In bipolar disorder (BD), during either manic or depressive episodes, a rapid thought process may be a core feature. This feature is frequently associated with ruminative characteristics of thought. Several studies have shown that patients in a depressive state increase rumination after experiencing negative affect, especially when they have low positive affect in daily life.[1] Therefore, rumination is considered to be an indicator of the onset and severity of depressive episodes, in addition to mediating differences in depressive symptoms between men and women.[2] However, rumination in BD or mania is much less studied.

Some authors consider rumination to be a coping strategy,[3] whereas others see it as a persistent, repetitive maladaptive phenomenon that occurs in response to life events, characterized by self-centeredness or focus on symptoms of distress and on its possible causes and consequences, thoughts that are difficult to control.[4] The most widely used definition of rumination as a psychological symptom is that of a process of perseverating thinking about one's own feelings and problems, instead of thinking in terms of the specific content of one's thoughts.[2,4]

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Rumination in depressive disorders has been studied since the early 1980s. However, interest in studying this phenomenon in other mental disorders has only emerged over the last few years,[5,6] after longitudinal studies involving patients with BD pointed to an association between BD and affective instability, self-esteem, and coping strategies.[7,8] As a result, the mental responses of patients with BD to emotional instability started to be assessed in an attempt to better understand its role in the development and maintenance of symptoms and of the illness itself. The objective of the present study was to conduct a systematic review of the literature about rumination in patients with BD, in the states of mania, depression, and euthymia.

Methods

The MEDLINE (PubMed), ISI Web of Knowledge, PsycINFO, and SciELO databases, in addition to Google Scholar, were searched using the terms ''bipolar disorder'' and ''rumination'' (rumination is not a Medical Subject Heading [MesH] term) and no time limits. The survey was conducted in January 2014.

A total of 105 references were found (24 in PubMed, 18 in ISI Web of Science, five in PsycINFO, 16 in SciELO, and 42 in Google Scholar). Of these, three were books, two were videos, four were articles written in Portuguese, and 22 were duplicates and therefore excluded (Figure 1). As a result, 74 journal articles were selected for abstract analysis and 36 for full-text analysis. The inclusion criteria were studies involving patients with BD and the use of at

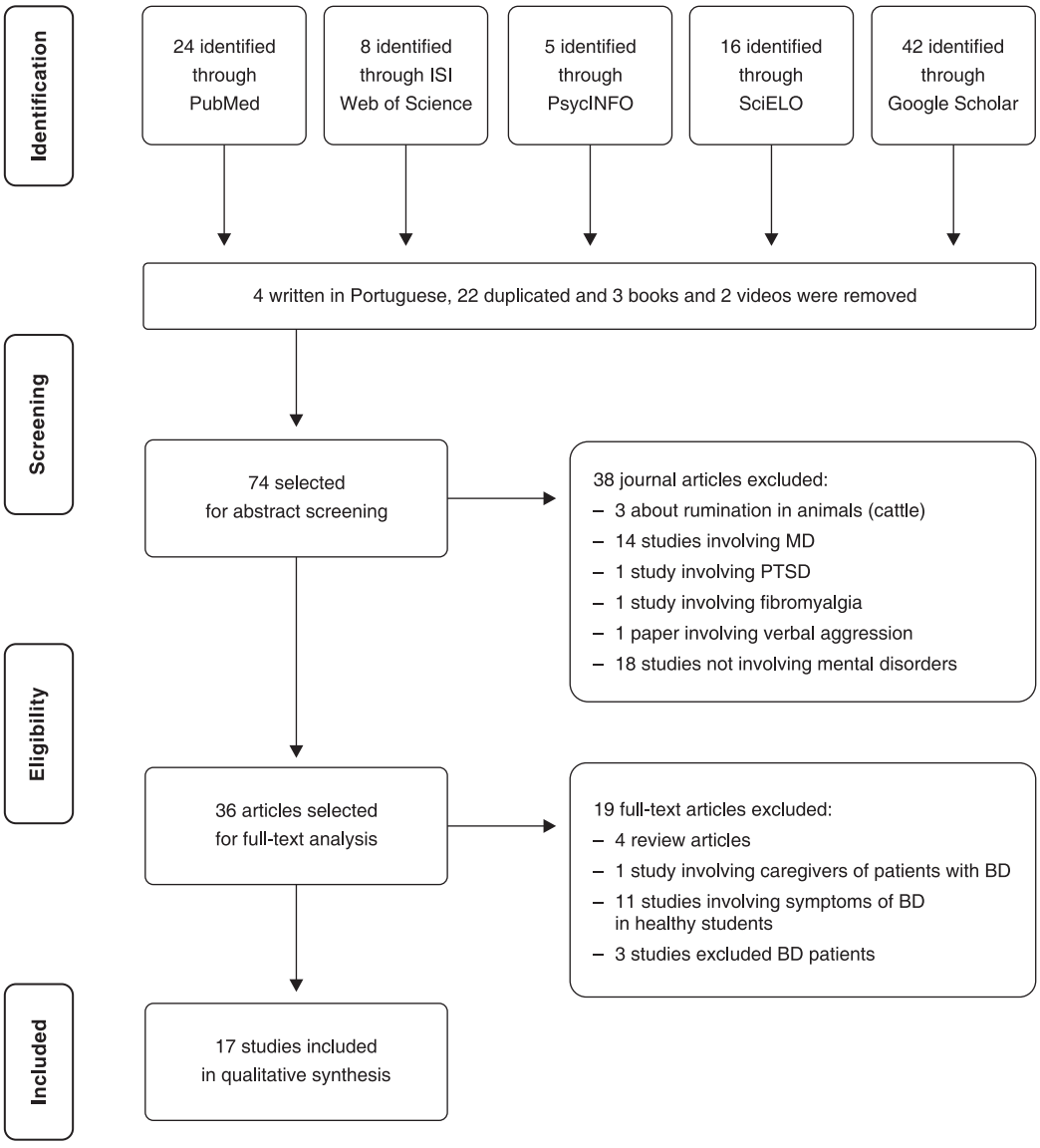

Figure 1 Flow diagram of study selection for a systematic review of rumination in BD. BD = bipolar disorder; MD = major depression; PTSD = posttraumatic stress disorder.

least one validated scale for assessment of rumination. Review articles and studies involving caregivers of patients with BD were excluded. After application of the inclusion and exclusion criteria, 17 articles were included in the review.

Results

The results of the studies included in the review are summarized in Table 1.

Rumination in BD

Despite the preliminary nature of studies involving patients with BD and the scarcity of data about rumination and mixed states,[8,23] rumination was found to be present in all phases of the illness, including during remission.[8,24] One aspect that stands out in patients with BD is that rumination may occur in response to both positive and negative affect[22] and remains present as a stable symptom in between depressive episodes.[20] Rumination is associated with hypomanic states when occurring in response to positive affect, and with depressive states when in response to negative affect.[25] Patients in the interepisodic phase have been shown to be more likely to ruminate when faced with positive and negative emotions when compared with healthy controls.[18] There is also a tendency among patients with BD to ruminate in response to negative affect when in hypomanic states, with a focus on their positive affective experiences and their own positive qualities.[7,22,25] Patients with BD use maladaptive cognitive strategies (such as rumination, catastrophizing, and self-blame) more frequently than their family members[17] and healthy controls,[9,10] and use adaptive strategies such as reappraisal and putting into perspective less frequently.[17]

Table 1 Summary of findings of the studies included in the review

Study	Design	N	M/F	Age (mean ± SD)	Age at onset (mean ± SD)	Rumination assessment	Diagnostic assessment	Psychological assessments	Results
Wolkenstein[9]	Cross-sectional	42 BD Rem 43 MD 39 HC	16/26 12/31 16/23	40.9±12.8 36.9±13.3 42.2±13.3	28.4±11.5* 28.4±12.4*	CERQ	SCID I SCID II	QIDS-SR HAM-D SRMI YMRS	-BD and MD reported more frequent use of self-blame, rumination, and catastrophizing than HC, and less frequent use of putting into perspective and positive reappraisal. -BD and MD did not differ in any CERQ subscale.
Gilbert[10]	Prospective	31 BD Rem 31 MD	11/20 10/21	30.9±9.76 31.71±11.15	12.9±10.6† 15.1±10.5†	RPA	SCID-IV BRMS IDS-C	PANAS HR‡ ECG‡	-Rumination and emotional inertia were different between BD and MD. -The use of maladaptive emotional strategies was differently associated with manic and depressive states. -6-month follow-up: induced rumination was not associated with depressive or manic symptoms.
Fletcher[11]	Cross-sectional	86 BD I 107 BD II 96 MD90 HC	155/224	39.7±11.4	18.4±7.0 19.4±10.2 20.8±11.3	RSQRP ACERQ	MINI	CIPM Brief COPE	-HC used more adaptive coping strategies than patients. -In BD, rumination was more focused on emotion and on the self than in MD when faced with positive affect; conversely, when faced with negative affect, BD engaged more in risk-taking than MD. -BD I and BD II used similar coping strategies. -The importance of psychological intervention in the treatment of BD II is reinforced.
Pavlickova[12]	Prospective	28 BD Rem 12 BD Dep 8 BD Hypo	14/34	45.4±10.8	27.2±9.7	RSQ	PANAS HRSD BRMS	ESM Momentary self-esteem Self-esteem fluctuations	-Rumination predicted lower positive affect; positive affect predicted decreases in rumination, whereas negative affect increased rumination. -Adaptive coping increases self-esteem and positive affect.
Rowland[13]	Cross-sectional	126 SZ 97 BD I 81 HC	73/53 36/61 37/44	45.5±11.0 51.3±12.1 44.6±12.9	N/A	CERQ	OPCRIT BED DIGS FIGS DASS HPS	None	-SZ and BD I showed more rumination, catastrophizing, and self-blame than HC, and less frequently used adaptive strategies (e.g., putting into perspective) in stressful situations. -In BD, rumination predicted depressive symptoms, anxiety symptoms, and hypomania. -These findings may reflect cognitive deficits in frontal executive functions in SZ and BD when faced with negative affect, with the use cognitive of repair [reappraisal?] strategies; both SZ and BD may present deficits in the ability to interpret emotional stimuli.
Rowland[14]	Cross-sectional	56 SZ 33 BD I 58 HC	32/24 18/15 29/29	44.6±10.4 40.7±11.3 33.9±12.2	N/A	CERQ	ISS PANSS	FEEST TASIT	-SZ ruminated more than BD and used more projection. -BD were more likely to blame themselves and less likely to engage in positive reappraisal than SZ. -Compared to HC, SZ showed impaired perception of positive and negative emotion; BD did not differ from HC.
Contreras[15]	Cross-sectional	164 BD I8 BD II 18 BD NOS 13 SZA DB 2 SZ 7 SMD	97/115	45.3±12.2	N/A	STAI	DIGS FIGS	None	-Rumination and worry may explain subsyndromal anxiety symptoms in Costa Rican patients with a history of mania or hypomania. -Methodological limitation: factor analytic study.
Kim[16]	Cross-sectional	227 MD 68 BD I 52 BD II 37 BD NOS 65 PD 16 GAD 11 OCD	177/299	16 to 88 years (range)	N/A	RSQ	SCID HRSD HRSA	None	-Rumination was found among individuals with MD, BD, GAD, and OCD, possibly indicating ineffective thought control. -Methodology: this study assessed the psychometric properties of RSQ to validate the Korean version of the scale.

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Study	Design	N	M/F	Age (mean ± SD)	Age at onset (mean ± SD)	Rumination assessment	Diagnostic assessment	Psychological assessments	Results
Green[17]	Cross-sectional	105 BD I 124 UR 63 HC	33/72 47/77 31/32	52.4±14.1 52.3±15.6 58.3±16.8	N/A	CERQ	DASS HPS	None	-BD more frequently presented maladaptive cognitive strategies such as rumination, catastrophizing, and self-blame in response to negative events than UR and HC. -BD I and UR reported more frequent use of maladaptive regulatory strategies than HC.
Gruber[18]	Cross-sectional	39 BD I 34 HC	11/28 12/22	42.5±13.8 38.2±11.1	19.5±12.1	RSQ RPA Emotion response to rumination induction	SCID YMRS DS-C PANAS	HR‡ ECG‡ RSA	-BD reported greater trait rumination about positive and negative emotion when compared with HC. -Rumination induction did not reveal differences between the groups. -Rumination about positive and negative affect in BD, as well as increased cardiovascular arousal, were associated with a greater frequency of lifetime depression and mania. -Methodology: illness course assessed retrospectively.
Liu[19]	Cohort	223 COMD 112 HC	N/A	N/A	N/A	RSQ	Suicide attempts	None	-COMD scored higher on maladaptive response styles and lower on adaptive styles. -Compared to COMD, probands with a history of suicide attempt were less likely to report the use of distracting activities to manage their depressed mood. -COMD who engaged in dangerous activities in response to depressed mood were more likely to attempt suicide (HR = 1.8, 95%CI 1.2-2.8).
Perlis[20]	Cohort	386 BD I 197 BD II	218/365	40.6±12.1	16.6±8.2	RSQ RPA CERQ	SCID ADEMINI CGI-S	None	-Great variation of symptoms in between depressive episodes in BD. -Rumination was a stable symptom during depressive episodes.
Van der Gucht[8]	Prospective	34 BD Man/Hypo/Mix30 BD Dep 43 BD Eut 41 HC	13/2 18/22 18/25 20/21	45.5±41-50‡ 46.2±42-49‡ 47.5±43-51‡ 47.9±43-52‡	23.9±21-27§ 21.0±17-25§ 24.0±22-26§	RSQ	SCID CSMS HRSD BRMS PANAS	Self-esteem diary Autobiographical memory CARROT PSI BIS/BAS PIT RSE	-BD in all phases showed high levels of sociotropy and autonomy, low self-esteem, self-esteem instability, rumination, and, less clearly, an impaired ability to recall specific autobiographical memories. -Vulnerability to depression was evident even in euthymic patients.
Gruber[21]	Cross-sectional	21 BD I 19 INS 20 HC	6/15 10/9	39.0±2.5 48.8±2.6	15.5±4.9 22.9±14.3‖	GRS	SCID IDS-C YMRS IDI DSISD BDI BAI	PSWQCCL	-Rumination and worry were transdiagnostic processes between insomnia and BD. -BD showed more negative automatic thoughts than HC; INS did not differ from HC.
Johnson[22]	Cross-sectional	28 BD 35 MD 44 HC	39/68	19.1±1.5	N/A	RSQRPA	SCID HPS IDD-L	None	-BD and MD ruminated more than HC in response to negative affect. -Patients in hypomania ruminated after negative affect but focused their thoughts on their own qualities and positive affect.
Simon[23]	Cross-sectional, ancillary to cohort	60 BD I 27 BD II 11 BD NOS	42/56	44.8±13.9	27.5±13.2†	RSQ	MINI SBQ ASI FQ PDSS-SR	PSWQ EACS FNE	-Higher RSQ scores were associated with greater suicidal ideation, and higher coping scores with lower suicidal ideation, in BD, during both depressive and manic episodes, in both males and females. -Rumination may mediate the relationship between anxiety and suicidal ideation.

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Table 1 (Continued)

Study	Design	N	M/F	Age (mean ± SD)	Age at onset (mean ± SD)	Rumination assessment	Diagnostic assessment	Psychological assessments	Results
Thomas[24]	Cross-sectional	14 BD Dep 40 BD Man 29 BD Rem 44 HC	11/3 10/20 11/18 14/30	38.3±12.2 45.9±12.4 45.8±11.2 37.4±12.7	N/A	RSQ	HRSD BRMS NART	None	-Rumination was greater in BD Rem and BD Dep when compared with BD Man and HC. -There was no correlation between rumination, sex, and IQ. -Risk-taking and active coping were associated with manic symptoms. -Methodological limitation: multiple groups with small sizes.

* Age at first treatment; † duration of illness (years); ‡ physiological measures; § 95% confidence interval; || average length of sleep disturbance.
ADE = Affective Disorders Evaluation; ASI = Reiss-Epstein-Gursky Anxiety Sensitivity Index; BD I = bipolar disorder type 1; BD II = bipolar disorder type 2; BD Dep = bipolar disorder in depressive episode; BD Eut = bipolar disorder in euthymic state; BD Hypo = bipolar disorder currently hypomanic; BD Man = bipolar disorder in manic episode; BD Man/Hypo/Mix = bipolar disorder in manic or hypomanic or mixed episode; BD NOS = bipolar disorder not otherwise specified; BD Rem = bipolar disorder in remission; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; BED = best estimate diagnosis; BAS = Behavioral Activation System Scale; BIS = Behavioral Inhibition System scale; BRMS = Bech-Rafaelsen Mania Scale; CARROT = Card Arranging Reward Responsivity Objective Test; CCL = Cognition Checklist; CERQ = Cognitive Emotion Regulation Questionnaire; CGI-S = Clinical Global Impression Scale for Current Severity; CIPM = Coping Inventory for Prodromes of Mania; COMD = childhood-onset mood disorder; CSMS = Cassidy Scale for Manic States; DASS = Depression and Anxiety Stress Scale; DIGS = Diagnostic Interview for Genetic Studies; DSISD = Duke Structured Interview for Sleep Disorders; EACS = Emotional Approach Coping Scale; ECG = electrocardiogram; ESM = Experience Sampling Method; F = female; FEEST = Ekman 60-Faces Task from the Facial Expressions of Emotion: Stimuli and Test; FIGS = Family Interview for Genetic Studies; FNE = Fear of Negative Evaluation scale; FQ = Fear Questionnaire; GAD = generalized anxiety disorder; GRS = Global Rumination Scale; HAM-D = Hamilton Depression Rating Scale; HC = healthy controls; HPS = Hypomanic Personality Scale; HR = heart rate; HRSA = Hamilton Rating Scale for Anxiety; HRSD = Hamilton Rating Scale for Depression; IDD-L = Inventory to Diagnose Depression - Lifetime; IDI = Insomnia Diagnostic Interview; IDS-C = Inventory of Depressive Symptomatology; INS = primary insomnia; IQ = intelligence quotient; ISS = Internal States Scale; M = male; MD = unipolar depression; MINI = Mini International Neuropsychiatric Interview; NART = National Adult Reading Test for IQ; OCD = obsessive compulsive disorder; OPCRIT = diagnostic interview for psychosis; PANAS = Positive and Negative Affect Scale; PANSS = Positive and Negative Syndrome Scale; PD = panic disorder; PDSS-SR = Self-Rated Panic Disorder Severity Scale; PIT = pragmatic inference task; PSI = Personality Style Inventory; PSWQ = Penn State Worry Questionnaire; QIDS-SR = Quick Inventory for Depressive Symptomatology - Self-Report; RPA = Responses to Positive Affect Questionnaire; RSA = respiratory sinus arrhythmia; RSE = Rosenberg Self-Esteem Scale; RSQ = Response Styles Questionnaire; SBQ = Suicide Behaviors Questionnaire; SCID = Structured Clinical Interview for DSM-IV; SD = standard deviation; SMD = substance-induced mood disorder; SRMI = Self-Report Manic Inventory; STAI = State-Trait Anxiety Inventory; SZA B = schizoaffective disorder, bipolar type; SZ = schizophrenia; TASIT = Awareness of Social Inference Test; UR = unaffected biological relatives of BD probands; YMRS = Young Mania Rating Scale.

Two studies have investigated the role played by rumination in the relationship between suicide attempts and mood disorders. In the first study, BD patients with higher rumination scores also showed higher suicidal ideation scores.[23] The second study assessed adults with childhood-onset mood disorder and found that patients who attempted suicide were less likely to use adaptive cognitive strategies to deal with their depressive symptoms than those who had never attempted suicide. Moreover, patients with the highest rumination scores were also the ones with the lowest scores for adaptive skills.[19]

A methodologically different study involving patients with BD was conducted to investigate the association between mood, self-esteem, rumination, and coping over time, controlled for depressive and manic symptoms.[12] That study revealed that low mood and self-esteem immediately led to rumination, whereas positive mood and high self-esteem could trigger risk-taking behaviors.[12] In the same study, high levels of negative affect and low levels of positive affect led to engagement in rumination at the subsequent time point; rumination, in turn, had a strong impact on mood, causing emotional inertia.[12] Those authors also found that rumination reduced positive affect but did not increase negative affect or alter self-esteem; coping and risk-taking, in turn, increased positive affect but did not alter negative affect; only coping resulted in increased self-esteem.[12]

The study above is in line with the hypothesis proposed by Dempsey et al.[26] in that rumination may contribute to deterioration of hypomanic and manic states by aggravating or sustaining them (tendency to keep thinking about the positive qualities of the self, positive affective experiences, and favorable life circumstances). Some recent neuroimaging studies have supported the hypothesis that rumination may maintain the mood state by establishing a vicious cycle.[27-29] In patients with BD, rumination in response to positive affect may be associated with the prospect of reward, initiating a thinking cycle that may maximize reward.[4,7]

Neurobiological findings about rumination in BD

From a neurobiological point of view, there is little information in the literature on rumination in BD patients; the findings published thus far cover different mental disorders, particularly depression. In patients with BD, the main areas showing functional abnormalities are those responsible for controlling emotion and executive functions, namely, areas of the prefrontal cortex (medial, dorsolateral, anterior cingulate, and orbital regions) and amygdala.[25] All these areas have shown abnormalities in studies investigating associations between rumination and neuroimaging findings[4,30] in other disorders, in line with the hypothesis that executive dysfunction may underlie the tendency to ruminate in patients with BD.[13,16] Moreover, several studies have confirmed that rumination has negative impacts on cognitive function in mood disorders, particularly on autobiographical memories, inhibition, cognitive flexibility, problem solving, working memory, and attentional bias towards negative

content.[30] It has been suggested that patients with BD may ruminate because they face difficulties inhibiting their persistent self-focusing behavior[11] – a process that may have been initiated in response to both positive and negative affect,[12] and needs extensive research.

Rumination has also been associated with changes in memory processing[8] and prefrontal activity.[31] Brain-derived neurotrophic factor (BDNF) is known to play a role in hippocampal function, synaptic plasticity in stressful situations, and prefrontal cortex functioning.[32] Preliminary evidence has pointed to reduced hippocampal volume and abnormalities in cognitive function primarily in the dorsolateral prefrontal cortex of patients with depression and BD.[30] Nolen-Hoeksema et al. suggested that rumination could be a mediator between the *BDNF* gene and depressive symptoms.[4] Another study involving 200 female adolescents and their mothers found that the Val/Val genotype of *BDNF* was associated with more frequent rumination and childhood-onset depression when compared with the Val/Met genotype; in mothers with adult-onset depression, in turn, Val/Met was more strongly associated with depressive symptoms.[33] In both the adolescents and their mothers, rumination was a significant mediator of the relationship between the Val/Val and Val/Met genotypes with regard to the presence of depressive symptoms.

Relation between mental function and rumination in BD

According to Michl et al., rumination may be the mechanism mediating the relationship between exposure to stressful situations and the onset of an internalizing psychopathology, based on the findings that 1) both rumination and traumatic events predict the onset of depression and anxiety; and 2) the brain region activated in a situation of social rejection is the same activated during self-reflection.[34] A recent study on rumination involving euthymic, BD, and depressed patients found a pattern in the use of emotional regulation strategies in patients when compared with healthy controls, namely, an increased use of maladaptive strategies and a reduced use of adaptive ones, suggesting a predisposition to relapse and to worse prognosis in the course of illness.[17] Within this perspective, Ghaznavi & Deckersbach[25] proposed a link between executive dysfunction (especially executive inhibitory control) and the tendency to ruminate in patients with BD in both depressive and manic states. According to those authors, evidence shows the same association in patients with major depression when compared with healthy controls. Taken together with the results of another article,[30] these findings underscore the difficulty in changing the focus of attention and performing new tasks among patients who engage in ruminative thoughts vs. those who do not.[25] These findings, however, are preliminary and need to be replicated.

Discussion

The study of rumination mechanisms in BD patients is a new area of interest. At this point in time, rumination seems to be present in all phases of the illness and to be independent of mood state in BD patients, but shows a close relationship with mood as well as with executive functions. It is possible that rumination has a negative impact on cognitive function, associated with executive dysfunction, particularly inhibitory control and the tendency to ruminate.

Rumination is not exclusive to patients with major depression. An experimental study has shown that inducing rumination in the context of a stressful situation has led to anxious and depressive moods among adolescents and adults, respectively.[35] Another study of rumination induction failed to find differences between patients with BD and healthy controls.[18] A recent study in which rumination was induced in patients with BD and depression found that rumination increases positive affect in both types of patients.[9] An association has also been found between frequent rumination and sexual violence.[36] Gruber et al. reported that rumination and worry were transdiagnostic symptoms between BD and insomnia.[21] In a study conducted by Watkins, rumination was associated with an increased chance of comorbidity with generalized anxiety, obsessive compulsive, and borderline personality disorders in depressed patients.[37] A recent study compared rumination in patients diagnosed with major depression, BD, panic disorder with or without agoraphobia, generalized anxiety disorder, and obsessive compulsive disorder. The lowest level of rumination was found in agoraphobic patients; surprisingly, patients with BD showed levels of rumination similar to those of depressed patients.[16] Another recent study, despite some important methodological limitations, hypothesized that rumination may explain the anxiety observed in patients with a history of mania and hypomania.[15] More recently, two studies compared social cognitive skills in patients with schizophrenia and BD and in healthy controls. In both studies, the authors found that patients with schizophrenia ruminate and blame themselves more frequently than the other two groups.[13,14] In the first study,[13] patients with schizophrenia and BD used adaptive strategies (e.g., putting into perspective) less than controls. Moreover, rumination in patients with BD predicted symptoms of depression, anxiety, and hypomania; little use of positive reappraisal of negative events also predicted the same symptoms. The authors suggest these findings may be associated with cognitive deficits in frontal executive functions (e.g., the ability to interpret a negative emotional stimulus using reappraisal strategies), as already demonstrated in schizophrenia and BD.[13] In the second study, patients with schizophrenia were found to use more projection than those with BD, and the latter were found to blame themselves more often and to engage less in positive reappraisal when compared with controls.[14] On the facial expression of emotion test, patients with schizophrenia scored worse than those with BD. The authors suggested that these findings evince poor use of social cognitive skills in these disorders, due to a possible dysfunction in the frontolimbic neural circuitry.[14]

Based on these findings, we may state that rumination does not appear only after the experience of negative affect or a stressful life event. Rather, rumination seems to be a phenomenon independent of mood state, but closely related to mood and to executive function, despite the lack of data

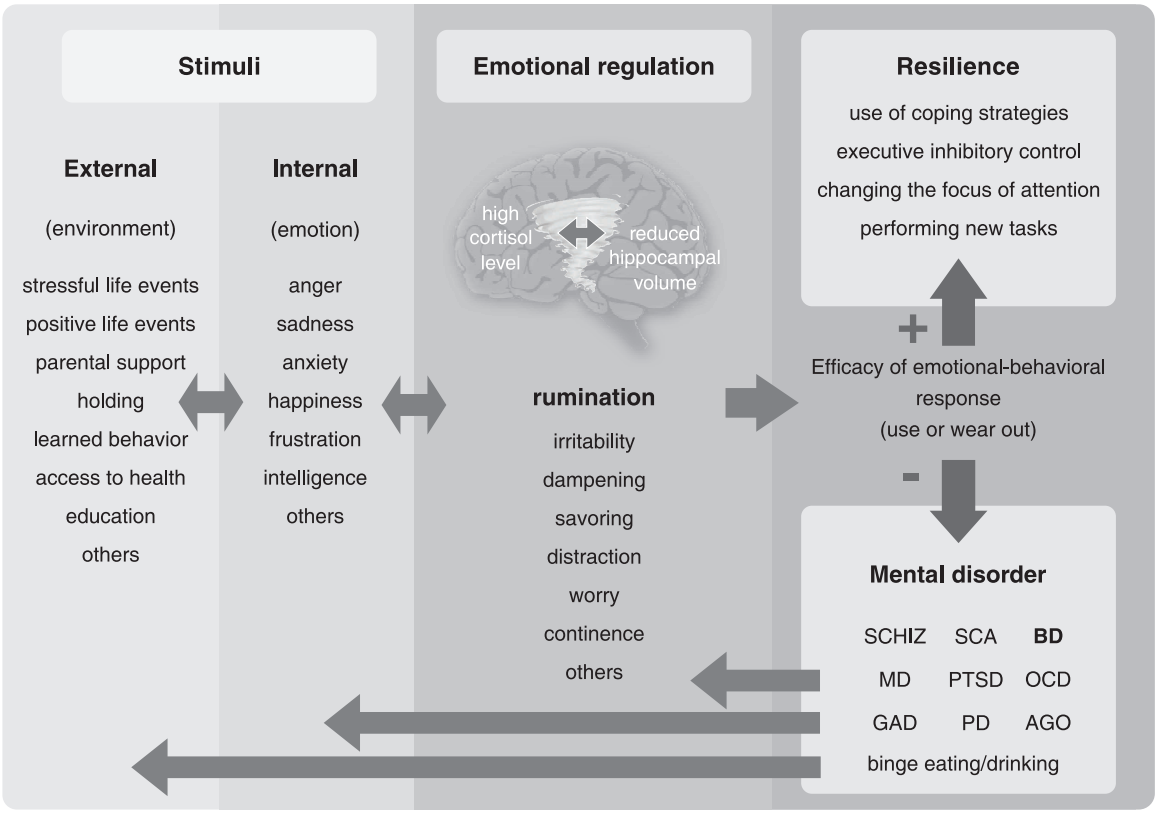

Figure 2 The rumination process in mental disorders. AGO = agoraphobia disorder; BD = bipolar disorder; GAD = generalized anxiety disorder; MD = major depression; OCD = obsessive compulsive disorder; PD = panic disorder; PTSD = posttraumatic stress disorder; SCA = schizoaffective disorder; SCHIZ = schizophrenia.

on ruminations and mixed state. In fact, one could speculate that rumination is a phenomenon present in several mental disorders. Depending on genetic load, environmental characteristics (holding, learned behavior), intelligence, and resilience, patients faced with a ruminative thought after a stressful life event may have as an outcome either the resolution of the situation, with tolerance to its external and internal effects, or the development of phobic, anxious, obsessive, depressive, manic, escapist (binge eating/drinking, self-mutilation), and psychotic symptoms. We hypothesize that an association may exist between rumination and reduced hippocampal volume and high cortisol levels (altered cortisol cascade), possibly as a result of genetic load, based on the reported association between stress and rumination[35,38] and between stress/anxiety/depressive symptoms and increased cortisol levels[30] (Figure 2).

In line with Watkins's proposition that rumination is a transdiagnostic symptom,[37] it may be worth studying as a dimensional symptom, i.e., within the recent research paradigm launched by the National Institute of Mental Health with the Research Domain Criteria (RDoC) project.[39] In this scenario, rumination could relate and integrate cognitive, emotional, and behavioral components with advances in genetic, molecular, cellular, and neural circuit research.[40] The goal would be to help improve the current diagnostic model, which groups symptoms into clusters and disregards the neurobiological bases of symptoms.[41] Obviously, this hypothesis requires wide further investigation before it can be considered valid and reliable.

Finally, achieving a better understanding of rumination may shed light on possible contributions towards the tendency to ruminate and may improve definitions of diagnostic boundaries and overlaps across mental illnesses in which rumination occurs. Learning more about mediators of the development of comorbidities, or about the factors involved in a poor prognosis, may be extremely important to help define initial treatment targets, which could be monitored and treated whenever present, thus improving executive, attentional, and memory functions.

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Disclosure

The authors report no conflicts of interest.

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