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Limbic Abnormalities in Affective Processing by Criminal Psychopaths as Revealed by Functional Magnetic Resonance Imaging

Kent A. Kiehl, Andra M. Smith, Robert D. Hare, Adrianna Mendrek, Bruce B. Forster, Johann Brink, and Peter F. Liddle

Background: *Psychopathy is a complex personality disorder of unknown etiology. Central to the disorder are anomalies or difficulties in affective processing.*

Methods: *Functional magnetic resonance imaging was used to elucidate the neurobiological correlates of these anomalies in criminal psychopaths during performance of an affective memory task.*

Results: *Compared with criminal nonpsychopaths and noncriminal control participants, criminal psychopaths showed significantly less affect-related activity in the amygdala/hippocampal formation, parahippocampal gyrus, ventral striatum, and in the anterior and posterior cingulate gyri. Psychopathic criminals also showed evidence of overactivation in the bilateral fronto-temporal cortex for processing affective stimuli.*

Conclusions: *These data suggest that the affective abnormalities so often observed in psychopathic offenders may be linked to deficient or weakened input from limbic structures.* Biol Psychiatry 2001;50:677–684 © *2001 Society of Biological Psychiatry*

Key Words: Psychopathy, limbic system, functional magnetic resonance imaging, emotion, affect, amygdala, anterior cingulate

Introduction

Psychopathy is a personality disorder believed to affect approximately 1% of the general population and approximately 15%–25% of incarcerated offenders (Hare 1991). Compared with other inmates, psychopathic offenders commit a disproportionate amount of repetitive, often violent, criminal acts (Hare and McPherson 1984; Hart et al 1994). Central to the disorder is a complex of features—glibness; superficiality; and lack of empathy, guilt, or remorse—that appear to be associated with difficulties or anomalies in the processing and production of affective material (Cleckley 1976; Hare 1993). Although the clinical symptomology of criminal psychopathy is well characterized (Hare 1991), relatively little is known regarding the neural systems mediating its affective abnormalities.

Most empirical research on the affective processes of psychopathic criminals has used behavioral methods or peripheral measures of neural activity (Patrick 1994). One of the most consistent findings from these studies is that criminal psychopaths fail to experience or appreciate the emotional significance of stimuli in the way that nonpsychopaths do (Christianson et al 1996; Day and Wong 1996; Kiehl et al 1999; Louth et al 1998; Patrick et al 1993; Patrick et al 1994; Williamson et al 1991). For example, data from our laboratory has shown that criminal psychopaths fail to show normal behavioral facilitation and event-related potential (ERP) differentiation between emotional and neutral words (Williamson et al 1991). Subsequent research has confirmed the presence of affective abnormalities in criminal psychopaths (Kiehl et al 1999). These deficits appear to be most prominent in response to negatively valenced emotional stimuli (Day and Wong 1996; Patrick et al 1993; Patrick et al 1994). Although ERPs have provided valuable information regarding the temporal features of these abnormalities, their limited spatial resolution has left the neural sources poorly characterized. One functional imaging study, using Single Photon Emission Computed Tomography (SPECT), found that psychopathic individuals show greater activation for affective than for neutral stimuli bilaterally in temporofrontal cortex (Intrator et al 1997). These latter data have been interpreted as supporting the notion that psychopathic individuals require more cognitive resources to process and evaluate affective stimuli than do comparison subjects. We note however that this latter study was limited in that it only assessed function in a 13.5 mm axial slice of cortex.

Researchers have suggested that a number of neural

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structures and systems may be implicated in psychopathic behavior. These regions include orbital frontal cortex (Damasio et al 1990), prefrontal cortex (Anderson et al 1999; Bechara et al 1994; Raine et al 2000), ventro-medial frontal cortex (Bechara et al 1999b), and limbic structures such as the amygdala (Bechara et al 1999b; Patrick et al 1993; Patrick et al 1994; Tranel and Damasio 1994) and cingulate (Dikman and Allen 2000; Tranel and Damasio 1994). Unfortunately, very little is known about the possible involvement of these structures in criminal psychopathy.

The purpose of the present study was to use whole brain functional magnetic resonance imaging (fMRI) to examine the neural systems underlying emotional processing in psychopathic offenders during performance of an affective memory task. The affective memory task consisted of eight repetitions of three phases (encoding, rehearsal, and recognition) plus rest. Unknown to the participants, four of the repetitions contained stimuli that were negative in affect, while in the remainder of the repetitions the stimuli were neutral in affect. Prior pilot research with this task revealed that affective stimuli elicit greater activation than do neutral stimuli in both limbic and neocortical brain regions, including the amygdala, hippocampal formation, and temporal and frontal cortex (see Table 1) (Kiehl et al 1998). In light of the substantial evidence indicating impaired processing of affect in psychopathy, we hypothesized that psychopaths would show less activation than healthy controls and criminal nonpsychopaths when processing affective words compared with neutral words, at those cerebral sites where healthy controls had exhibited significant activation for affective words compared with neutral words in the pilot study.

Methods and Materials

Criminal psychopaths ($n = 8$) and criminal nonpsychopaths ($n = 8$) were inmates from a maximum-security prison located in Abbotsford, British Columbia, Canada. Inmates were escorted to the University of British Columbia Hospital's magnetic resonance imaging (MRI) unit by the Correctional Services of Canada Regional Escort Team. Matched healthy control participants ($n = 8$) were recruited from the general population. All participants were free from any documented history of serious head injury (defined as a loss of consciousness for more than 1 hour) or psychotic illness (in self and first-degree relatives), were right-handed (Annett 1970), and spoke English as their first language. No participant met the DSM-IV criteria for substance abuse within the last 6 months. There were no group differences (criminal psychopaths: 5.5 (SD 3.2); criminal nonpsychopaths: 4.75 (SD 3.8) in the mean years of lifetime substance use (defined as self-reported use of any hard drug more than twice per week). There were no significant group differences in age (criminal psychopaths 33.9, SD 7.6; criminal nonpsychopaths 37.1, SD 7.1; controls 31.9, SD 8.4), parental socioeconomic status (based on the parental occupation section of the Hollingshead index of social position [Hollingshead and Redlich 1958]; criminal psychopaths 4.25, SD 1.4; criminal nonpsychopaths 4.25, SD 1.9; controls 3.1, SD 1.55), or IQ (measured with the National Adult Reading Test [Nelson and O'Connell 1978; Sharpe and O'Carroll 1991]; criminal psychopaths 111.2, SD 7.5; criminal nonpsychopaths 115.5, SD 5.9; controls 108.9, SD

Table 1. Summary of the Results of the Functional Imaging Data for the Affective Memory Task

Regions of Interest	Talairach Coordinates x	y	z	Pilot study z score	Control vs Psychopath Fixed Effects t; e	Control vs Psychopath Random Effects t; e	Nonpsychopath vs Psychopath Fixed Effects t; e	Nonpsychopath vs Psychopath Random Effects t; e
Frontal lobe								
1. Rostral Anterior Cingulate	0	38	8	4.55	8.20; 27	3.92; 27	7.64; 6	3.61; 11
2. Caudal Anterior Cingulate	−8	22	20	5.35	11.85; 27	3.76; 27	7.30; 27	2.18; 7
3. L Inferior Frontal Gyrus Parietal Lobe	−38	41	−8	7.38	6.12; 18	3.41; 27	7.69; 17	2.67; 15
4. Posterior Cingulate Gyrus	−8	−38	16	8.30	12.56; 27	2.71; 27	11.19; 27	2.20; 27
Temporal Lobe								
5. R Amygdala/Hippocampus	34	−12	−20	7.57	9.22; 27	2.03; 6	4.15[a]	2.85; 7
6. L Amygdala/Hippocampus	−19	4	−24	4.30	7.48; 2	1.83; 3	11.06; 6	ns
7. L Parahippocampus	−38	−26	−20	7.37	11.01; 12	4.20; 27	7.63; 5	ns
8. R Anterior Superior Temporal Gyrus	49	19	−24	6.85	9.19; 18	1.94; 10	ns	ns
9. L Anterior Superior Temporal Gyrus	−49	12	−32	6.55	5.56; 2	1.97; 2	ns	ns
10. Ventral Striatum	4	−8	−8	5.45	7.95; 27	3.22; 27	5.13; 2	2.13; 3

Regions of interest, Talairach coordinates (x, y, and z), and z scores from the pilot study of healthy controls are listed in columns 2, 3, and 4, respectively. All z scores from the pilot study are statistically significant after correction for number of effective comparisons. The remaining columns contain the results of the fixed-effects and random-effects analyses for the comparisons of the difference images (all emotional phases minus neutral phases) where psychopaths showed less affect-related activity than did healthy controls (control vs psychopath; columns 4 and 5) and criminal nonpsychopaths (nonpsychopath vs psychopath; columns 6 and 7). The degrees of freedom associated with the fixed-effects analyses are 7872.

t values associated with the random effects analyses with 21 degrees of freedom of 1.72, 2.08, 2.52, 2.83, and 3.82 correspond to one-tailed probability levels of .05, .025, .01, .005 and .0005, respectively. t, t value; e, spatial extent of activation (i.e., the number of significant voxels contiguous with the peak voxel in the region of interest); ns, nonsignificant; L, left; R, right.

[a] All t values reported for the fixed effects analyses have a probability level less than .001 corrected for multiple comparisons, except the value for the right amygdala/hippocampus for the comparison of criminal nonpsychopaths with psychopathic criminals where p = 0.1 after correction.

11.5; and Quick Tests [Ammons and Ammons 1962]; criminal psychopaths 102.7, SD 9.9; criminal nonpsychopaths 108.0, SD 5.86; controls 109.6, SD 17.5).

The Hare Psychopathy Checklist-Revised (PCL-R) was used to assess psychopathy (Hare 1991). The PCL-R is a reliable and valid measure of psychopathy in the prison system (Hare 1991; Stone 1995). Inmates with a score above the mean psychopathy score (23.6, SD 7.9) for the 1192 prison inmates presented in the PCL-R manual were defined as psychopaths. Inmates with scores below the mean were defined as criminal nonpsychopaths. The PCL-R scores can range from 0–40, and in our groups the range was 28–36 (mean 32.8, SD 2.9) for criminal psychopaths and 8–23 (mean 16.6, SD 6.0) for criminal nonpsychopaths. The Hare Psychopathy Checklist: Screening Version (PCL:SV) was used to assess psychopathy in the noncriminals. The PCL:SV is an abbreviated version of the PCL-R used in nonforensic populations. None of the noncriminals met the PCL:SV criteria for psychopathy.

All participants provided written informed consent before all research activities. This study protocol was approved by Human Subjects Committees of the Correctional Services of Canada, Vancouver Hospital, University of British Columbia branch, University of British Columbia Medical School and the University of British Columbia.

Materials and Procedure

The experimental procedure consisted of eight trials, with each trial comprising three sequential phases. In the first phase (encoding), participants were asked to memorize a list of 12 words presented serially, one at a time (500 m/sec duration, 1500 interstimulus interval). During the second phase (rehearsal), participants were instructed to mentally rehearse the list of words presented in the first phase. During this latter phase, the word "rehearse" was continuously displayed. The third phase (recognition) consisted of a recognition test, in which 12 words were presented and participants were instructed to indicate (yes or no), using the index and middle fingers of their right hand, if they recognized the word as being from the list that had been presented during the first phase. Half of the words presented during the third phase had been presented in the first phase. Participants were prompted with the word "encode" or "recall" (2000 msec duration; 500 msec ISI) to indicate the appropriate condition. Accuracy was stressed. A brief rest period followed the completion of the last phase. Each of the three phases and rest period lasted 25 sec. The encoding-rehearsal-recognition-rest sequence was repeated a total of eight times in two stimulus runs. On half of the trials, the word stimuli that were presented during encoding and subsequent recognition phases were uniformly neutral; in the remaining trials, word stimuli were uniformly negative. The participants were not informed explicitly of this word type manipulation. None of the words was repeated across trials (except the target words in the recognition phase). Stimulus words were selected from the seven-point pleasantness ratings given in Toglia and Battig (1978). Words rated as more than 1.3 standard deviations below the mean pleasantness rating were defined as negative (e.g., hate). Words within 1.3 standard deviations of the mean pleasantness rating were defined as neutral in affect (e.g., chair). In prior research, we found that criminal psychopaths are not impaired in accuracy of rating these stimuli as negative and neutral, respectively (Kiehl et al 1999). The word lists did not differ significantly in length (three to eight letters), imagery, or concreteness (Toglia and Battig 1978), or frequency (Francis and Kucera 1982).

An MRI-compatible fiber-optic response device (Lightwave Medical, Vancouver, B.C.) was used to acquire behavioral responses. All stimulus words were presented in lowercase letters, approximately, 5 × 3 visual degrees in size, and were presented (white on black background) in an outline of a rectangular box (6 × 4 visual degrees). Before entry into the scanning room, each participant performed two practice runs consisting of two repetitions of the three phases to ensure understanding of the instructions. The words presented in the practice runs were neutral in affect and were not used in the fMRI session.

Imaging

Imaging was implemented on a standard clinical General Electric 1.5 T whole body system fitted with a Horizon echo-speed upgrade. The participant's head was firmly secured using a custom head holder and external references were used to position the anterior commissure-posterior commissure (AC-PC) line at right angles to the slice-select gradient. Stimuli were presented to the participant by a computer-controlled projection system that delivered the words to a rear-projection screen located at the entrance to the magnet bore. A custom visual and auditory presentation package (VAPP: http://nilab.psychiatry.ubc.ca/vapp) was used to tightly couple the presentation of the stimuli with the acquisition of the MR scanner. The participant viewed this screen through a system of mirrors attached to the top of the head coil. The scanning room and magnet bore were darkened to allow easy perception of the words.

Conventional spin echo T_1 weighted sagittal localizers were acquired to confirm external landmarking and prescribe a subsequent 3D SPGR (TR/TE 11.2/21 msec, flip angle 60°, FOV 26 × 26 cm, 256 × 256 matrix, slice thickness 1.5 mm) volume acquisition. Functional image volumes were collected with a gradient-echo sequence (TR/TE 2500/50 msec, flip angle 90°, FOV 24 × 24 cm, 64 × 64 matrix, 62.5 kHz bandwidth, 3.75 × 3.75 mm in plane resolution, 4 mm slice thickness, 23 slices).

We performed repeated-measures Group (criminal psychopath, criminal nonpsychopath, control) X Condition (negative words, neutral words) analyses of variance (ANOVAs) on the accuracy data.

Functional images were reconstructed offline and the two runs were separately realigned using the procedure by Friston et al (1996) as implemented in Statistical Parametric Mapping (SPM99, Wellcome Department of Cognitive Neurology) (Friston et al 1995c). Translation and rotation corrections did not exceed 3 mm and 3 degrees, respectively, for any of the participants. A mean functional image volume was constructed for each participant for each run from the realigned image volumes. This mean image volume was then used to determine parameters for spatial normalization into the modified Talairach space employed in SPM99 using both affine and nonlinear components (Friston et al 1995a). In this space, coordinates are expressed relative to a rectangular coordinate frame with the

origin at the midpoint of the anterior commissure and the y axis passing through the posterior and anterior commisures. The normalization parameters determined for the mean functional volume were then applied to the corresponding functional image volumes for each participant. The normalized images were then smoothed with a 8 mm FWHM gaussian filter.

In pilot work employing healthy participants (Kiehl et al 1998) we identified 10 regions of interest in which greater hemodynamic activity was observed during performance of the affective encoding-rehearsal-recognition phases than the respective neutral phases. These regions included bilateral amygdala and anterior superior temporal gyrus, left parahippocampal gyrus, anterior (two regions) and posterior cingulate, ventral striatum and left inferior frontal gyrus. The exact coordinates for the site of most significant activation in each of these regions are listed in Table 1. A region was defined as a cube of volume 1000 mm^3 centered on the local maximum observed in the pilot study. A volume of 1000 mm^3 corresponds almost exactly to one resolution element (which is a measure of the extent of the spatial smoothness of the image).

On account of the relatively small sample size, we performed two analyses, a fixed-effects analysis and a random-effects analysis. In general, a fixed effects analysis has greater statistical power, but because the effects of interest are compared to the variance within subjects, the results apply only to the particular subjects in this study. The random effects analysis, in which the effects of interest are compared with the variance between subject, is less powerful, but the findings can be generalized to other samples with greater confidence. Both types of analysis were applied to test the hypothesis that criminal psychopaths showed less affect-related activity (emotional phases minus neutral phases) than criminal nonpsychopaths and noncriminal control participants in the 10 regions of interest identified in the pilot study. In the fixed effects analysis, a canonical delayed-box car (6 sec) response was used to model the event blocks. All reported results from the fixed-effects analysis are significant at the $p < .001$ corrected for multiple comparisons allowing for the number of voxels examined for the entire brain, unless otherwise noted (Friston et al, 1995b; 1995c).

In the random effects analysis, mean functional images were computed for the affective minus neutral phases for each participant by collapsing across each of the phases from both runs. In the computation of these adjusted mean images, a temporal delay of 6 sec was incorporated to account for the relatively slow onset of the hemodynamic response. This procedure yielded a single difference image (affective phases minus neutral phases) per participant. These difference images were then entered into a random-effects one-way (three groups) ANOVA. Planned comparisons were then made at each of the 10 regions of interest to examine our hypotheses that criminal psychopaths would show less affect-related activity than would criminal nonpsychopaths and noncriminal controls. Peak amplitude (maximal *t* score in each region of interest) and extent (number of voxels having a *t* score (21) greater than 1.72 contiguous with the maximal *t* score) are reported. Importantly, there were no significant group differences at any of the regions of interest for processing neutral stimuli relative to the resting baseline, indicating that differences in affective processing are not due to differences in the neutral baseline.

Although our primary hypotheses did not include examining group differences in affect minus neutral conditions at each phase of the encoding-rehearsal-recognition sequence, supplementary analyses are included in which each of the 10 regions of interest are examined separately for the encoding, rehearsal, and recognition phases (see Table 2).

Finally, we also performed an exploratory search of the entire brain to examine whether there were any brain regions in which criminal psychopaths showed greater affect-related activity than criminal nonpsychopaths and noncriminal control participants (see Intrator et al 1997).

Table 2. Summary Statistics of the Results of the Group Comparisons of the Difference Images (Emotional Minus Neutral) Separately for Each Phase (Encoding, Rehearsal, and Recognition) of the Memory Task from the Random-Effects Analysis

	Talairach Coordinates			Encode		Rehearse		Recognition	
Regions of Interest	x	y	z	Control t; e	Nonp t; e	Control t; e	Nonp t; e	Control t; e	Nonp t; e
Frontal Lobe									
1. Rostral Anterior Cingulate	0	38	8	3.02; 12	3.71; 9	ns	2.51; 5	4.05; 27	2.72; 5
2. Caudal Anterior Cingulate	−8	22	20	4.32; 27	2.55; 27	3.60; 27	2.29; 2	3.49; 27	2.59; 10
3. L Inferior Frontal Gyrus Parietal Lobe	−38	41	−8	4.83; 19	2.81; 3	2.98; 10	1.73; 1	2.50; 27	3.22; 27
4. Posterior Cingulate Gyrus	−8	−38	16	2.44; 27	2.65; 27	2.56; 17	2.83; 18	2.28; 6	2.36; 4
Temporal Lobe									
5. R Amygdala/Hippocampus	34	−12	−20	2.73; 13	ns	1.78; 1	ns	ns	ns
6. L Amygdala/Hippocampus	−19	4	−24	ns	ns	ns	ns	1.89; 4	ns
7. L Parahippocampus	−38	−26	−20	4.16; 27	3.57; 7	4.33; 5	ns	2.89; 27	2.69; 27
8. R Anterior Superior Temporal Gyrus	49	19	−24	3.20; 9	ns	2.32; 20	ns	2.70; 11	ns
9. L Anterior Superior Temporal Gyrus	−49	12	−32	2.21; 3	ns	2.65; 27	2.11; 2	2.70; 3	2.16; 5
10. Ventral Striatum	4	−8	−8	3.13; 27	2.93; 27	3.14; 27	2.81; 9	2.81; 27	3.49; 27

t values (21) and extent of activation are reported for each of these latter comparisons for criminal psychopaths versus noncriminal controls and criminal psychopaths versus criminal nonpsychopaths. t values (21) and extent of activation (i.e., the number of voxels above a t value of 1.72 contiguous with the peak voxel in the region of interest) are reported (t = t value; e = extent). t values (21) of 1.72, 2.08, 2.52, 2.83, and 3.82 correspond to one-tailed probability levels of .05, .025, .01, .005 and .0005, respectively. Control, results of comparison of the noncriminal control group versus criminal psychopaths; Nonp, results of comparison of the criminal nonpsychopaths versus criminal psychopaths; ns, nonsignificant; L, left; R, right; t, t value; e, spatial extent.

Results

BEHAVIORAL DATA. Consistent with previous research, negative words were recalled more accurately than were neutral words (main effect of Word, $F(1, 21) = 20.01$, $p < .000097$). There were no group differences in affective processing, relative to neutral processing (Group × Word interaction, $F(2, 21) = 4.82$, $p = .59$); however, the effect of word type was most pronounced in the criminal nonpsychopaths ($F(1, 21) = 9.44$, $p < .006$; percentage correct for neutral 83.60 (SD 4.91) and negative 90.63 (SD 5.10) words) and control participants ($F(1, 21) = 10.90$, $p < .003$; percentage correct for neutral 82.12% (SD 8.3) and negative 90.63% (SD 7.7) words). Psychopathic offenders also showed a statistical trend for more accurate recall of affective stimuli than for neutral stimuli ($F(1, 21) = 3.74$, $p < .067$), correctly classifying 84.25% (SD 4.4) and 88.63% (SD 6.06) of the neutral and negative words, respectively. Importantly, there were no overall group differences in accuracy, suggesting that all groups were actively engaged in performance of the task.

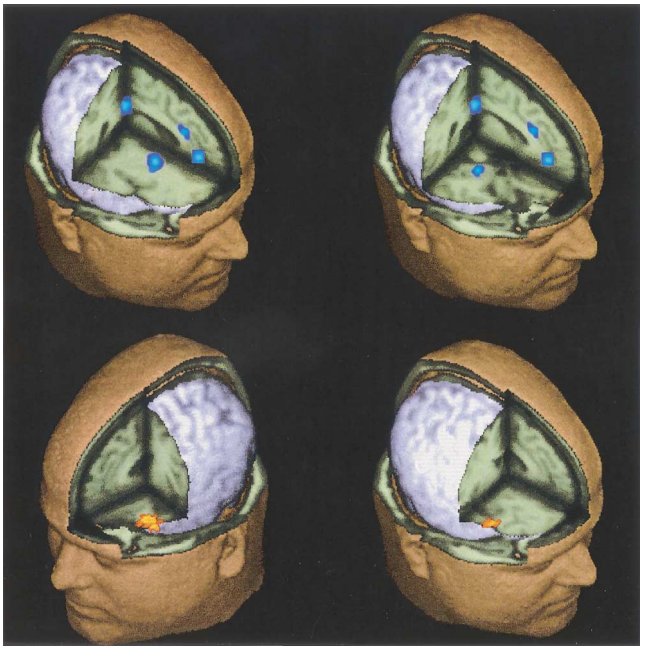

Figure 1. Rendering of the neural areas in which criminal psychopaths showed significantly less affect-related activity than noncriminal control subjects for the comparison of all affective phases versus all neutral phases from the random-effects analysis (top panels; depicted in blue color scheme, all voxels illuminated are statistically significant at the $p < .05$ level). Regions include (top left) posterior cingulate, caudal and rostral anterior cingulate, and ventral striatum (top right), right amygdala/hippocampus. The Talairach coordinates for these results are listed in Table 1. Also shown are the regions in which criminal psychopaths showed greater affect-related activity than noncriminal control subjects and criminal nonpsychopaths (bottom panels; depicted in orange, all voxels illuminated have a probability level $< .05$). These regions include bilateral inferior frontal gyrus (see text for details).

IMAGING DATA. The results of the fixed-effects and random-effects analyses of the imaging data revealed that criminal psychopaths showed less affect-related activity, compared to the neutral baseline, than did criminal nonpsychopaths and noncriminal controls in the rostral and caudal anterior cingulate, posterior cingulate, left inferior frontal gyrus, right amydgala, and ventral striatum. Criminal psychopaths also showed less affect-related activity than did noncriminal controls in the left amygdala and parahippocampal gyrus, and bilateral anterior superior temporal gyrus (see Table 1 and Figure 1).

Importantly, there were no group differences in the above regions for processing neutral stimuli compared to the resting condition. These data suggest that the observed abnormalities in these regions for criminal psychopaths are limited to anomalies in processing affective stimuli and are not due to difficulties in processing neutral stimuli (see also the results from the behavioral data).

Comparison of each phase of the encoding-rehearsal-recognition sequence revealed that during encoding noncriminal controls and criminal nonpsychopaths produced greater affect than neutral activity than did criminal psychopaths in the rostral and caudal anterior cingulate, left inferior frontal gyrus, posterior cingulate, left parahippocampal gyrus, and ventral striatum. Similar group differences also were observed during the recognition phase. Compared with noncriminals, criminal psychopaths showed less affect-related activity during encoding and rehearsal in the right amygdala and bilateral anterior superior temporal gyrus. This latter effect was observed in the left amygdala during recognition.

Interestingly, the exploratory random-effects analysis revealed that the criminal psychopaths exhibited greater activation than the noncriminal controls and criminal nonpsychopaths for affective than for neutral stimuli in a number of brain regions located outside the limbic system. These areas included the left anterior superior temporal gyrus/inferior frontal gyrus and right inferior frontal gyrus (criminal psychopaths greater than noncriminal controls: 44, 20, −12 $t(21) = 3.35$, $p < .001$, extent 12 voxels; −40, 24, −12, $t(21) = 2.85$, $p < .005$, extent 21 voxels; criminal psychopaths greater than criminal nonpsychopaths: 48, 32, −12, $t(21) = 2.25$, $p < .018$, extent 17 voxels; −40, 20, −24; $t(21) = 2.00$, $p < .029$, extent 30 voxels).

Discussion

This study was designed to elucidate and characterize the abnormal functional architecture underlying affective pro-

cessing in psychopathic offenders in the context of a memory task. The results support the hypothesis that criminal psychopathy is associated with abnormalities in the function of structures in the limbic system and frontal cortex while engaged in processing of affective stimuli. These structures primarily included anterior and posterior cingulate, inferior frontal gyrus, amygdala/hippocampal formation and ventral striatum.

Activation in the observed regions in the anterior and posterior cingulate have been associated with attentional processes (Heinze et al 1994; Maddock and Buonocore 1997; Posner and DiGirolamo 1998) and affective processes (Devinsky et al 1995; Mayberg et al 1999). For example, studies have shown that patients with damage to the anterior cingulate show impairments in electrodermal responding (Tranel and Damasio 1994). Criminal psychopathy has long been associated with reduced electrodermal responding to certain classes of stimuli (Hare 1965; Hare 1968; Lykken 1957). Combined with the results of the present data, these results suggest that some aspects of psychopathic behavioral may be related to abnormal function in cingulate cortex.

The amydgala, ventral striatum, and hippocampal formation typically are associated with processes related to emotion and memory (Adolphs et al 1998; Bechara et al 1999a; Irwin et al 1996). In particular, studies have shown that the amydgala is likely to be involved in processes related to fear conditioning (LaBar et al 1995). Numerous studies have shown that psychopaths are insensitive to several types of fear and punishment contingencies (Hare 1965; Hare 1968; Hare 1982; Hare et al 1978; Hare and Quinn 1971; Patrick et al 1994). In addition, Patrick and colleagues have shown that criminal psychopaths do not show the same pattern of startle potentiation during viewing of negatively valenced stimuli as do nonpsychopathic criminals and healthy control participants (Patrick et al 1993; Levenston et al 2000). There is a large body of animal research indicating that startle potentiation to negatively valenced stimuli is mediated by circuits in the limbic system, in particular, circuits in the amygdala (Patrick et al 1994). Taken together, our findings suggest that the neural systems associated with attentional processing of affective stimuli at both the limbic and paralimbic level are abnormal in criminal psychopaths.

It is important to note that psychopathic criminals did show a statistical trend for better memory recall of affective words than for neutral words during the recognition phases of the memory task. Criminal psychopaths showed greater activation for affective than for neutral stimuli in a number of brain regions, including bilateral inferior lateral frontal cortex. These latter regions are generally associated with semantic and decision-making processes (Kiehl et al 2000). These results are consistent with the hypothesis that criminal psychopaths employ nonlimbic cognitive strategies to process affective material (Williamson et al 1991). This interpretation is consistent with the findings of a recent brain imaging study that required participants to make lexical decisions about emotional and neutral words. Psychopathic individuals, but not control participants, showed greater activation for emotional than for neutral stimuli in bilateral frontotemporal cortices (Intrator et al 1997). This finding seemed to imply that this group of psychopaths used more cognitive resources to process affective information than did the healthy control participants. Presumably, the absence of appropriate limbic input regarding the affective characteristics of stimuli forces psychopathic individuals to use alternative cognitive operations and/or strategies to process affective material. These alternative strategies may recruit different neural structures than those used by most individuals, and perhaps additional cognitive resources, to aid in the processing of the affective stimuli. It should be noted, however, that the analyses that revealed the excessive affective activation in lateral frontal cortex in psychopaths were exploratory in nature and should be interpreted with caution.

At the present time, the etiology of these abnormalities is unknown; however, clinical data suggests that abnormalities in affective processing are present at an early age in this population (Frick 1998). It is important to note that these abnormalities in criminal psychopaths occur in the absence of any overt structural brain abnormalities. High resolution structural MRIs were evaluated in all participants and none had any evidence of overt structure brain pathology. Nevertheless, it may be possible that more sophisticated volumetric or morphologic analyses of the brain structure in psychopathic offenders may reveal subtle abnormalities.

There are a number of limitations in the present study that should be addressed in future work. The sample sizes for each group were small, which raises the possibility that some of the observed effects may be sample specific. The fixed-effects analysis revealed significantly smaller affective differentiation in the psychopaths relative to the controls at all 10 loci tested, but these findings could not be confidently generalized to other samples. The random-effects analysis revealed effects of modest significance at five of the sites, and effects of high significance ($p < .005$) at the remaining five sites. In addition, we cannot rule out the possibility that history of substance abuse may have contributed to the findings. All reasonable measures were made to reduce the possibility that substance abuse may have contributed to the observed effects, including recruiting inmates who were free from any DSM-IV diagnosis of substance abuse in the last 6 months and assessing lifetime history of self-reported substance use. Nevertheless, it is

possible that the three groups did differ in the their actual experience of drug use and the interpretation of the results must take this into account.

It is also relevant to note that the present study employed verbal material to examine affective differences between psychopaths and others. It may be possible that the some of the observed effects are limited to the abnormalities in processing this type of affective linguistic stimuli. Future research should consider examining emotional processes in psychopaths using different affective stimuli, such as faces or pictures, to identify common, and perhaps distinct, neuronal differences between psychopaths and others.

In summary, we have shown that processing of affective stimuli is associated with less limbic activation in criminal psychopaths than in criminal nonpsychopaths and noncriminal control participants. We have also shown that psychopathic offenders appear to use alternative neural systems to process affective stimuli. These findings support and extend previous lesion-based observations in psychopaths and provide in vivo visualization of the neural processes that may underlie the affective anomalies that clinicians have described in criminal psychopaths.

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