Blunted Rostral Anterior Cingulate Response During a Simplified Decoding Task of Negative Emotional Facial Expressions in Alcoholic Patients

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Background: Alcoholism is characterized by deficits in emotional functioning as well as by deficits in cognitive functioning. However, most brain imaging research on alcoholism has focused on cognition rather than emotion.

Method: We used an event-related functional magnetic imaging approach to examine alcoholics' brain blood oxygenation level dependent (BOLD) response to evaluation of emotional stimuli and to compare their response to that of nonalcoholic controls. The task used was a simplified variant of a facial emotion-decoding task in which subjects determined the intensity level of a target emotion displayed as a facial expression. Facial expressions of happy, sad, anger, disgust, and fear were used as stimuli.

Results: Alcoholics and controls did not differ in accurately identifying the intensity level on the simple emotional decoding task but there were significant differences in their BOLD response during evaluation of facial emotion. In general, alcoholics showed less brain activation than nonalcoholic controls. The greatest differences in activation were during decoding of facial expressions of fear and disgust during which alcoholics had significantly less activation than controls in the affective division of the anterior cingulate cortex (ACC). Alcoholics also had significantly less activation than controls in the affective division of the ACC, while viewing sad faces. Only to facial expressions of anger did the alcoholics show significant activation in the affective ACC and in this case, their BOLD response did not significantly differ from that of the controls.

Conclusion: Alcoholics show a deficit in the function of the affective division of the ACC during evaluation of negative facial emotions that can serve as cues for flight or avoidance. This deficit may underlie some of the behavioral dysfunction in alcoholism.

Key Words: Alcoholism, fMRI, Faces, Anterior Cingulate Cortex, Emotion, Cognition.

ALCOHOLISM IS A disease of the brain that can manifest itself structurally and functionally with detrimental behavioral concomitants. Alcoholics have been shown to be deficient in both cognitive and emotional processes. Studies have demonstrated compromises in a variety of cognitive functions including: judgment, problem solving, decision making, planning response flexibility, and inhibition of inappropriate behavior, attention, perception, memory, and language (Adams et al., 1993; Ahveninen et al., 2000; Cohen et al., 1997; Dao-Castellana et al., 1998; Deckel, 1999; Giancola and Moss, 1998; Kamarajan et al., 2005; Porjesz, 1993). Much less work has been performed examining the impairment of emotional processing in alcoholism.

Examinations of personality traits among both alcoholics and individuals at risk for the development of alcoholism suggest that 2 aspects of emotional function are disturbed in alcoholism. Alcoholics appear to be characterized by both a greater tendency to experience negative emotion as well as impulsivity and a lack of social constraint (Elkins et al., 2006; Sher et al., 1999). Recent functional imaging studies show that persons who are anxiety-prone show larger brain blood oxygenation level dependent (BOLD) activations to negative facial expressions than persons without increased anxiety-proneness (Stein et al., 2007). These results suggest that alcoholics who are anxiety-prone should show increased brain response to stimuli that evoke negative emotions However, recently, Miranda et al. (2003) demonstrated that alcoholics, particularly those with disorders characterized by a lack of constraint [antisocial personality disorder (ASPD) and conduct disorder] have a blunted startle response (lack of potentiated startle) to negative emotionally valenced stimuli, but do not differ from controls in their response to positively valenced emotional stimuli. Such a blunted response suggests insensitivity to aversive stimuli. In an earlier study, Miranda et al. (2002) found similarly altered emotionally modulation startle in young adults with a family history of alcoholism.

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A recent functional magnetic imaging (fMRI) study (Glahn et al., 2007) has supported Miranda's findings by showing that nonalcoholic, adult children of alcoholics have a blunted BOLD response in the amygdala to fearful facial expressions and that this hyporesponsivity is associated with behavioral disinhibtion.

Since previous work in our laboratory showed that the alcoholic patients treated at the National Institutes of Health (NIH) inpatient unit from which we recruit subjects suffer from a high incidence of both anxiety disorders and personality disorders characterized by impulsivity and lack of social constraint (Gilman et al., 2007; *in press*), we sought to determine if these subjects would show an elevated or a blunted brain response to facial expressions of negative emotion. To do this, we performed a functional magnetic resonance imaging (fMRI) examination of BOLD brain responses during a very simple facial emotion processing task in which subjects were required to identify the intensity level (high or low) of a facial expression and communicate their judgment by button press. The intensity-rating task was chosen because it is extremely easy and unlikely to elicit any performance differences between groups, while at the same time ensuring attention to and engagement in evaluating the expressions. Alcoholic and nonalcoholic subjects evaluated the intensity of facial expressions of happiness, sadness, fearfulness, anger, and disgust. In this way, we hoped to determine if differences in brain response to emotional facial expression (EFE) between alcoholics and nonalcoholics is limited to negative emotions. In addition, as our methods allowed us to measure BOLD response over most of the brain, we hoped to determine if particular brain regions showed consistent differences between alcoholics and nonalcoholics across various emotions.

MATERIALS AND METHODS

Subjects

Twenty-two right-handed male subjects (all values are given as mean ± SD; 11 alcoholic patients, age 35 ± 5.6 years; range 23 to 43; 11 healthy controls, age 36 ± 5.9 years; range 25 to 45) participated in the experiment. Healthy control subjects were free of any physical or mental illness (including substance use disorders), as determined by structured clinical interviews from the *Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition*. The patient group all met DSM-IV (American Psychiatric Association, 1994) criteria for a diagnosis of alcohol dependence. Duration of drinking history: 20 ± 6 years; Drinks consumed per day during the 6 month prior to hospitalization 14 ± 5.50; Average number of cigarette smoked a day: 10 ± 9; Days since last alcohol drink: 28 ± 15. Table 1 lists drinking history as well as NEO scores for both groups.

Healthy subjects were recruited through the normal volunteer office of NIH. Subjects were a mixture of employees at NIH and surrounding community. Healthy Subjects were paid $70.00 per scan session. None of the healthy controls reported drinking more that 3 drinks a day on a regular basis during their lifetime.

The alcoholic subjects were inpatients from the National Institute on Alcohol Abuse and Alcoholism treatment program. Patients were hospitalized for the 19 ± 4 days preceding scanning (Table 1) prior to testing and were unmedicated at the time of fMRI examination. Most had comorbid Axes II disorders. Only 2 subjects had no Axis I disorders other than alcohol dependence. Eight alcoholic patients had a history of substance abuse other than alcohol; however, for all patients alcohol was their primary drug of choice. Therefore, we could not test pure alcoholics as they had past substance abuse other then alcohol. For Axis I and Axis II disorders see Table 2.

Table 1. Scores Are Presented in Mean ± SD for Age, Years Drinking, Drinks per Day, Days Since Last Drink, Days of Hospitalization, Cigarettes per Day, and NEO Personality Factors

	Alcoholic Patients	Healthy Volunteers
Age	35.7 ± 5.61	36.2 ± 5.86
Years of drinking	20.1 ± 5.80	15 ± 6.30
Drinks consumed per day	13.6 ± 5.50	NA
Days since last drink	28.40 ± 15.03	NA
Days of hospitalization	18.73 ± 3.74	0.00 ± 0.00
Cigarettes consumed per day	10.00 ± 8.66	0.00 ± 0.00
Neuroticism	59.8 ± 13.0	53.6 ± 9.6
Extraversion	54.5 ± 10.9	46.9 ± 7.7
Openness	55.8 ± 7.3	54.9 ± 10.4
Agreeableness	44.0 ± 10.5	52.2 ± 10.5
Conscientiousness*	38.9 ± 7.4	55.4 ± 9.3

*$t(20) = 4.31$, $p < 0.0005$.

NA (not applicable) indicates that this measure was not collected from healthy volunteers.

The NEO personality inventory factor scores showed that the alcoholic subjects were significantly lower in conscientiousness than control subjects (Table 1). Both alcoholic patients and healthy controls were medically healthy as determined by a physical exam and blood and urine laboratory tests. All subjects had normal or corrected-to-normal vision. Subjects gave informed consent to participate. All procedures were reviewed and approved by the National Institute on Alcohol Abuse and Alcoholism Institutional Review Board. Healthy control subjects were compensated monetarily.

Subjects performed the Benton Facial Recognition Test (Benton et al., 1978) to determine if any difficulty in emotional processing/recognition was attributable to impaired perception per se. Score for patients was 47.25 ± 5.03 and score for controls was

Table 2. Number of Patients Who Have Been Diagnosed With Axis I and Axes II Disorders

Axis I	Number of Subjects	Axis II	Number of Subjects
Alcohol dependence	11	PD-NOS	7
Past sedative abuse/dependence	1	BP	3
Past cocaine abuse/dependence	6	OCPD	4
Past cannabis abuse/dependence	7	APD	2
Past hallucinogen abuse/dependence	2	Histrionic PD	1
Social phobia	4	Avoidant PD	1
Mood disorder	6		
Attention deficit disorder	5		
Posttraumatic stress disorder	2		
Generalized anxiety	1		

PD-NOS, personality disorder not otherwise specified; BP, borderline personality disorder; OCPD, obsessive compulsive personality disorder; APD, antisocial personality disorder.

47.87 ± 2.35 demonstrating equivalent performance in subjects groups. Therefore, any impairment in determining the intensity of facial emotion or differences in pattern of brain activation during evaluation of facial emotional intensity cannot be attributed to visual-perceptual abilities related to facial identification.

Visual Stimulation and Task

A total of 240 standardized emotional facial stimuli, 12 for each category of happy, sad, anger, fear, and disgust expressions were selected from a series of standardized EFE images (Matsumoto and Ekman, 1988) as well as a nonemotional control crosshair condition. The series were made up of a set of 2 intensity levels (120 low = 30% of maximal emotional expression intensity and 120 high = 70% of maximal emotional expression intensity). For each of the 5 emotions there were 2 different actors. Same male and female actors were used in the images of the low and high intensity conditions. These were interspersed with 60 fixation cross hair events. The total number of event of each type was therefore 24. The 70% intensity level was chosen over the 100% emotional expressions as it was more frequently encountered in real-life situations (Kornreich et al., 2003). Images were constructed and validated as described by Hess and Blairy (1995). The selected EFE were presented using an ASL laptop computer with Linux installed (ASL, Inc., Fremont, CA) with stimulus delivery software developed in the laboratory and were projected via an Epson 7200 LCD projector (Epson America, Inc., Long Beach, CA) for subject viewing inside the MRI scanner. Images were presented randomly in an event-related design during 2 scans each lasting 5 minutes and 16 seconds. During each scan, each EFE stimulus was presented for 2 seconds with a jittered interstimulus of between 2 and 14 seconds.

Prior to beginning the testing, participants were given a description of the task by the experimenter. Subjects were told that they had to judge the intensity of emotions portrayed in a series of images of faces. The participants were required to complete a practice run until they felt comfortable doing the task as well as to familiarize themselves with the procedure. For the intensity rating task, subjects were instructed to select the intensity level that matched the emotional intensity of the target face and indicate their choice by pressing a left or right button on a button box (Fig. 1). The experimenter addressed any questions that were raised by the subjects.

Brain Imaging

A General Electric 1.5 Tesla Excite MRI scanner with standard quadrature birdcage head coil was used for brain imaging. Single shot gradient recalled Echo-Planar Imaging (EPI) sequence was used for functional imaging. Functional imaging parameters: image matrix size 64×64, repetition time (TR) = 2 seconds, echo time (TE) = 40 milliseconds, flip angle 90°, squared field of view (FOV) = 240×240 mm, slice thickness = 4.8 mm. Each functional run was composed of 155 repetitions, thus lasting for 5 minutes, 16 seconds. Twenty-two axial slices covering most of the brain were prescribed. For high resolution, anatomical imaging (1 mm^3 cubic voxel) T1-weighted 3-dimensional spoiled gradient echo (3D SPGR) sequence was used.

Behavioral Data

The dependent measure for quantifying emotional intensity ratings were Accuracy scores (Accuracy of Response) and Reaction time to button press from the appearance of the target face (Speed of Response). We were interested in assessing whether there were differences in intensity ratings and speed of response between the patients and control groups. For that we conducted a repeated measures multiple analyses of variance approach (MANOVA) with Emotion Type (happy, sad, anger, fear, and disgust) and Intensity (low and high) as within subject factor and Group (alcoholics vs. controls) as the between subject factors. All analyses for the behavioral data were carried out with StatView (Statview Version 5.0.1; SAS Institute Inc., Cary, NC).

fMRI Data

We used a voxel-based statistical approach to identify significant activation maps using Analysis of Functional NeuroImages software package (Cox, 1996; Cox and Hyde, 1997). The first 4 volumes of each fMRI run were removed to ensure MRI signal steady state. Slice acquisition timing-correction, followed by interscan motion correction was performed separately, using 6-parameter rigid body transformation (Cox and Jesmanowicz, 1999), for the slice sets EPI time series. The reference volume for motion correction was chosen from the end of each time series as it was closest in time of acquisition to the reference high-resolution anatomical data set. Estimates of the motion parameters were used as regressors of no interest in the subsequent regression analyses. Voxel time series were scaled by the mean at each voxel to obtain normalized BOLD signal changes. This scaling is almost identical to scaling by the baseline as for fast-randomized event-related design, stimulus-induced changes are less than 1% of the baseline. Interstimulus intervals were composed of crosshairs and were between 2 and 14 seconds in duration.

For group analysis, high-resolution anatomical and accompanying functional data were transformed to the standardized space (Talairach and Tournoux, 1988). Voxel-wise percentage signal change data were entered into a 2-way repeated measures ANOVA with group as between subject factor and condition (expressions vs. fixation crosshair as well as high intensity expression vs. low expressions) as the within subject factor.

High Intensity Expressions—Fixation Comparison. First, to determine areas that were significantly activated during high intensity expression for both healthy controls and alcoholic patients, a within-subjects contrast was computed between high EFE versus the fixation crosshair across the 5 emotion types (happy, sad, anger, fear, and disgust) (Figs 2–11 and Table 5).

High Intensity Expressions—Low Intensity Expressions Comparison. Second, to determine areas that significantly activated during high intensity expression relative to 30% expression for both groups a within-subjects contrast was computed between decoding of high EFE versus decoding of low condition across the 5 emotion types (happy, sad, anger, fear, and disgust) for both healthy controls and alcoholic patients (Table 6). We do not report the results of the comparison between low (30%) emotional intensity expressions and fixation because the low (30%) intensity expressions were included in order to provide a contrast to the high (70%) intensity expressions so that the emotional decoding task could be performed during the scan and this comparison was expected to yield few differences.

Group Comparison

Third, to differentiate group related activation during decoding of 70% EFE for emotion type (happy, sad, anger fear, and disgust), a between group comparison was computed for contrasts of high EFE relative to fixation crosshair for alcoholic patients versus healthy controls and visa versa (Fig. 12 and Table 7).

A threshold adjustment method based on Monte-Carlo simulations was used to guard against identifying false-positive areas of activation (Forman et al., 1995). We only retained clusters of 7 or more contiguous voxels ($3.75 \times 3.75 \times 4.8$ $mm^3 \times 7 = 473$ mm^3) that were significant at $p < 0.005$, leading to a corrected p-value of 0.05 for the entire 3D volume. Finally, impulse response functions were extracted from regions of activation that were found to survive this threshold/cluster method and peak activation foci are reported.

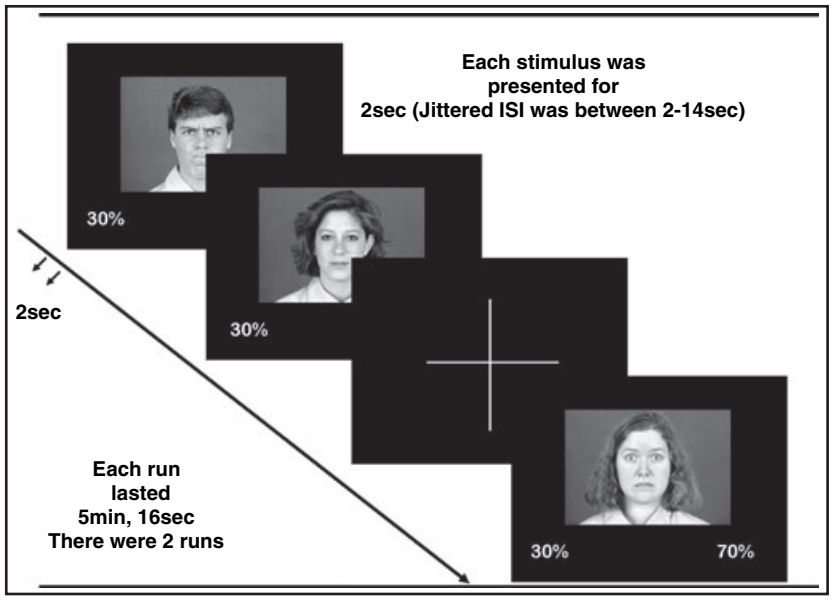

Fig. 1. Study design showing experimental timing and examples of stimuli, including the cross-hair (rest) condition.

As the focus of this investigation is emotional processing we report activations only in brain regions connected to limbic and medial frontal lobe structures. These include: the rostral and dorsal anterior cingulate cortex (ACC), as well as, the amygdala, striatum, hypothalamus, anterior insula, hippocampus, temporal lobe and orbital frontal cortex, dorsolateral prefronal cortex premotor, and parietal cortices as well as precentral gyrus (for review, see Bush et al., 2000 and Devinsky et al., 1995). We also included areas involved in face processing such as the fusiform gyrus (FFG) and other regions in the ventral visual stream.

RESULTS

Behavioral Data

Table 3 shows the mean ± SD of the accuracy scores for the patient and control groups. Alcoholics and nonalcoholic controls performed with similar accuracy in their ability to correctly identify high or low intensity emotional expression. We performed repeated measures of MANOVA. The effects of Emotion Type (happiness, sadness, anger fear, and disgust) and Group (Alcoholic patients and healthy controls) and Emotion Intensity (30% vs. 70%) on accuracy showed no significant difference between groups or any significant interactions between group and other factors. However, this analysis did show that both intensity of emotional expression and type of emotion affected accuracy [Interaction between intensity and emotion; $F(74,4) = 20.2$, $p < 0.0001$]. Inspection of Table 3 and post hoc t-test ($p < 0.001$) show that these effects were due to the difficulty both controls and alcoholics had in correctly identifying the intensity of the 70% sad expressions.

Table 4 shows the mean ± SD of the reaction times for the patient and control groups. Although the alcoholics tended to have a slightly slower speed of response across all emotional expressions and intensities this difference was not significant. Both intensity of the emotional expression and type of emotion significantly influenced reaction time [Interaction between intensity and emotion; $F(72,4) = 5.7$, $p < 0.0005$]. Inspection of Table 4 and post hoc t-test ($p < 0.005$) show that both controls and alcoholics were slow in responding to identify the intensity of the 70% sad expressions.

Neuroimaging Data

Voxels exceeding the significance threshold ($p < 0.05$ corrected, corresponding to $t > 2.7$) for group-specific differences (group contrasts) in brain activation (high EFE vs. baseline) and for condition specific differences in brain activation (high EFE vs. baseline and high EFE vs. low EFE) for both healthy subjects and for alcoholic patients for the 5 basic emotion in healthy controls and alcoholic patients for the first and second contrast analysis are summarized in Tables 5–7 and shown in Figs 2–12. Spatial coordinates are those of the largest response in each cluster.

Brain Activity Associated With 70% Emotional Faces Versus Fixation Crosshair Across All Emotions for Alcoholic Patients and for Healthy Controls

For all conditions, except disgust, we found only in healthy subjects increased activation in the inferior frontal gyrus; similarly, for all expressions except anger, we found activation in the superior parietal lobule only in the healthy controls.

Happy: Areas that were found commonly activated in both the healthy subjects and the patient group include middle frontal gyrus, cingulate gyrus, the insula, caudate, putamen, precentral gyrus as well as the FFG (Figs 2 and 7).

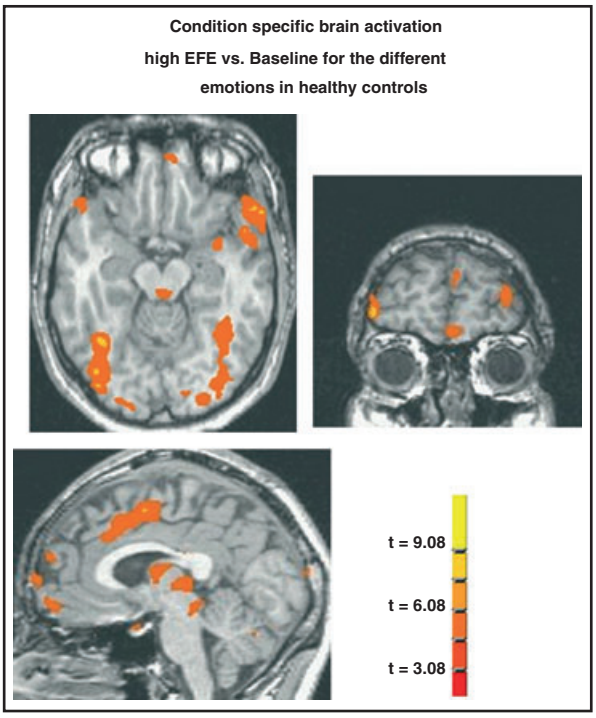

Fig. 2. Happy versus baseline in healthy controls. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.
Figures 2–11. Colorized group statistical map superimposed upon a coronal group averaged T1 structural image in Talairach space. Significance threshold clusters ≥7 contiguous voxels (p<0.05 corrected, corresponding to t > 2.7) for contrast 'high intensity' versus 'baseline' for 5 basic emotions (happy, sad, anger, fear, and disgusts) in healthy subjects (Figs 2–6) and in alcoholic patients (Figs 7–11). Activation foci show rostral anterior cingulate activity in healthy controls for decoding of all emotions except for happy. Alcoholic patients show activation foci in the subgenual gyrus only for decoding of anger EFE. Overall, there was less BOLD effect for decoding of all emotions in the patients group compared with the healthy controls and with EFE decoding for fear showing the most blunted response in patients. The color scale reflects the difference in percentage BOLD signal change.

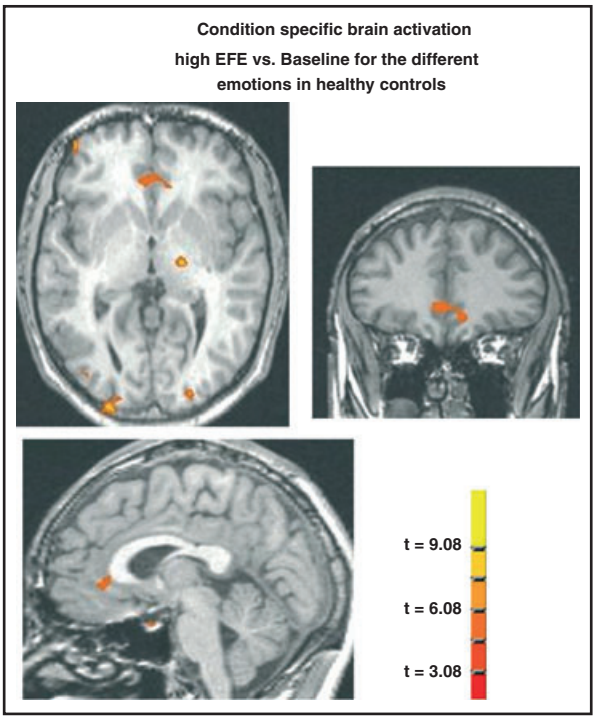

Fig. 3. Sad versus baseline in healthy controls. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

Sad: Sad EFE decoding elicited brain activation for both groups in the cingulate gyrus, insula as well as the precentral gyrus and FFG. In healthy subjects, EFE decoding elicited brain activation in the anterior cingulate, while in the alcoholic patients, the middle frontal gyrus showed increased activation (Figs 3 and 8).

Anger: For anger, we found in both groups brain activation in the middle frontal gyrus, precentral gyrus, and FFG. While in healthy subjects, we found additional activation in the medial frontal gyrus and subgenual gyrus (BA25), alcoholic patients showed activation in the subgenual region (BA25) as well as in the insula (Figs 4 and 9).

Fear: Both healthy subjects and alcoholic patients showed brain activation in the insula for EFE decoding of fear. Healthy controls showed additional activation in a number of other regions that include the middle frontal gyrus, the medial frontal gyrus, the anterior cingulate and subcollosal gyri as well as precentral gyrus and the FFG (Figs 5 and 10).

Disgust: Both subject groups show brain activation in FFG. Healthy subjects also showed brain activation in the middle frontal gyrus, anterior cingulate, the amygdala, insula, as well as precentral gyrus. Alcoholic patients showed additional activation only in the caudate nucleus (Figs 6 and 11).

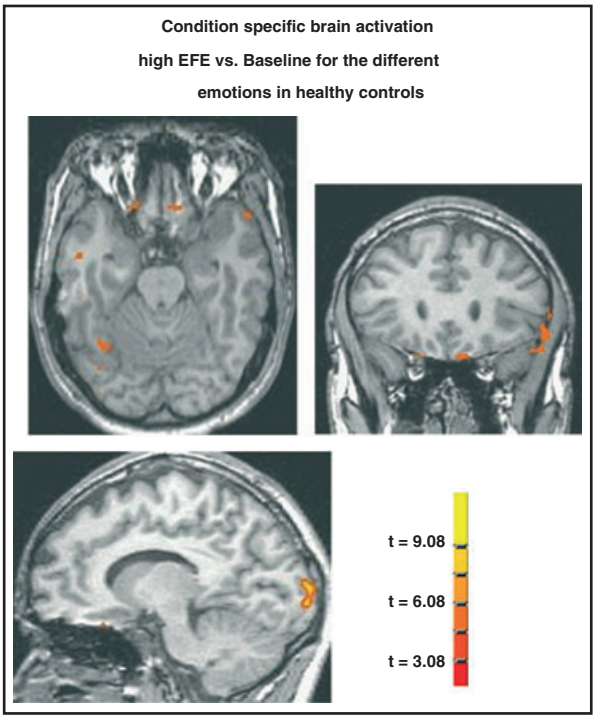

Fig. 4. Anger versus baseline in healthy controls. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

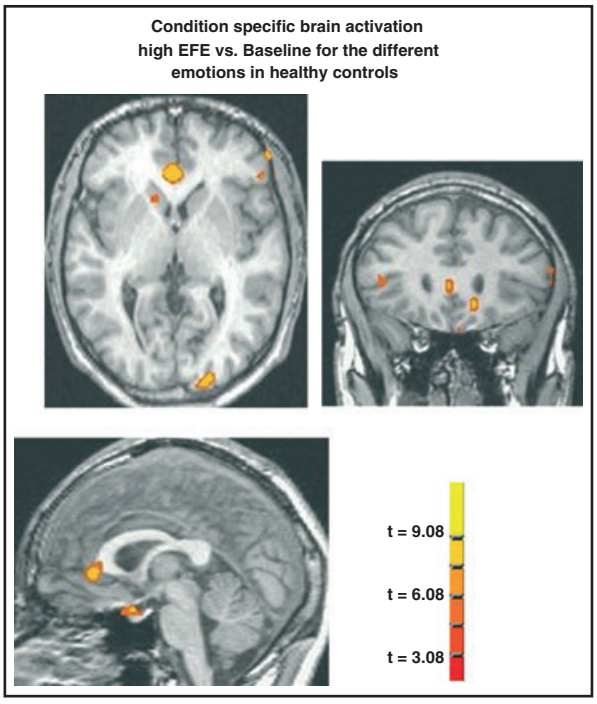

Fig. 5. Fear versus baseline in healthy controls. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

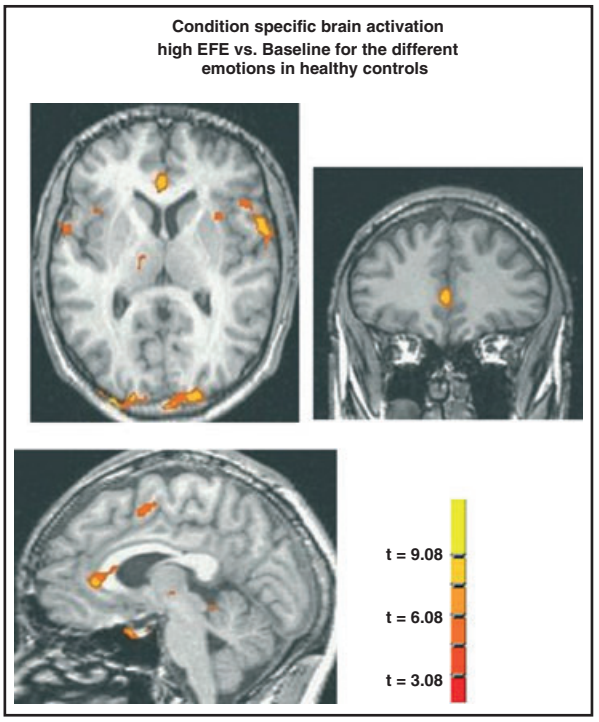

Fig. 6. Disgust versus baseline in healthy controls. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

Brain Activity Associated With 70% Emotional Faces Versus 30% Emotional Faces Across All Emotions for Alcoholic Patients and for Healthy Controls

Happy: For high versus low EFE, decoding for happy emotional expressions increased activation was found in the alcoholic patients in the medial frontal gyrus, insula, putamen, and precentral gyrus. The healthy nonalcoholic subjects had no significant activations when high to low intensity happy expressions were compared.

Sad: Alcoholic patients showed increased activation in the FFG.

Disgust: Compared with EFE decoding of other expression, disgust showed the most activation for both groups, particularly the healthy controls. In fact, among the controls, the only emotion for which the high–low intensity comparison was significant was disgust. Both groups showed common areas of activation in the middle frontal gyrus and FFG. Healthy subjects also showed increased activation in the inferior frontal gyrus, superior parietal lobule, and precentral gyrus. Alcoholic patients showed increased activation in the insula.

Differences in EFE Decoding Between Alcoholics and Controls for High (70%) Emotional Faces Versus Fixation Baseline

Happy: Healthy subjects show greater activation than alcoholic patients in response to happy faces in superior parietal lobule and precentral gyrus. Alcoholic patients, on the other hand, showed increased activation in the middle frontal gyrus, cingulate gyrus (near the border of the anterior and posterior cingulate), and amygdala-hippocampal areas.

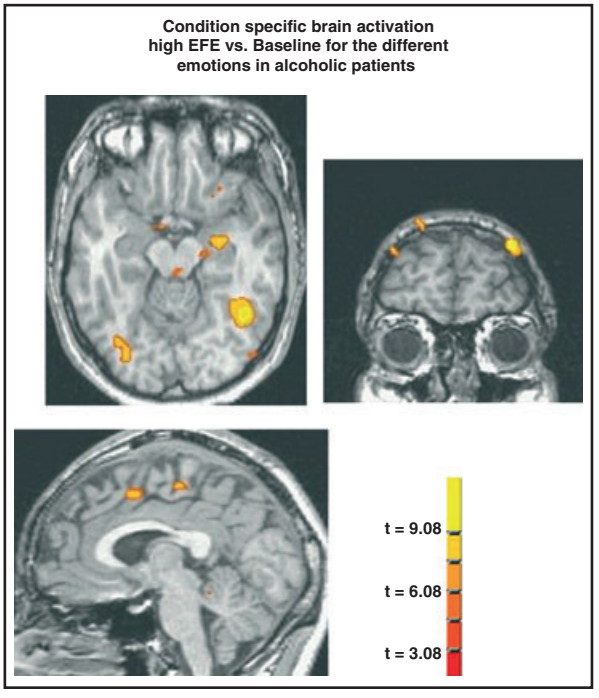

Fig. 7. Happy versus baseline in alcoholic patients. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

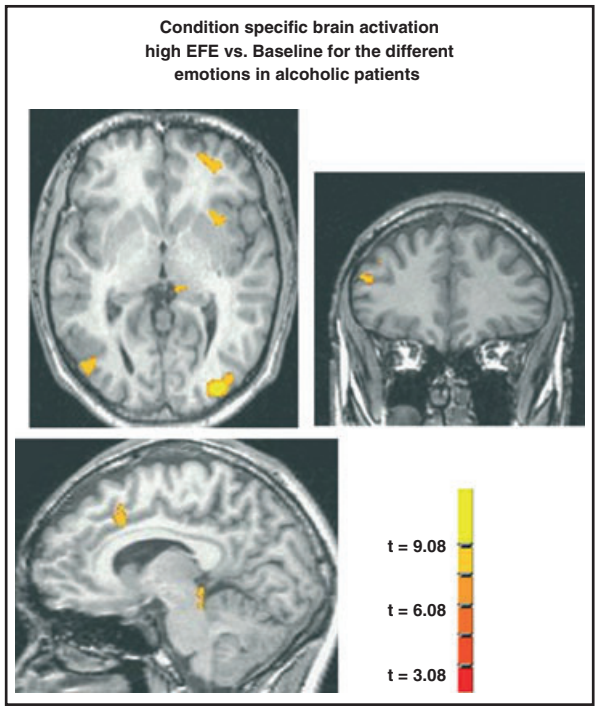

Fig. 8. Sad versus baseline in alcoholic patients. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

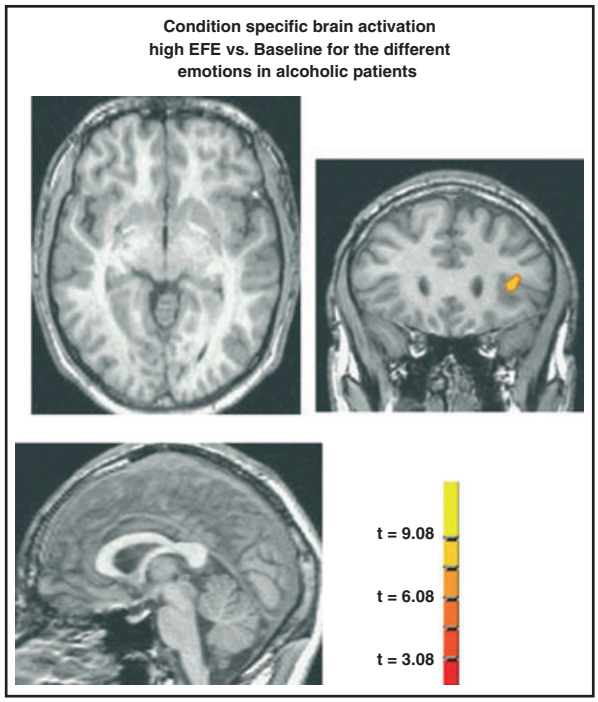

Fig. 10. Fear versus baseline in alcoholic patients. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

Sad: Healthy subjects showed greater activation than alcoholics in the anterior cingulate (affective division, Fig. 12*A*) and precentral gyrus. The more posterior cingulate gyrus as well as the insula showed greater activation in the alcoholic patients.

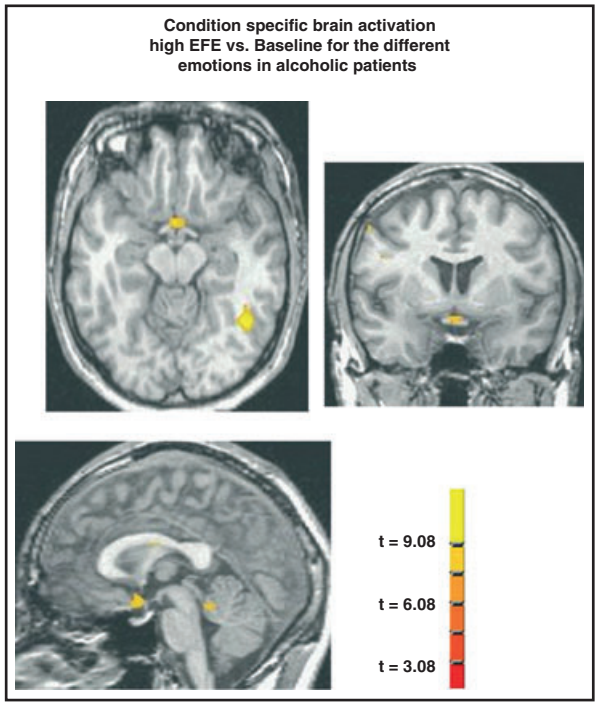

Fig. 9. Anger versus baseline in alcoholic patients. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

Anger: The precentral gyrus was commonly activated by both subject groups for anger. Healthy controls showed greater activation in the middle frontal gyrus and caudate. Patients showed increased activation in the insula.

Fear: The healthy subject group showed significantly greater activation than alcoholic subjects in a number of areas including the medial frontal gyrus, anterior cingulate (affective division, Fig. 12*B*), insula, hypothalamus, caudate, putamen, superior parietal lobule, and FFG.

Disgust: Similarly to fear, healthy subjects showed overall greater activation compared with the patient group in areas that included the inferior frontal gyrus, medial frontal gyrus, anterior cingulate (affective division, Fig. 12*C*), subcollosal gyrus, and cingulate gyrus, as well as the amygdala, insula, putamen, superior patrietal lobule, and precentral gyrus. Alcohlic patients demonstrated greater activation in the middle frontal gyrus.

DISCUSSION

The goal of this study was to examine the neural correlates of determining the intensity of human EFE decoding in alcoholic patients compared with healthy controls using fMRI. To our knowledge, this is the first study to examine brain activation during decoding of facial emotion among alcoholics. We used a multifactorial event-related fMRI design, which required determining the intensity of EFE for 5 basic emotions (happy, sad, anger, fear, and disgust). Thus, the

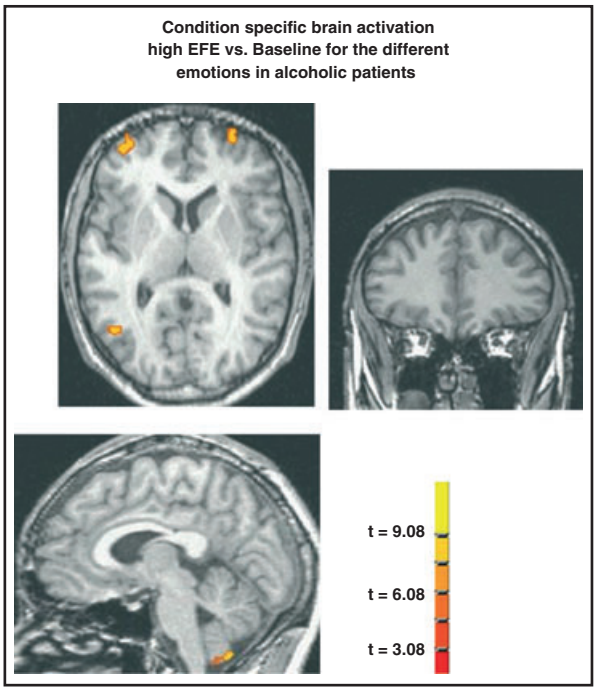

Fig. 11. Disgust versus baseline in alcoholic patients. Images are depicted in axial and coronal (**top 2 panels**) and saggital (**lower panel**) planes.

differences we find in BOLD activation patterns between alcoholics and nonalcoholics result not simply from differences in brain function during the perception of facial emotion, but also during the explicit evaluation of the intensity of facial emotion.

There were 2 major findings:

1. Alcoholic patients compared with healthy controls showed differential brain activation during decoding of all emotions with alcoholics generally showing less activation than controls. Evaluation of negative emotions produced the largest differences between alcoholic and controls with fear decoding showing the most blunting of activation in alcoholics. As both groups performed similarly in the accuracy and the speed of their judgments regarding emotional intensity, the differences we observed in brain activation were not simply caused by differences in performance, but rather reflect different functional approaches to decoding the emotional intensity of human facial expressions taken by alcoholics and controls.

2. The brain region that showed the most blunted brain response in the alcoholic patients compared with healthy controls during decoding of negative EFE was the rostral affective division of the ACC. The rostral, ventral portions of the ACC adjacent to and below the genu of the corpus callosum may be specialized for the higher order cognitive evaluation and decision making relative to affective stimuli (Bush et al., 2000). Our alcoholic subjects' brains appear to function in a way that does not make as much use of the rostral affective division of the ACC during EFE decoding of negative affect as the brains of our control subjects do. This difference may reflect inefficiency in the processing of negative emotional information among some alcoholics.

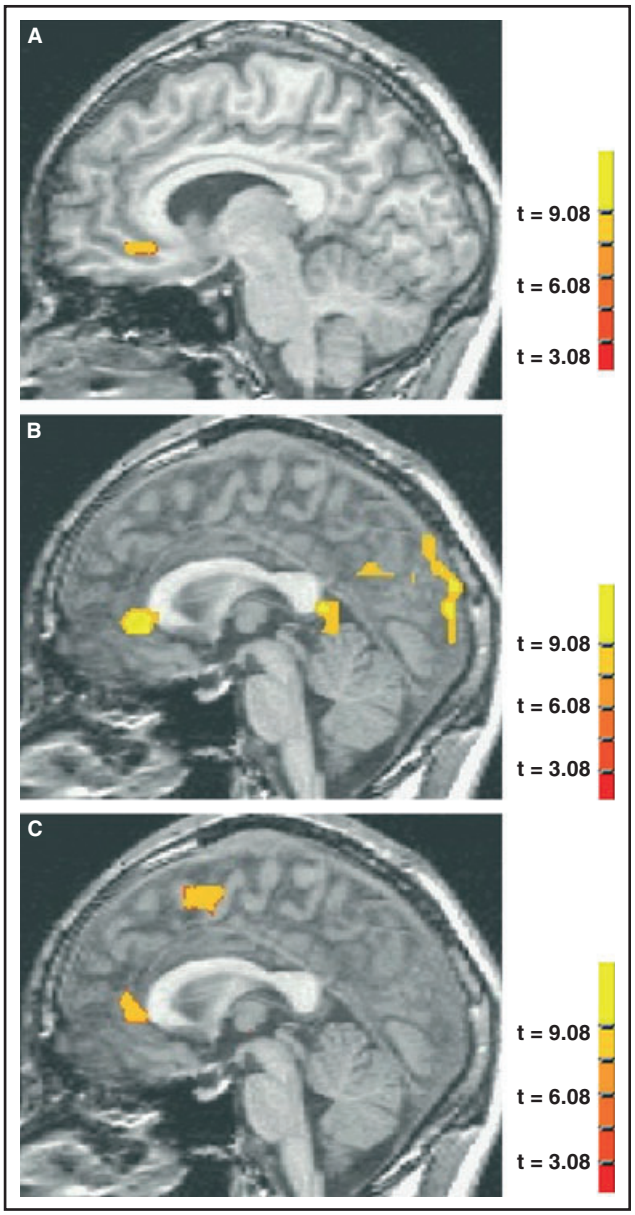

Fig. 12. (**A**) Image depicts cortical activation pattern for healthy controls relative to alcoholic patients during 70% emotional facial expression (EFE) decoding versus crosshair for Sad. Image is depicted in sagittal plane. The color scale reflects the difference in percentage brain blood oxygenation level dependent (BOLD) signal change. (**B**) Image depicts cortical activation pattern for healthy controls relative to alcoholic patients during 70% EFE decoding versus crosshair for Fear. Image is depicted in sagittal plane. The color scale reflects the difference in percentage BOLD signal change. (**C**) Image depicts cortical activation pattern for healthy controls relative to alcoholic patients during 70% EFE decoding versus crosshair for Disgust. Image is depicted in sagittal planes. The color scale reflects the difference in percentage BOLD signal change.

Behavioral Data

Unlike many neuropsychological studies of affect processing in alcoholic patients (Kornreich et al., 2001b, 2002;

Table 3. Accuracy Scores (percent correct)

	Alcoholic Patients		Healthy Controls	
	High Intensity (70%)	Low Intensity (30%)	High Intensity (70%)	Low Intensity (30%)
Happy	71.8 ± 41.8	96.7 ± 7.0	90.4 ± 9.8	89.2 ± 15.5
Sad	47.1 ± 30.4	96.7 ± 3.8	46.3 ± 30.8	92.1 ± 9.7
Anger	94.6 ± 6.8	98.3 ± 2.9	88.3 ± 10.4	94.6 ± 10.6
Fear	92.5 ± 15.4	96.2 ± 5.4	88.3 ± 12.7	95.8 ± 9.0
Disgust	96.25 ± 5.0	96.2 ± 4.6	93.3 ± 9.3	94.6 ± 9.4

Table 4. Speed of Response (milliseconds)

	Alcoholic Patients		Healthy Controls	
	High Intensity (70%)	Low Intensity (30%)	High Intensity (70%)	Low Intensity (30%)
Happy	849 ± 280	896 ± 127	801 ± 36	843 ± 127
Sad	1,107 ± 177	906 ± 135	964 ± 137	820 ± 141
Anger	883 ± 160	861 ± 127	831 ± 71	806 ± 116
Fear	906 ± 156	892 ± 113	825 ± 90	838 ± 133
Disgust	857 ± 146	919 ± 178	778 ± 68	805 ± 118

Philippot et al., 1999), but similar to (Cermak et al., 1989), we found comparable ability to identify the intensity of EFE among healthy controls and alcoholic patients. The inclusion of a slightly younger and perhaps medically healthier group of alcoholic patients in the current study (age: mean ± SD; 35 ± 5) may have lead to the better performance compared with those of other studies (age: mean ± SD; 41 ± 42) (see Kornreich et al., 2001a, 2003; Philippot et al., 1999; Uekermann et al., 2005). Also, it is likely that our task of intensity rating which required subjects to evaluate the EFE [choose between only 2 intensity values: high (70%) and low (30%)] of the portrayed emotion may have rendered the task easier to perform. Other studies using a similar task required that subjects accurately identify an expression whiles rating the intensity of faces on a scale from 1 (not at all) to 7 (very intensely) on a target emotion (Kornreich et al., 2001b, 2002). As the goal of our study was to compare brain activation during EFE decoding it was advantageous to use a task in which groups could perform similarly so that differences in performance would not confound the imaging results.

Neuroimaging Data

The area that showed the most consistent and robust differential brain response during EFE decoding was the rostral affective division of the anterior cingulate or subgenual anterior cingulate cortex (SACC). Although strictly speaking, not all the activation differences we found were below the genu of the corpus callosum; some were exactly level with the genu; however, all were within the region described as the affective division of the ACC by (see Bush et al., 2000 and Figs 3, 5, 6, and 12). The blunted BOLD activation in the rostral ACC in alcoholic patients is consistent with a variety of studies that have seen anomalies in the anterior cingulate area (O'Carroll et al., 1991; Samson et al., 1986) in alcoholic patients. Studies on cognitive functioning also reported an association between impaired performance on attention/executive tasks and anterior cingulate abnormalities (Adams et al., 1993; Goldstein et al., 2004).

Alcoholic patients have been suggested to share some commonalities with attention deficit disorder, antisocial personality disorder (ASPD) as well as other substance abuse disorders. These disorders all share certain characteristics such as inattention, impulsivity, risk taking and, as is the case with other substance abusers, sensation seeking. This description is particularly true for the alcoholics used as subjects in this study. Our alcoholic subjects had a high incidence of other substance abuse, personality disorders, and low scores in the NEO factor of conscientiousness. A number of imaging studies, most of them using a variety of cognitive control tasks, have reported a relationship between impaired performance and hypoactivity in the cognitive portion of the anterior cingulate in attention deficit/hyperactivity disorder (ADHD) subjects compared with healthy controls (Bush et al., 1999; Rubia et al., 1999). Deficient intentional control of behaviors (sensation seeking and impulsivity) (Ahveninen et al., 2000; Andrucci et al., 1989; Gorenstein and Newman, 1980) and lack of goal directed behavior (attention allocation/monitoring) may underlie impaired cognitive control processing, which could maintain alcohol dependence in our patient population.

EFE Decoding

Happy. Compared with EFE decoding of other emotional expressions, during the decoding of happy expressions alcoholic patients exhibited relatively little deficit in BOLD activation compared with healthy controls. If anything, the

Table 5. Condition Specific Cortical Activation Patterns Associated With High EFE Decoding Versus Crosshair Control in Healthy Subjects and Alcoholic Patients for the 5 Emotions

	Alcoholics Patients		Healthy Controls	
70% EFE vs. Baseline	Right	Left	Right	Left
Inferior frontal gyrus			64, 11, 27 (t = 4.10) BA9^{H} 45, 4, 27 (t = 5.35) BA9^{S} 45, 4, 31 (t = 4.13) BA9^{A} 41, 30, 12 (t = 3,31) BA46^{F} 49, 4, 31 (t = 3.43) BA9^{F}	−45, −0, 23 (t = 5.31) BA9^{H} −45, 4, 31 (t = 4.08) BA9^{S} −60, 30, 12 (t = 5.24) BA46^{F}
Middle frontal gyrus	56, 26, 23 (t = 3.04) BA46^{H} 30, 11, 46 (t = 4.03) BA6^{H} 49, 30, 23 (t = 4.80) BA46^{S} 49, 30, 31 (t = 3.19) BA9^{A}	−41, 4, 38 (t = 4.08) BA6^{H} −49, 15, 27 (t = 4.45) BA9^{H} −22, −4, 46 (t = 3.16) BA6^{S} −41, 15, 31 (t = 4.34) BA9^{S} −49, 15, 27 (t = 3.94) BA9^{A} −41, 34, 12 (t = 3.57) BA46^{A}	45, 30, 12 (t = 4.62) BA6^{H} 41, 34, 19 (t = 3.21) BA46^{F} 52, 4, 38 (t = 3.92) BA6^{D}	−49, 7, 49 (t = 3.30) BA6^{H} −45, 19, 23 (t = 4.88) BA46^{H} −45, 4, 53 (t = 3.86) BA6^{A} −34, −4, 61 (t = 3.10) BA6^{D} −45, 19, 23 (t = 3. 54) BA46^{D}
Medial frontal gyrus	11, −4, 49 (t = 3.92) BA6^{A}			−3, 56, −12 (t = 4.08) BA11^{H} −11, 26, −18 (t = 4.02) BA25^{A} −4, 26, −18 (t = 3.89) BA25^{F}
Anterior cingulate-affective division			8, 34, 1 (t = 3.92) BA24^{S} 4, 34, 4 (t = 5.34) BA24^{F} 4, 34, 8 (t = 4. 53) BA24^{D}	−1, 26, −3 (t = 4.02) BA24^{F}
Subcallosal gyrus-affective division		0, 4, −11 (t = 3.68) BA25^{A}		−11, 15, −14 (t = 3.33) BA25^{F} −11, 22, −14 (t = 2.86) BA25^{A}
Cingulate gyrus-cognitive division	7, −7, 46 (t = 4.37) BA24^{H} 7, 19, 38 (t = 3.95) BA32^{S}	19, −7, 34 (t = 3.67)^{H}		−7, 19, 31 (t = 3.63) BA32^{H} −4, 4, 46 (t = 3.75) BA24^{S} −7, 15, 34 (t = 3.22) BA32^{S} −7, 4, 38 (t = 3.34) BA24^{S}
Uncus-amygdala			22, −4, −22 (t = 3. 44) BA^{D}	
Insula	41, 4, 16 (t = 4.11) BA13^{H} 34, 7, 19 (t = 3.49) BA13^{S}	−34, 15, 12 (t = 3.48) BA13^{H} −34, 15, 4 (t = 4.17) BA13^{S} −30, 19, 12 (t = 3.44) BA13^{A} −30, 19, 12 (t = 4.14) BA13^{F}	37, 4, 19 (t = 5.12) BA13^{S} 37, 4, 19 (t = 4.48) BA13^{F} 41, 15, 8 (t = 3. 56) BA13^{D}	−37, −4, 16 (t = 4.92) BA13^{H} 34, −37, 19 (t = 3.21) BA13^{H} −34, 11, 8 (t = 3. 43) BA13^{D}
Caudate	11, 7, 16 (t = 4.15)^{H} body	−7, 15, 4 (t = 3.08)^{H} head −19, −26, 19 (t = 2.96)^{D} (and tail)		−15, 4, 19 (t = 3.32)^{H}
Putamen	30, 0, −3 (t = 3.64)^{H}	−30, −11, 1 (t = 4.57)^{H}	19, 11, 8 (t = 3.98)^{H}	−19, −4, 16 (t = 3.85)^{H}
Inferior parietal lobule			45, −67, 49 (t = 6.26) BA7^{H}	
Superior parietal lobule			37, −60, 49 (t = 3.35) BA7^{H}	−34, −64, 53 (t = 5.62) BA7^{H} −37, −56, 49 (t = 3.40) BA7^{S} −33, −64, 49 (t = 4.19) BA7^{F} −30, −45, 61 (t = 3. 93) BA7^{D}
Precentral gyrus	41, 15, 34 (t = 4.09) BA9^{H} 45, −4 49 (t = 3.86) BA6^{H} 37, 0, 34 (t = 3.58) BA6^{S} 45, −4, 34 (t = 3.75) BA6^{A}	−49, 4, 35 (t = 4.45) BA9^{H} −41, −4, 35 (t = 3.91) BA6^{H} −41, −4, 34 (t = 4.62) BA6^{S} −52, −4, 27 (t = 4.55) BA6^{A}	61, 11, 8 (t = 4.01) BA6^{H} 34, −11, 68 (t = 4.42) BA6^{S} 19, −56, 61 (t = 3.81) BA7^{F}	−41, −7, 53 (t = 5.89) BA6^{H} −30, −11, 68 (t = 5.42) BA6^{S} −26, −7, 46 (t = 3.48) BA6^{S} −41, −7, 61 (t = 5.14) BA6^{A} −37, −7, 57 (t = 5.45) BA6^{F} −64, 4, 12 (t = 5.08) BA6^{D}
Fusiform gyrus	41, −49, −7 (t = 4.54) BA37^{H} 41, −75, −14 (t = 3.22) BA19^{S} 37, 52, −15 (t = 5.02) BA37^{A} 30, −82, −11 (t = 4.70) BA19^{D}	−45, −49, −11 (t = 3.57) BA37^{S} −19, −94, −11 (t = 2.71) BA18^{S} −41, −56, −14 (t = 5.10) BA37^{D} −45, −67, −11 (t = 4.15) BA19^{D} −41, −79, −11 (t = 3.78) BA18^{D}	41, −75, −11 (t = 5.86) BA19^{H} 37, −45, −18 (t = 4.19) BA37^{H} 37, −56, −11 (t = 5.67) BA37^{S} 41, −71, −11 (t = 5.12) BA19^{S} 37, −56, −14 (t = 4.03) BA37^{A} 37, −56, −11 (t = 3.46) BA37^{F} 37, −52, −14 (t = 4. 07) BA37^{D} 22, −90, −14 (t = 4. 03) BA18^{D} 41, −71, −11 (t = 3. 47) BA19^{D}	−37, −49, −11 (t = 5.39) BA37^{H} −37, −75, −11 (t = 4.91) BA19^{H} −45, −26, −26 (t = 4.37) BA20^{H} −22, −90, −11 (t = 4.07) BA18^{S} −41, −22, −26 (t = 3.64) BA20^{S} −37, −56, −14 (t = 2.97) BA37^{S} −37, −75, −101 (t = 3.27)BA19^{A} −34, −49, −14 (t = 4. 61) BA37^{D} −37, −75, −14 (t = 3. 74) BA19^{D}

Foci of significant activation and their stereotaxic coordinates (Talairach & Tournoux atlas) and Brodmann's areas (where appropriate) are shown with t-values. Emotion for EFE decoding are presented in acronyms.

H, happy; S, sad; A, anger; F, fear; D, disgust; EFE, emotional facial expression.

Table 6. Condition Specific Cortical Activation Patterns Associated With High (70%) EFE Decoding Versus Low (30%) EFE for the 5 Emotions

70% EFE vs. 30% EFE	Alcoholic Patients		Healthy Controls	
	Right	Left	Right	Left
Inferior frontal gyrus			52, 41, 12 (t = 5.05) BA46^{D}	
Middle frontal gyrus	49, 34, 38 (t = 3.29) BA9^{D}	−52, 26, 31 (t = 3.62) BA9^{D}		−22, 4, 57 (t = 3.40) BA6^{D}
Medial frontal gyrus		−7, 41, 27 (t = 3.0) BA9^{H}	11, 15, −18 (t = 3.58) BA25^{D}	
Amygdala				−22, −7, −22 (t = 4.23)^{D}
Insula	41, −4, 1 (t = 2.98) BA13^{H} 45, −7, −3 (t = 3.74) BA13^{D}	−52, −30, 19 (t = 3.31) BA13^{H}		
Putamen	26, −19, 8 (t = 4.06)^{H}	−26, −4, 4 (t = 3.64)^{H}		
Superior parietal lobule			34, −64, 46 (t = 3.33) BA7^{D}	
Precentral gyrus		−37, 15, 34 (t = 3.85) BA9^{H}	56, 4, 12 (t = 4.59) BA6^{D}	−34, −7, 31 (t = 3.97) BA6^{D}
Fusiform gyrus		−26, −34, −18 (t = 3.24) BA 20^{S} −41, −45, −14 (t = 3.27) BA37^{D}		−30, −49, −7 (t = 3.87) BA37^{D}

Foci of significant activation and their stereotaxic coordinates (Talairach & Tournoux atlas) and Brodmann's areas (where appropriate) are shown with t-values. Emotion for EFE decoding are represented in acronyms.

H, happy; S, sad; A, anger; F, fear; D, disgust; EFE, emotional facial expression.

alcoholics seem to show greater activation during exposure to high intensity happy expressions than controls (see Table 6). Frigerio et al. (2002) found that alcoholic patients were able to decode low intensity facial expressions of happiness easier than other emotions, while Townshend and Duka (2003) found no differences between alcoholics and controls in decoding of happy expressions. One possible explanation for these findings is that happiness is a universal expression with some variant of a stereotypical signal, the smile (see Adolphs et al., 1996). Nevertheless, Kornreich et al. (2001b) found that recovering alcoholics compared with abstinent and nonalcoholic patients were less accurate in decoding happy expressions with a tendency to overestimate this expression. Also, Philippot et al. (1999) found that alcoholic patients made more errors in decoding accuracy for happy facial expression with a tendency to systematically rate the intensity higher than healthy controls. These authors moreover found that alcoholic patients are likely to believe that somebody presenting a happy face is actually in a negative mood.

Failure to find the rostral ACC activated during decoding of happy EFE for both healthy and patient groups is not surprising. Elliott et al. (2000) found that during an emotional cognitive control task, the anterior cingulate was recruited in response to sad but not happy words.

In healthy subjects, similar to Gorno-Tempini et al. (2001), we found ventromedial prefrontal cortex activation (rostral to the ACC) during explicit decoding of happy EFE. The ventromedial prefrontal is proposed to be involved in processing of social rewards. Functional imaging studies have shown an association between ventromedial prefrontal cortex activation and reward value response (for review, see Elliott et al., 2000) and during the viewing of positive images (Paradiso et al., 1999). Along similar lines, Wager et al. (1998) found that the medial prefrontal cortex was associated with approach behavior.

We also detected amygdala-hippocampal activation during decoding of happy expressions only in the alcoholic patient group. The amygdala and the ventromedial prefrontal cortex are functionally related to each other; the ventromedial prefrontal cortex has reciprocal connections with the limbic structures and is thought to play an important role in modulating emotional and social experiences. Voluntary evaluation of emotionally salient content has been shown to engage medial prefrontal cortices, while suppressing activity of the amygdala (Hariri et al., 2003; Taylor et al., 2003). Hariri et al. (2003) showed that limbic activation can be modulated by frontal control. In light of the limbic activation in the absence of ventromedial activation in alcoholic patients, it is possible that in the case of high intensity happy expressions, alcoholic patients may have responded to the arousal attribute displayed in happy faces with little in the way of prefrontal modulation on limbic activity.

Anger. Only during anger decoding did we observe activation by the alcoholic patients in any portion of the affective division of the cingulate cortex. This was in the subcallosal gyrus (BA25) and was detected only in the within group comparison of angry expressions compared with fixation. We also found similar activation in healthy subjects although the activation was less in spatial extend and intensity. Unlike the other negative emotions of fear, disgust and sadness where controls showed significantly greater activation than alcoholics in the affective division of the ACC, during anger decoding activation in subcallosal gyrus did not differ significantly between groups. Angry expressions are the one emotion that

Table 7. Group Specific Cortical Activation Patterns Associated With High EFE Decoding Versus Crosshair Control for the 5 Emotions

70% EFE vs, Baseline	Alcoholic Patients vs. Healthy Controls		Controls vs. Alcoholic Patients	
	Right	Left	Right	Left
Inferior frontal gyrus				−64, 15, 23 (t = 5.57) BA9^{D}
Middle frontal gyrus		−49, 19, 31 (t = 2.81) BA9^{S} −52, 30, 19 (t = 3.10) BA46^{S} −49, 34, 27 (t = 3.23) BA46^{D}		−26, 7, 42 (t = 2.93) BA6^{D}
Medial frontal gyrus				4, −15, 68 (t = 4,12) BA6^{A} −11, 30, −14 (t = 3,25) BA25^{F} −4, 26, −18 (t = 3,84) BA25^{F} −19, 11, 46 (t = 3.14) BA32^{D}
Anterior cingulate-affective division				−7, 30, −3 (t = 3.79) BA24^{S} −0, 34, 4 (t = 4.47) BA24^{F} −0, 37, 12 (t = 4.38) BA24/32^{D}
Subcallosal gyrus-affective division			7, 7, −11 (t = 3.76) BA25^{F}	
Cingulate gyrus-cognitive division	15, −4, 34 (t = 3.35)^{H} 11, −19, 42 (t = 3.76) BA24^{S}			7, 11, 42 (t = 3.82) BA32^{D}
Uncus-amygdala			22, −7, −22 (t = 4.44) BA^{D}	
Amygdala-hippocampus		−26, −11, −14 (t = 3.19)^{H}		
Insula	37, −11, 8 (t = 3.55)^{H}	−37, −7, 19 (t = 3.01) BA13^{A}	37, 15, 8 (t = 3.65) BA13^{D}	−37, −26, 4 (t = 3.75 BA13^{F} −37, 7, 8 (t = 3.06) BA13^{D}
Hypothalamus			4, −0, −14 (t = 3.80)^{F}	
Caudate			18, 21, 2 (t = 3.07)^{A} head 11, 19, 4 (t = 4,15 BA^{F}	−7, 11, −7 (t = 2.86)^{F} head
Putamen			30, −22, 1 (t = 4.53)^{F} 26, −0, 16 (t = 2.85)^{D}	
Superior parietal lobule				−34, −67, 49 (t = 4.03) BA7^{H} −30, −45, 61 (t = 4.48) BA7^{D} −28, −65, 47 (t = 3.50) BA7^{F}
Precentral gyrus	49, −4, 38 (t = 3.96) BA6^{A}		−64, −0, 19 (t = 3.79) BA6^{S} 45, −0, 31 (t = 3.61) BA6^{H} −45, −4, 23 (t = 3.90) BA6^{D}	−49, −7, 53 (t = 4.11) BA6^{H} −64, −0, 19 (t = 3.79) BA6^{S} −41, −7, 61 (t = 3. 66) BA6^{A}
Fusiform gyrus				−22, −67, −7 (t = 3.61 BA19^{F}

Foci of significant activation and their stereotaxic coordinates (Talairach & Tournoux atlas) and Brodmann's areas (where appropriate) are shown with t-values. Emotion for EFE decoding are represented by acronyms.

H, happy; S, sad; A, anger; F, fear; D, disgust; EFE, emotional facial expression.

appears to activate the affective cingulate among alcoholics. A possible explanation for this may be found in the strong relationship between chronic alcoholism and aggression. Alcoholics are known to be hostile (Handelsman et al., 2000; Tivis et al., 1998) and may thus be more sensitive to feelings of threat from angry faces. This may make them more motivated by angry facial expressions, and the increased activation in the subcallosal ACC to anger compared with other negative emotions among the alcoholics may reflect a hostile attribution bias among alcoholics (Dodge et al., 1990).

Sad. Healthy subjects activated the rostral ACC during EFE decoding of sadness but the alcoholic patients did not. Activation of the rostral ACC in healthy populations during processing of sadness is consistent with earlier studies using words (Whalen et al., 1998) and faces (Shafritz et al., 2006).

Fear and Disgust. Both fear and disgust EFE showed the lowest activation among alcoholic patients compared with other emotions, with the fear showing the most blunted effect.

Kornreich et al. (2001b) reported no difference in estimating the intensity of fear faces (EFE decoded) between recently detoxified alcoholic patients and healthy controls although the authors noted a possible floor effect. However, Townshend and Duka (2003) reported that the alcoholic subjects compared with social drinkers, showed enhanced fear responses to pictures of different facial expressions. In addition, the enhanced fear recognition found in the alcoholic group was related to the number of previous detoxifications. Deficits in decoding accuracy were observed in alcoholic patients for disgust facial expressions, which persisted with abstinence of 2 months and beyond (Kornreich et al., 2001a). Philippot et al. (1999) showed that alcoholics compared with controls showed a systematic bias for decoding of disgust stimuli attributing emotions of anger and contempt to facial expressions of disgust.

During EFE decoding of fear and disgust healthy subjects showed robust activation in the rostral affective division of the ACC but alcoholics show virtually no activation in this region. This was confirmed by the significant group differences in activation centered near the rostral tip of the corpus callosum for each emotion. Corresponding with Gorno-Tempini et al. (2001), we also found amygdala

activation during EFE decoding of disgust in the healthy subjects.

Darwin (1872) identified fight and flight as evolutionary attributes which favor survival. However, unlike anger, which is associated with fight, fear, and disgust may be more associated with flight. Plutchik (1980, 1993), and theories of emotion in general suggest that both fear and disgust often include behavioral components of avoidance. Inhibitory problems in alcoholic patients have been reported in a number of studies using a broad range of paradigms (Goldstein and Chotlos, 1965) and sensation seeking is well-known attribute found in this population group. The hypoactivity in alcoholic patients to faces showing disgust and more so for fear, fits well with the notion that alcoholics fail to effectively avoid cues that signal danger. Signals of fear and disgust may be ignored or not processed appropriately to induce retreat behavior. We propose that the hypoactivation for both these emotions in alcoholic patients accords with their temperamental trait, such as risk/sensation seeking personality (White, 1997).

CONCLUSION

There is evidence to suggest that the chronic deficit in social interaction and communication shown by alcoholics might be caused in part by difficulties in accurate interpretation of the emotional state of others (Philippot et al., 1999). Here, we present data pointing to different functional approaches to decoding and/or responding to EFE that may underlie such difficulties. The greatest deficit among alcoholics appears to be in brain activation during decoding of negative emotional faces in the affective division of the ACC. The location of this deficit in negative emotion decoding is consistent with recent findings showing that activation within the affective division of the ACC can be modulated by emotional valence, as sad faces induced more activation in rostral ACC during an inhibtion task than happy faces (Shafritz et al., 2006).

The findings of the current study have general implications for social behavior in alcoholic patients. Appropriate decision making in the context of social interaction requires the integration of emotional and cognitive information (Damasio et al., 2000). Hence, understanding of how these 2 neural systems interact to allow adaptive behavior in social settings may shed light on some of the problematic and psychopathological behaviors that are manifest in this patient population.

This study has several important limitations. It is a relatively small study involving only 11 subjects in each group. Also, the alcoholic subjects in this study had significant amounts of psychopathology and other substance abuse, in fact, on average they were more than a full standard deviation less conscientious, as measured by the NEO-PI, than the general population. Thus, it is uncertain if the blunted responses we found in the affective division of the ACC characterize relatively "pure" alcoholics as well as they do the more pathological sample we report on here.

It is uncertain if the lack of activation we find in the rostral affective ACC is secondary to loss of brain tissue in ACC of alcoholics or is purely functional in nature, i.e., is related to the way in which alcoholics process facial emotion. Although several positron emission tomography (PET) imaging studies have suggested reduced glucose use in the mesial frontal lobes of alcoholics (Dao-Castellana et al., 1998; Samson et al., 1986) no structural imaging studies have reported selective damage to the rostral ACC. O'Neill et al. (2001) showed region-specific structural recovery from chronic alcohol-induced brain injury, but also region-specific long-term structural damage in abstinent alcoholics. Pfefferbaum et al. (1997) provided in vivo evidence showing that the frontal lobes are especially vulnerable in older chronic alcoholics and that brain volume shrinkage is exaggerated in the prefrontal cortex in normal aging with additional loss in the anterior superior temporal cortex in alcoholism; moreover, the it was showed that continued alcohol abuse results in progressive brain tissue volume shrinkage over time (Pfefferbaum et al., 1998). More anatomically detailed structural studies in the future will be required to determine if the alcoholics' functional deficit in the affective division of the ACC is secondary to tissue loss. In addition, it is unknown whether the deficits we observe in rostral ACC function are secondary to prolonged and heavy alcohol use or precede heavy alcohol use. Studies in young adolescent children of alcoholics may be useful in this regard.

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