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RECOGNITION OF FACIAL EXPRESSIONS OF EMOTION

IN EUTHYMIC PATIENTS WITH BIPOLAR DISORDER

by

Syed Omar Ali

submitted to the

Faculty of the College of Arts and Sciences

of American University

in Partial Fulfillment of

the Requirements for the Degree of

Master of Arts

in

Psychology

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28 March 2001

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2001

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DEDICATION

I dedicate this thesis to my parents, Syed and Anjanie Ali.

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ABSTRACT

In this study, participants (i.e., 34 euthymic patients with bipolar disorder and 26 healthy controls) completed a computer-administered task, which measured the threshold of facial affect recognition. For the task, the participants viewed facial expressions of emotion (i.e., anger, disgust, happiness, sadness, fear, surprise, and neutral) obscured with static, that cleared up incrementally over a 17 sec time interval. Participants pushed a button when they thought they recognized the emotional expressions and earned points based upon their ability to recognize the expressions quickly (and correctly). Those participants responding correctly to more obscured expressions (i.e., more static) earned more points compared to participants responding correctly to less obscured expressions (i.e., less static). Participants then matched the emotional expressions of the images to one of seven key faces of emotion (i.e., non-

verbal matching) and to one of seven labels of emotion (i.e., verbal labeling). For non-verbal matching, the comparisons between the patients and the controls did not achieve statistical significance. For verbal labeling, patients made significantly fewer correct matches for anger and significantly more correct matches for fear, compared with the healthy controls. The patients were significantly less sensitive (i.e., had a higher threshold) to happy faces, compared with the healthy controls. Threshold (or sensitivity) of recognition for facial expressions may serve as a sensitive marker of bipolar disorder during asymptomatic periods and may have a meaningful effect on the social functioning of the patients.

ACKNOWLEDGEMENTS

The author acknowledges the generous support of the Theodore and Vada Stanley Foundation, and thanks the following individuals for their assistance with this work: Robert M. Post, M.D., Kirk D. Denicoff, M.D., Kamal Jajodia, M.D., Gabriela Obrocea, M.D., Earlian E. Smith-Jackson, R.N., Donna Owens, R.N., Madeline Gupta, R.N., Kathleen Noe, M.A., Maria Martinez, B.A., Karen Lutwin, B.A., David Luckenbaugh, M.A., Bryan D. Fantie, Ph.D., and Teresa K. Elliott, Ph.D. The author also thanks all of the participants that took part in this study.

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CHAPTER 1

INTRODUCTION

Bipolar disorder is an illness characterized by frequent changes of affect (i.e., mood), where periods of depression or mania can dominate the emotional disposition of the patient, interspersed with periods of normal mood and functioning (Goodwin & Jamison, 1990). According to the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th ed., American Psychiatric Association, 1994), three subtypes of bipolar disorder exist (i.e., Bipolar I, Bipolar II, and Bipolar Disorder Not Otherwise Specified). Patients with Bipolar I Disorder have a clinical course characterized by major depressive episodes and manic (or mixed) episodes, whereas patients with Bipolar II Disorder have a clinical course represented by major depressive episodes and hypomanic episodes. (These manic episodes can be longer in duration and greater in severity, compared to hypomanic episodes.) Patients with Bipolar Disorder Not Otherwise Specified have symptoms of the mood disorder that do not meet the criteria of either the Bipolar I or Bipolar II subtypes (DSM-IV, American Psychiatric Association, 1994). The treatment of bipolar disorder involves the use of psychoactive

medications (i.e., mood stabilizers, antidepressants, and neuroleptics) augmented with psychotherapy (Goodwin & Jamison, 1990). Furthermore, the treatment of bipolar disorder can be long-lasting because the illness is recurrent in nature.

Post, Rubinow, and Ballinger (1986; see also Post, 1992; Post & Weiss, 1989) postulate that the repeated pattern of mood episodes of bipolar disorder is associated with the sensitization of temporolimbic structures (i.e., the hippocampus and the amygdala), which contribute to mood (and memory) in all individuals (Frijda, 1986; Gloor, Olivier, Quesney, Andermann, & Horowitz, 1982; Madden, 1991). Specifically, Post et al. (1986) hypothesize that both environmental stressors and a genetic predisposition to mood disorders mediate the production of initial mood episodes in bipolar disorder. The initial mood episodes serve as a sensitization stimulus (or "kindling") for succeeding mood episodes, leading progressively to more severe episodes during the course of bipolar disorder (Post et al., 1986).

The data from neuroimaging studies may support the notion of temporolimbic involvement in bipolar disorder, because many investigators have found structural abnormalities of the temporal lobe and the hippocampus in patients with bipolar disorder. For example, Harvey, Persaud, Ron, Baker, and Murray (1994) observed larger left temporal lobe volumes in patients with bipolar disorder, compared

with healthy controls. Similarly, Kemmerer et al. (1994) reported increased hippocampal size in patients with bipolar disorder, compared with healthy controls. Other researchers, however, found a reduction in the temporal lobe (Altshuler et al., 1991; Hauser et al., 1989) or hippocampal size (Swayze, Andreasen, Alliger, Yuh, & Ehrhardt, 1992), compared with healthy controls. Some investigators, in contrast, observed no change in temporal lobe (Altshuler, Bartzokis, Grieder, Curran, & Mintz, 1998; Hauser et al., 2000; Johnstone et al., 1989; Roy et al., 1998; Swayze et al., 1992) or hippocampal size (Altshuler et al., 1998; Hauser et al., 1989; 2000; Strakowski et al., 1999), compared with healthy controls. Differences in the neuroimaging scanners (e.g., the strength of the magnet), the acquisition protocols (e.g., slice thickness), the measurement techniques of the structures (e.g., area vs. volume), and the types of patients used (e.g., older vs. younger) may account for the conflicting results.

A few investigators have reported functional as well as structural abnormalities of the amygdala in patients with bipolar disorder. Using structural magnetic resonance imaging (MRI), some researchers found bilateral enlargement of the amygdala in patients with mood disorders, compared with healthy controls (Altshuler et al., 1998; 2000; Strakowski et al., 1999). Other researchers, however, did not observe this bilateral enlargement of the amygdala, compared with healthy controls

(Mervaala et al., 2000; Pearlson et al., 1997; Sheline, Gado, & Price, 1998; Swayze et al., 1992). Using Positron Emission Tomography (PET), Abercrombie et al. (1998) and Drevets et al. (1992) reported statistically significant associations between the severity of mood symptoms and increased regional blood flow and glucose metabolism in the amygdala of patients with mood disorders. Furthermore, Drevets et al. (1992) found that blood flow and metabolism in the left amygdala were elevated abnormally (though to a lesser extent) in medication-free euthymic patients. This finding is of interest because it suggests that neuropsychological alterations associated with the amygdala (and related subcortical structures of the temporal lobe) can persist during periods of symptom remission in patients with bipolar disorder.

The amygdala has been of particular interest to investigators because studies highlight the role of this temporolimbic structure in mediating the recognition of facial expressions of emotion. For example, patients with congenital Urbach-Wiethe disease (associated with bilateral destruction of the amygdala through calcification; Adolphs, Tranel, Damasio, & Damasio, 1994; 1995; Tranel & Hyman, 1990), encephalitis (Broks et al., 1998; Calder et al., 1996), or bilateral amygdalotomy (Adolphs et al., 1999; Jacobson, 1986; Young et al., 1995; Young, Hellawell, Van De Wal, & Johnson, 1996) exhibit alterations in the recognition of facial affect. The data

from functional neuroimaging experiments in healthy controls are convergent with the aforementioned patient studies. While some investigators have reported selective activation of the amygdala in response to facial expressions of emotion (Blair, Morris, Frith, Perrett, & Dolan, 1999; Breiter et al., 1996; Morris et al., 1996; 1998; Phillips et al., 1997; Sprengelmeyer et al., 1999). Other researchers, however, did not (Hamann et al., 1996; Phillips et al., 1998; Sprengelmeyer, Rausch, Eysel, & Przuntek, 1998). Studies using both neuroimaging techniques and behavioral tasks, to my knowledge, have not been performed in patients with bipolar disorder. Such experiments could explore if alterations of facial affect recognition exist in euthymic patients with bipolar disorder, which could implicate abnormalities of the amygdala, and other neuroanatomical structures.

Cognitive alterations exist in euthymic patients with bipolar disorder. For example, euthymic patients performed poorly on tasks of executive functioning, such as the Controlled Oral Word Association Test (Atre-Vaidya et al., 1998; Ferrier, Stanton, Kelly, & Scott, 1999), the Wisconsin Card Sorting Test (Coffman, Bornstein, Olson, Schwarzkopf, & Nasrallah, 1990; Morice, 1990), and the Digit Span subtest of the Wechsler Adult Intelligence Scale – Revised (Ferrier et al., 1999), compared with healthy controls. Additionally, euthymic patients performed poorly on tasks of

visuospatial ability, including the Modified Raven's Matricies (Atre-Vaidya et al.), and tasks of psychomotor performance, such as the Trail Making Test (Coffman et al., 1990; Ferrier et al., 1999; Tham et al., 1997) and the Grooved Pegboard (Coffman et al.), compared with healthy controls. Euthymic patients also performed poorly on the California Verbal Learning Test, a task of verbal learning and memory, compared with healthy controls (Atre-Vaidya et al.; van Gorp, Altshuler, Theberge, & Mintz, 1999; van Gorp, Altshuler, Theberge, Wilkins, & Dixon, 1998). However, Calev, Korin, Shapira, Kugelmass, and Lerer (1986) observed that euthymic patients performed as well as healthy controls on tasks of verbal and non-verbal memory.

Numerous researchers have explored facial affect recognition in acutely depressed patients with either major depressive disorder or bipolar disorder (Archer, Hay, & Young, 1992; Asthana, Mandal, Khurana, & Haque-Nizamie, 1998; Cooley, & Nowicki, 1989; Feinberg, Rifkin, Schaffer, & Walker, 1986; Gaebel, & Wolwer, 1992; Gur, Erwin, Gur, Zwil, Heimberg, & Kraemer, 1992; Mandal, 1986; Mandal, & Bhattacharya, 1985; Mikhailova, Vladimirova, Iznak, Tsusulkovskaya, & Sushko, 1996; Persad, & Polivy, 1993; Walker, McGuire, & Bettes, 1984; Zuroff, & Colussy, 1986). These reports imply that alterations in facial affect recognition may be associated with the concurrent mood (i.e., depressed 'state'), rather than the other components (i.e.,

'traits') of affective illness, such as the duration and the severity of prior course of illness. Alterations in other cognitive domains, such as memory and perception, exist in acutely depressed participants, such as patients with affective disorders (Post et al., 2000; Veiel, 1997) and mood-induced healthy controls (Bower, 1981; Kenealy, 1986). For example, using a procedure developed by Velten (1968) to induce happy or sad moods in healthy controls, Bower (1981) observed that healthy controls exhibited mood-state-dependent learning and memory (i.e., the controls recalled a greater percentage of those experiences that were affectively congruent with the mood they were in during recall).

To examine if these facial affect recognition are associated with 'trait' rather than 'state' characteristics of mood disorders, a few experiments have explored facial affect recognition in depressed and euthymic patients with bipolar disorder. Rubinow and Post (1992) used a non-verbal photograph-matching task and a sentence-matching test, similar to tasks used by Kolb and Taylor (1981), to assess the perception of facial and verbal affect, respectively, in 17 acutely depressed patients with affective disorder (i.e., bipolar disorder or major depressive disorder), compared with 31 healthy controls. For the photograph-matching task, the participants examined 48 photographs of faces, and matched each with one of seven key photographs of faces (i.e., anger,

disgust, fear, happy, sad, surprise, and neutral), representing the basic emotional domains defined by Ekman, Friesen, and Ellisworth (1972). Similarly, for the sentence-matching test, the participants read 48 sentences describing the affective states of individuals, and matched each with one of seven key labels denoting the basic emotional domains. Rubinow and Post (1992) found that the patients performed poorly on the photograph-matching (but not sentence-matching) task, compared with the healthy controls. Furthermore, the investigators observed that the performance on the photograph-matching task by five medication-free euthymic patients was similar to that of the healthy controls. One should interpret the latter results with caution, however, given the small sample size and resulting low statistical.

Addington and Addington (1998) designed discrimination and labeling tasks to explore the non-verbal and verbal perception of facial affect, respectively, in 40 euthymic patients with bipolar disorder, compared with 40 healthy controls. In the discrimination task, the participants examined 42 pairs of photographs of faces. After viewing each pair, the participants decided if the facial expressions of emotion were similar or different. Addington and Addington (1998) used photographs of facial expressions which spanned the seven basic emotional domains of Ekman et al. (1972). In the labeling task, the participants examined 21 photographs of faces. After viewing

each photograph, the participants described the emotion of the face by selecting one (or more) labels which encompassed the seven basic emotional domains. Addington and Addington observed that the performance on both the discrimination task and the labeling task of the euthymic patients was similar to that of the healthy controls.

George et al. (1998) demonstrated that facial emotion recognition was mood-dependent in a male patient with rapid-cycling bipolar disorder. In the experiment, the patient examined photographs of happy and sad faces from the Pennsylvania Facial Discrimination Task (Erwin et al., 1992). After viewing each face, the patient rated the valence and degree of the emotion expressed using a 7-point scale, '1' representing 'very happy' to '7' representing 'very sad'. As a control measure, the patient examined the photographs again, and rated the age of each individual using a 7-point scale, '1' representing 'teens' to '7' representing '70s'. George et al. (1998) found that the patient judged neutral faces as sad and sad faces as very sad when acutely depressed. Furthermore, the emotional misjudgment disappeared when the patient reverted to a euthymic mood state. The patient's performance on the age discrimination control task was unaffected by mood state. While the study provided some evidence for the state-dependent nature of facial affect recognition in patients with mood disorders, the results were not conclusive. George et al. used facial expressions from only two

(i.e., happy and sad) of the seven (i.e., fear, anger, disgust, surprise, neutral) emotional domains, defined by Ekman et al. (1972). Thus, researchers have yet to determine if alterations in the recognition of facial expressions of fear, anger, disgust, and surprise in patients with mood disorders are either state- (i.e., mood) or trait- (i.e., illness) dependent.

The alterations of facial expressions of emotion are of interest, because they can reveal additional information on brain-behavior relationships, such as the association between the temporolimbic structures (e.g., the amygdala and the hippocampus) and the perception of emotion. In addition, alterations in the recognition for facial expressions of emotion can help investigators further understand features of bipolar disorder, such as the perception of emotion, and may result in improved treatment strategies. Subtle alterations, such as a higher threshold of recognition for facial expressions of emotion, may have a large impact on the social functioning of euthymic patients. Although Rubinow and Post (1992), Addington and Addington (1998), and George et al. (1998) examined the recognition of facial expressions of emotion in euthymic patients with bipolar disorder, their tasks may have been inadequate to assess subtle alterations, such as the threshold of recognition, associated with the perception of facial affect. Threshold of recognition may serve as a more

sensitive marker of bipolar disorder during asymptomatic periods. No experiments to date, to my knowledge, have explored the sensitivity of recognition in euthymic patients with bipolar disorder compared to healthy controls. Hence, the present study will explore both the accuracy and the sensitivity of facial affect recognition, in both euthymic patients with bipolar disorder and healthy controls, using a computer-administered task.

Hypotheses

The hypotheses of the present study are that the euthymic patients with bipolar disorder will be less accurate in recognizing specific facial expressions of emotion (e.g., fear and disgust), compared to the healthy controls, and that the euthymic patients will have a higher threshold of recognition (i.e., lower sensitivity) for facial expressions of emotion, compared to the healthy controls.

CHAPTER 2

METHOD

Participants

The participants included 34 patients (16 women, 18 men) with bipolar disorder who were part of an ongoing longitudinal treatment study at the outpatient clinic of the National Institute of Mental Health (NIMH) in Bethesda, Maryland (see Table 1). All of the patients met DSM-IV (American Psychiatric Association, 1994) criteria for bipolar disorder. Clinicians (i.e., psychiatrists, psychiatric nurses, and pre-graduate research assistants) screened the patients for psychiatric illnesses using the Structured Clinical Interview for DSM-IV Axis I Disorders – Patient Edition (SCID-I/P, Version 2.0) (First, Spitzer, Gibbon, & Williams, 1996), and excluded those with severe medical illnesses or other current Axis I disorders, such as substance abuse. The clinicians also evaluated the patients for neurological disorders and brain injury, and excluded those with current or past neurological ailments. The patients had a mean age of 48.6 (SE = 2.3) years and an average education of 16.3 (SE = 0.5) years. Over 75% of the patients were either employed or in school. Thirty-three of the 34 patients took

one or more mood stabilizing medications at task administration (i.e., lithium (N = 7), carbamazepine (N = 3), valproate (N = 7), lithium and carbamazepine (N = 9), lithium and valproate (N = 6), and carbamazepine and valproate (N = 1)).

The participants also included 26 healthy controls (17 women, 9 men) from the Washington, D. C. metropolitan area who responded to word-of-mouth advertising (see Table 1). Clinicians screened the participants for a history of psychiatric illnesses, current or prior substance abuse, neurological disorders, and other severe medical conditions. The controls had a mean age of 36.3 (SE = 2.7) years and an average education of 17.1 (SE = 0.2) years. All of the controls were either employed or in school. The institutional review boards of both the NIMH and American University reviewed the study protocol and all of the participants gave written informed consent before taking part in the experiment.

Assessments

Mood Ratings

The assessment of the patients' mood state took place during monthly visits to the outpatient clinic, using the clinician-administered versions of the Inventory of Depressive Symptomatology (IDS) (Rush, Giles, Schlesser, Fulton, Weissenberger, & Burns, 1996; Rush, Gullion, Basco, Jarrett, & Trivedi, 1996), the Mania Rating Scale

(MRS) (Young, Biggs, Ziegler, & Meyer, 1978), and the Life Chart Method (LCM) (Leverich & Post, 1996; 1998). Evaluation of the healthy controls' mood state took place during the testing session, using the self-administered version of the Beck Depression Inventory (BDI) (Beck, 1967; Beck & Beamesderfer, 1974).

General Intellectual Functioning

The assessment of the patients' general intellectual functioning took place during a separate testing session using the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III; Wechsler, 1997). Evaluation of the healthy controls' general intellectual functioning occurred during the same testing session as the threshold task using the Shipley Institute of Living Scale (Shipley, 1940).

Threshold Task

The assessment of the threshold of facial affect recognition occurred using a computer-administered task. In the task, participants viewed obscured images of facial expressions of emotion, which cleared up slowly over a short time interval. Participants responded when they thought they recognized the emotional expression of the images. A computer recorded both the accuracy and the sensitivity (i.e., the

threshold) of recognition for each image. The threshold task contained warm-up and test sections.

Stimulus Materials

For the warm-up section of the task, the stimuli included six black-and-white photographs of famous individuals (i.e., Prince Charles, Arnold Schwarzenegger, Denzel Washington, Brooke Shields, Robin Williams, and Tom Hanks). We obtained the warm-up stimuli from publicity photos of the famous individuals, which had appeared previously in the popular press.

For the test portion of the task, the stimuli included 35 black-and-white images of faces (15 women, 20 men), each having one of seven different emotional expressions (i.e., anger, disgust, fear, happiness, sadness, surprise, or neutral). We obtained the test stimuli from numerous still (or "paused") images of videotaped sessions of individuals who made various facial expressions of emotion (see Kolb and Taylor, 1990; 2000). We designed a stimulus presentation program using HyperCard 2.4.1 (Apple Computer, Inc., Cupertino, CA), to display each digitized image separately, in the center of a computer monitor, on a white background. Eight buttons (i.e., 'anger', 'disgust', 'fear', 'happiness', 'sadness', 'surprise', 'neutral', or 'other') appeared with each image. Fifteen expert judges (i.e., graduate students and

undergraduate research assistants from the Human Neuropsychology Laboratory) viewed and rated the emotional expressions of each image by clicking on one of the buttons using a mouse. If a judge selected the 'other' button, an additional button (i.e., 'don't know') and a blank line appeared on the computer screen. At that point, the judge either selected the 'don't know' button, or identified the emotional expression of the image by typing in a one-word description on the blank line.

After reviewing the judges' ratings of the images, we selected 35 of the images (five for each emotion) as test stimuli for the threshold task. The five images selected for each emotion represented a range of agreement by the judges. Thus, for two (of the five) images, 70% (n = 10) of the judges agreed on the emotional expression. Similarly, for two images, 80% (n = 12) of the judges agreed on the emotional expression, and for one image, 90% (n = 14) agreed. We used test stimuli with a range of agreement by the judges to ensure breadth of difficulty, thereby reducing the probability of floor or ceiling effects.

To create the stimuli for the threshold task, we used an optical scanner (UMAX Technologies, Inc., Fremont, CA) to digitize the photographs, storing the resulting JPEG (Joint Photographic Experts Group) files on the hard drive of a Power Macintosh G3 computer (Apple Computer, Inc., Cupertino, CA). Then, we imported

the JPEG files into Adobe PhotoShop 5.0 (Adobe Systems Inc., San Jose, CA) and applied a small (5%) layer of static (or "noise") to each photograph. We repeated the application of the static to each photograph 33 times, creating static layers of increasing density. This method produced a range of images (i.e., slightly obscure to completely obscure) for each photograph. The images ranged in size from 7.2 cm tall by 4.8 cm wide to 7.2 cm tall by 12 cm wide.

Task Procedure

The participants sat 40 to 60 cm from the computer screen and wore glasses or contact lenses, if needed, to see the stimuli clearly. We designed a stimulus presentation program using HyperCard 2.4.1 (Apple Computer, Inc., Cupertino, CA), to arrange and display the images from the highest to the lowest density of static. The computer presented the warm-up stimuli to the participants in the same order. The computer, however, presented the test stimuli to the participants in a randomized order. Warm-up and test stimuli appeared in the center of the computer screen on a white background. During the initial presentation of each stimulus, the participant viewed a completely obscured image. The images changed every 500 ms, starting with the most obscured one and progressing to the least obscured image over 17 seconds. To encourage speed and accuracy, the participants earned points based upon their ability to

recognize each test stimulus quickly (and correctly). Thus, those participants responding correctly to more obscured test stimuli earned more points compared to participants responding correctly to less obscured test stimuli. Participants received feedback on their responses to the test stimuli because the computer displayed (and kept a running total of) the number of points earned in the upper left corner of the screen. Participants had one chance to respond to each image. If the participant could not recognize the emotional expression of an image by the time the least obscured image had been shown for 500 ms (i.e., the participant did not respond), the participant received no points for that test stimulus and the computer presented the next test stimulus. The computer recorded the number of points earned for each test stimulus. Incorrect responses earned no points.

Warm-Up Section. For the warm-up section, the participants pressed the mouse button as soon as they recognized the face of the famous individual through the static. After pressing the mouse button, the computer prompted the participant to type in the name of the famous individual. The computer recorded the time taken to recognize each famous individual and the name typed in by the participant.

Test Section. Participants responded to each test stimulus using two modalities (i.e., non-verbal face-matching and verbal face-labeling), which allowed us to examine differences (if any) that may have existed between what the subjects saw and what they said they saw. During the task, participants pressed the mouse button as soon as they thought they recognized the emotional expression of the test stimulus through the static. After pressing the mouse button, the test stimulus disappeared and seven key faces corresponding to the seven basic emotions appeared on the computer screen. Six of the key faces were photographs taken from Life magazine (e.g., Kolb and Taylor, 1981), and one key face was taken from a set used by Ekman et al. (1972). The participants chose the key face they thought best matched the emotional expression of the test stimulus. The key faces disappeared after the participants responded and the computer recorded which of the key faces they chose. Next, the participants chose one of seven verbal labels (corresponding to the seven basic emotions) that they thought best matched the emotional expression of the test stimulus. The computer recorded the participants' responses (i.e., the labels chosen).

General Procedure

During monthly clinic visits, the clinicians assessed the patients' mood and their tolerance to psychotropic medications (see Denicoff et al., 1997 for further

details). The patients, who were euthymic (i.e., in remission of symptoms) for at least four weeks (determined by the LCM ratings), completed the four-hour study (i.e., WAIS-III and threshold task) during multiple clinic visits, which both helped to reduce fatigue and to ensure optimum performance.

The controls completed the threshold task, the mood rating (i.e., BDI), the Shipley Institute of Living Scale, and the demographic questionnaires either at NIMH or at their residences. The administration of the threshold tasks and the questionnaires (i.e., Shipley Institute of Living Scale, demographic and handedness inventories) took approximately two hours.

The administration of the threshold task occurred using two different Power Macintosh G3 computers (a desktop and a laptop model). The laptop model allowed for testing in the participants' residence. Both of the computers contained 300 MHz microprocessors. Experimenters were not blind to the diagnosis of the participants during the study. The participants took part in the study voluntarily, and none of the participants received monetary compensation for their time. All of the participants received debriefing after completing the study.

Statistical Analysis

Because the data did not satisfy all of the assumptions required for parametric analyses (e.g., normal distribution, homogeneity of variance), we analyzed the results with nonparametric statistical procedures (i.e., Mann-Whitney U tests and Spearman rank correlation coefficients). We performed data analysis on a PC (Dell Computer Corp., Round Rock, TX) running SPSS 8.0 (SPSS Inc., Chicago, IL) and SamplePower 1.2 (SPSS Inc., Chicago, IL) for Windows NT 4.0 (Microsoft Corp., Redmond, WA).

CHAPTER 3

RESULTS

We compared the demographic variables (i.e., age, education, and IQ; see Table 1) between the patients and the healthy controls using Mann-Whitney U tests. The patients were significantly ($U = 214.0$, $p < .001$) older than the healthy controls; however, none of the other comparisons was statistically significant. We evaluated the relationship between the demographic variables and the variables from the threshold task (for both the patients and the controls) using Spearman rank correlation coefficients. None of the associations was statistically significant. Similarly, we evaluated the variables from the threshold task by gender and by the computer used for administration (for both the patients and the controls) using Mann-Whitney U tests. Again, none of the comparisons was statistically significant. Finally, we examined the performance of the patients on the threshold task by previous mood state (i.e., the last episode being depression or mania) using Mann-Whitney U tests. None of the comparisons reached statistical significance.

For the face-matching response modality (i.e., number of correct face-face matches), none of the comparisons between the patients and the controls was statistically significant (see Figure 1). For the face-labeling response modality (i.e., number of correct face-label matches) the patients ($\underline{M}$ = 1.0, $\underline{SE}$ = 0.1) made significantly ($\underline{U}$ = 311.5, $\underline{p} < .05$) fewer correct matches for anger and significantly ($\underline{U}$ = 296.5, $\underline{p} < .05$) more correct matches for fear ($\underline{M}$ = 1.7, $\underline{SE}$ = 0.2), compared with the healthy controls ($\underline{M}$ = 1.5, $\underline{SE}$ = 0.2 and $\underline{M}$ = 1.2, $\underline{SE}$ = 0.2, respectively). None of the other comparisons between the patients and the controls was statistically significant (see Figure 2).

The patients ($\underline{M}$ = 7.5, $\underline{SE}$ = 0.7) had a significantly ($\underline{U}$ = 300.0, $\underline{p} < .05$) higher threshold (i.e., they scored less points) for recognizing happy faces, compared with the healthy controls ($\underline{M}$ = 9.1, $\underline{SE}$ = 0.7). None of the other comparisons between the patients and the controls was statistically significant (see Figure 3).

We performed post-hoc power analyses, using small, medium, and large effect sizes (i.e., 0.2, 0.4, and 0.6, respectively), the sample sizes (i.e., 34 and 26) and an alpha of .05 (two-tailed), to estimate the power of the data. We estimated the power to be .21 using a small effect size, .36 using a medium effect size, and .45 using a large effect size.

Although the patients had a lower threshold of recognition for sadness ($\underline{M}$ = 17.8, $\underline{SE}$ = 4.2, $\underline{N}$ = 11), compared to the healthy controls ($\underline{M}$ = 4.5, $\underline{SE}$ = 1.1, $\underline{N}$ = 5), the difference did not achieve statistical significance (see Figure 3). Further analyses revealed a bimodal distribution within the patient group for threshold of recognition for sadness. Five of the 11 patients had a significantly ($\underline{U} = 0$, $\underline{p} < .05$) higher threshold of recognition for sadness ($\underline{M}$ = 3.8, $\underline{SE}$ = 1.4), compared to the six other patients ($\underline{M}$ = 29.4, $\underline{SE}$ = 2.1). The high and low scoring patients did not differ significantly with respect to the demographic variables or the type of sadness stimuli to which they responded. Furthermore, the five patients with a high threshold of recognition for sadness did not differ significantly from the five healthy controls. The six patients with a low threshold of recognition, however, differed significantly ($\underline{U} = 0$, $\underline{p} < .05$) from the five healthy controls.

Although we did not expect the patients or the controls to be biased in their responses, we evaluated the data for the possibility of a response bias. For each emotional domain, we determined the percent of patients and controls who made correct and incorrect responses, quantifying by the type of response (see Tables 2 and 3). For example, for the face-matching response modality, 21.2% of the patients correctly identified angry faces, however, 15.9% of the patients chose 'disgust', 7.1% chose

'fear', 12.4% chose 'happy', 30.0% chose 'neutral', 5.3% chose 'sad', 5.3% chose 'surprise', and 2.9% made no response (see Table 2). If a relatively large proportion (e.g., 30% vs. 2.9%) of the patients (or the controls) had chosen one of the six possible incorrect responses, then this would have suggested that a response bias was present. Thus, hypothetically, if 3% of the patients correctly identified angry faces, 91% of the patients chose 'disgust', and 1% chose 'fear', 'happy', 'neutral', 'sad', 'surprise', or made no response, respectively, then the patients would have been biased in choosing 'disgust' for angry faces. The data suggest that both the patients and the controls were not biased, because for each emotional domain, the proportions of participants choosing incorrect responses were, for the most part, uniformly distributed across the six possible incorrect choices (see Tables 2 and 3).

We used an analytic technique, employed by Cottrell and Dailey (2000), to determine if the distributions of the responses within the face-matching and the face-labeling modalities were congruent between the patients and the controls. If the patients and the controls responded in a similar manner (i.e., made similar mistakes), then the association of the distribution of responses, between the patients and the controls, would be highly correlated. Using Spearman rank correlation coefficients, we determined that the patients and the controls had similar distributions of responses (i.e., made similar

mistakes), during both the face-matching ($r_s = .81$, $p < .001$) and the face-labeling ($r_s = .77$, $p < .001$) modalities.

CHAPTER 4

DISCUSSION

The results from this study suggest that the euthymic patients with bipolar disorder are both less accurate and sensitive in recognizing certain facial expressions of emotion, but both more accurate and sensitive in identifying other facial expressions of emotion. Specifically, the patients made significantly fewer correct matches for anger and significantly more correct matches for fear (when matching the emotional expressions of the faces to a verbal label), compared with the healthy controls. In addition, the patients were significantly less sensitive (i.e., had a higher threshold) to happy faces, compared to the healthy controls.

The patients were significantly less accurate in identifying angry faces verbally, compared with healthy controls. These data are convergent with observations by Scott, Young, Calder, Hellawell, Aggleton, and Johnson (1997), where a patient with bilateral lesions of the amygdala had difficulty recognizing anger (and fear) using auditory (i.e., words and sounds) emotion recognition tasks. Scott et al. (1997) postulated that the emotions of fear and anger are closely associated, because displays

of fear and anger by an individual represent the presence of an immediate threat in the environment. Furthermore, Scott et al. hypothesized that anger carries a clear intention which frightens the recipient (and induces fear). Davis (1992) and LeDoux (1995) speculated that alteration in the recognition of fear and anger after amygdala damage reflects involvement of the amygdala in both the assessment of threatening situations and the emotion of fear. While the amygdala is associated with the ability to recognize fear (Adolphs et al., 1994; Adolphs et al., 1995; Broks et al, 1998; Calder et al., 1996), its association with the ability to recognize anger is unclear. For example, Blair et al. (1999), using PET, observed that the recognition of the facial expression of anger was associated with activity in both the orbitofrontal and anterior cingulate cortex in healthy control participants. They found no relationship, however, with the recognition of facial expressions of anger and activation in the amygdala.

Based on the observations of Blair et al. (1999), our data indicate that alterations in the recognition of anger, in patients with bipolar disorder, may be associated with abnormal functioning of the orbitofrontal cortex and the cingulate cortex, rather than aberrant functioning of the amygdala. In fact, both structural and functional neuroanatomic data implicate the orbitofrontal and cingulate regions in the pathophysiology of mood disorders. Using histopathological techniques, Rajkowska et

al. (1999) found decreased neuronal size and decreased neuronal and glial densities in the orbitofrontal region of patients with major depressive disorder, compared with healthy controls. Using PET, Baxter et al. (1989) and Drevets et al. (1997) observed decreased blood flow and metabolism in the anterior cingulate of patients with either major depressive disorder or bipolar disorder, compared with healthy controls. Further studies, using both functional neuroimaging techniques and behavioral tests, such as the threshold task, are needed to explore systematically the neural basis for the recognition of facial expressions of anger, in patients with bipolar disorder.

Although the euthymic patients were less accurate in identifying fearful faces non-verbally, they were significantly more accurate in identifying fearful faces verbally, compared with the healthy controls. These results seem contradictory; however, they are congruent with the observations of Adolphs et al. (1994; 1995; 1998), Anderson and Phelps (2000), and Young et al. (1996). In these studies, patients with damage to the amygdala had a greater difficulty interpreting non-verbal cues (i.e., facial expressions) of emotion (especially fear), versus verbal cues (i.e., words). Patients with bipolar disorder do not have damage per se to the amygdala; however, structural and functional abnormalities exist (Abercrombie et al., 1998; Altshuler et al., 1998; Altshuler et al., 2000; Drevets et al., 1992; Strakowski et al., 1999). These structural

and functional abnormalities of the amygdala may account for the patients' difficulty in non-verbally recognizing fearful facial expressions. The neural basis for both the verbal and the non-verbal recognition of fearful facial expressions, in patients with bipolar disorder, warrants further exploration in future studies.

George et al. (1998) observed that a male patient with rapid-cycling bipolar disorder rated neutral faces as sad, and sad faces as very sad, during depressive episodes. Furthermore, George et al. found that this bias (i.e., trait marker of the illness) disappeared when the patient cycled into a euthymic interval. The data from the present study, however, differ from the observations of George et al. We found that euthymic patients with bipolar disorder were less accurate and had a significantly higher threshold for recognizing happy faces, compared to healthy controls, which may reflect an underlying presence (i.e., trait marker) of the illness.

There are some limitations with this study, which warrant consideration. For example, the patients were taking mood-stabilizing medications (i.e., lithium, carbamazepine, and/or valproate). The few studies that have examined the relationship of mood-stabilizing medications (or neuroleptic medications) on neuropsychological test performance in patients with mood disorders have yielded divergent results. Andrewes, Schweitzer, and Marshall (1990) reported that patients with mood disorders

performed more poorly on a psychomotor task while on the combination of lithium and carbamazepine, compared to either lithium or carbamazepine monotherapy. Furthermore, Andrewes et al. (1990) found that patients performed more poorly on a memory task while on lithium and the combination of lithium and carbamazepine, compared to carbamazepine monotherapy. However, Joffe, MacDonald, and Kutcher (1988) observed no relationship between lithium or carbamazepine prophylaxis and performance on neuropsychological tests of attention, concentration, visuomotor function, and memory in patients with bipolar disorder. Similarly, Prevey et al. (1996) found no association between carbamazepine and valproate treatment and performance on neuropsychological tasks of psychomotor functioning, concentration, cognitive flexibility, and memory in patients with epilepsy.

In the present study, the patients were on a large number of different mood-stabilizing medication regimens (or their combinations), which prevented an analysis of the effects of medication on the performance of the threshold task. While mood-stabilizing medications may have blunted task performance, their effects were not systematic across all of the variables, because the patients were more accurate in recognizing facial expressions of sadness and fear, compared with healthy controls.

Thus, it is unlikely that the mood-stabilizing medications affected the results in any systematic way.

The sample sizes of the patient and the healthy control groups were another limitation of this study. The number of patients in the present study was restricted to those in the NIMH clinic who were euthymic at the time of neuropsychological assessment. The number of healthy controls (particularly, age-matched healthy controls) was limited to those who were available and willing to participate in the study for no compensation. Threshold (or sensitivity) of recognition for facial expressions of emotion may be a subtle quality, which does not differ dramatically between the patients and the controls, but may still have a meaningful effect in social functioning. Thus, the paucity of significant findings in the present study may reflect the fact that patients are similar to controls. However, the paucity of significant findings could be due to the small sample sizes, which reduced statistical power (and the ability to detect smaller differences between the patients and the controls). Future studies are necessary to both replicate and extend the present results using a greater number of patients and controls.

Notably, patients had either a high or low threshold of recognition for sadness. Although it would be interesting to know why this bimodal distribution

emerged, the small sample sizes (i.e., $\underline{N} = 6$ and $\underline{N} = 5$ for low and high threshold of recognition, respectively) limited our ability to draw meaningful conclusions from the additional analyses performed (i.e., the comparisons of the demographic variables between the low and high threshold of recognition for sadness groups). Further research is needed to replicate this result (if possible) and explore its cause.

Curiously, the patients and the controls had similar distributions of responses, during both face-matching and face-labeling (see Tables 2 and 3). This suggests that the patients and the controls perceived the faces in the same way. In fact, many of the patients and some of the controls indicated to the experimenter that they were looking for specific features of the faces, such as the mouth or the eyes, to decipher the emotional expression through the static. However, our data differ from the observations of Sapin, Berrettini, Nurnberger, and Rothblat (1987), who explored facial information-processing strategies (i.e., the recognition of non-affected faces) in euthymic patients with bipolar disorder and healthy controls. They found that the patients relied on individual facial features during facial recognition, whereas the controls synthesized multiple elements (i.e., the features) of the faces during recognition. Hence, the strategies employed by euthymic patients with bipolar disorder

versus those used by healthy controls, during facial affect recognition require further study.

Both the patients and the controls achieved relatively low levels of performance for angry, disgusted, fearful, and sad facial expressions, but relatively high levels of performance for happy, surprised, and neutral facial expressions (see Figures 1 and 2). Davidson (2000) postulates that emotions possess a valence (i.e., they are either positive or negative). Anger, disgust, fear, and sadness are negative emotions, whereas happiness and surprise are positive emotions (neutral facial expressions have no valence). Given the present data, participants, regardless of any diagnosis, may have had a greater difficulty recognizing the negative emotions, compared to the positive (or the neutral) emotions merely because there were more possibilities within that group.

Although the patients were significantly older than the healthy controls, the correlations between age (and the other demographic variables) and both the patients' and controls' performance on the threshold task were not statistically significant. Mood and general intellectual functioning were also not correlated with either the patients' or the controls' performance on the threshold task. The experimenters were not blind to the diagnosis of the participants during the study,

leading to the possibility of experimenter bias; however, this was unlikely, because a computer administered and scored the affect recognition threshold task.

In summary, we found that euthymic patients are less accurate when labeling facial expressions of anger verbally, but more accurate when labeling facial expressions of fear verbally, compared with healthy controls. In addition, the patients were less sensitive (i.e., had a higher threshold) to happy faces, compared to the healthy controls. This study has a variety of implications for the treatment of bipolar disorder, because the ability to recognize facial expressions of emotion accentuates communication, and can reveal additional information during social interactions. Given the data from this and similar studies, clinicians can inform patients about the alterations in the recognition of facial expressions of emotion, especially those that persist during euthymic periods. Thus, this information allows patients to be more self-aware of limitations that may exist in their social functioning. This study also highlights the need for further research in the recognition of facial expressions of emotion in patients with bipolar disorder. Behavioral and neuroimaging methods, used simultaneously, can explore the relationships between alterations in facial affect recognition and structural and/or functional abnormalities of neuroanatomical structures.

APPENDIX

Table 1

Demographic Characteristics for the Participants

Variable	Patients			Controls		
	N	M	SE	N	M	SE
Age	34	48.6	2.3	26	36.3	2.7
Years of Education	34	16.3	0.5	26	17.1	0.2
IQ[a]	30	111.2	3.3	26	111.8	1.2
Mood						
IDS	34	6.0	0.8			
MRS	34	1.4	0.3			
Length of euthymic interval (days) prior to assessment[b]	34	736.3	156.1			
BDI				26	2.7	0.6

Table 1 (cont'd)

Variable	Patients N	Controls N
Gender		
Women	16	17
Men	18	9
Ethnicity		
Caucasian	32	19
African American	1	2
Asian American	0	4
Hispanic	1	1
Handedness[c]		
Right	30	23
Left	4	3
Diagnosis		
Bipolar I	22	
Bipolar II	12	

Table 1 (cont'd)

Note. [a]WAIS-III full-scale IQ reported for the patients, WAIS-R full-scale IQ (estimated from the Shipley Institute of Living Scale) reported for the controls. Four patients did not complete intelligence testing.
[b]Assessed using the Life-Chart Method (Leverich & Post, 1996; 1998).
[c]Assessed using the Handedness Inventory (Briggs & Nebes, 1975).

Table 2

Percents of Correct and Incorrect Responses Made by the Participants for the Face-Matching.

Participants' Responses[a]	Type of Facial Expression of Emotion Presented to the Participants						
	Anger	Disgust	Fear	Happy	Neutral	Sad	Surprise
No Response	2.9	7.1	7.1	7.1	4.1	13.5	6.5
	3.1	2.3	1.5	1.5	3.1	6.2	4.6
Anger	**21.2**	35.3	5.9	4.1	3.5	3.5	1.2
	28.5	38.5	10.0	2.3	6.2	9.2	4.6
Disgust	15.9	**12.9**	18.8	1.2	11.2	30.6	4.1
	16.9	**20.0**	16.9	3.1	8.5	27.7	4.6
Fear	7.1	7.6	**22.4**	4.1	4.1	6.5	14.1
	6.2	4.6	**29.2**	3.8	2.3	6.2	14.6
Happy	12.4	10.0	4.7	**65.9**	24.1	8.2	18.8
	6.9	16.2	5.4	**76.2**	21.5	11.5	16.2
Neutral	30.0	12.4	8.8	11.2	**48.2**	26.5	10.0
	33.1	11.5	6.9	10.8	**56.2**	33.1	10.7

Table 2 (cont'd)

Sad	5.3	4.1	20.6	3.5	0.6	**7.6**	8.2
	3.1	0	16.2	2.3	2.3	**4.6**	6.9
Surprise	5.3	10.6	11.8	2.9	4.1	3.5	**37.1**
	2.3	6.9	13.8	0	0	1.5	**37.7**

Note. [a]Within each cell, the top and bottom numbers are the percent of response for the patients and the controls, respectively. Bold numbers represent percents of correct responses. Underlined numbers denote large percents of incorrect responses.

Table 3

Percents of Correct and Incorrect Responses Made by the Participants for Face-Labeling.

Participants' Responses[a]	Type of Facial Expression of Emotion Presented to the Participant						
	Anger	Disgust	Fear	Happy	Neutral	Sad	Surprise
No Response	2.9	7.1	7.1	7.1	4.1	13.5	6.5
	3.1	2.3	1.5	1.5	3.1	6.2	4.6
Anger	**19.4**	35.3	8.2	1.8	2.4	5.9	2.9
	30.0	38.5	8.5	2.3	4.6	7.7	4.6
Disgust	10.6	**12.9**	9.4	1.2	2.9	12.9	2.9
	8.5	**20.0**	10.8	0.8	5.4	7.7	2.3
Fear	4.7	7.6	**34.7**	4.7	3.5	5.3	10.6
	4.6	4.6	**23.1**	0.8	1.5	0	10.0
Happy	12.9	10.0	2.9	**70.6**	23.5	8.8	20.6
	8.5	16.2	5.4	**76.9**	26.9	11.5	17.7
Neutral	29.4	12.4	11.2	10.0	**45.3**	24.1	10.6
	29.2	11.5	6.9	11.5	**51.5**	30.0	10.0

Table 3 (cont'd)

Sad	13.5	4.1	15.3	1.8	11.8	**23.5**	3.5
	14.6	0	26.9	3.8	6.9	**33.8**	5.4
Surprise	6.5	10.6	11.2	2.9	6.5	5.9	**42.4**
	1.5	6.9	16.9	2.3	0	3.1	**45.4**

Note. [a]Within each cell, the top and bottom numbers are the percent of response for the patients and the controls, respectively. Bold numbers represent percents of correct responses. Underlined numbers denote large percents of incorrect responses.

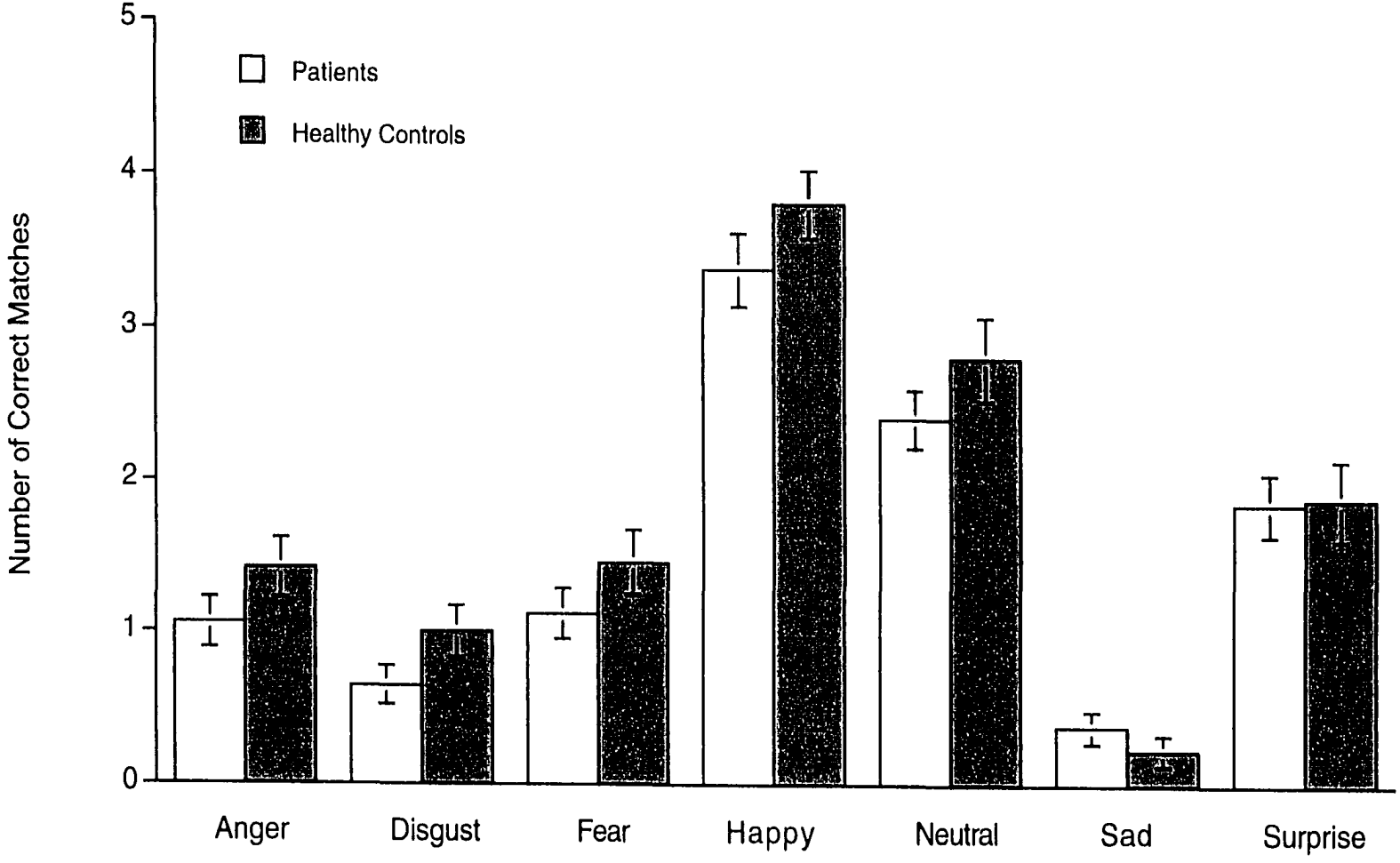

Figure 1: Mean (± SE) number of correct matches (by emotion) during face-matching

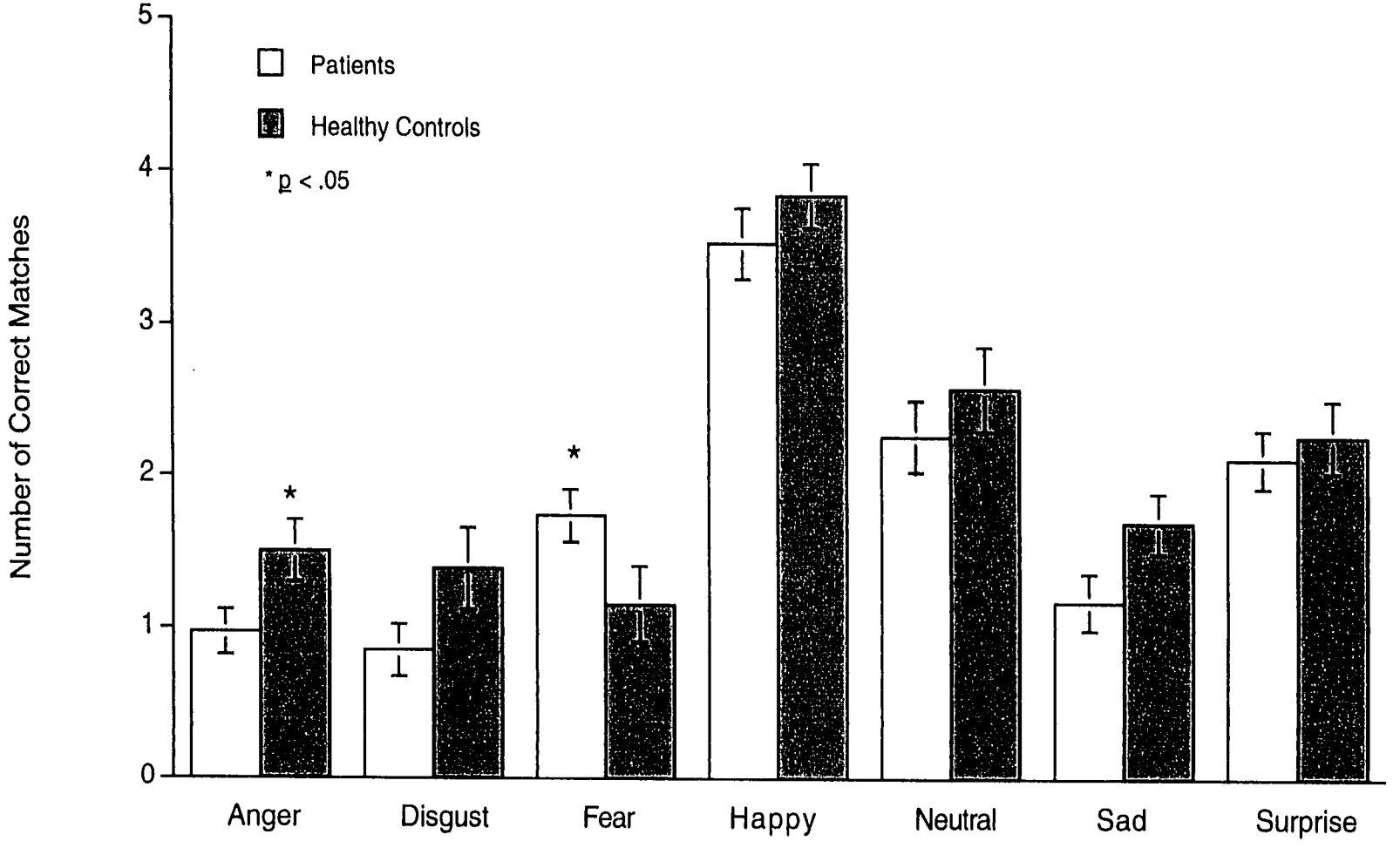

Figure 2: Mean (± SE) number of correct matches (by emotion) during face-labeling

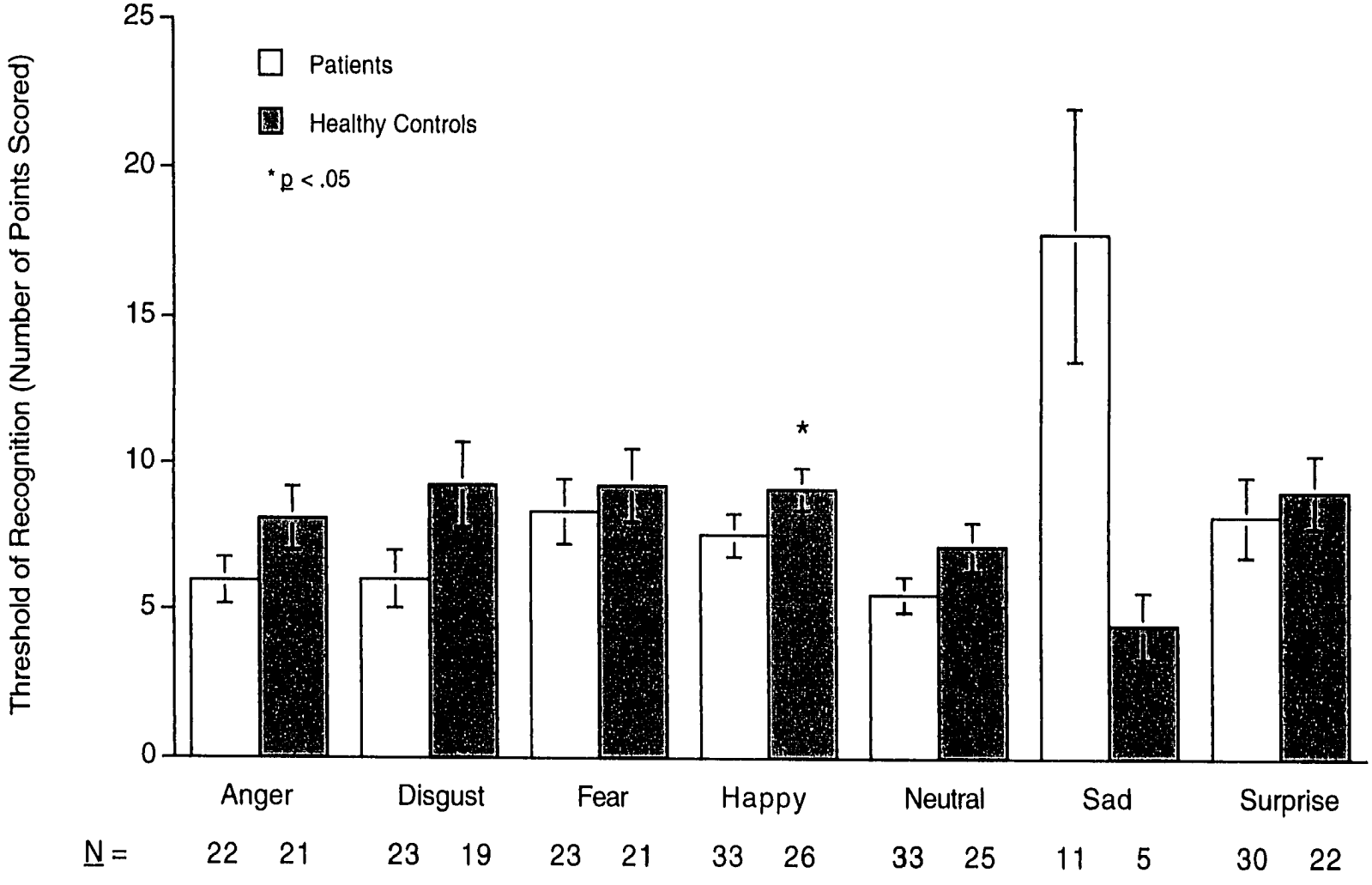

Figure 3: Mean (± SE) of the mean number of points scored (i.e., threshold of recognition) during face-matching

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