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Abstract

Background: Research has shown bipolar disorder to be characterized by dysregulation of emotion processing, including biases in facial expression recognition that is most prevalent during depressive and manic states. Very few studies have examined induced emotions when patients are in a euthymic phase, and there has been no research on complex emotions. We therefore set out to test emotional hyperreactivity in response to musical excerpts inducing complex emotions in bipolar disorder during euthymia.

Methods: We recruited 21 patients with bipolar disorder (BD) in a euthymic phase and 21 matched healthy controls. Participants first rated their emotional reactivity on two validated self-report scales (ERS and MAThyS). They then rated their music-induced emotions on nine continuous scales. The targeted emotions were wonder, power, melancholy and tension. We used a specific generalized linear mixed model to analyze the behavioral data.

Results: We found that participants in the euthymic bipolar group experienced more intense complex negative emotions than controls when the musical excerpts induced wonder. Moreover, patients exhibited greater emotional reactivity in daily life (ERS). Finally, a greater experience of tension while listening to positive music seemed to be mediated by greater emotional reactivity and a deficit in executive functions.

Limitations: The heterogeneity of the BD group in terms of clinical characteristics may have influenced the results.

Conclusions: Euthymic patients with bipolar disorder exhibit more complex negative emotions than controls in response to positive music.

Keywords: bipolar disorder; complex musical emotion; emotional reactivity; mixed model

.Introduction

Patients with bipolar disorder (BD) are generally assumed not to show any severe symptoms when they are in a euthymic state. However, there is increasing evidence that patients may exhibit subsyndromal symptoms, like cognitive impairments (Martinez-Aran et al., 2004) outside acute episodes and they may be one of the main cause of relapse (Henry et al., 2015). One of them-emotional reactivity-already seems to have been validated as an abnormal clinical feature in BD even between episodes. Self-report questionnaires indicate that patients experience higher levels of emotional lability and intensity than controls (Henry et al., 2008b). Researchers have also used emotion induction methods to test emotional reactivity in patients, such as showing them positive, neutral or negative pictures and asking them to assess the subjectively felt emotions triggered by the pictures (Dubois et al., 2012; M'bailara et al., 2009). These studies have shown that, compared with controls, patients with BD experience greater emotional intensity when exposed to neutral faces, even when they are in a euthymic state. However, there has been only limited research on this effect in the auditory modality. Some research on emotional prosody has shown that even patients in remission are selectively impaired on the recognition of emotions expressed by human voices (Bozikas et al., 2007; Van Rheenen and Rossell, 2013). However, only basic and discrete emotions have been studied so far, and the literature does not provide any information about complex emotion disturbances in BD.

Music is a powerful emotional and ecologically valid tool, and constitutes an ideal model for studying complex emotional experience. There is already a body of research on music-induced experiences in patients who have been diagnosed with depression (Aust et al., 2013; Kornreich et al., 2013; Naranjo et al., 2011). For example, a study by Punkanen and colleagues (Punkanen et al., 2011) showed that depressed patients' recognition of emotions expressed by musical stimuli is biased towards negative emotions such as sadness and anger. However, in this study, as in many others, participants were asked to recognize the emotions conveyed by the music, but not to assess their emotional experience when listening to the music. In the psychology of emotions and music psychology, a distinction is made between the *recognition* of emotions and the actual *experience* of emotions (Gabrielson and Juslin, 2003; Scherer, 2004). The recognition is viewed mainly as a cognitive process of assigning a label to an emotion expressed by the music. On the other hand, the experience of music-induced emotions involves the subjective feeling and also the physiological components of emotional reactions. For the present study we choose to ask participants to evaluate the actual experience of musical emotions, given that in BD the subjective emotional experience is compromised.

We therefore designed a study to test the experience of music-induced emotions in patients with BD. We chose music to study patients' emotional reactivity because this complex auditory and affective stimulus is an ecologically sound tool that often forms part of their daily lives. The emotions that can be induced by music go beyond the basic emotions that are important for survival, and include the complex affective experiences that can be encountered in the course of everyday life. Recent theoretical approaches suggest that domain-specific models are more appropriate for describing the emotional spectrum of affective responses to music (Zentner, 2010; Zentner et al., 2008) than either classic theories of *basic emotions* (e.g., fear, anger, or joy) (Ekman, 1992) or dimensional models that describe all affective experiences in terms of valence and arousal (Russell, 2003). The domain-specific model known as the Geneva Emotional Music Scale (GEMS) (Zentner et al., 2008) was derived from a series of field and laboratory studies in which participants rated their felt emotional reactions to music using an extensive list of adjectives (> 500 terms). Statistical analyses of the factors or dimensions that best described the organization of these emotional labels revealed that a nine-factor model, comprising Joy, Sadness, Tension, Wonder, Peacefulness, Power, Tenderness, Nostalgia, and Transcendence, best fitted the data (Zentner et al., 2008).

The aim of the present study was to explore the complex emotional responses (subjective feelings) triggered by musical stimuli in patients with BD outside acute episodes, looking for ecological emotional markers of BD regardless of mood state. Based on previous studies of emotional experience (Dubois et al., 2012; M'bailara et al., 2009), we hypothesized that all the emotional responses of patients in a euthymic state are exaggerated, compared with those of healthy controls (HC), all their emotional responses are exaggerated. Moreover, taking account of previous research on BD using emotional prosody and music (Bozikas et al., 2007; Erkkila et al., 2011), we hypothesized that there is a specific deficit in the experience of negative emotions.

Methods

Participants

One group of euthymic patients with BD and one group of HC took part in the study. The clinical group included 21 patients with BD (5 men, 16 women), all born in France and native French speakers. Their mean (± *SE*) age was 48.3 years (± 8.8, range = 33-63). Eighteen were right-handed and three were left-handed, according to the criteria of the Edinburgh Handedness Inventory (Oldfield, 1971). Their mean (± *SE*) education level was 13.1 years (± 2.7, range = 9-18). BD was diagnosed by the treating clinician and confirmed by a clinically trained psychiatry resident on the basis of the entire Mini International Neuropsychiatric Interview (MINI, (Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar, 1998)) and according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV (American Psychiatric Association, 1994)). All patients scored 16 or under on the Montgomery–Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) (*M* = 5, *SE* = 4.0, range = 0–16), and 11 or under on the Young Mania Rating Scale (YMRS) (Young et al., 1978) (*M* = 3, *SE* = 3.0, range = 0–11).

All the participants with BD were outpatients at the psychiatry department of the mental health hospital in Rennes, France. As far as comorbidities are concerned, according to the MINI, none of the patients in the sample exhibited either anxiety or phobic or addiction features, although eight patients had tobacco addiction (> one pack of cigarettes a day) in addition to their BD. There were no reports of either panic disorder or generalized anxiety disorder.

Nineteen patients had bipolar I disorder and six had bipolar II disorder. Their mean (± *SE*) age at onset was 34 years (± 11, range = 17-59). The mean (± *SE*) duration of their illness was 14 years (± 9, range = 2-37). Nine patients had a predominantly negative polarity, 11 had a predominantly positive polarity, and one had neither. For seven of them, the most recent episode had been a manic episode and for 14 of them it had been a major depressive episode. The minimum length of time since the last episode was two months for all the patients. The mean (± *SE*) number of previous hospitalizations per patient during BD was 6 (± 8.0, range = 1–38). The mean (± *SE*) number of previous suicide attempts per patient was 0.9 (± 1.5, range = 0–5).

Medication consisted of mood stabilizers (lithium, lamotrigine, valproic acid; $n = 18$), atypical antipsychotics used as mood stabilizers (quetiapine, olanzapine; $n = 10$), and antidepressants (clomipramine, venlafaxine, paroxetine, escitalopram; $n = 5$). Ten of them were only on one medication. The sociodemographic and illness-related characteristics of each patient in the euthymic BD patient group are set out in Table 1.

The HC group included 21 healthy individuals (4 men, 17 women) who were recruited from the general population and were given no reward for their participation. They were all native French speakers (except for one who had two native languages). Their mean (± *SE*) age was 46.2 years (± 7.6, range = 28–55). Eighteen HC participants were right-handed, one was left-handed, and one was ambidextrous. Mean (± *SE*) education level was 13.5 years (± 1.8, range = 11–17). Their health status was assessed by a clinically trained psychiatry resident on the basis of the MINI and according to DSM-IV criteria.

Exclusion criteria for all participants (BD and HC) were the wearing of hearing aids or a history of tinnitus or a hearing impairment, a history of neurological disorders, head trauma, anoxia, stroke and major cognitive deterioration, as attested by their score on the Mattis Dementia Rating Scale (MDRS) (Mattis, 1988). None of the participants scored under 130 on the MDRS, or displayed addictive or other psychiatric disorders (Axis 1 of the DSM-IV), except for BD in the patient group. Responses to a questionnaire indicated that none of the participants felt revulsion toward classical music or had any previous professional experience in the music field. The two groups were comparable for sex (Fisher's exact test, $p = 1$), age ($z = 0.39$, $p = 0.7$), education level ($z = -0.73$, $p = 0.46$), and handedness (Fisher's exact test, $p = 1$).

After giving a complete description of the study, oral and written informed consent was obtained from each participant, and the study was conducted in accordance with the Declaration of Helsinki.

Psychiatric and neuropsychological assessment

As indicated above, the severity of the patients' symptoms was assessed on the MADRS and the YMRS.

To measure emotional reactivity, we administered the Multidimensional Assessment of

Thymic States Scale (MAThyS) (Henry et al., 2008a), which defines bipolar mood states as a function of an inhibition/activation process, using a dimensional approach, and the Emotion Reactivity Scale (ERS) (Nock et al., 2008), which explores sensitivity to emotional stimuli in everyday life and the persistence of the emotion after exposure.

Given that performances on measures of cognitive functioning tend to be impaired in euthymic patients (for a review, see (Bourne et al., 2013; Quraishi and Frangou, 2002)), we administered a neuropsychological battery to all participants prior to the music-induced emotions session. This battery included the MDRS and a series of tests assessing frontal executive functions: the Wisconsin Card Sorting Test (WCST) (Grant and Berg, n.d.), Trail Making Test (TMT) (Reitan, 1955), Categorical and Literal Fluency test (Cardebat et al., 1990), Action (Verb) Fluency test (Woods et al., 2005), Digit/Symbol-Coding subtest of the Wechsler Adult Intelligence Scale-III (WAIS-III) (Wechsler, 1939), Stroop test (Stroop, 1935) and auditory memory spans. Finally, to ensure that participants had no auditory impairment, they all underwent the Montreal–Toulouse auditory agnosia battery (PEGA) (Agniel et al., 1992). None of the participants included in the study presented any major impairment.

Music-induced emotional experience

Stimulus material

The stimulus set comprised 12 excerpts (each lasting 45 s) of instrumental music composed in the past four centuries, taken from commercially available CDs (Supplementary Table 1). These stimuli were chosen to cover a subset of target emotions derived from the nine-dimension GEMS model (Zentner et al., 2008), but also to control for familiarity and reduce potential biases arising from memory and semantic knowledge.

All auditory stimuli were played binaurally through high-quality headphones. The loudness of the auditory stimuli was adjusted for each individual participant, prior to the session. Visual instructions were displayed on a 17-inch computer screen.

Experimental design

Before the session started, participants were instructed about the task and familiarized with the questionnaires and emotional terms that would be employed during the experiment. The instructions emphasized that answers to the questionnaires should only concern subjectively felt emotions, not the expressive style of the music (Gabrielson and Juslin, 2003; Zentner et al., 2008).

The musical stimuli consisted of 12 musical excerpts that had been assessed in a preliminary behavioral rating experiment featuring a different group of 20 healthy participants. In this preliminary study, stimuli were first assessed using the nine GEMS emotion categories. This assessment was then confirmed with a short version of the GEMS featuring just four emotion categories: Power, Tension, Wonder (GEMS categories Wonder + Joy) and Melancholy (GEMS categories Nostalgia + Sadness). Each of the 12 selected stimuli belonged to one of these four categories, and each category contained three musical stimuli (see Supplementary Table 1). Each musical excerpt lasted 45 seconds. Between each excerpt, we inserted a relaxation period, which allowed patients to settle and return to an emotional baseline. This baseline condition always lasted 20 seconds.

Before each excerpt, participants were instructed to listen attentively to the stimulus and to keep their eyes closed while it was being played. As soon as the stimulus came to an end, participants completed a set of emotion ratings. Participants were asked to rate how strongly they had experienced each of the nine GEMS emotional categories (Zentner et al., 2008) during the stimulus presentation. Visual analogue scales corresponding to these nine emotions (Joy, Sadness, Tension, Wonder, Peacefulness, Power, Tenderness, Nostalgia, and Transcendence) were displayed on the screen for each musical piece, together with scales for two additional descriptive adjectives (see Supplementary Table 2), in order to disambiguate the meaning of each emotional category, as in previous studies (Trost et al., 2012).

It is important to note that we explicitly emphasized to our participants that their judgments had to concern their subjectively felt emotional experience and not the expressiveness of the music. The final rating automatically triggered the relaxation time preceding the next stimulus presentation. Participants were instructed to answer spontaneously, but there was no time limit for responses. Therefore, the overall duration of the session varied slightly across participants (mean duration: 45 minutes).

The entire protocol was completed within a single session lasting approximately two hours.

Statistical analysis

For the sociodemographic, emotional reactivity and neuropsychological data, comparisons between the two groups (HC and BD) were performed using a Mann-Whitney test.

For the data of subjectively experienced musical emotions, we performed two types of analysis. First, we used the Mann-Whitney test to compare the performances of the two groups on categorical judgments, according to their percentages of correct responses.

Second, in order to test the influence of BD on the experience of music-induced emotions, we ran generalized linear mixed models (GLMMs) using the glmmADMB package (Fournier et al., 2012), with group (2 levels: BD vs. HC) and scale (9 levels) as fixed effects. We entered participant and musical excerpt as random effects, as interindividual variability in the way participants rated the scales and variability in the emotions induced by the musical excerpts had to be taken into account in the model. The emotion variables had a binomial distribution and an over-representation of zero scores on the subjective emotional scales for all the excerpts. A distribution with a zero over-representation represents a natural phenomenon in this kind of emotional paradigms, given that the evaluations for stimuli aiming to induce a certain emotion will be evaluated very low on non-target emotion categories. We therefore chose a negative binomial distribution in the model and performed a correction for the zero-inflation. It should be noted that the correction for zero-inflation did not exclude any data, but all observations were taken into account in the model. Complete and reduced models were calculated and compared by means of a likelihood ratio test, in order to assess the main effects and the interaction between the factors. We began by analyzing all the excerpts together. We then ran separate analyses for each type of stimulus (Melancoly, Power, Tension, Wonder).

To test whether the results for the emotional assessments could be explained by other psychological and neuropsychological variables (including emotional reactivity), we entered variables that differed significantly (with $p<0.001$) between patients and HC as covariates in the analyses with the GLMMs.

Statistical analyses were performed using Statistica 9.0 for the Mann-Whitney tests, and RStudio (Version 0.97.551) for the GLMMs, based on R (Version 3.0.1) and glmmADMB (Version 0.6.3). The significance threshold was set at $p = 0.05$.

Results

Emotional reactivity scores

Concerning the emotional reactivity scales, scores on the *emotional reactivity* subscale of the MAThyS did not differ significantly between the two groups (Mann-Whitney; $df = 1$, $z = 0.70$, $p = 0.48$). In addition, there was only a trend toward significance for the difference between the mean overall scores of the euthymic patients and HC on the MAThyS (Mann-Whitney; $df = 1$, $z = 0.79$, $p = 0.07$) (Table 2). HC had a mean overall score of 98.5 (*SD* = 21.8) on the MAThyS, with a mean score of 21.1 (*SD* = 4.7) on the emotional subscale (Table 2), while patients had a mean overall score of 107.3 (*SD* = 20.3), with a mean score of 20.8 (*SD* = 6.6) on the emotional subscale (Table 2).

The ERS scores differed significantly between the two groups (Mann-Whitney; $df = 1$, $z = 3.52$, $p < 0.001$). HC had a mean score of 22.9 (*SD* = 11.9), while patients had a mean score of 41.2 (*SD* = 15.3) (Table 2).

Neuropsychological assessments

As shown in Table 3, there was a significant difference between the two groups on the color-naming score of the Stroop Test, intended to measure attentional capacity. Concerning executive functions, the BD group performed significantly more poorly than the HC group on the TMT-B-A, the numbers of errors in the WCST, phonemic and categorical fluency, and the Digit/Symbol-Coding subtest of WAIS-III (Table 3). However, there was no significant difference between the two groups on action fluency, memory spans, the interference score of the Stroop test, or the number of perseverative errors in the WCST. Patients had lower MDRS and overall PEGA scores (Table 3).

Musical emotions

Categorical analysis of percentages of correct responses

The first step in our analysis consisted in comparing the performances of the two groups on categorical judgments, in terms of percentages of correct responses. A response was deemed to be correct when the participant rated the target scale (e.g., the Melancholy scale when the stimulus was "Melancholy") higher than all the other scales. There were no significant differences between the two groups, either on the overall score (z = -0.53, p = 0.60), or on the individual Melancholy, Power, Wonder and Tension scores (see Supplementary Table 3), with the BD group providing 52% of correct responses and the HC group 54%.

Generalized linear mixed models

In order to ascertain whether the BD patients and HC differed on the general emotional experience, we calculated complete (with interaction) and reduced (without interaction) GLMMs (glmmADMB), with group as the between-groups factor and scale as the within-groups factor. When all four types of stimuli were included, the likelihood ratio comparisons of the models revealed a significant main effect of scale, D(8) = 32.2, $p < 0.001$ (Table 4). However, the main effect of group was not significant, and there was no interaction with scale.

Because patients with BD were in a euthymic state, we only expected to observe subtle differences between the two groups on emotional experience. We therefore did not expect to find differences concerning the emotional evaluations of the target emotion category for one type of stimuli. But we looked for more specific differences between the two groups concerning the non-target emotion categories, by applying GLMMs to each type of stimulus. When we ran separate analyses for each type of stimulus, we found a significant main effect of scale in every case (Melancholy: D(8) = 103.1, $p < 0.001$; Power: D(8) = 91.2, $p < 0.001$; Tension: D(8) = 60.7, $p < 0.001$; Wonder: D(8) = 183.3, $p < 0.001$). No main effect of group emerged for any of the four target emotions. Only for the excerpts for the target emotion Wonder did we find a significant interaction between group and scale, D(8) = 32.3, $p < 0.001$. This interaction effect was significant because the two groups' assessments of these excerpts inducing Wonder (i.e., Wonder + Joy emotional categories) differed on the emotional categories Tension and Sadness (Tables 4 and 5, Fig. 1). Post hoc comparisons between group and the different levels of the scale factor failed to reveal any significant differences for the other three target emotions (see Supplementary Figs 1-3).

Covariate analyses

As the emotional reactivity measured by the ERS differed between the two groups, this score was entered as a covariate in the GLMMs to test whether this score could explain the significant results we had obtained. When we entered ERS as a covariate in the analyses for excerpts inducing the target emotion Wonder, we found that the significant interaction between group and scale disappeared for Tension ($p > 0.47$), but not for Sadness ($p < 0.001$). The other neuropsychological variables for which the two groups differed significantly ($p < 0.001$) were the subtest Code (Digit/Symbol-Coding) from the WAIS-III and the MDRS. When entering the standard score of the Code as covariate in the analyses for excerpts inducing Wonder, we found again that the significant interaction between group and scale disappeared for Tension ($p > 0.32$), but remained for Sadness ($p < 0.001$). Entering the MDRS as covariate did not affect the results, i.e. both effects for Tension ($p < 0.001$) and Sadness ($p < 0.001$) remained.

Discussion

In this study, we compared patients with BD and HC on the emotional experiences induced by music. Overall, we found that the subjective feelings experienced in response to music did not differ between patients and HC. However, when we took a closer look at more subtle differences for different types of music, we have found that the patients with BD reported a slightly different emotional experience. With the use of GLMMs, we showed that there were two specific effects in the BD group compared with HC: for positive musical excerpts that had been classified beforehand as inducing joy and wonder, the patients experienced more negative emotions, notably more tension and sadness, in comparison with HC.

Patients with BD have been shown to suffer from emotional hyperreactivity, not only during their mood episodes (Henry et al., 2003), but also during their euthymic periods (Henry et al., 2008b). M'Bailara and colleagues (M'bailara et al., 2009) found that patients in remission felt quite intense emotions towards neutral stimuli (neutral facial expressions drawn from the IAPS database), and similar results were reported by Dubois et al. (Dubois et al., 2012) using film clips taken from the battery developed by the group of Philippot (Schaefer et al., 2010). However, more specifically for music, Aust and colleagues (Aust et al., 2013) failed to find any differences in the emotional experience of music in remitted patients with unipolar depression..

Concerning the emotional experience of tension, Zeschel and colleagues (Zeschel et al., 2013) showed that 76.2% of the 42 patients with BD included in their study exhibited physical agitation during their euthymic periods. Although we did not find in our results that BD patients would be more stressed in general, we observed that patients with BD felt more agitated or tense than healthy participants when listening to music inducing wonder or joy. BD Zeschel and colleagues (Zeschel et al., 2013) showed that 76.2% of the 42 patients with BD included in their study exhibited physical agitation during their euthymic periods. patients' increased sensitivity to emotional stimuli and their inability to adequately control their emotional responses presumably also exacerbate their agitation when they are exposed to positive emotional stimuli (Phillips et al., 2008). Why this increased agitation of BD patients becomes visible in particular in response to joyful music still should be further investigated.

Concerning sadness, the euthymic patients in our study reported more negative emotional feelings when they listened to positive stimuli. This finding tallies with the negative emotional bias displayed by depressed patients, who tend to experience more negative emotions than HC. Regarding the recognition of emotions expressed in music, Punkanen et al. (Erkkila et al., 2011) found that, compared with HC, depressed patients had significantly higher scores on the recognition of anger and sadness for all musical excerpts. This misinterpretation of emotional valences was also described by Gur and colleagues in 1992 (Gur et al., 1992), when they showed that depressed patients recognize neutral faces as being rather sad, and happy faces as rather neutral. These observations suggest that there is a defect in negative emotion inhibition even when the stimulus is positive, similar to the atypical emotional response to visual stimuli observed in patients with schizophrenia (Strauss and Herbener, 2011). The findings described here are consistent with previous studies, which used both unipolar (Cohen and Minor, 2010) and bipolar (Strauss et al., 2010) scales to provide evidence that patients experience positive stimuli as aversive. In both cases, positive stimuli were rated in the unpleasant valence range more frequently by patients than by controls.

Another hypothesis would be that bipolar patients struggle so much to regulate their own positive emotions that it creates a chronic source of distress, which could be experienced as negative emotion (Gruber et al., 2013). In other words, this negative bias in subjective feelings could be a consequence of maladaptive emotion regulation strategies. Moreover, we found a significant difference between the two groups on processing speed (WAIS-III Digit/Symbol-Coding subscore), with a lower mean score for BD patients compared with HC.

This executive function deficit could lead to a lack of inhibition of subjective feelings (Banich, 2009) and partly explain these abnormalities in the emotion regulation process.

From a purely clinical point of view, we found that the emotional experience of euthymic patients with BD in daily life was different from that of HC. Both of the emotional reactivity scales used in this study had previously been validated in the scientific literature. The difference between the two groups on ERS scores (27) confirmed that patients are generally hyperreactive, and for daily-life events, the emotion persists for longer after the trigger than it does in HC., We found only a trend toward significance in the difference between patients and HC on mean MAThyS scores, but no difference concerning the emotional reactivity subscore of this scale. However, as the ERS represents a more appropriate instrument designed to specifically assess emotional reactivity we still assumed that our BD patients showed higher emotional reactivity than the HC. To test whether the negativity bias exhibited by the patients with BD in our study in response to pleasant music could be explained by this difference in emotional reactivity, we included the ERS score as a covariate in our analyses. Interestingly, in the analyses for pieces inducing Wonder, the emotional reactivity measured by the ERS seemed to mediate results for the evaluation of tension, whereas results for the evaluation of sadness remained significant even when we had controlled for the impact of emotional reactivity. The patients' more negative ratings on the tension scale of the emotion induced by the pleasant pieces therefore seems to have been due to their elevated level of emotional reactivity. However, our observation that patients with BD rated the pleasant musical pieces as sadder, compared with the HC cannot entirely be attributed to their higher level of emotional reactivity. This finding suggests that another factor influences patients' tendency to assess this kind of music differently from HC. Given that there is a particular affinity with depression and sad mood in BD, this result seems to be in line with the assumed malfunctioning of patients with BD for sadness.

Regarding emotion regulation strategies in BD, there is the hypothesis that bipolar patients struggle so much to regulate their own positive emotions that it creates a chronic source of distress, which could be experienced as negative emotion (Gruber et al., 2013). In other words, this negative bias in subjective feelings could be a consequence of maladaptive emotion regulation strategies. In a study by Wolkeinstein and colleagues (Wolkenstein et al., 2014), euthymic patients with BD and patients with major depressive disorder (MDD) reported increased rumination, catastrophizing, and self-blame, along with decreased positive reappraisal and perspective-taking, compared with HC. This suggests that deficits in the habitual use of emotion regulation strategies may characterize individuals with BD or MDD, even outside an acute episode, and thereby play a role in the recurrence of affective disorders. In fact, we found a significant difference between the two groups on processing speed (WAIS-III Digit/Symbol-Coding subscore), with a lower mean score for BD patients compared with HC. This executive function deficit could lead to a lack of inhibition of subjective feelings (Banich, 2009) and partly explain these abnormalities in the emotion regulation process. By adding the Code as covariate in the analysis we found that this executive function deficit in BD patients mediated the effect of increased experienced tension when listening to pleasant music. On the other hand, the effect that pleasant music was experienced as sadder in BD patients was not affected by the executive function deficit. These results suggest that an executive function deficit measured as a slowed processing speed in BD patients could be responsible for the increased experience of tension in response to pleasant music, which represents a maladaptive emotion regulation process. Interestingly, the effect of tension in this analysis was not mediated by a deficit in cognitive functioning in general (assessed by the MDRS). However, the finding that BD patients experience music usually inducing joy and wonder as sadder than HC does not seem to be due to such a deficit in processing speed, but another inherent factor in BD seems to sustain the propensity to experience positive stimuli more negative than HC.

However, our study had several limitations. We focused on the subjective feelings that are induced when listening to music. However, the emotional experiences evoked by music are highly subjective, and characterized by considerable interindividual variability. Furthermore, we chose classical music excerpts as auditory stimuli because we wished the latter to be as neutral as possible, in order to avoid potential recognition biases. Inevitably, patients and controls did not all have the same affinity with this type of music, and perceived it differently because of their musical preferences. Furthermore, it is important to note that unfortunately we had a broad spectrum of bipolarity among our patients. Some had very short illness duration or a very late onset. This heterogeneity may have influenced the results, and unfortunately our sample was not large enough to explicitly test the impact of specific clinical aspects. For example, it would have been interesting to test whether the negative bias we found was specific to one type of BD. In addition, as in many other studies, we were not able to include the patients' medication, as the different categories are difficult to compare.

Moreover, some patients were receiving multiple medication. Finally, we found significant differences between the two groups on the MDRS and the PEGA battery. Although the patients' scores were not pathological, they had poorer overall cognitive functioning, as could have been expected. As for their lower scores on the PEGA, these can be attributed to an attentional effect rather than to a sensory deficit.

For future directions, it would be necessary to corroborate our findings with a larger sample and with controlled groups for the type of BD and for medication. Nonetheless, once our results have been replicated, they might serve as markers for bipolar vulnerability, which could be helpful for early diagnosis and treatment. In conclusion, despite finding similar overall emotional patterns in patients and HC, which is what we had expected with this musical paradigm, we observed several differences between the two groups' emotional experience in response to music. The patients with BD exhibited not only a generally increased sensitivity to emotional events, but also a selective bias, such that they were more sensitive to negative emotions, even in response to positive stimuli. This negativity bias for positive emotional stimuli may reflect a specific pattern in the patients' daily lives, and reinforces the clinical reality of BD.

Conflict of interest

The authors report no conflicts of interest.

Author disclosure

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Table 1
Sociodemographic, clinical and psychiatric data for the group of patients with bipolar disorder outside their acute episodes

BD patients	Sex (M/F)	Age (years)	Education Level (years)	Handedness (right/left)	Type (1/2)	Duration of illness (years)	YMRS (max. 60)	MADRS (max. 60)	Mood stabilizer	Dose (mg/day)	Antidepressant	Dose (mg/day)
1	F	50	18	R	I	13	11	8	Quetiapine	700		
2	F	48	15	R	II	6	4	6	Lamotrigine	150		
3	F	37	9	R	I	13	2	5	Olanzapine CR	220 /14 days		
4	F	55	16	R	I	21	3	3	Quetiapine	300	Clomipramine	50
5	F	45	11	R	II	7	4	16	Lamotrigine	250	Clomipramine	50
6	M	39	13	R	I	19	3	4	Lithium CR	1200		
7	M	63	9	R	I	28	0	13	Lamotrigine + Olanzapine	300 + 5		
8	F	62	14	R	I	3	0	2	Lamotrigine + Risperidone	200 + 0.5	Escitalopram	10
9	F	40	15	R	II	18	4	3	Lamotrigine + Quetiapine	400 + 400		
10	F	33	14	R	II	8	1	4	Lamotrigine	300		
11	M	40	12	R	I	7	4	0	Quetiapine	600		
12	F	51	12	R	II	2	2	0	Olanzapine	5		
13	F	62	17	R	II	25	5	3	Lamotrigine	250		
14	F	47	12	R	I	14	2	13	Lithium + Valproate	900 + 1250		
15	F	54	12	R	I	37	3	2	Lithium CR	1000		
16	F	59	11	R	I	4	0	4	Lithium	800		
17	F	43	11	R	I	16	1	2	Lithium + Olanzapine	1200 + 10		
18	M	48	16	L	I	13	8	9	Lithium+Valproate+Quetiapine	1200 + 1500 + 100		
19	F	48	11	R	I	26	1	0	Valpromide	900	Venlafaxine	150
20	F	52	11	L	I	3	2	6	Lithium CR	800	Paroxetine	20
21	M	38.0	17	R	I	14	9	3	Quetiapine + Divalproate	100+1500		

Note. BD = bipolar disorder; duration of illness = length of time since the first symptoms of the first episode (in years); type = type of BD, Type I or II; MADRS = Montgomery–Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; Lithium CR = lithium controlled-release.

Table 2

Emotional reactivity in daily life in the BD group and the HC group

Group	HC	BD	
Scores	Mean ± *SD*	Mean ± *SD*	*p* value
MAThyS	98.5 ± 21.8	107.3 ± 20.3	0.074
SS_reactivity	20.1 ± 4.7	20.8 ± 6.6	0.481
ERS	22.9 ± 11.9	41.2 ± 15.3	< 0.001 ***

Note. HC = healthy controls; BD = bipolar patients; MAThyS = Multidimensional Assessment of Thymic States Scale; SS reactivity = subscore of emotion reactivity; ERS = Emotion Reactivity Scale.
* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

Table 3

Neuropsychological background data for the euthymic bipolar group and the healthy control (HC) group

		HC (n = 21)		Bipolar (n = 21)		Stat. val.(U)	p value
		mean	± *SE*	mean	± SE		
MDRS		142.3	1.6	139.7	3.2	116	< 0.001***
Auditory Memory Spans	direct	5.8	0.97	6.2	1.1	175.5	0.33
	indirect	4.4	1.1	4.1	0.8	179	0.49
WCST	Categories(max = 6)	6.0	0.0	5.7	0.7	168	0.18
	Errors	0.8	1.1	5.0	5.9	129.5	0.01*
	Perseveration errors	0.1	0.2	1.8	2.7	154	0.08
TMT	A (seconds)	33.9	10.4	36.9	14.2	217	0.68
	B (seconds)	70.0	23.1	101.2	58.6	153	0.04*
	B-A (seconds)	33.8	20.2	64.3	50.9	132	0.01*
Verbal Fluency	Phonemic (2 min)	27.9	5.2	20.9	9.0	110.5	0.01*
	Categorical (2min)	34.0	5.7	28.7	8.7	146	0.04*
	Action (Verb)(1min)	16.7	4.6	13.7	6.5	139	0.06
Stroop	Name	76.3	18.7	64.0	10.4	131.5	0.02*
	Colour	100.6	16.3	94.7	14.6	178	0.22
	D/L	42.9	8.5	33.7	13.3	118	0.01*
	Interference	1.2	7.4	-2.3	11.3	191	0.49
PEGA		9.7	0.7	9.3	0.9	136.5	0.03*
WAIS-III Code		74.9	16.1	53.5	14.7	71	< 0.001***

Note. HC = healthy controls; BD = bipolar patients; Stat. val. = statistical values; *df* = degrees of freedom; *SE* = standard error; MDRS = Mattis Dementia Rating Scale; TMT = Trail Making Test; WCST = Wisconsin Card Sorting Test; max. = maximum score; PEGA = Montreal−Toulouse auditory agnosia battery; WAIS-III Code = Wechsler Adult Intelligence Scale-III Digit/Symbol-Coding subtest. p values between bipolar and HC groups are reported (Mann-Whitney test for two independent groups).
* $p < 0.05$. ** $p < 0.0$. *** $p < 0.001$.

Table 4

Mixed model results for the target emotion wonder (wonder baseline) in the euthymic bipolar disorder (BD) group compared with the healthy control (HC) group.

	Estimate ± *SE*	*p* value
BD	0.02 ± 0.18	0.9
Emotion Scales		
Tension	- 0.72 ± 0.14	< 0.001 ***
Joy	- 0.03 ± 0.10	0.7
Nostalgia	- 0.26 ± 0.11	0.021 *
Peacefulness	- 0.12 ± 0.11	0.3
Tenderness	- 0.34 ± 0.11	0.002 **
Transcendence	- 0.27 ± 0.11	0.017 *
Power	- 0.17 ± 0.10	0.1
Sadness	- 1.11 ± 0.19	< 0.001 ***
Group x Scale		
BD x Tension	- 0.75 ± 0.21	< 0.001 ***
BD x Joy	0.00 ± 0.14	1.0
BD x Nostalgia	- 0.07 ± 0.16	0.6
BD x Peacefulness	- 0.07 ± 0.15	0.6
BD x Tenderness	0.11 ± 0.15	0.5
BD x Transcendence	- 0.15 ± 0.16	0.3
BD x Power	0.04 ± 0.15	0.8
BD x Sadness	- 1.10 ± 0.27	< 0.001 ***

Note. * $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

Table 5

Mixed model results for the target emotion Wonder (joy baseline) in the euthymic bipolar disorder group (BD) compared with the healthy control (HC) group.

	Estimate ± *SE*	*p* value
BD	0.02 ± 0.18	0.9
Emotion Scales		
Tension	- 0.68 ± 0.14	< 0.001 ***
Joy	- 0.03 ± 0.10	0.7
Nostalgia	- 0.22 ± 0.11	0.049 *
Peacefulness	- 0.08 ± 0.11	0.5
Tenderness	- 0.30 ± 0.11	0.005 **
Transcendence	- 0.23 ± 0.11	0.039 *
Power	- 0.13 ± 0.10	0.2
Sadness	- 1.07 ± 0.19	< 0.001 ***
Group x Scale		
BD x Tension	- 0.75 ± 0.21	< 0.001 ***
BD x Wonder	0.00 ± 0.14	1.0
BD x Nostalgia	- 0.07 ± 0.16	0.7
BD x Peacefulness	- 0.07 ± 0.15	0.6
BD x Tenderness	0.11 ± 0.15	0.5
BD x Transcendence	- 0.15 ± 0.16	0.3
BD x Power	0.04 ± 0.15	0.8
BD x Sadness	- 1.10 ± 0.27	< 0.001 ***

Note. * $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

Figure 1

Averaged emotion assessments for the three wonder-inducing musical stimuli provided by the patients with bipolar disorder (n = 21) and healthy controls (n = 21). Error bars indicate the standard error.