Metab Brain Dis (2014) 29:367–375
DOI 10.1007/s11011-013-9462-7

ORIGINAL PAPER

Mindfulness based cognitive therapy may improve emotional processing in bipolar disorder: pilot ERP and HRV study

Fleur M. Howells · H. G. Laurie Rauch · Victoria L. Ives-Deliperi · Neil R. Horn · Dan J. Stein

Received: 21 August 2013 / Accepted: 21 November 2013 / Published online: 7 December 2013

Abstract Emotional processing in bipolar disorder (BD) is impaired. We aimed to measure the effects of mindfulness based cognitive-behavioral therapy (MBCT) in BD on emotional processing, as measured by event related potentials (ERP) and by heart rate variability (HRV). ERP and HRV were recorded during the completion of a visual matching task, which included object matching, affect matching, and affect labeling. Individuals with BD ($n=12$) were compared with controls ($n=9$) to obtain baseline data prior to the individuals with BD undergoing an 8-week MBCT intervention. ERP and HRV recording was repeated after the MBCT intervention in BD. Participants with BD had exaggerated ERP N170 amplitude and increased HRV HF peak compared to controls, particularly during the affect matching condition. After an 8-week MBCT intervention, participants with BD showed attenuation of ERP N170 amplitude and reduced HRV HF peak. Our findings support findings from the literature emphasizing that emotional processing in BD is altered, and suggesting that MBCT may improve emotional processing in BD.

Keywords Matching task · Electroencephalography · Heart rate variability · Event-related potentials · N170 amplitude · High frequency peak · Face matching

F. M. Howells · N. R. Horn · D. J. Stein
Department of Psychiatry, Faculty of Health Sciences, University of Cape Town, Observatory 7925, South Africa

H. G. Laurie Rauch · V. L. Ives-Deliperi
Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Observatory 7925, South Africa

F. M. Howells (✉)
Department of Psychiatry, University of Cape Town, Office 105, J-2 Block Old Groote Schuur Hospital, Anzio Road, Observatory 7925, South Africa
e-mail: howellsfleur@gmail.com

Abbreviations

BD	Bipolar disorder
MBCT	Mindfulness based cognitive therapy
EEG	Electroencephalography
HRV	Heart rate variance
ERP	Event related potential
HF	High frequency

Introduction

Bipolar disorder (BD) is characterized by impaired emotional processing, even when mood has been stabilized and the individual is euthymic (Hassel et al. 2008; M'Bailara et al. 2009). Evidence from functional magnetic resonance imaging (fMRI) studies in BD disorder indicate that there are patterns of dis-connectivity between cortical and limbic structures, including the amygdala, during the processing of either positive (happy faces) or negative (angry or fearful faces) emotion (Almeida et al. 2009; Foland et al. 2008; Gruber et al. 2004; Malhi et al. 2007). Further work is, however, needed to determine the electroencephalographic correlates of impaired emotional processing in BD.

An early event related potential (ERP) component, the N170, often referred to as the 'face potential' may be useful in understanding the impaired emotional processing in BD. The 'face potential' is suggested to underlie the structural encoding of faces (Bentin et al. 1996; Eimer et al. 2010) arising from the fusiform gyrus (Deffke et al. 2007; Pizzagalli et al. 2002). The N170 is apparent during the processing of faces and is also evoked during matching of similar objects and words that do not carry any emotional valence (Thierry et al. 2007). However the N170 is even greater when both 'faces' and 'matching' are requisites of the task (Rossion et al. 2003). Exploration of the N170 component in BD is limited to few studies. In one study the authors used an emotional go/no-go task, a measure of behavioral inhibition, and found that in the go conditions individuals with BD showed decreased N170 amplitude compared to controls (Degabriele et al. 2011). A second study used an implicit association task, the dual valence task (DVT), where the participant is asked to classify facial affect or words that are emotionally valent. This study found that the N170 was decreased in BD compared to control participants, and during the simultaneous presentation of a face and a word individuals with BD showed greater response to the word (Ibanez et al. 2012). A third study which required the individual to identify either gender of a face, emotion of a face, else properties of a building, found no differences in the N170 in BD compared to control participants (Wynn et al. 2013). All three studies found no differences in N170 latencies in BD.

Previous work on the N170 ERP in BD has not studied processing of both "faces" and "matching". A task that includes both activation of the 'face potential' and matching of objects and words has been employed by Hariri et al. (2000) which successfully showed the functional activation (fMRI) of cortico-amygdala circuitry in healthy controls (Hariri et al. 2000) . This affect matching task is comprised of three matching conditions (object matching, affect matching, and affect labeling) and can be readily applied in an event-related potential EEG study, to address the N170 amplitude. Assessment of the N170 using such a task, may provide new insights on emotional processing in BD.

Within the peripheral nervous system, the high frequency (HF) peak of heart rate variability (HRV) is affected by mood (Hughes and Stoney 2000), and is suggested to serve as a marker of emotional regulation (Telles et al. 2011) however is often underutilized in psychiatric research (Henry et al. 2010). Interactions between the amygdala and cortex are known to modulate the hypothalamus and periaquaductal grey (Berntson et al. 1998; Green and Paterson 2008), via the caudal and rostral ventrolateral medullary brain areas, that closely abutt the rhythm generating pre-Botzinger complex forming part of the ventral respiratory group in the lower brain stem (Green and Paterson 2008), and controls breathing frequency (Spyer and Gourine 2009). The HRV HF peak is a marker of breathing frequency (Gilbey et al. 1984; Hirsch and Bishop 1981) and is therefore under indirect modulatory control of cortical-amygdala neurocircuitry. It is useful to incorporate HRV HF as a peripheral measure of emotional regulation in ERP studies where emotional processing is being investigated.

Mindfulness Based Cognitive Therapy (MBCT) combines meditative practices and aspects of cognitive behavioral therapy, and may be useful in addressing impaired emotional processing in BD (Miller et al. 1995). The aim of meditative practices is to "reduce or eliminate irrelevant thought processes through training of internalized attention" (Rubia 2009). Indeed, pilot studies of MBCT in BD have reported improvement of depressive symptoms (Miklowitz et al. 2010; Williams et al. 2008), manic symptoms, anxiety and suicidal ideation (Miklowitz et al. 2010), improved mindfulness (Ives-Deliperi et al. 2013), and attentional readiness (Howells et al. 2012). In addition MBCT has already been shown to improved ERP contingent negative variation (Ikemi 1988; Travis et al. 2002) and decreased HRV HF (Telles et al. 2011) in healthy controls.

In the present study we aimed to determine the effects of MBCT in BD on emotional processing, as measured centrally by the ERP N170 amplitude and peripherally by the HRV HF peak. We hypothesized that (1) individuals with BD would show deficits in emotional processing, as reflected in alterations in ERP N170 amplitude and HRV HF peak during the completion of a matching task that includes affect, and (2) MBCT would improve emotional processing, as evidenced by normalization in ERP N170 amplitude and HRV HF peak.

Methods

Participants

Twenty-one participants were recruited for the present study. Twelve individuals with euthymic bipolar I disorder (age 37±7.3 years, 10 females and 2 males) and 9 control individuals (age 29±6.4 years, 7 females and 2 males) with no prior psychiatric history and no reported first degree relatives with a mood disorder. The study was approved by the Faculty of Health Sciences Human Ethics Committee of the University of Cape Town, and the participants signed informed consent. The study was conducted in accordance with the Declaration of Helsinki (WMA General Assembly 2000).

All BD participants were receiving mood stabilizers, with 8 receiving lithium. Other prescribed medications included antipsychotics (8 participants), antidepressant (2 participants), and or anxyolytic (2 participants) medications. Medications were held constant throughout the present study. Comorbidities present in the BD cohort included: impulse control disorders (1 participant with trichotillomania and with compulsive buying, 1 participant with compulsive buying), anxiety disorders (3 participants with panic disorder and agoraphobia), and substance abuse disorders (1 participant with a past history of alcohol and cannabis dependence, 1 participant with a past history of benzodiazepine and diet pill dependency, 1 participant with current alcohol abuse).

Experimental design

Each of the participants underwent a Structured Clinical Interview (SCID) for DSM-IV Disorders, to confirm the diagnosis of bipolar 1 disorder and to exclude psychiatric disorders in the control group. Each of the participants completed a visual matching task, during which time they underwent electrophysiological record of brain wave activity (electroencephalography (EEG)) and cardiac activity (electrocardiography (ECG)). The participants with BD then completed an 8-week MBCT intervention; thereafter the visual matching task and electrophysiological recording were repeated.

Each testing day, clinical scales were administered; these included the Young Mania Rating Scale (YMRS) (Young et al. 1978) and the Hospital Anxiety and Depression Scale (HADS) (Snaith and Zigmond 1986) in order to confirm mood state, i.e. euthymic state was an inclusion criterion. The electrophysiological data was obtained within an hour session, between 09h00 and 13h30. The recording session was completed in a quiet, dimly lit room to reduce distraction. The researcher conducting the experiments was with the participant at all times during the testing. All stages of the testing session were programmed in Eprime 1.1, which sent digital inputs of stimuli to Acqknowledge 4.1 (Biopac Systems Inc.) software, via an MP150 Biopac acquisition system, that also collected the EEG (EEG 100C amplifier modules, with an electro-oculogram (EOG) amplifier) and ECG data (ECG 100C amplifier module).

Matching task

The visual matching task was adapted from Hariri et al. 2000 (Hariri et al. 2000). The paradigm consisted of seven experimental blocks: three blocks of object matching (20 trials per block) were interwoven with two blocks of affect matching (30 trials per block) and two blocks of affect labeling (30 trails per block), i.e. for each condition the participant completed 60 trials. Stimuli were presented for a maximum of 5000 msec or until the participant had responded to presented trial. Inter-stimuli were present between trials, a blank screen, for 1500 msec. A counter-balance number of either scared or happy or angry facial expressions were used. Each time a participant completed the task, the images within the each condition were different and the correct number of trails and counter-balance of images were presented. Balance of ethnicity was also included (Ekman and Friesen 1978).

Electrophysiological recordings

EEG data were collected to determine ERP waveforms, and ECG data were collected to determine HRV measures, using a Biopac Acquisition system.

Electroencephalography (EEG)

A standard 10/20 linked ears reference montage EEG system was used, the individuals were grounded peripherally, through the ECG amplifier. Brain frequency activity and event-related potentials (ERPs) were obtained from: F_3, F_4, C_3, C_4, P_3, and P_4. The data was sampled at 500 Hz and band pass filtered FIR with a Hamming window (0.5–30 Hz). Electrooculography (EOG) data were used to assist in removal of EOG artifact, through an automated independent component analysis within Acqknowledge 4.1.

To obtain the ERP waveforms from the matching task, epochs 200 msec prior to stimulus and 800 msec post target presentation were extracted to give a 1 s window. This was performed for object matching trials, affect matching trials, and affect labeling trials. The extraction was set to reject ERPs that had deflections greater than +100 μV or less than −100 μV. This was then followed by visual inspection of the averaged ERP of each participant. The average individual ERP was baseline corrected for 200 msec prior to stimulus presentation. ERPs for each of the conditions was visually inspected and the N170 (100–250 msec window) wave component was extracted.

Electrocardiogram (ECG)

ECG activity was recorded with three electrodes, positioned as per Eindhoven's triangle, and ECG lead II was used for the analysis. The data were sampled at 500 Hz and band pass filtered 0.5–35 Hz. HRV data were analyzed from the R-R interval tachograms derived from the ECG traces using Acqknowledge 4.1 software. Tachograms were extracted for each condition of the task; this was achieved by removing data of the two conditions that did not pertain to the condition under analysis. The tachograms were visually inspected to determine correct recognition of QRS complexes; missed and ectopic beats were corrected. A 250 s tachogram was used for the HRV analysis with software from the Biomedical Signal Analysis Group (Department of Applied Physics, University of Kuopio, Finland); an autoregressive model order of 16 with an interpolation rate of 5 Hz was used.

We calculated the low frequency (LF) power in the 0.04–0.15 Hz band and the high frequency (HF) power in the 0.15–0.4 Hz band in $msec^2$. The calculated $msec^2$ power values for LF and HF were transformed via natural logarithm to normalize the distributions, and this is reported as InLF, and InHF. In addition, peak frequencies were calculated in both the LF and HF bands (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). The HRV frequency domain analyses were conducted for each of the matching task's conditions: object matching, affect matching, and affect labeling.

Mindfulness based cognitive therapy (MBCT)

A previously developed 8-week MBCT program for major depression was used (Segal et al. 2002; Williams et al. 2008). The program was modified to include psychoeducation and focused on the early warning signs of mania (Williams et al. 2008). The MBCT intervention was led by an experienced therapist with recognized expertise in the delivery of cognitive therapy and MBCT. During their participation in the present study, participants were encouraged to continue with all of their outpatient appointments, medications and other services. None of the participants reported using non-MBCT meditation or yoga for therapeutic purposes during their participation in the present study.

Statistical analysis

Statistica 10 (StatSoft Incorporated 2011) was used for the statistical analyses. To determine differences between the BD and healthy control groups, independent-sample t-tests were performed. To determine the effects of MBCT in BD, EEG and ECG measures were compared before and after treatment using dependent-sample t-tests. To determine differences across the three task conditions, Friedman ANOVAs were performed, as the data was non-parametrically distributed, and if significant were followed by Wilcoxon Matched Pairs tests.

Results

The individuals with BD reported higher mean Young Mania Rating Scale (YMRS) scores (3.41±3.02) than controls ($P<0.001$). There were no significant differences in the Hospital Anxiety ($bipolar_{anxiety}$ = 8.41±4.48, $control_{anxiety}$ = 7.33±4.58) and Depression ($bipolar_{depression}$ = 5.08±2.93, $control_{depression}$ = 3.33±2.59) rating scores between the groups. After MBCT, individuals with BD showed no change in the Hospital Anxiety and Depression rating scores or in their YMRS scores, indicative of stable euthymia.

Electrophysiological group differences

ERP N170

During object matching individuals with BD showed significantly increased N170 amplitude over the right frontal cortex (F_4 $t=-2.4$; $p<0.05$), bilateral central cortices (C_3 $t=-3.37$, C_4 $t=-3.13$; $p<0.05$), and bilateral parietal cortices (P_3 $t=-2.65$, P_4 $t=-2.22$; $p<0.05$) compared with controls (Fig. 1). Compared with baseline findings, after MBCT, BD individuals showed decreased N170 amplitude over the left frontal (F_3 $t=3.6$; diff = 8.01, Std.Dv.Diff = 7.71; $p<0.05$) and left central cortices (C_3 $t=2.72$, diff = 3.28, Std.Dv.Diff = 4.18; $p<0.05$). No differences were found in N170 latencies (Fig. 1).

During affect matching individuals with BD showed increased N170 amplitudes bilaterally over frontal cortices (F_3 $t=-2.45$, F_4 $t=-2.36$; $p<0.05$), central cortices (C_3 $t=-2.51$, C_4 $t=-2.4$; $p<0.05$), and parietal cortices (P_3 $t=-2.73$, P_4 $t=-3.37$; $p<0.05$) compared with controls (Fig. 2). Compared with baseline findings, after MBCT, BD individuals showed decreased N170 amplitude bilaterally over frontal cortices (F_3 $t=2.32$, diff = 11.86, Std.Dv.Diff = 17.65; F_4 $t=2.38$, diff = 12.59, Std.Dv.Diff = 18.33; $p<0.05$), central cortices (C_3 $t=2.47$, diff = 12.69, Std.Dv.Diff = 17.8; C_4 $t=2.38$, diff = 11.8, Std.Dv.Diff = 17.18; $p<0.05$), and parietal cortices (P_3 $t=2.43$, diff = 11.83, Std.Dv.Diff = 16.82; P_4 $t=2.9$, diff = 11.63, Std.Dv.Diff = 13.88; $p<0.05$). No differences were found in N170 latencies (Fig. 2).

During affect labeling individuals with BD showed increased N170 amplitude bilaterally over parietal cortices (P_3 $t=-2.23$, P_4 $t=-3.26$; $p<0.05$) compared with controls

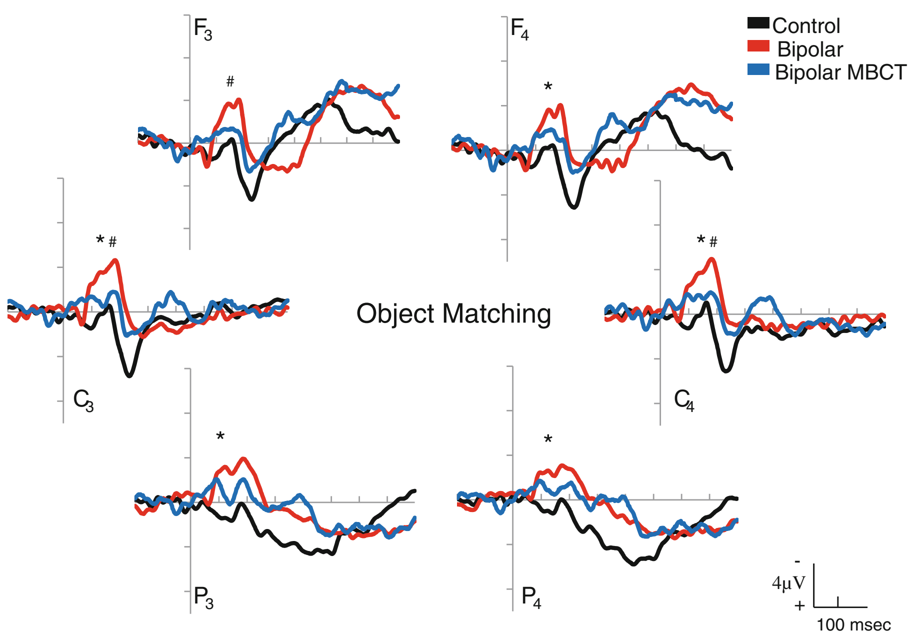

Fig. 1 Object matching grand mean event-related potentials (ERPs) for frontal (F_3 & F_4), central (C_3 & C_4), and parietal (P_3 & P_4) cortices. *Individuals with bipolar disorder showed greater N170 amplitudes over the right frontal cortex, central cortices, and parietal cortices compared with control participants. #Post MBCT individuals with bipolar disorder showed attenuated N170 responses over the left frontal and central cortices ($p<0.05$, $Controls_n$ = 9, $Bipolar_n$ = 12)

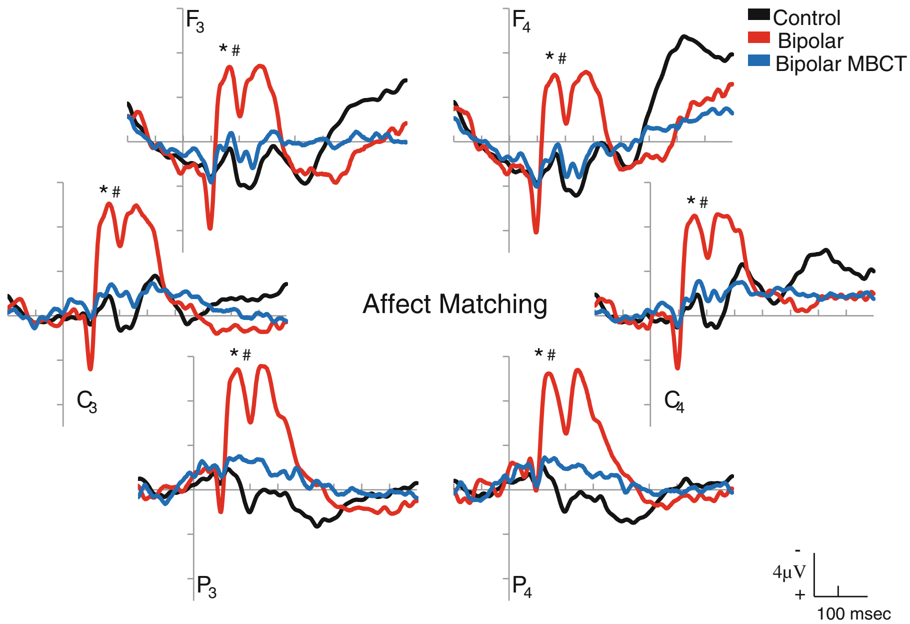

Fig. 2 Affect matching grand mean event-related potentials (ERPs) for frontal (F_3 & F_4), central (C_3 & C_4), and parietal (P_3 & P_4) cortices. *Individuals with bipolar disorder showed greater N170 amplitudes for all electrodes compared with control participants. #Post MBCT individuals with bipolar disorder showed attenuation of the N170 response for all electrodes. Within the bipolar prior to MBCT intervention affect matching N170 response was greater than their object matching or their affect labeling N170 response ($p<0.05$, $\text{Controls}_n = 9$, $\text{Bipolar}_n = 12$)

(Fig. 3). Compared with baseline findings, after MBCT, BD individuals showed decreased N170 amplitude bilaterally over parietal cortices (P_3 $t=2.21$, diff = 4.14, Std.Dv.Diff = 6.48; P_4 $t=2.41$, diff = 3.87, Std.Dv.Diff = 5.56; $p<0.05$). No differences were found in N170 latencies (Fig. 3).

HRV

During object matching individuals with BD showed a tendency for increased HF peaks in their HRV spectrograms ($t=-2.11$; $p=0.051$) compared with controls (Table 1). Compared with baseline findings, after MBCT, BD individuals showed a significant decrease in their HF peak during object matching ($t=2.45$, diff = 0.05, Std.Dv.Diff = 0.068; $p<0.05$) (Table 1).

During affect matching individuals with BD showed a significantly increased HF peaks ($t=-2.14$; $p<0.05$) compared with controls (Table 1). Compared with baseline findings, after MBCT, BD individuals showed a significant decrease in their HF peak during affect matching ($t=3.06$, diff = 0.032, Std.Dv.Diff = 0.04; $p<0.05$) (Table 1).

During affect labeling individuals with BD showed no differences when compared with controls (Table 1). However, compared with baseline findings, after MBCT, both

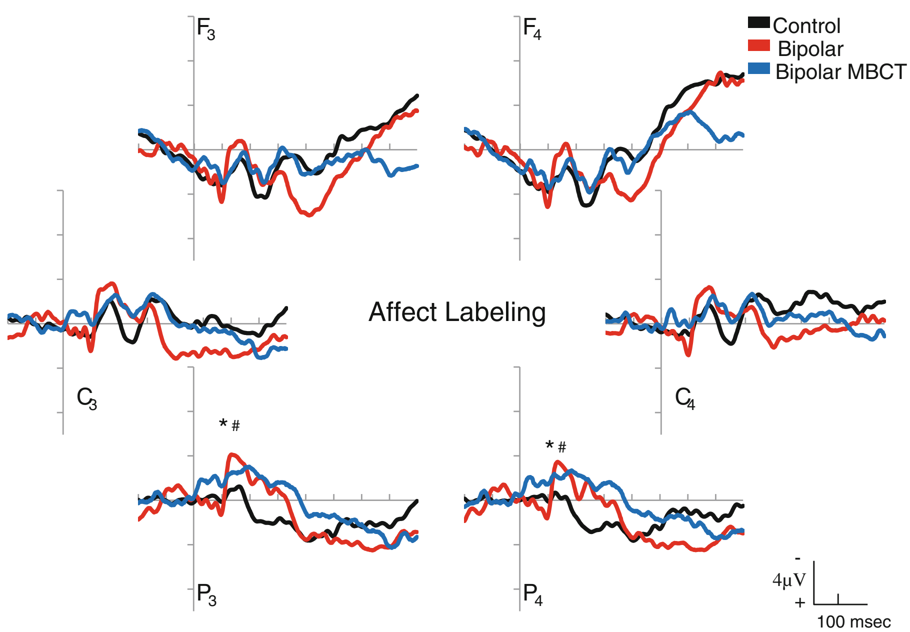

Fig. 3 Affect labeling grand mean event-related potentials (ERPs) for frontal (F_3 & F_4), central (C_3 & C_4), and parietal (P_3 & P_4) cortices. *Individuals with bipolar disorder showed greater N170 response over the parietal cortex compared with controls. #Post MBCT individuals with bipolar disorder showed attenuation of the N170 response over the parietal cortices. Within the bipolar prior to MBCT intervention affect labeling N170 response was greater than their object matching N170 response ($p<0.05$, $\text{Controls}_n = 9$, $\text{Bipolar}_n = 12$)

Table 1 Heart rate variability (HRV) frequency domain variables for control participants, individuals with bipolar disorder prior and post mindfulness based cognitive therapy during the completion of a matching task's conditions

	Object matching						Affect matching						Affect labeling					
	Control		Bipolar		Bipolar MBCT		Control		Bipolar		Bipolar MBCT		Control		Bipolar		Bipolar MBCT	
	MEAN	*STDDEV*	MEAN	*STDDEV*	MEAN	*STDDEV*	MEAN	*STDDEV*	MEAN	*STDDEV*	MEAN	*STDDEV*	MEAN	*STDDEV*	MEAN	*STDDEV*	MEAN	*STDDEV*
Natural log of low frequency power (ln.msec^2)	5.48	*0.56*	5.19	*1.07*	5.04	*1.45*	4.94	*0.45*	4.86	*0.79*	4.70	*1.57*	5.44	*0.36*	5.01	*1.02*	5.04	*1.32*
Natural log of high frequency power (ln.msec^2)	4.54	*1.32*	4.41	*1.10*	4.16	*1.29*	4.81	*1.30*	4.50	*0.58*	4.47	*1.15*	4.51	*1.31*	4.24	*0.60*	4.39	*1.00*
Low frequency peak (0.04–0.0.15 Hz, msec^2)	0.10	*0.03*	0.09	*0.02*	0.09	*0.02*	0.10	*0.01*	0.09	*0.02*	0.09	*0.02*	0.09	*0.02*	0.10	*0.01*	$^{\#}$ 0.09	*0.02*
High frequency peak (0.15–0.4 Hz, msec^2)	0.25	*0.05*	^{t} 0.31	*0.07*	$^{\#}$ 0.26	*0.04*	0.26	*0.05*	* 0.31	*0.04*	$^{\#}$ 0.28	*0.03*	0.27	*0.04*	0.30	*0.04*	$^{\#}$ 0.26	*0.04*

*Significant differences and ^{t} tendency towards significant difference between control participants and participants with bipolar disorder and task conditions. $^{\#}$ Significant differences between participants with bipolar disorder prior and post mindfulness based cognitive therapy for task conditions. nControl = 9, nBipolar = 12, nBipolar MBCT = 12, p <0.05 and t <0.1

the HF and LF peaks in the cardiac spectrogram of the BD individuals decreased (HF peak $t = 2.54$, diff = 0.03, Std.Dv.Diff = 0.042; LF peak $t = 2.71$, Diff = 0.01, Std.Dv.Diff. = 0.015; $p < 0.05$) (Table 1).

Physiological within group task condition differences

ERP N170

Prior to MBCT individuals with BD showed differences in ERP N170 amplitudes between the task's conditions for frontal, central, and parietal electrodes (F_3 Chi $Sqr_{(2,11)} = 10.17$, F_4 Chi $Sqr_{(2,11)} = 8.67$, C_3 Chi $Sqr_{(2,11)} = 8.67$, C_4, Chi $Sqr_{(2,11)} = 8.67$, P_3 Chi $Sqr_{(2,11)} = 14.0$, P4 Chi $Sqr_{(2,11)} = 12.17$, $p < 0.05$). Further analysis revealed N170 amplitude for affect matching was greater compared with object matching and affect labeling conditions for all electrodes (F_3, F_4, C_3, C_4, P_3, P_4). In addition, over the parietal cortices (P3 & P4) N170 amplitude was greater for affect labeling than object matching within the bipolar group (Table 2).

Within both the control group, and within the BD group assessed after MBCT, no differences in ERP N170 wave component were found between task conditions (OM, AM, AL) (Table 2).

HRV

In individuals with BD assessed after MBCT, there were significant differences in the HF peaks of the HRV spectrograms across the task's conditions (Chi $Sqr_{(2,11)} = 6.36$; $p < 0.05$), such that the affect matching HF peak was greater than object matching and affect labeling HF peaks (Table 2).

Within both the control group and the BD group prior to MBCT, no differences in HRV measures were found between task conditions (Table 2).

Discussion

The main findings of the present paper are: (1) emotional processing in BD was impaired, as evidenced by increased ERP N170 amplitude and increased HRV HF peak compared with controls; (2) MBCT improved emotional processing in BD, as evidenced by decreased ERP N170 amplitude and decreased HRV HF peak.

Emotional processing in bipolar disorder

Impaired emotional processing was apparent in the BD participants when compared with control participants. This was evidenced by an exaggerated physiological response to the affect matching condition, with increased ERP N170 amplitude and increased HRV HF peak in BD. The N170 amplitude and HF peak can be viewed as indirect measures of the modulatory control achieved by communication between cortex and amygdala during emotional processing (Ahs et al. 2009; Hariri et al. 2000).

During the affect matching condition, the participant was required to match a central face bearing emotional valence with a face of similar emotional valence (having a choice of two faces to choose from), the N170 wave component was greater in BD than controls (Fig. 2) and it was greater when compared with object matching and affect labeling (Table 2). Classically the N170 ERP wave component is measured over the temporal cortex with mastoid references (Jeffreys and Tukmachi 1992), however our aim was to assess the involvement of the frontal cortex, including the dorsolateral prefrontal cortex (frontal EEG electrodes) and anterior cingulate cortex (central EEG electrodes). Previous studies in BD that have explored the N170 ERP component have not employed the combination of affect and matching, their studies found decrease N170 ERP component, which may seem contradictory however they address different cognitive processes (Degabriele et al. 2011; Ibanez et al. 2012; Wynn et al. 2013). These data support the reported dysfunction of emotional processing in BD.

HRV HF peak was increased in BD, supporting the use of peripheral measures of arousal in the study of emotional processing (Gilbey et al. 1984; Hirsch and Bishop 1981; Telles et al. 2011), supporting the involvement of the cortico-limbic pathways that have been reported in fMRI studies of emotional processing in BD (Almeida et al. 2009; Foland et al. 2008; Gruber et al. 2004). Further use of HRV parameters may serve well in understanding emotional processing and its deficits.

Table 2 Event related potential (ERP) N170 and Heart rate variability (HRV) parameter differences between task conditions and within groups: control participants, individuals with bipolar disorder prior and post mindfulness based cognitive therapy

	Object matching vs. Affect matching	Object matching vs. Affect labeling	Affect matching vs. Affect labeling
Control	~	~	~
Bipolar prior to MBCT	for all EEG electrodes N170 OM < AM	for P3 & P4 electrodes N170 OM < AL	for all EEG electrodes N170 AM > AL
Bipolar post MBCT	HRV High frequency peak OM < AM	~	HRV High frequency peak AM > AL

Significant event-related potential N170 and heart rate variability differences between task conditions within groups (control participants, individuals with bipolar disorder, and individuals with bipolar disorder post mindfulness based cognitive therapy). nControl = 9, nBipolar = 12, nBipolar MBCT = 12, $p < 0.05$

Emotional processing in bipolar disorder is improved by mindfulness based cognitive therapy

MBCT improved emotional processing in BD, as measured by the attenuation of the N170 amplitude and decreased HRV HF peak. The exaggerated physiological response to emotional processing in BD (Table 2), as seen by the increased ERP N170 amplitude and increased HRV HF peak, were attenuated after MBCT (Fig. 2, Table 1). There have been few studies on the physiological effects of MBCT, with a single study showing improvement of attentional readiness and attenuation of non-relevant information processing during attentional processes on EEG (Howells et al. 2012). However, meditative practices have shown attenuation of ERP contingent negative variation (Ikemi 1988; Travis et al. 2002) and attenuation of HF HRV in healthy individuals (Telles et al. 2011). Our findings are consistent with this work, and extend it by showing that MBCT led to attenuation of an exaggerated N170 amplitude and decreased HRV HF peak in BD. However further study is required to understand the underlying physiological mechanisms by which MBCT facilitates these changes.

Limitations

First, although medication was stable in the BD group, we did not assess the effects of medication on EEG and/or ECG measures, primarily due to our limited number of participants in this pilot study. Second, mood was also stable in the BD cohort, however previous studies report improved depression and anxiety ratings (Deckersbach et al. 2012; Ives-Deliperi et al. 2013; Segal et al. 2002; Williams et al. 2008), our results may be superficially seen as lack of MBCT effect due to study design, however our physiological findings support changes in neural systems of emotional processing. Third, the healthy control group did not undergo MBCT and were not age-matched, which limits our understanding of the effects of MBCT on EEG and ECG measures. Fourth, these investigations are applied techniques and do not directly assess the cortico-amygdala network activity and caution should be applied in accepting the presented findings. Fifth, greater fidelity is required in administration of MBCT intervention, resources to ensure that this is possible are a major consideration for future large scale studies (Crane et al. 2012; Weck et al. 2011). Finally, the limited number of participants and design of the present study was severely lacking (Kraemer et al. 2002) - however this study provides further proof of concept towards large scale studies that will be able to address emotional processing in BD by using multimodal physiological record, and the effects of MBCT, not only at a self-report or clinical level but directly addressing changes within the individuals physiology.

Conclusions

This pilot study provides novel neurophysiological data on the mechanisms underlying the effects of MBCT on emotional processing in BD. The findings support a previous literature emphasizing impairment in emotional processing in BD, and indicate that MBCT led to improvement of emotional processing in BD, as assessed by N170 amplitude and HRV HF peak. Further study is required to understand comprehensively the neurobiological mechanisms which underlie these specific changes

Acknowledgments The authors wish to thank the International Society of Affective Disorders (ISAN) for funding the present project (PIs VI-D and NRH). FMH wishes to thank the Brain and Behavior Initiative, the Research Committee of the University of Cape Town and the National Research Foundation Innovation postdoctoral fellowships during the time in which this project was conducted. The authors are also grateful to the Department of Human Genetics, and Professor Rajkumar Ramesar, for access to their research cohort, and Sister Gameda Benefeld for her time and clinical diagnoses of participants; Dr Matthew Watkins, clinical psychologist, for implementing the MBCT intervention in the present study; Ms Candice Kotze, research assistant, for her great efforts in the logistical organization and during the data collection period of the present study; and Dr Leesha Singh, psychiatrist, for her time in verifying participants' psychiatric diagnoses. In addition, we would like to thank the research participants for their time and effort as part of this pilot study of MBCT in BD.

Competing interests Authors declare that there are no conflicts of interest related to the present paper.

References

Ahs F, Sollers JJ 3rd, Furmark T, Fredrikson M, Thayer JF (2009) High-frequency heart rate variability and cortico-striatal activity in men and women with social phobia. Neuroimage 47:815–820

Almeida JR, Versace A, Mechelli A, Hassel S, Quevedo K, Kupfer DJ, Phillips ML (2009) Abnormal amygdala-prefrontal effective connectivity to happy faces differentiates bipolar from major depression. Biol Psychiatry 66:451–459

Bentin S, Allison T, Puce A, Perez E, McCarthy G (1996) Electrophysiological studies of face perception in humans. J Cogn Neurosci 8:551–565

Berntson GG, Sarter M, Cacioppo JT (1998) Anxiety and cardiovascular reactivity: the basal forebrain cholinergic link. Behav Brain Res 94: 225–248

Crane RS, Kuyken W, Williams JM, Hastings RP, Cooper L, Fennell MJ (2012) Competence in teaching mindfulness-based courses: concepts, development and assessment. Mindfulness (N Y) 3:76–84

Deckersbach T, Holzel BK, Eisner LR, Stange JP, Peckham AD, Dougherty DD, Rauch SL, Lazar S, Nierenberg AA (2012) Mindfulness-based cognitive therapy for nonremitted patients with bipolar disorder. CNS Neurosci Ther 18:133–141

Deffke I, Sander T, Heidenreich J, Sommer W, Curio G, Trahms L, Lueschow A (2007) MEG/EEG sources of the 170-ms response to faces are co-localized in the fusiform gyrus. Neuroimage 35:1495–1501

Degabriele R, Lagopoulos J, Malhi G (2011) Neural correlates of emotional face processing in bipolar disorder: an event-related potential study. J Affect Disord 133:212–220

Eimer M, Kiss M, Nicholas S (2010) Response profile of the face-sensitive N170 component: a rapid adaptation study. Cereb Cortex 20:2442–2452

Ekman P, Friesen WV (1978) Facial action coding systems (FACS): a technique for the measurement of facial action. Consulting Psychologists Press, Palo Alto

Foland LC, Altshuler LL, Bookheimer SY, Eisenberger N, Townsend J, Thompson PM (2008) Evidence for deficient modulation of amygdala response by prefrontal cortex in bipolar mania. Psychiatry Res 162:27–37

Gilbey MP, Jordan D, Richter DW, Spyer KM (1984) Synaptic mechanisms involved in the inspiratory modulation of vagal cardio-inhibitory neurones in the cat. J Physiol 356:65–78

Green AL, Paterson DJ (2008) Identification of neurocircuitry controlling cardiovascular function in humans using functional neurosurgery: implications for exercise control. Exp Physiol 93:1022–1028

Gruber SA, Rogowska J, Yurgelun-Todd DA (2004) Decreased activation of the anterior cingulate in bipolar patients: an fMRI study. J Affect Disord 82:191–201

Hariri AR, Bookheimer SY, Mazziotta JC (2000) Modulating emotional responses: effects of a neocortical network on the limbic system. Neuroreport 11:43–48

Hassel S, Almeida JR, Kerr N, Nau S, Ladouceur CD, Fissell K, Kupfer DJ, Phillips ML (2008) Elevated striatal and decreased dorsolateral prefrontal cortical activity in response to emotional stimuli in euthymic bipolar disorder: no associations with psychotropic medication load. Bipolar Disord 10:916–927

Henry BL, Minassian A, Paulus MP, Geyer MA, Perry W (2010) Heart rate variability in bipolar mania and schizophrenia. J Psychiatr Res 44:168–176

Hirsch JA, Bishop B (1981) Respiratory sinus arrhythmia in humans: how breathing pattern modulates heart rate. Am J Physiol 241: H620–H629

Howells FM, Ives-Deliperi VL, Horn NR, Stein DJ (2012) Mindfulness based cognitive therapy improves frontal control in bipolar disorder: a pilot EEG study. BMC Psychiatry 12:15

Hughes JW, Stoney CM (2000) Depressed mood is related to high-frequency heart rate variability during stressors. Psychosom Med 62:796–803

Ibanez A, Urquina H, Petroni A, Baez S, Lopez V, do Nascimento M, Herrera E, Guex R, Hurtado E, Blenkmann A, Beltrachini L, Gelormini C, Sigman M, Lischinsky A, Torralva T, Torrente F, Cetkovich M, Manes F (2012) Neural processing of emotional facial and semantic expressions in euthymic bipolar disorder (BD) and its association with theory of mind (ToM). PLoS One 7:e46877

Ikemi A (1988) Psychophysiological effects of self-regulation method: EEG frequency analysis and contingent negative variations. Psychother Psychosom 49:230–239

Ives-Deliperi VL, Howells F, Stein DJ, Meintjes EM, Horn N (2013) The effects of mindfulness-based cognitive therapy in patients with bipolar disorder: a controlled functional MRI investigation. J Affect Disord

Jeffreys DA, Tukmachi ES (1992) The vertex-positive scalp potential evoked by faces and by objects. Exp Brain Res 91:340–350

Kraemer HC, Wilson GT, Fairburn CG, Agras WS (2002) Mediators and moderators of treatment effects in randomized clinical trials. Arch Gen Psychiatry 59:877–883

M'Bailara K, Chevrier F, Dutertre T, Demotes-Mainard J, Swendsen J, Henry C (2009) Emotional reactivity in euthymic bipolar patients. Encéphale 35:484–490

Malhi GS, Lagopoulos J, Sachdev PS, Ivanovski B, Shnier R, Ketter T (2007) Is a lack of disgust something to fear? A functional magnetic resonance imaging facial emotion recognition study in euthymic bipolar disorder patients. Bipolar Disord 9:345–357

Miklowitz DJ, Alatiq Y, Geddes JR, Goodwin GM, Williams JM (2010) Thought suppression in patients with bipolar disorder. J Abnorm Psychol 119:355–365

Miller JJ, Fletcher K, Kabat-Zinn J (1995) Three-year follow-up and clinical implications of a mindfulness meditation-based stress reduction intervention in the treatment of anxiety disorders. Gen Hosp Psychiatry 17:192–200

Pizzagalli DA, Lehmann D, Hendrick AM, Regard M, Pascual-Marqui RD, Davidson RJ (2002) Affective judgments of faces modulate early activity (approximately 160 ms) within the fusiform gyri. Neuroimage 16:663–677

Rossion B, Joyce CA, Cottrell GW, Tarr MJ (2003) Early lateralization and orientation tuning for face, word, and object processing in the visual cortex. Neuroimage 20:1609–1624

Rubia K (2009) The neurobiology of meditation and its clinical effectiveness in psychiatric disorders. Biol Psychol 82:1–11

Segal ZV, Williams JMG, Teasdale JD (2002) Mindfulness-base cognitive therapy for depression: a new approach to preventing relapse

Snaith RP, Zigmond AS (1986) The hospital anxiety and depression scale. Br Med J (Clin Res Ed) 292:344

Spyer KM, Gourine AV (2009) Chemosensory pathways in the brainstem controlling cardiorespiratory activity. Philos Trans R Soc Lond B Biol Sci 364:2603–2610

StatSoft Incorporated (2011) STATISTICA data analysis software system. 10

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) Heart rate variability: standards of measurement, physiological interpretation, and clinical use. Eur Heart J 17:354–381

Telles S, Singh N, Balkrishna A (2011) Heart rate variability changes during high frequency yoga breathing and breath awareness. Biopsychosoc Med 5:4

Thierry G, Martin CD, Downing P, Pegna AJ (2007) Controlling for interstimulus perceptual variance abolishes N170 face selectivity. Nat Neurosci 10:505–511

Travis F, Tecce J, Arenander A, Wallace RK (2002) Patterns of EEG coherence, power, and contingent negative variation characterize the integration of transcendental and waking states. Biol Psychol 61: 293–319

Weck F, Bohn C, Ginzburg DM, Stangier U (2011) Assessment of adherence and competence in cognitive therapy: comparing session segments with entire sessions. Psychother Res 21:658–669

Williams JM, Alatiq Y, Crane C, Barnhofer T, Fennell MJ, Duggan DS, Hepburn S, Goodwin GM (2008) Mindfulness-based cognitive therapy (MBCT) in bipolar disorder: preliminary evaluation of immediate effects on between-episode functioning. J Affect Disord 107:275–279

WMA General Assembly (2000) World medical association declaration of Helsinki: ethical principles for medical research involving human subjects. Adopted by the 18th WMA general assembly, Helsinki, Finland, June 1964, and amended by the 52nd WMA general assembly, Edinburgh, Scotland, October 2000

Wynn JK, Jahshan C, Altshuler LL, Glahn DC, Green MF (2013) Event-related potential examination of facial affect processing in bipolar disorder and schizophrenia. Psychol Med 43:109–117

Young RC, Biggs JT, Ziegler VE, Meyer DA (1978) A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry 133:429–435

Authors' contributions

FH developed the EEG and HRV protocol, undertook the EEGs, analyzed the EEG data, and drafted the manuscript. HGLR analyzed the HRV data and contributed to writing of the manuscript. NH and VID designed the broader study of BD within which this protocol fell, recruited and evaluated participants, and commented on the manuscript. DS gave input on both the design of the broader bipolar protocol and the current EEG protocol, and contributed to the writing of the manuscript.