A NEUROIMAGING INVESTIGATION OF AFFECTIVE, COGNITIVE, AND LANGUAGE FUNCTIONS IN PSYCHOPATHY

By

KENT ANTHONY KIEHL

B.Sc., University of California, Davis, 1993
M.A., University of British Columbia, 1996

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF
THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
in
THE FACULTY OF GRADUATE STUDIES
Department of Psychology

We accept this thesis as conforming
to the required standard

THE UNIVERSITY OF BRITISH COLUMBIA

February, 2000

In presenting this thesis in partial fulfilment of the requirements for an advanced degree at the University of British Columbia, I agree that the Library shall make it freely available for reference and study. I further agree that permission for extensive copying of this thesis for scholarly purposes may be granted by the head of my department or by his or her representatives. It is understood that copying or publication of this thesis for financial gain shall not be allowed without my written permission.

Department of Psychology

The University of British Columbia
Vancouver, Canada

Date March 1, 2005

DE-6 (2/88)

Abstract

Psychopathy is a complex personality disorder defined by a constellation of affective and behavioral characteristics. There is accumulating behavioral evidence suggesting that the condition is associated with impairments in affective, cognitive, and language functions. However, relatively little is known regarding the neural systems underlying these abnormalities. The present thesis is comprised of five experiments designed to elucidate and characterize the abnormal functional architecture underlying these abnormalities in psychopathic criminals. In Experiments 1 and 2, functional magnetic resonance imaging (fMRI) was used to elucidate the neural systems underling abnormal semantic and affective processes in these individuals. In Experiments 3, 4 and 5, event-related potentials (ERPs) were used to characterize the temporal features of cognitive and language functions in psychopaths.

The results from Experiment 1 revealed that compared to control participants, psychopaths performed more poorly and failed to showed the appropriate neural differentiation between abstract and concrete stimuli during a lexical decision task. These deficits were located in the right anterior superior temporal gyrus.

The results from Experiment 2 indicated that psychopaths, relative to control participants, showed less activation for processing affective stimuli than for neutral stimuli in several neural regions, including the right amygdala/hippocampal formation, left parahippocampal gyrus, ventral striatum, and in the anterior and posterior cingulate. Psychopaths did show greater activation for processing affective than for neutral stimuli in regions located outside the limbic system, including bilateral inferior frontal gyrus. These

latter data suggesting that psychopaths used different neural systems than did controls for performing the task.

The results from Experiments 3 and 4 indicated that psychopathy is associated with abnormalities in the P3 ERP component elicited by target stimuli during visual and auditory oddball tasks. In addition, the psychopaths' ERPs to visual and auditory target stimuli were characterized by large fronto-central negativities in the 350-600 millisecond time window. These fronto-central ERP negativities are similar to those observed for patients with temporal lobe damage.

In Experiment 5, using a standard sentence processing paradigm, no group differences were observed between psychopaths and nonpsychopaths in the amplitude of the N400 potential elicited by terminal words of sentences that were either congruent or incongruent with the previous sentence context. These results indicate that the abnormal fronto-central ERP negativities observed in previous studies of language function in psychopaths are not related to processes involved in the generation of the N400.

Taken together, these data suggest that one of the cardinal abnormalities in psychopathy is abnormal semantic processing of conceptually abstract information and affective information and that these abnormalities are related to the function of neural circuits in the anterior temporal lobes and lateral frontal cortex.

Table of Contents

List of Tables

List of Figures

Acknowledgments

There are many friends and colleagues who have contributed to final product presented in this thesis. I would like to start by acknowledging my UC Davis family. My deepest gratitude goes out to Carolyn Aldwin and Rick Levenson for adopting me into their family and for comforting me during my deepest personal losses. I would also like to thank them for training me how to think critically about neuroscience data. To Debra Long, for always being willing to take the time to answer the questions of a persistent, if not overbearing, undergraduate student. To Michael Szymanski, for the seminal lecture on event-related potentials that changed my life. To Ron Mangun, for taking a chance on an unknown undergraduate student and for teaching me the intricacies of event-related potential and positron emission tomography data collection and analyses. To Joe Hopfinger and Todd Handy, for your friendship and collaboration that is only in its infancy.

At the University of British Columbia, I would first like to acknowledge Bob Hare, for taking a chance on an enthusiastic undergraduate student. Your dedication and enthusiasm for your work has, and continues to, inspired me.

To my committee members, Janet Werker, John Pinel, and Don Wilkie, for their patience and assistance with having to read yet another dissertation. To Dimitri Papageorgis, who I know is looking down upon me, thanks for showing me how to be an instructor.

To the hard working undergraduates -Sara Johnston, Derek Mitchell and Erin Fennell - who spent many difficult days with me at the prison. To Andra Smith, it seems like that bike ride in Stanley Park was only a few days ago – who would have guessed the course the next six years would take? We have to proclaim victory though – we got them scanned!

I would like to thank Tony Gray, Arthur Jones and Scott Morrison for coding elegant and flexible programs. To John McDonald, for your friendship and collaboration.

I owe a lot to the members of the Radiology and Physics departments. I would like to thank Drs. Alex McKay and Ken Whittall for helping us get the fMRI program started. To Dr. Forster, for supporting our imaging work throughout the years – we could not have done this anywhere else in the world. To the MRI technicians, Karen Smith, Trudy Shaw and Sylvia Renneberg, for putting up with our 'difficult' patients.

I would like to acknowledge the staff and guards at the Regional Health Centre. To Johann Brink, for helping me get started. To David Kolton for his clinical acumen. Big thanks goes out the Correctional Services of Canada Regional Escort Team for transporting our subjects. To the inmates, for their participation and cooperation and for keeping the last 6 years from being anything but boring.

To my extended family, for understanding why I have been so close these last six years, yet so far away. I am sorry that I have not called more often, but they only give you one phone call in prison.

I have lost touch with two friends of mine over the last few years who contributed much to making me the person I am today. To Brock and Jake – where ever you are, I wish you the best.

I would like to thank my fellow students in Dr. Liddle's lab – to Kristin 'Scully' Laurens, your dedication to research is inspiring. To Alan Bates, for helping to collect so much of the data – you have a great future ahead of you. To the rest of the lab, Adrianna, Adrien, Carol, Lisa and Steph, thanks for your understanding and support – now get back to work.

I do not know if I can put into words the appreciation I feel for my supervisor, Peter Liddle. I am often left in awe of his enthusiasm and undying dedication to his work. His work ethic is nothing short of amazing. He has tried, repeatedly, to cultivate my thinking, writing, and understanding as a scientist. Moreover, he has shown me how to be a better person. Peter, please accept my deepest gratitude for all that you have done over the years.

This work would not have been completed without funding from the Medical Research Council of Canada, Norma Calder Foundation, John Wacker Foundation, BC Medical Services Foundation, and BC Health. I have been fortunate to be generously supported over the last four years by the Michael Smith Scholarship, Medical Research Council of Canada.

Much of the work presented in this thesis was done in collaboration with others. However, any faults in its presentation or logic are mine and mine alone.

Dedication

This thesis is dedicated to the memory of my father, Jeff Kiehl. Without his enduring patience, guidance, forgiveness and unconditional love, I never would have been able to even begin, much less complete, such an accomplishment. Dad, I wish you could be here to share this with me.

1. Introduction

1.1 General Introduction

Psychopathy is a complex personality disorder of unknown etiology. The modern concept of psychopathy can be traced back to the psychiatrist Pinel (1792), who labeled the condition 'madness without delirium'. This term was used to denote the lack of morality and behavioral control in these individuals that occurred despite the absence of any psychotic symptoms or defects in intellectual function.

In the 200 years that followed, the condition has been through an evolution in terminology but many of the defining characteristics have remained unchanged. These characteristics were most clearly delineated, and the current diagnostic criteria established, by the writings of the psychiatrist Hervey Cleckley (Cleckley, 1976). In his 40 years of clinical work Cleckley came to narrow the syndrome he called psychopathy to 16 characteristics (see Table 1). In subsequent years, Hare and colleagues operationalized and transformed these characteristics into items on the Hare Psychopathy Checklist (Hare, 1980), and its successor, the Hare Psychopathy Checklist-Revised (PCL-R; Hare, 1991; see Table 2). The PCL-R is now the most widely accepted diagnostic instrument for psychopathy. There is a substantial literature attesting to the reliability and validity of the PCL-R as a measure of psychopathy in offenders and forensic patients (Fulero, 1996; Hare, 1980; 1996; Hare & Hart, 1993; Hare, Hart, & Harpur, 1991a; 1991b; Harpur, Hakstian, & Hare, 1988; 1989; Hart & Hare, 1989; 1996). Factor analyses of the PCL-R have revealed two correlated dimensions or factors (Harpur et al., 1988; 1989).

Table 1. Cleckley's (1976) 16 characteristics of psychopathy

1)	Superficial charm and good intelligence
2)	Absence of delusions and other signs of irrational thinking
3)	Absence of nervousness or psychoneurotic manifestations
4)	Unreliability
5)	Untruthfulness and insincerity
6)	Lack of remorse or shame
7)	Inadequately motivated antisocial behavior
8)	Poor judgment and failure to learn from experience
9)	Pathologic egocentricity and incapacity for love
10)	General poverty in major affective reactions
11)	Specific loss of insight
12)	Unresponsiveness in general interpersonal relations
13)	Fantastic and uninviting behavior with drink and sometimes without
14)	Suicide rarely carried out
15)	Sex life impersonal, trivial, and poorly integrated
16)	Failure to follow any life plan

Table 2. Items on the Hare Psychopathy Checklist-Revised (PCL-R; Hare, 1991).

1)	Glibness and superficial charm
2)	Grandiose senses of self-worth
3)	Need for stimulation/proneness to boredom
4)	Pathological lying
5)	Conning/ manipulative
6)	Lack of remorse or guilt
7)	Shallow affect
8)	Callous/lack of empathy
9)	Parasitic lifestyle
10)	Poor behavioral controls
11)	Promiscuous sexual behavior
12)	Early behavioral problems
13)	Lack of realistic, long term goals
14)	Impulsivity
15)	Irresponsibility
16)	Failure to accept responsibility for own actions
17)	Many short-lived marital relationships
18)	Juvenile delinquency
19)	Revocation of conditional release
20)	Criminal versatility

Factor 1 includes items related to emotional and interpersonal relationships (e.g., superficial charm, egocentricity, grandiosity, deceitfulness and manipulativeness, and absence of remorse, guilt, or empathy). Factor 2 items reflect impulsive and antisocial behaviors (e.g., impulsivity, poor behavioral controls, proneness to boredom, poor life planning, and irresponsibility). This latter factor is most closely related to the Diagnostic and Statistical Manual of Mental Illness (DSM IV) classification of Antisocial Personality Disorder (APD; American Psychiatric Association, 1994). It is important to note that although APD was intended to capture the essential components of psychopathy, it has been criticized for overly relying on antisocial behaviors, while excluding the affective and interpersonal characteristics considered to be central to the construct of psychopathy (Hare, 1996; Hare et al., 1991b; Hart & Hare, 1996; Widiger et al., 1996). In the following experiments, all inmates were assessed with the Hare Psychopathy Checklist-Revised.

Utilizing these modern assessment techniques, researchers have found that psychopathy is associated with abnormalities in a number of cognitive and language domains, including affective and semantic processes. The present thesis is comprised of a series of experiments that seek to elucidate and characterize the neural architecture underlying these cognitive and language abnormalities in criminal psychopaths. Before beginning a detailed review of the relevant research it may be helpful to briefly describe the experimental methods used in this background research and employed in the experiments to follow.

1.2 Event-related potentials

Event-related potentials (ERPs) have been used successfully for over 30 years to characterize the time course and scalp topography of the neural activity associated with information processing in health and disease. ERPs are stimulus-locked segments of the ongoing electroencephalogram (EEG). ERPs are typically averaged over many comparable stimulus events (e.g., abstract words) in order to remove 'noise' resulting from ongoing brain activity not relevant to the processing of the stimulus of interest. The resulting series of peaks and troughs, often labeled 'components', are plotted as function of time versus amplitude. These components can be referred to in regards to their functional significance (e.g., mismatch negativity) or, more commonly, they can be labeled according to their polarity (e.g., negative wave [N]; positive wave [P]) and by their ordinal position after stimulus onset. ERP components can also be referred to by their polarity and latency in milliseconds from stimulus onset. A P1 for example, would be the first positive component following the stimulus. The N400, on the other hand, would be a negative component of the ERP peaking approximately 400 milliseconds after stimulus onset.

ERPs provide precise characterization, on the order of milliseconds, of the temporal structure of information processing. However, characterizing the spatial distribution of the neural generators underlying these components is difficult, as there is no unique solution to the 'inverse problem'. The inverse problem refers to determining the unique dipole distribution believed to have generated the scalp potentials. Additionally, if one was seeking to determine a description in terms of a sum of dipoles, one would also need to determine the relative strength of the dipoles.

1.3 Functional magnetic resonance imaging

Functional magnetic resonance imaging (fMRI) takes advantage of the fact that as neurons are engaged in a cognitive operation a commensurate increase in local blood flow occurs. This enhanced blood flow supplies the metabolically active neurons with an increased supply of oxygenated blood. Importantly, the increase in blood flow exceeds the amount needed to meet the additional demand for oxygen, leading to an increase in the concentration of oxygenated hemoglobin, and a corresponding dilution of deoxyhemoglobin. Deoxygenated hemoglobin is a paramagnetic compound that causes spin packets in the magnetic field to dephase rapidly (T2* relaxation) which results in a loss of MR signal. A local increase in the ratio of oxygenated/deoxygenated hemoglobin concentration then produces a decrease in spin dephasing, which results in a net increase in MR signal. This effect was termed the blood oxygen level dependent (BOLD) contrast by Kwong and colleagues (Kwong et al., 1992). The resulting signal from each region in the brain can then be plotted and analyzed as a function of intensity versus time. Currently, the temporal and spatial resolution of fMRI is on the order of seconds and millimeters, respectively. Functional MRI has been used in the past 9 years to characterize the neural correlates of many domains of cognitive function and is readily being applied to the study of psychopathology (D'Esposito, Zarahn, & Aguirre, 1999).

1.4 Cognitive and language abnormalities in psychopaths

Early empirical research sought to elucidate cognitive impairments in psychopathy by examining the relationship between psychopathy and hemispheric lateralization for language function (Day & Wong, 1996; Hare, 1979; Hare & Jutai, 1988; Hare & McPherson, 1984; Jutai, Hare, & Connolly, 1987; Raine, O'Brien, Smiley, Scerbo, & Chan, 1990). The impetus for exploring this relationship arose from clinical observations of psychopathic individuals. Numerous clinicians noted that the actual behavior of psychopathic individuals is often strikingly inconsistent with their verbalized reports (Cleckley, 1976; McCord & McCord, 1964), leading some to speculate that psychopathy was associated with language abnormalities (Flor-Henry, 1972).

Subsequent research found that abnormalities in language processes are most prevalent when psychopathic individuals were required to perform tasks involving semantic processing (Hare, 1979; Hare & Forth, 1985; Hare & McPherson, 1984). For example, in a task that placed no explicit demands on affective processing, Hare and Jutai (1988) observed that psychopathic individuals made more errors than did control participants in an abstract semantic categorization task. However, psychopathic individuals performed no worse than control participants for a simple recognition task or categorical judgment task, suggesting that the observed cognitive abnormalities were present only when processing abstract semantic information (see also Hare, 1979).

More recently, Kiehl, Hare, McDonald and Brink (1999) observed that psychopathic individuals performed more poorly than control participants during a task (Task 2 in their study) that required classifying word stimuli as either concrete (e.g., table) or abstract (e.g.,

justice). Previous studies have demonstrated that healthy subjects respond more quickly and accurately to concrete words than to abstract words in lexical decision and concrete/abstract discrimination tasks (Day, 1977; Holcomb, Kounios, Anderson, & West, 1999; James, 1975; Kounios & Holcomb, 1994; Kroll & Merves, 1986). These data led to theories that the cognitive operations, and by inference, the neural systems, involved in processing concrete and abstract words are disassociated (Holcomb et al., 1999; Kiehl et al., 1999b; Paivio, 1986; Paivio, 1991; Schwanenflugel, Harnishfeger, & Stowe, 1988; Schwanenflugel & Stowe, 1989). Consistent with the hypothesis that psychopathic individuals have difficulty processing abstract words, Kiehl et al., (1999a) found that psychopathic individuals made more errors than did nonpsychopaths when having to classify word stimuli as abstract. They also recorded event-related potential (ERP) data during their procedure and observed that psychopathic individuals failed to show the normal ERP differentiation between concrete and abstract words (Tasks 1 and 2). In noncriminals and in criminal nonpsychopathic individuals concrete words elicit greater ERP negativity in the 300-800 millisecond window than do abstract words (Kounios & Holcomb, 1994; Paller, Kutas, Shimamura, & Squire, 1987). This latter effect is strongest at fronto-temporal electrode sites suggesting frontal-temporal generators are involved in the differentiation of concrete and abstract words. Given that the differentiation between concrete and abstract words appears to be most robust 300-500 ms post-stimulus, it has been argued that this differentiation is due to modulations of semantic generators also believed to contribute to the N400 potential typically observed in word and sentence processing tasks (Kutas & Hillyard, 1980b; 1983; 1984). Recent evidence suggests that the amplitude of the N400 may reflect processes related to the integration of a words meaning within ongoing cognitive context (Holcomb, 1993). Using this interpretation, it would appear

that psychopaths differ from others in the degree and extent of cognitive processes required to perform language tasks.

Abnormalities in semantic processing also have been observed in psychopathic individuals to emotional stimuli. Day and Wong (1996) found that psychopathic individuals did not show the same hemispheric laterality in behavioral performance as did control participants for processing negatively valenced word stimuli. These results were interpreted as support for the hypothesis that psychopathic individuals do not make use of the connotative-emotional processes based in the right hemisphere (Day & Wong, 1996). Williamson, Harpur and Hare (1991) found that psychopathic individuals did not show the normal behavioral facilitation and ERP differentiation between emotional and neutral words during a lexical decision task (see also Kiehl et al, 1999a, Task 3).

Evidence for abnormalities in language processing also comes from analyses of the speech of psychopathic individuals. Gillstrom and Hare (1988) found that psychopathic individuals use more 'beats', defined as language-related hand gestures incongruent with the semantic content of their speech, than do control participants. This finding was interpreted as evidence that psychopathic individuals compartmentalize their speech into smaller, more discrete units than do others. Psychopathic individuals also do not differentiate, in voice analyses, between affective and neutral words (Louth, Williamson, Alpert, Pouget, & Hare, 1998). Brinkley, Bernstein & Newman (1999) found that psychopathic individuals performed more poorly at resolving action in spoken narratives than did control participants. Interestingly, the performance of the psychopathic individuals did improve however, when they were provided with more concrete, tangible story guides.

Recent evidence from neuroimaging studies of affective processing in psychopathic individuals has also revealed abnormalities in semantic processing. Using Single Photon Emission Computed Tomography (SPECT), Intrator et al. (1997) found that psychopathic individuals show greater activation for affective than for neutral stimuli bilaterally in temporo-frontal cortex. These latter data have been interpreted as supporting the notion that psychopaths require more cognitive resources to process and evaluate affective stimuli than do comparison subjects.

Thus, on balance, accumulating evidence suggests that psychopathy is associated with abnormalities in semantic processing. In particular, these abnormalities appear to be strongest when accessing right hemisphere resources for processing conceptually abstract information of both emotionally valenced stimuli and affectively neutral stimuli.

1.5 Role of right hemisphere in language processing

Since the classic work of Broca and Wernicke, language functions have generally been assumed to reside in left hemisphere neural systems. However, more recent evidence from language studies suggests that the right hemisphere may play an important role in language processing. For example, patients with right hemisphere brain damage show deficits in verbal reasoning ability (Caramazza, Gordon, Zurif, & DeLuca, 1976), in interpretation of verbal humor (Brownell, Michel, Powelson, & Gardner, 1983), in understanding prosody of speech (Ross, 1981) and in comprehension and production of the connotative meanings of words and figures of speech (Gardner & Denes, 1973; Winner & Gardner, 1977).

Recent evidence from neuroimaging studies have further implicated the right hemisphere in language functions. Beauregard et al. (1997), using PET, observed that passive viewing of abstract words relative to baseline produced neuronal activation in the right inferior frontal gyrus (Beauregard et al., 1997). This right hemisphere activation was found for abstract word processing but not for concrete words minus baseline comparisons or for emotional words minus baseline comparisons (Beauregard et al., 1997). D'Esposito et al. (1997) also found activation of the right superior frontal gyrus during passive viewing of abstract words, when compared with active processing of concrete words. Similarly, several areas in the right hemisphere, including prefrontal cortex and middle temporal gyrus, have been found to be activated during comprehension of metaphors (Bottini et al., 1994). Kiehl et al. (1999b) found that a region in the right anterior superior temporal gyrus extending into the inferior frontal gyrus was more strongly activated for processing abstract stimuli than for concrete stimuli during a lexical decision task, suggesting that there is a right hemisphere neural pathway or system involved in processing abstract word stimuli. Thus, on balance, these data suggest that the right hemisphere may play a special role in interpreting the abstract representations of language and also affective connotations of language.

1.6 The functional significance of the fronto-central ERP negativities in psychopaths

Several studies have reported that long-latency ERPs (later than 300 ms) are different in psychopaths than in nonpsychopaths, especially during visual language tasks. Psychopaths consistently show a large frontally distributed negative wave with a latency of approximately 500 milliseconds to word stimuli. Williamson et al. (1991) reported that psychopaths

exhibited a larger fronto-central N500 to word stimuli during a lexical decision task than did nonpsychopaths. The task employed by Williamson et al. required a Go/No-go decision, raising the possibility that the prominent N500 of the psychopaths was related to poor response inhibition. There is accumulating evidence that psychopathy is associated with deficits in response inhibition (Kiehl, Smith, Hare, & Liddle, 1999c; Lapierre, Braun, & Hodgins, 1995; Smith et al., 1999). However, Kiehl et al. (1999a) reported that psychopaths exhibited a large centro-frontal negative wave with latency about 350 milliseconds during three different language tasks, all of which employed a Go/Go design. Moreover, Kiehl et al. (1999c) observed fronto-central ERP negativities in psychopaths to Go trials but not during No Go trials during a Go/No Go response inhibition study. It is unlikely therefore, that the abnormal late centro-frontal negative waves exhibited by psychopaths can be attributed entirely to difficulties in response inhibition. While both Williamson et al. (1991) and Kiehl et al. (1999a) employed tasks that demanded linguistic processing, the late negative wave in both studies was elicited for all word types (i.e., positive, negative, and neutral words in Williamson et al., 1991; concrete and abstract words (Tasks 1 and 2) and positive and negative words (Task 3) in Kiehl et al., 1999a), raising the possibility that it is independent of stimulus content.

Based on the similar topography of the psychopathic individuals' N350 (Kiehl et al., 1999a) and N500 (Williamson et al., 1991) Kiehl et al. (1999a) suggested that there were at least two possible explanations for the functional significance of these components. The tasks employed by Williamson et al. and Kiehl et al. (1999a) (see also Kiehl et al., 1999c) involved both lexico-semantic processing and required a concurrent behavioral response. Thus, in the 300-600 milliseconds after a word stimulus is presented both semantic and decision-making

processes are engaged and will elicit overlapping ERP components of opposite polarity. In general, presentation of a word stimulus in the absence of any online task demands will elicit a large ERP negativity in the 300-500 ms time window (N4 or N400). There is extensive evidence that links the N400 component to processes related to integrating word meanings within ongoing context (Kutas, 1997; Kutas & Van Petten, 1994). Thus, one interpretation of the psychopaths' fronto-central ERP negativities offered by Kiehl et al. (1999a) and Williamson et al. (1991) was that they may be related to an abnormally large N400. To the extent that the amplitude of the N400 reflects cognitive operations involved in processing the semantic meanings of words, these data are consistent with the hypothesis that psychopathy is associated with abnormal semantic processing. This latter interpretation is strengthened by the fact that abnormally large N400s have been reported in other psychopathological conditions with conceptual and empirical links to psychopathy (Blackwood, Whalley, Christie, & Blackburn, 1987; Ford, et al., 1994; McCarley, Faux, Shenton, & Nestor, 1991). However, there are no studies to date that have examined the relationship between psychopathy and the semantic processing related to the generation of the N400.

The other interpretation offered by Kiehl et al. (1999a) for the functional significance of the psychopaths' N350 was that it was related to an abnormally small P3 potential. The P3 as used here, refers to a family of positive ERP potentials occurring at a latency of 300 milliseconds or more. In general, any task that requires a binary decision (Go/No Go; Go/ Go tasks) will elicit a large positive component in the ERP. Since the discovery of the P3 more than 30 years ago (Sutton, Tueting, Zubin, & John, 1967), there has been considerable effort to delineate the functional significance of this component(s). In general, these studies suggest that the P3 is sensitive to changes in the allocation of attentional resources and

processes involved in contextual updating and decision making (Alexander et al., 1995a; Pritchard, 1981). Since defective allocation of attentional resources and abnormal decision making processes are postulated features of psychopathy (Harpur & Hare, 1990; Kosson, 1996; Kosson & Newman, 1986; Newman, 1998) it may be possible that the large fronto-central negativities seen in psychopaths might results from a lack of attenuation from a typically large positive potential. Although P3 responses have been well characterized in a number of clinical conditions, relatively little is known about them in psychopathy. These studies are summarized below.

1.7 ERP studies of psychopathy

There have been six ERP studies on psychopathy defined according to PCL (an early version of the PCL-R, Hare, 1980) or PCL-R scores (Forth & Hare, 1989; Jutai & Hare, 1983; Jutai et al., 1987; Kiehl et al., 1999a; Raine & Venables, 1988; Williamson et al., 1991). Five reported information concerning P3s, though only two studies employed paradigms in which the salience of stimuli was manipulated in a manner expected to elicit a P3 response. These were the study by Jutai et al. (1987), which employed an auditory phoneme discrimination task, and the study by Raine and Venables (1988), which employed a visual continuous performance task.

Jutai et al. (1987) found no significant difference between psychopaths and nonpsychopaths in the amplitude or latency of the P3, though they did observe a late positive wave (at 600 milliseconds) in psychopaths' waveforms for target stimuli (phonemes) during a dual task procedure (playing video games and making phonemic discriminations). Visual

inspection of the waveforms in their study indicated that the P3 amplitude was smaller in the psychopaths than in nonpsychopaths. It should noted that Jutai et al. did not record from parietal electrodes, usually the optimal site for detection of P3. In contrast, Raine and Venables (1988) reported that the amplitude of parietal P3 to target stimuli in the visual modality was greater in psychopaths than in nonpsychopaths.

In the remaining three studies that reported information about P3, there was no evidence indicating that P3 amplitude was abnormal in psychopaths. However, these studies did not employ paradigms that manipulated the salience of the stimuli. Overall, the findings provide equivocal information about the nature of P3 in psychopathy. The only study (Raine &Venables, 1988) that reported significant P3 differences found *larger* P3s in psychopaths than in nonpsychopaths. This finding was contrary to the expectation that psychopaths would have abnormally low P3 amplitude to oddball stimuli, as is observed in other patient groups with impaired ability to allocate attentional resources (Blackwood et al., 1987; Pfefferbaum, Roth, & Ford, 1995). It should be noted that Raine and Venables (1988) used visual stimuli, whereas many of the studies in other disorders employed auditory stimuli. The unexpected result obtained by Raine and Venables (1988) justifies further exploration of the P3 elicited by visual stimuli.

With regard to the P3 elicited by non-salient stimuli, all the studies that have reported relevant data (Jutai, Hare, & Connolly, 1987; Forth & Hare, 1989; Raine & Venables, 1988) have found that psychopaths do not differ from nonpsychopaths. This effect is consistent with the observation that psychopaths have a normal, or enhanced, ability to ignore irrelevant material (Jutai, 1989; Jutai & Hare, 1983).

Overall, the results of studies of ERP components with a latency of 300 milliseconds or longer in psychopaths raise two major questions. First, does the visual P3 elicited by oddball stimuli have abnormally low amplitude and long latency in psychopaths, as would be expected from the evidence that impaired allocation of attentional resources is a characteristic of the condition? Secondly, can the late fronto-central negative waves reported by Williamson et al. (1991) and Kiehl et al. (1999a) be elicited by visual stimuli that do not involve linguistic processing?

1.8 Summary

Accumulating evidence suggests that psychopathy is associated with abnormalities in semantic processing for stimuli of affective connotations and for non-affective conceptually abstract stimuli. Although several of the studies investigating semantic processes in psychopaths have used ERPs to assess the temporal features of the psychopaths' information processing abnormalities, little is known regarding the neural sources underlying these processes. ERP studies of cognitive and language function in psychopathy have also observed large late fronto-central ERP negativities in the psychopaths' waveforms to language and task-relevant stimuli. The functional significance of these component(s) is unclear and may be related to abnormalities in attentional processes, decision making processes (e.g., P3) and/or semantic processes (e.g., N4).

1.9 Rationale and Hypotheses for Experiment 1

The purpose of the Experiment 1 was to use functional magnetic resonance imaging to elucidate the neural architecture underlying lexico-semantic processing in criminal psychopathic individuals during performance of a concrete/abstract lexical decision task (Kiehl et al., 1999a; 1999b). Previously, using a similar task, we observed that psychopathic individuals failed to show the normal ERP differentiation between concrete and abstract words (Kiehl et al., 1999a). Moreover, we observed that for the psychopathic individuals, all word stimuli elicited a large fronto-central negativity (N350) suggesting aberrant semantic processing (see also Williamson et al., 1991).

Prior fMRI research from our laboratory has shown that lexical decisions to concrete and abstract stimuli are associated with activation of bilateral fusiform gyrus, anterior cingulate, left middle temporal gyrus, right posterior superior temporal gyrus and left and right inferior frontal gyrus (Kiehl et al., 1999b). A direct comparison between the abstract and concrete stimuli epochs yielded a significant area of activation in right anterior temporal cortex suggesting that this right hemisphere site is implicated in differentiating abstract from concrete words. Kiehl et al. (1999b) interpreted this effect as support for the notion that there is a right hemisphere pathway involved in processing abstract words.

Given that psychopathic individuals have difficulty processing abstract information (Hare & Jutai, 1988; Kiehl et al., 1999a), in particular information that draws on right hemisphere resources, we hypothesized that we would observe reduced neural differentiation between abstract and concrete stimuli in the right hemisphere for psychopathic individuals relative to control participants. We specifically hypothesized that this effect would be present

in the right anterior superior temporal gyrus. We also expected psychopathic individuals to be slower and less accurate than control individuals when processing abstract words (Hare & Jutai, 1988; Kiehl et al., 1999a).

1.10 Rationale and Hypotheses for Experiment 2.

Psychopathy has long been associated with deficits or abnormalities in affective processing (Christianson et al., 1996; Day & Wong, 1996; Hare, 1993; Kiehl et al., 1999a; Patrick, 1994; Patrick, Bradley, & Lang, 1993; Patrick, Cuthbert, & Lang, 1994; Williamson et al., 1991). However, relatively little is known regarding the neural architecture underlying these abnormalities. Most empirical research on the affective processes of psychopaths has used behavioral methods or peripheral measures of neural activity (Patrick, 1994).

One of the most consistent findings from these studies is that psychopaths fail to experience or appreciate the emotional significance of stimuli in the way that nonpsychopaths do (Christianson et al., 1996; Patrick et al., 1993; 1994; Williamson et al., 1991). For example, Williamson et al. found that 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 psychopaths (Kiehl et al., 1999a). These anomalies appear to be most prominent in response to negatively valenced emotional stimuli (Patrick et al., 1993; 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.

Here we investigate the neural systems underlying affective processing in psychopaths and controls using functional magnetic resonance imaging during an affective memory task. Prior research with this affective memory task in control participants revealed that affective stimuli elicit greater activation than do neutral stimuli in both limbic and cortical brain regions, including the amygdala, hippocampal formation, and temporal and frontal cortex (Kiehl et al., 1998b). Our primary hypothesis was that psychopaths, relative to control participants, would show less activation in these limbic and cortical structures during processing of the affective stimuli. We also expected the psychopaths to show less behavioral differentiation between affective and neutral stimuli than would control participants.

1.11 Rationale and Hypotheses for Experiments 3, 4 and 5.

Several studies have reported that long-latency ERPs (e.g., 300-600 ms post-stimulus) are different in psychopaths than in nonpsychopaths, especially during visual language tasks. The most consistent feature is the appearance in psychopaths of a large frontally distributed negative wave with a latency of approximately 450 milliseconds. There are (at least) two possible explanations for the functional significance of these components. First, the fronto-central ERP negativities may be related to aberrant semantic processes that would lead to an abnormally large ERP component structure in the 300-600 millisecond post-stimulus time window (e.g., N400). Second, the large fronto-central ERP negativities in psychopaths may be related to defective attentional, contextual updating and decision making processes. These abnormal processes may lead to small positive potentials in similar time windows (e.g., P3), the result of which might be augmented late ERP negativity seen in psychopaths.

In Experiment 3 we required participants to respond to nonlinguistic task-relevant visual stimuli (visual oddball task). This paradigm engages processes related to attentional control and decision making, but no explicit demands are placed on semantic processing. The visual oddball task is well characterized and is know to elicit a robust P3 in healthy participants (Alexander et al., 1995). We expected that the P3 elicited by the salient (oddball) stimuli would be smaller and would have longer latencies in psychopaths than in nonpsychopaths. We also hypothesized that the psychopaths, but not nonpsychopaths, would exhibit a late centro-frontal negative wave even though the stimuli do not require linguistic processing. Lastly, we expected that the amplitude and latency of the P3 elicited by the non-salient stimuli (e.g., nontargets) would be the same in psychopaths as in nonpsychopaths, consistent with the observation that psychopaths have a normal, or enhanced, ability to ignore irrelevant material (Jutai, 1989; Jutai & Hare, 1983).

In Experiment 4, we examined the neural response to auditory oddball stimuli. ERPs elicited by task-relevant auditory stimuli have been shown to be abnormal in a number of psychopathological conditions (Blackwood et al., 1987; Ford, 1998; McCarley, Hsiao, Freedman, Pfefferbaum, & Donchin, 1996). Also, the cognitive processes generating the P3 are believed to be modality nonspecific. Thus, any abnormalities observed in psychopaths during the visual oddball task should also be observed in the auditory oddball task. Therefore, the predictions for Experiment 4 were the same as Experiment 3.

In Experiment 5 ERPs were recorded while participants were engaged in a standard sentence processing task that required semantic processing but no concurrent decision making processes. The primary aim of this experiment was to examine the integrity of the neural systems underlying semantic processes in the absence of concurrent task demands to attempt

to isolate and characterize the conditions in which large fronto-central negativities are elicited. The specific hypothesis was that psychopaths, relative to nonpsychopaths, would show a larger N400 to the terminal words of sentences that were either congruent or incongruent with the previous sentence context. This latter effect would be consistent with the hypothesis that psychopathy is associated with abnormal semantic activation.

In summary, the aim of experiments 3-5 is to determine if the fronto-central ERP negativities previously observed in psychopaths during language tasks (Kiehl et al., 1999a; Williamson et al., 1991) are due to abnormalities in semantic processes (i.e., N4) and/or in combination with abnormalities in attentional/contextual updating processes (i.e., P3).

2.0 Experiment 1

Methods

2.1 Participants. Criminal psychopathic individuals (n=8; all male) were inmates from a maximum-security prison located in Abbotsford, British Columbia, Canada. Psychopathic inmates were transported the University of British Columbia Hospital's MRI unit by the Correctional Services of Canada Regional Escort Team. Noncriminal control participants (n=8; all male) were recruited from the general population. The noncriminal control group was matched with the psychopathic group on gender, age, parental socioeconomic status (assessed with the Hollingshead criteria for parental social position), education level, and IQ, measured with the National Adult Reading Test (NART; Sharpe & O'Carroll, 1991) and Quick Tests (Ammons & Ammons, 1962; 1979a; 1979b). These data are summarized in Table 3. There were no group differences on any of these measures (all p's $> .50$).

All participants were free from any history of head injury or psychotic illness (in self and first-degree relatives), were right-handed (Annett, 1970), and spoke English as their first language. All participants had normal or corrected to normal vision. No participants met the criteria for substance abuse according to the DSM IV criteria within the last 6 months.

Two clinicians used the Hare Psychopathy Checklist-Revised (PCL-R) to assess psychopathy (Hare, 1991). The PCL-R is a reliable and valid measure of psychopathy (Fulero, 1996; Hare, 1980; 1991; Hare et al., 1990a; 1990b; 1991b; Harpur et al., 1988; 1989; Harpur & Hare, 1994; Hart & Hare, 1989; Hart, Hare, & Harpur, 1992). Each of the 20 items on the PCL-R is scored on a 3-point scale (0-2) according to the extent to which it applies to the inmate. All inmates had a PCL-R score above 28 (which range from 0 – 40) on the PCL-

R (mean 32.8, SD 2.9), which is above the mean score on the PCL-R (23.6, SD 7.9) listed in the test manual for normative data of 1192 prison inmates (Hare, 1991). None of the control participants had a criminal history.

2.2 Materials. Stimulus words (3 to 8 letters in length) were selected from the word norms of Toglia and Battig (1978) and were either concrete or abstract. Words rated as more than .75 standard deviations above or below the mean concreteness rating contained in the word norms were defined as concrete and abstract, respectively. The word lists for each task did not differ in word frequency or length (Francis & Kucera, 1982). Furthermore, only affectively neutral words (at or within one standard deviation of the mean pleasantness rating given in Toglia and Battig, 1978) were selected in order to eliminate any confound of emotionality. We developed sets of pronounceable pseudowords by selectively altering one letter of each of the concrete and abstract words.

2.3 Procedure. Stimuli were presented to the participant by a computer controlled projection system that delivered a visual stimulus to a rear-projection screen located at the entrance to the magnet bore. The participant viewed this screen through a mirror system attached to the top of the head coil. The scanning room and magnet bore were darkened to allow easy visualization of the experimental stimuli.

Two stimulus runs were presented, each consisting of a series of four thirty second lexical decision blocks alternating with a baseline session. Each run was prefaced by a ten second rest session that was collected to allow for T_1 effects to stabilize. These images were not included in any subsequent analyses. During the lexical decision blocks 15 letter stimuli

(350 ms duration; 1650 ms inter-stimulus interval) were randomly presented. All stimuli were presented in capital letters. During the baseline session, the characters "*****" were continuously displayed for 29.5 seconds (500 ms inter-stimulus interval). Stimulus runs were balanced such that equal proportions of word and pseudoword stimuli were presented. Lexical decision blocks consisted of either concrete words and associated pseudowords or abstract words and associated pseudowords. The word and its associated pseudoword did not appear during the same run. Concrete and abstract lexical decision blocks were presented in a random order. The participant was not informed of the concrete/ abstract manipulation. Participants were instructed to respond with one hand each time the letter stimuli presented formed a real English speaking word and to respond with their other hand if the letter stimuli did not form an English speaking word. The hand used to make the response was counter-balanced across participants. Reaction time and accuracy were equally stressed. A commercially available MRI compatible fiber-optic response device (Lightwave Medical, Vancouver, B.C.) was used to acquire behavioral responses. A custom visual (and auditory) presentation package (VAPP; http://www.psychiatry.ubc.ca/sz/nilab/software/vapp/) was used to precisely control the timing of the experimental stimuli and recording of all behavioral data. Prior to entry into the scanning room, each participant performed a practice block of lexical decisions, repeated twice, to ensure he understood the instructions. None of the stimuli used in the practice blocks were used in the fMRI session.

Reaction times were computed on trials for which the participant responded correctly within 1500 ms post-stimulus. Errors included incorrect responses within 1500 ms post-stimulus or any response with a latency of greater than 1500 ms following the onset of the target stimulus. We performed 2 Group (Psychopath, Control) X 2 Word (concrete, abstract)

X 2 Lexical (real word, pseudoword) repeated-measures analyses of variance (ANOVAs) on the reaction time and accuracy data. Planned comparisons were then performed to test our hypothesis that psychopathic individuals would respond slower and be less accurate for the lexical decisions for abstract words than would control participants.

2.4 Image acquisition. Functional data was collected using a clinical GE 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. Conventional spin echo T_1 weighted sagittal localizers were acquired to confirm external land-marking. Functional image volumes were collected with a gradient-echo sequence (TR/TE 2500/50 ms, flip angle 90°, FOV 24 x 24 cm, 64 x 64 matrix, 62.5 kHz bandwidth, 3.75 by 3.75 mm in plane resolution, 4 mm slice thickness, 23 slices) effectively covering the entire brain (except for the ventral cerebellum).

2.5 Image processing. 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 (SPM96, Wellcome Department of Cognitive Neurology; Friston et al., 1995b). The realignment procedure is used to control for head movement during the scanning period and involves minimizing the sum of the squares of the differences between the first image and subsequent images using an iterative algorithm. The translation (in x, y and z directions) and rotation (about the origin (centered at the anterior commisure) in x, y, and z degrees) corrections did not exceed 2.5 mm and 2.5 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 SPM96 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. Because each brain differs in size and shape, spatial normalization procedures are commonly used in functional imaging studies to allow voxel-based comparisons to be made within and across groups of participants. Additionally, transforming all individual brains into a standard space (e.g., Talairach space) facilitates comparisons with other studies that have employed similar spatial normalization procedures. The normalization parameters determined for the mean functional volume were then applied to the corresponding functional image volumes for each participant.

Adjusted mean functional images were then created for the lexical decision blocks and rest session by collapsing across the time points in each of the three conditions. In the computation of these adjusted mean images a temporal delay of 6 seconds was incorporated to account for the relatively slow onset of the hemodynamic response and the data were high pass filtered (.1 Hz) to remove noise associated with low frequency confounds (e.g., respiratory artifact; see Holmes, Josephs, Buchel, & Friston, in press).

These adjusted mean images (concrete stimuli, abstract stimuli, and rest) were then smoothed with a 10 x 10 x 10 mm Gaussian kernel. The smoothed adjusted mean images were then entered into a two stage analyses. Both stages of analyses employed univariate tests at each voxel in the adjusted mean images using the General Linear Model (GLM; Friston et

al., 1995b). The application of the GLM to each voxel generates values for a statistical parameter such as the F statistic or the t statistic for each voxel. These statistics are employed to construct statistical parametric maps (SPMs) in which the value in each voxel represents the value of the statistic of interest. A map in which voxel values represent values of F is known as an SPM{F} while a map in which voxel values are values of t is known as an SPM{t} (Friston et al., 1995b). The SPM{t} can then be transformed into a SPM{Z}using a probability integral transformation. These SPM{Z}s can then be displayed (usually by colorizing) or rendered onto structural MRIs in Talairach space for illustration. Because multiple voxels were examined, a correction for multiple comparisons based on the theory of Gaussian fields was employed (Worsley, 1994; Worsley & Friston, 1995). Reported statistical levels are significant at the voxel level (Worsley & Friston, 1995) and were all greater than $p < .05$ corrected for multiple comparisons unless otherwise noted.

In the first stage, we performed a confirmatory analysis in the control participants by comparing the concrete and abstract stimuli versus the rest condition. These latter analyses were performed to determine whether we could replicate the results of our previous study (Kiehl et al., 1999b) in this new sample of healthy participants. We also performed an identical analysis in the psychopathic group.

In the second stage we compared the differences between the abstract and concrete stimuli between groups. Here we tested our hypothesis that control participants would show greater activation for processing of abstract stimuli than for concrete stimuli than would psychopathic individuals (i.e., Group x Condition interaction).

Results

2.6 Behavioral data. Consistent with our hypothesis, psychopathic individuals were significantly slower to respond to abstract words than were control participants [planned comparison, $F(1, 14) = 4.40$, $p < .05$]. However, control participants were, in general, faster to respond than were the psychopathic individuals [main effect of Group, $F(1,14) = 9.17$, $p < .009$]. Post hoc tests also revealed that psychopaths were slower to respond to concrete words than were control participants. There were no group differences in accuracy for real word stimuli. However, psychopathic individuals were less accurate than were control participants for responding to the pseudoword stimuli [Group x Lexical interaction, $F(1,14) = 8.99$, $p < .0096$]. Summary statistics of the behavioral data are presented in Table 4.

Overall, real word stimuli were responded to faster than were pseudoword stimuli [main effect of Lexical, $F(1,14) = 32.62$, $p < .0001$]. Concrete words were responded to more quickly than were abstract words [Lexical x Word interaction, $F(1,14) = 10.59$, $p < .0058$]. Concrete stimuli (words and pseudowords) were classified more accurately than were abstract stimuli [main effect of Word, $F(1,14) = 7.94$, $p < .0137$].

2.7 Imaging data. Illustrations of the areas of activation for the concrete stimuli versus baseline and abstract stimuli versus baseline comparisons for the control participants and psychopathic individuals are illustrated in Figures 1 and 2, and 3 and 4, respectively.

The psychopathic individuals showed a very similar pattern of activation as was observed for the control participants for the two comparisons of the word stimuli versus baseline (see Tables 5 and 6). For the psychopathic individuals, activation for both

Table 3. Demographic data for the criminal psychopaths and control participants for Experiment 1.

Group	Age Mean(SD)	Years of formal education Mean (SD)	NART score Mean (SD)	Quick test Mean (SD)	Hollingshead parental social position index Mean (SD)
Controls	27.9 (5.0)	12.4 (.74)	111.82 (7.0)	104.75 (5.4)	4.25 (3.4)
Psychopaths	33.9 (7.6)	11.13 (1.46)	111.19 (7.5)	102.75 (9.9)	4.25 (1.4)

Table 4. Behavioral data for the criminal psychopaths and control participants for the concrete/abstract lexical decision task in Experiment 1.

Reaction times (milliseconds)	Control Participants Mean (SD)	Psychopaths Mean (SD)
Concrete words	608.5 (65.7)	678.6 (52.0)
Abstract words	640.6 (80.2)	714.5 (59.2)
Pseudoconcrete stimuli	709.2 (81.2)	845.6 (113.9)
Pseudoabstract stimuli	700.5 (86.3)	833.9 (93.1)
Percentage correct		
Concrete words	94.3 (3.5)	96.2 (3.4)
Abstract words	89.5 (3.6)	88.5 (11.9)
Pseudoconcrete stimuli	95.0 (3.3)	91.3 (5.7)
Pseudoabstract stimuli	93.6 (3.7)	85.0 (9.9)

Figure 1. Cortical surface rendering of the areas of activation for the control participants for the concrete stimuli versus baseline comparison. These renderings depict 4 views: top left, right hemisphere; top right, left hemisphere; bottom left, left hemisphere mid-sagittal slice; bottom right, right hemisphere mid-sagittal slice. The areas of activation are thresholded at a z-score of 4.0 or greater.

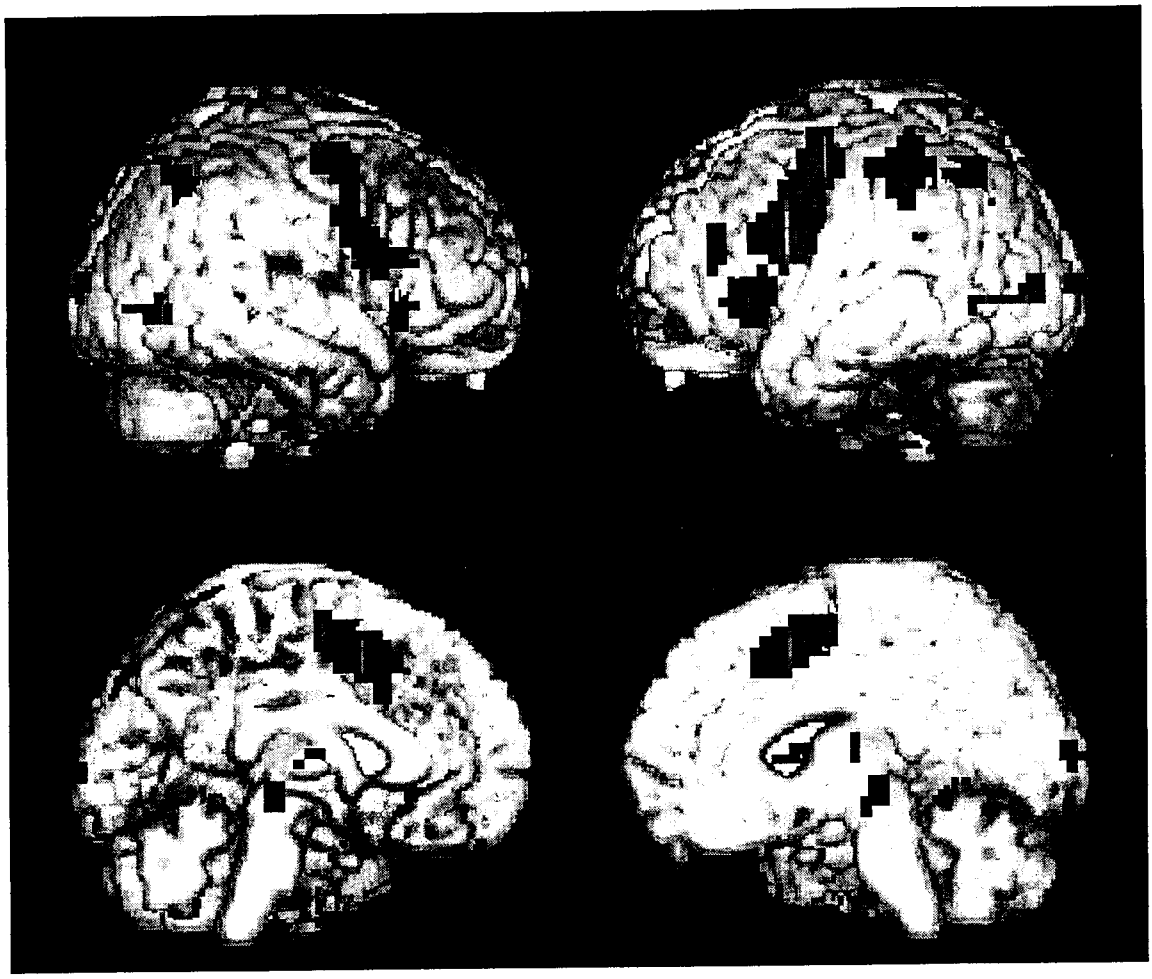


Figure 2. Cortical surface rendering of the areas of activation for the control participants for the abstract stimuli versus baseline comparison. These renderings depict 4 views: top left, right hemisphere; top right, left hemisphere; bottom left, left hemisphere mid-sagittal slice; bottom right, right hemisphere mid-sagittal slice. The areas of activation are thresholded at a z-score of 4.0 or greater.

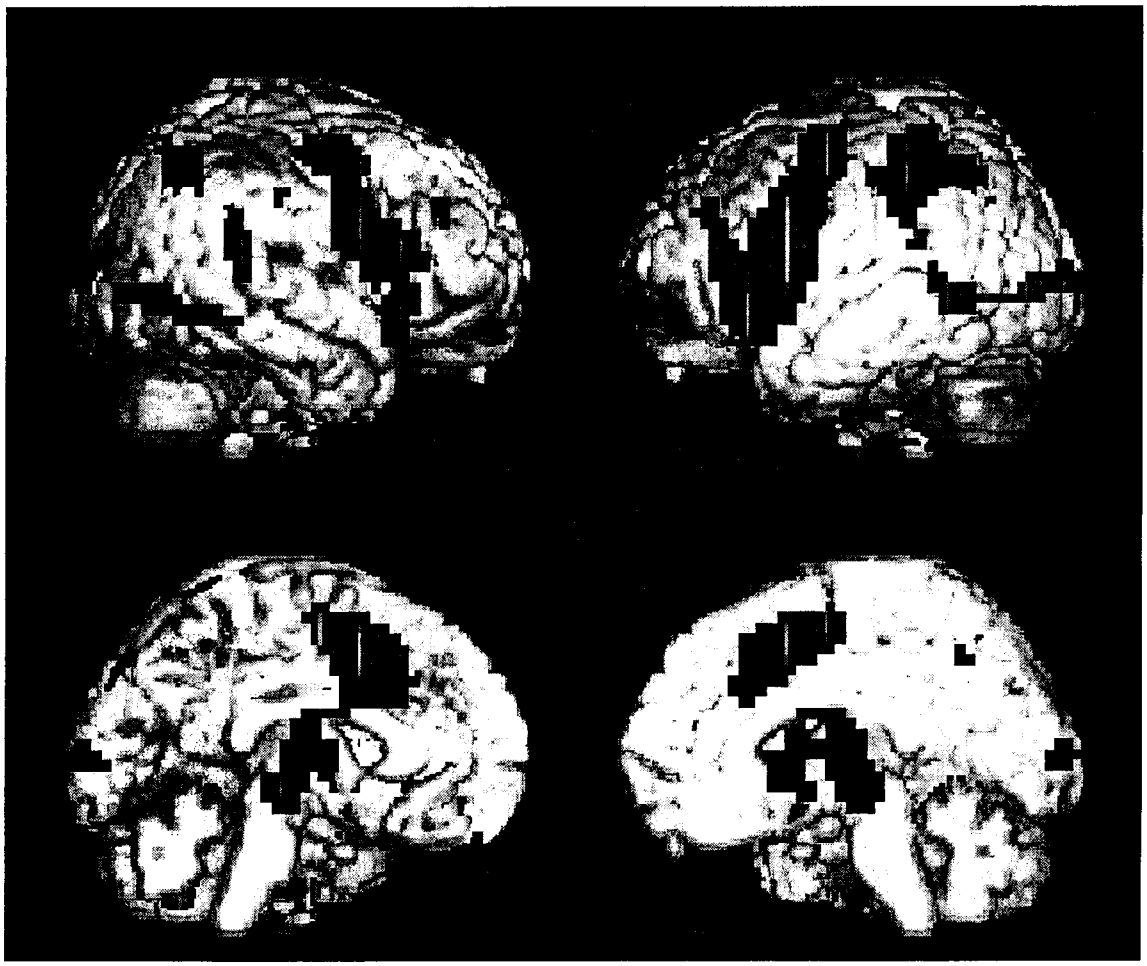


Figure 3. Cortical surface rendering of the areas of activation for the psychopathic participants for the concrete stimuli versus baseline comparison. These renderings depict 4 views: top left, right hemisphere; top right, left hemisphere; bottom left, left hemisphere mid-sagittal slice; bottom right, right hemisphere mid-sagittal slice. The areas of activation are thresholded at a z-score of 4.0 or greater.

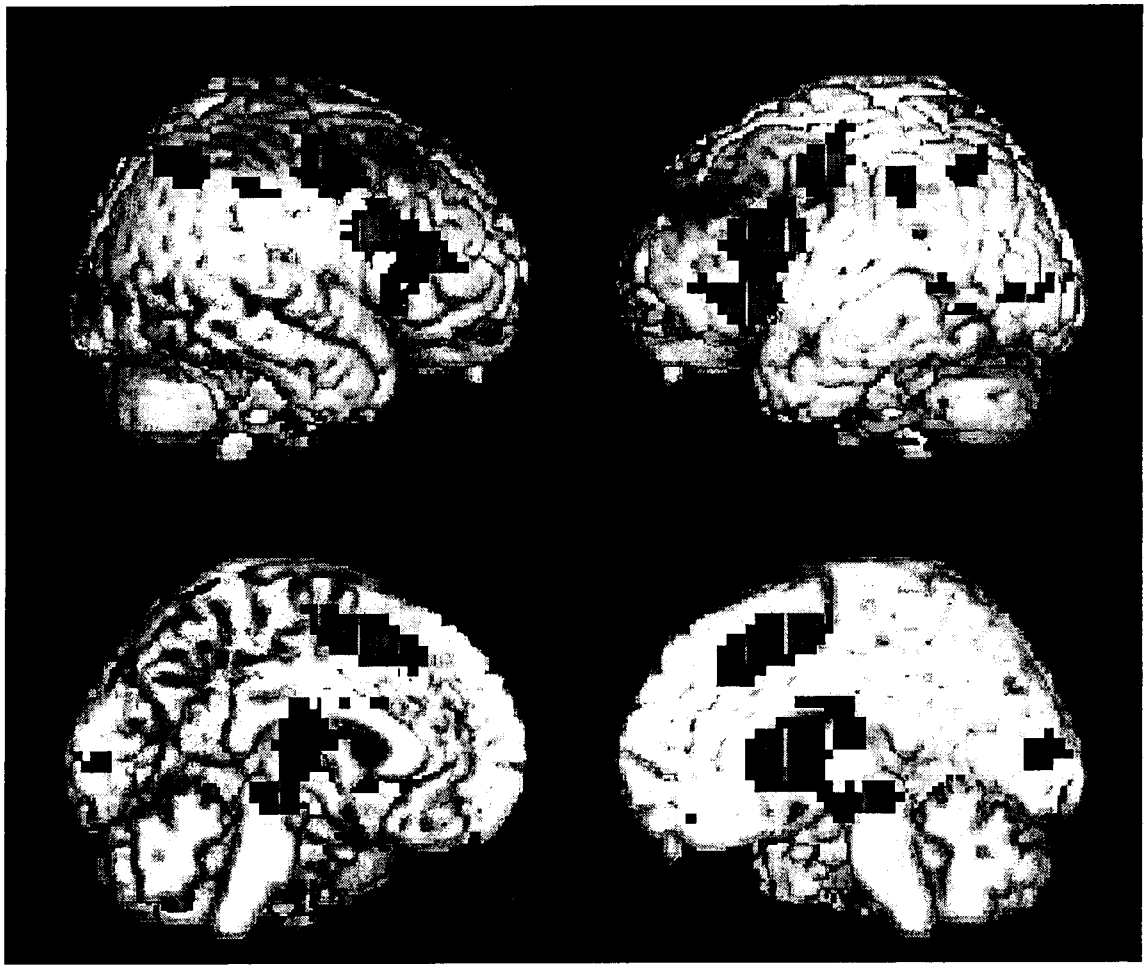


Figure 4. Cortical surface rendering of the areas of activation for the psychopathic participants for the abstract stimuli versus baseline comparison. These renderings depict 4 views: top left, right hemisphere; top right, left hemisphere; bottom left, left hemisphere mid-sagittal slice; bottom right, right hemisphere mid-sagittal slice. The areas of activation are thresholded at a z-score of 4.0 or greater.

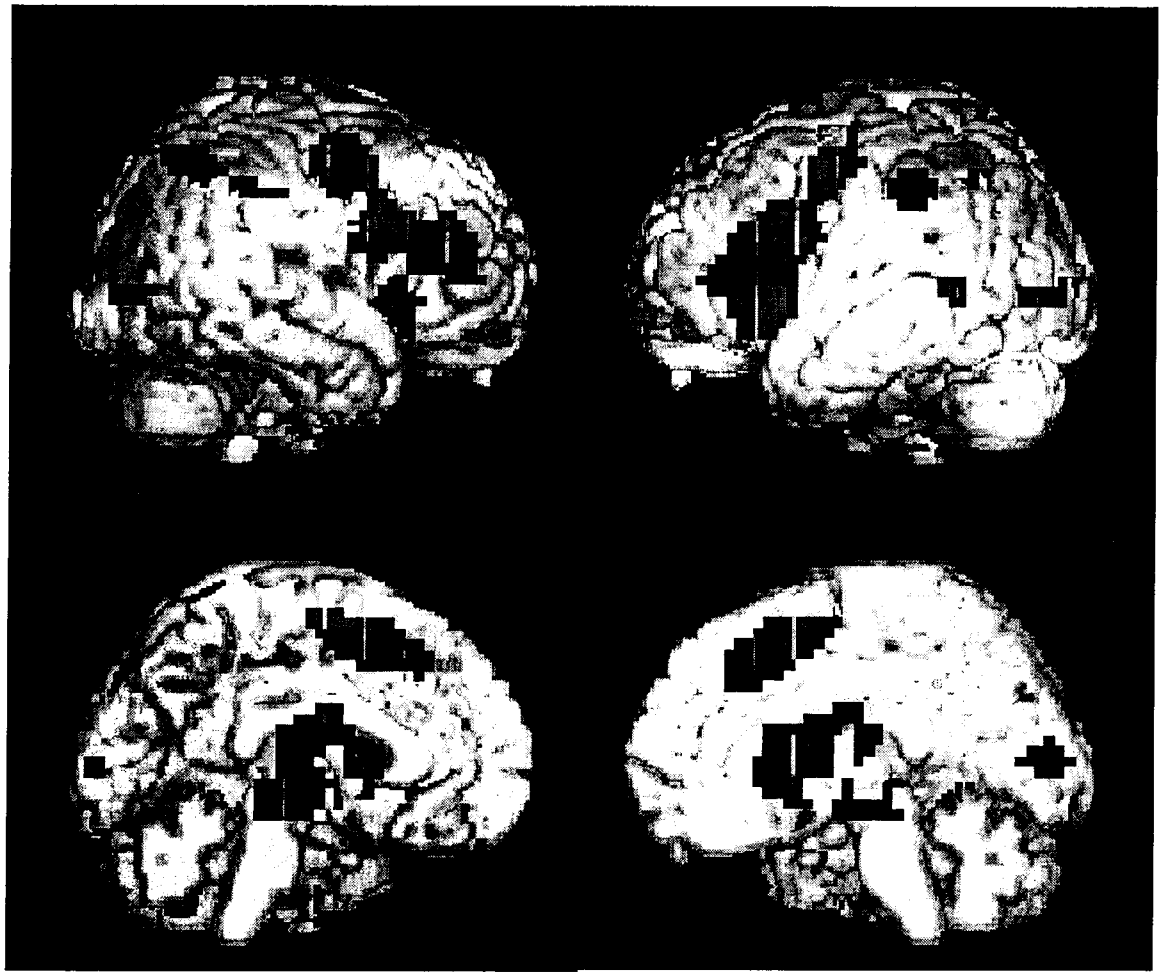


Table 5. Summary of the significant areas of activation for the comparison of the concrete stimuli versus the baseline condition. Talairach coordinates and z-scores are given from our previous study (Kiehl et al., 1999b). Control participants and psychopathic individuals' z-scores and Talairach coordinates are listed for the same anatomical locations as in Kiehl et al., 1999 (at or within on smoothing element, 12 x 12 x 12 mm). L = left; R = right. [a] Denotes a z-score in Kiehl et al. (1999) that was not reported in the original study because the significance level only reached trend levels ($p < .15$). Note: *** $p \leq .001$, ** $p \leq .01$, * $p \leq .05$, ns = nonsignificant

	Region	Talairach coordinates x	y	z	Kiehl et al., 1999b z-score	Control participants z-score (Talairach coordinates: x,y,z)	Psychopathic individuals z-score (Talairach coordinates: x,y,z)
	Frontal lobe						
1.	R Insula	41	26	0	4.26[a]	5.69*** (34,26,0)	5.13*** (34,22,0)
2.	L Inferior Frontal Gyrus	-49	8	32	7.68***	6.88*** (-45,4,32)	6.84*** (-49,15,24)
3.	R Inferior Frontal Gyrus	52	4	32	7.68***	6.21*** (44,8,24)	6.98*** (45,11,24)
4.	Cingulate Gyrus	0	11	40	7.65***	6.84*** (4,8,48)	7.06*** (-4,11,50)
5.	L Middle Frontal Gyrus	-34	0	60	7.10***	5.72*** (-34,-4,64)	6.34*** (-44,-4,50)
6.	R Middle Frontal Gyrus	38	4	52	6.91***	4.99** (34,-4,56)	6.97*** (41,-4,48)
7.	L Inferior Frontal Gyrus	-30	0	44	5.80***	6.24*** (-34,-8,48)	6.34*** (-45,-4,48)
8.	L Insula	-30	34	4	5.36**	6.36** (-34,24,4)	6.51*** (-38,22,0)
9.	L Insula	-34	22	8	4.81*	6.36*** (-34,24,4)	6.51*** (-38,22,0)
	Parietal Lobe						
10.	R Superior Parietal Lobule	30	-60	48	7.00***	5.11** (34,-56,40)	5.74*** (34,-52,44)
11.	L Inferior Parietal Lobule	-30	-52	40	7.58***	5.52***(-26,-56,48)	5.19** (-25,-50,40)
12.	L Inferior Parietal Lobule	-45	-34	48	4.55**	4.64* (-45,-34,40)	4.75* (-45,-34,44)
	Temporal lobe						
13.	L Middle Temoral Gyrus	-52	-52	4	5.46**	5.49** (-41.-71.0)	4.64* (56.-49.4)
14.	R Superior Temporal Gyrus	56	-38	16	5.47**	3.99 (ns) (60,-38,20)	Nonsignificant
	Occipital Lobe						
15.	R Fusiform Gyrus	40	-74	-12	5.92***	4.57* (49,-71,-4)	4.70* (-38,-75,-4)
16.	L Fusiform Gyrus	-41	-60	-12	7.97***	5.49*** (-41,-71,5)	4.69* (-38,-56,-4)

Table 6. Summary of the significant areas of activation for the comparison of the abstract stimuli versus baseline condition. Talairach coordinates and z-scores are given from our previous study (Kiehl et al., 1999). Control participants and psychopathic individuals' z-scores and Talairach coordinates are listed for the same anatomical locations as in Kiehl et al., 1999 (at or within on smoothing element, 12 x 12 x 12 mm). L = left; R = right. [a] Denotes a z-score in Kiehl et al. (1999) that was not originally reported because the significance level reached trend levels ($p < .15$). Note: *** $p \leq .001$, ** $p \leq .01$, * $p \leq .05$.

	Region	Talairach coordinates x	y	z	Kiehl et al., 1999 z-score	Control participants z-score (Talairach coordinates: x,y,z)	Psychopathic individuals z-score (Talairach coordinates: x,y,z)
	Frontal lobe						
1.	L Inferior Frontal Gyrus	-49	8	32	7.93***	7.27***(-49,8,32)	6.93*** (-49,15,24)
2.	R Inferior Frontal Gyrus	52	8	28	7.72***	7.16*** (45,8,28)	7.21*** (45,11,24)
3.	Cingulate Gyrus	0	11	40	7.97***	7.16*** (-8,8,48)	7.14*** (-4,11,52)
4.	R Middle Frontal Gyrus	38	4	52	7.26***	6.03*** (34,-4,52)	7.09*** (41,-4,52)
5.	L Middle Frontal Gyrus	-34	0	56	7.05***	6.94*** (-34,-8,52)	5.28** (-38,-11,52)
6.	L Inferior Frontal Gyrus	-30	0	44	6.83***	6.94*** (-34,-8,52)	5.28** (-38,-11,52)
7.	L Inferior Frontal Gyrus	-56	19	16	6.35***	7.13*** (-52,11,24)	4.91** (-64,15,12)
8.	L Insula	-30	34	4	6.04***	6.95*** (-38,25,0)	5.84*** (34,24,0)
9.	R Inferior Frontal Gyrus	41	26	0	4.64*	6.68*** (34,22,0)	5.84*** (34,22,0)
	Parietal lobe						
10.	L Parietal Lobe	-41	-34	44	6.23***	5.73*** (-45,-34,36)	4.86** (-45,-34,40)
11.	L Inferior Parietal Lobule	-30	-52	40	7.66***	6.28***(-26,-52,44)	5.10** (-25.-52.44)
12.	R Superior Parietal Lobule	30	-56	48	7.59***	6.06*** (34,-52,40)	4.96** (34,-52,40)
	Temporal lobe						
13.	R Superior Temporal Gyrus	56	-38	16	7.06***	5.01*** (60,-38,20)	Nonsignificant
14.	L Middle Temporal Gyrus	-52	-52	4	6.66***	5.05** (-49,-52,0)	5.22** (-56,-49,4)
15.	R Superior Temporal Gyrus	56	11	0	5.00*	5.77*** (49,20,10)	Nonsignificant

	Occipital lobe						
16.	L Fusiform Gyrus	-41	-60	-12	8.02***	5.70*** (-49,-70,5)	Nonsignificant
17.	R Fusiform Gyrus	38	-74	-12	5.59**	5.45** (45,-64,-4)	4.72** (38,-84,0)
	Deep Grey						
18.	L Thalamus	-8	-19	-8	4.30[a]	5.29*** (-4,-22,-4)	6.08*** (-12,-20,-4)
19.	R thalamus	4	-22	-8	4.37[a]	5.30*** (4,-22,-8)	5.89*** (4,-22,-12)

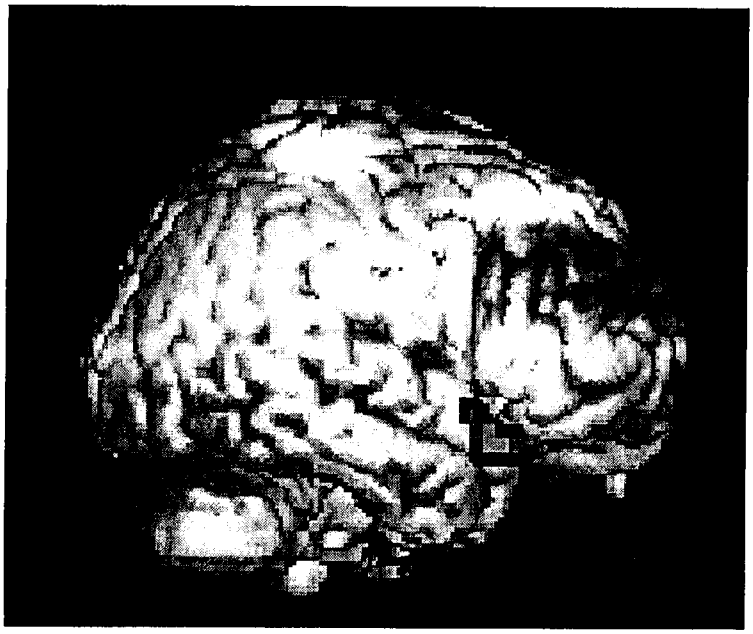
comparisons was observed in bilateral in the superior parietal lobules, anterior cingulate, inferior frontal gyrus, insula, precuneus, bilateral fusiform gyrus, left middle temporal gyrus and right posterior superior temporal gyrus. However, no significant activation was observed in the right anterior superior temporal gyrus for the psychopathic individuals for the abstract versus baseline comparison (see Tables 5 and 6).

In the control participants, the pattern of activation for the concrete stimuli versus baseline and abstract stimuli versus baseline comparisons largely confirmed previous results using this task (Kiehl et al., 1999b). In both studies, processing of concrete stimuli and abstract stimuli (relative to the baseline condition) elicited activation in the bilateral superior parietal lobules, anterior cingulate, inferior frontal gyrus, insula, precuneus, bilateral fusiform gyrus, left middle temporal gyrus and right posterior superior temporal gyrus (see Tables 5 and 6). In addition, significant activation was found in bilateral premotor cortex consistent with the fact that the lexical decision was indicated with a button press using either the right or left hand. In the control participants, we observed significant activation bilaterally in the thalamus for processing abstract words. In our previous study, activation of the thalamus only reached trend levels (see Tables 5 and 6). Comparison of the abstract stimuli versus baseline revealed a very similar pattern of activation to the concrete stimuli versus baseline comparison. As in our previous study, activation in the right anterior superior temporal gyrus was observed for the abstract stimuli versus baseline comparison that was not observed for the concrete stimuli versus baseline comparison.

In the second stage analyses, as predicted, control participants produced greater activation for processing of abstract, compared to concrete, stimuli than did the psychopathic individuals in the right anterior superior temporal gyrus (Talairach coordinates, 52, 15, -10;

z-score 3.35, $p < .001$; see Figure 5). There was also a trend for greater activation during the processing of abstract stimuli relative to that for concrete stimuli for control participants than psychopathic individuals in the right lateral frontal cortex (Talairach coordinates, 34, 11, 32, $p < .0001$, uncorrected for multiple comparisons).

Figure 5. Cortical surface rendering of the areas in which control participants show significantly greater activation for processing of abstract stimuli than for concrete stimuli than did psychopathic individuals. The region was located in the right anterior superior temporal gyrus (Talairach coordinates, x= 52, y = 15, z = -10). The displayed area of activation is thresholded at a z-score of 3.0 or greater.



2.8 Summary and Discussion of Experiment 1

This study was designed to elucidate the abnormal functional neural architecture underlying lexico-semantic processing in psychopathy. Consistent with previous research, psychopathic individuals performed more poorly, manifest as slower reaction times, than did control participants for processing of abstract word stimuli (Hare & Jutai, 1988; Kiehl et al., 1999a). Psychopaths also responded less accurately than control participants for classifying pseudoword stimuli. Some have argued that the cognitive operations associated with processing of pseudoword stimuli are similar to those for processing real word stimuli (see Kounios & Holcomb, 1994). One could also argue that pseudoword stimuli are more similar to abstract word stimuli than to concrete word stimuli. This suggests that the poor behavioral performance of the psychopathic individuals for processing pseudoword stimuli may be related to difficulties in lexico-semantic processing of abstract representations of linguistic stimuli.

In general, the pattern of neural activation associated with processing concrete and abstract stimuli was similar in the psychopathic individuals and control participants. However, psychopathic individuals showed clear deficits in activating the right anterior superior temporal gyrus and surrounding cortex for processing abstract stimuli and they failed to show the appropriate neural differentiation in this region for abstract and concrete stimuli relative to control participants.

The anterior superior temporal gyrus is a multimodal association cortex with rich connections with frontal and parietal cortex (Mendola et al., 1999). In general, the anterior temporal lobe is believed to be involved in a circuit that integrates the outcome of sensory

analyses with previously stored semantic information (Mendola et al., 1999). Removal of the nondominant hemisphere, for treatment of intractable epilepsy, results in impairment in the recall and recognition of visual and auditory patterns that are difficult to code verbally. One might argue that these stimuli are more abstract than concrete and effective processing of these stimuli may rely on the function of this region of cortex (Doyon & Milner, 1991; Kimura, 1963; Meier & French, 1965; Miller & Milner, 1985; Shankweiler, 1966; Smith & Milner, 1988; Warrington & James, 1967).

It is important to note that the right hemisphere abnormalities observed in the psychopathic individuals do not appear to be due to any gross structural brain pathology. High-resolution structural MRI scans were collected in all participants and none had any overt brain pathology. It may be possible that more detailed analyses of the structural MRI data may reveal subtle structural brain abnormalities in the psychopathic offenders, but at this time there is no evidence to support the view that the cognitive abnormalities observed in the present study are due to structural brain damage. In other words, it appears that the abnormalities observed in the psychopathic individuals in the present study are functional, rather than structural, in nature.

In summary, these data suggest that psychopathy is associated with abnormalities in semantic processing of conceptually abstract information. These abnormalities appear to be localized to the right anterior superior temporal gyrus and surrounding cortex. These data are consistent with the hypothesis that psychopathy is related to right hemisphere abnormalities, particularly in the temporal lobe.

3. Experiment 2

Methods

3.1 Participants. Criminal psychopaths (n=8; all male) were inmates from a maximum-security prison located in Abbotsford, British Columbia, Canada. Matched noncriminal control participants (n=8; all male) were recruited from the general population. The two groups of participants were matched for gender (all male), age [Psychopaths 33.9 (SD 7.6); Controls 31.9 (SD 8.4)], parental socioeconomic status [Psychopaths 4.25 (SD 1.4); Controls 3.1 (SD 1.55)], and IQ (measured with the National Adult Reading Test [Psychopaths 111.2 (SD 7.5); Controls 108.9 (SD 11.5)] and Quick Tests [Psychopaths 102.7 (SD 9.9); Controls 109.6 (SD 17.5)]). There were no group differences on any of these measures (all p's > .35). All participants were free from any history of head injury 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 criteria for substance abuse according to the DSM IV criteria within the last 6 months. The Hare Psychopathy Checklist-Revised (PCL-R) was used to assess psychopathy (Hare, 1991). All inmates scored above the mean psychopathy score [23.6, SD 7.9] for the 1192 prison inmates presented in the PCL-R manual. The range of PCL-R scores in our sample was 28-36 (mean 32.8, SD 2.9). The 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.

3.2 Stimuli. Stimulus words were either neutral or negative in connotation, and were selected from the 7-point pleasantness ratings given in Toglia and Battig (1978). Words rated as more that 1.3 standard deviations above 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. The word lists did not differ significantly in length (3-8 letters), imagery or concreteness (Toglia & Battig, 1978), or frequency (Francis & Kucera, 1982).

3.3 Task and Procedure. The experimental procedure consisted of three phases. In the first phase (encoding), participants were asked to memorize a list of twelve words presented serially, one at a time (500 ms duration, 2000 ms ISI). During the second phase (rehearsal), participants were instructed to mentally rehearse the list of words presented in the first phase. The third phase (recognition) consisted of a recognition test, in which twelve words were presented and participants were instructed to indicate (yes or no), using the index and middle fingers of their right hand, whether they recognized the word as being from the list presented during the first phase. Half of the word stimuli presented during the third phase were presented in the first phase. Accuracy was stressed. At the completion of the last phase, a brief rest period ensued. Each phase and rest period lasted 25 seconds. Eight total repetitions of the three phases (plus rest period) were presented in two stimulus runs. Unknown to the participants, half of the phases contained word stimuli (i.e., all stimuli from phase 1 and phase 3) that were either negative or neutral in affect. A MRI compatible fiber-optic response device (Lightwave Medical, Vancouver, B.C.) was used to acquire behavioral responses. All stimuli were presented (white on black background) in an outline of a rectangular box (6 x 4

visual degrees). Word stimuli were all presented in lower case letters and were approximately 5 x 3 visual degrees in size. Prior to 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. All of the word stimuli presented in the practice runs were neutral in affect and none were used in the fMRI session. Stimuli were presented to the participants in the same manner as Experiment 1.

3.4 Behavioral data analyses. We performed repeated-measures Group (psychopath, control) X Condition (negative, neutral) analyses of variance (ANOVAs) on the accuracy data. Planned comparisons were used to determine if both groups showed the expected greater accuracy recognition of emotional stimuli than for neutral stimuli.

3.5 Image acquisition. Image acquisition was performed in the same manner as for Experiment 1.

3.6 Image processing. As in Experiment 1, 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 (SPM97, Wellcome Department of Cognitive Neurology). Translation and rotation corrections for this Experiment 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 SPM97 using both affine and nonlinear components

(Friston et al., 1995a). The normalization parameters determined for the mean functional volume were then applied to the corresponding functional image volumes for each participant.

Adjusted mean functional images were then created for the affective and neutral phases for each participant by collapsing across all three phases for each condition. In the computation of these adjusted mean images, variations in global intensity were removed using proportional scaling and a temporal delay of 6 seconds was incorporated to account for the relatively slow onset of the hemodynamic response. These adjusted mean images were analyzed by comparing the differences between affective and neutral stimuli between the two groups. We were primarily interested in the areas in which greater activation was observed for processing of affective stimuli than for neutral stimuli and where these differences were significantly different between psychopaths and controls.

Results

3.7 Behavioral data. Consistent with previous research, negative words were recalled more accurately than were neutral words (main effect of Word, $F(1, 14) = 19.42$, $p < .0006$). This effect was most pronounced in the control participants (planned comparison: $F(1, 14) = 16.93$, $p < .001$), who correctly classified 82.12% (SD 8.3) and 90.63 (SD 7.7) of the neutral and negative words, respectively, during the recognition condition. Psychopaths also showed a statistical trend for more accurate recall of affective stimuli than for neutral stimuli (planned comparison: $F(1, 14) = 4.49$, $p < .06$), 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 both groups were actively engaged in performance of the task.

3.8 Imaging data. Analyses of the imaging data revealed that control participants showed significantly greater activation for processing of affective than for neutral stimuli than did the psychopathic individuals in the following regions: anterior and posterior cingulate, left posterior fusiform gyrus, left posterior hippocampal gyrus, right anterior parahippocampal gyrus, extending into the amygdala and the ventral striatum (see Figure 6). Other areas where psychopathic individuals showed little differentiation between negative and neutral stimuli included the left inferior frontal gyrus and right superior parietal lobule. However, these latter areas did not reach statistical significance after the stringent correction for multiple comparisons employed in SPM 96 ($p < .0001$ uncorrected).

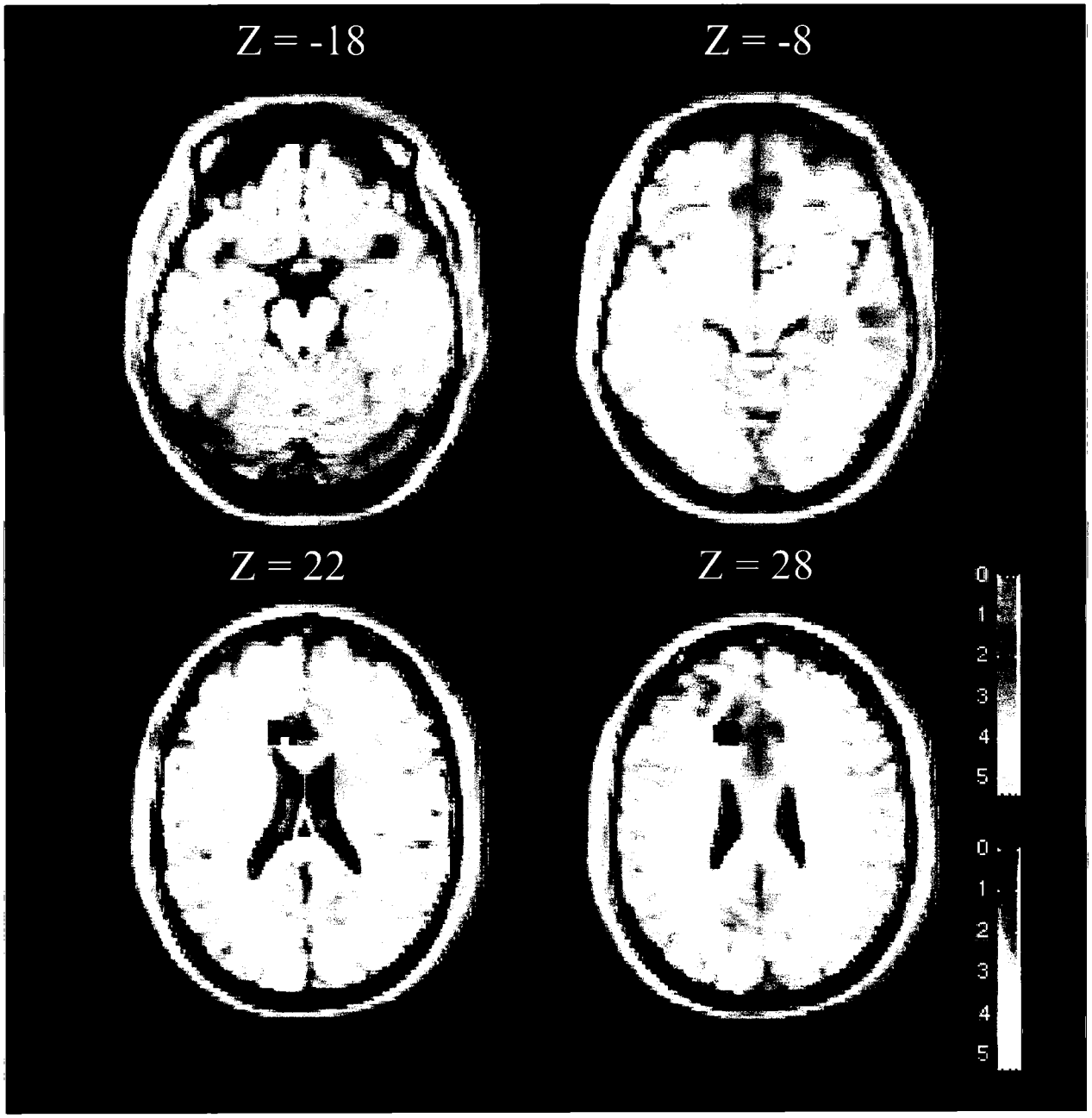
Interestingly, psychopaths did show greater activation for processing of affective than for neutral stimuli in a number of brain regions located outside the limbic system. These areas included the left anterior superior temporal gyrus/inferior frontal gyrus, right inferior frontal gyrus, left precentral gyrus, left and right parietal lobe, and middle temporal gyrus (Figure 6).

Figure 6 legend.

Group statistical parametric maps (SPM{Z}s) rendered onto four transverse slices of a standard reference brain in Talairach space. The z-levels depicted for the four slices are -18, -8, 22, 28 mm below and above the anterior commisure/posterior commisure line, respectively. Left hemisphere is on the left side of each slice. Areas depicted in blue indicate areas in which controls show significantly greater emotional than neutral differentiation than do psychopaths. These areas include: slice 1: right hippocampus/amygdala (34, -11, -20; z-score 4.74); left parahippocampal gyrus (-38, -22, -16; z-score 4.93); left fusiform gyrus (-49, -38, -12; z-score 5.05); slice 2: right putamen/ventral striatum (15, 11, -8; z-score 4.75); slice 3 and 4: left anterior cingulate (-15, 26, 28; z-score 5.20); left posterior cingulate (-8, -38, 16; z-score 5.36). Depicted in red are areas in which psychopaths show greater emotional than neutral differentiation than do controls. These areas include: slice 1: left anterior superior temporal gyrus (-45, 22, -24; z-score 5.31) extending into the inferior frontal gyrus (-38, 26, -20; z-score 4.89); slice 2: right inferior frontal gyrus (64, 22, 16; z-score 4.71); slice 3: right posterior superior temporal gyrus (34, -52, 24; z-score 4.70); left middle temporal gyrus (-64, 8, 28; z-score 5.13); and the left postcentral gyrus (-49, -19, 24; z-score 5.08). This latter effect was also observed in the right precuneas (19, -34, 44; z-score 4.84; data not depicted). Color bars on the bottom right corner indicate the range of z-score units for the two comparisons. A z-scores of 4.50 is equivalent to a probability level of $p = .05$, corrected for multiple comparisons.

See next page for Figure 6

Figure 6. See previous page for legend.



3.9 Summary and Discussion for Experiment 2

This study was designed to elucidate and characterize the abnormal functional architecture underlying affective processing in psychopathic offenders. Psychopathic offenders showed reduced affective-neutral differentiation than did control participants in the hippocampal/amygdala formation, ventral striatum, and in the anterior and posterior cingulate.

In general, the observed regions of activation in the anterior and posterior cingulate and posterior fusiform gyrus have been associated with attentional mechanisms (Heinze et al., 1994; Maddock & Buonocore, 1997; Posner & Rothbart, 1998). The amydgala, ventral striatum, and hippocampal formation typically are associated with processes related to emotion and memory (Adolphs, Tranel, & Damasio, 1998; Bechara, Damasio, Damasio, & Lee, 1999; Irwin et al., 1996). Taken together, these findings suggest that the neural systems associated with attentional processing of affective stimuli and that impart affect at both the limbic and neocortical level are abnormal in psychopaths .

The finding that the areas observed to differentiate affective from neutral stimuli in psychopaths included regions generally associated with semantic and decision-making processes are consistent with the hypothesis that psychopaths employ non-limbic cognitive strategies to process affective material (Williamson et al., 1991). The observation that psychopathic individuals showed greater activation for affective than neutral stimuli in bilateral anterior superior temporal gyrus/inferior frontal gyrus is consistent with the findings of a recent brain imaging study that required participants to make lexical decisions about affective and neutral stimuli. Psychopaths, but not nonpsychopaths, produced greater activation for processing of affective than neutral stimuli in bilateral fronto-temporal cortices (Intrator et al.,

1997). These latter data have been interpreted as supporting the notion that psychopaths require more cognitive resources to process affective information than do normal individuals. Presumably, in the absence of appropriate limbic and cortical input regarding the affective characteristics of stimuli forces psychopaths 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.

At the present time the etiology of these abnormalities is unknown. However, an extensive body of clinical data suggests that abnormalities in emotional processing are present at an early age in this population (Frick, 1998).

In summary, this experiment has shown that processing of affective stimuli is associated with less limbic activation in psychopaths than in control participants. This experiment has also shown that psychopaths appear to use alternative neural systems to process affect. These findings provide the first visualization of the neural processes that may underlie affective anomalies that clinicians have described in psychopaths.

4.0 Experiment 3

Method

4.1 Participants. The participants were 21 male inmates from a federal forensic psychiatric facility near Vancouver, British Columbia. They were participants in a violent offender or sex-offender treatment program. Volunteers were selected for the study if they were between 18 and 55 years of age, had normal, or corrected-to-normal vision, were free from any reported serious head injury or neurological impairment, had no DSM-IV Axis I diagnosis (American Psychiatric Association, 1994), and were right handed (Annett, 1970). Volunteers participated in two sessions: a videotaped semi-structured interview and the experimental recording session. Information from the interview and an extensive review of institutional files were used by two clinicians to independently complete the PCL-R on each inmate. Each of the 20 items on the PCL-R is scored on a 3-point scale (0-2) according to the extent to which it applies to the inmate. The mean and standard deviation of PCL-R total scores (which can range from 0 to 40) for the entire sample were 25.9 and 9.1, respectively. Because of the continuing debate as to whether psychopathy is discrete condition or a dimension of personality (Cooke, 1998; Cooke & Michie, 1997), we performed both categorical and correlational analyses. For the purposes of categorical analyses, an approximate median split was used to create two groups. Inmates with a PCL-R score of 29 or above (n = 11) were defined as Psychopaths (mean = 33.2, standard deviation = 2.2), and those with a PCL-R score of 27 or below (n = 10) were defined as Nonpsychopaths (mean = 17.9, standard deviation = 6.8). Using this procedure all but one of the Psychopaths had a PCL-R score above 30 (the suggested cutoff point for psychopathy given by Hare, 1991). Three of the

Nonpsychopaths had scores above the recommended cutoff of 20 on the PCL-R (Hare, 1991). The liberal cutoff point on the PCL-R for inclusion into the Nonpsychopathic group would, if anything, lend to a conservative bias to our experimental hypotheses. The kappa coefficient for two independent raters for classification into Psychopathic and Nonpsychopathic groups by PCL-R scores was 1.00. The inter-rater reliability for two raters for total PCL-R scores was 0.86.

Mean age and years of formal education were 27 and 33, and 10.5 and 10.8 years for Psychopaths and Nonpsychopaths, respectively. The two groups did not differ significantly on either of these measures ($p > .20$). Participants were rated as average to above average intelligence by a psychiatric screening interview completed for participation in the treatment programs. We paid each inmate $5.00 for the PCL-R interview and $10.00 for the experiment. The total of $15.00 was equivalent to 2 days prison wage. As an additional incentive, we told the participants that the participant who had the best reaction time and accuracy would receive an extra $10.00. The study was conducted in accordance with Institutional and University ethical standards.

4.2 Stimuli. Each stimulus, displayed on a computer monitor, consisted of a white square on a black background. The target stimulus was a four-by-four centimeter square and the nontarget stimulus was a six-by-six centimeter square. The larger stimuli subtended a visual angle of 8.5 by 8.5 degrees, and the smaller stimuli subtended an angle of 3.8 by 3.8 degrees.

4.3 Event-related Potential Recording. Scalp potentials were recorded from tin electrodes (ElectroCap International) placed over prefrontal (F7, Fpz, F8), frontal (F3, Fz, F4), temporal

(T3, T4), central (C3, Cz, C4), and parietal (P3, Pz, P4) sites according to the International 10-20 System of electrode placement. Vertical eye movements were monitored from an electrode on the supra orbital ridge of the right eye. All electrodes were referenced to an electrode located at the right mastoid process. One additional channel, left mastoid to right mastoid, was recorded for the purposes of allowing digital re-referencing to an average of left and right mastoids (Nunez, 1981; Nunez, 1990). Electrical impedance was checked before and after the experiment. In all cases, the electrode impedances were below 5 Kohms.

The EEG channels (Grass Model 8-18C) were amplified with a bandpass of .1 to 70 Hz, digitized on-line at a rate of 256 samples per second, and recorded on computer hard disk. The sampling epoch was 1300 milliseconds, beginning with a 100 millisecond pre-stimulus baseline period. Artifact rejection was performed before averaging to evaluate trials contaminated by blinks (greater than 50 microvolts) or amplifier blocking. These rejected trials did not exceed 5% of trials in any condition and there were no group differences in the number of trials averaged in any condition. The ERPs were then digitally filtered with a zero-phase shift 20 Hz low pass filter to reduce electromyographic noise.

4.4 Procedure. The experiment was conducted in a dimly-lit room in a quiet part of the institution. After attachment of the electrodes the inmate sat in a comfortable chair approximately 60 cm from the computer monitor. He previewed the stimuli and was told to respond as quickly and accurately as possible, by pressing a designated button on a computer keyboard whenever a small square (the target) appeared, but not to respond when a large square (nontarget) appeared. The hand used to respond was counterbalanced across participants. The stimulus duration was 50 milliseconds, with a random 750 – 1250 inter-

stimulus interval. Two hundred trials were presented in 2 blocks of 100. Within each block 25 % of the trials were the target stimuli and 75% of the trials were nontarget stimuli. The participant performed a block of 10 practice trials, repeated twice, to insure he understood the instructions before beginning the experiment.

4.5 Data analysis. We performed separate t-tests on the reaction time, percentage of correct hits and errors of commission. ANOVAs were performed on the ERP data; one for lateral sites and one for midline sites. These analyses included factors of Group (psychopath vs. nonpsychopath) × Condition (target vs. nontarget) × Site (prefrontal, frontal, central, parietal, and temporal for lateral analyses; prefrontal, frontal, central, and parietal for midline analyses). For lateral sites, there also was a factor for Hemisphere (left and right). Two ERP components were measured (relative to the 100 ms prestimulus baseline); the P300 and the N550. For the P300 we performed both peak amplitude and latency measurements. In order to reduce the effect of latency jitter on the P300 peak amplitude measurement, we also quantified the P300 as the mean amplitude in the 325 – 425 millisecond window. Analysis of the mean amplitude measurement of the P300 largely confirmed the peak amplitude analysis. The amplitude of the N550 was quantified as the mean value in the 550-650 window. Following the ANOVA, planned comparisons were performed on the predicted effects. Type I error rate was maintained below .05 by using the Dunn-Bonferroni correction. Other effects of interest were tested using simple effects analyses or Tukey's multiple comparisons. The Geisser-Greenhouse correction was used for any repeated measures that contained more than one degree of freedom in the numerator (Geisser & Greenhouse, 1958). All probability levels are reported using epsilon-adjusted degrees of freedom. The McCarthy and Wood (1985)

correction was applied to any Group x Site or Group x Hemisphere interaction. In all cases, this correction did not decrease the probability level below significance.

We also performed correlation analyses comparing the P300 amplitude and the amplitude of the N550 with PCL-R total scores. All participants were included in these analyses.

Results

4.6 Behavioral data. Participants had no difficulty correctly responding to or correctly classifying the two stimuli. There were no group differences in any of the three behavioral measures (all p's > .05). The behavioral results are presented in Table 7.

4.7 Event-related Potentials. Grand mean ERPs for the Psychopaths and Nonpsychopaths are presented in Figures 7 and 8 for the target and nontarget stimuli, respectively.

4.7.1 P300 peak amplitude. Analyses of the lateral sites yielded a main effect of Group [$F(1, 19) = 5.75$, $p < .03$] and a Group × Condition interaction [$F(1, 19) = 4.82$, $p < .05$]. This pattern of results indicated four things: 1) the P300 to target stimuli was larger for nonpsychopaths than for psychopaths; 2) the P300 was larger for targets than for nontargets for nonpsychopaths; but 3) this latter effect was not significant for psychopaths; and 4) there were no ERP differences between psychopaths and nonpsychopaths for the nontarget stimuli. P300 amplitude measurements for Psychopaths and Nonpsychopaths are summarized in Table 8.

There was a significant Group × Hemisphere interaction [$F(1, 19) = 4.54$, $p < .05$]. This effect indicated that the P300 was more lateralized (right hemisphere) in Nonpsychopaths than in Psychopaths.

At midline sites there was a significant Group × Condition interaction [$F(1, 19) = 5.66$, $p < .03$] and a Group × Site interaction [$F(3, 57) = 4.76$, $p < .006$, $\varepsilon = .55$], and a Group × Condition × Site interaction [midline, $F(3, 57) = 5.55$, $p < .002$, $\varepsilon = .55$]. As with the lateral analyses, 1) Nonpsychopaths had a larger P300 for the target stimuli than did Psychopaths; and 2) Nonpsychopaths, relative to Psychopaths, showed greater central and posterior P300 differentiation between target and nontarget stimuli. There was no P300 difference between conditions for Nonpsychopaths at frontal sites. There was a trend for Psychopaths to show a slightly larger P300 to target than to nontarget stimuli at the anterior site (Fpz).

In general, the P300 was larger for target than for nontarget stimuli [main effect of Condition: lateral, $F(1, 19) = 18.70$, $p < .00001$; midline, $F(1, 19) = 5.66$, $p < .004$] with this effect being greater at right than left hemisphere central and parietal sites [Condition × Site × Hemisphere interaction: lateral, $F(4, 76) = 5.73$, $p < .002$, $\varepsilon = .68$; Condition × Site interaction: midline, $F(3, 57) = 4.75$, $p < .006$, $\varepsilon = .55$]. Across stimulus types the P300 was larger at central and parietal sites than at anterior or temporal sites [main effect of Site: lateral, $F(4, 76) = 23.36$, $p < .001$, $\varepsilon = .40$; midline, $F(3, 57) = 11.13$, $p < .001$, $\varepsilon = .54$]. The results of the correlational analyses between PCL-R scores and the peak amplitude of the P300 to target stimuli are summarized in Table 9. Significant negative correlations were found at central and parietal sites, indicating that the smaller P300 to target stimuli was characteristic of psychopathy.

Table 7. Behavioral data for Psychopaths and Nonpsychopaths for the visual oddball task in Experiment 3.

	Reaction times (ms)	Percentage of Correct Hits	Errors of Commission
	Mean (Std)	Mean (Std)	Mean (Std)
Psychopaths	416 (45.9)	96.2 (1.1)	0.54 (0.7)
Nonpsychopaths	403 (30.5)	94.0 (5.1)	1.80 (1.9)

Table 8. Mean P300 and N550 amplitude measurements for target and nontarget stimuli for psychopaths and nonpsychopaths at prefrontal (F7, Fpz, F8), frontal (F3, Fz, F4), central (C3, Cz, C4), parietal (P3, Pz, P4) and temporal (T3, T4) electrode locations.

PCL-R	F7	Fpz	F8	F3	Fz	F4	C3	Cz	C4	P3	Pz	P4	T3	T4
P300 peak amplitude														
Target stimuli														
Psychopaths	5.0	6.5	4.3	5.8	5.3	6.0	4.9	4.1	6.3	6.2	7.4	7.0	2.8	4.0
Nonpsychopaths	5.8	5.6	5.9	7.6	7.9	9.0	9.3	10.7	11.0	9.4	11.1	10.0	4.0	6.6
Nontarget stimuli														
Psychopaths	2.5	3.4	3.0	4.7	5.2	4.6	5.5	6.9	5.6	4.3	5.2	4.3	2.5	3.2
Nonpsychopaths	1.7	2.7	3.1	3.7	4.9	4.6	5.5	6.7	6.1	5.0	6.3	5.3	2.8	3.4
N550 mean amplitude														
Target stimuli														
Psychopaths	-1.8	-2.2	0.0	-2.3	-3.3	-1.2	-0.7	-2.2	-0.7	0.2	0.6	1.0	-0.7	0.9
Nonpsychopaths	0.5	0.7	2.6	0.8	1.0	2.5	3.4	3.3	4.3	2.3	3.4	2.7	0.8	2.6
Nontarget stimuli														
Psychopaths	1.3	2.2	2.0	1.8	1.8	2.1	1.9	2.3	2.4	0.6	1.3	0.8	0.9	1.7
Nonpsychopaths	1.0	1.9	2.2	1.0	2.1	2.2	2.1	2.7	2.7	0.5	1.3	0.6	1.6	1.3

Figure 7. Grand-averaged ERPs to target stimuli for Experiment 3. By convention, negative amplitude is plotted up.

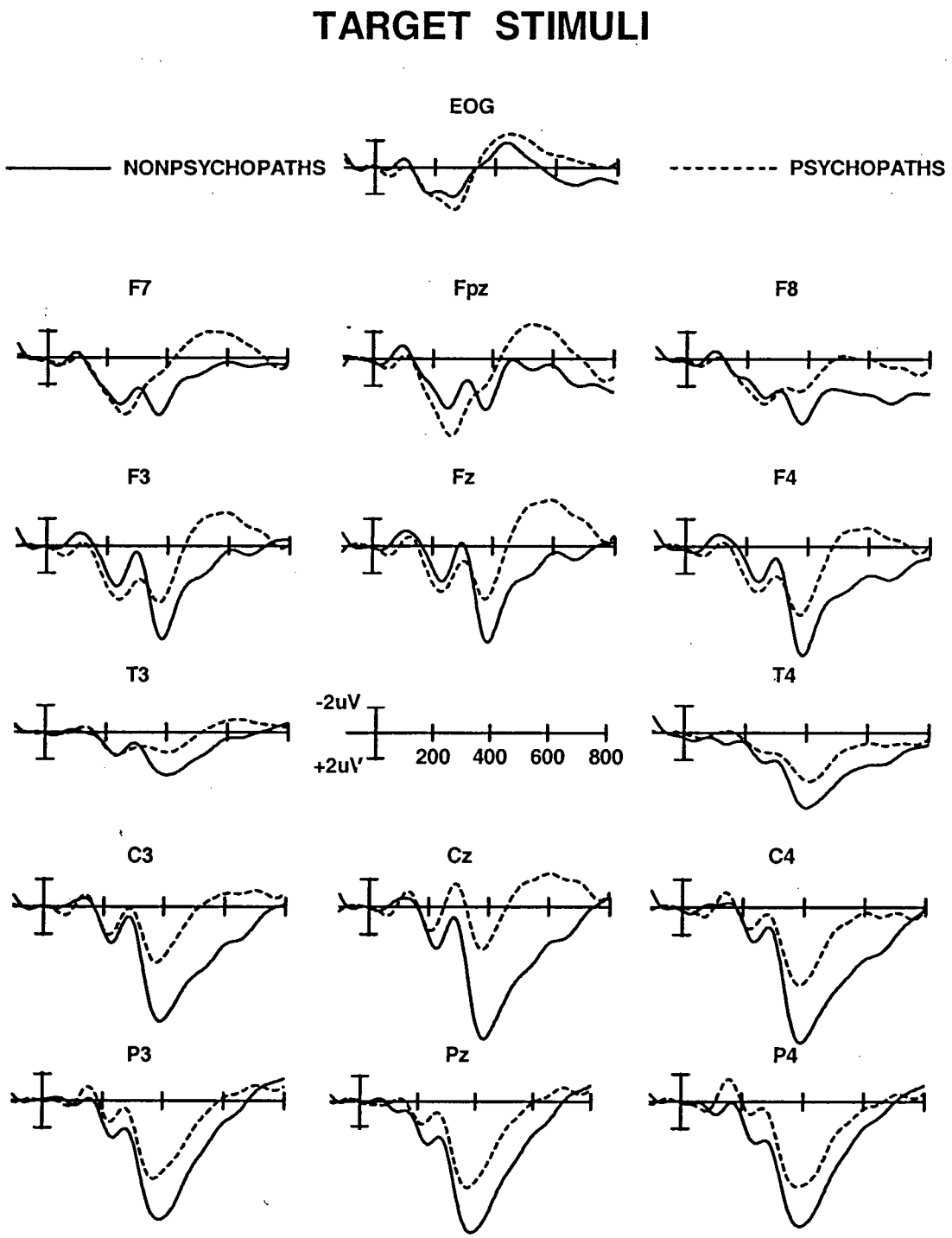
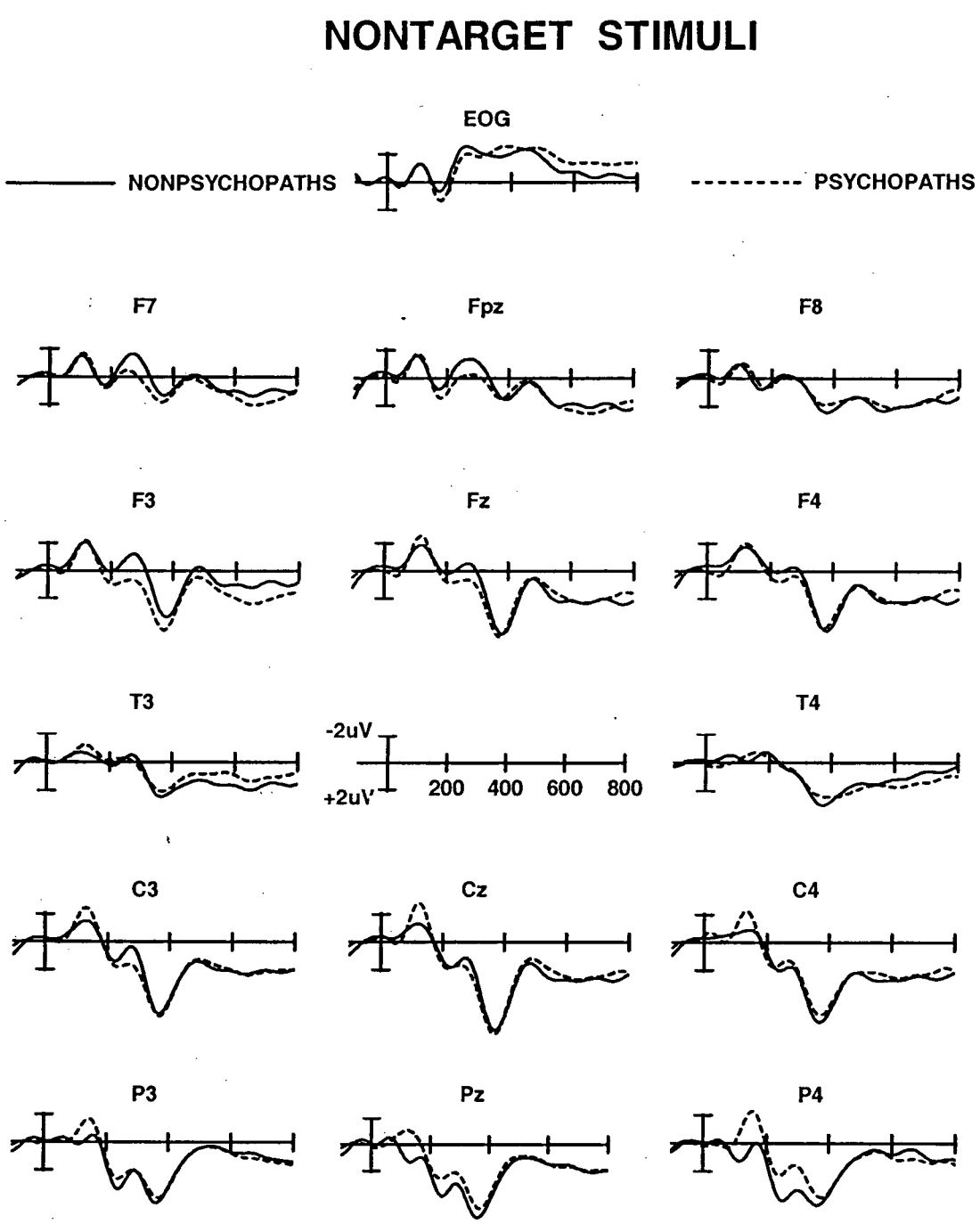


Figure 8. Grand-averaged ERPs to nontarget stimuli for Experiment 3. By convention, negative amplitude is plotted up.



4.7.2 P300 peak latency. The P300 was earlier at prefrontal sites than at any other scalp site [main effect of Site: midline, $F(3, 57) = 5.70$, $p < .01$; lateral, $F(4, 76 = 10.67$, $p < .001$], an effect found only for the target condition and not the nontarget condition [Condition × Site interactions: midline, $F(3, 57) = 13.64$, $p < .0001$; lateral, $F(4, 76) = 9.46$, $p < .001$]. Latency measurements also were faster over left hemisphere sites than at right hemisphere sites [main effect of Hemisphere: $F(1, 19) = 8.68$, $p < .008$]. There were no P300 peak latency differences between Psychopaths and Nonpsychopaths.

4.7.3 N550 mean amplitude. Analyses of this time window confirmed that Psychopaths had a larger N550 than did Nonpsychopaths [main effect of Group: lateral, $F(1,19) = 9.43$, $p < .007$; midline, $F(1, 19) = 14.04$, $p < .002$] an effect found for the target stimuli but not for the nontarget stimuli [Group × Condition interactions: lateral, $F(1, 19) = 7.20$, $p < .02$; midline, $F(1, 19) = 10.01$, $p < .008$]. The N550 was more anterior than posterior [main effect of Site: lateral, $F(4, 76) = 5.46$, $p < .006$, $\varepsilon = .60$; midline, $F(3, 57) = 7.26$, $p < .004$, $\varepsilon = .56$; Condition × Site interactions: lateral, $F(4, 76) = 7.19$, $p < .002$, $\varepsilon = .56$; midline, $F(3, 57) = 10.51$, $p < .002$, $\varepsilon = .58$] and more prominent over the left hemisphere than the right hemisphere [main effect of Hemisphere: $F(1, 19) = 20.53$, $p < .0001$; and Condition × Hemisphere interaction: $F(1, 19) = 11.10$, $p < .005$]. N550 amplitude measurements for Psychopaths and Nonpsychopaths are summarized in Table 8.

As for the P300 results, significant negative correlations were found between PCL-R scores and the N550 amplitude measurements at frontal and central sites (see Table 9).

Table 9

Correlations between psychopathy (PCL-R score) and P300 and N550 amplitude measurements for target stimuli at prefrontal (F7, Fpz, F8), frontal (F3, Fz, F4), central (C3, Cz, C4), parietal (P3, Pz, P4) and temporal (T3, T4) electrode locations.

PCL-R	F7	Fpz	F8	F3	Fz	F4	C3	Cz	C4	P3	Pz	P4	T3	T4
P300 peak amplitude														
R	-.10	.12	-.10	-.22	-.29	-.30	-.52	-.58	-.54	-.47	-.50	-.50	-.40	-.45
p value	.65	.60	.67	.34	.20	.18	.02	.007	.02	.03	.02	.02	.08	.05
N550 mean amplitude														
R	-.37	-.46	-.26	-.51	-.56	-.51	-.55	-.61	-.47	-.43	-.49	-.34	-.48	-.24
p value	.10	.04	.24	.02	.008	.02	.01	.003	.03	.05	.02	.14	.03	.29

4.8 Summary and Discussion for Experiment 3

This study was designed to assess the topographic variation in the P300 response while psychopaths and nonpsychopaths performed a visual oddball task. We predicted that the P300 response to target stimuli would be smaller in psychopaths than in nonpsychopaths consistent with the hypothesis that psychopathy is associated with an impaired ability to allocate attentional resources. The ERP results clearly supported this prediction. As Figure 7 illustrates, the P300 response to the target stimuli was significantly smaller for psychopaths than for nonpsychopaths. This effect was present despite the fact that there were no behavioral differences between groups. This finding may be due to the simplicity of the behavioral task (e.g., ceiling effects) or, more likely, representative of the greater sensitivity of ERP measures to group differences in information processing. This latter conclusion is consistent with a number of other ERP studies on psychopathy (Jutai et al., 1987; Raine & Venables, 1988; Kiehl et al., 1999a) which found ERP differentiation occurred with little or no behavioral differences between experimental conditions.

The reduced P300 amplitude for target stimuli in psychopaths apparently contradicts the finding by Raine and Venables (1988) of an enhanced P300 to visual target stimuli, making it necessary to examine the methodology of both studies. First, with regard to paradigm, Raine and Venables (1988) employed a visual continuous performance task (CPT), whereas in this study we employed a visual oddball task. In the CPT the participant must discriminate between multiple different nontarget stimuli, whereas in the oddball paradigm all nontargets are identical. With regard to participant classification, both studies distinguished psychopaths from nonpsychopaths by performing a median split on scores on the PCL (Raine & Venables,

1988) or its revision, the PCL-R (present study) in a prison sample. Raine and Venables (1988) did not report the median score in their sample. However, if that sample was representative of the larger British prison population from which it was drawn (PCL-R mean score 17.8, standard deviation 8.6, as reported in Hare, 1991), the median score was probably substantially lower than the median score of 29 in the present experiment. However, the results of the correlational analysis suggest that differences between studies in the median values should not affect the findings.

The psychopaths' P300 deficit to target stimuli supports the longstanding idea that psychopathy is characterized by an inability or deficiency in sustaining attention or appropriately allocating attentional resources to task (Cleckley, 1976; Hare, 1993; Kosson, 1996; Kosson & Newman, 1986). Because this performance "deficit" was present only for the target condition and not the nontarget condition, it appears to indicate that it is a specific, rather than a global deficit in psychopathy. It might be that psychopaths are abnormal in their ability to mobilize and rapidly focus attention to stimuli to which they are required to respond. Once focused, it may be extremely difficult for them to re-mobilize and switch attentional resources (cf. Jutai & Hare, 1983)

We have provided further confirmation that psychopaths exhibit an abnormal late centro-frontal negativity in a task that requires a decision and response. However, in contrast to Williamson et al. (1991) and Kiehl et al. (1999a), we observed this negativity for a task that places no explicit demands on linguistic processing. This raises the question of what aspect of processing is responsible for the negativity? Williamson et al. employed a Go/No-go paradigm, indicating that the late negativity might be due at least in part to response inhibition. Our observation that the late negativity only occurred in response to the target stimuli

indicates that it is unlikely to be due to response inhibition, confirming the conclusion of Kiehl et al. It remains to be determined what other processes these negative waves represent. It should be noted that the larger N550 in psychopaths than in nonpsychopaths may have been due, at least in part, to the psychopaths' reduced P300. Alternatively, the small P300 of the Psychopaths may be related to the presence of the large N550.

One additional interesting effect found in this study was that the peak amplitude of the P300 was greater over the right than over the left hemisphere electrode sites in nonpsychopaths but not in psychopaths. There is a relatively large body of evidence that suggests psychopathy is associated with weakly or unusually lateralized cerebral hemispheres (Day & Wong, 1996; Hare & Jutai, 1988; Hare & McPherson, 1984). This hemispheric asymmetry in nonpsychopaths is very similar that found in healthy participants during a visual discrimination task (Alexander et al., 1995b). Indeed, the morphology and scalp distribution of the P300 for the nonpsychopaths in our study very closely resembles that of healthy participants in Alexander et al's study. Interestingly, Alexander et al. interpreted the right frontal-central asymmetry of the P300 to be reflective of processes involved in the sustained engagement of attentional focus. These findings suggest that future research examining the relationships among psychopathy, cerebral asymmetry, and attentional processes will be fruitful.

In summary, this experiment attempted to clarify the relationships between psychopathy and the P300 response elicited by target stimuli during a visual oddball task. The present results are consistent with the clinical literature on psychopathy and support the hypothesis that psychopathy is associated with difficulties in the effective modulation and allocation of attentional resources.

5.0 Experiment 4

Methods

5.1 Participants. The participants were 80 male inmates from a federal maximum-security prison facility near Vancouver, British Columbia. Volunteers were selected for the study if they were between 18 and 55 years of age, were free from any reported serious head injury or neurological impairment and had no DSM-IV Axis I diagnosis (American Psychiatric Association, 1994). Volunteers participated in two sessions: a videotaped semi-structured interview and the experimental recording session. Information from the interview and an extensive review of institutional files were used complete the PCL-R on each inmate. Each of the 20 items on the PCL-R is scored on a 3-point scale (0-2) according to the extent to which it applies to the inmate. Inter-rater reliability for two raters for a subset of the inmates (n=30) was .83. The total population of 80 inmates was broken into two samples. Within each sample, inmates with a PCL-R score of 30 or above were defined as Psychopaths and those with a PCL-R score below 30 were defined as Nonpsychopaths. Sample 1 was comprised of 23 Psychopaths [mean PCL-R score 32.5 (SD 1.7)] and 21 Nonpsychopaths [mean PCL-R score 20.85 (SD 5.99)] collected by the present author. Sample 2 was a replication sample collected by a research assistant and was comprised of 18 Psychopaths [mean PCL-R score 33.94 (SD 2.48)] and 18 Nonpsychopaths [mean PCL-R score 20.35 (SD 6.39)]. Statistical analyses were performed separately for each sample.

For Sample 1, the mean age and years of formal education were 33.9 and 35.8, and 11.0 and 11.4 years for Psychopaths and Nonpsychopaths, respectively. For Sample 2, mean

age and years of formal education were 32.5 and 31.4, and 10.4 and 11.2 years for Psychopaths and Nonpsychopaths, respectively. The National Adult Reading Test (NART) and Quick tests were used to assess IQ. NART and Quick scores were unavailable for 4 inmates. For Sample 1 the NART and Quick scores for Psychopaths were 108.9 (SD 9.6) and 103.2 (SD 11.85) and for Nonpsychopaths they were 107.6 (SD 10.3) and 103.5 (SD 8.5), respectively. For Sample 2 the NART and Quick scores for Psychopaths were 112.3 (SD 7.3) and 105.45 (SD 10.8) and for Nonpsychopaths they were 110.9 (SD 9.36) and 105.8 (SD 9.21), respectively. For both samples, there were no group differences in age, years of formal education, NART or Quick scores (all p's > .50).

We paid each inmate $5.00 for the PCL-R interview and $10.00 for the experiment. The total of $15.00 was equivalent to 2 days prison wage. The study was conducted in accordance with Institutional and University ethical standards.

5.2 Stimuli. The target (1500 hz tones), novel (e.g., ramped tones, random sounds) and nontarget (1000 hz tones) stimuli were presented with a probability level of .125, .125 and .75, respectively. All stimuli were 200 milliseconds in duration with a random 1000 – 1500 ms inter-stimulus interval. The only constraint on the order of stimulus presentation was that two low probability stimuli could not occur after each other, otherwise the presentation of stimuli was random. Six runs of 64 stimuli were collected. Participants were instructed to respond as quickly and accurately as possible to the target stimuli and to ignore the nontarget and novel stimuli. The hand used to respond to the target stimuli was counterbalanced across participants. Two runs of 20 stimuli were given as practice.

5.3 Event-related Potential Recording. Scalp potentials were recorded from tin electrodes (ElectroCap International) placed over 29 electrode sites according to standard placement guidelines of the International 10-20 System. Vertical and horizontal electrooculargram (EOG) were monitored from a bipolar electrode pair located on the lateral and supra orbital ridges of the right eye. All EEG electrodes were referenced to the nose. Two additional channels, left and right mastoids were recorded. Electrical impedances were maintained below 10 kohms throughout the experiment. The EEG channels (SA instruments) were amplified (20,000 gain) with a bandpass of .01 to 100 Hz, digitized on-line at a rate of 256 samples per second, and recorded on computer hard disk. The length of the recording epoch was 1200 milliseconds with a 100 millisecond pre-stimulus baseline. Single-trials with voltages greater than (+ or -) 75 microvolts at any electrode site or EOG artifact were excluded. Four participants (all nonpsychopaths from Sample 2) were excluded because of excessive artifacts (greater than 40% of target trials). After exclusion of these participants, there were no significant group differences in the number of trials averaged in any condition. The ERPs were digitally filtered with a zero-phase shift 30 Hz low pass filter to reduce electromyographic contamination and ambient electrical noise.

Three components were analyzed by measuring the peak amplitude, relative to a 100 millisecond prestimulus baseline, in the following latency windows 175-265 ms (N2), 275-425 ms (P3), and 425-625 ms (N475). These windows were centered upon the peak latency of each of the components in the grand average waveforms. Separate ANOVAs were performed on midline, medial and lateral sites. These ANOVAs included factors of Group [Psychopath and Nonpsychopath], Condition [nontarget, target and novel], and Site [frontal (F7, F3, Fz,

F4, F8), fronto-central (Fc7, Fc3, Fcz, Fc4, Fc8), central (T3, C3, Cz, C4, T4), temporo-parietal (Tp7, P3, Pz, P4, Tp8), and temporo-occipital (T5, O1, Oz, O2, T6)]. For medial and lateral ANOVAs there was an additional factor of Hemisphere [right and left]. Midline (Fpz) and medial (Fp1, Fp2) ANOVAs also included an additional level of Site [prefrontal]. Following the ANOVA, planned comparisons were performed on the predicted effects. Type I error rate was maintained below .05 by using the Dunn-Bonferroni correction. Other effects of interest were tested using simple effects analyses or Tukey's multiple comparisons. The Geisser-Greenhouse correction was used for any repeated measures containing more than one degree of freedom in the numerator (Geisser & Greenhouse, 1958). The McCarthy and Wood (1985) correction was applied to any Group x Site or Group x Hemisphere interaction and is only reported in conditions in which the observed effect became nonsignificant. In addition to the ANOVAs we also performed a correlation analyses between the peak amplitude of the ERP components and PCL-R total scores using the entire sample (n=76). Correlation analyses were not performed separately for PCL-R factor 1 and factor 2 scores as the correlation between these factors was extremely high (r = .86), making any inferences regarding the relationship between factor structure difficult.

Results

5.4 Behavioral data.

5.4.1 Sample 1. There were no significant group differences in the percentage of correct hits [Psychopaths 97.28 (SD 6.07); Nonpsychopaths 98.0 (SD 3.6)], reaction times [Psychopaths 486.90 ms (SD 92.8); Nonpsychopaths 459 ms (SD 62.9)], or numbers of false alarms to novel [Psychopaths 0.82 (SD 1.6); Nonpsychopaths 1.0 (SD 1.5)] or nontarget stimuli [Psychopaths 9.1 (SD 5.7); Nonpsychopaths 8.52 (SD 4.4)]; all p's > .25).

5.4.2 Sample 2. As in Sample 1, there were no significant group differences in the percentage of correct hits [Psychopaths 93.6 (SD 12.4); Nonpsychopaths 98.8 (SD 2.3)], reaction times [Psychopaths 424 ms (SD 79.3); Nonpsychopaths 404 ms (SD 88.8)], or numbers of false alarms to novel [Psychopaths 1.7 (SD 1.4); Nonpsychopaths 2.5 (SD 3.0)] or nontarget stimuli [Psychopaths 12.7 (SD 7.6); Nonpsychopaths 15.6 (SD 7.6)]; all p's > .13).

5.5 Event-related potentials. Grand mean group (across both samples) ERPs for target, novel, and nontarget stimuli are presented in Figures 9, 10, and 11, respectively. Grand mean ERPs for target, novel and nontarget stimuli for Sample 1 are presented in Figures 12, 13, and 14, respectively. The replication group (Sample 2), grand mean ERPs for target, novel and nontarget stimuli are presented in Figures 15, 16, and 17, respectively.

Figure 9. Grand mean ERPs (both samples) for target stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

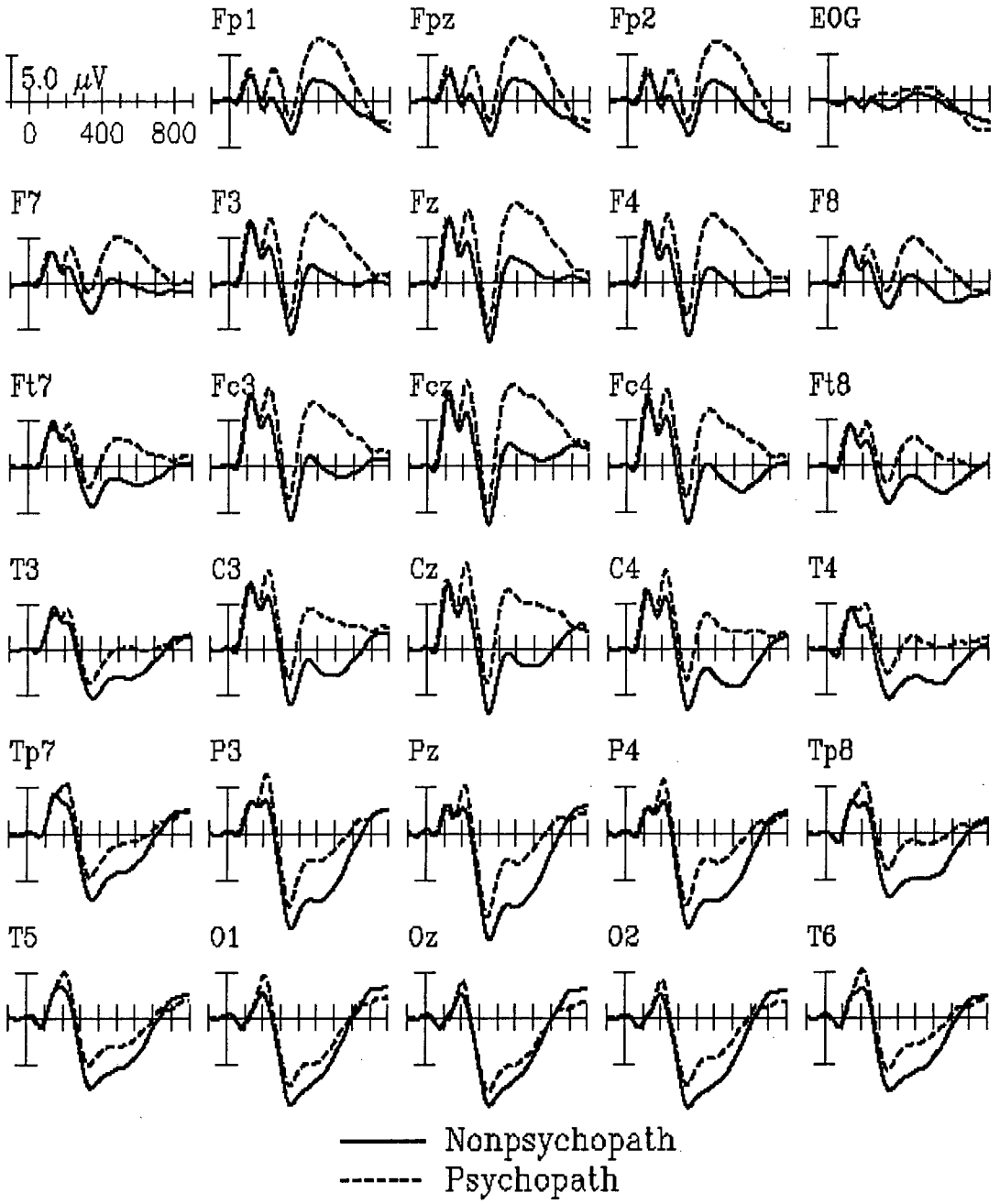


Figure 10. Grand mean ERPs (both samples) for novel stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

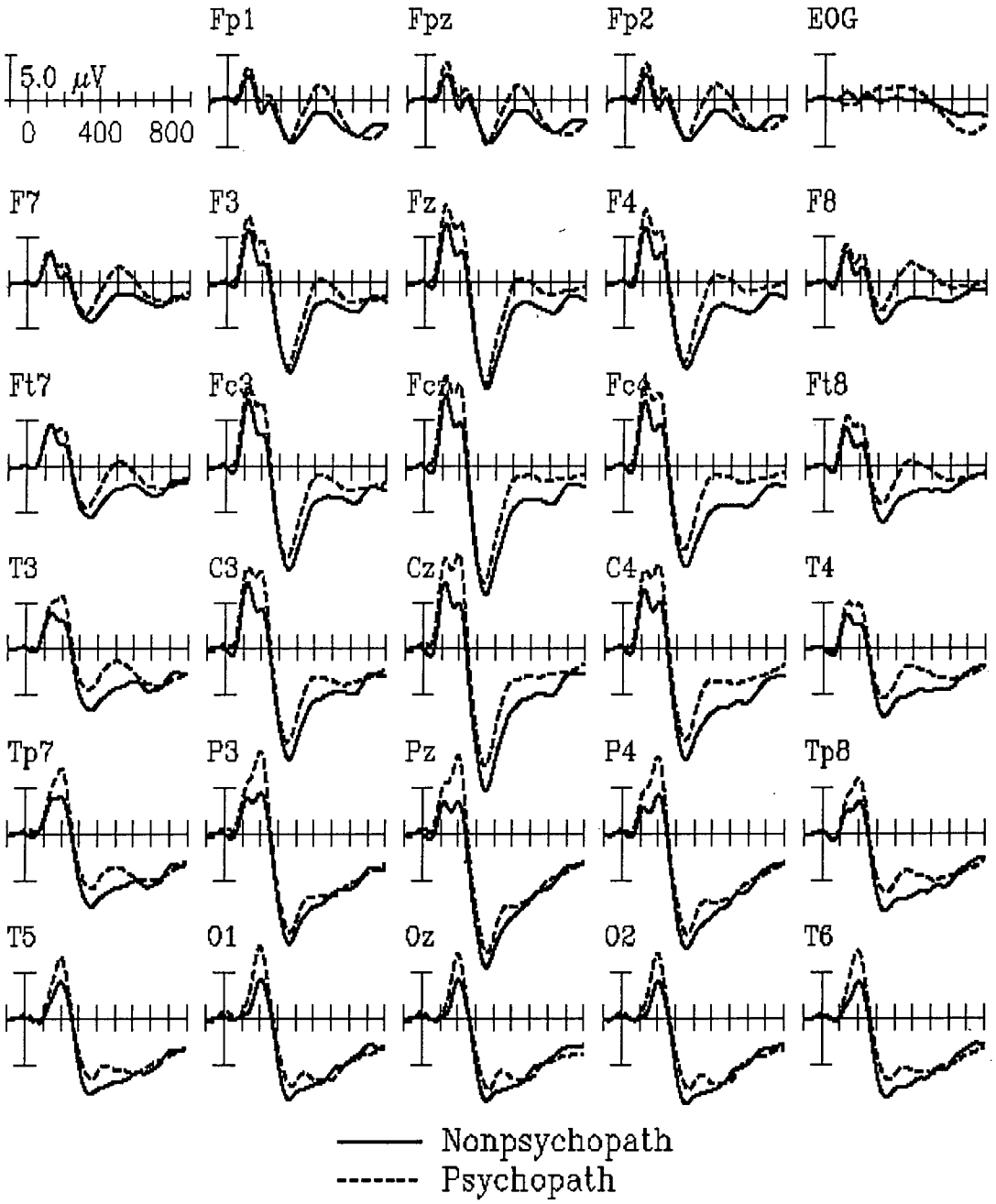


Figure 11. Grand mean ERPs (both samples) for nontarget stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

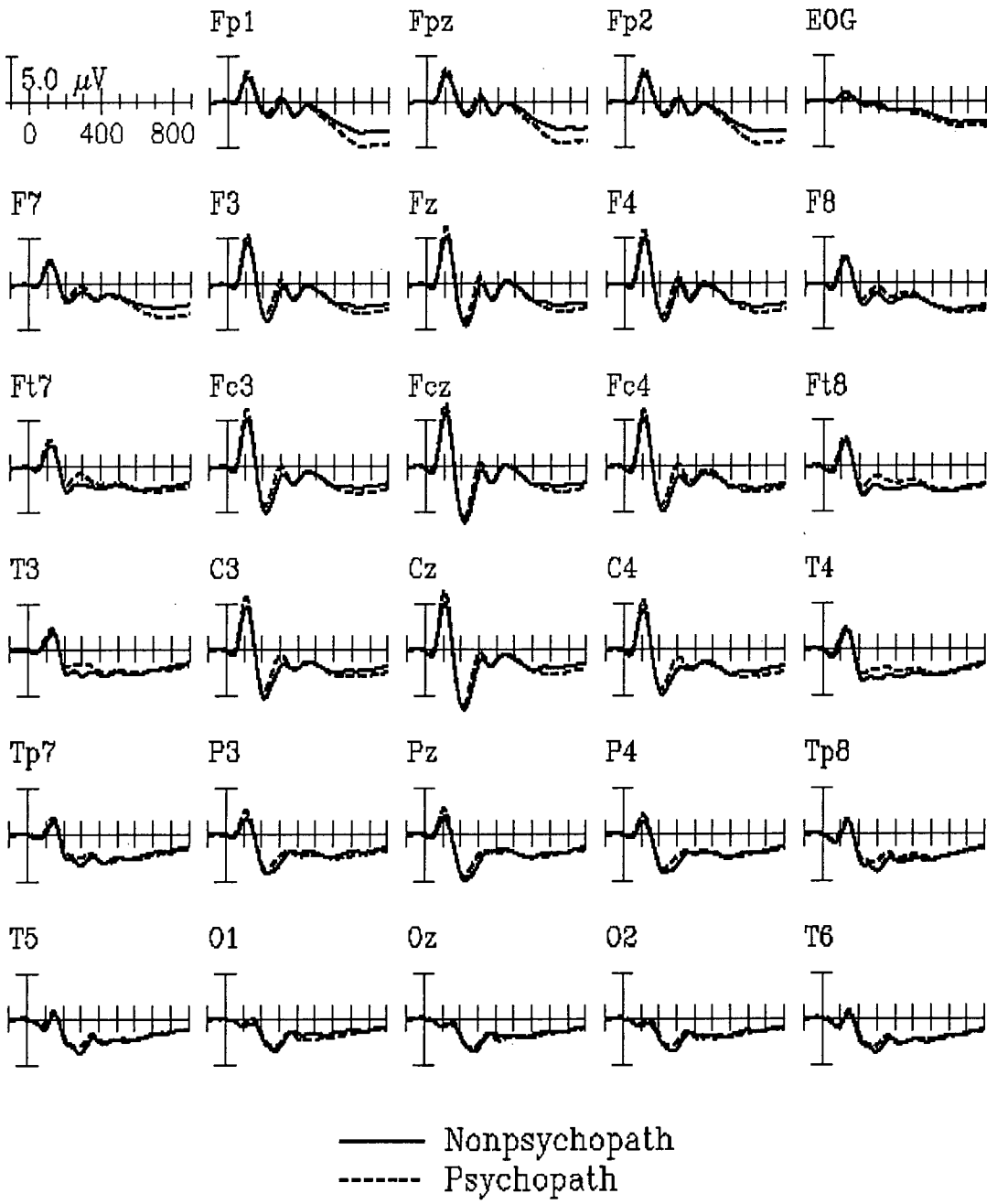


Figure 12. Grand mean ERPs (Sample 1) for target stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

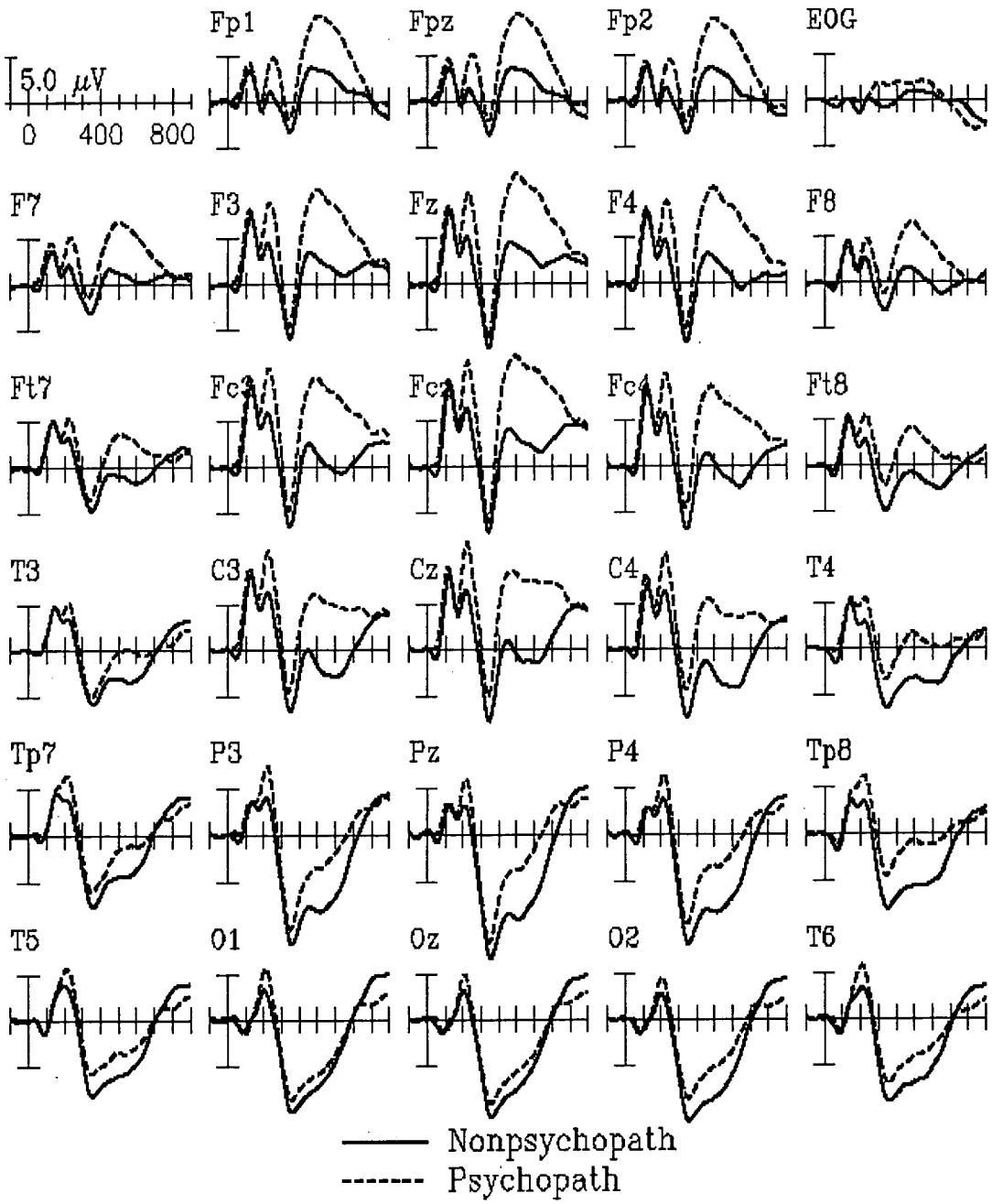


Figure 13. Grand mean ERPs (Sample 1) for novel stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

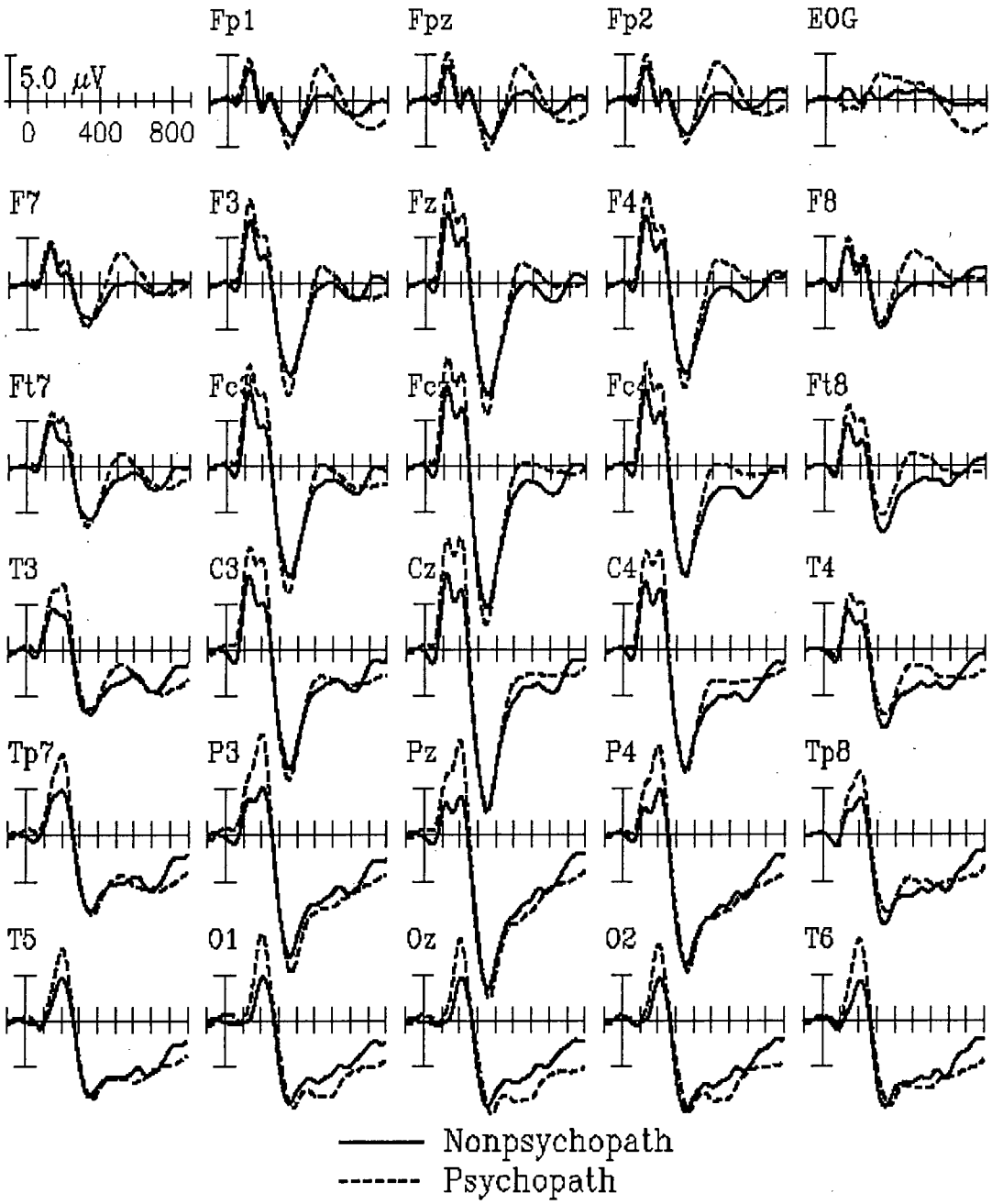


Figure 14. Grand mean ERPs (Sample 1) for nontarget stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

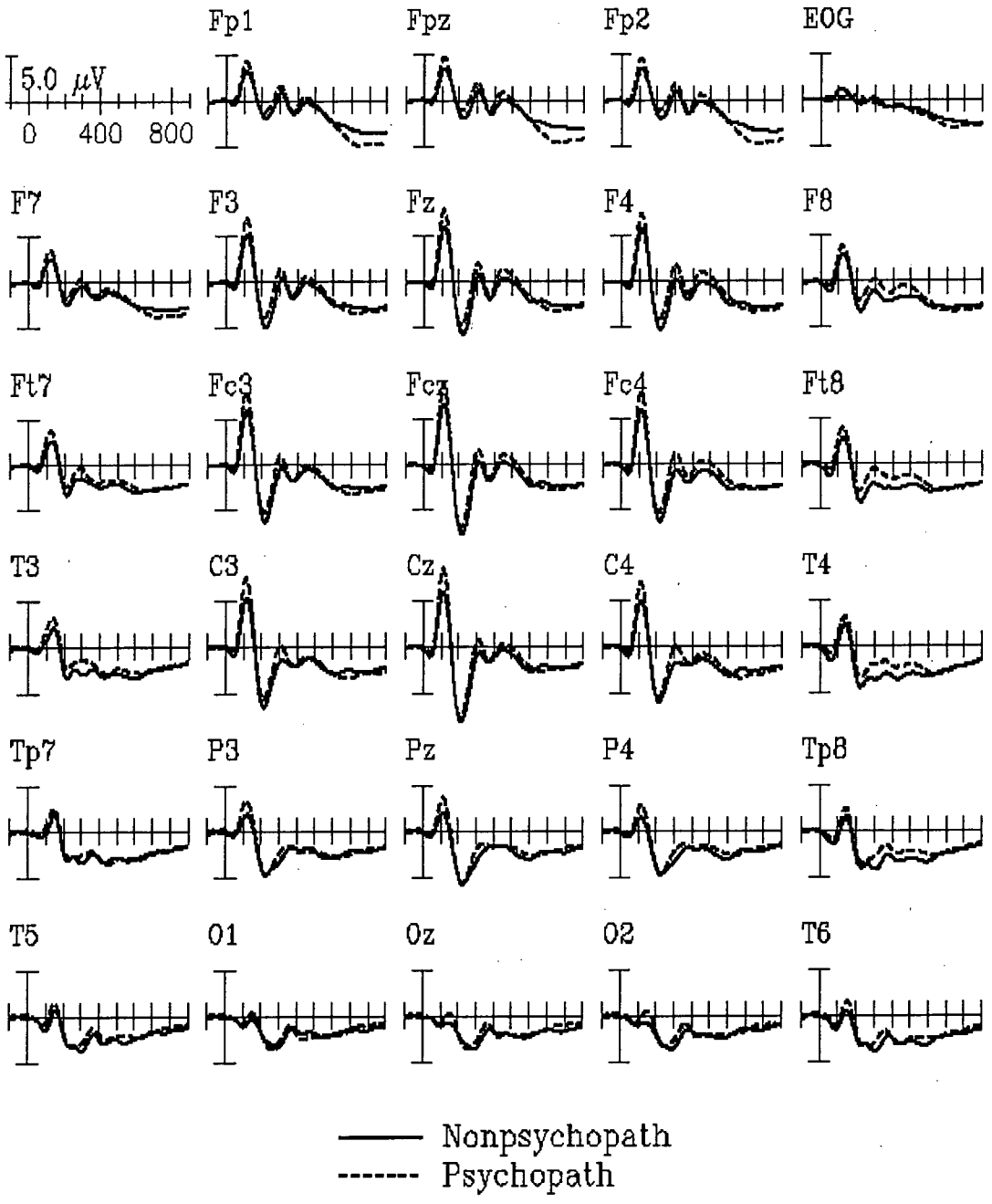


Figure 15. Grand mean ERPs (Sample 2) for target stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

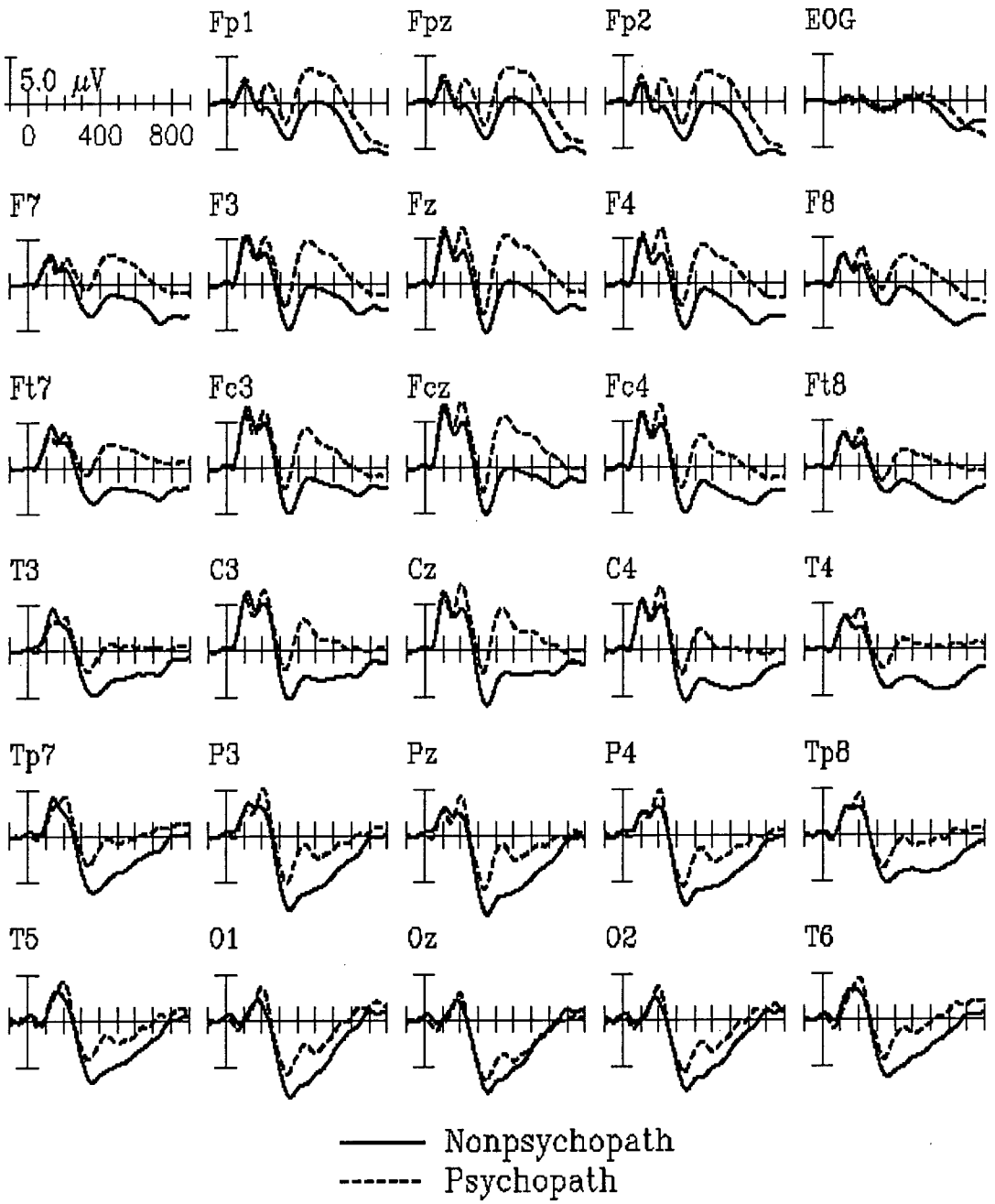


Figure 16. Grand mean ERPs (Sample 2) for novel stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

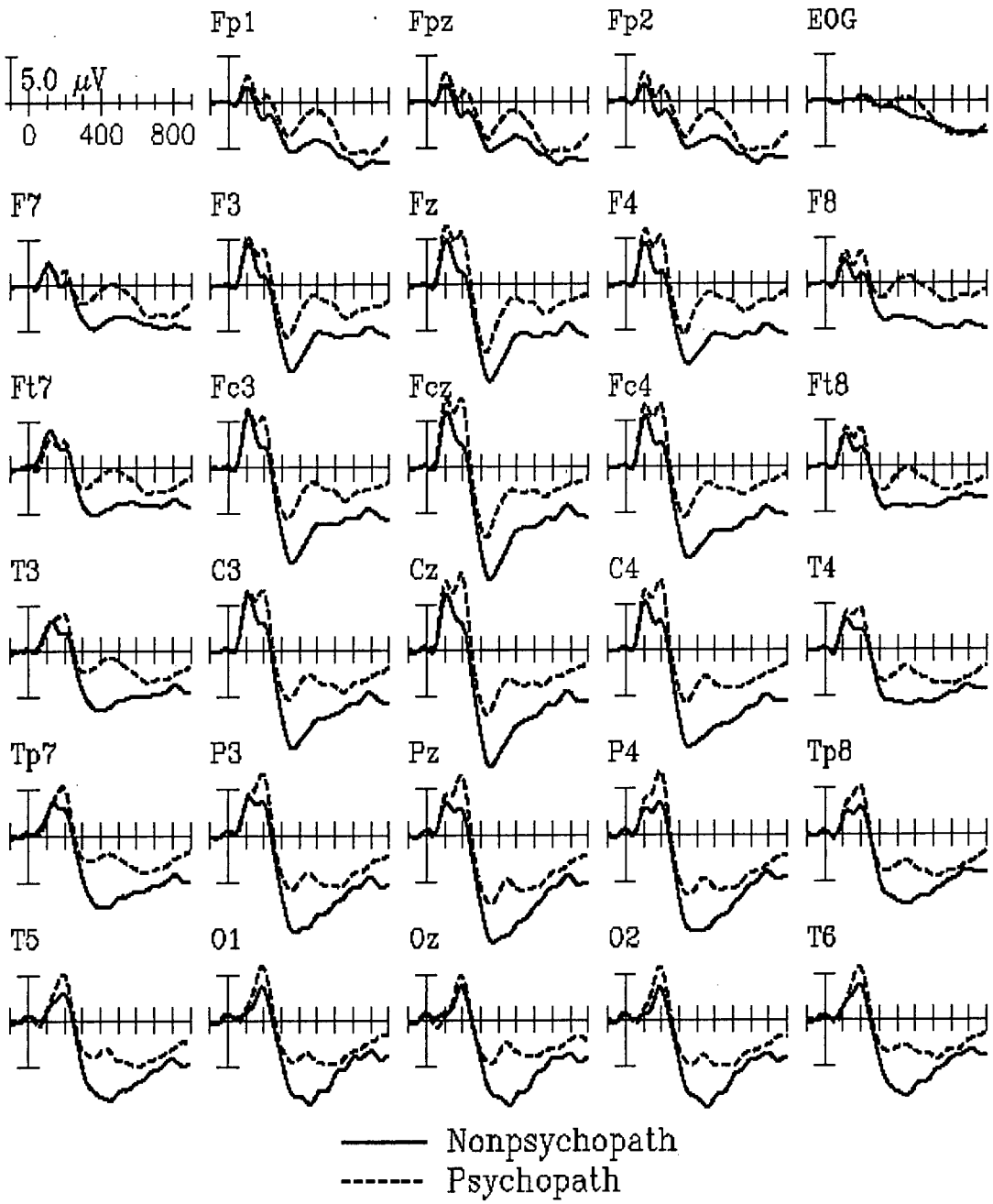
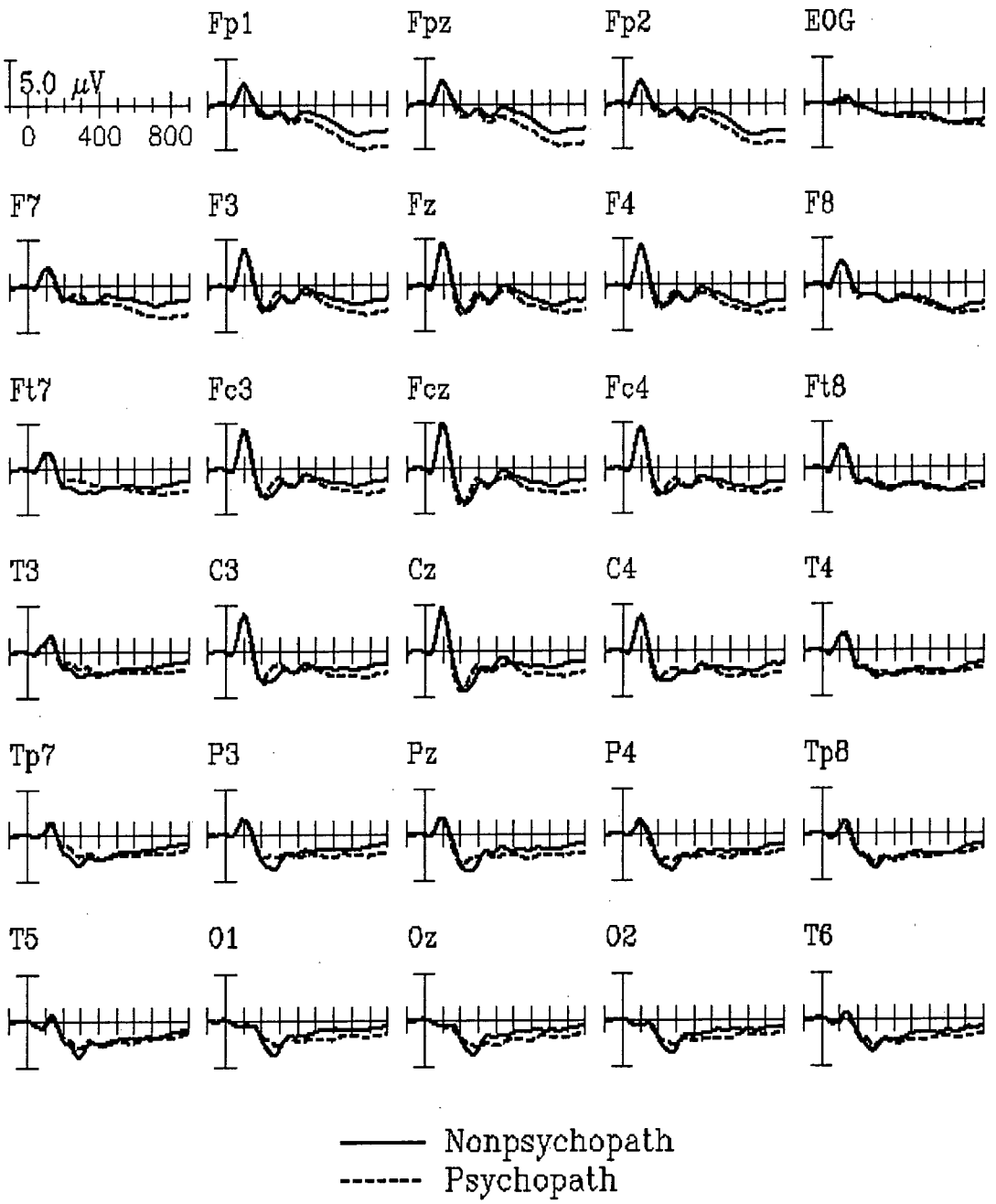


Figure 17. Grand mean ERPs (Sample 2) for nontarget stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.



N2 peak amplitude analyses.

5.5.1 Sample 1. The N2 peak amplitude for target stimuli was larger for Psychopaths than for Nonpsychopaths. This effect was greatest at fronto-central sites. The N2 elicited by novel stimuli was larger for Psychopaths than for Nonpsychopaths at centro-parietal sites [main effect of Group, midline, $F(1, 42) = 4.01$, $p < .05$; medial, $F(1, 42) = 4.57$, $p < .038$; lateral $F(1, 42) = 5.62$, $p < .022$; Group x Condition X Site trend, midline, $F(10, 420) = 2.28$, $p < .063$; medial $F(10, 420) = 2.13$, $p < .083$; Group x Condition trend, medial, $F(2, 84) = 2.4$, $p < .10$; Group x Condition x Site trend, lateral, $F(8, 336) = 2.188$, $p < .096$].

Across all participants the N2 was larger for target and novel stimuli than for nontarget stimuli [main effect of Condition, midline, $F(2, 84) = 65.33$, $p < .001$; medial, $F(2, 84) = 68.68$, $p < .001$; lateral, $F(2, 84) = 54.14$, $p < .001$]. For target stimuli, the N2 had a fronto-central distribution, asymetrically larger on the left hemisphere than the right hemisphere [Condition X Site interaction, midline, $F(10, 420) = 35.94$, $p < .001$, medial, $F(10, 420) = 33.01$, $p < .000$, lateral, $F(8, 336) = 12.74$, $p < .001$; Site x Hemisphere interaction, medial, $F(5, 210) = 6.26$, $p < .001$; Condition x Site x Hemi interaction, medial, $F(10, 420) = 4.08$, $p < .001$, lateral $F(8, 336) = 2.57$, $p < .039$; main effect of Site, midline, $F(5, 210) = 11.06$, $p < .001$, medial, $F(5, 210) = 10.91$, $p < .001$, lateral, $F(4, 168) = 7.45$, $p < .005$].

5.5.2 Sample 2. The N2 elicited by target and novel stimuli was larger for Psychopaths than for Nonpsychopaths at midline sites [Psychopathy x Condition interaction, $F(2, 60) = 3.40$, $p < .05$].

There were no significant group effects at medial or lateral sites and no group differences in the N2 elicited by nontarget stimuli.

As in the Sample 1 above, across all participants, the N2 was larger for target and novel stimuli than for nontarget stimuli [main effect of Condition, midline, $F(2, 60) = 52.62$, $p < .001$, medial, $F(2, 60) = 54.00$, $p < .001$, lateral, $F(2, 60) = 57.76$, $p < .001$]. The target N2 was maximal at fronto-central sites, while the novel N2 had a more posterior distribution [Condition x Site interaction, midline, $F(10, 300) = 29.85$, $p < .001$, medial, $F(10, 300) = 32.28$, $p < .001$, lateral, $F(8, 240) = 12.98$, $p < .001$; main effect of Site, midline, $F(5, 150) = 14.83$, $p < .001$, medial, $F(5, 150) = 18.00$, $p < .001$, lateral, $F(4, 120) = 11.11$, $p < .001$].

P3 peak amplitude analyses.

5.5.3 Sample 1. There were no overall group differences in the amplitude of the P3. At temporal sites the P3 was slightly larger on the left (Ft3, T3, T5) than the right hemisphere (Ft4, T4, T6) for Psychopaths, this effect was reversed for Nonpsychopaths [Group x Site x Hemisphere interaction, lateral, $F(4, 168) = 2.53$, $p < .04$; nonsignificant after application of the McCarthy and Wood (1985) correction].

Across all participants, the P3 was larger for target and novel stimuli than for nontarget stimuli [main effect of Condition, midline, $F(2, 84) = 58.85$, $p < .001$, medial, $F(2, 84) = 48.59$, $p < .001$, lateral, $F(2, 84) = 23.10$, $p < .001$]. The target P3 had a posterior distribution, while the P3 elicited by novel stimuli had a fronto-central distribution [Condition x Site interaction, midline, $F(10, 420) = 32.41$, $p < .001$, medial, $F(10, 420) = 23.61$, $p < .001$, lateral, $F(8, 336) = 11.29$, $p < .001$]. Interestingly, as Alexander et al., (1996)

observed, the target P3 in the present sample was slightly larger over the right hemisphere than the left hemisphere at fronto-central electrodes and this hemispheric asymmetry switched at parietal electrodes [Condition x Site x Hemisphere interaction, lateral, $F(8, 336) = 2.56$, $p < .029$; main effect of Site, midline, $F(5, 210) = 31.18$, $p < .001$, medial, $F(5, 210) = 28.51$, $p < .001$], lateral, $F(4, 168) = 39.70$, $p < .001$].

5.5.4 Sample 2. The P3 for target stimuli and novel stimuli was slightly smaller for Psychopaths than for Nonpsychopaths at medial sites. This latter effect was limited to the P3 for novel stimuli at lateral sites [Group x Condition interaction, midline, $F(2, 60) = 2.43$, $p < .10$, medial, $F(2, 60) = 3.08$, $p < .05$, lateral, $F(2, 60) = 4.23$, $p < .019$; main effect of Group, midline, $F(1, 30) = 3.26$, $p < .081$, medial, $F(1, 30) = 4.01$, $p < .05$, lateral, $F(1, 30) = 3.78$, $p < .061$]. We note however, that the Psychopaths' small P3 for target stimuli may have been due to the large fronto-central negativity in the 350-600 millisecond window (see below).

As in sample 1, the P3 was larger for target and novel stimuli than for nontarget stimuli [main effect of Condition, midline, $F(2, 60) = 33.23$, $p < .001$, medial, $F(2, 60) = 28.41$, $p < .001$, lateral, $F(2, 60) = 12.53$, $p < .001$]. The P3 for target stimuli was maximal at parietal sites, while the P3 to novel stimuli had a more fronto-central distribution [Condition x Site interaction, midline, $F(10, 300) = 20.56$, $p < .001$, medial, $F(10, 300) = 13.56$, $p < .001$,lateral, $F(8, 240) = 6.02$, $p < .002$; main effect of Site, midline, F 5(, 150) = 12.78, $p < .001$; medial, $F(5, 150) = 12.72$, $p < .001$, lateral, $F(4, 120) = 30.55$, $p < .001$]. There were no hemispheric asymmetries for the P3 in this sample.

N475 peak amplitude analyses.

5.5.5 Sample 1. As predicted, the N475 elicited by target stimuli was significantly larger for Psychopaths than for Nonpsychopaths [Group x Condition interaction, midline, $F(2, 84) = 3.44$, $p < .05$, medial, $F(2, 84) = 3.92$, $p < .038$, lateral, $F(4, 168) = 6.23$, $p < .008$; main effect of Group, midline, $F(1, 42) = 4.39$, $p < .042$, medial, $F(1, 42) = 4.57$, $p < .038$, lateral, F 1, 42) = 3.67, $p < .062$]. This effect was largest at fronto-central electrode sites [Group x Condition x Site interaction, midline, $F(10, 420) = 2.076$, $p < .025$, medial, $F(10, 420) = 2.02$, $p < .030$, lateral, $F(8, 336) = 2.32$, $p < .020$; Group x Site interaction, midline, $F(5, 210) = 5.57$, $p < .007$, medial, $F(5, 210) = 6.04$, $p < .006$]. At many sites, the N475 elicited by target stimuli was more than twice the amplitude in Psychopaths as it was in Nonpsychopaths.

Across participants, the N475 was larger for target stimuli than for novel or nontarget stimuli [main effect of Condition, midline, $F(2, 84) = 17.53$, $p < .001$, medial, $F(2, 84) = 13.33$, $p < .001$, lateral, $F(2, 84) = 7.85$, $p < .002$], this effect having a fronto-central distribution. [main effect of Site, midline, $F(5, 210) = 86.36$, $p < .001$, medial, $F(5, 210) = 94.91$, $p < .001$, $F(4, 168) = 105.23$, $p < .001$; Condition x Site interaction, midline, $F(10, 420) = 28.444$, $p < .001$, medial, $F(10, 420) = 25.68$, $p < .001$, lateral, $F(8, 336) = 28.393$, $p < .001$; Site x Hemisphere interaction, medial, $F(5, 210) = 3.78$, $p < .015$; Condition x Site x Hemisphere interaction, medial, $F(10, 420) = 2.74$, $p < .027$].

5.5.6 Sample 2. As in Sample 1, N475 elicited by target stimuli was significantly larger for Psychopaths than for Nonpsychopaths. This effect was greatest at fronto-central sites [Group

x Condition x Site interaction, midline, $F(10, 300) = 1.78$, $p < .06$; Group x Condition interaction, midline, $F(2, 60) = 7.23$, $p < .002$, medial, $F(2, 60) = 7.20$, $p < .002$, lateral, $F(2, 60) = 6.15$, $p < .004$; main effect of Group, midline, $F(1, 30) = 6.29$, $p < .018$, medial, $F(1, 30) = 6.95$, $p < .013$, $F(1, 30) = 8.52$, $p < .007$].

Across all participants, the N475 was larger for target than for novel or nontarget stimuli, an effect greatest at fronto-central electrodes [Condition x Site interaction, midline, $F(10, 300) = 12.70$, $p < .001$, medial, $F(10, 300) = 13.36$, $p < .001$, lateral, $F(8, 240) = 10.95$, $p < .001$; main effect of Condition, midline, $F(2, 60) = 18.38$, $p < .001$, medial, $F(2, 60) = 15.25$, $p < .001$, lateral, $F(2, 60) = 7.16$, $p < .001$; main effect of Site, midline, $F(5, 150) = 19.84$, $p < .001$, medial, $F(5, 150) = 17.36$, $p < .001$, lateral, $F(4, 120) = 27.17$, $p < .001$].

5.6 Correlation analyses. Correlations between PCL-R total scores and the amplitude of the N2, P3, and N475 ERP components are presented in Table 10. These analyses revealed that psychopathy scores were negatively related to the N2 for target and novel stimuli at centro-parietal electrodes. There were no significant correlations between psychopathy scores and the peak amplitude of the P3 for target or novel stimuli. Using mean amplitude measurements of the P3 (to control for latency jitter) we observed that there were significant correlations between psychopathy scores and the target P3 at frontal sites. There was a strong negative relationship between psychopathy scores and the peak amplitude of the N475. Consistent with the ANOVA results, these correlations were strongest at fronto-central sites.

Table 10. Correlations between psychopathy PCL-R total scores and the amplitude of the N2, P3, and N475 ERP components for target and novel stimuli. Correlations are based upon the entire sample of participants (n=76). Note: p.a. = peak amplitude; m.a. = mean amplitude; ***p < .01; **p < .05; *p < .10

Electrode Site	N2 p.a. target	N2 p.a. novel	P3 p.a. target	P3 p.a. novel	P3 m.a. target	P3 m.a. novel	N475 p.a. target	N475 p.a. novel
FP1	-.229**	-.102	-.068	-.025	-.143	-.006	-.223**	-.142
FPZ	-.226**	-.102	-.070	.020	-.150*	.013	-.257**	-.122
FP2	-.202*	-.093	-.077	.003	-.161*	-.001	-.250**	-.106
F7	-.199*	-.139	-.137	-.090	-.199**	-.066	-.237**	-.141
F3	-.192*	-.188*	-.047	-.011	-.137	-.035	-.272***	-.139
FZ	-.193*	-.207*	-.028	.008	-.125	-.030	-.296***	-.158*
F4	-.184	-.181	-.058	-.018	-.161*	-.058	-.310***	-.193**
F8	-.156	-.121	-.170*	-.120	-.227**	-.139	-.273***	-.226**
FT7	-.136	-.125	-.095	-.093	-.162*	-.068	-.212**	-.102
FC3	-.184	-.212*	-.069	-.037	-.149*	-.061	-.270***	-.153*
FCZ	-.184	-.228**	-.048	-.013	-.144*	-.052	-.291***	-.189**
FC4	-.177	-.214*	-.110	-.056	-.191**	-.089	-.320***	-.219**
FT8	-.152	-.189*	-.155*	-.140	-.174*	-.121	-.232**	-.197*
T3	-.103	-.208*	-.079	-.128	-.109	-.130	-.169*	-.112
C3	-.168	-.250**	-.105	-.078	-.174*	-.097	-.249**	-.135
CZ	-.209*	-.286**	-.097	-.067	-.177*	-.096	-.270***	-.202**
C4	-.185*	-.237**	-.138	-.057	-.187**	-.079	-.293***	-.196**
T4	-.212*	-.151	-.176*	-.102	-.178*	-.044	-.263**	-.150*
TP7	-.189*	-.233**	-.116	-.105	-.146*	-.105	-.154*	-.096
CPZ	-.213*	-.301***	-.103	-.039	-.158*	-.070	-.239**	-.120
TP8	-.241**	-.201*	-.182*	-.049	-.177*	-.019	-.262***	-.103
P3	-.238**	-.280**	-.116	-.021	-.152*	-.053	-.205**	-.023
PZ	-.229**	-.315***	-.091	-.011	-.128	-.044	-.200**	-.051
P4	-.229**	-.282**	-.125	-.003	-.144*	-.031	-.215**	-.061
T5	-.224**	-.206*	-.138	-.045	-.149*	-.039	-.165*	-.082
T6	-.222**	-.276**	-.129	-.024	-.130	-.033	-.166*	-.036
O1	-.243**	-.285**	-.122	-.013	-.134	-.037	-.114	-.018
OZ	-.188*	-.219*	-.060	.026	-.077	-.008	-.026	-.062
O2	-.236**	-.272**	-.136	.004	-.137	-.017	-.156*	-.027

5.7 Summary and Discussion for Experiment 4

This experiment was designed to examine the modality specificity of the late fronto-central negative waves that have been observed in the event-related potentials of psychopaths for tasks that employ visual stimuli (Kiehl et al., 1999a; Williamson et al., 1991). Consistent with these studies, a large fronto-central negativity (N475) was observed in the psychopaths' ERPs to task relevant stimuli. This effect was robust in both samples of psychopaths. There was some evidence of a smaller P3 to target and novel stimuli for psychopaths compared to nonpsychopaths; however, this reduction in P3 amplitude may have been due to the overlapping N475 in the psychopaths' waveforms. We also observed that the N2 for both target and novel stimuli was larger for psychopaths than for nonpsychopaths. In general, there appeared to be a negative shift in the psychopaths' ERPs to target stimuli that began as early as 100 milliseconds and proceeded until about 800 milliseconds post-stimulus.

The finding that the P3 was not reliably reduced is somewhat at odds with the findings from Experiment 3, in which we observed that the P3 to visual oddball stimuli was reduced in psychopaths relative to nonpsychopaths. However, as noted in Experiment 3, the small P3 of the psychopaths to target stimuli may have been due to the large overlapping fronto-central negativity (N550). However, in the present study the mean amplitude of the P3 to target stimuli was negatively correlated with PCL-R scores at frontal sites.

Studies have now shown that large fronto-central negativities are present in psychopaths' ERPs to visual word stimuli, visual oddball stimuli, visual target stimuli in a Go/No go task, and auditory oddball stimuli. Given the ubiquity in which these odd waveforms seem to be found, what might be their functional significance?

Although the tasks in which fronto-central ERP negativities have been observed for psychopaths are quite different, they do due share a number of methodological similarities. First, each of the tasks required a speeded behavioral response raising the possibility that the some of the observed effects may be due to processes related to motor preparation and execution. To explore this possibility, we investigated the response-locked potentials for target stimuli in the present study. There were no group differences in these potentials, nor was there any evidence of any fronto-central ERP negativities.

Additionally, research from our laboratory has shown that these fronto-central negativities are present in psychopaths' ERPs for task relevant stimuli that do not require a manual response. In two studies, one employing visual stimuli and one employing auditory stimuli, we have observed that fronto-central ERP negativities are observed when psychopaths are required to silently count, rather than manually respond, to low probability target stimuli (Kiehl, 1999). Thus, on balance, these data suggest that the observed fronto-central ERP negativities do not appear to be due to processes related to motor control.

Another similarity common to each of the aforementioned tasks is that they required processes required to attentional control. As we discussed in the summary for Experiment 3, there is growing evidence for abnormalities in attentional processes in psychopathy. However, the N2 potential has also been associated with attentional processes and this component was larger for psychopaths than for nonpsychopaths. This latter effect suggests greater allocation of attentional processes for processing target stimuli for psychopaths than for nonpsychopaths. Some have argued that psychopaths tend to 'overfocus' on stimuli of immediate relevance, ignoring otherwise potentially important cues (Jutai, 1989; Jutai & Hare, 1983). In the present study, such an 'overfocusing' should have led to behavioral differences

between groups. If psychopaths were processing the stimuli faster than were nonpsychopaths because of this greater allocation of attentional resources, then we should have observed superior response speeds for psychopaths than for nonpsychopaths for processing target stimuli. No such effect was observed. We note however, that the absence of group differences in performance in the present study may have been due to ceiling effects. Additionally, if psychopaths were 'overfocusing' on the task relevant stimuli, we might also have observed a greater number of false alarms to nontarget and/or novel stimuli for psychopaths compared to nonpsychopaths. Again, no such effects were observed.

Thus, we are still left with no definitive explanation for the presence of these fronto-central negativities in the psychopaths' ERPs to task relevant stimuli. In Experiments 1 and 2, functional abnormalities were observed in psychopaths in frontal, temporal, and limbic structures. This raises the possibility that the fronto-central ERP negativities in psychopaths may be related to abnormalities in frontal, temporal or limbic structures. Evidence from studies of the intracranial electrode recordings (Halgren, 1980; Halgren et al., 1995a; 1995b; Halgren, Marinkovic, & Chauvel, 1998), event-related fMRI studies of healthy participants (Kiehl, Laurens, Duty, Forster, & Liddle, 1998a; McCarthy, Luby, Gore, & Goldman-Rakic, 1997; Menon, Ford, Lim, Glover, & Pfefferbaum, 1997; Opitz, Mecklinger, Von Cramon, & Kruggel, 1999) and psychopathological populations (Kiehl & Liddle, 1999), and from patients with brain damage (Knight, 1984; 1996; Knight, Grabowecky, & Scabini, 1995; Knight & Nakada, 1998; Knight, Scabini, Woods, & Clayworth, 1989) indicate that frontal, temporal, and limbic structures are implicated in auditory and visual oddball tasks. Thus, an examination of auditory and visual ERP studies of patients with damage to frontal, temporal and/or limbic structures may reveal similar late fronto-central ERP negativities. This search

revealed that fronto-central ERP negativities to oddball stimuli have been found in patients who have undergone anterior temporal lobe resection for treatment of intractable epilepsy (Johnson, 1988; 1989; Johnson & Fedio, 1987; Rugg, Pickles, Potter, & Roberts, 1991; Scheffers, Johnson, & Ruchkin, 1991). Additionally, fronto-central ERP negativities to target stimuli are observed for patients with temporal lobe damage due to cerebral infarction (Yamaguchi & Knight, 1993; 1995). Paller and colleagues have shown that fronto-central ERP negativities are elicited by target stimuli in monkeys with induced temporal lobe lesions (Paller, Zola-Morgan, Squire, & Hillyard, 1988). To our knowledge, fronto-central ERP negativities to oddball stimuli have not been observed in frontal or parietal lobe damaged patients (Yamaguchi & Knight, 1993; 1995). These data suggest that the most plausible interpretation of the fronto-central ERP negativities for psychopaths is that they are related to the presence of temporal lobe abnormalities. This latter interpretation is supported by the fact that the N2 component elicited by target stimuli is larger for patients with temporal lobe damage than for control participants (Johnson, 1989; Yamaguchi & Knight, 1993). Moreover, the P3 component in these latter patients appears to be only slightly abnormal at frontal sites. Thus, the similarities between psychopaths and patients with temporal lobe damage are present for the N2, P3 and N475 components of the ERP elicited by target stimuli. Additional similarities between psychopaths and patients with temporal lobe abnormalities are discussed in the General Discussion.

If the fronto-central ERPs in psychopaths are related to abnormal function of the temporal lobe and removal of the temporal lobe also causes these potentials, then where might these potentials be generated? Studies of the intracranial sources of the P3 suggest that the polarity inversions (e.g., electrical negativities in the 300-600 millisecond post-stimulus time

window) are found in the amygdala, anterior cingulate cortex, and inferior lateral frontal cortex (Halgren, 1999; Halgren et al., 1995a; 1995b). Given that fronto-central ERP negativities are present for patients in which the amygdali are removed, this suggests that the most likely candidate for the neural generator(s) of the fronto-central negativities is the anterior cingulate and/or inferior lateral frontal cortex. Consistent with this notion, preliminary source localization analyses, performed with Brain Electrical Source Analyses (BESA) software, have revealed that a single dipole in the anterior cingulate appears to be a plausible solution to the inverse problem for the psychopaths' N475. Using a two-dipole model, we have observed that the best solution for the additional dipole is in the right inferior lateral frontal cortex. It is important to note that these latter analyses were preliminary and that some have argued that source modeling of ERP components later than 300 ms may be an ill-posed question given the number of possible generators and the mathematical uncertainty of determining a unique solution to account for all these putative sources (Halgren et al., 1998).

The interpretation that psychopathy is associated with aberrant activity in the anterior cingulate is consistent with a number of other lines of research. In Experiment 2 we observed that compared with control participants, psychopaths failed to show greater neural activation for affective stimuli than for neutral stimuli in the anterior cingulate. Additionally, we have observed that psychopathy is associated with a reduced error-related negativity (ERN) for error trials during a Go/No go task (Gehring, 1993; Gehring, Coles, Meyer, & Donchin, 1990; Gehring, Goss, Coles, & Meyer, 1993). The ERN is believed to be generated in the anterior cingulate (Kiehl, Liddle, & Hopfinger, in press; Scheffers, Coles, Bernstein, & Gehring, 1996; Tucker, 1998). Thus, the small ERN for psychopaths is consistent with the hypothesis that psychopathy is associated with anterior cingulate abnormalities.

In summary, the N2, P3, and N475 components of the ERP were different for psychopaths than for nonpsychopaths for auditory target stimuli. The enlarged N2 and N475 and reduced frontal P3 in psychopaths are similar to ERP abnormalities found in patients with temporal lobe damage. This suggests that the most plausible interpretation for the presence of the late fronto-central ERP negativities in psychopaths is that they are an electrophysiological signature of anterior temporal lobe abnormalities.

6.0 Experiment 5

Methods

6.1 Participants. The participants were 50 male inmates from a federal maximum-security prison facility near Vancouver, British Columbia. Volunteers were selected for the study if they were between 18 and 55 years of age, were free from any reported serious head injury or neurological impairment and had no DSM-IV Axis I diagnosis (American Psychiatric Association, 1994). Forty-eight inmates were right hand dominant and two were left hand dominate (Annett, 1970). Volunteers participated in two sessions: a videotaped semi-structured interview and the experimental recording session. Information from the interview and an extensive review of institutional files were used complete the PCL-R on each inmate. Each of the 20 items on the PCL-R is scored on a 3-point scale (0-2) according to the extent to which it applies to the inmate.

Inmates with a PCL-R score of 30 or above (n = 25) were defined as Psychopaths (mean = 33.5, SD = 2.), and those with a PCL-R score below 30 (n = 25) were defined as Nonpsychopaths (mean = 20.1, SD = 6.6). The mean age and years of formal education were 32.5 and 32.1, and 10.1 and 10.9 years for Psychopaths and Nonpsychopaths, respectively. The NART and Quick IQ measures were 107.8 (SD 10.0) and 102.7 (SD 12.6), and 106.8 (11.4) and 103.3 (11.76) for Psychopaths and Nonpsychopaths, respectively. There were no differences between the Psychopaths and Nonpsychopaths on any of these measures (p's > .50).

We paid each inmate $5.00 for the PCL-R interview and $10.00 for the experiment. The total of $15.00 was equivalent to 2 days prison wage. The study was conducted in accordance with Institutional and University ethical standards.

6.2 Stimuli. One hundred sentences (eight to ten words in length) were presented one word at a time (500 ms stimulus duration and ISI) on a computer monitor. Equal proportions of the sentences ended with a word that was either semantically congruent (e.g.. The man went to the store to buy a loaf of bread.) or semantically incongruent (e.g., The man went to the store to buy a loaf of milk.) with the previous sentence context. The sentences were the same as those used by Niznikiewicz et al. (1997). The order of sentence presentation was random. Letter stimuli were approximately 2 x 1 visual degrees. All stimuli were presented white on black background in a continuously displayed rectangular box. A prompt (asterisk) was presented 1000 ms after the offset of the last word to indicate that the participant should make the sense/no sense discrimination. The hand used to make judgment was counterbalanced across participants. ERPs were analyzed only for correctly classified terminal words. As an additional measure to attempt to further reduce the possibility that motor responses might confound the results, accuracy was stressed and response time was de-emphasized.

6.3 Event-related Potential Recording Scalp potentials were recorded from tin electrodes (ElectroCap International) placed over 29 electrode sites according to standard placement guidelines of the International 10-20 System (see Figure 1). Vertical and horizontal electroocularogram (EOG) were monitored from a bipolar electrode pair located on the

lateral and supra orbital ridges of the right eye. All EEG electrodes were referenced to the nose. Two additional channels, left and right mastoids were recorded. Electrical impedances were maintained below 5 kohms throughout the experiment. The EEG channels (SA instruments) were amplified (20,000 gain) with a bandpass of .01 to 100 Hz, digitized on-line at a rate of 256 samples per second, and recorded on computer hard disk. The length of the recording epoch was 1200 ms with a 100 ms pre-stimulus baseline. Single-trials with voltages greater than (+ or -) 75 microvolts at any electrode site or EOG artifact were excluded. Four participants (three nonpsychopaths and one psychopath) were excluded because of excessive artifacts (greater than 40% of trials). After exclusion of these participants, there were no significant group differences in the number of trials averaged in any condition. The ERPs were digitally filtered with a zero-phase shift 30 Hz low pass filter to reduce electromyographic contamination and ambient electrical noise.

The analyses proceeded in two stages. Two components were analyzed, the N400 and P600. The N400 is typically measured as the peak amplitude in the 300-500 ms post-stimulus time window in the difference wave of incongruent minus congruent stimuli. However, several studies of the N400 in psychopathological populations have shown that relying solely on the difference wave measurements can lead to misleading results. For example, in the literature on the N400 and schizophrenia for example, early studies reported that the N400 (measure in difference waves) was smaller for schizophrenic patients than for controls (Adams et al., 1993; Grillon, Ameli, & Glazer, 1991). However, subsequent research has shown that the N400 is larger for schizophrenic patients than for control participants for both congruent and incongruent sentence

endings (Nestor et al., 1997; Niznikiewicz et al., 1997). This indicates that the baseline measurement is important for determining group differences. For these reasons, separate analyses were performed on both the peak amplitude of the N400 and P600 measured in the difference wave and from incongruent and congruent conditions.

In the first set of ANOVAs, the N400 and P600 were measured in the difference wave only. In the second set of ANOVAs, the N400 and P600 were measured for both congruent and incongruent sentence endings. The N400 and P600 were quantified as the peak amplitude (relative to the 100 ms prestimulus baseline) in the 300-500 ms and 500-800 millisecond time windows, respectively. These windows were centered upon the peak latency of each of the components in the grand average waveforms. Separate ANOVAs were performed on midline, medial and lateral sites. The first set of ANOVAs included factors of Group [Psychopath and Nonpsychopath], and Site [frontal (F7, F3, Fz, F4, F8), fronto-central (Fc7, Fc3, Fcz, Fc4, Fc8), central (T3, C3, Cz, C4, T4), temporo-parietal (Tp7, P3, Pz, P4, Tp8), and temporo-occipital (T5, O1, Oz, O2, T6)]. For medial and lateral ANOVAs there was an additional factor of Hemisphere [right and left]. Midline (Fpz) and medial (Fp1, Fp2) ANOVAs also included an additional level of Site [prefrontal]. For the second set of ANOVAs there was an additional factor of Condition [Incongruent and Congruent]. The Geisser-Greenhouse correction was used for any repeated measures containing more than one degree of freedom in the numerator (Geisser & Greenhouse, 1958). Following the ANOVA, planned comparisons were performed on the predicted effects. Type I error rate was maintained below .05 by using the Dunn-Bonferroni correction. Other effects of interest were tested using simple effects analyses or Tukey's multiple comparisons.

Results

6.4 Behavioral data. Across all participants performance was more accurate for classifying congruent words than for classifying incongruent words [main effect of Condition, $F(1, 44) = 5.41$, $p < .025$]. There were no significant group differences in the number of errors committed [Psychopaths, congruent stimuli, 2.45 (SD 2.79); incongruent stimuli, 3.86 (SD = 4.25); Nonpsychopaths, congruent stimuli, 1.58 (SD 1.24); incongruent stimuli, 2.91 (SD 2.73)].

6.5 Event-related potentials. Grand mean group ERPs for congruent terminal words, incongruent terminal words and for the incongruent-congruent difference waves are presented in Figures 18, 19, and 20, respectively.

N400 peak amplitude analyses.

6.5 1. Difference wave analyses. There were no significant group differences in the amplitude of the N400 at midline, medial or lateral sites. Across all participants, the N400 was largest at centro-parieto-temporal sites [main effect of Site, midline, $F(5, 220) = 11.31$, $p < .001$, medial, $F(5, 220) = 11.02$, $p < .001$]. Consistent with previous research, this effect was slightly larger over the right than the left hemisphere [Site x Hemisphere interaction, lateral, $F(5, 220) = 3.13$, $p < .017$; main effect of Hemisphere, lateral, $F(1, 44) = 4.80$, $p < .034$].

Figure 18. Grand mean ERPs for congruent terminal words of sentences for psychopaths (dashed) and for nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

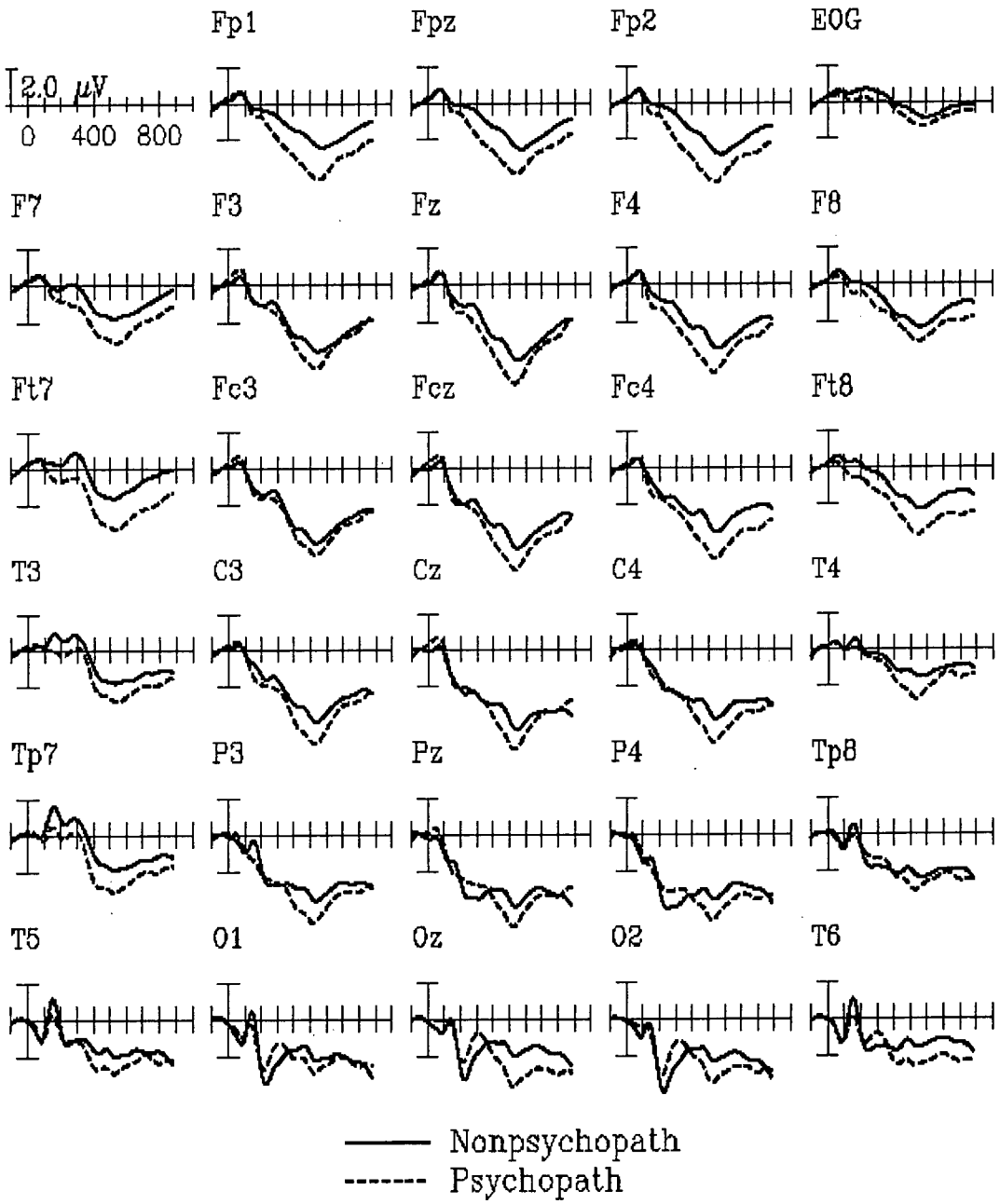


Figure 19. Grand mean ERPs for incongruent terminal words of sentences for psychopaths (dashed) and for nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

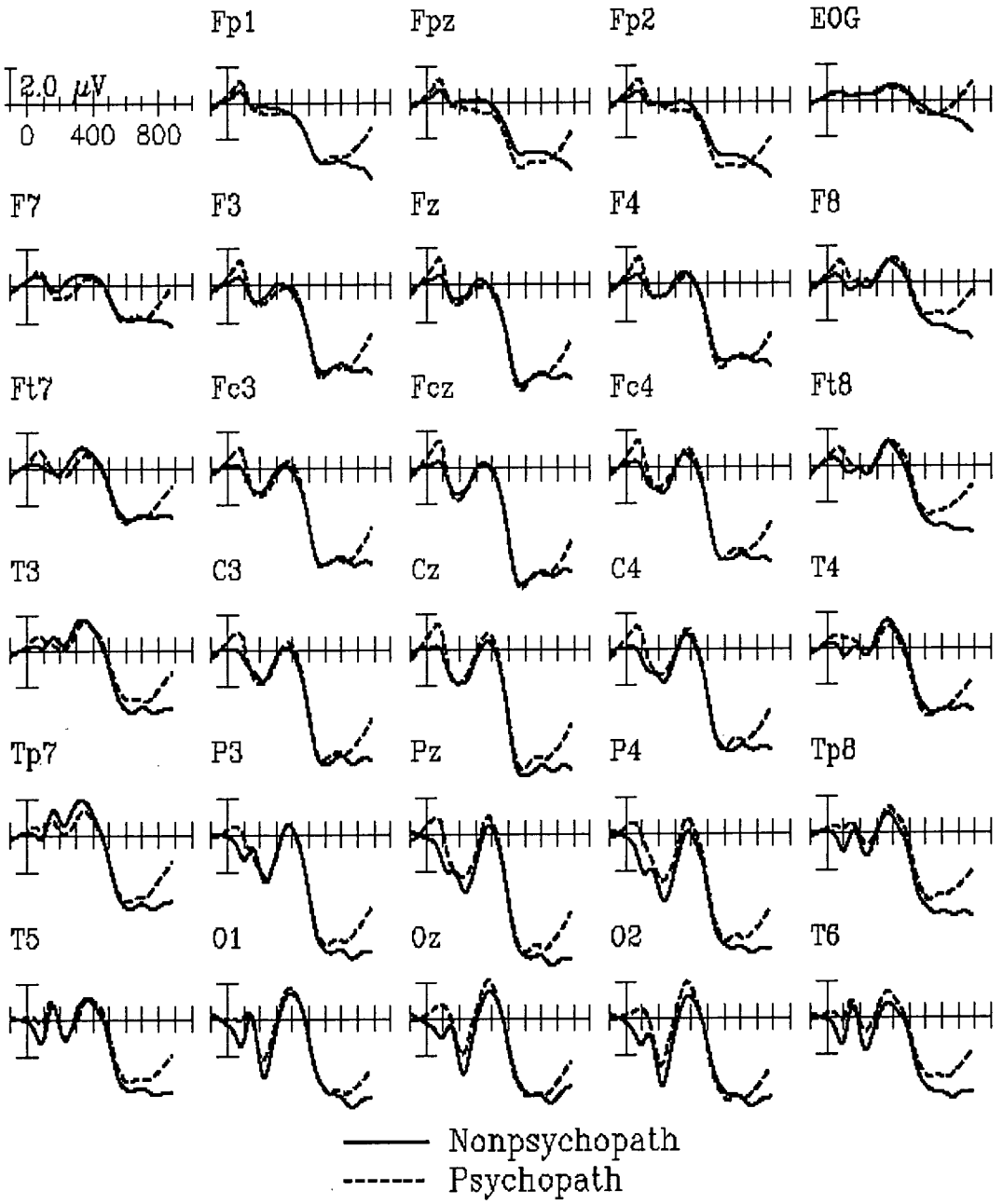
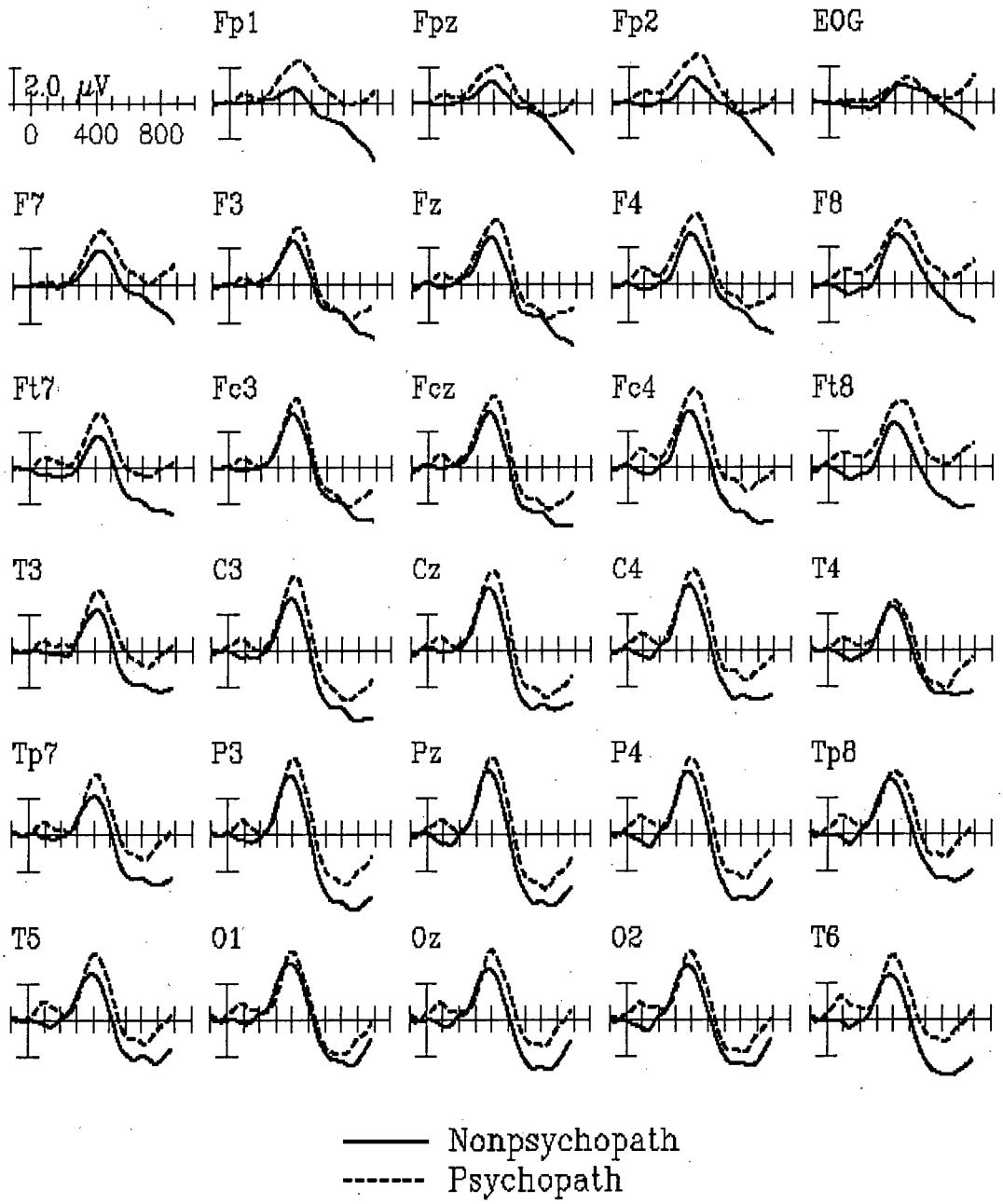


Figure 20. Grand mean ERP difference waves for incongruent minus congruent terminal words of sentences for psychopaths (dashed) and for nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.



6.5.2 Two condition analyses. As in the difference wave analyses, there were no significant group differences in the N400 elicited by congruent or incongruent terminal words. Across all participants, N400 was larger for incongruent than for congruent sentence endings [main effect of condition, midline, $F(1, 44) = 18.62$, $p < .001$, medial, $F(1, 44) = 18.68$, $p < .001$, lateral, $F(1, 44) = 10.82$, $p < .002$] this effect was largest at centro-temporo-parietal sites [Condition x Site interaction, midline, $F(5, 220) = 7.56$, $p < .001$, medial, $F(5, 220) = 7.14$, $p < .001$]. The N400 for incongruent stimuli was slightly larger over left hemisphere temporo-parietal and occipital sites than the analogous right hemisphere sites [Condition x Site x Hemisphere, medial, $F(5, 220) = 3.08$, $p < .018$, Condition x Site x Hemisphere interaction, lateral, $F(4, 176) = 2.73$, $p < .049$; Condition x Hemisphere interaction, medial, $F(1, 44) = 7.53$, $p < .009$, lateral, $F(1, 44) = 8.99$, $p < .004$; Site x Hemisphere interaction, medial, $F(5, 220) = 4.68$, $p < .029$, lateral, $F(4, 176) = 4.31$, $p < .010$; Main effect of Site, midline, $F(5, 220) = 6.04$, $p < .001$, medial, $F(5, 220) = 5.49$, $p < .011$]. There we no hemispheric asymmetries for the N400 elicited by congruent terminal words.

P600 peak amplitude analyses

6.5 3 Difference wave analyses. There were no significant group differences in the amplitude of the P600. The P600 difference wave was largest centro-parietal sites [main effect of Site, midline, $F(5, 220) = 11.45$, $p < .001$, medial, $F(5, 220) = 10.18$, $p < .001$, lateral, $F(4, 176) = 15.61$, $p < .001$], an effect slightly larger on the right than the left hemisphere [Site x Hemisphere interaction, medial, $F(5, 220) = 3.02$, $p < .019$; Site x Hemisphere, lateral, $F(4, 176) = 2.97$, $p < .033$].

6.5.4 Two condition analyses. As in the difference wave analyses, there were no significant group differences in the amplitude of the P600. Across all participants, the P600 was larger for incongruent stimuli than for congruent stimuli [main effect of condition, midline, $F(1, 44) = 9.42$, $p < .004$, medial, $F(1, 44) = 6.48$, $p < .01$]. This latter effect was stongest at centro-parietal sites [Condition x Site interaction, midline, $F(5, 220) = 8.83$, $p < .001$, medial, $F(5, 220) = 7.98$, $p < .001$], lateral, $F(4, 176) = 13.01$, $p < .001$; Main effect of Site, midline, $F(5, 220) = 20.64$, $p < .001$; medial, $F(5, 220) = 10.16$, $p < .001$, lateral, $F(4, 176) = 8.12$, $p < .001$; Site x Hemisphere interaction, medial, $F(5, 220) = 3.03$, $p < .019$].

6.6 Summary and Discussion for Experiment 5

This study was designed to examine the relationship between psychopathy and semantic processes related to the generation of the scalp recorded N400 ERP. In general, sentence processing studies of the N400 elicited by terminal word stimuli suggest that this component is related to processes involved with accessing and integrating word meanings within ongoing context. Previous studies of language functioning in psychopathy have consistently observed the presence of large fronto-central ERP negativities in psychopaths' waveforms elicited by linguistic stimuli. One interpretation offered for the functional significance of these components was that they were related to abnormal semantic activation akin to that believed to generate N400 potentials. However, the data from the present experiment do not support this interpretation. In the present study, there were no group

differences in the amplitude of the N400 elicited by either congruent or incongruent word stimuli assessed at 29 scalp electrodes. Indeed, across all participants, the N400 was similar in amplitude and topography as is that found in studies of noncriminals (Niznikiewicz et al., 1997).

Source localization studies of the N400 have suggested that there are generators located in the anterior temporal lobe. Specifically, these studies have found that regions just anterior to the amygdala generate negative field potentials in the 300-500 millisecond post-stimulus time window (Guillem, N'Kaoua, Rougier, & Claverie, 1995; McCarthy, Nobre, Bentin, & Spencer, 1995; Nobre & McCarthy, 1995). These studies have also implicated the fusiform gyrus in the generation of the N400. Recent event-related fMRI data from our lab has confirmed that the anterior temporal lobes are activated during processing of congruent and incongruent terminal words of sentences. We have observed that greater activation is found for processing of incongruent terminal words than for congruent words bilaterally in the medial anterior temporal lobe and in left lateral frontal cortex (Kiehl, Laurens, & Liddle, 1999).

The results of Experiments 1 and 2, and the interpretation offered for the results from Experiments 3 and 4, strongly suggest that psychopathy is associated with functional abnormalities in the anterior temporal lobe. In Experiment 1 we found that psychopathy was associated with abnormalities in the right anterior superior temporal gyrus (Talairach coordinates, x = 56, y = 15, z = -10) during performance of a concrete/abstract lexical decision task. The right hemisphere (x = 38, y = 22, z = -28) region we observed to differentiate incongruent from congruent stimuli in our event-related fMRI study appears to fall approximately 30 mm medial and 25 mm inferior to the region we observed abnormalities

for psychopaths in Experiment 1. In Experiment 2, we observed that psychopaths failed to show greater activation for processing affective stimuli than for neutral stimuli in the right amydgala/ parahippocampal region (Talairach coordinates, x = 34,y = -11, z = -20) and left parahippocampal formation (Talairach coodinates, x = -38, y = -22, z = -16). Comparison of these latter sites with those found to be greater activated for processing of incongruent than for congruent stimuli suggest these sites were approximately 30 mm distance from each other (x = -34, y = 22, z = -25; left hemisphere site from Kiehl, Laurens, and Liddle, 1999) Thus, to the extent that the scalp recorded N400 is generated in the anterior temporal lobe, it would appear to be located distal to those sites in which we have observed abnormalities in psychopathy.

To summarize, there were no group differences between psychopaths and nonpsychopaths in the amplitude of the N400 or P600 for either congruent or incongruent terminal words of sentences. The present data do not support the hypothesis that psychopathy is associated with abnormalities in processes related to the generation of the N400 ERP.

7.0 General Discussion

7.1 Summary of results

This thesis is comprised of five experiments that were designed to elucidate the functional neural architecture and characterize the temporal features of information processing abnormalities in affective, cognitive and language functions in criminal psychopaths. Experiments 1 and 2 sought to elucidate the neural systems underlying semantic and affective processes in psychopathy using fMRI. Experiments 3, 4 and 5 examined the temporal features of cognitive and language function in psychopaths using ERPs.

In Experiment 1 we observed that psychopaths performed more poorly and showed significantly less neural differentiation between abstract and concrete stimuli than did control participants. These deficits were located in the right anterior superior temporal gyrus. In Experiment 2 we observed that psychopaths, relative to control participants, showed reduced neural differentiation between affective and neutral stimuli in several neural regions, including the right amygdala/hippocampal junction, left parahippocampal formation, ventral striatum, and in the anterior and posterior cingulate. Psychopaths did show greater activation for affective than for neutral stimuli in regions located outside the limbic system, suggesting that they used alternative neural systems for performing the task (see also Intrator et al., 1997).

In Experiment 3 we observed that psychopathy was associated with abnormalities of the P3 component of the ERP elicited by visual oddball stimuli. In Experiment 4 we observed that psychopathy was associated with abnormalities of the N2 and P3 components of the ERP elicited by auditory oddball stimuli. These data are consistent with the growing literature

showing that psychopaths differ from others in the modulation and allocation of attentional resources (Harpur & Hare, 1990). The most prominent difference between psychopaths and control participants was that the psychopaths' ERPs to visual and auditory target stimuli were characterized by a large fronto-central negativity in the 350-600 millisecond time window. These fronto-central ERP negativities are also observed in patients with temporal lobe damage, suggesting, as do the results from Experiments 1 and 2, that psychopathy is associated with functional abnormalities in the temporal lobe(s).

Experiment 5 examined the neural systems underlying semantic processes related to the generation of the N400 ERP. In sentence processing studies, this component of the ERP is believed to be related to semantic processes associated with integrating word meanings within the ongoing discourse (Kutas & Hillyard, 1980a; 1980b; 1983; Kutas & Van Petten, 1994). In this experiment we used the classic N400 paradigm (e.g., Kutas & Hillyard, 1980b) in which participants are required to judge whether the terminal words of sentences were either congruent or incongruent with the previous sentence context. We did not observe any group differences between psychopaths and nonpsychopaths in behavioral performance or in the amplitude of the N400 elicited by either congruent or incongruent terminal words. Taken together with the results from Experiments 3 and 4, these data suggest that the functional significance of the late fronto-central ERP negativities that have been reported in previous ERP studies of language processes in psychopathy (Kiehl et al., 1999a; Williamson et al., 1991) are not due to abnormalities in processes related to the generation of the N400.

7.2 Evidence for abnormalities in abstract processing in psychopaths.

The findings from Experiment 1 add to the accumulating evidence suggesting that psychopathy is associated with abnormalities in processing conceptually abstract information. Studies have shown that psychopathic individuals have difficulty processing abstract words (current data from Experiment 1; Kiehl et al., 1999a), performing abstract categorization tasks (Hare & Jutai, 1988; Kiehl et al., 1999a), and understanding and interpreting proverbs (Gillstrom, 1994). These data suggest that psychopathy is associated with deficits or impairments in semantic processing of abstract material.

ERP studies have shown that differentiating abstract words from concrete words (Kiehl et al., 1999a; Kounios & Holcomb, 1994; Paller et al, 1987) begins to occur in the processing stream at approximately 200 milliseconds post stimulus. Psychopaths however, do not show this same ERP differentiation between abstract words and concrete words during a concrete/abstract lexical decision task or during a concrete/abstract discrimination task (Kiehl et al., 1999a). These data suggest that abnormalities in information processing begin to occur in psychopaths as early as 200 milliseconds after a word stimulus is presented. It is also important to note that in these latter tasks psychopaths differed from nonpsychopaths in their ERPs to all word stimuli. That is, beginning as early as 200 ms post stimulus psychopaths' ERP to concrete and abstract words, as well as to pseudoconcrete and pseudoabstract stimuli, were associated with greater fronto-central ERP negativities than were nonpsychopaths' ERPs. In Experiment 1, we observed that psychopaths failed to activate the right anterior superior temporal gyrus for processing abstract words relative to baseline and failed to use this region for differentiating abstract stimuli from concrete stimuli in a manner consistent with

that found in controls. The anterior superior temporal gyrus is a multimodal association cortex believed to be involved in a circuit that integrates the outcome of sensory analyses with previously stored semantic information (Mendola et al., 1999). This latter interpretation of the function of the anterior superior temporal gyrus suggests that this region would exert its influence on information processing at approximately 150-250 millisecond post stimulus. This information, combined with the ERP data from Kiehl et al. (1999a) showing that the differences between psychopaths and others for semantic processing occur at approximately 200 ms post stimulus, suggest that the anterior superior temporal gyrus may be the site at which information processing difficulties begin in psychopaths. The fact that the right anterior superior temporal gyrus was not activated for processing abstract word stimuli (even compared to baseline) suggests a focal abnormality in the psychopaths' information processing stream. One might speculate that if this region is not functioning appropriately, alternative systems may be recruited for performing computations on abstract material.

7.3 Evidence for abnormalities in affective processing in psychopaths.

Studies have also shown that psychopathy is associated with abnormalities in processing affective information. Psychopaths have difficulty processing affectively valenced word (Day & Wong, 1996; Intrator et al., 1997; Kiehl et al., 1999a; Williamson et al., 1991), and speech (Louth et al., 1998) stimuli, making judgments regarding emotional polarity (Williamson, Harpur, & Hare, 1990), and interpreting emotional metaphors (Hayes, 1995). Psychopaths also fail to show the normal 'narrowing' of details when recalling affective information as do nonpsychopaths (Christianson et al., 1996). The results from Experiment 2

indicate that psychopaths perform in a similar manner as do controls for memory for affective stimuli; however the neural systems engaged in these cognitive operations are quite different between psychopaths and controls. Psychopaths did not show the same pattern of activation for affective (compared to neutral) stimuli as did controls in multiple limbic sites, including the amygdala, hippocampus, and anterior and posterior cingulate. Unlike Experiment 1, psychopaths did show evidence of using alternative neural systems for performing the task. These regions included bilateral inferior frontal gyrus. This suggests that in the absence of input from the limbic system, psychopaths were forced to use a different system(s) to perform the task than were noncriminals. Evidence for abnormalities in limbic function also comes from other research in psychopathy. Patrick and colleagues have shown that psychopaths do not show the same pattern of startle potentiation during viewing of negatively valenced stimuli as do nonpsychopaths (Patrick, Bradley, & Lang, 1993). 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 (reviewed by Patrick, 1994). Although more research is needed in this area, these data suggest that the abnormal emotional behavior of psychopaths may be related to deficits in limbic function.

In summary, psychopathy is associated with abnormalities in semantic processing of conceptually abstract information and also abnormalities in processing affective information. At the present time it is unclear whether these abnormalities in semantic processing are related to that same cognitive process or different cognitive processes or some combination thereof. What is clear from the present data is that the neural systems that underlie these abnormalities appear to include lateral frontal and anterior temporal cortex. We note that these two regions are highly interconnected via the uncinate fasciculus. This raises the possibility that some of

the observed abnormalities in psychopaths may be related to disruption of function of circuits linking frontal cortex with temporal cortex. Indeed, perhaps a more precise characterization of the observed abnormalities in psychopaths would be that there appears to be an abnormal relationship between activity in frontal and temporal cortex (including limbic system). That is, some areas in the temporal lobe (and limbic system) appear to show abnormally small changes in response to stimuli while some frontal areas appear to show abnormally large changes. In Experiment 1 psychopaths failed to activated the right anterior superior temporal gyrus for processing of abstract words. In Experiment 2 psychopaths showed reduced activity associated with affective processing in the amygdala, hippocampal formation, and anterior and posterior cingulate. However, psychopaths showed greater activation associated with processing affective stimuli than did controls bilaterally in the inferior frontal gyrus. It is also plausible to suggest that the abnormal fronto-central ERP negativities in psychopaths (Experiments 3 and 4) occur from weakened input from temporal lobe structures which may lead to excessive activation of frontal cortex. Indeed, the similarity between the observed psychopathological and neural abnormalities in psychopaths and those observed in patients with temporal lobe damage (or temporal lobectomy for treatment of epilepsy) deserves further comment.

7.4 The relationship between psychopathy and the temporal lobes.

Similarities between patients with temporal lobe abnormalities and criminal psychopathic individuals exist on several levels. On the behavioral level, detailed psychological and personality assessments of the patients with temporal lobe epilepsy suggests

a high incidence of psychopathic-like behavior. Indeed, some studies have reported that pre-operatively the prevalence of psychopathic-like behaviors are as high as 70% of patients with anterior temporal lobe epilepsy (Hill, Pond, Mitchell, & Falconer, 1957). Interestingly, removal of the anterior temporal lobe appears to alleviate these behavioral problems in the majority of cases. Hill and colleagues (1957) reported that improvements in personality functioning following temporal lobectomy included reduced hostility, more appropriate sexual behavior (e.g., reduced use of prostitutes and sexual fetishes), increased warmth in social relationships, and increased empathy. It is also noteworthy that little or no intellectual deficits were observed in these patients after surgery for their epilepsy (Falconer & Serafetinides, 1963; Hill et al., 1957). Note that removal of the anterior temporal lobe reduced the psychopathic traits, implying that these traits might reflect pathological temporal lobe over-activity or disruption in circuits that involve the anterior temporal lobes.

Similarities between patients with temporal lobe abnormalities and criminal psychopathic individuals also come from the ERP data from the present series of experiments. Data from these studies have revealed the presence of large fronto-central ERP negativities in the 300-800 millisecond post-stimulus time window in psychopaths for a variety of stimuli. These abnormal fronto-central ERP negativities have been elicited by word stimuli (Kiehl et al., 1999a; Williamson et al., 1991), simple visual stimuli (Experiment 3; (see also Braverman, 1993), and task relevant auditory stimuli (Experiment 4). A number of interpretations of functional significance of these fronto-central ERP negativities have been suggested, including abnormalities in attentional, executive, and semantic processes (Kiehl et al., 1999a; Williamson et al., 1991). Examination of ERP data from similar tasks with patients with anterior temporal lobe abnormalities indicate that these patients also show strong evidence for

abnormal fronto-central negativities (Johnson, 1989; Yamaguchi & Knight, 1993). Indeed, the similarities in waveform morphology and topography between these two groups are striking.

Paller and colleagues (1988) have also shown that fronto-central ERP negativities are elicited by auditory oddball stimuli in monkeys following temporal lobe lesions (Paller, McCarthy, Roessler, & Allison, 1992; Paller et al., 1988). As noted in the summary and discussion for Experiment 1, it is important to note that these abnormalities in psychopaths occur in the absence of any overt structural brain abnormalities. High resolution structural MRIs have now been evaluated in 23 psychopathic offenders and none have any evidence of overt structure brain pathology (Kiehl, 1999). It is relevant to note that neither psychopaths nor temporal lobe damaged (or temporal lobectomy) patients show any evidence of behavioral impairment in visual or auditory oddball tasks.

As mentioned in the discussion for Experiment 4, given that fronto-central ERP negativities exist in patients who have had severe damage to the temporal lobe, were might these potentials be generated? Halgren and colleagues have reported that negative polarity inversions in the 300-500 ms post-stimulus time window for auditory target stimuli are found in the anterior cingulate, amygdala and inferior lateral frontal cortex (Halgren, 1999; Halgren et al., 1995a; 1995b). Recent event-related fMRI studies of the hemodynamic response to visual and auditory oddball stimuli have confirmed that these sites are implicated in the processing of task-relevant stimuli (see Kiehl et al. 1998a). In Experiment 2 abnormalities in affective processing in psychopaths were observed in the left anterior cingulate, right amygdala and bilaterally in the inferior lateral frontal cortex. These latter data suggest that the abnormal fronto-central ERP negativities may also be related to abnormal function of these

neural structures. However, it is important to reiterate that localizing the neural sources underlying ERP components is difficult. Perhaps future studies should combine the high temporal resolution of ERPs with the high spatial resolution of fMRI to elucidate the neural systems that underlie the fronto-central ERP negativities in psychopaths.

7.5 Relationship between semantic processing abnormalities and other theories of psychopathy.

7.5.1 Low fear hypothesis

The observation that abnormalities in semantic processing of conceptually abstract material and affective information are a prominent feature of psychopathy may throw light upon several of the existing theories of psychopathy. For example, the low fear hypothesis of psychopathic behavior posits that psychopathic individuals suffer from a chronic need for stimulation, compounded by a relative fearlessness of novel and dangerous situations (Lykken, 1957; 1982; 1995; Patrick, 1994; Patrick et al., 1993; 1994; see Levenson, 1990; 1992; Levenson, Kiehl, & Fitzpatrick, 1995, for criticisms of this view). If the semantic (and perhaps limbic) systems that normally incorporate the meaning of fearful stimuli are not functioning normally, then this may lead to augmented appetitive behavior that would otherwise be inhibited. Moreover, failing to process the meaning of contextual cues related to emotional, including learned fearful stimuli, may lead to psychopathic behaviors.

7.5.2 Response modulation hypothesis

The hypothesis that abnormalities in semantic processing may be a fundamental feature in psychopathy might also help explain Newman and colleagues finding that psychopathic individuals are less likely than nonpsychopathic individuals to show interference to contextual cues (Newman, Schmitt & Voss, 1997). This latter study was designed to evaluate the generality of the response modulation hypothesis of psychopathy (Newman, 1998). Briefly, the response modulation hypothesis argues that psychopaths suffer from an information processing deficit that impedes their ability to 'automatically' process contextual cues that, in nonpsychopathic individuals, normally augment behavior. There is now large body of literature suggesting that psychopathy is associated with a failure to accommodate these contextual cues to modulate behavior (see Newman, 1998, for a review). In clarifying their use of the term 'automatic', Newman et al., indicated that "the term is used to indicate that psychopaths do not consider the **meaning** (emphasis mine) of their words, their actions, and situational cues in a spontaneous way". Interestingly, patients with right hemisphere lesions show reduced interference effects for language stimuli compared to left hemisphere brain damage patients or control participants (Doyon & Milner, 1991). Studies have also shown that word meanings can be accessed automatically (e.g., in the absence of awareness) up to 600 ms post-stimulus (Luck, Vogel, & Shapiro, 1996). Using ERPs we have shown that abnormalities in differentiating the semantic aspects of word stimuli occur in psychopaths as early as 200 milliseconds post-stimulus (Kiehl et al., 1999a). Thus, the deficits in psychopaths for accommodating contextual cues, those that are possibly semantic in nature, may lead to

less interference, at least in part, because of a relative deficit (or advantage) in abstracting the meaning of the contextual cue.

7.5.3 'Acquired sociopathy' model of psychopathy

Several previous investigators have emphasized the probable involvement of frontal cortex in psychopathy. For example, Damasio and colleagues have suggested that 'acquired sociopathy', a condition putatively related to psychopathy, is the result of damage to the orbital frontal cortex (Damasio, 1994; Damasio, Tranel, & Damasio, 1990; Hare, 1993). In Experiment 2, we observed that, compared with controls, psychopaths generated excessive activation in the lateral aspects of the orbital cortex for processing affective stimuli. Unfortunately, due to susceptibility artifact in the frontal sinuses, we were unable to directly examine the role of the medial orbital cortex in these experiments. We also observed that, relative to control participants, psychopaths showed reduced activation for processing affective stimuli in the anterior cingulate. Additional evidence for anterior cingulate abnormalities in psychopathy comes from recent evidence demonstrating that psychopathy is associated with reductions in the amplitude of the error-related negativity (ERN; Kiehl, Bates & Liddle, 1999). The ERN is associated with processes related to error detection and is believed to be generated in the anterior cingulate cortex (Kiehl, Liddle & Hopfinger, in press). Thus, although there may be some similarities between 'acquired sociopathy' and psychopathy, the present data do not appear to address this relationship directly. It is important to reiterate, however, that psychopathy does not appear to be related to gross structural lesions akin to those known to cause 'acquired sociopathy'.

7.5.4 Left hemisphere dysfunction

Some theorists have also argued that psychopathy is associated with dominant or left hemisphere frontal abnormalities (Flor-Henry, 1972). However, there have been mixed results supporting this view (Hare, 1979; Jutai, Hare, & Connolly, 1987). In the present series of experiments we have observed differences between psychopaths and others in cognitive and language functions located in both the left and right hemispheres. Moreover, from the available evidence, it would appear that psychopathy is associated with both left and right hemisphere dysfunction.

7.6 Limitations of the present studies

There are a number of limitations in the present series of experiments that should be addressed in future work. In Experiments 1 and 2 the sample sizes for each group were small, which raises the possibility that some of the observed effects may be sample specific. According to current estimates, sample sizes of approximately 9 participants per group are adequate for delineating group effects in positron emission tomography (PET) studies (Holmes, 1999). Because fMRI typically has better signal-to-noise ratios than do PET studies, the sample sizes in the present study appear to be adequate. Nevertheless, future studies should consider employing larger sample sizes. Functional imaging studies, including the present studies, also commonly employ fixed-effect models for data analyses, which means that the results of Experiments 1 and 2 must be qualified as case studies.

A second limitation of the Experiments 1 and 2 is that we did not use an incarcerated nonpsychopathic control group. This raises the issue that some of the observed effects in the psychopathic group may be due to the effects of incarceration or criminality per se rather than psychopathy. In our previous ERP studies that provided the basis for proposing Experiments 1 and 2 we observed that the nonpsychopathic inmates' behavioral data and ERPs to concrete and abstract words (Task 1 and Task 2; Kiehl et al., 1999a) and to affective words (Task 3, Kiehl et al., 1999a; Williamson et al., 1991) were very similar to those observed for noncriminal controls (Kounious & Holcomb, 1994; Paller et al., 1987; Kiehl, 1999). In addition, numerous other studies have shown that the performance of nonpsychopathic inmates parallels that of noncriminals in various cognitive and psychophysiological measures (e.g., Christianson et al., 1996; Hare, 1984; Hart, Forth, & Hare, 1990; Patrick et al., 1993; Newman et al., 1997; Smith, Arnett, & Newman, 1992). Moreover, in Experiments 3, 4, and 5, the performance and ERP data of the incarcerated nonpsychopaths was very similar to that observed in studies of noncriminals. Therefore, in view of the major logistical difficulties in performing MRI studies in inmates of a maximum-security prison, we elected to study only psychopathic offenders. It is important to note that the control groups employed in Experiments 1 and 2 were matched with the psychopathic groups on gender, age, education, IQ measures, socio-economic status and handedness. Nevertheless, we cannot exclude the possibility that the observed differences between psychopaths and non-inmate controls might be due to factors associated with criminality or incarceration. However, we consider that the taking into account the previous ERP studies using similar tasks, in which the nonpsychopathic inmate controls exhibited normal ERPs, make such an explanation unlikely. Furthermore, the available evidence indicates that incarceration itself does not impair abstract

thinking. For example, Goethals (1981) has shown that length of incarceration is unrelated to impairments in performance in Raven's progressive matrices test, a test of abstract thinking (Goethals, 1981).

Lastly, we cannot rule out the possibility that history of substance abuse may have contributed to the findings of Experiments 1 and 2. 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 six months, requiring urine samples for drug testing at the time of study, and examining the prison records for history of failed urine tests. Nevertheless, the two groups did likely differ in the their history of drug use and the interpretation of the results must take this into account.

7.7 Implications for treatment of psychopathy

These data may have important implications for treatment and management of psychopaths. Difficulty understanding and comprehending conceptually abstract and affective information may be part of the reason why psychopathic individuals are so resistant to psychological treatment (Grann, Langstroem, Tengstroem, & Kullgren, 1999; Hare, 1998; Losel, 1998; Rice, Harris, & Cormier, 1992; Wallace, Vitale, & Newman, 1999). Many treatment programs used in forensic settings teach information that is not only abstract in content but also affective (e.g., role playing, empathy modules). If psychopathy is associated with impairments in interpreting and understanding these types of information, then psychopathic individuals may be at a distinct disadvantage in these programs and may require

alternative treatment regimes. Moreover, perhaps treatment and management of psychopathic individuals would be particularly improved if these programs emphasized concepts in more concrete forms.

7.8 Suggestions for future research

Currently, cognitive and language abnormalities have only been characterized in samples of adult psychopathic populations. However, the limited published evidence does indicate that language abnormalities are present in adolescent psychopathic individuals (Raine et al., 1990). This raises the issue of when do these abnormalities originate? Unfortunately, very little is known about the onset and course of psychopathy (for review see Frick, 1998) and even less is known about the cognitive correlates of the syndrome at young ages. Clearly, anecdotal and clinical evidence suggest that psychopathy is present at a very early age. Indeed, some have even linked psychopathic-like behavior to attachment theory in children as early as 6 months of age (Magid & McKelvey, 1988). Modern psychopathy assessment techniques are currently investigating identifying these individuals as a very early age (Forth & Burke, 1998; Frick, 1998). Future studies should consider employing the tasks used in the present series of experiments to examine the possibility that these abnormalities may be present at younger ages. Indeed, these tasks may prove to be useful in evaluating individuals at risk for psychopathy.

7.9 Conclusion

The results from studies of affective and semantic processes in psychopaths suggest that the disorder is related to difficulties in processing abstract material and also processing affective information. These abnormalities appear to involve sites in the anterior temporal lobes and inferior frontal lobes, including the limbic system (Experiments 1 and 2). The results from Experiments 3 and 4 suggest a link between psychopathy and abnormalities in the temporal and frontal lobes. Together, these data suggest that one of the cardinal abnormalities in psychopathy is abnormal processing of affective information and also conceptually abstract information and that these abnormalities are related to the function of neural circuits in the anterior temporal lobes and lateral frontal cortex.

8.0 References

American Psychiatric Association (1994): Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Washington D.C.

Adams, J., Faux, S. F., Nestor, P. G., Shenton, M., Marcy, B., Smith, S., & McCarley, R. W. (1993). ERP abnormalities during semantic processing in schizophrenia. Schizophrenia Research, 10, 247-257.

Adolphs, R., Tranel, D., & Damasio, A. R. (1998). The human amygdala in social judgment. Nature, 393, 470-474.

Alexander, J. E., Bauer, L. O., Kuperman, S., Morzorati, S., SJ, O. C., Rohrbaugh, J., Porjesz, B., Begleiter, H., & Polich, J. (1996). Hemispheric differences for P300 amplitude from an auditory oddball task. International Journal of Psychophysiology, 21, 189-196.

Alexander, J. E., Porjesz, B., Bauer, L. O., Kuperman, S., Morzorati, S., O'Connor, S. J., Rohrbaugh, J., Begleiter, H., & Polich, J. (1995a). P300 hemispheric amplitude asymmetries from a visual oddball task. Psychophysiology, 32, 467-475.

Alexander, J. E., Porjesz, B., Bauer, L. O., Kuperman, S., Morzorati, S., SJ, O. C., Rohrbaugh, J., Begleiter, H., & Polich, J. (1995b). P300 hemispheric amplitude asymmetries from a visual oddball task. Psychophysiology, 32, 467-475.

Ammons, R. B., & Ammons, C. H. (1962). The Quick Test (Qt): Provisional Manual. Psychological Reports, 11, 111-161.

Ammons, R. B., & Ammons, C. H. (1979a). Use and Evaluation of the Quick Test (Qt): Partial Summary Through October, 1979: I. Published Papers. Psychological Reports, 45, 943-946.

Ammons, R. B., & Ammons, C. H. (1979b). Use and Evaluation of the Quick Test (Qt): Partial Summary Through October, 1979: II. Reviews, Theses, Unpublished Reports and Papers. Psychological Reports, 45, 953-954.

Annett, M. (1970). A classification of hand preference by association analysis. British Journal of Psychology, 61, 303-321.

Beauregard, M., Chertkow, H., Bub, D., Murtha, S., & et al. (1997). The neural substrate for concrete, abstract, and emotional word lexica: A positron emission tomography study. Journal of Cognitive Neuroscience, 9, 441-461.

Bechara, A., Damasio, H., Damasio, A. R., & Lee, G. P. (1999). Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. Journal of Neuroscience, 19, 5473-5481.

Beeman, M., Friedman, R. B., Grafman, J., Perez, E., Diamond, S., & Lindsay, M. B. (1994). Summation priming and coarse semantic coding in the right hemisphere. Journal of Cognitive Neuroscience, 6, 25-45.

Blackwood, D. H., Whalley, L. J., Christie, J. E., & Blackburn, I. M. (1987). Changes in auditory P3 event-related potential in schizophrenia and depression. British Journal of Psychiatry, 150, 154-160.

Bottini, G., Corcoran, R., Sterzi, R., Paulesu, E., Schenone, P., Scarpa, P., Frackowiak, R. S., & Frith, C. D. (1994). The role of the right hemisphere in the interpretation of figurative aspects of language. A positron emission tomography activation study. Brain, 117, 1241-1253.

Braverman, E. R. (1993). Brain electrical activity mapping (BEAM) in patients who commit violent crimes: Are bitemporal abnormalities a characteristic? Journal of Orthomolecular Medicine, 8, 154-156.

Brinkley, C. A., Bernstein, A., & Newman, J. P. (1999a). Coherence in the narratives of psychopathic and nonpsychopathic criminal offenders. Personality & Individual Differences, 27, 519-530.

Brinkley, C. A., Newman, J. P., Harpur, T. J., & Johnson, M. M. (1999b). Cohesion in texts produced by psychopathic and nonpsychopathic criminal inmates. Personality & Individual Differences, 26, 873-885.

Brownell, H. H., Michel, D., Powelson, J., & Gardner, H. (1983). Surprise but not coherence: Sensitivity to verbal humor in right-hemisphere patients. Brain & Language, 18, 20-27.

Caramazza, A., Gordon, J., Zurif, E. B., & DeLuca, D. (1976). Right-hemispheric damage and verbal problem solving behavior. Brain & Language, 3, 41-46.

Christianson, S.-A., Forth, A. E., Hare, R. D., Strachan, C., Lidberg, L., & Thorell, L.-H. (1996). Remembering details of emotional events: A comparison between psychopathic and nonpsychopathic offenders. Personality & Individual Differences, 20, 437-443.

Cleckley, H. (1976). The mask of sanity. (5th ed.). St. Louis, MO: Mosby.

Cooke, D. J. (1998). Psychopathy across cultures. In D. J. Cooke, A. E. Forth, & R. D. Hare (Eds.), Psychopathy: Theory, Research, and Implications for Society (pp. 13-46). Dordrecht, Netherlands: Kluwer Academic Publishers.

Cooke, D. J., & Michie, C. (1997). An item response theory analysis of the Hare Psychopathy Checklist--Revised. Psychological Assessment, 9, 3-14.

Damasio, A. R. (1994). Decartes' error: Error, reason, and the human brain. New York: Grosset / Putnam.

Damasio, A. R., Tranel, D., & Damasio, H. (1990). Individuals with sociopathic behavior caused by frontal damage fail to respond to autonomically to social stimuli. Behavioral Brain Research, 41, 81-94.

Day, J. (1977). Right-hemisphere language processing in normal right-handers. Journal of Experimental Psychology: Human Perception & Performance, 3, 518-528.

Day, R., & Wong, S. (1996). Anomalous perceptual asymemetries for negative emotional stimuli in the psychopath. Journal of Abnormal Psychology, 105, 648-652.

D'Esposito, M., Detre, J. A., Aguirre, G. K., & Stallcup, M. (1997). A functional MRI study of mental image generation. Neuropsychologia, 35, 725-730.

D'Esposito, M., Zarahn, E., & Aguirre, G. K. (1999). Event-related functional MRI: Implications for cognitive psychology. Psychological Bulletin, 125, 155-164.

Doyon, J., & Milner, B. (1991). Right temporal-lobe contribution to global visual processing. Neuropsychologia, 29, 343-360.

Falconer, M. A., & Serafetinides, E. A. (1963). A follow-up study of surgery in termporal lobe epilepsy. Journal of Neurology, Neurosurgery & Psychiatry, 26, 154-165.

Flor-Henry, P. (1972). Psychiatric syndromes considered as manifestations of lateralized temporal-limbic dysfunction. Paper presented at the Third International Congress of Psychosurgery.

Ford, J. M. (1998). Schizophrenia: The broken P300 and beyond. Paper presented at the Annual meeting of the Society for Psychophysiological Research, Denver, CO.

Ford, J. M., White, P., Lim, K. O., Pfefferbaum, A., & et al. (1994). Schizophrenics have fewer and smaller P300s: A single-trial analysis. Biological Psychiatry, 35, 96-103.

Forth, A. E., & Burke, H. C. (1998). Psychopathy in adolescence: Assessment, violence, and developmental precursors. In D. J. Cooke, A. E. Forth, & R. D. Hare (Eds.), Psychopathy: Theory, Research, and Implications for Society (pp. 205-229). Dordrecht, Netherlands: Kluwer Academic Publishers.

Forth, A. E., & Hare, R. D. (1989). The contingent negative variation in psychopaths. Psychophysiology, 26, 676-682.

Francis, W. N., & Kucera, H. (1982). Frequency analysis of English usage. Boston: Houghton Mifflin.

Frick, P. J. (1998). Callous-unemotional traits and conduct problems: Applying the two-factor model of psychopathy to children. In D. J. Cooke, A. E. Forth, & R. D. Hare (Eds.), Psychopathy: Theory, Research, and Implications for Society (pp. 161-188). Dordrecht, Netherlands: Kluwer Academic Publishers.

Friston, K. J., Ashburner, J., Frith, C. D., Poline, J.-B., Heather, J. D., & Frackowiak, R. S. J. (1995a). Spatial registration and normalization of images. Human Brain Mapping, 2, 165-189.

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J.-P., Frith, C. D., & Frackowiak, R. S. J. (1995b). Statistical parametric maps in functional imaging; A general linear approach. Human Brain Mapping, 2, 189-210.

Friston, K. J., Williams, S., Howard, R., Frackowiak, R. S. J., & Turner, R. (1996). Movement-related effects in fMRI time-series. Magnetic Resonance in Medicine, 35, 346-355.

Fulero, S. (1996). Review of the Hare-Psychopathy Checklist-Revised. In J. C. Conoley & J. C. Impara (Eds.), 12th Mental Measurements Yearbook (pp. 453-454). Lincoln: Buros Institue.

Gardner, H., & Denes, G. (1973). Connotative judgments by aphasic patients on a pictorial adaptation of the semantic differential. Cortex, 9, 183-196.

Gehring, W. J. (1993). The error-related negativity: Evidence for a neural mechanism for error-related processing. Unpublished Dissertation. U Illinois, Urbana-Champaign, US.

Gehring, W. J., Coles, M. G. H., Meyer, D. E., & Donchin, E. (1990). The error-related negativity: An event-related brain potential accompanying errors. Psychophysiology, 27, S43.

Gehring, W. J., Goss, B., Coles, M. G., & Meyer, D. E. (1993). A neural system for error detection and compensation. Psychological Science, 4, 385-390.

Geisser, S., & Greenhouse, S. W. (1958). An extension of Box's results on the use of the F distribution in multivariate analysis. Annals of Mathemathical Statistics, 29, 885-891.

Gillstrom, B. J. (1994). Abstract thinking in criminal psychopaths. Unpublished Dissertation, University of British Columbia, Vancouver.

Goethals, J. (1981). Imprisonment and cognitive impairment. Journal of Clinical Psychology, 37, 418-422.

Grann, M., Langstroem, N., Tengstroem, A., & Kullgren, G. (1999). Psychopathy (PCL-R) predicts violent recidivism among criminal offenders with personality disorders in Sweden. Law & Human Behavior, 23, 205-217.

Grillon, C., Ameli, R., & Glazer, W. M. (1991). N400 and semantic categorization in schizophrenia. Biological Psychiatry, 29, 467-480.

Guillem, F., N'Kaoua, B., Rougier, A., & Claverie, B. (1995). Intracranial topography of event-related potentials (N400/P600) elicited during a continuous recognition memory task. Psychophysiology, 32, 382-392.

Halgren, E. (1980). Endogenous potentials generated in the human hippocampal formation and amygdala by infrequent events. Science, 210, 803-805.

Halgren, E. (1999). Personal communication.

Halgren, E., Baudena, P., Clarke, J. M., Heit, G., Liégeois, C., Chauvel, P., & Musolino, A. (1995a). Intracerebral potentials to rare target and distractor auditory and visual stimuli. I. Superior temporal plane and parietal lobe. Electroencephalography and Clinical Neurophysiology, 94, 191-220.

Halgren, E., Baudena, P., Clarke, J. M., Heit, G., Marinkovic, K., Devaux, B., Vignal, J. P., & Biraben, A. (1995b). Intracerebral potentials to rare target and distractor auditory and visual stimuli. II. Medial, lateral and posterior temporal lobe. Electroencephalography and Clinical Neurophysiology, 94, 229-250.

Halgren, E., Marinkovic, K., & Chauvel, P. (1998). Generators of the late cognitive potentials in auditory and visual oddball tasks. Electroencephalography & Clinical Neurophysiology, 106, 156-164.

Hare, R. D. (1979). Psychopathy and laterality of cerebral function. Journal of Abnormal Psychology, 88, 605-610.

Hare, R. D. (1980). A research scale for the assessment of psychopathy in criminal populations. Personality & Individual Differences, 1, 111-119.

Hare, R. D. (1984). Performance of psychopaths on cognitive tasks related to frontal lobe function. Journal of Abnormal Psychology, 93, 133-140.

Hare, R. D. (1991). Manual for the Hare Psychopathy Checklist-Revised. Toronto: Multi-Health Systems.

Hare, R. D. (1993). Without conscience: The disturbing world of the psychopaths among us. New York: Pocket Books.

Hare, R. D. (1996). Psychopathy – A clinical construct whose time has come. Criminal Justice and Behavior, 23, 25-54.

Hare, R. D. (1998). Psychopaths and their nature: Implications for the mental health and criminal justice systems. In E. Theodore Millon, E. Erik Simonsen, & et al. (Eds.), Psychopathy: Antisocial, criminal, and violent behavior . (pp. 188-212): New York, NY, USA.

Hare, R. D., & Forth, A. E. (1985). Psychopathy and lateral preference. Journal of Abnormal Psychology, 94, 541-546.

Hare, R. D., Harpur, T. J., Hakstian, A. R., Forth, A. E., & et al. (1990a). The revised Psychopathy Checklist: Reliability and factor structure. Psychological Assessment, 2, 338-341.

Hare, R. D., Harpur, T. J., Hakstian, A. R., Forth, A. E., Hart, S. D., & Newman, J. P. (1990b). The revised Psychopathy Checklist: Description statistics, reliability, and factor structure. Psychological Assessessment, 2, 338-341.

Hare, R. D., & Hart, S. D. (1993). Psychopathy, mental disorder, and crime. In H. Sheilagh (Ed.), Mental disorder and crime. (pp. 104-115): Sage Publications, Inc, Newbury Park, CA, US.

Hare, R. D., Hart, S. D., & Harpur, T. J. (1991a). Psychopathy and the DSM-IV criteria for antisocial personality disorder. Special Issue: Diagnoses, dimensions, and DSM-IV: The science of classification. Journal of Abnormal Psychology, 100, 391-398.

Hare, R. D., Hart, S. D., & Harpur, T. J. (1991b). Psychopathy and the DSM-IV criteria for antisocial personality disorder. Journal of Abnormal Psychology, 100, 391-398.

Hare, R. D., & Jutai, J. W. (1988). Psychopathy and cerebral asymmetry in semantic processing. Personality & Individual Differences, 9, 329-337.

Hare, R. D., & McPherson, L. M. (1984). Psychopathy and perceptual asymmetry during verbal dichotic listening. Journal of Abnormal Psychology, 93, 141-149.

Harpur, T. J., Hakstian, A. R., & Hare, R. D. (1988). The factor structure of the Psychopathy Checklist. Journal of Consulting and Clinical Psychology, 56, 741-747.

Harpur, T. J., & Hare, R. D. (1990). Psychopathy and attention. In T. E. James (Ed.), The development of attention: Research and theory. Advances in psychology, 69. (pp. 429-444): North-Holland, Amsterdam, Netherlands.

Harpur, T. J., & Hare, R. D. (1994). Assessment of psychopathy as a function of age. Journal of Abnormal Psychology, 103, 604-609.

Harpur, T. J., Hare, R. D., & Hakstian, A. R. (1989). Two-factor conceptualization of psychopathy: Construct validity and assessment implications. Psychological Assessment, 1, 6-17.

Hart, S. D., Forth, A. E., & Hare, R. D. (1990). Performance of criminal psychopaths on selected neuropsychological tests. Journal of Abnormal Psychology, 99, 374-379.

Hart, S. D., & Hare, R. D. (1989). Discriminant validity of the Psychopathy Checklist in a forensic psychiatric population. Psychological Assessment, 1, 211-218.

Hart, S. D., & Hare, R. D. (1996). Psychopathy and Antisocial Personality Disorder. Current Opinion In Psychiatry, 9, 129-132.

Hart, S. D., Hare, R. D., & Harpur, T. J. (1992). The Psychopathy Checklist--Revised (PCL-R): An overview for researchers and clinicians. In P. M. James C. Rosen (Ed.), Advances in psychological assessment, Vol. 8. (pp. 103-130): Plenum Press, New York, NY.

Heinze, H. J., Mangun, G. R., Burchert, W., Hinrichs, H., Scholz, M., Munte, T. F., Gos, A., Scherg, M., Johannes, S., & Hundeshagen, H. (1994). Combined spatial and temporal imaging of brain activity during visual selective attention in humans. Nature, 372, 543-546.

Hill, D., Pond, D. A., Mitchell, W., & Falconer, M. A. (1957). Personality changes following temporal lobectomy for epilepsy. Journal of Mental Science, 103, 18-27.

Holcomb, P. J. (1993). Semantic priming and stimulus degradation: Implications for the role of the N400 in language processing. Psychophysiology, 30, 47-61.

Holcomb, P. J., Kounios, J., Anderson, J. E., & West, W. C. (1999). Dual-coding, context-availability, and concreteness effects in sentence comprehension: An electrophysiological investigation. Journal of Experimental Psychology: Learning, Memory, & Cognition, 25, 721-742.

Holmes, A.P., Josephs, O., Buchel, C., & Friston, K.J. (in press). Statistical modelling of low frequency confounds in fMRI . Human Brain Mapping.

Intrator, J., Hare, R., Stritzke, P., Brichtswein, K., Dorfman, D., Harpur, T., Bernstein, D., Handelsman, L., Schaefer, C., Keilp, J., Rosen, J., & Machac, J. (1997). A brain imaging (single photon emission computerized tomography) study of semantic and affective processing in psychopaths. Biological Psychiatry, 42, 96-103.

Irwin, W., Davidson, R. J., Lowe, M. J., Mock, B. J., Sorenson, J. A., & Turski, P. A. (1996). Human amygdala activation detected with echo-planar functional magnetic resonance imaging. Neuroreport, 7, 1765-1769.

James, C. (1975). The role of semantic information in lexical decisions. Journal of Experimental Psychology: Human Perception and Performance, 14, 130-136.

Johnson, R., Jr. (1988). Scalp-recorded P300 activity in patients following unilateral temporal lobectomy. Brain, 111, 1517-1529.

Johnson, R., Jr. (1989). Auditory and visual P300s in temporal lobectomy patients: evidence for modality-dependent generators. Psychophysiology, 26, 633-650.

Johnson, R., Jr., & Fedio, P. (1987). Task-related changes in P300 scalp distribution in temporal lobectomy patients. Electroencephalography and Clinical Neurophysiology. Supplement, 40, 699-704.

Jutai, J. W. (1989). Psychopathy and P-sub-3 amplitude: A commentary on Raine. International Journal of Psychophysiology, 8, 17-22.

Jutai, J. W., & Hare, R. D. (1983). Psychopathy and selective attention during performance of a complex perceptual-motor task. Psychophysiology, 20, 146-151.

Jutai, J. W., Hare, R. D., & Connolly, J. F. (1987). Psychopathy and event-related brain potentials (ERPs) associated with attention to speech stimuli. Personality & Individual Differences, 8, 175-184.

Kiehl, K.A. (1999). Unpublished observations.

Kiehl, K.A., Bates, A., & Liddle, P.F. (1999). Abnormal error processing in criminal psychopaths: An event-related potential study. manuscript in preparation.

Kiehl, K. A., Hare, R. D., McDonald, J. J., & Brink, J. (1999a). Sematic and affective processing in psychopaths: An event-related potential study. Psychophysiology, 36, 765-774.

Kiehl, K. A., Laurens, K. R., Duty, T. L., Forster, B. B., & Liddle, P. F. (1998a). Neural sources involved in auditory target detection and novelty processing: An event-related fMRI study. manuscript submitted for publication.

Kiehl, K. A., & Liddle, P. F. (1999). An event-related fMRI study of an auditory oddball task in schizophrenia. manuscript submitted for publication.

Kiehl, K. A., Liddle, P. F., & Hopfinger, J. B. (in press). Error processing and the rostral anterior cingulate: An event-related fMRI study. Psychophysiology.

Kiehl, K. A., Liddle, P. F., Smith, A. S., Mendrek, A., Forster, B. B., & Hare, R. D. (1999b). Neural pathways involved in the processing of concrete and abstract words. Human Brain Mapping, 7, 225-233.

Kiehl, K. A., Smith, A. M., Hare, R. D., & Liddle, P. F. (1999c). An event-related potential investigation of response inhibition in schizophrenia and in psychopathy. manuscript submitted for publication.

Kiehl, K. A., Smith, A. M., Mendrek, A., Forster, B. B., Hare, R. D., & Liddle, P. F. (1998b, June). Activation of the amygdala during an affective memory task. Paper presented at the International Society for Human Brain Mapping, Montreal, Canada.

Kiehl., K. A., Laurens, K. R., & Liddle, P. F. (1999). Reading anomalous sentences: An event-related fMRI study of semantic processing. manuscript submitted for publication.

Kimura, D. (1963). Right temporal-lobe damage: Perception of unfamiliar stimuli after damage. Archives of Neurology, 8, 264-271.

Knight, R. (1996). Contribution of human hippocampal region to novelty detection. Nature, 383, 256-259.

Knight, R. T. (1984). Decreased response to novel stimuli after prefrontal lesions in man. Electroencephalography & Clinical Neurophysiology, 59, 9-20.

Knight, R. T., Grabowecky, M. F., & Scabini, D. (1995). Role of human prefrontal cortex in attention control. Advances in Neurology, 66, 21-36.

Knight, R. T., & Nakada, T. (1998). Cortico-limbic circuits and novelty: a review of EEG and blood flow data. Reviews in the Neurosciences, 9, 57-70.

Knight, R. T., Scabini, D., Woods, D. L., & Clayworth, C. C. (1989). Contributions of temporal-parietal junction to the human auditroy P3. Brain Research, 502, 109-116.

Kosson, D. S. (1996). Psychopathy and dual-task performance under focusing conditions. Journal of Abnormal Psychology, 105, 391-400.

Kosson, D. S., & Newman, J. P. (1986). Psychopathy and the allocation of attentional capacity in a divided-attention situation. Journal of Abnormal Psychology, 95, 257-263.

Kounios, J., & Holcomb, P. J. (1994). Concreteness effects in semantic priming: ERP evidence supporting Dual-Coding theory. Journal of Experimental Psychology: Learning, Memory and Cognition, 20, 804-823.

Kroll, J. F., & Merves, J. S. (1986). Lexical access for concrete and abstract words. Journal of Experimental Psychology: Learning, Memory, & Cognition, 12, 92-107.

Kutas, M. (1997). Views on how the electrical activity that the brain generates reflects the functions of different language structures. Psychophysiology, 34, 383-398.

Kutas, M., & Hillyard, S. A. (1980a). Event-related brain potentials to semantically inappropriate and surprisingly large words. Biological Psychology, 11, 99-116.

Kutas, M., & Hillyard, S. A. (1980b). Reading senseless sentences: brain potentials reflect semantic incongruity. Science, 207, 203-205.

Kutas, M., & Hillyard, S. A. (1983). Event-related brain potentials to grammatical errors and semantic anomalies. Memory and Cognition, 11, 539-550.

Kutas, M., & Hillyard, S. A. (1984). Brain potentials during reading reflect word expectancy and semantic association. Nature, 307, 161-163.

Kutas, M., & Van Petten, C. K. (1994). Psycholinguistics electrified: Event related brain potential investigations. In M. A. Gernsbacher (Ed.), Handbook of Psycholinguistics (pp. 83-143). San Diego: Academic Press.

Kwong, K. K., Belliveau, J. W., Chesler, D. A., Goldberg, I. E., Weisskoff, R. M., Poncelet, B. P., Kennedy, D. N., Hoppel, B. E., Cohen, M. S., & Turner, R. (1992). Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. Proceedings of the National Academy of Sciences of the United States of America, 89, 5675-5679.

Lapierre, D., Braun, C. M. J., & Hodgins, S. (1995). Ventral frontal deficits in psychopathy: Neuropsychological test findings. Neuropsychologia, 33, 139-151.

Levenson, M. R. (1990). Risk taking and personality. Journal of Personality & Social Psychology, 58, 1073-1080.

Levenson, M. R. (1992). Rethinking psychopathy. Theory & Psychology, 2, 51-71.

Levenson, M. R., Kiehl, K. A., & Fitzpatrick, C. M. (1995). Asssessing psychopathic attributes in a noninstitutionalized population. Journal of Personality and Social Psychology, 68, 151-158.

Losel, F. (1998). Treatment and management of psychopaths. In D. J. Cooke, A. E. Forth, & R. D. Hare (Eds.), Psychopathy: Theory, Research, and Implications for Society (pp. 303-354). Dordrecht, Netherlands: Kluwer Academic Publishers.

Louth, S. M., Williamson, S., Alpert, M., Pouget, E. R., & Hare, R. D. (1998). Acoustic distinctions in the speech of male psychopaths. Journal of Psycholinguistic Research, 27, 375-384.

Luck, S. J., Vogel, E. K., & Shapiro, K. L. (1996). Word meanings can be accessed but not reported during the attentional blink. Nature, 383, 616-618.

Lykken, D. T. (1957). A study of anxiety in the sociopathic personality. Journal of Abnormal & Social Psychology, 55, 6-10.

Lykken, D. T. (1982). Fearlessness: Its carefree charm and deadly risks. Psychology Today, 16, 20-28.

Lykken, D. T. (1995). The antisocial personalities. Hillsdale, N.J.: Lawrence Erlbaum Associates.

Maddock, R. J., & Buonocore, M. H. (1997). Activation of left posterior cingulate gyrus by the auditory presentation of threat-related words: an fMRI study. Psychiatry Research, 75, 1-14.

Magid, K., & McKelvey, C. A. (1988). High risk. (Bantam ed.). Toronto ; New York: Bantam Books.

McCarley, R. W., Faux, S. F., Shenton, M. E., & Nestor, P. G. (1991). Event-related potentials in schizophrenia: Their biological and clinical correlates and a new model of schizophrenic pathophysiology. Schizophrenia Research, 4, 209-231.

McCarley, R. W., Hsiao, J. K., Freedman, R., Pfefferbaum, A., & Donchin, E. (1996). Neuroimaging and the cognitive neuroscience of schizophrenia, Schizophrenia Bulletin 22, 703-725.

McCarthy, G., Luby, M., Gore, J., & Goldman-Rakic, P. (1997). Infrequent events transiently activate human prefrontal and parietal cortex as measured by functional MRI. Journal of Neurophysiology, 77, 1630-1634.

McCarthy, G., Nobre, A. C., Bentin, S., & Spencer, D. D. (1995). Language-related field potentials in the anterior-medial temporal lobe: I. Intracranial distribution and neural generators. Journal of Neuroscience, 15, 1080-1089.

McCarthy, G., & Wood, C. C. (1985). Scalp distributions of event-related potentials: An ambiguity associated with analysis of variance models. Electroencephalography and Clinical Neurophysiology, 62, 203-208.

McCord, W. M., & McCord, J. (1964). The psychopath: an essay on the criminal mind. Princeton, N.J.: Van Nostrand.

Meier, M. J., & French, L. A. (1965). Some personality correlates of unilateral and bilateral EEG abnormalities in psychomotor epileptics. Journal of Clinical Psychology, 21, 3-9.

Mendola, J. D., Rizzo, J. F., 3rd, Cosgrove, G. R., Cole, A. J., Black, P., & Corkin, S. (1999). Visual discrimination after anterior temporal lobectomy in humans. Neurology, 52, 1028-1037.

Menon, V., Ford, J. M., Lim, K. O., Glover, G. H., & Pfefferbaum, A. (1997). Combined event-related fMRI and EEG evidence for temporal-parietal cortex activation during target detection. Neuroreport, 8, 3029-3037.

Miller, L., & Milner, B. (1985). Cognitive risk-taking after frontal or temporal lobectomy: II. The synthesis of phonemic and semantic information. Neuropsychologia, 23, 371-379.

Nestor, P. G., Kimble, M. O., BF, O. D., Smith, L., Niznikiewicz, M., Shenton, M. E., & McCarley, R. W. (1997). Aberrant semantic activation in schizophrenia: a neurophysiological study. American Journal of Psychiatry, 154, 640-646.

Newman, J. P. (1998). Psychopathic behavior: An information processing perspective. In D. J. Cooke, A. E. Forth, & R. D. Hare (Eds.), Psychopathy: Theory, Research, and Implications for Society (pp. 81-104). Dordrecht, Netherlands: Kluwer Academic Publishers.

Newman, J. P., Schmitt, W. A., & Voss, W. D. (1997). The impact of motivationally neutral cues on psychopathic individuals: assessing the generality of the response modulation hypothesis. Journal of Abnormal Psychology, 106, 563-575.

Niznikiewicz, M. A., O'Donnell, B. F., Nestor, P. G., Smith, L., Law, S., Karapelou, M., Shenton, M. E., & McCarley, R. W. (1997). ERP assessment of visual and auditory language processing in schizophrenia. Journal of Abnormal Psychology, 106, 85-94.

Nobre, A. C., & McCarthy, G. (1995). Language-related field potentials in the anterior-medial temporal lobe: II. Effects of word type and semantic priming. Journal of Neuroscience, 15, 1090-1098.

Nunez, P. L. (1981). Electric fields of the brain. New York: Oxford University Press.

Nunez, P. L. (1990). Physical principles and neurophysiological mechanisms underlying event-related potentials. In J. W. Rohrbaugh, R. Parasuraman, & R. Johnson, Jr. (Eds.), Event-related brain potentials (0 ed., pp. 19-36). New York: Oxford University Press.

Opitz, B., Mecklinger, A., Von Cramon, D. Y., & Kruggel, F. (1999). Combining electrophysiological and hemodynamic measures of the auditory oddball. Psychophysiology, 36, 142-147.

Paivio, A. (1986). Mental representaions: A dual coding approach. London: Oxford University Press.

Paivio, A. (1991). Dual coding theory: Retrospect and current status. Canadian Journal of Psychology, 45, 255-287.

Paller, K. A., Kutas, M., Shimamura, A. P., & Squire, L. R. (1987). Brain responses to concrete and abstract words reflect processes that correlate with later performance on test of recall and stem-completion priming. In R. Johnson, J. Rohrbaugh, & R. Parasuraman (Eds.), Current trends in brain potential research (pp. 360-365). Amsterdam: Elsevieer.

Paller, K. A., McCarthy, G., Roessler, E., & Allison, T. (1992). Potentials evoked in human and monkey medial temporal lobe during auditory and visual oddball paradigms. Electroencephalography & Clinical Neurophysiology, 84, 269-279.

Paller, K. A., Zola-Morgan, S., Squire, L. R., & Hillyard, S. A. (1988). P3-like brain waves in normal monkeys and in monkeys with medial temporal lesions. Behavioral Neuroscience, 102, 714-725.

Patrick, C. J. (1994). Emotion and psychopathy: Startling new insights. Psychophysiology, 31, 319-330.

Patrick, C. J., Bradley, M. M., & Lang, P. J. (1993). Emotion in the criminal psychopath: Startle reflex modulation. Journal of Abnormal Psychology, 102, 82-92.

Patrick, C. J., Cuthbert, B. N., & Lang, P. J. (1994). Emotion in the criminal psychopath: Fear image processing. Journal of Abnormal Psychology, 103, 523-534.

Pfefferbaum, A., Roth, W. T., & Ford, J. M. (1995). Event-related potentials in the study of psychiatric disorders. Archives of General Psychiatry, 52, 559-63.

Posner, M. I., & Rothbart, M. K. (1998). Attention, self-regulation and consciousness. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 353, 1915-1927.

Pritchard, W. S. (1981). Psychophysiology of P300. Psychological Bulletin, 89, 506-540.

Raine, A., O'Brien, M., Smiley, N., Scerbo, A., & Chan, C. J. (1990). Reduced lateralization in verbal dichotic listening in adolescent psychopaths. Journal of Abnormal Psychology, 99, 272-277.

Raine, A., & Venables, P. H. (1988). Enhanced P3 evoked potentials and longer P3 recovery times in psychopaths. Psychophysiology, 25, 30-38.

Rice, M. E., Harris, G. T., & Cormier, C. A. (1992). An evaluation of a maximum security therapeutic community for psychopaths and other mentally disordered offenders. Law & Human Behavior, 16, 399-412.

Ross, E. D. (1981). The aprosodias. Functional-anatomic organization of the affective components of language in the right hemisphere. Archives of Neurology, 38, 561-569.

Rugg, M. D., Pickles, C. D., Potter, D. D., & Roberts, R. C. (1991). Normal P300 following extensive damage to the left medial temporal lobe. Journal of Neurology, Neurosurgery & Psychiatry, 54, 217-222.

Scheffers, M. K., Coles, M. G. H., Bernstein, P., & Gehring, W. J. (1996). Event-related brain potentials and error-related processing: An analysis of incorrect responses to go and no-go stimuli. Psychophysiology, 33, 42-53.

Scheffers, M. K., Johnson, R., & Ruchkin, D. S. (1991). P300 in patients with unilateral temporal lobectomies: The effects of reduced stimulus quality. Psychophysiology, 28, 274-284.

Schwanenflugel, P. J., Harnishfeger, K. K., & Stowe, R. W. (1988). Context availability and lexical decisions for abstract and concrete words. Journal of Memory & Language, 27, 499-520.

Schwanenflugel, P. J., & Stowe, R. W. (1989). Context availability and the processing of abstract and concrete words in sentences. Reading Research Quarterly, 24, 114-126.

Shankweiler, D. (1966). Effects of temporal-lobe damage on perception of dichotically presented melodies. Journal of Comparative & Physiological Psychology, 62, 115-119.

Sharpe, K., & O'Carroll, R. (1991). Estimating premorbid intellectual level in dementia using the National Adult Reading Test: A Canadian study. British Journal of Clinical Psychology, 30, 381-384.

Simon, B., Holzberg, J. D., Alessi, S. L., & Garrity, D. A. (1951). The recognition and acceptance of mood in music by psychotic patients. Journal of Nervous & Mental Disease, 114, 66-78.

Smith, A. S., Kiehl, K. A., Hare, R. D., Forster, B. B., Brink, J., & Liddle, P. F. (1999). A fMRI study of response inhibition in psychopathy. manuscript submitted for publication.

Smith, M. L., & Milner, B. (1988). Estimation of frequency of occurrence of abstract designs after frontal or temporal lobectomy. Neuropsychologia, 26, 297-306.

Smith, S. S., Arnett, P. A., & Newman, J. P. (1992). Neuropsychological differentiation of psychopathic and nonpsychopathic criminal offenders. Personality & Individual Differences, 13, 1233-1243.

Sutton, S., Tueting, P., Zubin, J., & John, E. R. (1967). Information delivery and the sensory evoked potential. Science, 155, 1436-1439.

Toglia, M. P., & Battig, W. F. (1978). Handbook of semantic word norms. Hillsdale, NJ: Erlbaum.

Tucker, D. M. (1998). Error processing and the brain: An overview of current research. Paper presented at the Annual meeting of the Society for Psychophysiological Research, Denver, CO.

Wallace, J. F., Vitale, J. E., & Newman, J. P. (1999). Response modulation deficits: Implications for the diagnosis and treatment of psychopathy. Journal of Cognitive Psychotherapy, 13, 55-70.

Warrington, E. K., & James, M. (1967). Disorders of visual perception in patients with localized cerebral lesions. Neuropsychologia, 5, 253-266.

Widiger, T. A., Cadoret, R., Hare, R., Robins, L., Rutherford, M., Zanarini, M., Alterman, A., Apple, M., Corbitt, E., Forth, A., Hart, S., Kultermann, J., Woody, G., & Frances, A. (1996). DSM--IV antisocial personality disorder field trial. Journal of Abnormal Psychology, 105, 3-16.

Williamson, S., Harpur, T. J., & Hare, R. D. (1990, August). Sensitivity to emotional valence in psychopaths. Paper presented at the Annual meeting of the American Psychological Association, Boston.

Williamson, S., Harpur, T. J., & Hare, R. D. (1991). Abnormal processing of affective words by psychopaths. Psychophysiology, 28, 260-273.

Winner, E., & Gardner, H. (1977). The comprehension of metaphor in brain-damaged patients. Brain, 100, 717-729.

Worsley, K.J., & Friston K.J. (1995). Analysis of fMRI time-series revisited - Again Neuroimage, 2, 173-181.

Worsley, K.J. (1994). Local maxima and the expected Euler characteristic of excursion sets of Chi^2, F and t fields. Advances in Applied Probability, 26, 13-42.

Yamaguchi, S., & Knight, R. T. (1993). Association cortex contributions to the human P3. In W. Haschke, A. I. Roitbak, & E.-J. Speckmann (Eds.), Slow potential changes in the brain (pp. 71-84). Boston: Birkhauser.

Yamaguchi, S., & Knight, R. T. (1995). Contributions of anterior and posterior association cortex to the human somatosensory P3. Electroencephalography and Clinical Neurophysiology. Supplement, 44, 130-139.