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Remembering that Neutral Feeling? Enhanced Memory for Neutral, but not Positive or Negative, Emotional Stimuli in Bipolar I Disorder

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Abstract

Bipolar disorder (BD) is a chronic psychiatric disorder that is associated with heightened and persistent positive emotion (Gruber, 2011; Johnson, 2005). Yet we know less about underlying cognitive processes that may influence these observed biases in emotionality. One promising approach is to examine cognitive processes, such as declarative memory, that may serve as an important window into understanding how individuals with BD remember emotion-laden stimuli. The current study presented standardized positive, negative and neutral emotion eliciting images to remitted BD I adults (*n*=26) and healthy controls (CTL; *n*=24) and measured accuracy in recall after a subsequent 60-minute delay period. Results suggest that the BD group exhibited increased memory accuracy for neutral images compared to the CTL group; however, groups did not differ in positive or negative memory accuracy. Findings may provide insight into potential cognitive processes that maintain heightened positive emotional responding in BD.

Keywords: emotion, memory, bipolar disorder

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Bipolar disorder (BD) is a severe and chronic psychiatric illness that often causes impairment in multiple domains of life (Coryell et al., 1993) and has been ranked as one of the top ten causes of disability worldwide (e.g., Murray, Lopez, & Lopez, 1996). Recent laboratory-based models stress the importance of emotion regulation difficulties in BD (Gruber, 2011a; Gruber, Harvey, & Gross, 2012; Phillips & Vieta, 2007). A critical next step is to characterize mechanisms that may underlie and contribute to these observed patterns of emotion disturbance. One promising route towards identification of such mechanisms is to explore differences in memory recall for emotional material, which has been shown to play an important role in maintaining disorders of negative emotion such as depression and anxiety (e.g., Bradley, Mogg, & Williams, 1995; Bremner et al., 2003; Browning, Holmes, & Harmer, 2010; Hertel, 1998; Joormann & Gotlib, 2008; Lyubomirsky, Caldwell, & Nolen-Hoeksema, 1998; Sorenson, Furman, & Gotlib, 2014; Yeh & Hua, 2009). However, less is known about the role of emotional memory in contributing to disturbances in positive emotion, a characteristic of BD. This paper will examine potential group differences, for the first time, in emotional memory among adults with bipolar disorder compared to healthy controls.

Emotional Disturbance in Bipolar Disorder

Recent research suggests that individuals with BD experience heightened positive affect that persists across a myriad of contexts (Gruber, 2011a; Gruber, 2011b). For example, adults with remitted BD self-report greater positive affect in response to emotional films (Gruber, Harvey & Purcell, 2011), static images (M'Bailara et al., 2009), and reward-related tasks (Meyer, Johnson, & Winters, 2001) compared to healthy controls. This persistent and pervasive positive

emotionality might have implications for reward seeking, goal striving, and risk taking behavior observed in BD (e.g., Alloy, Abramson, Urosevic, Bender, & Wagner, 2009; Johnson, 2005). People with BD, relative to controls, also exhibit extended durations of self-reported positive affect during laboratory studies in which positive affect is induced (Farmer et al., 2006). In addition, BD individuals exhibit increased psychophysiological correlates of emotional responding (e.g., respiratory sinus arrhythmia) in response to positive and negative stimuli such as films, photos, and autobiographical memories (Gruber, Harvey, & Johnson, 2009; Gruber, Johnson, Oveis, & Keltner, 2008; Sutton & Johnson, 2002). Neuroimaging studies further suggest that individuals with BD experience heightened positive affect by showing that those with BD exhibit increased activity to positive stimuli in brain regions typically associated with emotional salience and reward (e.g., amygdala, putamen, ventral striatum, and orbitofrontal cortex; Johnson, Gruber, & Eisner, 2007). Heightened positive emotionality differentiates BD from other mood disorders, such as major depressive disorder (Gruber, Oveis, Keltner & Johnson, 2011; Kring & Bachorowski, 1999; Watson, Clark, & Carey, 1988), and has important implications for psychosocial treatments aimed at reducing positive emotionality (e.g., Johnson & Fulford, 2009). In sum, BD has been associated with heightened positive emotion responding across positive, negative, and neutral contexts.

BD is not only characterized by periods of heightened positive emotionality but is also characterized by recurrent bouts of depression so abnormalities in negative emotionality might also be expected (Judd et al., 2003). However, research has generated mixed findings. On the one hand, people with BD do not differ from healthy controls in their momentary emotional responses to negative stimuli (e.g., Cuellar, Johnson, & Ruggero, 2009; Ruggero & Johnson, 2006; Sutton & Johnson, 2002). On the other hand, research suggests that individuals with BD

report increased dispositional tendencies towards neuroticism and behavioral inhibition, both of which are associated with increased negative affect (e.g., Alloy et al., 2008; Kasch, Rottenberg, Arnow, & Gotlib, 2002; Meyer et al., 2001; Murray, Goldstone, & Cunningham, 2007). In sum, BD is robustly associated with heightened positive emotionality and with mixed evidence for negative emotionality which is primarily more trait-like and less apparent in momentary emotion assessments (Johnson et al., 2007). Given the importance of emotional processing in BD, an important next-step is to explore potential cognitive processes that may influence heightened emotionality in BD.

Emotional Memory as a Window into Understanding Bipolar Disorder

A critical next step in understanding emotion disturbance in BD involves isolating cognitive processes that may contribute to emotion-related disturbances in individuals with BD (Gruber, 2011b). Cognitive processes, such as memory, have long been recognized as contributing to, and being affected by, emotional states (e.g., Bradley, Greenwald, Petry, & Lang, 1992; Charles, Mather, & Carstensen, 2003; D'Argembeau & Van, 2005; Hamann, Ely, Grafton, & Kilts, 1999; Ochsner, 2000). We will first review what is known about emotional memory in healthy adults, followed by reviewing critical gaps in this literature on emotional memory in adults with BD.

Emotional Declarative Memory in Healthy Adults. Declarative/explicit memory is a type of long-term memory that involves the conscious recall of information and experience; its converse is non-declarative/implicit memory which is unconscious memory for information and experience. There are two distinct types of declarative memory: semantic, which is memory for facts and general knowledge, and episodic, which is memory for experience. Emotional memory can be declarative or non-declarative and involves the storage and recall of information about the

emotional significance of events; this includes both event details and the physiological response that was present when the event occurred (Hamann, 2001; LeDoux, 1993). Emotional declarative memory, a type of episodic memory, is therefore defined as the conscious recall of information about an emotional stimuli. The majority of empirical research shows that people have better declarative memory for emotional stimuli than neutral stimuli and better memory for negative affective stimuli than positive affective stimuli (e.g., D'Argembeau & Van, 2005; Kensinger & Corkin, 2003); however, findings about the enhancement of memory by emotion are mixed.

A growing body of evidence suggests that emotion only improves memory accuracy to an extent and has a stronger impact on one's subjective sense of memory vividness than on memory accuracy (Phelps, 2012; Phelps & Sharot, 2008). Much of this work even suggests that emotionally arousing stimuli result in lower memory accuracy than neutral stimuli even though the emotional stimuli are perceived as being remembered with more detail. Studies have found that details for how participants, from all across the country, recall hearing about the September 11th, 2001 terrorist attacks change over time but their confidence in their memory accuracy is consistently high (Hirst et al., 2009; Talarico & Rubin, 2003). Multiple laboratory-based studies presented negative and neutral emotional IAPS images (e.g., Rimmele, Davachi, Petrov, Dougal, & Phelps, 2011), negative and neutral emotional stories (e.g., Christianson & Loftus, 1991), or both images and stories (e.g., Adolphs, Tranel, & Buchanan, 2005) to adult participants and found that emotion enhanced overall recognition accuracy, central details, and memory confidence but impaired memory for contextual or peripheral items. In conclusion, it seems that emotion enhances memory in some circumstances and impairs memory in others (Jones, O'Gorman, & Byrne 1987; Mather, 2007).

A study by Sharot and Phelps (2004) presented neutral and negative emotion words to college students and found faster forgetting for neutral words than for negative words, more accurate recognition of negative words than of neutral words over time, and higher recognition rates for negative than for neutral words after a delay period; this study concluded that high arousal stimuli result in superior consolidation and thus, high arousal stimuli are not advantageous to short-term or working memory but are advantageous to long-term memory. A study by Kensinger and Corkin (2003) presented neutral words and negative words from the Affective Norms for English Words (ANEW; Bradley & Lang, 1999) to test the memory of healthy adult participants. They found that memory was better for negative than neutral words. Many other studies, of similar design, have reached the same conclusion (Canli, Zhao, Brewer, Gabrieli, & Cahill 2000; Dietrich et al., 2001). A study by D'Argembeau and Van (2005) presented positive, negative, and neutral emotional images to test the emotional declarative memory of college students. They found that negative images were better recognized than positive images and that both negative and positive images were better recognized than neutral images. However, there is also research suggesting that when participants were assigned to an emotion condition (positive or negative) and were then asked to recall non-emotional information, those in the positive emotion condition did better, overall, than the negative emotion condition; however, the negative emotion condition remembered more information directed towards goals and outcomes (Levine & Burgess, 1997). This study suggests that specific emotions enhance memory for specific aspects of events.

While findings are mixed, most research suggests that emotional memory produces more accurate recall than non-emotional memory. Some research shows that emotion serves not only to increase the likelihood of remembering an event but also the amount of detail recalled about

the event (Kensinger & Corkin, 2003) while other research shows the opposite (e.g., Phelps & Sharot, 2008). It is also still unclear whether emotional memory is best for negatively valenced stimuli or positively valenced stimuli.

One possible explanation for the phenomenon that emotion enhances memory is that we remember best what we attend to most; emotional stimuli seem to be attended to more than neutral stimuli and thus, emotional memory is superior to non-emotional memory. However, research has shown, by testing emotional memory in varying attention conditions, that there is more to emotional memory than just attention (Christianson, Loftus, Hoffman, & Loftus, 1991; Sharot & Phelps, 2004). A second possible explanation is that the amygdala, an almond-shaped brain structure that is important for processing emotional information, enhances the function of the medial temporal lobe, a brain structure largely responsible for memory (Cahill & McGaugh, 1998; Dolcos, LaBar, & Cabeza, 2004), and thus increases memory for affective stimuli. A third potential explanation is that emotion serves to highlight what is important for our future experiences and our survival and because of this our brain has better recall for emotional stimuli (Phelps & Sharot, 2008). A final explanation is that the heightened distinctiveness with which emotional stimuli are encoded and re-experienced may be the cause of the observed differences in emotional and non-emotional memory (Ochsner, 2000).

In conclusion, there is an abundance of research on the topic of emotion and memory, yet, findings are mixed. The majority of research agrees that emotional declarative memory is more successful than non-emotional declarative memory; however, it is still unclear whether emotional declarative memory for negative affective stimuli or memory for positive affective stimuli is superior.

Emotional Declarative Memory in Bipolar Disorder. With respect to BD, there are several lines of evidence that converge to suggest potential impairments in emotion relevant memory. First, we will review evidence for general memory impairments in BD and then we will review the little research, to date, on emotional memory impairments in BD. Individuals with BD are characterized by a wide range of cognitive impairment, generally (Deckersbach et al., 2004; Hawkins et al., 1997; Rubinsztein, Michael, Paykel, & Sahakian, 2000; Tham et al., 1997; van Gorp, Altshuler, Theberge, Wilkins, & Dixon, 1998; Van Rheenen & Rossell, 2014), as well as in declarative memory, specifically (e.g., Bearden et al., 2006; van Gorp, Altshuler, Theberge, & Mintz 1999; Van Rheenen & Rossell, 2014). One study looked at declarative versus procedural memory (a type of non-declarative memory) in a group of euthymic bipolar participants (with and without a history of alcohol abuse) and healthy controls (van Gorp et al., 1999). Declarative memory was measured by administering the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987) to both the BD and healthy control groups. The California Verbal Learning Test assess verbal learning and verbal memory, a type of declarative memory, by testing people's memory for a list of words at various delay periods using free recall (memory for target words with no aid), cued recall (memory for target words with the help of categorical hints), and recognition memory recall (memory for target words with the help of a list of words). They found that the BD participants performed significantly worse on the CVLT compared to healthy controls in terms of number of words learned. However, the two groups did not differ on tests of procedural memory; thus, the BD group demonstrated impaired declarative memory but not impaired procedural memory. Another study also used the CVLT and again found significant impairments in declarative memory in the BD group (Bearden et al., 2006).

A study by Van Rheenen and Rossell (2014) administered the Hopkins Verbal Learning Test-Revised (HVLT-R: Brandt & Benedict, 2001) to euthymic and symptomatic BD participants and healthy controls. The HVLT-R tests verbal memory and learning, specifically immediate recall, delayed recall, and recognition for groups of words. They found that both euthymic and symptomatic BD participants had difficulty in learning the HVLT-R word list and demonstrated impairment in delayed recall and recognition of words compared to healthy controls. Other research has also shown impairments in verbal memory in participants with BD using a battery of neuropsychological tests (Cavanagh, Van Beck, Muir, & Blackwood, 2002; Clark, Iversen, & Goodwin, 2001). Taken together, the research suggests potential difficulties in declarative memory specifically in BD. The research shows that there is something distinct about the declarative memory system, for those with BD show impairment in declarative memory but not impairment in some other types of memory (such as procedural memory). This impaired declarative memory seems to imply that declarative emotional memory in BD would also be impaired which may shed light on the cognitive mechanisms behind the emotion disturbance characteristic of BD.

While there is much research about impairment in declarative memory in those with BD, there is a dearth of work on emotional declarative memory in BD, to date. Some work suggests that there may be a link between naturally occurring affect states in BD and the strength of internal images that are remembered (Holmes, Coughtrey, & Connor, 2008; Holmes, Geddes, Colom, & Goodwin, 2008; Holmes & Mathews, 2010). No work yet demonstrates how this extends to externally presented images. One study by Malhi, Lagopoulos, Sachdev, Ivanovski, and Shnier (2005) found that remitted BD patients had less subcortical and cortical activation to affective stimuli suggesting a potential deficit in affective processing. Other research shows that

the amygdala, which has been found to be abnormal in BD patients (Altshuler, Bartzokis, Grieder, Curran, & Mintz, 1998; Wang et al., 2009), acts as a modulator of explicit (conscious) emotional memory (Hamann, 2001). This means that the amygdala plays a key role in enhancing emotional memory, for both positive and negative stimuli, by regulating and monitoring the encoding and consolidation of emotional memories. Patients with unilateral or bilateral amygdala damage show impaired emotional declarative memory, yet another example of the strong connection between the amygdala and memory for emotional stimuli (Adolphs, Cahill, Schul, & Babinsky, 1997; Adolphs, Tranel, & Denburg, 2000; Cahill, Babinsky, Markowitsch, & McGaugh, 1995).

All three of these studies, looking at amygdala damage and emotional memory, used the same stimuli: a story consisting of approximately 12 slides, each with an image on it, shown in sequence, accompanied by a narrative. Together, the slides and narrative tell a story of a boy and his mother who visit his father in the hospital. The story can be broken into three sections – the first and third are characterized as non-emotional (e.g., the mother leaves the hospital to make a phone call and go home) and the second is emotional (there are images of surgery). Slide number 7 in particular is a scene of a car crash victim's leg being surgically re-attached and was rated, by all groups, as having the highest emotional intensity rating. The first study (Adolphs et al., 2000) looked at memory for this story in participants with unilateral amygdala damage compared to control groups. This study found that the control groups all had the best memory for slide 7, as determined by a questionnaire about the story. They also found that the group with unilateral amygdala damage did not have the best memory for slide 7 (their memory, on average, was best for a non-emotional slide). The second study (Adolphs et al., 1997) looked at bilateral amygdala damage compared to control groups. This study also found that the control groups had the best

memory for slide 7 and that the bilateral amygdala damaged group did not remember slide 7 any better than the other non-emotional slides. This, again, was measured by administering a questionnaire about the stimuli. The third study (Cahill et al., 1995) found the same results. These studies concluded that amygdala damage impairs long-term declarative memory for emotionally arousing stimuli. All evidence suggests that individuals with BD, a disorder commonly associated with amygdala abnormalities, will have impairments in emotional declarative memory.

Yet, the current research has several important scientific gaps. To date, only two studies specifically looked at emotional memory in BD participants. The first study looked at memory for emotional and neutral story stimuli in BD participants and healthy controls (Kauer-Sant'anna et al., 2008). Researchers found that overall memory scores, as determined by a questionnaire, were lower for the BD group than the healthy control group and that the BD group had poorer memory for the emotional phase of the story. The BD group also rated the neutral story condition as more emotional than the healthy controls. They concluded that memory retrieval for emotionally bound information is blunted in individuals with BD. While this study does directly test emotional declarative memory in remitted BD participants, it fails to look at both types of emotional memory; emotional memory for positive stimuli was not tested and thus, they were unable to research a valence effect. While this study shows that emotional memory is impaired in BD, it does not offer insight into whether memory for positive affective stimuli is abnormal in BD.

The other study looking at emotional memory in BD is an fMRI study that used neutral and emotionally positive IAPS images to test the memory of BD participants, healthy controls, and participants with schizophrenia (Whalley et al., 2009). After viewing each image, while in an

fMRI, participants were asked which images were recognized and not recognized. This study found that emotional stimuli were remembered better than neutral stimuli across all three groups and that memory accuracy was not significantly different between the three groups. Their main finding was that the BD group had greater hippocampal activation, compared to healthy controls and participants with schizophrenia, when exposed to emotional stimuli versus neutral stimuli. The primary goal of this study was not to test behavioral differences in emotional memory between healthy controls and individuals with psychopathology but instead was to test differences in brain activation across the three groups. This experiment also lacked negative affective stimuli, which was excluded from this study because they were only interested in brain activation generally, not the possibility of a valence effect.

The Present Investigation

Examining emotional memory in individuals with BD may provide critical insights into identifying potential factors that cause individuals with BD to be vulnerable to relapse, to engage in risk taking behavior, to engage in reward seeking behavior, and to exhibit poor emotion regulation. Despite the prevalence of emotional and cognitive difficulties in BD, there is a dearth of research on emotional memory in BD. This study will fill the gap in research by examining memory for positive, negative and neutral stimuli in individuals with remitted BD compared to healthy adults. We focused on remitted BD participants so as to determine if there are group differences in emotional declarative memory independent of current mood symptoms. We used well validated positive, negative, and neutral static photo stimuli drawn from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008). We gathered memory accuracy ratings as well as individualized positive and negative emotion intensity ratings for each image. This enabled us to test the following aims:

Aim 1: Group Differences in Overall Memory Accuracy. The first aim of this study was to test to see if individuals with BD have impaired declarative memories compared to healthy controls across all images. We predicted that BD participants would have significantly lower memory accuracy scores across all images compared to healthy controls (**Hypothesis 1**). This hypothesis is based on previous research showing that people with BD exhibit general difficulties in declarative memory for non-emotional stimuli (Deckersbach et al., 2004; Martínez-Arán et al., 2004; Martínez-Arán et al., 2014; van Gorp et al., 1999; Wolfe, Granholm, Butters, Saunders, & Janowsky, 1987).

Aim 2: Group Differences in Emotional Memory Accuracy. The second aim of this study was to test if declarative memory for emotional stimuli (i.e., positive and negative) is particularly impaired in individuals with remitted BD compared to healthy controls. We predicted that participants with BD would have lower memory accuracy scores for positive and negative images compared to healthy controls, but no group differences would emerge for neutral memory accuracy scores (**Hypothesis 2**). This hypothesis is based on previous research showing that memory retrieval for emotional information is impaired in BD (Kauer-Sant'anna et al., 2008), that individuals with BD show less brain activation to affective stimuli suggesting a potential deficit in affective processing (Malhi et al., 2005), and that BD is associated with amygdala abnormalities, a brain structure largely associated with enhancing emotional memory (Adolphs et al., 2000; Altshuler et al., 1998; Hamann, 2001).

Aim 3: Associations of Illness Duration with Memory Accuracy. The final aim of this study was to test if illness duration predicted memory accuracy scores within the BD group. We predicted that a longer illness duration in the BD group would be associated with decreased memory accuracy scores for emotional (i.e., positive and negative) images (**Hypothesis 3**). This

hypothesis is based off of previous research showing that for participants with BD, lifetime illness duration is associated with impaired verbal memory scores (van Gorp et al., 1998) and impaired general memory performance (Landau, Raymont, & Frangou, 2003).

Method

Participants

All participants were recruited as part of a larger study on emotion and mood. Participants were individuals diagnosed with BD type I, currently in remission (n = 26), and healthy control individuals who did not meet current or past criteria for any DSM-IV-TR Axis I disorders (n = 24). In order to minimize the effects of phasic mood states on the obtained results, we focused on BD participants in remission (i.e., not in a current manic, depressed, or mixed mood phase for at least the past month). Exclusion criteria included a lifetime history of stroke, severe head trauma, neurological disease, autoimmune disorder, severe medical condition (e.g., cardiovascular disease, fibromyalgia, HIV/AIDS), alcohol or substance abuse in the past six months, and impaired cognitive functioning as indicated by a score of less than 24 on the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975). Given that BD is highly comorbid with other disorders (e.g., Kessler et al., 2005), BD participants were not excluded based on psychiatric comorbidities with the aforementioned exception of substance and alcohol use disorders. See **Table 1** for demographic information and clinical characteristics.

Measures of Clinical Functioning

Diagnostic Evaluation. All Axis I diagnoses were assessed using the Structured Clinical Interview for DSM-IV (SCID-IV; First, Spitzer, Gibbon, & Williams, 2007). Trained interviewers (i.e., clinical psychology doctoral candidates and research fellows) administered the

SCID-IV. Additional measures of illness duration, age of onset, and lifetime number of manic and depressive episodes were also obtained (see **Table 1**).

Mood Symptoms. The Young Mania Rating Scale (YMRS; Young, Biggs, Ziegler, & Meyer, 1978) was used to measure current manic symptoms. The YMRS is an 11-item, clinician rated measure of current manic symptoms with scores ranging from 0 to 60, with higher scores indicating greater manic severity. Scores ≥ 7 represent clinically significant mania symptom levels. Current symptoms of depression were measured using the Inventory of Depressive Symptomatology-Clinician (IDS-C; Rush, Gullion, Basco, Jarrett, & Trivedi, 1996). The IDS-C is a 30-item, clinician-rated measure of current symptoms of depression. IDS-C scores range from 0 to 84, with higher scores indicating greater depressive severity. Scores ≥ 11 represent clinically significant depressive symptom levels. The IDS-C has been validated in individuals with BD (Trivedi et al., 2004) and strongly correlates with other measures of depression severity (Rush et al., 1996). Current remitted status (i.e., neither manic, depressed, nor mixed mood state) for the BD group was determined using the SCID-IV mood module criteria for the past month and cutoff scores on the YMRS (≤ 7) and IDS-C (≤ 11) for the past week. The CTL group also scored below these cutoffs.

Illness Duration. We assessed illness course parameters (the number of total lifetime manic and depressive episodes and the number of manic and depressive episodes experienced in the last 12 months) using the National Institute of Mental Health retrospective Life-Charting Methodology (NIMH-LCMr; Leverich & Post, 1993). The NIMH-LCMr procedure involves charting a participant's course of illness from the date of illness onset. The NIMH-LCMr has been well validated and used in samples of bipolar participants (e.g., Denicoff et al., 1997; Leverich & Post, 1993).

Global Functioning. The Global Assessment of Functioning Scale (GAF; Spitzer, Gibbon, Williams, & Endicott, 1996) was used to assess global functioning in the past week. The GAF assesses overall psychological, social, and occupational functioning on a scale from 1 (lowest level of functioning) to 100 (highest level of functioning).

Measures of Baseline Cognitive Functioning

We included two additional measures of baseline cognitive functioning to ensure that our results were robust to potential impairments in more general cognitive functioning between groups.

General Cognitive Functioning. In order to assess participants' general cognitive functioning, the Mini Mental State Examination was utilized (MMSE; Folstein et al., 1975). The MMSE is a 30-item assessment that takes approximately ten minutes to administer and screens for cognitive functioning in such domains as orientation, recall, calculation, attention, naming, repetition, comprehension, reading, writing, and drawing (Cockrell & Folstein, 2002). The MMSE scores range from 0 to 30, with 30 reflecting the highest functioning. Threshold eligibility was set at ≥ 24, and all participants met or exceeded this score.

Working Memory. Working memory was measured as a potential confound given that remitted individuals with BD have been found to experience lasting cognitive impairments, including difficulties with executive functioning and sustained attention (Latalova, Prasko, Diveky, & Velartova, 2011). The letter-number sequencing subtest of the Wechsler Adult Intelligence Scale-IV (WAIS-IV; Wechsler, 2008) was utilized to measure working memory. In this test, the experimenter reads aloud a series of increasingly long lists of randomly ordered numerical digits and alphabetical letters. After the list is read aloud, participants verbally repeat back all numbers (in numerical order) first, followed by all letters (in alphabetical order). This

subtest takes approximately ten minutes to administer. Raw scores (ranging from 0 to 21) are calculated as the total number of trials correct, from which WAIS-IV age-norm scaled scores are computed for final analysis.

Emotional Memory Task

For the emotional memory task, participants viewed 175 individually presented images that were derived from the International Affective Picture System[1] (IAPS; Lang et al., 2008). The images were displayed to the participant in an individual testing room in front of a 26" high-resolution Sony computer monitor using E-prime software. Of the total 175 images viewed, 148 images were previously viewed[2] and 27 were introduced as unseen distracter images. Specific images were classified according to valence; of the 148 previously viewed images, 62 were positive images, 58 were negative images, and 28 were neutral images. Across all participants, the positive images were rated as more positive (M=5.12, SD=1.74) compared to both negative (M=1.67, SD=0.63) and neutral (M=2.74, SD=1.57) images, F=122.72, p<.001. Also, across all participants, the negative images were rated as more negative (M=5.69, SD=1.70) compared to

[1]**ERC and EATS Images**: 4000, 2025, 8120, 4609, 4601, 4606, 4624, 5830, 4610, 8531, 8465, 8311, 8420, 8497, 8320, 7284, 4210, 4290, 4659, 4664, 4681, 4800, 4810, 5621, 5629, 8030, 8179, 8185, 8186, 8191, 8400, 7330, 7350, 6190, 1301, 7360, 9102, 2490, 9120, 6010, 6836, 9470, 2312, 2278, 9440, 9160, 2691, 2700, 6831, 3530, 3068, 3150, 9420, 9252, 3000, 2800, 9181, 3180, 3261, 2053, 3230, 9410, 3140, 7285, 4651, 7475, 2092, 4532, 1942, 8460, 4625, 8600, 7195, 4653, 5991, 1900, 5890, 8130, 2240, 8280, 1650, 2331, 4660, 8501, 2050, 1750, 1710, 2340, 5700, 4200, 1811, 8470, 9042, 8230, 2055.1,1525, 9001, 7361, 3300, 9180, 9622, 6213, 9920, 3220, 7380, 2900.1, 6510, 9320, 2710, 6250, 2730, 3160, 2683, 9040, 3100, 3181, 6350, 2205, 9571, 9405, 2215, 2383, 7130, 7705, 2441, 2480, 7186, 9210, 2214, 9070, 7035, 7235, 2890, 7010, 7185, 7179, 7233, 7034, 2487, 5530, 5395, 7500, 2745.1, 2191, 7100, 5740, 7550, 2880, 4220
New Images: 1720, 1999, 2070, 2440, 2493, 3030, 3301, 4650, 4656, 5390, 5520, 5660, 5731, 5990, 6200, 6360, 7009, 7025, 7187, 7359, 7481, 7510, 8117, 8231, 9000, 9041, 9910

[2]Images were previously viewed on one of two earlier laboratory tasks including: 1) **The Emotion Regulation Choice task** (ERC; Sheppes et al., 2011, 2014) contained two counterbalanced conditions: a negative and positive condition. At the start of each condition, participants completed a 60 second resting baseline in front of a blank computer screen. They also completed baseline emotion ratings using the modified Differential Emotions Scale (mDES; Cohn, Fredrickson, Brown, Mikels, & Conway, 2009; Fredrickson, Tugade, Waugh, & Larkin, 2003) and the Positive and Negative Affect Schedule (PANAS; Mackinnon, Jorm, Christensen, Korten, Jacomb, & Rodgers, 1999). At the beginning of each condition, participants completed a practice ERC session in which they were taught the meaning of reappraisal and distraction, and practiced the strategies aloud with the experimenter using practice photos. These photos matched the valence of the upcoming task accordingly. In order to begin the task, participants had to demonstrate understanding of the task through correctly defining both terms, describing the difference between the two strategies, and completing multiple practice examples where they correctly implemented each strategy. For the ERC task trials, 30 negative and 34 positive photos were selected from the International Affective Photo System (IAPS; Lang, Bradley, & Cuthbert, 2008). Each photo was presented for a brief period (500 ms) after which participants pressed a button on the keyboard to select a regulation strategy (distraction or reappraisal) to decrease their emotional intensity while viewing that photo. Participants then viewed the photo again (5,000 ms) while implementing their chosen strategy. After each photo, participants separately rated how positively and negatively they felt on a 1 (not at all) to 9 (very) scale (Sheppes et al., 2011, 2014). This task took approximately 25 minutes; or 2) **Eye-Tracking Attention Task**: participants' visual gaze was measured with an Applied Science Laboratories eye tracker, Model 504 (Bedford, MA). The tracker records the movements and position of participants' left eye sixty times per second with a camera and a non-invasive beam of infrared light. The visual fixations were defined as those series of gazes in which an individual stays within 1° visual angle for 100 ms or longer (Manor & Gordon, 2003). Visual fixations to each image were recorded throughout the presentation of emotional pictures on a 15x12 inches Dell desktop computer and calculated using Gaze Tracker software (Eye Response Technologies, Inc., Charlottesville, VA). The design and procedures used were based on those used in prior eye tracking research (e.g., Wadlinger & Isaacowitz, 2008). During the task, participants viewed 84 images and were given the following instructions: "watch each image naturally, as you would if at home while watching TV. You can look anywhere on the screen, but try not to turn your head away from the screen." Each trial consisted of a single emotional picture, displayed at a size of 12x10.25 inches (5.0s), followed by a buffer slide with a fixation cross (0.5*s*) to realign gaze to the center of the screen. The participants' visual gaze was continuously recorded throughout the task. Participants were assigned to one of three groups (each group had the images in different orders) to eliminate an order effect. This task took approximately 20-30 minutes.

both positive (*M*=1.43, *SD*=0.48) and neutral (*M*=1.40, *SD*=0.54) images, *F*=164.01, *p*<.001. Each image was presented for approximately 5,000 milliseconds. After viewing each image, participants were asked to provide three ratings for the image including a memory accuracy score (i.e., "have you seen this image before?") answered categorically (yes/no) and two emotion intensity ratings where they separately rated how positive and negative the image was on a 1 (*not at all*) to 9 (*very much*) Likert scale. To eliminate possible order effects, the order of the 175 images was randomized. This task took approximately 25-30 minutes to complete.

Procedure

After obtaining informed consent, trained clinical psychology faculty, graduate students, or post-baccalaureate researchers administered the SCID-IV, YMRS, IDS-C, GAF, MMSE and WAIS-IV Working Memory Task. Next, participants viewed the 148 target images across two separate tasks spaced approximately 10-15 minutes apart. After a delay of approximately 60 minutes, during which participants completed tasks not relevant to the present investigation, they completed the Emotional Memory Task. After completing the task, participants were debriefed and compensated for their participation.

Results

Demographic and Clinical Characteristics

As seen in **Table 1**, BD and CTL participants did not significantly differ with respect to age, gender, ethnicity, or years of education. Not surprisingly, the BD group scored lower on global functioning than the CTL group. Although all groups scored below YMRS (≤ 7) and IDS-C (≤ 11) cutoffs, the BD group scored higher than CTL participants on both the YMRS and IDS-C. However because both groups scored well below clinically significant thresholds, and there are considerable concerns about the statistical validity of controlling for current symptoms (e.g., Miller & Chapman, 2001), we opted not to control for current symptoms in the present analyses.

The groups did not differ on the baseline MMSE or WAIS-IV working memory measure, suggesting observed differences in memory accuracy for our main analyses were not better accounted for by general cognitive impairment differences between the groups.

Main Analyses

Group Differences in Memory Accuracy. To test Hypotheses 1 and 2, a 2 (Group: BD, CTL) x 3 (Image: Neutral, Negative, Positive) repeated-measures analysis of variance (ANOVA) was conducted for memory accuracy scores. A Greenhouse-Geisser correction was used when assumptions for sphericity were not met and adjusted *F* and *p* values are reported. Effect sizes for significant results are reported as partial eta squared (η_p^2). All reported *p* values are two-tailed. Means and standard deviations are presented in **Table 2**.

Results indicated a significant main effect of Image, $F(2, 96)=6.14$, $p=0.003$, $\eta_p^2=0.11$, with pairwise comparisons indicating that all participants had higher memory accuracy scores for both positive (M=88.0%, SD=0.14) and negative (M=89.6%, SD=0.14) images compared to neutral (M=83.4%, SD=0.17) images ($p=0.01$). Across both groups negative images had higher memory accuracy scores compared to neutral images ($p=0.006$) and positive images had higher memory accuracy scores compared to neutral images ($p=0.038$). However, there was not a significant difference between memory accuracy scores for negative images versus positive images ($p=0.070$). The Group main effect was not significant, $F(1, 48)= 0.152$, $p=0.698$, $\eta_p^2=0.003$. These results were qualified by a significant Group x Image interaction, $F(2, 96)=6.57$, $p=0.009$, $\eta_p^2=0.12$.

Three follow-up univariate ANOVAs were conducted separately for neutral, negative, and positive images. Results indicated a significant effect for the BD group to exhibit higher memory accuracy scores than the CTL group for the neutral images, $F(1,49)=4.073$, $p=0.049$,

η_p^2=0.078. No group differences emerged for positive, $F(1,49)=0.444$, p=0.508, η_p^2=0.009, or negative, $F(1,49)=0.42$, p=0.520, η_p^2=0.009 images.

Memory Accuracy and Associations with Illness Duration. To test Hypothesis 3, we conducted bivariate correlations linking memory accuracy scores for neutral, positive and negative images with illness duration for the BD group specifically. No significant correlations between memory accuracy and illness duration emerged (ps> .20); however, increased memory accuracy for negative and positive images were associated with decreased number of lifetime depressive episodes (r= -0.47, p=0.028 and r= -0.505, p=0.016) but not for neutral images (r= -0.21, p= 0.36).

Potential Confounds: Emotion Intensity Ratings. We examined the potentially confounding role of self-reported emotion intensity on memory accuracy to explain our observed group difference for accuracy of neutral images. Specifically, we examined if self-reported positive and negative emotion intensity was associated with memory accuracy scores across images. We found a significant Group x Image interaction for positive intensity ($F(2,47)=3.33$, p=0.04, η_p^2= 0.124) and a near significant interaction for negative intensity ($F(2,47)=2.88$, p=0.066, η_p^2=0.109).

Follow-up univariate ANOVAs were conducted separately for positive intensity ratings for negative, positive, and neutral images. For neutral images, we found a trend for group difference, $F(1,49)=2.43$, p=0.13, η_p^2=0.048, in that the BD group (M=3.07, SD=1.86) rated neutral images more positive than the CTL group (M=2.38, SD=1.14). We did not find significant group differences in negative intensity ratings for neutral images, $F(1,49)=1.13$, p=0.294, η_p^2=0.023.

We ran a follow-up ANOVA to see if this difference in positive ratings influenced how well the BD group remembered the neutral images. We looked at memory accuracy for neutral images while controlling for positive intensity ratings for the neutral images. We found that the group differences in memory accuracy scores become trending, instead of significant, when we control for positive intensity ratings, $F(1,49)=3.96$, $p=0.052$, $\eta_p^2=0.078$.

Discussion

BD is characterized by emotion disturbance especially for positive emotions. This study aimed to further understand this feature by looking at one important and potentially associated cognitive process, emotional declarative memory, which may help understand these emotion related difficulties. Emotional memory has been shown to play a role in the maintenance of depression and anxiety, thus we were curious to explore whether emotional memory also plays a role in disorders of positive affect like BD (e.g., Bradley et al., 1995; Bremner et al., 2003; Browning et al., 2010; Hertel, 1998; Joormann & Gotlib, 2008; Lyubomirsky et al., 1998; Sorenson et al., 2014; Yeh & Hua, 2009). Given the importance of emotional memory, the present study tested overall memory accuracy scores and emotional memory accuracy scores of participants with BD versus healthy controls. To our knowledge, the current study is the first to test memory for neutral, positive, *and* negative affective stimuli in individuals with remitted BD compared to a healthy control group. Our findings demonstrate that participants with BD have better memory for neutral stimuli compared to healthy controls and that this may be partially explained by increased positive intensity ratings attributed to the neutral image.

Aim 1 & 2: Group Differences in Memory Accuracy

The first hypothesis focused on the overall differences in memory accuracy between both groups. We predicted that participants with BD would remember fewer images overall, as

compared to healthy controls. Our results indicated that there were no group differences between the BD group and control group in overall memory accuracy scores. This finding is inconsistent with our hypothesis and with previous literature showing impairment in declarative memory in participants with BD (Bearden et al., 2006; van Gorp et al., 1999; Van Rheenen & Rossell, 2014). Several possible explanations may shed insight into these divergent results. First, our finding might be different from previous research because our BD group is not representative of the BD population; our BD group had slightly higher working memory scores on the WAIS-IV than the healthy control group. However, BD has widely been associated with cognitive impairments (Deckersbach et al., 2004; Hawkins et al., 1997; Rubinsztein et al., 2000; Tham et al., 1997; van Gorp et al., 1999; Van Rheenen & Rossell, 2014). Thus, it is possible that our specific BD sample had better memories than most BD individuals or that our specific CTL sample was not representative in that they had worse memories than the majority of healthy controls. Second, this divergent result might be due to the nature of the tasks studied. Previous research has mostly focused on impairments in verbal memory, whereas our study tested visual memory. Verbal memory and visual memory, as tested in these studies, are both forms of declarative memory but they are associated with distinct brain regions. Thus, the differences in results might be due to differences in study stimuli and in the nature of memory tested.

Our second hypothesis was that participants with BD would have impaired emotional memory compared to healthy controls. Thus, the BD participants would demonstrate decreased memory accuracy for negative and positive images, but not neutral images, compared to our healthy control group. Inconsistent with this prediction, we did not find differences in memory accuracy scores for positive or negative images. This diverges from previous research showing that participants with BD have impaired memory retrieval for emotionally bound information

(Kauer-Sant'anna et al., 2008). The fact that memory for positive and negative affective stimuli is unimpaired in our BD participants might suggest that participants with BD experience positive and negative stimuli similarly to healthy controls and that the processing of emotional stimuli is not necessarily the cause of emotion dysregulation in BD. Our study differs from the research that found impairments in emotionally bound information in BD in the following important ways: that study only looked at negative and neutral stimuli, used a story instead of images, and had a week long delay period. It is possible that because of our positive stimuli condition, less salient affective stimuli, and much shorter delay period, our emotional memory results were not significant. Since they only looked at negative affective stimuli, it makes sense that the BD group had impairments in memory since assigning heighted positive affect to negative stimuli, which seems to be a feature of BD, might have the effect of cancelling out salience. It is also possible that we did not find significant differences in emotional memory between the two groups due to our small sample size. The BD group did have lower memory accuracy scores for positive and negative stimuli, but not at a significant level; it is possible that with a larger sample size, the results would have been significant. Our results are, however, consistent with some previous research showing that people, in general, have the best memory recall for emotional stimuli compared to neutral stimuli (D'Argembeau & Van, 2005; Kensinger & Corkin, 2003).

Our results also indicated that the BD group had significantly increased memory accuracy scores for neutral images. This unanticipated finding seems to suggest that individuals with BD process stimuli, even neutral stimuli, with greater affect than do healthy controls. It suggests a salience effect, in that those with BD may assign increased salience to both emotional (i.e., positive and negative) and non-emotional (i.e., neutral) stimuli. “Assignment of salience” can be defined as the process by which a stimulus is evaluated as important to the motivational structure

of an individual (e.g., Cunningham & Brosch, 2012) as well as the degree to which a stimulus contains personal meaning or significance (e.g., Phan, Wager , Taylor, & Liberzon, 2004). In the sense that this finding suggests a salience effect, it converges with previous literature, for previous research has suggested that BD participants have persistent and heightened positivity across all contexts (Gruber et al., 2008). This finding has important implications. Individuals with remitted BD, as seen in this study, remember neutral images more accurately than healthy controls. This seems to be because they assign salience to neutral stimuli. If this is in fact the reason, it suggests that participants with BD are most likely remembering personal life events with more emotionality as well. Our findings, as well as previous research, also indicate that participants impose positive affect, specifically, onto neutral stimuli (Gruber et al., 2008; Gruber et al., 2013). In the present study, we found a trend for the BD group to rate neutral images as more positive than the healthy control group. We found that this difference in positive intensity ratings somewhat influences memory accuracy.

Since it seems to be the case that individuals with BD experience self-reported elevations in and greater physiological arousal related to positive emotion, regardless of stimulus condition, it seems that BD participants are remembering neutral images with better accuracy because they assign positive affect to the neutral stimuli. This has many implications and may be the cause of some of the characteristic behaviors seen in BD. Risk taking and reward seeking behavior are common symptoms of BD, even after such behaviors lead to devastating consequences. One possible implication of our finding is that better memory for neutral events might lead to continued reward seeking behavior, even after such behavior causes negative consequences, because the events are remembered with greater positive valence. Thus, a rewarding behavior that leads to negative affect is experienced differently in BD than in non-psychiatric populations.

Assigning positive affect to neutral stimuli also has important implications for mania - a key feature of BD. Mania is characterized by feeling extremely high, hyper, and excited (American Psychiatric Association, 2000, *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed., text revision). The fact that participants with remitted BD find neutral stimuli more positive than healthy controls may suggest why those with BD are vulnerable to relapse; if participants view the world with heightened positivity, it follows that they would experience increased overall positive affect which might, in turn, lead to mania.

Aim 3: Associations of Illness Duration with Memory Accuracy.

Our third hypothesis was to test to see if illness duration predicted memory accuracy scores within the BD group. The results suggested that there was no relationship between memory accuracy scores and illness duration; however, increased memory accuracy for negative and positive images were associated with a decreased number of lifetime depressive episodes. Memory accuracy for neutral images was not associated with number of lifetime depressive episodes. These findings are partly consistent with previous research; previous research suggests that with longer illness duration comes increasingly impaired declarative memory. Our findings were consistent with our hypothesis. We predicted that memory accuracy scores for emotional images (i.e., positive and negative) would be higher with shorter illness duration. This finding seems to suggest that memory for neutral stimuli is not affected by number of manic or depressed episodes or illness duration, unlike memory for emotional stimuli which is affected by number of depressive episodes. Thus, it seems that, since memory for neutral stimuli in BD is actually improved by the heightened positive affect seen in BD, memory for neutral stimuli is not negatively correlated with lifetime number of depressive episodes as overall memory is

suggested to be. This finding further supports our idea that memory for neutral stimuli is affected by the positivity effect seen in BD.

Limitations and Future Directions

Findings from the present study should be interpreted within the confines of several limitations. First, although the images used in the present study are standardized and reliable elicitors of emotions, it could be argued that the results may not be generalizable to everyday emotional experiences in the lives of BD patients. Thus, it will be important for future studies to assess more ecologically valid stimuli that are both dynamic in nature (e.g., remembering the temporal sequence of an emotional event) and personally salient (e.g., autobiographical memories). Second, we acknowledge that our sample sizes were relatively modest despite mirroring sample sizes typically reported in experimental psychopathology research (e.g., van Gorp et al., 1999). Future studies would benefit from larger sample sizes. Third, the sample consisted largely of Caucasian participants and results may not generalize to a more diverse sample. Fourth, the BD group was not excluded on the basis of comorbidities to ensure a more ecologically valid sample. Although this represents a strength of the study, future studies would be helpful in examining how the presence of specific comorbid disorders influences emotional declarative memory. Fifth, given the possible confound of psychotropic medication, future paradigms with random assignment to different medication classes are warranted. Specifically, future research might include a control group that is matched on the same comorbid conditions, as well as random assignment of BD individuals on different medication classes (e.g., antidepressants, mood stabilizers, anxiolytics). Finally, the images used to test memory were spread across two very different tasks (the ERC and EATS tasks). The EATS task was a simple, uninstructed, passive viewing task but the ERC task had regulation instructions and many other

components. The instructions and regulation in the ERC task may confound the memory results since adding other components, aside from viewing, may cause increased attention to each image. If participants only attended to some of the images, or have greater attention to some of the images, they may have higher memory accuracy scores for those specific images and thus, memory accuracy scores may be confounded. However, the ERC task did not consist of any neutral images, thus, it seems that the main finding that the BD group had better memory for neutral images would not be affected by this possible confound. Future research, only using images previously seen in passive and uninstructed tasks, should be conducted so as to avoid this potential confound. This study specifically focused on examining accuracy in whether an emotional image was accurately identified (i.e., remembered). Future studies should expand upon this work to additionally examine accuracy in remembering previous *emotional experiences* themselves. This could be examined by assessing self-reported emotion responses when participants view an emotional image initially and retrospective reports on how they remember feeling when re-presented with the image following a delay period. This would assess not just how well they remember the content of the images seen but how well they remember feeling in response to evocative images.

Conclusion and Implications

Despite these caveats, the present investigation provides important insights into underlying cognitive mechanisms associated with positive emotional disturbance in a severe and chronic psychiatric disorder. Specifically, the present investigation isolated a specific process of interest – emotional declarative memory – in order to examine if and how it is impaired in BD. Results from the present study indicated that neutral stimuli are remembered with better accuracy in individuals with BD than in healthy controls. This finding seems to suggest a "salience effect" in BD, meaning that BD individuals experience cross-contextual stimuli with heightened salience. Previous research shows that those with BD experience positive, negative, and neutral stimuli

with greater positive affect. This apparent bias towards attending to positive emotion may be the cause of better memory for neutral stimuli in BD because individuals with BD are assigning positive emotion to neutral events. In fact, our study found exactly that - the participants with BD rated neutral stimuli as having more positive intensity compared to the control group, which may have impacted the BD group's memory accuracy scores for neutral images. This positivity may cause the typical reward seeking, risk taking, and poor emotion regulation seen in BD; if events are remembered with heightened positive affect it seems to follow that reward related events that lead to negative outcomes are remembered more positively in BD, and thus repeated. The observed salience effect may also lead to relapse because experiencing heightened positivity has the potential to trigger mania in individuals with BD. This abnormality in declarative memory and observed salience effect may also come at the expense of negative emotions and lead to many of the defining features of BD.

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Table 1. *Demographic and Clinical Characteristics.*

	BD 26	CTL 24	Statistic
Demographic			
Age (Yrs)	35.04 (12.34)	33.25 (10.53)	F= 0.30
Female (%)	53.8 %	58.3 %	χ^2= 0.48
Caucasian (%)	84.6 %	91.7 %	χ^2= 1.92
Education (Yrs)	15.58(1.88)	15.96 (2.71)	F=0.34
Employed/Student (%)	69.2 %	54.2 %	χ^2=1.20
Partnered (%)	42.3 %	66.7 %	χ^2=2.98
Cognitive			
MMSE	28.35 (1.90)	28.46 (1.84)	F=0.05
Working Memory	12.00 (2.90)	11.50 (3.48)	F=0.31
Clinical			
YMRS	1.65 (1.85)	0.67 (.87)	F=5.66 *
IDS-C	3.96 (3.04)	2.83 (2.67)	F=1.93
GAF	71.12 (7.11)	88.58 (4.66)	F=103.59 **
Mania Duration (Yrs)	17.50 (13.37)	--	--
Depression Duration (Yrs)	18.18 (13.96)	--	--
# Depressive Episodes	22.55 (32.33)	--	--
# Manic Episodes	30.35(84.97)	--	--

Note: BD=Bipolar I disorder group; CTL=Healthy control group; Employed=Employed or student status full-time or part-time; Partnered=Married or Live-in-Partner; MMSE=Mini Mental State Exam; Working Memory=WAIS-IV working memory section; YMRS=Young Mania Rating Scale; IDS-C=Inventory to Diagnose Depression; GAF=Global Assessment of Functioning. Mean values are displayed with standard deviations in parentheses where applicable.

*p< .05; **p< .01

Table 2. *Group Differences in Positive, Negative, and Neutral Memory Accuracy*

	BD	CTL	Statistic
Positive Accuracy	86.75% (0.154)	89.38% (0.121)	F=0.44
Negative Accuracy	88.33% (0.165)	90.90% (0.107)	F=0.42
Neutral Accuracy	87.90% (0.096)	78.51% (0.215)	F=4.07*

Note: BD = Bipolar disorder group; CTL = Healthy control group. Scores refer to accuracy rated on a 0-100% scale. *p< .05