Brain potentials implicate temporal lobe abnormalities in criminal psychopaths

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Abstract

Psychopathy has long been associated with abnormalities in attention and orienting during processing of task-relevant or salient stimuli. Event-related potential (ERP) studies have shown that psychopaths are characterized by a number of ERP component abnormalities, the most prominent of which is an aberrant negativity at frontal and central scalp sites during cognitive tasks that require rapid identification and processing of salient stimuli. However, delineating the functional significance of these ERP negativities in psychopaths has been complicated by the relative complexity of the tasks (often linguistic) in which they have been observed. To address this issue, we selectively manipulated the salience of stimuli using a simple three-stimulus auditory oddball task, consisting of low probability task-relevant targets, low probability task-irrelevant novel stimuli, and frequent task-irrelevant standard stimuli. ERPs were recorded during performance of this task in 80 incarcerated offenders classified as psychopathic or nonpsychopathic based on scores on the Hare Psychopathy Checklist-Revised. The primary hypothesis was that in psychopaths the ERPs elicited by the salient targets would include abnormal late negativities, a hypothesis based on evidence that salient targets engage orienting processes for which psychopaths are known to be deficient. Consistent with the hypothesis, psychopaths showed larger fronto-central ERP negativities (N550) than those shown by nonpsychopaths during processing of the target stimulus. Psychopaths were also characterized by an enhanced N2 and mildly reduced frontal P3 components during salient stimulus processing. Similar ERP modulations of salient stimuli have been reported in patients with anterior and lateral temporal lobe brain damage, including the amygdala and anterior superior temporal gyrus. These data suggest that the aberrant late ERP negativities observed in psychopathy are related to dysfunction of the medial and lateral aspects of the temporal lobe.
These data support the new hypothesis that psychopathy may best be conceptualized as a disorder of the paralimbic system – a system which embraces parts of the temporal lobe and frontal lobe.

Introduction

Psychopathy is a personality disorder defined by a cluster of interpersonal, affective and behavioral characteristics, including glibness, impulsivity, poor behavioral controls, shallow affect, and lack of empathy, guilt, and remorse (Hare, 1991, 1993). Although there is good agreement regarding the assessment and behavioral correlates of psychopathy (Hare, 2003), relatively little is known about the neurocognitive processes implicated in the disorder. One cognitive domain that has been shown to be abnormal in psychopathy involves attentional and orienting processes (see reviews by Arnett, 1997; Hare, 2003; Kosson & Harpur, 1997; Newman & Lorenz, 2002). In general, psychopaths tend to exhibit relatively small increases in skin conductance in anticipation of a variety of noxious stimuli (e.g., Flor, Birbaumer, Hermann, Ziegler et al., 2002; Hare, Frazelle, & Cox, 1978; Hare & Quinn, 1971; Lykken, 1957), as well as in response to emotional stimuli, including threatening images (Blair, Jones, Clark, & Smith, 1997), slides of mutilated faces (Mathis, 1970), and emotional sounds, both positive and negative (Verona, Patrick, Curtin, Bradley et al., 2004). The skin conductance response is a component of the orienting reflex (Hare, 1973; Sokolov, 1963), suggesting that psychopathy is associated with abnormal orienting/attentional responses to salient or novel stimuli. This perspective has been incorporated into the response modulation hypothesis (Newman & Lorenz, 2002), a conceptual framework in which psychopaths are described as having difficulty in attending and responding to important contextual cues while engaged in goal-directed behavior.

Event-related potential (ERP) studies have been used to study aspects of the orienting response for many years, particularly with “oddball” paradigms. In a typical oddball task, low probability task-irrelevant novel stimuli, and low- probability task-relevant target stimuli, are presented against a background of frequent or standard stimuli. Both novel and target stimuli are associated with a sequence of electrocortical components, the most prominent of which is a large broadly distributed positive wave, termed P3 or P300 (Sutton, Braren, Zubin, & John, 1965). The P3 elicited by target stimuli has a parietal maximum topography while novel stimuli

elicit a P3 with a fronto-central maximum, also known as the P3a (Courchesne, Hillyard, & Galambos, 1975). The P3s elicited by novel and target stimuli are believed to be related to processes involving attentional capture, allocation of cognitive resources, and contextual updating – all components linked to 'orienting processes'.

There have been only eight published ERP studies on psychopathy (Flor, Birbaumer, Hermann, Ziegler et al., 2002; Forth & Hare, 1989; Jutai & Hare, 1983; Jutai, Hare, & Connolly, 1987; Kiehl, Hare, McDonald, & Liddle, 1999; Kiehl, Smith, Hare, & Liddle, 2000; Raine & Venables, 1988; Williamson, Harpur, & Hare, 1991). Seven studies have reported information concerning P3s, though only four studies employed paradigms in which the salience of stimuli was manipulated in a manner expected to elicit a canonical P3 response (Jutai, Hare, & Connolly, 1987; Kiehl, Hare, McDonald, & Liddle, 1999; Kiehl, Smith, Hare, & Liddle, 2000; Raine & Venables, 1988). Jutai et al. (1987) found no difference between psychopaths and nonpsychopaths in the amplitude or latency of the P3. Visual inspection of the waveforms in their study indicated that the P3 amplitude was smaller, albeit nonsignificantly, in the psychopaths than in nonpsychopaths. However, Jutai et al. did not record from parietal electrodes, which is the optimal site for detection of the P3. In contrast, Raine and Venables (1988) reported that the amplitude of parietal P3 to visual target stimuli was greater in psychopaths than in nonpsychopaths. More recent studies have reported that the P3 elicited during visual oddball tasks is substantially smaller over frontal, central and parietal sites in psychopaths than in nonpsychopaths (Kiehl, Hare, McDonald, & Liddle, 1999; Kiehl, Smith, Hare, & Liddle, 2000). In the remaining P3 studies, there was little evidence indicating that the P3 was abnormal in psychopaths. However, these latter studies did not employ paradigms that manipulated the salience of the stimuli. In summary, the evidence regarding abnormality of the P3 in psychopathy is inconclusive, but suggests that under some circumstances the P3 may be reduced in psychopaths. However, perhaps more illuminating is that abnormal late (i.e., later than 300ms post-stimulus) ERP negativities appear to be uniquely characteristic of psychopaths during tasks that manipulate the salience of the stimuli.

To date, abnormally large late ERP negativities, maximal at frontal and central sites, have been reported in psychopaths during a contingent negative variation task (Forth & Hare, 1989), emotional lexical decision task (Williamson, Harpur, & Hare, 1991), a concrete/abstract discrimination task, a concrete/abstract lexical decision task, and an emotional polarity discrimination task (Tasks 1, 2, and 3, respectively, in Kiehl, Hare, McDonald, & Brink, 1999), as well in a response inhibition task (Kiehl, Smith, Hare, & Liddle, 2000), and a visual oddball task (Kiehl, Hare, McDonald, & Liddle, 1999). One common denominator of the studies that have observed late ERP negativities in psychopaths is that the eliciting stimuli were task-relevant or salient and engaged attention, orienting, and decision making processes (for review see Kiehl, in press). Still unresolved, however, are the neural systems implicated in salient stimulus processing in general and psychopathy in particular.

One method used to investigate the potential generators underlying the processing of salient, or oddball, stimuli was to record ERPs in patient populations with localized brain insults. The main tenet here is that if the circuits involved in salient stimulus processing are damaged it should lead to observable abnormalities in the scalp recorded ERPs. These studies found that frontal, temporal, parietal, and limbic structures are engaged during processing of oddball stimuli (see review by Soltani & Knight, 2000). Interestingly, in patients with temporal lobe damage several studies found clear evidence for late fronto-central ERP negativities during processing of target stimuli (Johnson, 1993; Yamaguchi & Knight, 1993). Patients with temporal lobe damage, relative to controls or patients with parietal lobe damage, had enlarged N2b's, smaller P3s, and late fronto-central negativities (Yamaguchi & Knight, 1993). Similar effects were observed in epilepsy patients following resection of the amygdala and anterior superior temporal gyrus for the treatment of intractable epilepsy (Johnson, 1993). These data suggest that the medial and lateral temporal lobes are implicated in the elicitation of late ERP negativities during the context of auditory oddball tasks.

Another avenue available for examining the neural circuits implicated in target detection is event-related functional magnetic resonance imaging (fMRI). These studies have shown that in healthy participants target

stimuli elicit activity in diverse and widespread neuronal networks, including medial (i.e., bilateral amygdala) and lateral temporal lobe, anterior and posterior cingulate, and frontal and parietal cortex (Clark, Fannon, Lai, Benson et al., 2000; Kiehl, Laurens, Duty, Forster et al., 2001a; Kiehl, Laurens, Duty, Forster et al., 2001b; Kiehl & Liddle, 2003). The results are in close parallel to the intra-cranial electrode data recorded from patients with brain pathology during similar tasks (Clarke, Halgren, & Chauvel, 1999a, b). Thus, there is substantial evidence suggesting that the medial and lateral aspects of the temporal lobe are implicated in salient stimulus processing tasks. However, the suggestion that the primary processing deficit in psychopaths is related to the salience of the stimuli is hampered by the fact that the tasks shown to elicit the late ERP abnormalities in psychopaths often involved relatively complex stimuli and decision-making (e.g., about different classes of language stimuli). Thus, it has been difficult to isolate the neurocognitive processes underlying the late ERP negativities observed in psychopaths. To address this issue, the present study employed an auditory 'oddball' task to selectively manipulate the salience of the stimuli. The primary hypothesis was that during processing the salient stimuli psychopaths' ERPs would be characterized by late ERP negativities.

Methods

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 to 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. One sample (n=44) was collected by the first author (KK) and a subsequent sample (n=36) was collected by the second author (AB). To control for the effect of these different experimenters, time of data acquisition, and to illustrate the reproducibility of the results, the two samples were analyzed separately. 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 consisted of 23 Psychopaths [mean PCL-R score 32.5 (SD 1.7)) and 21 Nonpsychopaths [mean PCL-R score 20.85 (SD 5.99)). Sample 2 consisted of 18 Psychopaths [mean PCL-R score 33.94 (SD 2.48)) and 18 Nonpsychopaths [mean PCL-R score 20.35 (SD 6.39)).

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). Each inmate was paid $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.

Stimuli. The target (1500 hz tones), novel (e.g., ramped tones, random sounds) and standard (1000 hz tones) stimuli were presented with a probability level of .10, .10 and .80, 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 one after the 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 stimulus and to ignore the standard and novel stimuli. The hand used to respond to the target stimulus was counterbalanced across participants. Two runs of 20 stimuli were given as practice.

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 electrooculargrams (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 (N550). 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 (standard, 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).

Results

Behavioral data. Sample 1. There were no significant group differences (all p's > .25) 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 stimuli (Psychopaths, 0.82, SD = 1.6; Nonpsychopaths, 1.0, SD = 1.5)) or standard stimuli (Psychopaths, 9.1, SD = 5.7; Nonpsychopaths, 8.52, SD = 4.4).

Sample 2. As in Sample 1, there were no significant group differences (all p's > .13) 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 stimuli (Psychopaths 1.7, SD = 1.4; Nonpsychopaths, 2.5, SD = 3.0), or standard stimuli (Psychopaths, 12.7, SD = 7.6; Nonpsychopaths, 15.6, SD = 7.6).

Event-related potentials. Grand mean ERPs for target, novel and standard stimuli for Sample 1 are presented in Figures 1, 2, and 3, respectively. Sample 2 grand mean ERPs for target, novel and standard stimuli are presented in Figures 4, 5, and 6, respectively. Grand mean ERPs (across both samples) are presented in Figures 7, 8, and 9 for target, novel and standard stimuli, respectively.

N2 amplitude analyses.

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 standard 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, asymmetrically 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).

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 standard stimuli.

As in the Sample 1 above, across all participants, the N2 was larger for target and novel stimuli than for standard 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 amplitude analyses.

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).

Across all participants, the P3 was larger for target and novel stimuli than for standard 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, $F (4, 168) = 39.70$, $p < .001$).

Sample 2. The P3 for target stimuli and novel stimuli was slightly, though significantly, 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 standard 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.

N550 amplitude analyses.

Sample 1. As predicted, the N550 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 N550 elicited by target stimuli was more than twice the amplitude in Psychopaths as it was in Nonpsychopaths.

Across participants, the N550 was larger for target stimuli than for novel or standard 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).

Sample 2. As in Sample 1, N550 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 N550 was larger for target than for novel or standard 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).

Discussion

Consistent with hypothesis, analyses of the electrophysiological data revealed that psychopathic inmates, relative to demographically matched nonpsychopathic inmates, showed an aberrant large late ERP negativity during target detection (N550). Psychopaths also had an enlarged N2b and a slightly reduced fronto-central P3 (Sample 2 only) during target detection. The N550 ERP negativity was nearly twice the amplitude in psychopaths as in nonpsychopaths (see Figures 1, 4 and 7). These data demonstrate that a simple salient stimulus discrimination between tone types is sufficient to elicit late ERP negativities in psychopaths. Thus, the late ERP negativities do not appear to be necessarily related to language stimuli or other complex task demands as employed in prior studies (Kiehl, Hare, McDonald, & Brink, 1999; Kiehl, Smith, Hare, & Liddle, 2000; Williamson, Harpur, & Hare, 1991).

The auditory oddball task has also been well studied in patients with neurological conditions. Examination of this literature reveals that in patients with selective damage to medial and anterior lateral temporal lobe, abnormalities in the scalp recorded waveforms include a large early negativity (N2b), mildly reduced fronto-central positivity (P3), and an enlarged late negativity (N550) (Johnson, 1989; Johnson & Fedio, 1987; Yamaguchi & Knight, 1993). This sequence of electrophysiological abnormalities appears to be exclusive to patients with medial and anterior lateral temporal lobe lesions or damage (see Figure 10). That is, these abnormalities have not been observed in patients with frontal lobe or parietal lobe damage during similar tasks (Knight, Scabini, Woods, & Clayworth, 1989; Yamaguchi & Knight, 1993). A comparison of the ERPs elicited by salient target stimuli for the psychopaths and the patient studies is shown in Figure 10. The similarities exist at multiple ERP components, with the enhancement of the N2b, mild reduction of the P3, and enlarged late ERP negativity. These data suggest that psychopathy is associated with impairments in the medial and lateral aspects of the temporal lobe during auditory target detection.

Support for the view that psychopathy is associated with medial and anterior lateral temporal lobe function also comes from hemodynamic imaging studies of psychopathy (Kiehl, Smith, Hare, Forster et al., 2001; Kiehl, Smith, Mendrek, Forster et al., 2004; Veit, Flor, Erb, Hermann et al., 2002). These studies suggest that during processing of certain types of linguistic and emotional stimuli the anterior superior temporal gyrus [Kiehl, 2004 #1723], amygdala (Kiehl, Smith, Hare, Forster et al., 2001; Veit, Flor, Erb, Hermann et al., 2002), and hippocampus (Laakso, Vaurio, Koivisto, Savolainen et al., 2001) appear to be dysfunctional in psychopaths. Additional support for the hypothesis of abnormal medial and anterior lateral temporal lobe function in psychopathy comes from behavioral studies of patients with temporal lobe epilepsy. There is some evidence that suggests patients with temporal lobe epilepsy have a high incidence of psychopathic-like behavior (Hill, Pond, Mitchell, & Falconer, 1957). Removal of the dysfunctional anterior temporal lobe in these epilepsy patients appears to reduced hostility, increase warmth and empathy in social relationships, and decrease inappropriate sexual behavior (Hill, Pond, Mitchell, & Falconer, 1957). Moreover, a number of studies have shown that psychopaths have problems with processing certain aspects of affective speech and face stimuli (Blair, Jones, Clark, & Smith, 1997; Kosson, Suchy, Mayer, & Libby, 2002; Louth, Williamson, Alpert, Pouget et al., 1998) that are similarly impaired in patients with amygdala damage (see review in Kiehl, in press). Overall, these converging results are consistent with the hypothesis that medial and anterior lateral temporal lobe structures play a prominent role in psychopathy.

It is relevant to note the medial and anterior lateral aspects of the temporal lobe may be conceptualized as part of the larger paralimbic system. The paralimbic system, defined by similarities in the structure of neurons and number of layers of cortex, was described by Brodmann (1909). The paralimbic system embraces classic limbic structures such as the amygdala and hippocampus and also includes anterior superior temporal gyrus, cingulate cortex and orbital frontal cortex (Mesulam, 2000). It is noteworthy that abnormalities in these latter brain regions are potentially implicated in psychopathy. The anterior cingulate, for example, is known to

be involved in error monitoring (Kiehl, Liddle, & Hopfinger, 2000; Swick & Turken, 2002), response inhibition (Liddle, Kiehl, & Smith, 2001), and affective processing (Kiehl, Smith, Hare, Forster et al., 2001). Psychopathy is associated with abnormalities in error monitoring (Dikman & Allen, 2000), response inhibition (Kiehl, Smith, Hare, & Liddle, 2000; Lapierre, Braun, & Hodgins, 1995) and affective processing (Kiehl, Smith, Hare, Forster et al., 2001). Indeed, regional abnormalities during affective processing have been observed in the anterior and posterior cingulate in psychopathy (Kiehl, Smith, Hare, Forster et al., 2001). These data support the argument that the anterior cingulate is implicated in psychopathy.

It is probable that the orbital frontal cortex plays a crucial role in the neuronal circuitry involved in psychopathy. Patients with damage to the orbital frontal cortex may have a condition termed 'pseudopsychopathy' (Blumer & Benson, 1975) or 'acquired sociopathic personality' (Damasio, 1994) characterized by problems with reactive aggression, grandiosity, motivation, empathy, planning and organization, impulsivity, irresponsibility, insight, and behavioral inhibition (Malloy, Bihrle, Duffy, & Cimino, 1993; Stuss, Benson, & Kaplan, 1983). However, dysfunction of the orbital frontal cortex does not fully account for the constellation of symptoms that comprise psychopathy. For example, unlike psychopaths, patients with orbital frontal damage rarely show instrumental aggression and callousness (Hare, 1993). The extant evidence suggests that a broad view, including medial and anterior lateral temporal lobe, anterior cingulate, and orbital frontal cortex, are implicated in psychopathy. These structures collectively form the paralimbic system.

ERPs associated with oddball processing are abnormal in a range of psychiatric conditions with conceptual links to psychopathy. However, the abnormalities are of a different nature than those observed in psychopathy. For example, Antisocial Personality Disorder (ASPD), which is most closely related to the behavioral facet of psychopathy, but only weakly correlated with the interpersonal and affective characteristics of psychopathy, is associated with P3 reductions during oddball tasks (L. O. Bauer, 2001b; L. O. Bauer &

Hesselbrock, 1999; L. O. Bauer, O'Connor, & Hesselbrock, 1994). However, these ERP studies of ASPD have not revealed any evidence of fronto-central ERP negativities as seen in psychopaths. Thus, as with other psychiatric conditions, ASPD is associated with subtle cognitive abnormalities that lead to a reduced P3. These data suggest that meaningful differences in neurobiology can be observed between ASPD and psychopathy. Similarly, studies have shown that the P3 is reduced in patients with alcoholism (Oscar-Berman, 1987; Romani & Cosi, 1989) and substance abuse problems (Amass, Lukas, Weiss, & Mendelson, 1989; D. L. Bauer, 2001a; Kouri, Lukas, & Mendelson, 1996; Noldy & Carlen, 1997). Psychopathy is known to be co-morbid with substance abuse (Hare, 2003; Hemphill, Hart, & Hare, 1994). However, as with ASPD, no studies of alcohol or substance abuse have shown evidence of late ERP negativities during salient stimulus processing tasks. Nevertheless, it is important to consider whether substance abuse contributed to any of the observed group differences. All participants in the present study were completing a nine month intensive violent or sex offender treatment program. This program mandated alcohol and substance abstinence and participants were randomly tested, as often as every month. Thus, it is unlikely that any of the observed group differences in the present study were related to current substance abuse.

It is often desirable to examine the relevant contribution of the interpersonal/affective (PCL-R Factor 1) and the lifestyle/antisocial (PCL-R Factor 2) features of psychopathy. However, the present samples, drawn from a very select high security sample, were found to have Factor 1 and Factor 2 scores that correlated .86. This correlation is much higher than the typical correlation between factors scores of .5 (Hare, 2003). Thus, post hoc analyses examining Factor 1 and Factor 2 scores did not reveal anything more than the group comparisons using total scores.

In summary, the data from the present study suggest that psychopathy is associated with functional abnormalities in the medial and anterior lateral aspects of the temporal lobe. The medial and anterior lateral aspects of the temporal lobe are part of a larger paralimbic system which includes the anterior and posterior

cingulate and orbital frontal cortex. These results, in conjunction with converging evidence from electrophysiological and hemodynamic studies in psychopathy and with studies of lesion patients, suggest that psychopathy may best be conceptualized as a disorder of the paralimbic system rather than a disorder of a single brain region (i.e., orbital frontal cortex).

Figure Legends

Figure 1. 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 2. 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 3. Grand mean ERPs (sample 1) for standard stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

Figure 4. 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 5. 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 6. Grand mean ERPs (sample 2) for standard stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

Figure 7. 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 8. 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 9. Grand mean ERPs (both samples) for standard stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

Figure 10. Comparison of the ERP elicited by auditory oddball stimuli in criminal psychopaths (present data), patients with temporal lobe damage (Yamaguchi & Knight, 1993) and patients who had undergone anterior temporal lobectomy for the treatment of intractable epilepsy (Johnson, 1989). All three groups are typified by an enhanced N2b, diminished frontal P3, and enlarged late negativity (N550), relative to control participants. All plots are from fronto-central electrode sites and are scaled to similar amplitude and epoch.

Figure 1. 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.

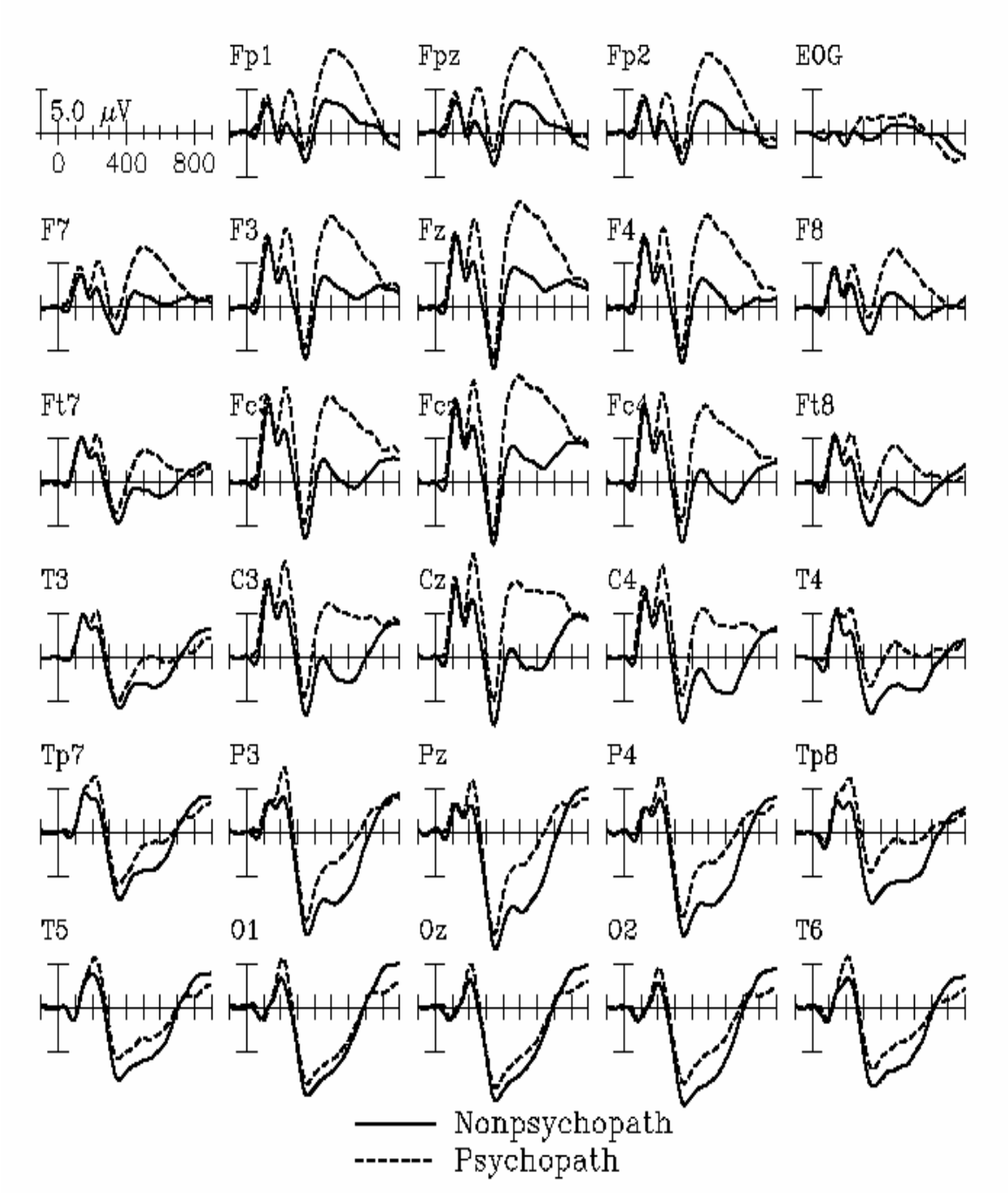


Figure 2. Grand mean ERPs (Sample 1) for novel stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

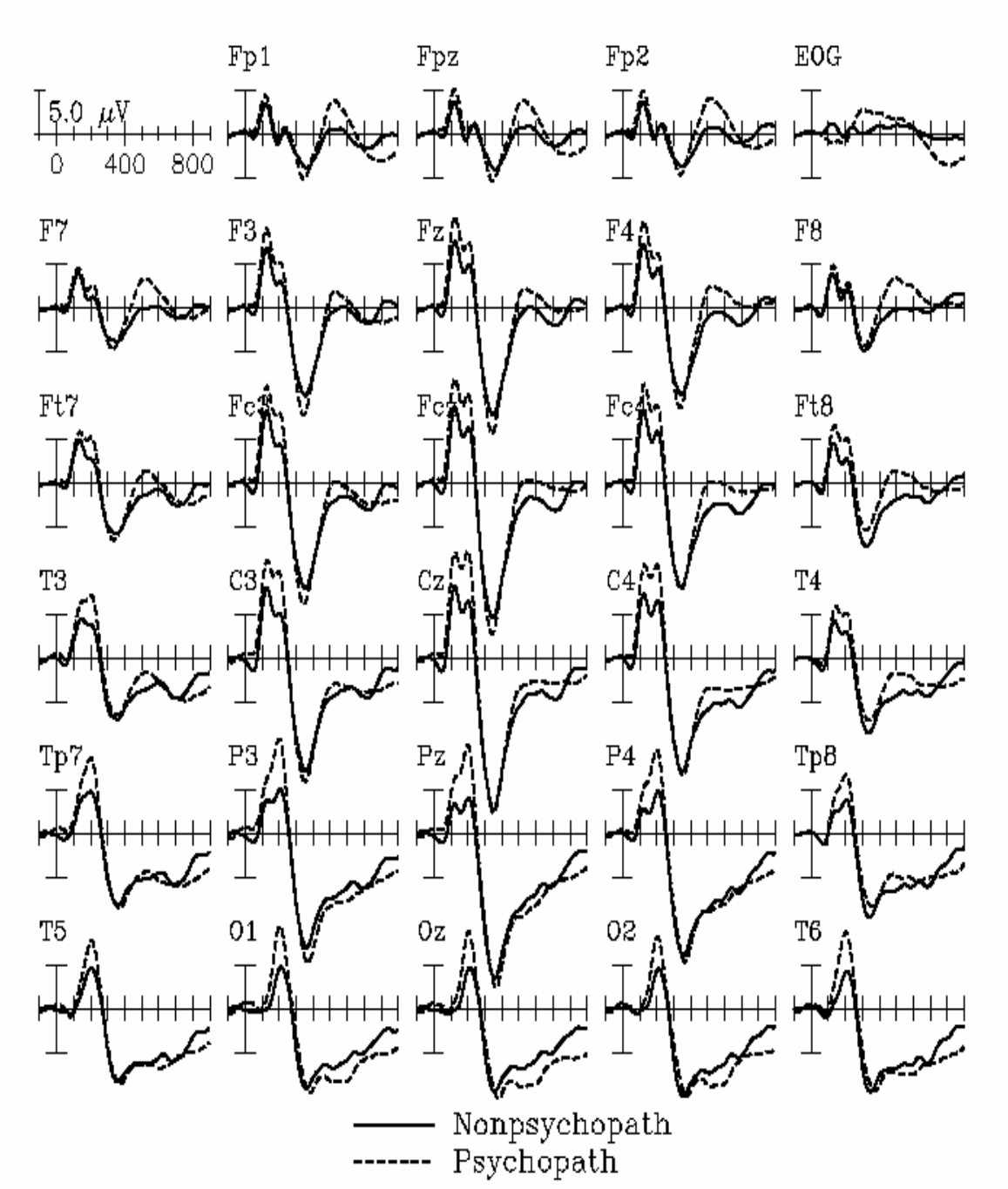


Figure 3. Grand mean ERPs (Sample 1) for standard stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

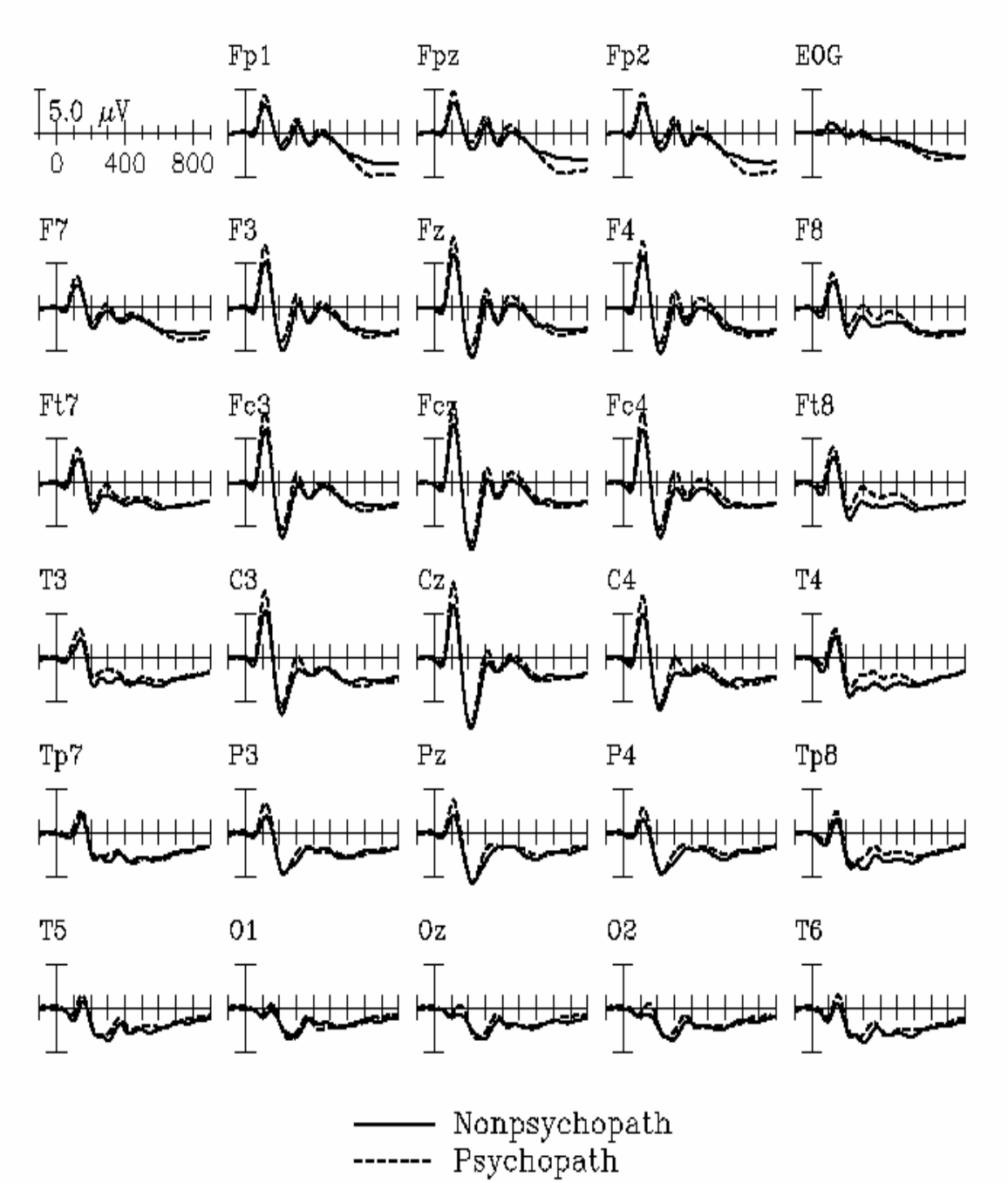


Figure 4. Grand mean ERPs (Sample 2) for target stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

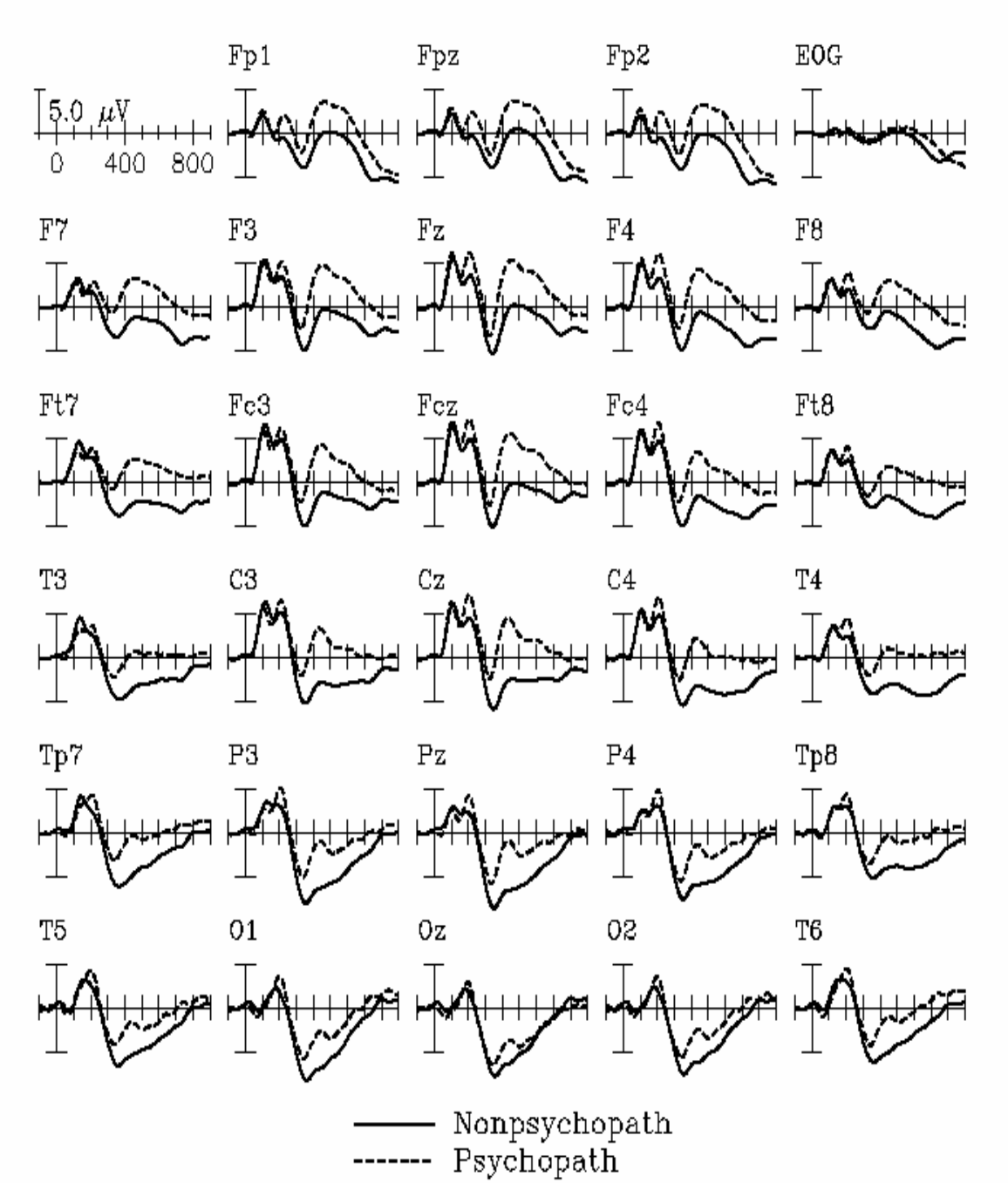


Figure 5. Grand mean ERPs (Sample 2) for novel stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

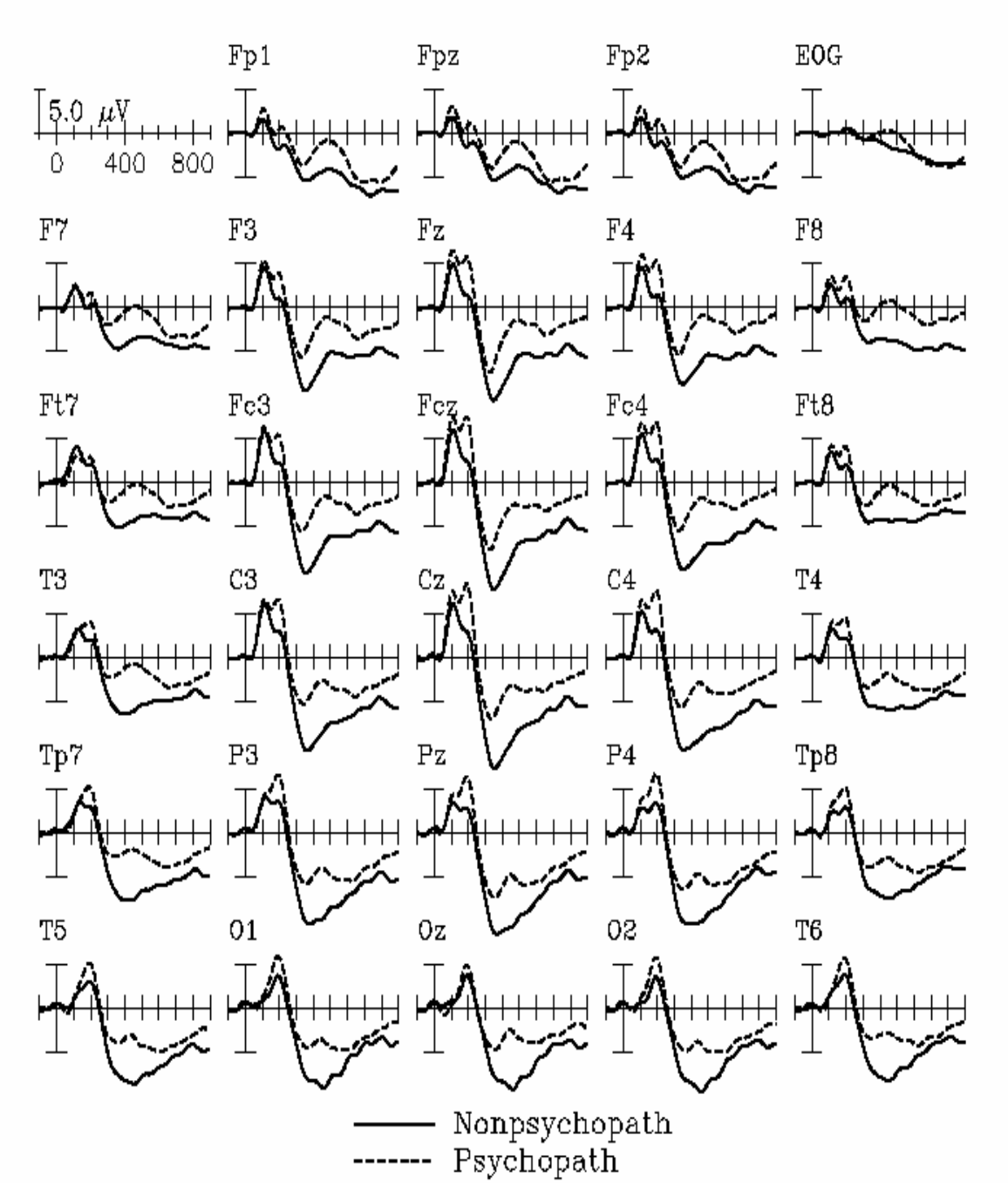


Figure 6. Grand mean ERPs (Sample 2) for standard stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

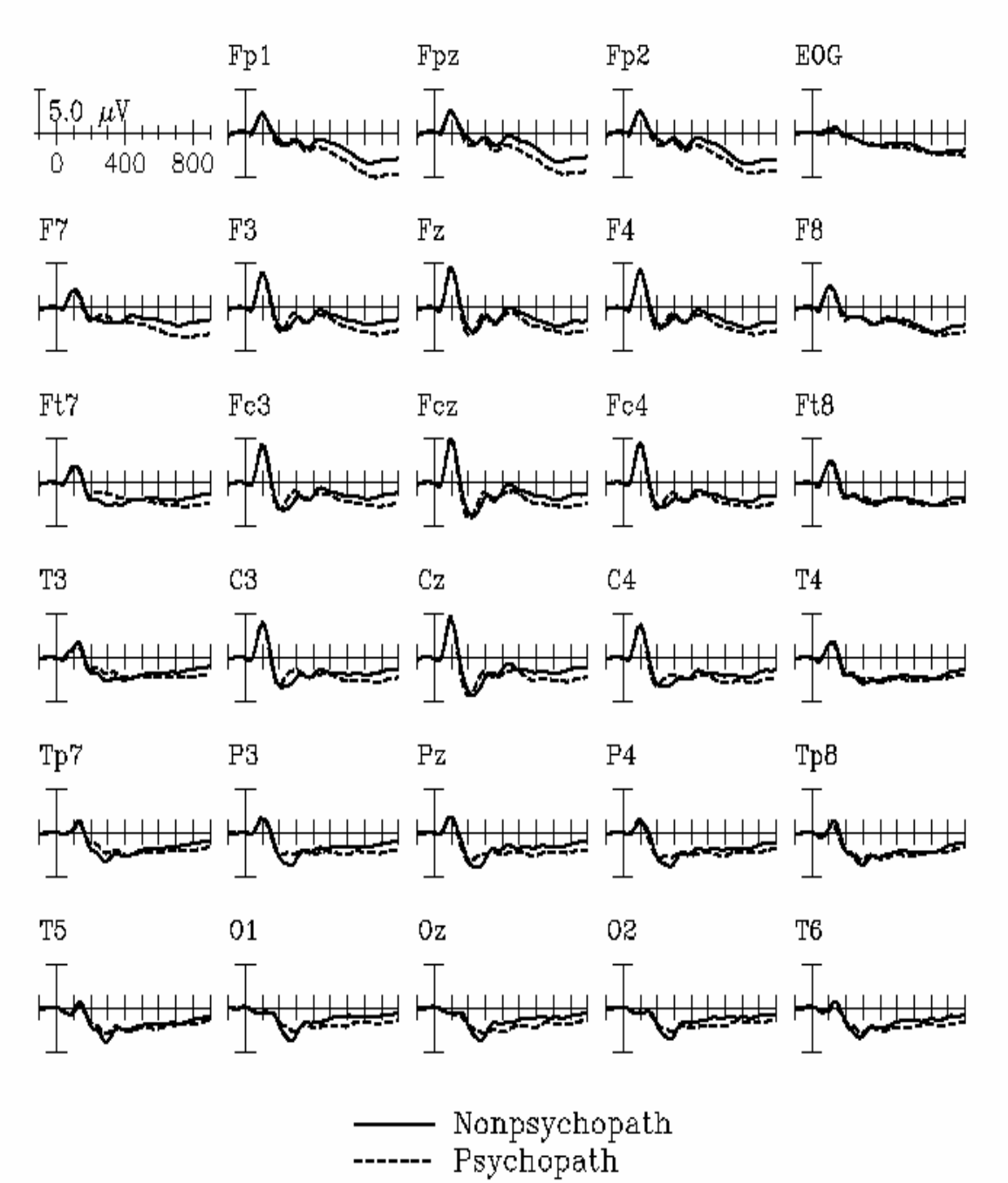


Figure 7. Grand mean ERPs (both samples) for target stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.

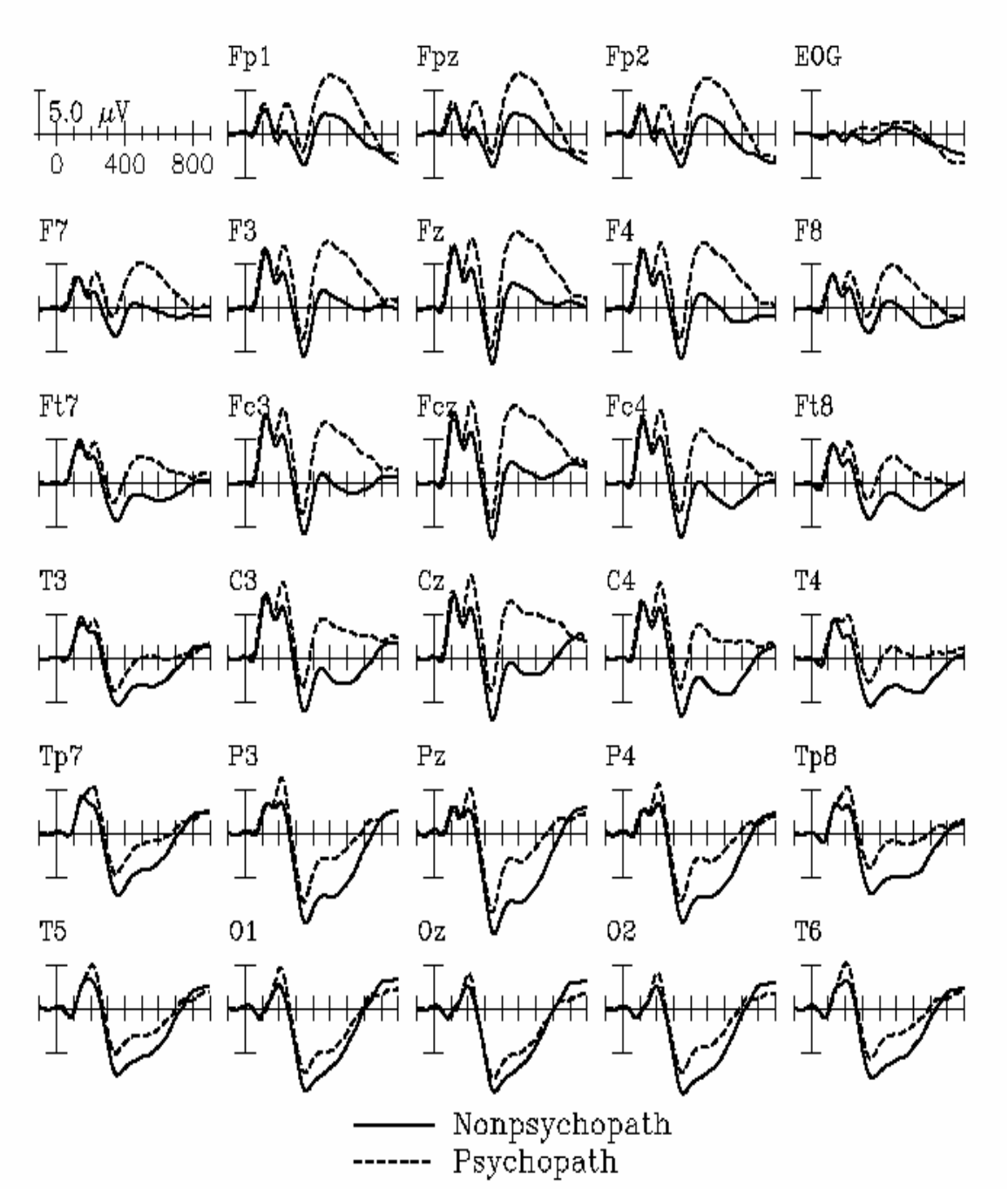
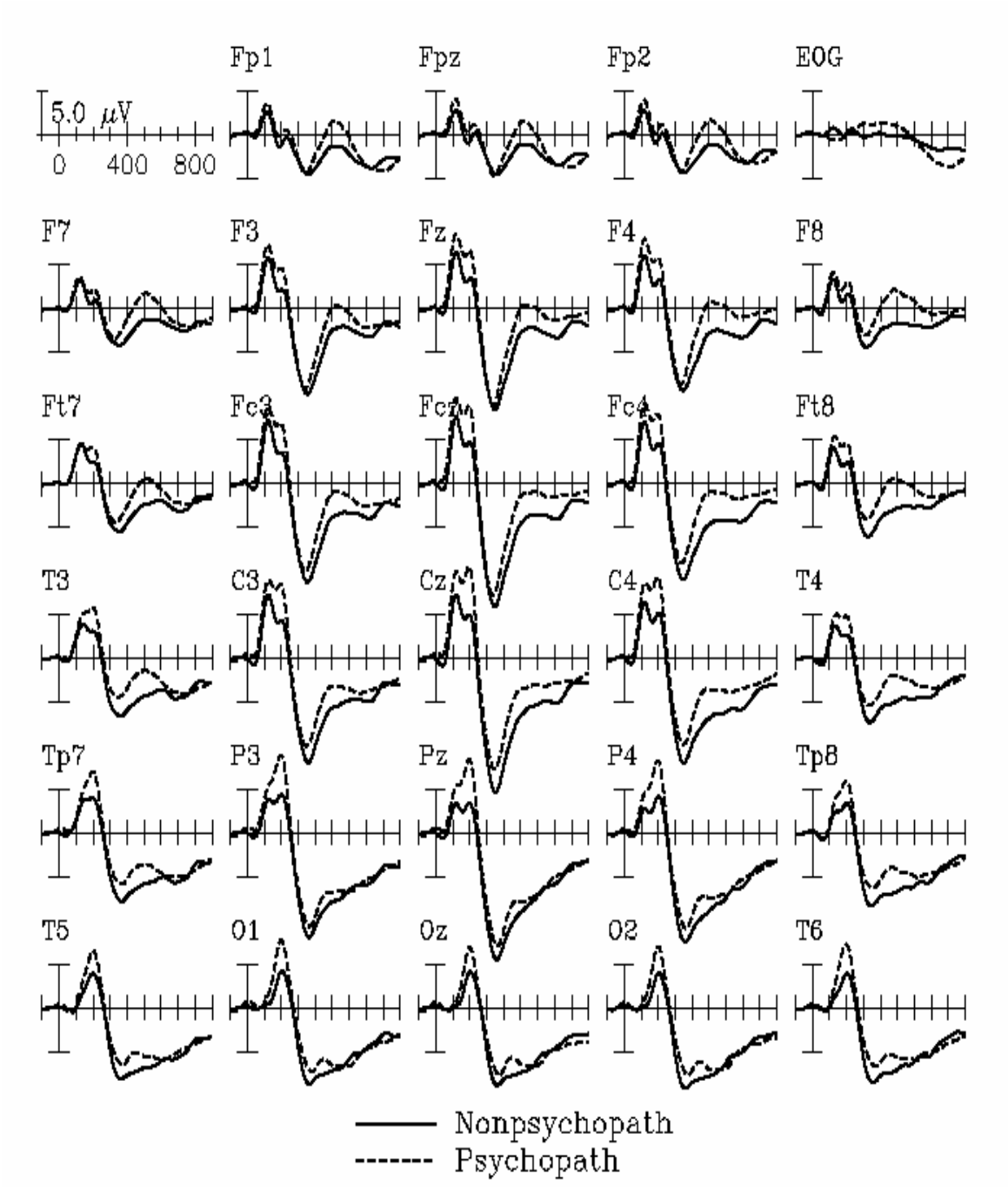


Figure 8. Grand mean ERPs (both samples) for novel stimuli for psychopaths (dashed) and nonpsychopaths (solid). By convention, negative amplitude is plotted up. Tick marks are in units of 100 milliseconds.



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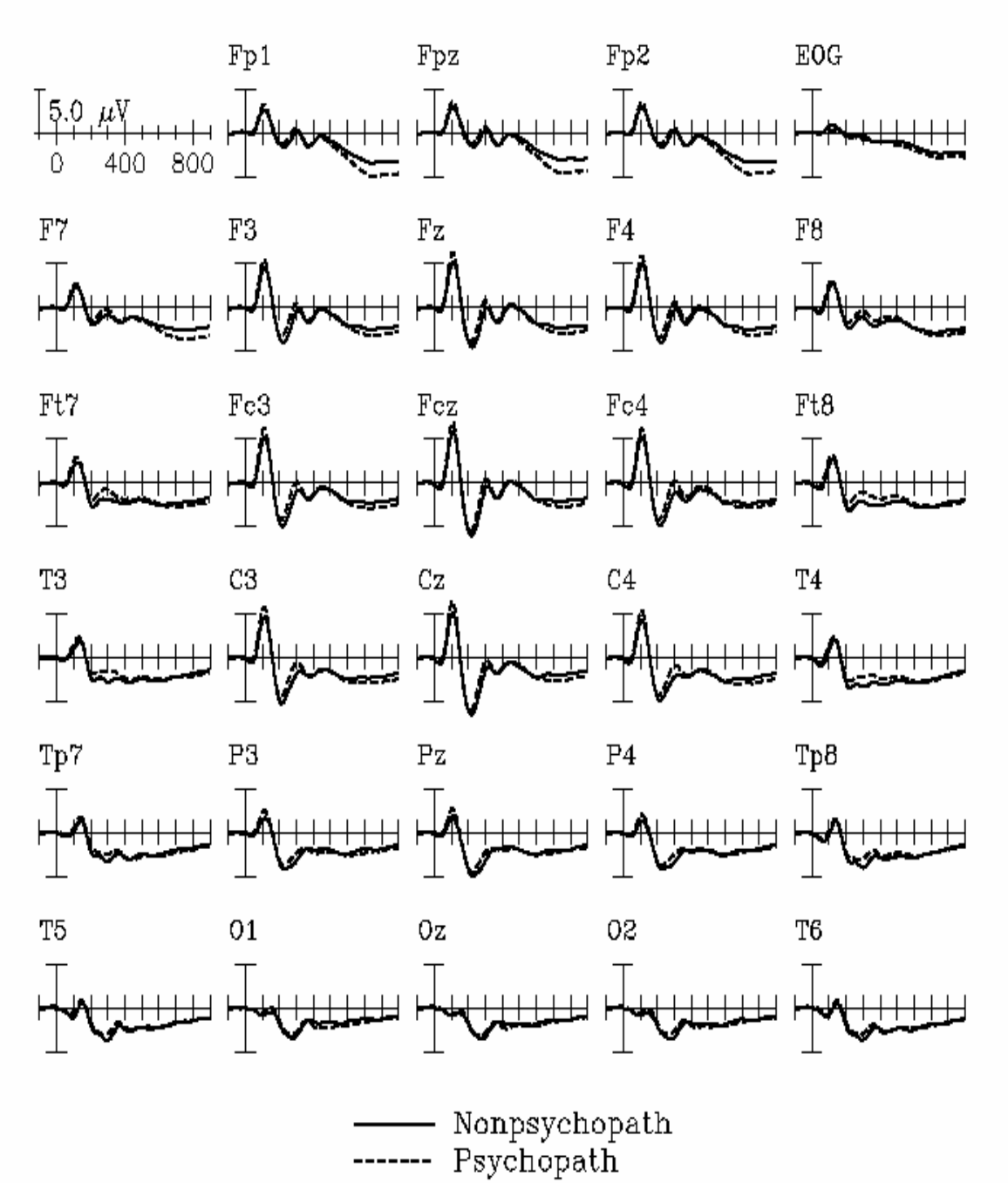

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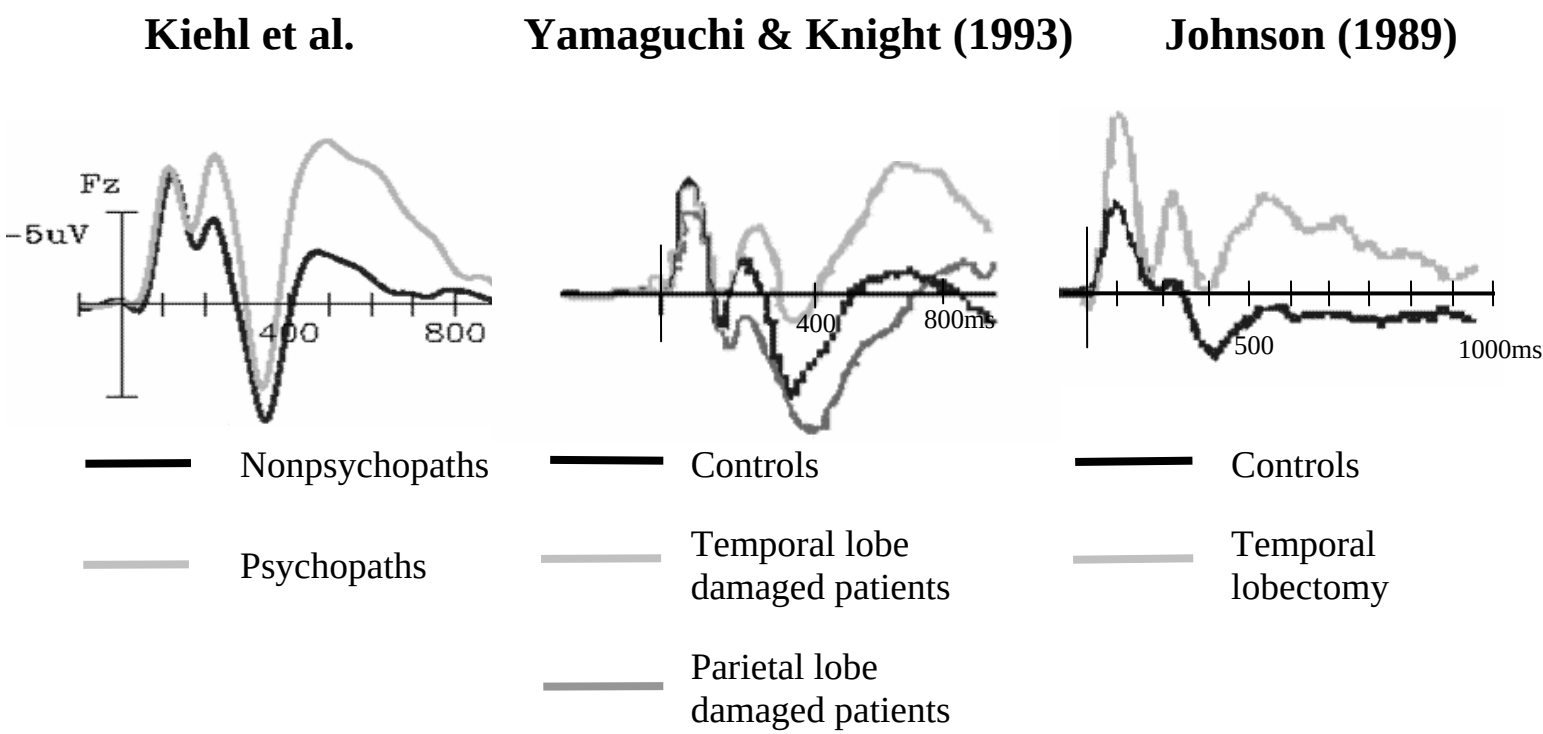

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